Title: Development and Implementation of a Tobacco and ENDS Treatment Intervention for Adolescents and Young Adults in the Pediatric Hospital

Clinical Trial: NCT05936099

Date: August 30 2024

STATISTICAL DESIGN AND POWER

Aim 2: Evaluate preliminary efficacy and implementation outcomes of our tobacco and ENDS use intervention

Design: We will conduct a prospective, pilot trial with 3-month follow up to assess preliminary efficacy and implementation outcomes (Table 3). Hospitalized AYAs (n=144) with current (past 30-day) ENDS use (including those with co-use of cigarettes) will be randomized 2:1 to receive our novel intervention or control intervention that will consist of brief advice and printed quit line referral (see Figure 2). We will evaluate preliminary efficacy (i.e., 30-day self-reported abstinence with biochemical verification) as the primary outcome. We will also assess self-reported motivation and confidence to quit immediately post-intervention and at 3-month follow up and implementation outcomes (i.e. acceptability, feasibility, and fidelity).

Data Sources: AYAs: surveys, electronic health record; Parents/Guardians: surveys; Hospital Provider (i.e., Dr. Masonbrink: survey, audio-recording of sessions; Health educator: survey, field notes, audio-recording of sessions

Assessments:

AYA Participants: We will use confidential, web-based surveys administered via Research Electronic Data Capture (REDCap) to capture AYA data pre- and post-intervention, 3-month follow up (Research Strategy Table 3 and 4, Appendix). The health educator will recruit, screen, consent, and randomize eligible participants. AYAs who decline to participate will be asked to provide age, sex, race and ethnicity to facilitate identification of participation bias. Randomization of consented participants will be stratified on sex and age using a 2:1 ratio within strata via computer generated assignment sequence placed in sequentially numbered sealed envelopes. *Control participants* will receive brief advice from the health educator regarding tobacco and ENDS use cessation and printed referral to a quit line. *Intervention participants* will receive the intervention developed in Aim 1, administered by the same health educator and Dr. Masonbrink. All participants will complete a pre- and post-intervention survey and a 3-month survey sent via email, text message, and/or mailed paper survey so the research team is not directly involved in outcome data collection.

Parents/guardians of AYAs will be asked to complete a post-intervention survey. The health educator will complete brief survey items and field notes after each session. The AYA intervention and control sessions will be audio-recorded and reviewed by Drs. Masonbrink and Catley to assess fidelity and provide feedback. Dr. Catley will review audio-recordings of Dr. Masonbrink's sessions (e.g., Assist: NRT prescription) to assess fidelity and give feedback.

Participant demographics and clinical characteristics (e.g., age of initiation, nicotine dependence) will be assessed at baseline. The outcome measures, method of assessment, relevant stakeholders and detailed description are depicted in Table 3 and sample survey items in Table 4. *Preliminary efficacy* will be assessed via self-reported 30-day point prevalence tobacco/ENDS abstinence using the timeline follow-back method at 3-month follow-up.[73] To obtain a biochemically verified outcome and to encourage accurate self-reporting we will assess salivary cotinine via mailed samples from all participants (not currently on NRT) who report abstinence. Although accurate verification will not be possible with participants who are occasional users or using NRT, this will also allow us to evaluate the feasibility of collecting saliva by mail in this population which will be informative for future studies with daily ENDS users. Secondary efficacy outcomes will include self-reported motivation and confidence to quit immediately post-intervention and at 3-month follow up.[65, 74,75] We will assess *acceptability* with the overall intervention and intervention components via survey immediately post intervention (AYAs and parents) and at 3 month follow-up (AYAs). Acceptability will also be evaluated via participant enrollment and session completion rates. *Feasibility* will be assessed via intervention duration in minutes from audio recordings and Dr. Masonbrink and the health educator will complete a brief survey and record field notes to assess feasibility (e.g., impact on workflow, disruption, suitability). To assess *fidelity* we will review audio recordings and rate health educator intervention and control sessions based on a previously developed fidelity rating scales.

AYA participants: We will use confidential, web-based surveys administered via Research Electronic Data Capture (REDCap) to assess post-intervention outcome measures including preliminary efficacy using previously validated survey questions to assess self reported 30-day abstinence and acceptability using 5-point

Parents/Guardians: We will use confidential, web-based surveys administered via Research Electronic Data Capture (REDCap) to assess post-intervention 5-point Likert scale implementation items among parents/guardians of AYA participants (Research Strategy Tables 3 and 4, Appendix).
Hospital Provider (Dr. Masonbrink: We will use confidential, web-based surveys administered via REDCap to assess post-intervention 5-point Likert scale items and audio-recording of sessions to examine feasibility and fidelity (Research Strategy Table 3 and 4, Appendix).
Health Educator: We will use confidential, web-based surveys administered via REDCap to assess post-intervention 5-point Likert scale implementation items and will take field notes (Table 3 Research Strategy, Appendix). We will use field notes, audio-recording of sessions and survey items by the health educator to examine feasibility and fidelity.

Analysis:
We will use level of significance α=0.05 and all analyses will be conducted using SAS v 9.4 (SAS Institute, Cary, NC, USA).
Measures and Statistical Analysis:
Participant demographics and clinical characteristics (e.g., age of initiation, nicotine dependence) will be assessed at baseline. The outcome measures, method of assessment, relevant stakeholders and associated outcome measures are depicted in Table 3 and sample survey items in Table 4.
To assess *preliminary efficacy*, differences in self-reported and biochemically verified 30-day tobacco/ENDS use abstinence at 3-month follow up (primary outcome) will be analyzed using a generalized linear model assuming an underlying binomial distribution and logit link function to compare between study arms. Motivation and Confidence to quit will be analyzed using a repeated measures analysis of variance. Potential differential outcomes based on sex and demographic factors will be explored. Chi-square (categorical variables) and Wilcoxon Rank Sum (continuous variables) tests will be used to assess participation bias. For *acceptability*, we will calculate the proportion of AYA participants and parents/guardians in the intervention arm with mean ratings of satisfaction and acceptability of ≥ 4 on the 5-point Likert scale. In addition, frequencies and percentages will be used to describe the enrollment and session completion rate. For *feasibility* we will conduct thematic analysis of field notes and conduct simple descriptive analyses (means, frequencies, percentages) of the brief survey items completed by Dr. Masonbrink and the health educator and session length data. *Fidelity* will be summarized utilizing similar descriptive analyses of the fidelity ratings (e.g., percentage of intervention steps completed; mean rating of key MI skill adherence). Potential differential outcomes based on sex and demographic factors will be explored. Chi-square (categorical variables) and Wilcoxon Rank Sum (continuous variables) tests will be used to assess participation bias.

Sample Size Our proposed *sample size* [n=144 (96 treatment, 48 control)] is well within the recommendations for behavioral intervention development pilot trials based on what is feasible to recruit in our hospital and judged to be sufficient to evaluate efficacy (i.e., self-reported/biochemically verified abstinence) in a preliminary behavioral design trial.[63,64] With respect to percentage reporting self-reported and/or biochemically confirmed abstinence at 3-mo follow up the margin of error (ME) around our observed outcomes depends on the observed proportion with the largest ME occurring when the proportion is 50%. Our sample size is sufficient to provide a ME of 10% (if the proportion is 50%) or less. A study fully powered to determine efficacy will be the focus of an R01 hybrid implementation trial informed by this study.