Study Title: Alcohol Cessation Among Head and Neck Cancer Survivors: A Pilot RCT of a Tailored Text Message-Based Intervention

Funded by United States Department of Defense: W81XWH-22-1-0186

PI: Michael Diefenbach, PhD

Study Protocol and Statistical Analysis Plan

Version Date: 9/9/2025

Northwell Health

RESEARCH PROTOCOL

Protocol Title:	Alcohol Cessation among Head and Neck Cancer Survivors: A Pilot RCT of a tailored text message based intervention
Principal Investigator:	Michael Diefenbach, PhD
Primary Contact Name:	Sherene Lambert
Primary Contact Phone:	516-253-7870
Primary Contact E-mail:	Slambert7@northwell.edu
Date Revised:	September 9, 2025
IRB Number:	22-0362

Guidelines for Preparing a Research Protocol

Instructions:

- You do not need to complete this document if you are submitting an *Application for Exemption* or *Application for a Chart Review*.
- Do not use this template if:
  - Your study involves an FDA regulated product. In this case, use the *Clinical Trial Protocol Template.*
  - Your study has a protocol from a sponsor or cooperative group. In this case, use the *Protocol Plus*.
  - Your study is a registry or repository for data and/or samples, In this case, use *Protocol Template – Registry Studies.* .
- If a section of this protocol is not applicable, please indicate such.
- Do not delete any of the text contained within this document.
- Please make sure to keep an electronic copy of this document. You will need to use it, if you make modifications in the future.
- Start by entering study information into the table above, according to these rules:
  - Protocol Title: Include the full protocol title as listed on the application.
  - Investigator: include the principal investigator's name as listed on the application form
  - Date Revised: Indicate the date at which the protocol was last revised
  - IRB Number: Indicate the assigned IRB number, when known. At initial submission, this row will be left blank.
- Once the table information in entered, proceed to page 2 and complete the rest of the form.

↓ Continue to next page to begin entering information about this study ↓

1. PREVIOUS STUDY HISTORY

Has this study ever been reviewed and rejected/disapproved by another IRB prior to submission to this IRB?

☒ No ☐ Yes – if yes, please explain:

2. BRIEF SUMMARY OF RESEARCH

- *The summary should be written in **language intelligible to a moderately educated, non-scientific layperson**.*
- *It should contain a clear statement of the rationale and hypothesis of your study, a concise description of the methodology, with an emphasis on what will happen to the subjects, and a discussion of the results.*
- *This section should be ½ page*

Head-and-neck cancers (HNC) account for 4 percent of cancer diagnoses in the United States and for more than 66,000 annual cancer diagnoses. **The prevalence rate of HNC among Veterans is 150% higher than the rate in the general population.** Together with smoking, alcohol drinking is a major risk factor for HNC, responsible for approximately one-third of the cases worldwide. Overwhelming evidence from population-based studies show that alcohol drinking significantly increases the risk of recurrence of the primary HNC and of second primary malignancies, as well as negatively impacts HNC survivors' psychosocial health. Hence, several organizations (i.e., American Cancer Society, American Society of Clinical Oncology, and the World Cancer Research Fund) have issued guidelines recommending that individuals with HNC reduce or avoid alcohol altogether. Despite these recommendations, a substantial proportion of HNC survivors continue to use alcohol.

Objective. The overall goal of the proposed research is to: 1) adapt an existing evidence-based text message alcohol cessation intervention for HNC survivors in both civilian and VA settings (i.e., at two sites, Northwell Health and the Brooklyn VA Medical Center); and 2) preliminarily evaluate, in a two-arm pilot RCT, the acceptability and preliminary efficacy of the intervention, as well as feasibility of conduct a future RCT.

Hypotheses. We hypothesize that:
H1: The tailored text-message intervention will be 1) feasible to evaluate in a large-scale RCT, defined as achieving an enrollment rate of ≥70% in this pilot; and 2) acceptable to participants, defined as a score ≥4 on a 5-point Likert scale ranging from "not at all" to "extremely" acceptable.
H2: Compared to our control condition of alcohol assessment and feedback (AF), the tailored text messages will result in a 30% increase in cessation among survivors (assuming also a 20% increase in cessation in the AF arm).

3. INTRODUCTION/BACKGROUND MATERIAL/PRELIMINARY STUDIES AND SIGNIFICANCE

- *Describe and provide the results of previous work by yourself or others, including animal studies, laboratory studies, pilot studies, pre-clinical and/or clinical studies involving the compound or device to be studied.*
- *Include information as to why you are conducting the study and how the study differs from what has been previously researched, including what the knowledge gaps are.*
- *Describe the importance of the knowledge expected to result*

Head and Neck Cancer (HNC) is cancer of the oral cavity, pharynx, and larynx. HNC accounts for 4 percent of cancer diagnoses in the United States. HNC is particularly elevated in service members and veterans. A recent report by Zevallos and colleagues on national trends in HNC in the VA system demonstrated that the **prevalence of HNC among Veterans is at 6% and thus 150% higher than the rate of the general population at 4%.** Between 2006 and 2012 (the latest reported timepoint) there were significant increases in incidence of HNC among Veterans of White and African American descent and across all age cohorts. In addition, the rate of patients who never smoked and were diagnosed with HNC increased from 8% to 15.7% in 2012. Although not as prevalent as lung or prostate cancer, the rise in incidence among HNC is concerning and there is an urgent need to halt the rising incidence of HNC through interventions targeting behaviorally-based modifiable factors.

Survivors of HNC often cope with severe long-term changes in their function and quality of life (QOL) as a result of treatment. They may require lifelong rehabilitation and behavioral modification to adjust to the changes in oral, salivary, and swallowing function, in addition to pain and restricted neck and arm mobility. These functional challenges have a profound impact on a patient's social life and QOL, which has been shown to correlate with overall survival in this population.

The International Agency for Research on Cancer (IARC) has indicated that a causal relationship exists between alcohol use and the development of HNC and upper aerodigestive tract cancers, including oral cavity, oropharyngeal, hypopharyngeal, esophageal, and laryngeal cancers. Evidence suggests that alcohol is responsible for 26.4% of all lip and oral cavity cancers, 30.5% of pharyngeal cancers, 21.6% of all laryngeal cancers, and 16.9% of all esophageal cancers. Combined with tobacco use, alcohol accounts for approximately 75% of oral cancers. The pathway from alcohol consumption to the development of cancers is not entirely understood; however, research has demonstrated that alcohol permanently damages the DNA strands in the cell through acetaldehyde, a product of metabolizing alcohol. Other possible mechanisms through which alcohol leads to cancer are through nutritional deficiencies, genetic variations, and, for females, changes in estrogen pathways. In one study, compared to abstainers or light drinkers, those consuming 3-4, 5-7, 8-11, or greater than 12 drinks per day had odds ratios of developing HNC of 2.1, 5.0, 12.2, and 21.1, respectively. The pooled relative risk of developing HNC was 1.21 for those consuming less than 1 drink per day; which is in stark contrast to a relative risk of developing HNC of 5.24 for those consuming greater than 4 drinks per day. A meta-analysis of the association between the amount of alcohol drinking and risk of HNC showed that light drinkers had a relative risk of 1.13 for developing oral cavity and pharynx cancers, compared to 1.83 for moderate drinkers, and 5.13 for heavy drinkers. In addition, the relative risk for developing larynx cancers is 0.87 for light drinkers, 1.44 for moderate drinkers, and 2.65 for heavy drinkers. Estimates attribute 3.5%

of cancer deaths in the United States and 4.2% of cancer deaths globally directly to alcohol intake.

Recent data published by the Rand organization provides evidence of a pattern of binge and heavy drinking across all service branches of the US military Binge drinking over the past 30 days ranges from 24.1% to 44.9% with an average across all branches of 34.0%. Heavy drinking ranges from 5.0% to 15.3% with an average across all branches of 9.8%. Combining the 30-day average of binge and heavy drinking, shows that almost 44% of military personnel engage in this unhealthy behavior.

Available data show that those who continue to consume alcohol following a primary HNC are at increased risk of developing second primary malignancies. In one multicenter study of 13 population-based cancer registries, comprising nearly 100,000 individuals with a primary HNC, 13% of second primary tumors were alcohol-related cancers. A multicenter study from the International Head and Neck Cancer Epidemiology Consortium, consisting of over 4,000 individuals with HNC, showed that consumption of greater than 1 alcoholic drink per day increased the risk of second primary cancers, among those with laryngeal cancer (hazard ratio: 2.11, 95% CI: 1.13-3.94). This relationship was confirmed in a second study of cancers of the upper aerodigestive tract; individuals continuing to consume alcohol post-diagnosis had a 1.3 times greater risk of developing a second primary tumor, compared to those who did not use alcohol following initial diagnosis. Furthermore, consumption of more than 14 drinks per week was associated with a 50% increase in risk of developing a second primary tumor and premature death.

Studies also strongly suggest that individuals with HNC, who continue to drink, are not only at risk of developing a second primary tumor but are also at greater risk of cancer recurrence. In a retrospective review study of 482 individuals treated for a primary HNC diagnosis, risk of recurrence was associated with consuming 8-14 alcoholic beverages per week. Further research is needed to elucidate the relationship between the quantity of alcohol consumed and recurrence risks in survivors of HNC. Negative effects of continued alcohol consumption go beyond the development of second primary cancers and recurrences, however. Evidence suggests that HNC survivors, who continue to use alcohol, are at an increased risk of needing a gastrostomy tube feeding in the future and developing osteoradionecrosis of the jaw; they also have a poorer disease prognosis and are more likely to suffer from social effects, such as unemployment and work disability. Conversely, the absence of alcohol use by HNC survivors was significantly associated with better QOL. A history of heavy alcohol consumption over the years, has been linked to future physical and mental health problems. Habitual alcohol use, even at moderate levels is detrimental to cancer patients and survivors and cessation efforts without assistance and support are difficult for most survivors.

Several organizations have issued guidelines recommending that HNC survivors reduce or avoid alcohol altogether. In 2016, the American Cancer Society published guidelines for HNC survivorship, recommending that "primary care physicians counsel HNC survivors to achieve a dietary pattern that is high in fruits, vegetables, and whole grains, and low in saturated fats, sufficient in dietary fiber, and avoids alcohol consumption. In addition, the World Cancer Research Fund recommends limiting alcohol consumption generally, and for cancer prevention, not to drink alcohol at all. Lastly, the American Society of Clinical Oncology recommends reduced alcohol consumption to prevent cancer. Despite these strong recommendations, evidence suggests that HNC survivors continue to use alcohol throughout all stages of the cancer trajectory, including after initial cancer diagnosis,

during treatment, into early survivorship, and through long-term survivorship. A literature review on the prevalence and effects of alcohol consumption after oral cancer diagnosis indicates that between 34% and 57% of survivors of cancer of the upper aerodigestive tract (HNC and esophageal cancers) continue to drink after diagnosis. In a study retrospectively assessing alcohol use *before* HNC diagnosis, compared to immediately following diagnosis, the prevalence of alcohol use decreased by 16.7%, and the proportion of problem drinkers decreased from 46.6% to 24.5%. Although this is a considerable decrease, a quarter of the sample with newly diagnosed HNC continues to abuse alcohol. Other longitudinal research suggests that 44.5% of individuals with HNC were still drinking 12 months after diagnosis, with 21.4% of these individuals categorized as problem drinkers (defined as those who scored 3 or more on the Michigan Alcoholism Screening Test). During early and long-term survivorship, a substantial proportion of HNC survivors continue to consume alcohol. In a population-based study of HNC survivors longer than 6 months post-treatment, there was a mere 13% drinking cessation rate; 62% of the sample considered themselves current drinkers. Of those current drinkers, about a quarter of the sample (i.e., 26%) reported that they consume alcohol at least 4 times per week. A study of HNC survivors 5 years post-treatment reported that 38.9% continued to use alcohol. Studies suggest that HNC survivors are often unaware of the relationship between alcohol and HNC, and do not receive adequate information from their providers about the impact of alcohol on their disease course. In one study, between 15-50% of those surveyed did not recall having received any recommendation regarding alcohol consumption. Thus, education about, and raising awareness of, the risks of alcohol consumption among HNC survivors is a necessary first step to achieve alcohol reduction and cessation. **Therefore, there is an urgent need for alcohol cessation interventions for this growing group of HNC survivors, to prevent second malignancies and cancer recurrences, as well as to improve their psychosocial functioning. This need is escalated for military and veteran populations, who are prone to risky drinking behavior and for whom mission readiness depends upon their physical and mental health. Our proposal seeks to adapt and preliminarily evaluate an existing evidence-based alcohol cessation intervention, delivered via an existing text-message based platform called Bottle Cap, for HNC survivors in both civilian and VA settings.**

One study, using an educational pamphlet, showed that knowledge of alcohol abuse as a risk factor for cancer increased from 15% to 27% from pre- to post-reading.35 Yet, few studies have aimed to reduce alcohol use specifically in the HNC population. In another study, researchers developed and tested a tailored smoking, alcohol, and depression nurse-administered intervention, consisting of cognitive behavioral therapy and medications, compared to usual care, for individuals with HNC. Rates of alcohol consumption declined in both groups, but there was no difference in the number of problem drinkers at the 6-month assessment point. In a randomized controlled trial (RCT) of 105 individuals with HNC, focused on tobacco cessation, researchers compared a provider-delivered smoking cessation intervention with a usual-care-advice control condition; results showed that participants experienced reduced smoking, but an *increase* in alcohol use 12 months post-intervention. Survivors may have substituted alcohol for tobacco. We found only three relevant studies (described above) targeting patients with HNC, none of them recent. These studies focus mainly on smoking cessation and mental health outcomes, with alcohol cessation a secondary intervention target. One study was designed to improve knowledge of alcohol as a risk factor for cancer recurrence among patients with HNC and achieved a 12% increase in knowledge. Another study consisted of a nurse-administered cognitive behavioral therapy and medication intervention, implemented during the beginning of treatment, targeting smoking, alcohol abuse, and depression. At six months post diagnosis,

although alcohol, smoking and depression decreased, the number of problem drinkers did not differ between the intervention and control conditions. In contrast and according to our own data, 40% of patients drink shortly after treatment completion, and another 14% resume alcohol consumption over the next 21 months. Thus, we observed a rising proportion of patients consuming alcohol, that after 2 years post diagnosis, exceeded the proportion of drinkers post baseline. The main conclusion of our study is that intervention implementation at the beginning of treatment is likely ineffectual, as patients often refrain from drinking during treatment, and intervention messages are less effective several months after delivery. Therefore, we are implementing our intervention and baseline assessment at the 3-month follow-up visit after treatment completion and from that point follow-up for 6-months to measure the success of our intervention. Finally, the last and third study in the literature focused on smoking cessation among patients with HNC. Although smoking decreased, drinking increased within 12 months by 17%. This suggests that alcohol might serve as a substitute for tobacco use, and that specific alcohol cessation messages are crucial for cessation. The proposed intervention incorporates the following four lessons learned from these prior studies: 1) Optimal intervention implementation is at Month 3 after treatment completion, when, according to our data, patients are most likely to resume alcohol consumption; 2) there is a need for alcohol cessation specific messages; 3) there is a need for sustained intervention content delivery, as can be achieved through phone texts; and 4) a 9 months follow-up assessment from end of treatment is ideal. Advances in technology have made electronically administered interventions attractive as an alternative to interventions administered in a more traditional manner. Although not yet evaluated in HNC samples, the extant literature on electronically administered interventions indicates their utility and efficacy. A review of the current literature shows that individuals who drink are interested in using text-message-based interventions and smartphone-based applications to reduce alcohol use. More specifically, use of an Addiction Comprehensive Health Enhancement Support System, a smartphone app, by those with alcohol dependence was high and sustained over time (94% used it in Week 1; 80% continued into Week 16). A meta-analytic review of 28 electronic intervention trials for alcohol misuse and alcohol use disorders showed a small reduction in consumption (approximately 1 drink per week) in adults and college students at 6 months. More recently, a two-arm RCT, comparing an intervention group receiving a 6-week text message intervention, and a control group that was referred to treatment as usual at the local student health care center, showed that, at 3-month follow-up, total weekly alcohol consumption decreased in both groups, but no significant between-group difference was seen, potentially due to lack of power and the need to refine the intervention. Yet, Muench et al. found that daily automated texts can help problem drinkers reduce drinking frequency and quantity significantly more than weekly self-tracking messages. **Therefore, we will deliver our alcohol cessation intervention content through text-messages.**

The investigative team has successfully recruited HNC patients and survivors into research studies. Members of the research team (Diefenbach & Teckie) have a history of collaboration working with HNC patients and survivors. They developed and evaluated the LogPal IOS application to record disease and treatment related side effects among patients diagnosed with HNC, which demonstrates that patients diagnosed with HNC are willing to participate in research using smartphone-based interventions and are adherent to research protocols. LogPal uses the ecological momentary assessment technique to record patients' symptom reports. LogPal prompts patients twice a week, at a time of their choosing, to complete a 25-item list of validated symptoms. The application was pilot tested among 36 survivors of HNC who just completed treatment. Eighty percent of the patients who were approached accepted. Patients were asked to complete the assessments for 2 months.

Adherence to the app was very high; 90% of enrolled patients completed all assessments. Patients reported that the app was easy to use, the questions were relevant to their recovery, and did not take much time to answer. Members of our research team, under the leadership of Co-I Jonathan Morgenstern, Ph.D., have decades-long experience in the development and implementation of alcohol cessation interventions. They have demonstrated their effectiveness (NIAAA R34AA021502), and developed the Bottle Cap platform for text message intervention delivery. *Findings support the use of text messaging interventions in reducing alcohol use among a population of drinkers and demonstrate high retention rates among users.*

In sum, the present application builds on wide-ranging pilot data with large sample sizes, is based upon extensive experience in alcohol cessation research conducted by the investigative team, can draw on the evidence-based resources the team has developed and evaluated, and answers an urgent need for alcohol cessation interventions for HNC survivors. This project is of high significance for military and veteran populations, for whom both alcohol drinking and HNC is elevated, as HNC survivors who continue to drink alcohol are at risk for poor physical and mental health outcomes, which impedes mission readiness for them and their family members.

4. OBJECTIVE(S)/SPECIFIC AIMS AND HYPOTHESES

- *A concise statement of the goal(s) of the current study.*
- *The rationale for and specific objectives of the study.*
- *The goals and the hypothesis to be tested should be stated*.

The primary goal of the proposed work is to assess the acceptability of the proposed intervention, to estimate effect sizes for the two arms, as well as to determine feasibility of a future RCT.

We have structured the proposed research into two phases: An **Adaptation Phase** and a **Preliminary Evaluation Pilot Phase**. The below discusses the overall goals across both sites; note that the VA IRB will review the conduct of research at that site and the Northwell Health IRB will review the conduct of research at our site.

During the Adaptation Phase (Aim 1), we will adapt the intervention; specifically, we will adapt alcohol cessation text messages by tailoring them to HNC survivors in both civilian and VA settings. This will be completed through rapid development and evaluation cycles, as guided by the ORBIT model, and with the help of our Patient Advisory Board (PAB) in both civilian (n=15) and veteran (n=15) patients, as well as HNC health care providers (n=5).

During the evaluation phase (Aim 2), we will assess acceptability and preliminary efficacy of the intervention in a 2-arm pilot 6-month longitudinal RCT. HNC survivors (baseline N=138) will be enrolled from Northwell Health and the Brooklyn VA Medical Center, at the 3-month post treatment completion follow-up visit, when alcohol resumption is most likely to occur according to our pilot data. We will randomize survivors to either the control condition (AF; n=69) or the text message intervention arm, consisting of: AF plus HNC tailored texts for civilians (n=34) and AF plus HNC tailored texts for Veterans (n=35), for a total of n=69. We expect 15% attrition over 6 months for a final sample size of N=120. Our primary outcome is alcohol cessation at 6 months post-baseline.

Hypothesis. During our preliminary evaluation phase (Aim 2 pilot RCT), we will compare our alcohol cessation text-message intervention to a control condition (assessment and feedback, AF).
H1: The tailored text-message intervention will be: 1) feasible to evaluate in a future large-scale efficacy RCT, defined as achieving a consent rate of 70% during this pilot; and 2) acceptable to participants, defined as a score ≥4 on a 5-point Likert scale ranging from "not at all" to "extremely" acceptable.
H2: Compared to the control condition (AF), the tailored text messages will result in a 30% difference in alcohol cessation rate among HNC survivors in both civilian and VA settings, (assuming also a 20% increase in alcohol cessation in the AF condition).

5. RESOURCES AVAILABLE TO CONDUCT THE HUMAN RESEARCH

- *Explain the feasibility of meeting recruitment goals of this project and demonstrate a potential for recruiting the required number of suitable subjects within the agreed recruitment period*
    - *How many potential subjects do you have access to?*
- *Describe your process to ensure that all persons assisting with the trial are adequately informed about the protocol and their trial related duties and functions*

The multidisciplinary research team is led by Dr. Michael A. Diefenbach, PhD, (PI) a health/social psychologist and behavioral scientist with expertise in behavioral theory, intervention development, qualitative and quantitative research methods, and software design. Dr. Maged Ghaly, MD, (Co-I) a radiation oncologist at the Center for Advanced Medicine/Monter Cancer Center, will support the proposed research during all phases with her expertise in HNC. Together, they collected the alcohol prevalence data among survivors of HNC and developed the LogPal phone application to record treatment-related symptoms and recovery progress among HNC survivors. Dr. Allison Marziliano, Ph.D., (Co-I) brings complimentary expertise in the assessment of psychosocial response to illness and particularly how physical illness impacts individuals' social isolation, loneliness and relationships with others, which are the primary focus of our secondary outcomes. Drs. Diefenbach, Ghaly and Marziliano also completed a recent review article on alcohol use among HNC survivors. In addition, Dr. Jonathan Morgenstern, PhD, (Co-I) originator of the Bottle Cap platform and an expert in designing alcohol cessation interventions, and Dr. Svetlana Levak, Ph.D, (Co-I) an expert in designing text messages, will contribute to the research by providing expertise on the existing evidence-based alcohol intervention. Stephanie Izard, MS, a biostatistician, rounds out the Northwell team.

This protocol will discuss/describe research procedures associated with Northwell Health patients. We have requested an exemption from the requirement to rely on a single IRB (sIRB) for cooperative research according to 45 CFR 46.114. As such, the VA IRB will cover the conduct of research for our collaborating researchers.

The team at the VA is comprised of Drs. David Schwartz (Co-I) and Jonathan Wallach (Co-I), Chief of Radiation Oncology and Assistant Professor in Radiation Oncology, respectively, at the Veterans Hospital, Brooklyn, who will provide the military and veteran-related expertise and assist with recruitment of Veterans into the study.

The team will have weekly research meetings to ensure timely achievement of milestones and completion of the proposed study and all research members are adequately informed about trial-related duties.

Northwell Health (NWH) is the largest health system in New York State, encompassing 24 hospitals and 500 ambulatory sites in Long Island, the 5 boroughs of New York City, and Westchester County. HNC is mainly treated at: NWH's Monter Cancer Center on Long Island. While we will be mainly recruiting from Monter Cancer Center, we will not exclude NWH patients based off of their treatment location and we will open recruitment to HNC patients at all NWH facilities.

Based on the medical records, the NWH system treats 41 patients/month for HNC, yielding a patient pool of 1230 patients over the 30 months recruitment period. Based on the 40% drinking rate and a high consent rate based on prior recruitment experience this gives us a sufficient pool of patients to recruit N=138 HNC survivors, n=69 survivors per arm across the NWH and the VA sites. In the event that the VA site is unable to meet their enrollment goal, Northwell will continue enrolling additional patients to ensure that the overall target accrual of N=138 patients is met

6. RECRUITMENT METHODS

- *Describe the source of potential subjects*
- *Describe the methods that will be used to identify potential subjects*
- *Describe any materials that will be used to recruit subjects. A copy of any advertisements (flyers, radio scripts, etc.) should be submitted along with the protocol.*
- *If monetary compensation is to be offered, this should be indicated in the protocol*

Aim 1: Adaption Phase
The study team has access to an existing HNC Patient Advisory Board (PAB), which was originally established to aid in the development of the LogPal software program. This group of male and female survivors will be the primary pool of potential participants to achieve Aim 1. If needed, the study team plans to further recruit civilian HNC survivors from Northwell Health as needed to reach complete data goals for Aim 1 (n=15Northwell patients), via phone calls and mailed (email and/or physical) outreach recruitment methods, after first scanning the EMR to identify eligible participants. Additionally, 3 treating HNC providers who treat potential participants that we may approach for participation in this research will be identified to also participate in Aim #1.

Aim 2: Preliminary Evaluation Phase
Research coordinators (RC) at NWH will scan the EMR records facilitated by patient lists generated by our data analyst to identify eligible survivors due for their first standard of care clinical visit after treatment. To supplement these efforts, the study team will use the Oncora and ARIA databases which are used by Northwell's radiation oncology department to create patient cohorts for research purposes. We will use the filtering capabilities within these databases to create lists of eligible HNC survivors within the Northwell system.

Eligibility and permission to approach will be confirmed by the collaborating providers; if the provider does not respond to the request within one week, they will be assented by default. Study staff will contact survivors by phone and via myNorthwell to assess interest in the study. Once eligibility has been established, interested patients will be asked to meet study RCs after the regularly scheduled appointment, and to expect that the visit will be extended by 45-60 minutes. At the end of the clinic visit, the HNC survivor will meet with the RC to give informed consent, record baseline data, and assess drinking patterns with the AUDIT questionnaire and the Time-Line Follow Back (TLFB) alcohol use assessment procedure. Patients will also have the option to elect to consent and complete questionnaires virtually. Randomization will occur after the patient is consented. The RC will access the randomization website and provide alcohol use feedback, plus, if randomized to the intervention arm, register the HNC survivor with the Bottle Cap platform.

Survivors who have consented to participate will be block randomized to either AF or the intervention text messaging arm. This procedure will ensure that even numbers per condition across sites are maintained overall.

7. ELIGIBILITY CRITERIA

- *Describe the characteristics of the subject population, including their anticipated number, age, ranges, sex, ethnic background, and health status. Identify the criteria for inclusion or exclusion of any subpopulation.*
- *Explain the rationale for the involvement of special classes of subjects, such as fetuses, pregnant women, children, prisoners or other institutionalized individuals, or others who are likely to be vulnerable. You cannot include these populations in your research, unless you indicate such in the protocol*
- *Similarly, detail exclusionary criteria: age limits, special populations (minors, pregnant women, decisionally impaired), use of concomitant medications, subjects with other diseases, severity of illness, etc.*

Healthcare Workers (Aim 1)
Inclusion Criteria:

1) Employed as a physician or nurse
2) Currently treating head and neck cancer patients (surgically or with radiation)

Exclusion Criteria:
N/A

Patient Advisory Board (Aim 1) and Participants (Aim 2)
Inclusion Criteria:

1) Adult male or female patients 18 years or older
2) Diagnosed with primary cancer of: pharynx (nasopharynx, oropharynx, hypopharynx), larynx (all subsites), oral cavity (all subsites)
3) Having completed surgical, radiation, and/or chemotherapy treatment;
4) Post-treatment completion status of at least 3 months;
5) Able to communicate and read in English;
6) Possess a telephone with text messaging capability; and
7) Confirmation of alcohol consumption.

Exclusion Criteria:

1) Non-English speaker
2) Non-drinker
3) Previously enrolled in Aim 1 **(for Aim 2 only)**]
4) Clinically significant depression, as indicated by an assessment of ≥ 16 on the CES-D 11-item Iowa short form scale **(Aim 2 only)**

8. NUMBER OF SUBJECTS

- *Indicate the total number of subjects to be accrued locally. If applicable, distinguish between the number of subjects who are expected to be pre-screened, enrolled (consent obtained), randomized and complete the research procedures.*
- *If your study includes different cohorts, include the total number of subjects in each cohort.*
- *If this is multisite study, include total number of subjects across all sites.*

Aim 1
For this phase of the research, we will enroll until 15 PAB members and up to 5 healthcare workers complete Aim #1 research procedures at Northwell.

Aim 2
For this phase of the research, we will enroll until 69 HNC survivors to each of the study arms at Northwell Health (34 in the control arm and 35 in the intervention arm) complete Aim #2 research procedures, in order to contribute to the overall target accrual of 138 patients for the study (69 from Northwell, 69 from the VA). In the event that the VA is unable to enroll 69 HNC survivors to each of the study arms at their site, Northwell will enroll additional patients to ensure that we meet the overall target accrual for the study.

9. STUDY TIMELINES

- *Describe the duration of an individuals participation in the study*
- *Describe the duration anticipated to enroll all study subjects*
- *The estimated date of study completion*

Aim 1
Aim 1 participants may be asked to attend 3-5 virtual or in-person interviews that may last up to 1 hours each. We anticipate we will conduct Aim 1 study activities for up to 6 months. The estimated date of completion of this aim is September 1, 2023.

Aim 2
For Aim 2, total study duration will be 6 months for all participants. All participants will be required to complete enrollment and baseline questionnaires and follow-up assessments at 3-months and 6-months post-enrollment, which will take 1 hour to complete. Participants randomized to receive tailored text messages will receive up to 3 messages, up to 3 times a week for the first 3 months of their participation in Aim 2. For all participants, study participation will be complete after the 6-month follow-up assessment. We estimate the date of completion of Aim 2 to be March 31, 2026.

10. ENDPOINTS

- *Describe the primary and secondary study endpoints*
- *Describe any primary or secondary safety endpoints*

For Aim 1: Our main endpoint is a new library of text messages on Bottle Cap tailored to head and neck cancer survivors, both Civilian and Veterans.

For Aim 2: Our primary endpoint is alcohol cessation, a binary variable (drinking is occurring or drinking is not occurring) created based on data collected as part of the Time-Line Follow Back (TLFB) procedure and the alcohol use disorders identification test (AUDIT). While both TLFB and AUDIT will be used to collect data for this outcome, TLFB will be supersede the AUDIT as the primary outcome measure if conflicting responses are provided. Feasibility of conducting a future large-scale efficacy RCT, defined as a recruitment rate of 70% (number of survivors recruited over approached) in the pilot RCT, will also be assessed as a primary endpoint. Our secondary endpoint is alcohol reduction which will be assessed as a percent change using the same methods described above for the primary endpoint (i.e., TLFB and AUDIT).

Our secondary outcomes are quality of life (measured with the Head and Neck Quality of Life instrument, a widely used 20-item Likert scale measure that evaluates quality of life related to eating, communication, pain, and emotion in the last 4 weeks), overall health (measured with the SF-12 Questionnaire), depression (measured with the Patient Health Questionnaire (PHQ-2)) with additional resources and linkage to care provided, social isolation (measured with the Lubben Social Network Scale) and loneliness (measured with the De Jong Gierveld Loneliness Scale). Additionally, during our Aim 2 pilot RCT, we will evaluate acceptability of the intervention, defined as a positive evaluation of the intervention as indicated by a mean value of 4 on a 5-point scale, with higher values = higher acceptability.

11. RESEARCH PROCEDURES

- *Include a detailed description of all procedures to be performed on the research subject and the schedule for each procedure.*
- *Include any screening procedures for eligibility and/or baseline diagnostic tests*
- *Include procedures being performed to monitor subjects for safety or minimize risks*
- *Include information about drug washout periods*
- *If drugs or biologics are being administered provide information on dosing and route of administration*
- *Clearly indicate which procedures are only being conducted for research purposes.*
- *If any specimens will be used for this research, explain whether they are being collected specifically for research purposes.*
- *Describe any source records that will be used to collect data about subjects*
- *Indicate the data to be collected, including long term follow-up*

Aim 1

The study team will work closely with the HNC patient advisory board (PAB) to participate in multiple interviews aimed to adapt an existing alcohol cessation messaging program (Bottle Cap) for HNC survivors based on the ORBIT model. If needed, the study team will screen the EMR for potential eligibility ((type of HNC, date(s) of treatment, age, sex, race, and education, etc.) to meet enrollment objectives. After consent is obtained, the study team will collect basic demographic information and may ask participants to participate in 3-5 interviews either in person or via tele or video conference. During these interviews, participants may be asked to give quantitative and qualitative feedback on a set of text messages (see attached document) that aim to help people to stop drinking alcohol based on their opinions regarding their efficacy. Interviews may be audio/visual recorded to ensure accuracy. Participant are informed of this in the consent document for Aim #1. Based on interview feedback, we will select the text messages that will be used in the Aim #2 intervention.

Participants will also be asked about their personal experiences in order to create new messages. Overall, we plan to adapt 50 messages in 3-5 rounds of adaptation sprints. All newly adapted messages will be incorporated into Bottle Cap's message library. We will submit a modification if the text messages differ significantly in content than those already created and submitted for review, or if the nature of the questions could change the risk/benefit ratio initially documented by the IRB.

Participants will be compensated up to $125 for their participation in Aim 1; $125 will be evenly divided among the total number of interviews needed to compensate participants for their involvement with each interview.

Aim 2

All participants will be initially screened via EMR records for potential eligibility (type of HNC, date(s) of treatment, age, sex, race, and education, etc.). A waiver of authorization for this access has been requested below. Study staff will seek permission to approach potential participants from the HNC survivor's provider before inviting the patient to extend an existing scheduled appointment to participate in the study. At the end of the clinic visit, the HNC survivor will meet with the study staff to obtain informed consent, schedule another time to discuss the study or obtain contact information to send the consent document (i.e., via REDCap or mail). After consent, the coordinator will record baseline data and all assessments. Participants that are found to have clinically significant depression (≥ 16 on the CES-D Iowa short form) will be withdrawn from the study and referred to social work.

Consented participants will then be block-randomized into one of 2 arms:

i. **Control condition: Assessment and Feedback (AF)**. Regardless of drinking level ascertained during the baseline questionnaires, the patient will receive feedback about their reported alcohol consumption from study coordinators (i.e. not through Bottle Cap). Feedback will be provided by study coordinators one time, in person or virtually (depending on how the participant elects to receive their baseline visit), after the baseline measures are completed, and include assessment of alcohol levels and recommending alcohol cessation. The feedback will emphasize that, according to leading medical associations, any consumption of alcohol is not advisable for cancer survivors, as continued

alcohol use is associated with a higher risk of cancer recurrence and reduced quality of life. A sample feedback statement is "one or two drinks might not seem much, but it can increase your chances of cancer recurrence". Smoking cessation information will also be provided as per usual care. Patients will be urged to stop smoking and referred to a smoking cessation program if so desired. Participants will be asked to complete two follow-up questionnaires, one at 3 and one at 6 months post baseline, during scheduled follow-up visits. No further effort will be required.

ii. **Intervention condition.** Survivors recruited from NWH who are randomized into the intervention condition will receive all research activities given in the control condition, plus the HNC-tailored alcohol cessation program. Study staff will register the survivor at the Bottle Cap website and confirm the person's gender and age. Survivors will receive text messages three times a week, usually during the late afternoon/early evening period, when the risk of alcohol drinking is greatest, for a period of 3 months. Participants will be asked to complete two follow-up questionnaires, one at 3 and one at 6 months post baseline. As with the control condition arm, all study activities will end after 6 months.

All participants will receive up to $100 compensation at the end of the study for their participation in Aim 2.

It should be noted that participants will have the option of completing all assessments electronically (i.e., via REDCap link), via hard copy (i.e., mailed form), and over the phone or in-person with the CRC/RA. In the event that participants opt to complete the questionnaire via mailed copy, over the phone or in-person, the CRC/RA will input participant responses into REDCap. For this study, all data collected will be coded and entered into REDCap (Research Electronic Data Capture), a vetted HIPAA compliant (Health Insurance Portability and Accountability Act) web-based application that manages research surveys and databases.

12. STATISTICAL ANALYSIS

- *Describe how your data will be used to test the hypotheses.*
- *State clearly what variables will be tested and what statistical tests will be used.*
- *Include sample size calculations.*
- *If this is a pilot study, state which variables will be examined for hypothesis generation in later studies.*

Aim 1:
All newly adapted Bottle Cap messages will be reviewed by the Patient Advisory Board (PAB), which consists of at least 15HNC survivors from Northwell Health and 15 HNC survivors from the VA, as well as 5 clinicians (oncologists, surgeons, nurses, etc.) who care for HNC patients and survivors. Members of the PAB will be asked to rate, on a yes/no binary scale, whether a message is motivating and convincing. If 80% of members

rate a message on a binary scale as both motivating and convincing it will be included in the message bank. Further, during the individual interviews with members of the PAB, we will collect qualitative feedback on how best to adapt the messages so they are tailored to HNC survivors' unique issues related to alcohol use, as well as use language that resonates with civilians or VA members. Feedback supported by ≥ 2 HNC survivors will be integrated into the text messages.

Aim 2:

Power Analysis:

The proposed recruitment sample size of 69 participants per arm (138 participants total) is based on feasibility and availability of resources during the recruitment time frame, as estimated by the PI of this study. Assuming 15% attrition, recruitment of 69 participants per arm will yield an analytic sample size of approximately 60 participants per arm (120 participants total). One of the main goals of this study is to estimate the cessation rate in both the control arm and intervention arms. Therefore, in Table 1 we used two sample sizes to calculate the 95% exact confidence intervals (CI) and widths/precision corresponding to four cessation rates. The limits are dependent on the observed proportion, but a sample size of 60 per arm will produce a two-sided 95% confidence interval with a maximum width equal to 25% when the sample proportion is as high as 40%.

Our secondary objective will be to compare the cessation rate of the two arms to obtain a preliminary effect size estimate to be used in future trials. Since this analysis will be used for exploratory, hypothesis-generating purposes, we will not be powered to detect a difference (yet to be determined) in the cessation rate between the two arms in this pilot study.

Of note, a fully powered study with proportions of 20% cessation in the control arm and 30% cessation in the intervention arm would require a sample size of 294 per arm (2-sided alpha=0.05, power=80%). Assuming 15% attrition, approximately 346 participants would need to be recruited per arm in a fully powered study. As recommended in published literature, the minimum sample size requirements for a pilot study are 10% of the fully powered study, which would be approximately 35 participants per arm based on these assumptions. We have chosen to exceed these minimum requirements in order to have more confidence in the pilot study's capacity for testing all aspects of the trial design and estimating effects.

Table 1. 95% CI and width/precision of estimation per arm for varying rates.

Sample size per arm	Cessation rate	95% CI	95% CI width
60	10%	10% (4%, 21%)	17%
60	20%	20% (11%, 32%)	21%
60	30%	30% (19%, 43%)	24%
60	40%	40% (28%, 53%)	25%
69	10%	10% (4%, 20%)	16%
69	20%	20% (12%, 32%)	20%
69	30%	23% (20%, 43%)	23%
69	40%	24% (29%, 53%)	24%

This study will include descriptive and univariate analyses.

Variables to be used in the main analyses (including covariates): We will collect data on demographics, health history and treatment type, physician cessation advice, overall health, and alcohol use. Additionally, we will collect data on acceptability of the text-message based intervention and feasibility of conducting a future RCT of the intervention. Our primary analyses will involve a binary measure of alcohol cessation using the TLFB and AUDIT scales. In order to facilitate a binary measure, the AUDIT questionnaire will be modified to include branching logic to not present the remaining questions of the questionnaire to participants should their response to the first question of "How often do you have a drink containing alcohol?" be "never". the TLFB will be supersede the AUDIT as the primary outcome measure if conflicting responses are provided. Secondary exploratory analyses will involve measures of quality of life, depression, social isolation, and loneliness as well as percent change of alcohol cessation.

Statistical Analyses:
Summary scales of standardized measures will be computed. Univariate and descriptive analyses will be performed on all continuous outcome variables and, normalizing and/or variance stabilizing transformations will be conducted. We will examine the data for outliers and use descriptive and inferential statistical techniques for data characterization. We will compare differences between the AF and intervention arms with a 2x2 chisquare test on the proportions of cessation in the groups. In addition, the rate of cessation between civilian and Veteran patients will be preliminarily evaluated through a t-test or analysis of variance procedure.

Stratification of data:
Patients, who have consented to participate, will be randomized to either the intervention or to the comparison condition (assessment and feedback about alcohol use). This procedure will ensure that an even number of participants will be allocated to the two arms, and that even numbers per condition across sites (i.e., Northwell and VA) are maintained overall. The Quantitative Intelligence team will develop and implement the randomization procedure, using a secure, HIPAA-compliant, web-based application that allows investigators or the research coordinator to randomize subjects into RCTs, using their personal computer and allows for multicenter, stratified, and single/double blinded RCTs, using permuted blocks.

13. SPECIMEN BANKING

- *If specimens will be banked for future research, describe where the specimens will be stored, how long they will be stored, how they will be accessed and who will have access to the specimens*
- *List the information that will be stored with each specimen, including how specimens are labeled/coded*
- *Describe the procedures to release the specimens, including: the process to request release, approvals required for release, who can obtain the specimens, and the information to be provided with the specimens.*

NA

14. DATA MANAGEMENT AND CONFIDENTIALITY

- *Describe the data and specimens to be sent out or received. As applicable, describe:*
  - *What information will be included in that data or associated with the specimens?*
  - *Where and how data and specimens will be stored?*
  - *How long the data will be stored?*
  - *Who will have access to the data?*
  - *Who is responsible for receipt or transmission of data and specimens?*
- *Describe the steps that will be taken to secure the data during storage, use and transmission.*

The research material collected will include quantitative and medical record abstraction data at the time of screening. The quantitative and electronic medical record data will be collected specifically for the proposed research project. The medical chart data is collected to contact the patient at follow-up time points. Signed hard-copy informed consents will be kept in a locked file cabinet at 600 Community Drive, Suite 300, Manhasset, NY 11030. Only the study personnel will have access to links between subjects and subject identities. Access to the Northwell Health SharePoint PHI drive containing electronic data is restricted to study personnel.

Data will be collected through REDCap (Research Electronic Data Capture), a vetted HIPAA-compliant (Health Insurance Portability and Accountability Act) web-based application that manages research surveys and databases. All data will be de-identified prior to conducting analyses. Only the PI and IRB approved study team will have access to the links that can associate the subject record to the individuals. These links will be maintained in REDCap. Subjects will sign an informed consent form prior to partaking in the study that states the potential risk of loss of confidentiality. This risk will be mitigated by storing data appropriately, ensuring only study personnel have access to the data, and that there are data use agreements in place before data is shared.

Research data and documentation will be maintained securely and stored in REDCap and on Northwell's SharePoint PHI drive according to applicable regulatory requirements (Policy 100.97 Records Retention and Destruction and GR021 Research Data Ownership and Management for additional information).

The Principal Investigator will meet with the study staff on a regular basis to ensure data accuracy and protocol adherence. To ensure the validity and integrity of study data, the PI will also oversee all data management responsibilities across both sites.

15. DATA AND SAFETY MONITORING PLAN

A specific data and safety monitoring plan is only required for greater than minimal risk research. For guidance on creating this plan, please see the Guidance Document *on the HRPP website.*

Part I – this part should be completed for all studies that require a DSMP.
Part II – This part should be completed when your study needs a Data and Safety Monitoring Board or Committee (DSMB/C) as part of your Data and Safety Monitoring Plan.

Part I: Elements of the Data and Safety Monitoring Plan

- *Indicate who will perform the data and safety monitoring for this study.*
- *Justify your choice of monitor, in terms of assessed risk to the research subject's health and well being. In studies where the monitor is independent of the study staff, indicate the individual's credentials, relationship to the PI, and rationale for selection*
- *List the specific items that will be monitored for safety (e.g. adverse events, protocol compliance, etc)*
- *Indicate the frequency at which accumulated safety and data information (items listed in # above) will be reviewed by the monitor (s) or the DSMB/C.*
- *Where applicable, describe rules which will guide interruption or alteration of the study design.*
- *Where applicable, indicate dose selection procedures that will be used to minimize toxicity.*
- *Should a temporary or permanent suspension of your study occur, in addition to the IRB, indicate to whom will you report the occurrence.*

Oversight Responsibilities:
The Principal Investigator (PI), Dr. Michael Diefenbach, has oversight responsibility for the conduct of this research. The PI will supervise the research, ensure that each individual engaged in research is qualified to do so by virtue of education, training and experience to perform the delegated task. He will protect the rights, safety and welfare of participants by ensuring that the research is conducted in accordance with all federal regulatory requirements, state law and Northwell Health policies (including IRB SOPs) and with the IRB-approved plan, and is conducted in accordance with the IRB approved plan, and ensure the accuracy, security and integrity of the research data and data analysis.

Monitoring Responsibilities:
Study data are accessible at all times for review by the PIs and named co-investigators. The PI and co-investigators will review study on a monthly basis. Coordinators will be able to monitor study procedure adherence through remote monitoring. Any technical issues with the Bottle Cap messaging will be addressed directly by the study team and a dedicated Bottle Cap technical and customer support group.

- Reportable events (unanticipated problems, deviations, violations, etc.) will be reviewed by the PIs at each site and reported to their respective IRBs in a timely manner and in accordance with local IRB Policy.

All events determined to be reportable at the collaborating VA site will be communicated to the Northwell Health PI to assess changes as/if needed to the research.

In addition to reportable events, deviations will also be monitored. Deviations can be the results of actions of the participant or of the study team. For example, situations in which the investigator failed to perform tests or examinations as required by the protocol or failures on the part of study subjects to complete scheduled visits as required by the

protocol, would be considered protocol deviations. Protocol deviations can be major or minor.

Major Protocol Deviation: A deviation that affects subject safety, rights, welfare or data integrity.

Examples of major protocol deviations include (but are not limited to):

- Use of study procedures not approved by the IRB
- Failure to report unanticipated problems to the IRB and/or sponsor
- Enrollment of subjects (or use of their identifiable data) after IRB-approval of study expired

Minor protocol deviation: A deviation that does not affect subject safety, rights, welfare or data integrity.

Examples of minor protocol deviations include (but are not limited to):

- Deviations from the approved study procedure that do not affect subject safety or data integrity
- Omitting an approved portion of the protocol

The PIs will determine if a deviation is major or minor. Major protocol deviations will be reported to the IRB within ten (10) working days of discovery. Minor protocol deviations will be reported at the time of continuing review or check-in by the IRB.

For this study, research procedures are limited to receipt of text messages and completion of questionnaires/surveys. As such, we do not expect adverse events (AE) to occur. However, if they do, adverse events will be reported to the IRB per reporting guidelines, unless they are attributable to a medically indicated procedure accompanying participation in this protocol. Non-serious adverse events will not be reported in the IRB at each occurrence but will be reported in summary form at the time of continuing review and protocol termination. Serious adverse events will be reported using the serious adverse event report form.

Despite all of our efforts to maintain the privacy and data security of our participant's information, unanticipated problems, such as a stolen computer may occur, although it is highly unlikely. OHRP considers unanticipated problems, in general, to include any incident, experience, or outcome that meets all of the following criteria:

1. unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
2. related or possibly related to participation in the research; and
3. suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Unanticipated problems can be "acts of God", power failures, breaches of confidentiality, loss of study data, etc. since they could have an adverse effect on study subjects.

Related: An event is "related" if it is likely to have been caused by the research procedures.

Probably/Possibly Related: An event is considered to be probably or possibly related to the research if there is a greater than 50% chance that the event was caused by the study procedures.

Should an unanticipated event related to the research that exposes individuals other than the research participants (e.g., investigators, research assistants, students, the public, etc.) to potential risk, the event will be reported in a timely manner but not more than five (5) working days after discovery by the PI.

The PIs, as well as the IRB and other oversight committees, have the authority to stop or suspend the study or require modifications.

Part II: Data and Safety Monitoring Board or Committee

- *When appropriate, attach a description of the DSMB.*
- *Provide the number of members and area of professional expertise.*
- *Provide confirmation that the members of the board are all independent of the study.*

16. WITHDRAWAL OF SUBJECTS

- *Describe anticipated circumstances under which subjects will be withdrawn from the research without their consent*
- *Describe procedures for orderly termination*
- *Describe procedures that will be followed when subjects withdraw from the research, including partial withdrawal from procedures with continued data collection.*

Circumstances in which participates may be withdrawn from the research without their consent may include the following:

- failure to follow instructions,
- failure to adhere to scheduled in-person or virtual interviews,
- it is not in the participant's best interest to continue on this study, or
- the study is stopped.

This decision may be made by the PIs, or the IRB.

Participants will be able to withdraw from the study at any time. The consent form will make explicit to patients that they may discontinue the study at any time without penalty and without prejudice to their medical care.

Any subjects withdrawn from the research will be instructed that per the consent form we may still use information we have already collected for research purposes but will not

continue to collect any further data. The subject will have their information removed from any future correspondence that was planned for the study.

17. RISKS TO SUBJECTS

- *Describe any potential risks and discomforts to the subject (physical, psychological, social, legal, or other) and assess their likelihood and seriousness and whether side effects are reversible. Where appropriate, describe alternative treatments and procedures that might be advantageous to the subjects.*
- *Include risks to others , like sexual partners (if appropriate)*
- *Discuss why the risks to subjects are reasonable in relation to the anticipated benefits and in relation to the importance of the knowledge that may reasonably be expected to results*
- *Describe the procedures for protecting against or minimizing any potential risks, including risks to confidentiality, and assess their likely effectiveness.*

There is a slight risk that participants might be distressed or uncomfortable when being asked questions about their cancer or drinking habits. All research personnel with patient contact will be trained by Dr. Diefenbach and the Co-Is to be vigilant and sensitive to expressions of distress. All participants will be encouraged to contact the PI if any concerns arise.

The risks to subjects are reasonable in that this is a minimally invasive study, no subject's treatment will be altered in any way and the only potential risk is that of distress with questions being asked which they are free to skip. The risks are outweighed by the anticipated benefits and knowledge to be gained that may help HNC survivors in addition to providing subjects with enhanced knowledge and awareness of the risks of alcohol consumption after cancer treatment.

The procedures to protect subjects against or minimize the described risks in addition to risks to confidentiality include allowing participants to skip or choose not to respond to any questions that may cause them distress. Confidentiality will be protected by ensuring that all patient information gathered will be kept on Northwell's secured server and in password protected files that only the research team has access to. Further, information will only be accessed when needed and the research team will be trained to ensure confidentially and the correct procedures when accessing and saving patient information are used.

In the future, we may publish results of this study on data sharing websites (e.g., Open Science Framework), in scientific journals, and may present it at scientific meetings. If we do we will not identify the subject. All data included in the publication will be de-identified.

18. RESEARCH RELATED HARM/INJURY

- *Describe the availability of medical or psychological resources that subjects might need as a result of anticipated problems that may be known to be associated with the research.*
- *If the research is greater than minimal risk, explain any medical treatments that are available if research-related injury occurs, who will provide it, what will be provided, and who will pay for it.*

This study presents no greater than minimal risk to participants, thus research related harm/injury is not expected.

Patients may be at risk for slight emotional distress, which might result from being asked questions about personal cancer and treatment experiences. Participants will be informed during the interview sessions and at the beginning of the assessment that potentially sensitive topics will be discussed and that they may skip any part that would make them uncomfortable. In accordance with Monter's standard of care procedures, any participant who expresses distress throughout the duration of this study, for any reason, will be referred by the study team to a licensed social worker from our institution. Patients will also be referred to social work if they are clinically depressed or found to have severe substance abuse, as evaluated by our baseline assessment of standardized measures

19. POTENTIAL BENEFIT TO SUBJECTS

- *Explain what benefits might be derived from participation in the study, noting in particular the benefit over standard treatment (e.g. a once-a-day administration instead of four times a day, an oral formulation over an IV administration).*
- *Also state if there are no known benefits to subjects, but detail the value of knowledge to be gained*

This research is designed to test the acceptability of this type of intervention program. We also want to test how well it works so we can try this approach with more people in a larger research study. Because we are looking at how well this works, participants may indirectly benefit from learning more about alcohol and its effect on cancer survivors. Information we gather from participants' responses may help future cancer and HNC patients to cut down (reduce) their alcohol drinking.

20. PROVISIONS TO PROTECT PRIVACY INTERESTS OF SUBJECTS

- *Describe the methods used to identify potential research subjects, obtain consent and gather information about subjects to ensure that their privacy is not invaded.*
- *In addition consider privacy protections that may be needed due to communications with subjects (such as phone messages or mail).*

The researchers take the issue of privacy very seriously. Study information will be stored in a Northwell-approved database drive to store PHI, and it will only be accessible to research staff listed on the approved IRB protocol. Names or other identifying information

will not be shared with those outside the research team, except as indicated in the "Data Management and Confidentiality" section above for the purposes of sending research communications. Phone numbers and email will only be used for study-related communications. Any phone calls or emails will be sent to participants through the respective study site's secured server and calls made at each study location in a secured area.

21. COSTS TO SUBJECTS

- *Describe any foreseeable costs that subjects may incur through participation in the research*
- *Indicate whether research procedures will be billed to insurance or paid for by the research study.*

This study uses text messaging to deliver notifications, reminders, and study questionnaires. Completing the surveys will require cellular data if a participant is not connected to Wi-Fi. Standard message and data rates from the participant's wireless carrier may apply. Study participants will not be compensated for any costs related to data usage or sending or receiving text messages by the study or by members of the study team.

If referred for counseling or medical care, the study will not be responsible for any costs associated for future counseling or medical care needed by participants.

22. PAYMENT TO SUBJECTS

- *Describe the amount of payment to subjects, in what form payment will be received and the timing of the payments.*

Patients participating on the adaptation interviews (Aim 1) will receive up to $125 for their participation via a ClinCard delivered at the end of Aim 1 activities (i.e. all interviews are complete). Patients participating in the pilot RCT (Aim 2) will receive up to $100 for their participation via a ClinCard upon completion of Aim 2 assessments ($25 baseline, $25 3-month, $50 6-month).

23. CONSENT PROCESS

If obtaining consent for this study, describe:

- *Who will be obtaining consent*
- *Where consent will be obtained*
- *Any waiting period available between informing the prospective participant and obtaining consent*
- *Steps that will be taken to assure the participants' understanding*

- *Any tools that will be utilized during the consent process*
- *Information about how the consent will be documented in writing. If using a standard consent form, indicate such.*
- *Procedures for maintaining informed consent.*

Each subject will receive written explanations of the purposes, procedures, and risks of this study in language appropriate for the individual's level of understanding. All questions will be answered via email or phone, and if all inclusion criteria are met, and the subject volunteers to participate, digital written informed consent will be obtained.

Consent may be obtained in person (hardcopy consent form) or electronically (written, electronic consent via REDCap).

For in person consent: The site research coordinators, who have experience obtaining informed consent at NWH will describe the study in detail, answer questions, and obtain written informed consent. The study investigator or research coordinator will not enroll a potential subject until the person administering the consent is satisfied that the subject understands all parts of the study. A copy of the informed consent will be provided to the patient at the end of the consultation process.

For eConsent: The e-consent document will contain all of the elements of informed consent required by applicable federal regulation for the protection of human subjects and elements of authorization required by the HIPAA Privacy Rule, and will begin with a concise and focused presentation of the key information that is most likely to assist participants in understanding the reasons why he/she might or might not want to participate in the research. Because consent will be obtained remotely, the electronic consent form will be designed such that the form is easy to navigate. The system will also incorporate electronic strategies to encourage participants to access all of the consent material before documenting his/her consent via electronic signature.

In the event a participant experiences difficulty navigating our electronic consent form, the study team will mail a written copy of the consent form to the participant. If the participant agrees to participate, they will be directed to sign the consent form and return back to the study team. This can be accomplished electronically (i.e., scanned copy of consent form sent to the study team) or via mail (i.e., study team provides stamped return envelope for participants to mail back consent form).

Research coordinators will review names and signatures of all completed consent forms. PDF copies of signed consent forms will be stored in a HIPAA-secured, Northwell approved storage drive with protected access to only the PI and research personnel listed on the study protocol. A copy of the signed form will be made available to participants.

Participants may contact a member of the research team with questions about the research. Each page of consent materials will contain a direct number to a research phone and a designated encrypted email inbox. Both the research phone and email inbox will be monitored daily by consenting coordinators.

In the state of NY, any participants under the age of 18 are considered children. If your study involves children, additional information should be provided to describe:

- *How parental permission will be obtained*
- *From how many parents will parental permission be obtained*
- *Whether permission will be obtained from individuals other than parents, and if so, who will be allowed to provide permission. The process used to determine these individual's authority to consent for the child should be provided*
- *Whether or not assent will be obtained from the child*
- *How will assent be documented*
- *Whether child subjects may be expected to attain legal age to consent to the procedures for research prior to the completion of their participation in the research. If so, describe the process that will be used to obtain their legal consent to continue participation in the study. Indicate what will occur if consent is not obtained from the now-adult subjects.*

NA

If the study involves cognitively impaired adults, additional information should be provided to describe:

- *The process to determine whether an individual is capable of consent*
- *Indicate who will make this assessment*
- *The plan should indicate that documentation of the determination and assessment will be placed in the medical record, when applicable, in addition to the research record.*
- *If permission of a legally authorized representative will be obtained,*
  - *list the individuals from who permission will be obtained in order of priority*
  - *Describe the process for assent of subjects; indicate whether assent will be required of all, some or none of the subjects. If some, which subjects will be required to assent and which will not.*
  - *If assent will not be obtained from some or all subjects, provide an explanation as to why not*
  - *Describe whether assent will be documented and the process to document assent*
  - *Indicate if the subject could regain capacity and at what point you would obtain their consent for continued participation in the study*

NA

If the study will enroll non-English speaking subjects:

- *Indicate what language(s) other than English are understood by prospective subjects or representatives*
- *Indicate whether or not consent forms will be translated into a language other than English*

- *Describe the process to ensure that the oral and written information provided to those subjects will be in that language*
- *If non-English speaking subjects will be excluded, provide a justification for doing so*

A primary goal for this pilot research study is to test virtual research delivery capabilities and use of mobile messaging and coaching to help HNC survivors stop and/or reduce drinking. This study builds upon the work originally done by Jon Morgenstern, Ph.D. under protocol 17-0390 (Bottle Cap) and is of high significance for military and veteran populations for whom both alcohol drinking and HNC is elevated. HNC survivors who continue to drink alcohol are at risk for poor physical and mental health outcomes, which impedes mission readiness for them and their family members. We are focused on soliciting feedback from participants on the ease of platform use, if the research delivery was satisfactory, if the messaging was deemed useful, etc. Currently, Bottle Cap is available in English only. Having a platform capable of accurately displaying research requirements and study related material is especially important for speakers whose language involves characters that may not be easily displayed electronically or may introduce formatting errors. We aim to be transparent that further research is needed to assess feasibility in the same delivery with non-English speaking individuals. Presently we hope to collect enough information to justify a future expansion of the Bottle Cap program to other disease groups (e.g., head and neck cancer patients or other at-risk cancer patients). Funds for such an expansion can then also be used to expand to Spanish. Please note that a simple translation of messages into Spanish is not sufficient to generate an effective alcohol cessation program. Alcohol consumption behavior is triggered by cultural and individual factors, which need to be thoroughly explored, before text messages in another language can be crafted. Hence, this requires a substantial investment in time and resources. With regard to the current study, we are aware that lack of representation undermines generalizable results and impacts public trust in science, thus we are committed to enrolling a racially and ethnically diverse population in this protocol. However, note that the majority of patients diagnosed with head and neck cancer are White. We will make all efforts to include minority patients into the study and we intend to advertise the research without restriction. Race and ethnicity (not just English proficiency) are strongly correlated with income, employment, and other social determinants of health, which, by definition, affect health outcomes and success with alcohol cessation. We will collect information on all of these factors to help inform the research design. We do not believe that focusing on native English-speaking participants in this pilot study - those that may be from ethnically and racially diverse populations - will negatively impact equitable access, participant comprehensibility or applicability to the diverse populations that may be solicited for participation in future clinical trials using Bottle Cap.

24. WAIVER OR ALTERATION OF THE CONSENT PROCESS ☐ N/A

Complete this section if you are seeking an alteration or complete waiver of the consent process.

- *Describe the possible risks of harm to the subjects involved in this study and explain why the study involves no more than minimal risk to the subject:*
- *Explain why the waiver/ alteration will not adversely affect the rights and welfare of subjects*
- *Explain why it is impracticable to conduct this research if informed consent is required*
- *Explain why it is not possible to conduct this research without using the information or biospecimens in an identifiable form*
- *If appropriate, explain how the subjects will be provided with additional pertinent information after participation. If not appropriate to do so, explain why.*

Complete this section if you are obtaining informed consent but you are requesting a waiver of the documentation of consent (i.e., verbal consent will be obtained). *To proceed with a waiver based on these criteria, each subject must be asked whether they wish to have documentation linking them to this study.* ***Only complete subsection 1 OR subsection 2.***

SUBSECTION 1

- *Explain how the only record linking the subject to the research would be the consent document.*
- *Explain how the principal risk of this study would be the potential harm resulting from a breach in the confidentiality*
- *Indicate whether or not subjects will be provided with a written statement regarding the research.*

SUBSECTION 2

- *Describe the possible risks of harm to the subjects involved in this study and explain why the study involves no more than minimal risk.*
- *Confirm that the research only involves procedure for which consent is not normally required outside the research context.*
- *Indicate whether or not subjects will be provided with a written statement regarding the research.*

25. WAIVER OF HIPAA AUTHORIZATION ☐ N/A

Complete this section if you seek to obtain a full waiver of HIPAA authorization to use and/or disclose protected health information.

- *Describe the risks to privacy involved in this study and explain why the study involves no more than minimal risk to privacy:*
- *Describe your plan to protect identifiers from improper use or disclosure and to destroy them at the earliest time.*
- *Indicate why it is not possible to seek subjects' authorization for use or disclosure of PHI.*
- *Indicate why it is not possible to conduct this research without use or disclosure of the PHI.*
- *Indicate if PHI will be disclosed outside NSLIJ Health System, and if so, to whom. Note: PHI disclosed outside NSLIJ Health System, without HIPAA authorization needs to be tracked. Please see guidance at www.nslij.com/irb for information about tracking disclosures.*

We request a waiver of authorization for record review and screening purposes only for both Aim #1 and Aim #2.

The description of the PHI for which use or access is as follows: Patient, date of birth (DOB), medical record number (MRN), Provider, Procedure, Procedure Date/Encounter Date, cancer type, details, etc.

Collection of this information is necessary for recruitment/screening procedures. The use of this protected health information involves no more than a minimal risk to the privacy of individuals, based on our adequate plan to protect the identifiers from improper use and disclosure as described above.

The health information collected for this recruitment/screening purpose will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study. The research could NOT practicably be conducted without the waiver or alteration for eligibly/recruitment/screening. In addition, the research could NOT practicably be conducted without access to and use of the protected health information.

The study team is aware that waiver of authorization does not authorize subject contact. Treating providers will be consulted prior to contact. The study team is also aware that HIPAA regulations require that accounting logs be maintained when researchers access patient records under a waiver of authorization including those approved for recruitment purposes.

Complete this section if you seek to obtain a partial waiver of the patient's authorization for screening/recruitment purposes *(i.e., the researcher does not have access to patient records as s/he is not part of the covered entity)*

Note: Information collected through a partial waiver for recruitment cannot be shared or disclosed to any other person or entity.

- *Describe how data will be collected and used:*
- *Indicate why you need the PHI (e.g.PHI is required to determine eligibility, identifiers are necessary to contact the individual to discuss participation, other)*
- *Indicate why the research cannot practicably be conducted without the partial waiver (e.g. no access to medical records or contact information of the targeted population, no treating clinician to assist in recruitment of the study population, other)*

26. VULNERABLE POPULATIONS:

Indicate whether you will include any of these vulnerable populations. If indicated, submit the appropriate appendix to the IRB for review:

- ☐ *Children or viable neonate*
- ☐ *Cognitively impaired*
- ☐ *Pregnant Women, Fetuses or neonates of uncertain viability or nonviable*
- ☐ *Prisoners*
- ☒ *NSLIJ Employees, residents, fellows, etc*
- ☐ *poor/uninsured*
- ☐ *Students*
- ☐ *Minorities*
- ☐ *Elderly*
- ☐ *Healthy Controls*

If any of these populations are included in the study, describe additional safeguards that will be used to protect their rights and welfare.

Aim 1 will enroll health care workers to participate in informational interviews. Potential participants will be given documents explaining that participation in this research will not impact their employment or standing with Northwell Health. Individuals with a supervisory relationship over an employee will not enroll any individual who reports to them in this study. Employee participation or non-participation in this study will have no bearing on an individual's position at Northwell Health.

27. MULTI-SITE HUMAN RESEARCH (COORDINATING CENTER)

If this is a multi-site study where you are the lead investigator, describe the management of information (e.g. results, new information, unanticipated problems involving risks to subjects or others, or protocol modifications) among sites to protect subjects.

The central site investigator, Michael A. Diefenbach, Ph.D., is responsible for the overall oversight of the data collected at NWH and Brooklyn VA in addition to the monitoring of the data, assuring protocol compliance, and conducting the safety reviews during regular meetings or more frequently if needed. The central site investigator will also be responsible for compiling the data sheets, day to day oversight of research and ensuring the integrity and privacy of the data. During the review process the principal investigators, along with the other investigators, will evaluate whether the study should continue unchanged, require modification/amendment, or be closed to enrollment. To aid in this study progress, data and safety concerns will be reviewed after every month and will include the research team. Outside of these scheduled meetings, safety concerns can be raised at any time and by anyone. The principal investigators or the Institutional Review Board (IRB) have the authority to stop or suspend the study or require modifications.

All research data including any subject contact information and protected health information obtained both from the baseline and follow-up measures will be held in strict confidence in a coded format, identified only by a study ID number. After data entry, subject information will not have the patient's name, but will be identified only by a study ID number. The database, that will be password-protected, stored, and backed up daily on a protected server, will be designed using REDCap, a secure web-based application designed to support data capture for research studies. All data obtained in the study will be used exclusively for the purposes of the proposed research, which are clearly outlined in the informed consent signed by the patient. Ongoing protection of confidentiality will be adhered to throughout the study period and thereafter. In addition, the PI, Dr. Diefenbach will meet with the study staff at NWH on a regular basis to ensure data accuracy and protocol adherence. Further and as mentioned prior, meetings with the Brooklyn VA study team will also ensure protocol adherence. To ensure the validity and integrity of study data, Dr. Diefenbach will also oversee all data management responsibilities and will discuss all data management issues with the study team at both sites. The VA site will provide a copy of the research data collected to Northwell at the conclusion of the study.

28. REFERENCES/BIBIOGRAPHY

Provide a reasonable list of references directly related to the study. Any diagrams for new medical devices or brief reprints from journals might also prove useful.

1. Marziliano, A., Teckie, S., & Diefenbach, M. (2020). Alcohol-related Head and Neck Cancer: A Summary of the Literature. Head and Neck, 42, 732-738. Available from: https://pubmed.ncbi.nlm.nih.gov/31777131/
2. Wotman, M., Teckie, S., Marziliano, A., Orner, D., Yi, J., Mulvany, C., Ghaly, M., Parashar, B., & Diefenbach, M. (2021). Patterns of alcohol use among early head and neck cancer survivors: A cross-sectional survey study using the Alcohol Use Disorders Identification Test (AUDIT). Oral Oncology. Available from: https://pubmed.ncbi.nlm.nih.gov/34077813/

3. Meadows, S.O., Engel, C.C., Collins, R.L., Beckman, R.L., Breslau, J. Litvin Bloom, E., Dunbar, M. S., Gilbert, M., Grant, D., Hawes-Dawson, J., Brooks Holliday, S., MacCarthy, S., Pedersen, E.R., Robbins, M.W., Rose, A.J., Ryan, J., Schell, T.L., & Simmons, M.M. (2018). Department of Defense Health Related Behaviors Survey (HRBS): Results for the Active Component. Santa Monica, CA: RAND Corporation. Available from: https://www.rand.org/pubs/research_reports/RR4222.html
4. Muench, F., K. van Stolk-Cooke, A. Kuerbis, G. Stadler, A. Baumel, S. Shao, J. R. McKay & Morgenstern, J. (2017). A Randomized Controlled Pilot Trial of Different Mobile Messaging Interventions for Problem Drinking Compared to Weekly Drink Tracking. PLoS One, 12, e0167900. Available from: https://pubmed.ncbi.nlm.nih.gov/28146560/
5. Zevallos J.P., Kramer J.R., Sandulache V.C., Massa, S.T., Hartman, C.M., Mazul, A.L., Wahle, B.M., Gerndt, S.P., Sturgis, E.M, & Chiao, E.Y. (2021). National trends in oropharyngeal cancer incidence and survival within the Veterans Affairs Health Care System. Head & Neck. 2021;43:108–115. Available from: https://onlinelibrary.wiley.com/doi/epdf/10.1002/hed.26465