The effect of nicotine and tobacco message framing on use among diverse groups of young adults

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Table of Contents

I. OBJECTIVES

Summary. Through the proposed K99/R00 studies, Dr. Joanne Patterson will receive direct training in communications and tobacco regulatory science, and application of this knowledge to mentored research *to develop and gain skills necessary to develop anti-tobacco messages that effectively communicate the risks of polytobacco use to lesbian, gay, bisexual, and transgender polytobacco users.* Using a conceptual model based on the Extended Parallel Process Model (EPPM)[1-3] and message impact framework[4] *we will develop and refine anti-tobacco messages targeting young adult polytobacco users*; specifically, lesbian, gay, bisexual, and transgender young adults—a polytobacco use disparities population (Aim 1, Phases 1 and 2).

Brief Background*. Between 21-40% of lesbian, gay, bisexual, and transgender (LGBT) young adults (YA)[5-8] (vs 12-21% of non-LGBT YA[9,10]) report polytobacco use, defined as using more than one tobacco product including electronic nicotine delivery systems (ENDS).* This difference is alarming as polytobacco use is associated with nicotine dependence[11] and continued tobacco use[12-16] into adulthood, which may widen existing tobacco disparities.[17] Markedly low tobacco risk perceptions[8,18-24] among LGBT YA may reinforce polytobacco use.[25] National anti-tobacco communications are a successful strategy for increasing public knowledge about tobacco health risks and decreasing tobacco use;[26-29] however, they may not engage YA LGBT polytobacco users for two reasons: ***First, existing YA anti-tobacco communications are not framed to specifically address polytobacco use risks. Second, LGBT populations report low engagement with non-targeted anti-tobacco communications.[30,31]*** The proposed study will use experimental methods to address these concerns. ***This proposal directly supports the FDA's mandate to educate the public about the risks of tobacco[32] by addressing the FDA research priority of Communications: The study goal is to determine effective communication of polytobacco use risk to at-risk LGBT YA.*** We propose to:

Aim 1 (NCT05393869). Identify absolute and relative risk anti-tobacco messages that effectively communicate polytobacco risks to LGBT young adults (K99). *Hypothesis:* Messages emphasizing relative (vs absolute) risk of polytobacco use will most effectively increase tobacco risk perceptions. *Hypothesis:* AR and RR messages emphasizing quit efficacy will increase intentions to quit all tobacco while AR and RR messages emphasizing switch efficacy will increase intentions to switch to exclusive ENDS use.

Aim 2 (NCT05972941). Determine the effects of cultural targeting on LGBT young adult polytobacco users' attention to anti-tobacco messages and perceived effectiveness (K99). Hypothesis: Exposure to culturally targeted messages will result in greater engagement with and perceived effectiveness of anti-polytobacco messages among LGBT YA.

Aim 3. (NCT06644664) (a) Assess the feasibility of delivering MMS anti-tobacco messages developed in the K99 to LGBT young adults via texting; and (b) Estimate effect sizes of exposure to anti-tobacco messages on risk perceptions and tobacco use over time (R00). *Hypothesis*: LGBT young adult polytobacco users exposed to *any* anti-tobacco messages (vs not exposed) will report greater risk perceptions and reduced tobacco use.

A team of exceptional NIH-funded researchers will provide mentorship for the proposed K99/R00 mentored research: *Amy Ferketich*, a tobacco prevention and control expert, with experience leading health communications studies to inform tobacco regulatory policy will provide primary mentorship with collaborative support from a team of co-mentors. This team is comprised of *Elizabeth Klein* and *Darren Mays* who are experts in leveraging psychophysiological measurement for health communications studies; and *Theodore*

Wagener, Director of the Center for Tobacco Research and expert in lab-based tobacco studies. A Mentoring Advisory Committee will provide further mentoring support and include *Michael Pennell*, biostatistician and expert in the statistical analysis of psychophysiological data and experimental studies, *Michael Slater*, health communications expert, and *Paul Nini*, an expert in applied visual communications design.

II. BACKGROUND and RATIONALE

This K99/R00 proposal addresses the FDA research priority area of Communications. The rationale for the scientific aims is the following. While tobacco regulation has contributed to steady declines in combustible tobacco use, there has been a marked increase in the use of novel tobacco products, including electronic nicotine delivery systems (ENDS).[6,33] Polytobacco use, defined as using more than one tobacco product including ENDS, is increasing[34] and is high in LGBT populations.[5,21,35-37] Between 22-40% of LGBT young adults (YA)[5-7] (vs 12-21% of non-LGBT YA[9,10]) report past 30-day polytobacco use. This is concerning as many polytobacco users progress to exclusively using combustible tobacco.[38,39] Both LGBT people[8] and polytobacco users[8,18-24] are also less likely to perceive tobacco as harmful, which may reinforce tobacco use.[25] The Food and Drug Administration (FDA) Center for Tobacco Products (CTP) is mandated to educate the public about the risks of tobacco products.[26-29,32] Yet, no evidence describes how to effectively frame anti-tobacco messages to communicate risks to LGBT YA. Anti-tobacco campaigns may use cultural targeting[40] to increase engagement, but this strategy demonstrates mixed effectiveness for health communications.[41-45] If culturally-targeted anti-tobacco messages are not more engaging than non-targeted messages, then general anti-tobacco campaigns may reach LGBT YA. We propose to develop and test anti-tobacco messages for an at-risk group, LGBT YA, with the goal of increasing risk perceptions and reducing tobacco use over time.

While anti-tobacco communications effectively reduce cigarette smoking[46,47] by preventing initiation[48-51] and progression,[50,52] no campaigns have specifically addressed polytobacco use. Existing campaigns (e.g., *The Real Cost*, *This Free Life*) focused on communicating *absolute risks* (AR) of *specific tobacco products (e.g., "cigarette smoking leads to lung cancer")* with the goal of preventing uptake in non-users or experimental users. YA polytobacco users have established tobacco patterns, so anti-tobacco campaign goals must also aim to: (1) prevent uptake of additional products, and (2) promote total tobacco cessation, or (3) harm reduction[53] by switching to lower risk products, like ENDS.[54,55] The FDA's regulatory plan places tobacco products on a risk continuum,[56] yet little evidence describes the effect of *relative risk* (RR) communications *(e.g., "cigarettes contain 9 times more cancer-causing chemicals than ENDS)* on risk perceptions and tobacco use.[57-59] Among smokers, RR communications increase intentions to quit smoking[58] and switch to ENDS.[57,58] RR messages may also influence quitting and switching behaviors in polytobacco users.

Targeting is a broadly supported communications strategy[40] to increase engagement with anti-tobacco communications. LGBT adults engage less with anti-tobacco campaigns than heterosexuals;[30,31] however, they report high exposure,[30,60,61] engagement,[30,62] and receptivity[60,63] to LGBT-targeted tobacco industry marketing.[60,63,64] Tobacco marketing messages emphasize LGBT community values of choice and pride.[65] These values have been leveraged in health campaigns targeting LGBT people,[66,67] including *This Free Life*, the FDA's first anti-tobacco campaign for LGBT YA who occasionally smoke.[68] The campaign's culturally targeted smoking prevention messages reached perceived effectiveness ratings similar to prior youth[49,69] and adult[70] anti-tobacco campaigns. Yet, no studies have *tested* if LGBT culturally targeted (vs non-targeted) messages are more engaging or effective for reducing polytobacco use.[71] Targeted anti-tobacco campaigns

are costly.[72,73] To manage costs[74] anti-tobacco communications must effectively engage audiences. ***If cultural targeting does not increase engagement and effectiveness of anti-tobacco messages, then the FDA may be able to reach at-risk LGBT people via campaigns targeting YA more generally***.

A conceptual model based on the Extended Parallel Process Model (EPPM)[1-3] and message impact framework[4] will guide the proposed research (Figure 2). Together they posit that, upon exposure to anti-tobacco messages, a person proceeds through three steps: attention, reaction, and formation of attitudes and intentions. These steps determine whether a person engages in the behavior promoted in the message.[75] The EPPM includes four key variables: perceived susceptibility, perceived severity, response efficacy and self-efficacy.[25,76] The model predicts that messages which cause a high perceived threat and high efficacy will result in action (quitting, switching). **The effectiveness of high threat[58,77,78] messages for behavior change is well established; however, less is known about how to effectively frame efficacy messages. Prior anti-tobacco campaigns have omitted efficacy statements entirely[1] or encouraged tobacco avoidance/cessation.[28,79] Yet for polytobacco users, both cessation *and* harm reduction efficacy messages may be needed**. Recent studies have applied combination efficacy messages that emphasize total tobacco cessation, while stating that if smokers are not ready to quit, switching to exclusive ENDS use can reduce health risks.[58,80] However, combined quit/switch messages may be confusing for users.[81] We will investigate optimal framing of threat/efficacy messages to communicate absolute and relative risk of

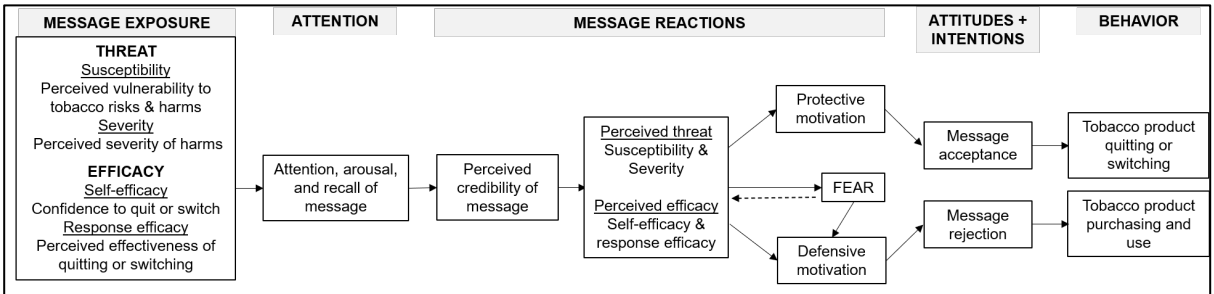

Figure 2. Conceptual model based on the Extended Parallel Process Model (1992) and Noar's (2017) Message Impact Framework

polytobacco use.

Bio-behavioral methods may be used to objectively quantify attention to culturally targeted anti-tobacco messages. Studies using self-report after anti-tobacco message exposure have revealed important information about behavioral intentions to use tobacco[27,82-84]; however, self-report outcomes are subject to social desirability bias[85] and can be enhanced by bio-behavioral methods.[86-88] More specifically, psychophysiological measures can clarify which messages capture polytobacco users' attention (eye-tracking) and evoke emotional responses (skin conductance).[89] These processes are prerequisite steps that inform risk perceptions, behavioral intentions and, ultimately, behaviors.[89] Bio-behavioral methods are used in studies of tobacco advertising[90-92] and warnings,[87,93,94] and will be used here to objectively study attention to anti-tobacco messages.

Anti-tobacco messages delivered via texting may effectively increase tobacco risk perceptions and reduce tobacco use. Texting-based communications have demonstrated effectiveness for increasing cessation in YA smokers[95-97] and preliminary efficacy[97] for changing risk perceptions and behaviors in YA waterpipe users. It is possible that anti-tobacco mobile multimedia messages (i.e., text plus graphic; MMS) may be similarly applied to communicate polytobacco use risks and reduce polytobacco use in LGBT YA. Over 96% of YA own a mobile device with MMS,[98] and 75% use it to seek health information.[99] By delivering anti-

tobacco messages via texting we can target content[95] to LGBT YA and, using MMS, mimic real-life exposure to anti-tobacco communications that LGBT YA may encounter while seeking health information using their device.

The proposed research will have an impact on the growing field of tobacco regulatory science. This study will provide results that can directly inform future FDA anti-tobacco public education efforts. At the completion of the study, we will have conducted an evaluation of the effectiveness of absolute and relative risk anti-tobacco ENDS messages that includes both formative and summative evaluation.[100]

III. PROCEDURES

A. K99/R00 Research Design Overview

Using qualitative and experimental designs, the proposed K99/R00 research is scientifically rigorous in its application of formative and summative evaluation.[100] Aims are synergistic and focused on developing and evaluating effective anti-tobacco messages for LGBT YA. Aim 1 (NCT05393869) is formative evaluation and focuses on optimal message framing for AR and RR anti-tobacco messages. Aim 1 outcomes are presented in ***Table 1.***

NOTE: Aim 1 studies (Phase 1 and 2) have been proposed and approved. As the K99 is transitioning to the R00 phase (August 2022), we are now proposing the Aim 2 formative focus groups and Aim 2 eye-tracking study (NCT05972941). Amendments will be submitted for the future Aim 3 RCT (NCT06644664; ***planned fall 2023).***

	Table 1. Overview of primary and secondary outcome measures for K99/R00 studies, by specific aim		
Aim	**Phase**	**Domain**	**Outcome Measure**
1	1 + 2	Cognitive	*General*[70,101] and *health-specific*[102] *perceived effectiveness*
1	2	Cognitive	EPPM constructs*: self-efficacy* to quit tobacco,[103] *response efficacy,*[103] and *reactance*[104]
1	2	Cognitive	*Risk perceptions:* Significance, severity, and seriousness of health threats from tobacco use,[105] absolute/relative risks of polytobacco use (vs exclusive ENDS use)
1	1+ 2	Behavioral	*Behavioral intentions* to use tobacco; intentions quit all tobacco, intentions to switch to exclusive ENDS use[58]
1	1	Qualitative	Acceptability and perceived effectiveness, recommendations for further refining

B. AIM 1 Phase 1 study *procedures*

(K99 Grant Year 1) In Aim 1 (NCT05393869) we will develop anti-tobacco messages and assess effectiveness.

In Aim 1 Phase 1, we will use multi-methods to gain feedback on textual anti-tobacco messages and gain insights about visual elements (images, fonts, colors) that are appealing to young adult polytobacco users. Phase 1 studies will include the following:

- Aim 1, Phase 1: Study 1 – FOCUS GROUPS will explore terminology and message themes used in absolute and relative risk anti-tobacco messages and quit/switch efficacy statements

- Aim 1, Phase 1: Study 2 – ONLINE RATING SURVEY will quantitatively assess how young adults rate absolute and relative polytobacco risk messages and quit/switch efficacy statements for perceived effectiveness and reactance

- Aim 1, Phase 1: Study 3 – IN-DEPTH INTERVIEWS will explore qualitatively how young adults perceive 8 absolute risk and 8 relative risk anti-tobacco messages.

Aim 1, Phase 1: Study 1 – FOCUS GROUPS: Focus group participants will be asked to share their opinions on possible textual anti-tobacco messages (**Table 2**). Anti-tobacco risk statements will pe presented in two sets; communicating either absolute (e.g., "*tobacco smoke contains 69 cancer-causing chemicals, including arsenic and formaldehyde*") or relative risk *(e.g., "combustible tobacco products contain 9 times more cancer-causing chemicals than ENDS).* Messages will address FDA-regulatory topics[106]; for example: addiction, toxic exposure, and health effects **(see supplemental documents for sample risk statements).** We will then present examples of efficacy statements including quit only (e.g., "*Quit all tobacco products to reduce health risks."*), switch only (e.g., *"Switch to using e-cigarettes to reduce health risks."*), or quit plus switch messages (e.g., *"Quit all tobacco products to reduce your risk of cancer. If you're not ready to quit, switch to e-cigarettes only."*). Focus group feedback will be used to further develop text for anti-tobacco messages that will be further tested in Aim 1, Phase 2 (NCT05393869). (**see supplemental documents A for sample efficacy statements).** Focus group participants will also be asked to provide feedback on the acceptability, appeal, and comprehension of specific terms (e.g., "traditional cigarettes" vs. "combustible cigarettes", "e-cigarettes" vs. "nicotine vapes" vs "vapes").

To assess graphics that are appealing to using adult polytobacco users, we will present examples of existing anti-tobacco messages from FDA and Truth anti-tobacco campaigns **(see samples in supplemental documents)**. We will ask focus group participants to identify the graphic components that are more and less appealing from existing anti-tobacco ads. We will use focus group feedback to add visual elements to the textual anti-tobacco messages that will be further tested in Aim 1, Phase 2. Graphics will mirror visual styles of existing campaigns[107] using bold colors and images of YA[108] to represent topics conveyed in text. Messages and images will be refined based on focus group feedback.

Table 2. Message sets for formative message testing in a 2x3 between subjects experiment (Aim 1 Phase 2)

		THREAT	
		ABSOLUTE RISK (AR)	**RELATIVE RISK (RR)**
EFFICACY	**Quit only (Q)**	Set 1: AR/Q (n = 8)	Set 2: RR/Q (n = 8)
	Switch only (S)	Set 3: AR/S (n = 8)	Set 4: RR/S (n = 8)
	Combined quit + switch (QS)	Set 4: AR/QS (n = 8)	Set 6: RR/QS (n = 8)

Aim 1, Phase 1: Study 2 –ONLINE RATING SURVEY: In Phase 1, Study 2 we will conduct an online survey to quantitatively examine young adults' perceptions of 8 absolute risk and 8 relative risk anti-tobacco messages and quit/switch efficacy statements. To reduce participant burden, each participant will view a random sample of messages as follows: n = 5 absolute and relative risk anti-tobacco messages (of N = 24), and n = 3 (of N = 12) efficacy messages. They will be asked to rate absolute and relative risk antitobacco messages and quit/switch efficacy statements for perceived message effectiveness, likeability, and reactance.

Aim 1, Phase 1: Study 3 –IN-DEPTH INTERVIEWS: Interviewees will be asked to share their reactions to the 24 textual anti-tobacco messages tested in Study 2. Specifically, interviewees will be asked to rate their top 5 (of N =12) absolute risk and top 5 (of N =12) relative risk antitobacco messages. We will then qualitatively explore their rationale for their top 5 selected messages.

Aim 1, Phase 2: ONLINE FACTORIAL EXPERIMENT (NCT05393869): Using a 2x3 factorial experiment (Table 2), plus control group design we will test the influence of AR and RR message framing on perceived effectiveness, tobacco risk perceptions, and behavioral intentions in young adult ever polytobacco users. Participants will be randomized to one of 8 conditions, including 6 experimental sets of AR and RR anti-tobacco messages(**Table 3**) and a control set of AR or RR regulatory control messages. We will present 8 messages within each experimental and control set. An expert panel of scientists, selected and invited by the mentoring team, will review all messages, which we will further refine based on expert feedback prior to testing in Aim 1, Phase 2 (NCT05393869).

B.1 Sample

Participants for Aim 1, Phase 1 studies will be young adults (age 18-35 years) who live in the United States. and are susceptible to multiple nicotine and tobacco product use (i.e., have used combustible tobacco or e-cigarettes at least once).

In the Aim 1 Phase 1 focus groups and interviews, participants expressed concern that relative risk messages comparing combustible cigarette and ENDS use could increase young adult non-users' curiosity and intentions to use ENDS. The goal of anti-tobacco messages being tested in this study is to increase harm perceptions and decrease use intentions among susceptible nicotine and tobacco users, However, we also do not want to negatively impact nonusers. After conferring with the mentoring committee and scientific experts, in Phase 2, we will address this concern by empirically testing whether responses to absolute and relative risk messages vary by nicotine and tobacco user type. As such, our sample will include young adults (age 18-35 years) who live in the United States. Per the Aim 1, Phase 1 studies, half of our sample will include young adults who are susceptible to multiple nicotine and tobacco product use (i.e., have used combustible tobacco or e-cigarettes at least once) and half of the sample will comprise U.S. young adult nonusers.

For Aim 1, Phase 1, Study 1--FOCUS GROUPS: The maximum overall sample size will be N = 58. However, our analytic sample size will start with 3 focus groups of size 6-8 individuals (N = 18-24 total participants). This sample size is standard in “usability research,” where existing messages are tested to uncover issues of effectiveness, and newly designed prototypes are tested to improve any communication issues. *If we do not reach thematic saturation, we will conduct additional focus groups until thematic saturation is achieved, up to a total analytic sample size of N = 48 participants.* We have inflated the overall sample size to 29 participants for each round of focus groups (N = 58) to allow for 20% dropout.

Recruitment will occur online via social media, on OSU’s campus, and in the Columbus community. On campus, we will reach out to student groups and we will place flyers in residence halls and other buildings. We have used these methods in the past with success. We will also work with the Office of Minority Health at Columbus Public Health to reach a racially, ethnically, and economically diverse group of young men and women. Co-investigator Ferketich has partnered with this office in the past and they have helped successfully recruit young people through their community connections. We will also partner with The Equitas Health Institute to reach LGBT young adults. Both the PI (Patterson) and Co-I (Ferketich) have relationships with The Equitas Health Institute through the College of Public Health. Focus groups will be balanced by gender and sexual orientation.

Aim 1, Phase 1: Study 2 –ONLINE RATING SURVEY: The overall sample size will be N = 550. Participants will be recruited via Prolific (https://www.prolific.co/), a platform for online subject recruitment for research, which is supported by Isis Innovation of the University of Oxford. In recent years, Prolific has been extensively

used in social science research and by the PI in prior studies. Prolific enables researchers to recruit participants to perform tasks such as filling out surveys, opinion polls, cognitive psychological studies, and many others. Researchers advertise their studies on Prolific, and participants choose only those studies that interest them. Participants are paid for completing the studies. In the PI's prior research using Prolific to recruit young adults into survey studies, approximately 3% of survey participants had inconsistencies between the prescreening questions asked by Prolific (e.g., age range) and demographic questions reported as part of the survey (e.g., numerical age). Data for these participants was not included in analyses, as we could not confirm that they met study eligibility criteria. As our analytic sample size is N = 500 participants; we have inflated our overall sample size is inflated by 10% to account for estimated inconsistencies between prescreening and survey responses.

We will monitor enrollment with the goal of recruiting a balance of young adult participants by age (younger: age 18-25, older: age 26-35), gender, and sexual orientation. From current population-based estimates, we expect that study participants will be 57% non-Hispanic white, 19% non-Hispanic black, 15% Hispanic, and 6% Asian, and the remaining representing other race groups.

As of October 2021, there are 11,731 active Prolific users who are aged 18-35, living in the United States, and have ever used nicotine or tobacco. Of these, 3,374 identify as women; 4465 identify as NOT heterosexual (i.e., homosexual, bisexual, other non-heterosexual sexual orientation), and 472 identify as transgender or nonbinary/genderqueer.

Aim 1, Phase 1: Study 3 – IN-DEPTH INTERVIEWS. For interviews, the maximum overall sample size will be N = 20. However, our initial analytic sample size will be N = 8 participants. *If we do not reach thematic saturation, we will conduct additional interviews until thematic saturation is achieved, up to a total analytic sample size of N = 16 participants.* We have inflated the overall sample size to 20 participants to allow for 20% dropout.

Recruitment will occur online via social media, via email listservs, on OSU's campus, and in the Columbus community. We will invite prior focus group participants to participate in in-depth interviews. On campus, we will reach out to student groups and we will place flyers in residence halls and other buildings. We have used these methods in the past with success. We will also partner with The Equitas Health Institute to reach LGBT young adults. Both the PI (Patterson) and Co-I (Ferketich) have relationships with The Equitas Health Institute through the College of Public Health. We will aim to balance interviews by gender and sexual orientation.

For the Aim 1, Phase 2—ONLINE FACTORIAL EXPERIMENT (NCT05393869): The overall sample size will be N = .2940. Participants will be recruited via Prolific (https://www.prolific.co/), a platform for online subject recruitment for research, which is supported by Isis Innovation of the University of Oxford. In recent years, Prolific has been extensively used in social science research and by the PI in prior studies. Prolific enables researchers to recruit participants to perform tasks such as filling out surveys, opinion polls, cognitive psychological studies, and many others. Researchers advertise their studies on Prolific, and participants choose only those studies that interest them. Participants are paid for completing the studies. In the PI's prior research using Prolific to recruit young adults into survey studies, approximately 3% of survey participants had inconsistencies between the prescreening questions asked by Prolific (e.g., age range) and demographic questions reported as part of the survey (e.g., numerical age). Data for these participants was not included in analyses, as we could not confirm that they met study eligibility criteria. In our phase 1 study, <1% of the sample reported inconsistencies between prescreening and survey responses. As our analytic sample size is

N = 2800 participants (n = 400 participants per experimental or control group); we have inflated our overall sample size is inflated by 5% to account for estimated inconsistencies between prescreening and survey responses.

We will monitor enrollment with the goal of recruiting a balance of young adult participants by age (younger: age 18-25, older: age 26-35), gender, and sexual orientation. From current population-based estimates, we expect that study participants will be 57% non-Hispanic white, 19% non-Hispanic black, 15% Hispanic, and 6% Asian, and the remaining representing other race groups.

B.2. Measurement / Instrumentation

For Aim 1, Phase 1: Study 1--FOCUS GROUPS: A focus group guide will be developed and will be used to facilitate the research for preliminary work. Participants will be asked about their opinions on a series of absolute and relative risk polytobacco use statements, efficacy statements, and visual elements of anti-tobacco communication campaigns. Participants will also be asked their thoughts on the types of images to pair with anti-tobacco risk statements.

For Aim 1, Phase 1: Study 2—ONLINE RATING SURVEY: Primary outcome measures are presented in **Table 1**. Baseline questionnaires will assess EC and combustible tobacco use,[109] pro- and anti-tobacco advertising exposure,[110] receptivity,[111] social media use and risk perceptions[105] and behavioral intentions.[58] Post-viewing their randomly assigned messages participants will be asked to rate each message for perceived message effectiveness,[70,101] likeability,[112] and reactance.[104] Finally, sociodemographic questions also include age, race/ethnicity, education level, location (state, zip code, rurality), sexual orientation[113] and gender identity.[114]

For Aim 1, Phase 1: Study 3—IN-DEPTH INTERVIEWS: An interview guide will be developed and will be used to facilitate the research. Specifically, interviewees will be asked to rate their top 5 (of N =12) absolute risk and top 5 (of N =12) relative risk antitobacco messages. We will then qualitatively explore their rationale for their top 5 selected messages. We will also ask participants to share their opinions on the types of images to pair with anti-tobacco risk statements.

For Aim 1, Phase 2-ONLINE FACTORIAL EXPERIMENT (NCT05393869): Primary outcome measures are presented in **Table 1**. These measures were largely selected from the Tobacco Regulatory Research PhenX Toolkit.[115,116] Baseline questionnaires will assess ENDS and combustible tobacco use,[109] pro- and anti-tobacco advertising exposure,[110] receptivity,[111] social media use, risk perceptions,[105] self- and response efficacy,[103] and behavioral intentions.[58] Post-viewing their assigned message condition, all participants will be asked about their responses to the posts including perceived acceptability, attitude toward, and effectiveness of the messages. All baseline measures (excluding social media use and prior anti-tobacco message exposure) will be asked post-viewing all messages. Finally, sociodemographic questions also include age, race/ethnicity, education level, location (state, county, rurality), sexual orientation[113] and gender identity.[114]

The purpose of the R00 Phase is to identify which anti-polytobacco messages most strongly influence LGBT YA's attention, tobacco risk perceptions, and behavioral intentions (Aim 2: NCT05972941) and evaluate the impact of exposure to anti-polytobacco communications delivered by mobile multimedia messaging (MMS) on tobacco use over time in YA polytobacco users of diverse sexual orientations and gender identities (Aim 3: (NCT06644664)*)*

C. AIM 2 Study (NCT05972941) Procedures (R00 Grant Year 1)
Overview

- Our Aim 2 goal is to identify if culturally targeted (CT) or non-targeted (NT) anti-polytobacco messages are most effective for engaging LGBT YA. Using the most effective NT messages from Aim 1 (12 RR; 12 AR), we will create a set of CT messages. Message framing will remain consistent between CT and NT messages; however, CT messages will include graphics representing LGBT values per the PI's formative research and extant literature.[39,40] Focus groups with LGBT tobacco users will be used to elicit recommendations for refining CT messages, which we will change accordingly. Then, an expert panel of scientists and LGBT community members will review CT messages prior to testing as part of our Community Advisory Board for this study and beyond. In the Aim 2 clinical trial (NCT05972941), a virtual eye-tracking study, participants will be randomized to view CT or NT messages in our virtual lab where we will assess eye-tracking, self-reported perceived effectiveness, risk perceptions, and behavioral intentions. We aim to determine the effects of cultural targeting on attention to anti-polytobacco messages and perceived effectiveness among LGBT young adult polytobacco users. The most effective messages (CT or NT) will be tested in Aim 3 for their influence on risk perceptions and tobacco use.

- **Aim 2 Focus groups:** Focus groups will take place in-person or online via CarmenZoom in a secure, private space. Eligible participants will complete a verbal informed consent and online baseline survey. A PDF of the informed consent will be made available for download as part of the online baseline survey. Consent will be reaffirmed prior to commencing discussions and audio-recording. Participants will receive $30 for their time.
- **Aim 2 Eve-tracking experiment (NCT05972941):** The eye-tracking experiment will take place virtually using iMotions, an online platform for remote eye-tracking data collection, and Qualtrics survey software. Eligible participants will complete written informed consent via RedCap. A PDF of the informed consent will be made available to participants for download. Participants will receive $50 for the eye-tracking survey. Participants will be contacted one-week after participating for a follow-up survey to assess recall. Participants will receive $20 for participating in the follow-up survey.

C.1. Sample

Participants for Aim 2 studies must: (1) be 18-35 years old; (2) be able to speak English fluently; (3) an *ever user of ENDS and combustible tobacco who currently use ENDS, combustible cigarettes, or both ENDS and combustible cigarettes,* (4) self-identify as LGBTQ+, (5) reside in the US (United States); (6) have access to a laptop or desktop computer with a camera for virtual eye-tracking, and (7) for eye-tracking study only, not have problems that would preclude eye-tracking (i.e., no glaucoma, cataracts).

- Focus groups: Using targeted social media, online (i.e., listserv), and print advertising,[41-43] we will recruit up to 4 focus groups of 6-8 LGBT young adults.
- Virtual eye-tracking: Using targeted online, social media, print and venue-based engagement ,[41-43] and crowdsourcing, we will enroll up to N=300 LGBT YA to ensure our analytic sample size of N=108. We will monitor enrollment with the goal of recruiting a balance of young adult participants by age (younger: age 18-25, older: age 26-35), gender, and sexual orientation. From current population-based estimates of LGBT people, we expect that study participants will be 58% non-Hispanic white, 12% non-Hispanic black, 20% Hispanic, and 2% Asian, and the remaining representing other race groups.

Participants will be recruited using primarily a mix of convenience and snowball sampling, an effective strategy with difficult to locate populations, and which the PI has successfully used to recruit LGBT populations into intervention studies. Online, we will engage community members via social media and organizational listervs to

distribute study information. We will also use targeted social media advertising. We will complement online recruitment by distributing print flyers on The Ohio State University and other university campuses via LGBT organizations.

C.2 Measurement / Instrumentation

For Aim 2 focus groups, a focus group guide will be developed and will be used to facilitate the research for preliminary work. Focus groups: Via semi-structured interview, we will ask participants about polytobacco use patterns, risk perceptions, and responses to CT messages.

For the Aim 2 eye-tracking experiment (NCT05972941), outcomes of interest are as follows:

Primary;	Attention	During exposure	Visual attention measured by eye-tracking on areas of interest (text, graphic): first fixation, dwell time (milliseconds), heat map
Primary;	Perceived effectiveness	Post-exposure to each message	Includes general perceived effectiveness (e.g., "The messages I received messages were worth remembering") and health-specific perceived effectiveness ("The messages I received made me concerned about the health effects of polytobacco use")
	EPPM Construct		Psychological reactance
Primary;	Risk Perceptions	Pre- and post-test	We will ask participants to report the significance, severity, and seriousness of health threats from tobacco use, absolute/relative risks of polytobacco use (and vs exclusive ENDS use)
Primary;	Behavioral Intentions	Pre- and post-test	Behavioral intentions to use tobacco; intentions quit all tobacco, intentions to switch to exclusive ENDS use
Secondary;	EPPM Constructs	Pre- and post-test	Self-efficacy to quit tobacco, response efficacy

For the 1-week follow-up a survey will be developed. Questions will quantitatively assess recent tobacco and ENDS use and health risk perceptions. Message recall will be assessed using quantitative and qualitative survey items.

IV. DETAILED STUDY PROCEDURES

A. Aim 1, Phase 1: Study 1- FOCUS GROUP Procedures

Prescreening and consent. Participants will be recruited from OSU student organizations, flyers on campus, Reddit, other social media, or through word of mouth from participants who completed the study. The recruitment materials will include a study phone number and an OSU email address that will be set up for the study. Individuals who are interested in the study will be asked to call or email the study email address. An IRB-approved research team member will call the individual and go through the screener that explains the study and determines eligibility.

Eligible participants will complete a verbal informed consent. The research team member will read the informed consent script and verbally explain the online questionnaire and focus group process. The research team member will indicate that participation in the questionnaire and focus group is voluntary. The eligible participant will be given an opportunity to ask questions and have all questions answered to their satisfaction. Once the eligible participant understands the consent form and process, then and only then will the eligible participant be asked to give verbal consent. Eligible participants that do not consent will be released at this time. Consenting participants will be emailed the informed consent script for their records. A PDF copy of the informed consent script will also be made available for download as part of the online questionnaire.

The research team member will ask eligible and consented participants for an email address for online questionnaire distribution and to send information for the future focus group. After the call has concluded, the research team member will email participants a link to a short questionnaire distributed via Qualtrics with questions about tobacco use, intentions to quit smoking, and demographic characteristics.

Focus group procedures. On the day of focus group, OSU IRB approved study personnel will provide an opportunity for verbal reconsent immediately preceding the focus group. Prior to audio-recording, the IRB-approved research team member will re-affirm participant consent. The research team member will indicate that participation in the focus group is voluntary and that participants may withdraw participation at any time. Eligible participants who do not reaffirm consent to focus group participation will be released at this time.

Focus groups will take place online via CarmenZoom in a secure, private space. A growing body of evidence describes the use of web-based videoconferencing platforms—also known as Voice over Internet Protocol (VoIP)-mediated technologies (e.g., CarmenZoom, Skype, FaceTime)—for collecting data in qualitative studies.[117-121] Zoom, in particular, has been cited by qualitative interview participants as straightforward, easy to use, and preferred for its "robust but simple privacy and security options" (e.g., secure webinar options and local device- or server-based recording).[117] Online focus group are also a feasible option for conducting qualitative human subjects research during the COVID-19 pandemic where meeting in groups may not be preferred in order to protect participants' health and wellbeing.

All focus groups will be audio-recorded and transcribed for subsequent analysis. Focus group length is anticipated to be about 90 minutes. Audio-recorded data will capture participants' verbal ratings and reactions to polytobacco use risk statements (absolute and relative risk), quit efficacy statements, and visual elements of existing national anti-tobacco campaigns. Specifically, participants will be asked to rate and then describe their reactions to anti-tobacco messages, including whether they believe the message effectively communicates tobacco risk (absolute or relative) and whether the message would be effective at preventing polytobacco use among young adults. Then, they will be asked to provide their opinion about how to visually represent that idea. They will also be asked about their reactions to self-efficacy statements promoting quitting and, if participants are not ready to quit, switching to lower harm products. Finally, participants will be asked to share their reactions to visual elements (images, fonts, colors) used in existing FDA and Truth© anti-tobacco campaigns. Participants will receive $30 via Amazon gift card distributed via email in appreciation of their time.

Aim 1, Phase 1: Study 1-FOCUS GROUP data will be used to further develop/refine text and graphics for anti-tobacco messages that will be further tested in Aim 1, Phase 2 (NCT05393869).

B. Aim 1, Phase 1: Study 2—ONLINE RATING SURVEY Procedures

Prescreening and consent. Participants will be recruited via Prolific, an online platform open to participants who are compensated for completing surveys and online behavioral experiments. Prolific is an efficient online recruitment platform, ideal for pilot studies, as it can deliver a high number of participants, per day, at low cost (recommended, minimum $0.175 per minute of survey participation time). Data quality provided by Prolific

samples is high and comparable to that from traditional college student samples.[122] Prolific offers access to over 38,000 United States nationals. Prolific samples are young; approximately 1/3 of the Prolific population reports ages < 35 years old, which makes Prolific an ideal pool for recruiting young adult survey participants. Prolific is also a viable method for recruiting hard-to-reach populations for survey research, including LGBT populations.[123]

Prescreening will be conducted via Prolific. Prolific is able to segment our population of interest for age (18-35 years) and currently residing the United States. It can also help us track gender and sexual orientation in order to balance recruitment. We are able to add in a custom pre-screening question to assess for prior history of ever nicotine or tobacco use (i.e., use of combustible tobacco or e-cigarette products at least once).

Participants who meet eligibility criteria will be directed to an online survey administered via Qualtrics. Consent will be completed online prior to the Qualtrics survey.

Qualtrics survey procedures. Following online consent, participants will be directed to complete a survey that includes questions assessing tobacco use, including exposure to tobacco related advertising, coupons, and discounts; harms perceptions and tobacco-related behavioral intentions (i.e., quit, switch). It is estimated that the survey will take 20 minutes to complete.

Participants will answer baseline survey questions before viewing a random sample of 5 messages (of N = 24); they will rate each message for perceived effectiveness[70,101,102], likeability,[112] and reactance.[104] After viewing all messages, participants will complete a post-survey and receive $0.175/minute (estimated $3.50) via Prolific for participating.

As per Prolific procedures, participants are paid via Prolific only when submitted work is approved by the study team. Participants are redirected back to Prolific at the end of the Qualtrics survey via a Completion URL, which proves that they have completed the study. This code is given to the participants who submit a complete and valid response to the survey. The study team compares the Qualtrics surveys to the participants redirected back to Prolific via the URL. If a survey participant is not matched to a redirect URL, a participant is not paid.

To contextualize data quality, we will include an instructional manipulation check[124] at the end of the survey. A participant's answer to this question will not affect payment for survey participation; rather, it will be used during data analysis to identify potential problematic survey responses for in-depth data checks. Participants will be asked the following:

> *Research suggests that, when making decisions and answering questions, people prefer not to pay attention and minimize their efforts. Some studies show that over 50% of people do not carefully read questions. You will be compensated for survey participation regardless of your answer to this question. If you are reading this question and have read all the other questions, please select the box marked 'other" and type 'yes" in the box below. Thank you for participating in our survey!*
>
> - *Yes*
> - *No*
> - *Other:_____*

C. Aim 1, Phase 1: Study 3:-IN-DEPTH INTERVIEW Procedures

Prescreening and consent. Participants will be recruited from OSU student organizations, flyers on campus, Reddit, other social media, email listservs, or through word of mouth from participants who completed the Phase 1 Focus group or interview study. The recruitment materials will include a study phone number and an OSU email address that will be set up for the study. Individuals who are interested in the study will be asked to call or email the study email address. An IRB-approved research team member will call the individual and go through the screener that explains the study and determines eligibility.

Eligible participants will complete a verbal informed consent. The research team member will read the informed consent script and verbally explain the online questionnaire and interview process. The research team member will indicate that participation in the questionnaire and interview is voluntary. The eligible participant will be given an opportunity to ask questions and have all questions answered to their satisfaction. Once the eligible participant understands the consent form and process, then and only then will the eligible participant be asked to give verbal consent. Eligible participants that do not consent will be released at this time. Consenting participants will be emailed the informed consent script for their records. A PDF copy of the informed consent script will also be made available for download as part of the online questionnaire.

The research team member will ask eligible and consented participants for an email address for online questionnaire distribution and to send information for the interview. After the call has concluded, the research team member will email participants a link to a short questionnaire distributed via Qualtrics with questions about tobacco use, intentions to quit smoking, and demographic characteristics.

Interview procedures. On the day of interview, OSU IRB approved study personnel will provide an opportunity for verbal reconsent immediately preceding the interview. Prior to audio-recording, the IRB-approved research team member will re-affirm participant consent. The research team member will indicate that participation in the interview is voluntary and that participants may withdraw participation at any time. Eligible participants who do not reaffirm consent to interview participation will be released at this time.

Interviews will take place online via CarmenZoom in a secure, private space. A growing body of evidence describes the use of web-based videoconferencing platforms—also known as Voice over Internet Protocol (VoIP)-mediated technologies (e.g., CarmenZoom, Skype, FaceTime)—for collecting data in qualitative studies.[117-121] Zoom, in particular, has been cited by qualitative interview participants as straightforward, easy to use, and preferred for its “robust but simple privacy and security options” (e.g., secure webinar options and local device- or server-based recording).[117] Online interviews are also a feasible option for conducting qualitative human subjects research during the COVID-19 pandemic where meeting in-person may not be preferred in order to protect participants’ health and wellbeing.

All interviews will be audio-recorded and transcribed for subsequent analysis. Interview length is anticipated to be about 60 minutes. Audio-recorded data will capture participants’ verbal ratings and reactions to antitobacco risk statements (absolute and relative risk), quit efficacy statements, and visual elements of existing national anti-tobacco campaigns. Specifically, participants will be asked to rate their top 5 of both absolute and relative risk anti-tobacco messages, including whether they believe the message effectively communicates tobacco risk (absolute or relative) and whether the message would be effective at preventing polytobacco use among young adults. Then, they will be asked to provide their opinion about how to visually represent that idea. They will also be asked about their reactions to self-efficacy statements promoting quitting and, if participants are not ready to quit, switching to lower harm products. Participants will receive $30 via Amazon gift card distributed via email in appreciation of their time.

D. Aim 1, Phase 2: ONLINE FACTORIAL EXPERIMENT (NCT05393869) Procedures

Prescreening and consent. Participants will be recruited via Prolific, an online platform open to participants who are compensated for completing surveys and online behavioral experiments. Prolific is an efficient online recruitment platform, ideal for pilot studies, as it can deliver a high number of participants, per day, at low cost (recommended, minimum $0.175 per minute of survey participation time). Data quality provided by Prolific samples is high and comparable to that from traditional college student samples [122]. Prolific offers access to over 38,000 United States nationals. Prolific samples are young; approximately 1/3 of the Prolific population reports ages < 35 years old, which makes Prolific an ideal pool for recruiting young adult survey participants. Prolific is also a viable method for recruiting hard-to-reach populations for survey research, including LGBT populations [123].

Prescreening will be conducted via Prolific. Prolific is able to segment our population of interest for age (18-35 years) and currently residing the United States. It can also help us track gender and sexual orientation in order to balance recruitment. We are able to add in a custom pre-screening question to assess for prior history of ever nicotine and tobacco use.

Participants who meet eligibility criteria will be directed to an online survey administered via Qualtrics. Consent will be completed online prior to the Qualtrics survey.

Qualtrics survey procedures. Following online consent, participants will be directed to complete a survey that includes questions assessing tobacco use, including exposure to tobacco related advertising, coupons, and discounts; harms perceptions and tobacco-related behavioral intentions (i.e., quit, switch); and online/social media use questions.

Participants will answer baseline survey questions before random assignment to 1 of 6 experimental conditions in the 2 (Threat: Absolute/Relative Risk) X 3 (Efficacy: Quit, Switch, Quit plus Switch) design. Participants will view 8 randomly-ordered, anti-tobacco messages within their assigned condition; they will rate each message for perceived effectiveness[70,101,102] and reactance.[104] After viewing all messages, participants will complete a post-survey and receive $0.225/minute (estimated $4.50) via Prolific for participating.

As per Prolific procedures, participants are paid via Prolific only when submitted work is approved by the study team. Participants are redirected back to Prolific at the end of the Qualtrics survey via a Completion URL, which proves that they have completed the study. This code is given to the participants who submit a complete and valid response to the survey. The study team compares the Qualtrics surveys to the participants redirected back to Prolific via the URL. If a survey participant is not matched to a redirect URL, a participant is not paid.

To contextualize data quality, we will include an instructional manipulation check[124] at the end of the survey. A participant's answer to this question will not affect payment for survey participation; rather, it will be used during data analysis to identify potential problematic survey responses for in-depth data checks. Participants will be asked the following:

> *Research suggests that, when making decisions and answering questions, people prefer not to pay attention and minimize their efforts. Some studies show that over 50% of people do not carefully read questions. You will be compensated for survey participation regardless of your answer to this question. If you are reading this question and have read all the other questions, please select the box marked 'other" and type 'yes" in the box below. Thank you for participating in our survey!*
>
> - *Yes*

- *No*
- *Other:*_____

E. Aim 2: Focus Group Procedures

Prescreening and consent. Participants will be recruited from OSU student organizations, flyers on campus, Reddit, other social media, or through word of mouth from participants who completed the study. The recruitment materials will include a study phone number and an OSU email address that will be set up for the study. Individuals who are interested in the study will be asked to take an online screener or, if they have questions, to call or email the study email address.

Individuals who are deemed eligible via the online screener will be asked to share their contact information. An IRB-approved study team member will contact eligible individuals to review informed consent. Eligible participants will complete a verbal informed consent. The research team member will read the informed consent script and verbally explain the online questionnaire and focus group process. The research team member will indicate that participation in the questionnaire and focus group is voluntary. The eligible participant will be given an opportunity to ask questions and have all questions answered to their satisfaction. Once the eligible participant understands the consent form and process, then and only then will the eligible participant be asked to give verbal consent. Eligible participants that do not consent will be released at this time. Consenting participants will be emailed the informed consent script for their records.

The research team member will ask eligible and consented participants for an email address for online questionnaire distribution and to send information for the future focus group. After the call has concluded, the research team member will email participants a link to a short questionnaire distributed via Qualtrics with questions about tobacco use, intentions to quit smoking, and demographic characteristics. A PDF copy of the informed consent will be available for download as part of the online baseline survey.

Focus group procedures. On the day of focus group, OSU IRB approved study personnel will provide an opportunity for verbal reconsent immediately preceding the focus group. Prior to audio-recording, the IRB-approved research team member will re-affirm participant consent. The research team member will indicate that participation in the focus group is voluntary and that participants may withdraw participation at any time. Eligible participants who do not reaffirm consent to focus group participation will be released at this time.

Focus groups will take place in-person or online via CarmenZoom in a secure, private space. A growing body of evidence describes the use of web-based videoconferencing platforms—also known as Voice over Internet Protocol (VoIP)-mediated technologies (e.g., CarmenZoom, Skype, FaceTime)—for collecting data in qualitative studies.[117-121] Zoom, in particular, has been cited by qualitative interview participants as straightforward, easy to use, and preferred for its “robust but simple privacy and security options” (e.g., secure webinar options and local device- or server-based recording).[117] Online focus group are also a feasible option for conducting qualitative human subjects research with national samples.

All focus groups will be audio-recorded and transcribed for subsequent analysis. Focus group length is anticipated to be about 60-90 minutes. Audio-recorded data will capture participant’ responses to questions about nicotine and tobacco use, public education messages about nicotine and tobacco, and textual and visual elements of LGBT cultural targeting.

Sources of Materials: Information from focus groups (conducted via CarmenZoom) will be obtained in this study to pre-test culturally targeted anti-polytobacco messages. Focus groups will either be conducted in-person and audio-recorded or will be conducted remotely using CarmenZoom

(https://resourcecenter.odee.osu.edu/carmenzoom), an enterprise-wide web conferencing tool that allows individuals to connect via videoconference or telephone.

- For in-person focus groups we will use a digital audio recorder. Post focus group, audio data will be immediately downloaded and transferred to One Drive for secure long-term storage. Only the focus group identification number will be used to identify the data source.

- For remote focus groups, researchers will use CarmenZoom's videoconferencing platform to enable CarmenZoom's secure audio-recording feature. Participants will be asked to call into the meetings via telephone only. CarmenZoom stores audio-recorded sessions and protects sensitive data using real-time encryption of meetings and automatic cloud-based recording and storage to the OSU Carmen Zoom online remote server networks (i.e., "the cloud") for 180 days. These recordings will be downloaded and transferred to Microsoft Teams/One Drive for secure long-term storage. Only the focus group identification number will be used to identify the data source.

Participants will receive $30 via Amazon gift card distributed via email in appreciation of their time.
Aim 2 focus group data will be used to further develop/refine text and graphics for anti-tobacco messages that will be further tested in the Aim 2 eye-tracking study.

F. Aim 2: Virtual Eye-Tracking Experiment (NCT05972941) Procedures
Prescreening, consent, and study procedures:

Participants will complete an online screener via RedCap after viewing a social media ad or flyer, receiving an email from participating in another study, or via word-of-mouth from other participants. Eligibility screeners will include 'nedCAPTCHA', a module that provides the use of a classic image CAPTCHA with distorted text, a math problem, or a custom question/answer challenge. These CAPTCHAs are similar to the 'I am not a robot' button or the 'Click all of the traffic lights' CAPTCHAs often seen in online forms. nedCAPTCHA is highly recommended by OSU OCIO for projects using the Public Survey Link option in REDCap. The module will help prevent bots from completing surveys. Eligible participants will asked to report an email address and telephone number for future contact if enrolled into the study.

As the eye-tracking component of this survey requires that participants complete the survey on a laptop or desktop with a webcam, we will include a question at the end of the eligibility screener asking participants if they are currently participating on a desktop/laptop with webcam. If participants meet all other eligibility criteria, but they are taking the screener on a device other than a laptotop or desktop with webcam (e.g,. a tablet or smart phone), they will be directed to the following opt-in statement: "I have a desktop computer or laptop but I am currently on my phone or tablet. Please email me a link to the consent form and I will complete the iMotions task on my laptop/desktop." Research study staff will then contact eligible and interested participants via email, phone call or text to complete the informed consent and participate in the online eye-tracking experiment. After reviewing the consent form, participants will be asked to electronically indicate their consent to participate. Online consent will be documented in REDCap.

If eligible participants indicate that they are currently taking the eligibility screener on a laptop or desktop with webcam, they will be immediately directed to an informed consent describing the study purpose and detail

about the survey and the embedded remote eye-tracking experiment. After reviewing the consent form, participants will be asked to electronically indicate their consent to participate. Online consent will be documented in REDCap.

Consented participants will be directed to the online survey. At the beginning of the survey, we will ask participants to confirm that they are taking the survey in a well-lit area and that their face and eyes are clearly viewable on their webcam. We will include example images of good vs. poor lighting. If participants respond, "I am using a desktop computer or laptop. I am in an area that is well lit, and I can see my face and eyes clearly," then they will be directed to the survey. If they respond, "I have a desktop computer or laptop, but I am currently in an area that is not well lit and I cannot see my face or eyes clearly on my webcam. Please email me a link to the survey, and I will complete the iMotions task when I am in an area with better lighting," then research staff will then email these participants a direct link to the survey that they can take at a convenient time. We will send up to 9 survey reminders via email, phone call or text.

Once the survey begins, participants will complete baseline questionnaires before proceeding to the remote eye-tracking experiment. At this point, participants will be randomly assigned to 1 of 2 experimental conditions (CT or NT messages). iMotions provides an online platform for remote eye-tracking data collection using a webcam connected to a desktop or laptop computer to track eye movements during the study. Participants will be informed that their webcam needs to be turned on during the study. Prior to viewing images, calibration procedures will be conducted to assure data quality; if participants cannot be calibrated, participation will end. Participants will view a series of randomized messages (8 messages, for 10 seconds each, within assigned conditions. A 10 second viewing time is greater than needed (6 seconds) to assess visual attention.

Message versions will include similar messaging and imagery but different layouts to mitigate viewing bias, as we anticipate that a majority of participants will tend to read left to right and top to bottom. After each message, participants will report perceived effectiveness and reactance. To re-center eyes, participants will view an "X" centered on-screen for 10 seconds. Post eye-tracking, participants will complete demographic and contextual questions prior to exiting the survey. Participation is expected to last 20 minutes. Participants will receive a $50 gift card.

We will contact participants 1-week post-experiment via a RedCap survey to assess message recall, recent nicotine and tobacco use, and risk perceptions. Participation is expected to take 10-15 minutes, for which they will receive a $20 gift card.

Participants may be recontacted to resolve discrepant data entries. We will recontact participants via the study email address or phone to resolve the problem. <u>If we are unable to resolve the discrepancy, we are unable to provide a study incentive.</u>

Participants will also be asked if they would be willing to be contacted to participate in future studies. Depending on their preferred contact method (e.g., email or phone), we will keep a list of those who say “yes” to being contacted for future studies saved in REDCap.

All research-related data will be saved on a password protected computer on The Ohio State University server. Upon completion of data collection, all data will be de-identified and stored on The Ohio State University Microsoft Teams/OneDrive.

Participants who have consented to version 1 of the consent form will be asked to consent to version 2 which specifically outlines details related to facial recording. Participants will be sent an individual email using the secure databasing platform, REDCap and will be given the option to consent or decline study participation electronically within REDCap. We will recontact participants up to 9 times to seek reconsent.

At the end of data analysis, participants will be emailed once their face recording data has been deleted.

Sources of Materials

Information from an online survey with embedded remote eye-tracking will be obtained in this study to experimentally test the effect of exposure to anti-polytobacco messages with and without cultural targeting on message effectiveness and reactance, and tobacco harm perceptions. Data from the pre- and post-eye-tracking surveys will be collected in Qualtrics. Data from the embedded remote eye-tracking study will be collected via iMotions, a secure, online data collection platform. No self-report or eye-tracking data collected are directly linked to participant identifying information: self-report and eye-tracking data collected through iMotions are tracked using a unique, numeric participant identifier. Remote eye tracking is performed through the respondent's own webcam and allows for recording and analysis of responses to images tracking visual attention. Webcam recordings of facial data will be recorded and stored within the I-motions software. Post-participation, the data will be downloaded. Facial recording data will be reviewed by staff members for compliance-related purposes only, and will not be used for analysis. All survey and eye-tracking data will be stored on The Ohio State University Microsoft Teams/OneDrive. Data collected in follow-up surveys will be collected and stored in RedCap and linked to the participant’s personal identifier. At the conclusion of the study, all facial recognition data will be deleted.

V. RISKS, BENEFITS, SAFETY PLANS

A. Risks associated with the study

Potential risks are minimal for the focus group and survey studies. Some of the questions may upset individuals; however, we have used these questions and procedures in many previous studies without upsetting participants. A potential risk is loss of confidentiality In our screener, we collect participant contact information. Also, iMotions eye-tracking software saves facial data to track eye movements; however, this information will only be used to track participant compliance to study procedures, will not be used during data analysis, and will be deleted upon study completion. We will not use facial recording information for any other purpose, and because all study data including facial recording is stored on a secure password-protected University-sponsored laptop, we do not believe this represents an increase in risk for study participants. Participant privacy is protected because participants will consent to research before any study activities are performed. Because facial recordings are collected, participants are informed of this at several points throughout the study

and will be given the option to discontinue participation at any time. For Aim II Eye Tracking Study, we are collecting facial recordings because it is a requirement of the software. We are only using facial recordings for compliance purposes. We also collect first and last name, email address, zip code, county, and sexual orientation from participants, which may be sensitive. Participants provide this by self-report and may skip any question that is uncomfortable. We have rigid procedures in place to protect against loss of confidentiality. Participant identifiers will be kept in password-protected files, stored on secure OSU servers.

B. Benefits associated with the study

There are no direct benefits to be gained by participants. However, the anticipated societal benefit resulting from this study is considerable, given the increasing prevalence of polytobacco use, including ENDS. Societal benefits include increased public health resulting from this study providing evidence that directly informs and strengthens FDAs tobacco public education efforts. Few studies have been conducted on effectively communicating tobacco risk to polytobacco users and at the same time, there is mounting evidence that LGBT young adult polytobacco users, a vulnerable population from a tobacco control perspective, are largely misinformed of the risks of combustible tobacco and ENDS use.

VI. DATA ANALYSIS

A. Aim 1, Phase 1: Study 1—FOCUS GROUPS Data Analysis

For focus groups, the goal is to refine messages and determine which images should be matched to the AR and RR anti-tobacco messages. These images will then move on to Aim 1 Phase 2 of this study. We will qualitatively summarize the feedback in response to each focus group question.

> Sample size justification: For Aim 1 Phase 1: Study 1—FOCUS GROUPS: A planned analytic sample size of N = 24 participants is standard for usability research, where the aim is to test existing messages to improve any communication issues. If we do not reach thematic saturation during the first round of focus group, we will enroll up to an additional 24 participants (for a maximum analytic of N = 48).The sample size was inflated to 29 participants for each round of focus groups to allow for 20% dropout; resulting in a maximum overall sample size of N = 58 focus group participants.

B. Aim 1, Phase 1: Study 2-ONLINE RATING SURVEY Data Analysis

For online rating survey data, we will describe mean and median values of participants' ratings of perceived message effectiveness, likeability, and reactance.

In exploratory analyses, we will l assess whether there are systematic differences in participants' ratings *by message type (AR vs RR), gender, LGBT status (vs non-LGBT)*, *race/ethnicity, age (e.g., 18-24 vs 25-35)* and *tobacco user typ*e (e.g., current, former, never polytobacco user). We will test mean differences between groups using t-tests or ANOVA. If there are violations of assumptions (e.g., normality) we will test median differences between groups using Wilcoxon rank-sum test (two groups) or Kruskal Wallis test (more than 2 groups).

We will also run exploratory regression models to evaluate the effect of risk message type (e.g., absolute risk vs. relative risk) and efficacy message type (e.g., quit; switch; combination) on messages on perceived message effectiveness, likeability, and reactance; controlling for pro- and anti-tobacco marketing exposure, baseline risk and efficacy perceptions and behavioral intentions. For models testing the effect of efficacy

messages, we will conduct overall F-tests to determine if there is an effect of efficacy message type in each model. If so, pairwise t-tests will be conducted, and Holm's procedure will be used to control Type I error rate.

Sample Size Justification**:** For Aim 1, Phase 1, Study 2--ONLINE RATING SURVEY: An analytic sample size of 200 participants per group will allow us to detect differences between two groups in terms of perceived message effectiveness. Assuming a pooled standard deviation of 1.0 units, the study would require a minimum sample size of n = 199 for each group to achieve power of 80% and two-sided significance level of p = .05 for detecting a 0.25 unit difference in perceived message effectiveness scores, which has been reported previously in the literature.[58] Under these same parameters, we will be able to detect a 0.25 unit difference in PME scores with 75% probability assuming a significance level of p = 0.1. As multi-group comparisons are exploratory, we believe this a prior sample size calculation is appropriate. As our desired analytic sample size is N = 500 participants (n = 250 participants per experimental group; AR vs RR messages); we have inflated our overall sample size is inflated by 10% to account for estimated inconsistencies between prescreening and survey responses, resulting in an overall sample size of N = 550.

C. Aim 1, Phase 1: Study 3—IN-DEPTH INTERVIEWS:

For in-depth interviews the goal will be to refine messages and determine which images should be matched to the AR and RR anti-tobacco messages. These images will then move on to Aim 1 Phase 2 of this study. We will qualitatively summarize the feedback in response to each focus group question using rigorous and accelerated data reduction (RADaR) analytic methods.[125] Used in applied research, RADaR organizes transcribed textual data from qualitative interviews into data tables; which are then organized and iteratively reduced, coded, and analyzed using team-based coding.

Sample size justification: For Aim 1, Phase 1: Study 3—IN-DEPTH INTERVIEWS our planned analytic sample size of N = 8 is designed to maximize the information power of qualitative research in which an initial sample of 6- 8 participants for is recommended for qualitative interviews. The aim of these interviews is to test existing messages to improve any communication issues. If we do not reach thematic saturation, we will enroll additional participants up to a maximum of N = 16. We have inflated the overall sample size to 20 participants to allow for ~20% dropout.

D. Aim 1, Phase 2: ONLINE FACTORIAL EXPERIMENT (NCT05393869) Data Analysis

We will fit linear regression models to evaluate the effect of condition on perceived effectiveness, risk perceptions, and behavioral intentions. Covariates will include exposure to pro- and anti-tobacco marketing, and baseline risk perception and behavioral intention items (per respective models). Baseline and post-viewing scores may be transformed if violations of assumptions are detected. We will conduct overall F-tests to determine if there is an effect of condition in each model. If so, pairwise t-tests will be conducted, and Holm's procedure will be used to control Type I error rate. Exploratory analyses will be conducted to determine if there is an interactive effect between Condition x Topic. *Responses will be examined by gender and sexual orientation to determine if there are systematic differences*.

Sample Size Justification**:** For the Aim 1, Phase 2: ONLINE FACTORIAL EXPERIMENT (NCT05393869) an analytic sample size of 400 participants per group will allow us to detect the best message in terms of risk perception score with 75% probability assuming the mean score in the best group is at least 0.1 standard deviations better than the mean score in the second best group.[126] As effect sizes of 2 or greater are reported in the literature for this outcome, we do not consider smaller differences to be of interest. As our analytic sample size is N = 2800 participants (n = 400 participants per experimental or control group); we have inflated our overall sample size is inflated by 5% to account for estimated inconsistencies between prescreening and survey responses, resulting in an overall sample size of N = 2940.

E. Aim 2 Focus groups Data Analysis

We will use directed content analysis[47] to summarize feedback on perceived polytobacco use risks and recommendations for refining CT messages.

Sample Size Justification: We will recruit up to 4 focus groups of size 6-8 LGBT polytobacco users (N = 24-32), a standard sample size[48,49] in formative qualitative research.

F. Aim 2 Eye-tracking (NCT0597294) Data Analysis

Hypothesis: Psychophysiological data will indicate that culturally targeted messages attract greater attention.

Anti-polytobacco messages will be divided into text and graphic AOIs. Dwell time on the textual message (in milliseconds) is the primary eye-tracking outcome. We will use linear regression models to compare message type (CT vs NT) and framing (RR vs AR) on average dwell time and proportion of time viewing AOIs.

Hypothesis: Exposure to targeted messages will result in greater perceived effectiveness of anti-polytobacco messages.

Generalized linear models (GLMs) will be fit to examine differences in perceived effectiveness by message type (CT vs NT). Covariates will include baseline measures in applicable models and prior exposure tobacco communications. We will also investigate gender differences. Exploratory analyses: We will conduct exploratory analyses on secondary outcomes of interest. Specifically, we will fit generalized linear models (GLMs) to examine differences in EPPM constructs, risk perceptions, behavioral intentions, and 1-week recall by message type (CT vs NT).

Sample size justification: Virtual lab study. Differences in dwell time from eye-tracking antitobacco communications studies (PI: Klein) provide the basis for estimates. Assuming a 1.1 second standard deviation, 108 participants (n = 54 per arm) will provide a 95% chance of detecting an 0.6 second mean difference in dwell time on AOIs, at 80% power. Data from our prior tobacco warning studies indicate up to a 0.8 second difference in dwell time between conditions (Klein, unpublished). A 0.6 second difference in dwell time is scientifically important as the brain can register stimuli within 0.03 seconds per fMRI. The enrollment number of n=300 will account for any duplicate responses, high abandonment rate forthe I-motions portion of the survey after consent has been completed, and any low-quality eye tracking data recorded due via remote I-motions software.

Research question: How does culturally targeting influence message recall?
For quantitative survey responses, generalized linear models (GLMs) will be fit to examine differences in message recall by message type (CT vs NT). Covariates will include baseline measures in applicable models and prior exposure tobacco communications. We will also investigate gender differences.
For qualitative survey responses, we will summarize the feedback in response to each focus group question using rigorous and accelerated data reduction (RADaR) analytic methods.[125] Used in applied research, RADaR organizes transcribed textual data from qualitative interviews into data tables; which are then organized and iteratively reduced, coded, and analyzed using team-based coding.

Sample size justification: All participants who complete the eye-tracking survey will be contacted to complete a one-week follow-up survey. Even with an estimated 30% attrition, the estimated analytic sample size (N=76) would be adequate for formative qualitative research.

VII. DATA SAFETY and MONITORING PLAN

The Ohio State University Comprehensive Cancer Center Data Safety Monitoring Committee (DSMC) will be the DSMC of record and, thus, will be responsible for reviewing the study. The PI will submit a summary report of the study's progress, including all subsite activities and data status to the DSMC on an annual basis. All adverse events related to the study will be recorded by the investigators. The study investigators will evaluate adverse events and study data during their weekly meetings and make a determination of whether any adverse events affect the risk/benefit ratio of the study and whether modifications to the protocol (e.g., Potential risks) or consent procedures are required.

Serious unanticipated events are not anticipated. In the unlikely case that such serious adverse events occur, they will be reviewed by the OSUCCC – James Data and Safety Monitoring Committee (DSMC). All reportable serious adverse events will be reported within 48 hours to the OSU IRB and any appropriate funding and regulatory agencies. The investigators will specify whether the serious unanticipated adverse event is related to the study. Adverse events will be reported to the NCI when frequency and magnitude clearly exceed expectations.

The OSU IRB provides annual review of all open protocols and hence this is one level of monitoring that will occur. In this annual report, the investigator is required to report the number of subjects enrolled and treated, any adverse events that have occurred, and a summary of the findings from either the study or the literature that would affect the safety of the participants or the ethics of the trial. The PI will provide a summary of the Data Safety and Monitoring Plan annually as part of the progress report to the National Cancer Institute (NCI).

All data and safety monitoring will adhere to the policies and procedures of the OSU Comprehensive Cancer Center's Data and Safety Monitoring Plan which has been approved by NCI.

VIII. Dissemination Plan

The study will be uploaded to clinicaltrials.gov and the results and accomplishments from this study will be made available to the public. We will disseminate the results and accomplishments from this trial to the research community and to the public at large through peer-reviewed scientific journal manuscripts and national conferences for the tobacco control, public health and medical communities. Additionally, the findings from this trial may be used to provide evidence informing the development of anti-tobacco messages for

national tobacco public education campaigns. Finally, members of our Community Advisory Board may receive study results and accomplishments.

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