A text-based reduction intervention for smokeless tobacco cessation

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2. SIGNIFICANCE

Smokeless tobacco use is associated with morbidity and mortality and disproportionally affects rural and medically underserved populations. Underserved smokeless tobacco users (those who live in rural areas and/or those who live in medically underserved areas, areas with high poverty levels and few primary care providers[10]) are at increased risk for poor health outcomes, given high rates of smokeless tobacco usage. Smokeless tobacco is used mostly by males, with national rates of use reported to be more than twelve times higher among males (6%) compared to females (0.4%).[11] Smokeless tobacco use rates in certain sub-populations of the U.S., such as male residents of Southern and Western states (13-17%) and rural residents (6%), are significantly higher than population norms.[11,12] Clearly, we need effective interventions to reduce smokeless tobacco use targeted to those most at risk in these underserved areas, where residents have little access to and use of proven tobacco cessation treatments. The high rate of use coupled with less access to programs creates a disparity that increases underserved residents' risk for in the short term oral mucosal lesions[13 14,15], periodontal disease[16], and precancerous oral lesions.[17] Long-term use may increase the risk for ischemic heart disease [18] and head and neck cancers especially oral cancers.[19] Just one year of smokeless tobacco use is associated with over 6 million Disability Adjusted Life Years lost and over a quarter of a million deaths.[18] This disparity is compounded by the lack of health care providers and the burden of traveling far distances to health care facilities in underserved populations. Further, many rural Americans do not receive consistent cessation advice and have less access to cessation services than their urban counterparts.[20] Therefore, innovative interventions that provide consistent access to cessation services are needed.

Reducing smokeless tobacco use in response to situational cues is imperative for cessation success. Research supports that people use tobacco in response to stimuli or environmental and situational cues,[21 22] yet many smokeless tobacco cessation interventions do not address stimulus control. For example, Coffey and Lomardo examined the importance of sensory and behavioral cues in smokeless tobacco use and found that cues modulated urge, affect, and stress.[22] Current smokeless tobacco cessation interventions do not address chewing behaviors that may be driven by cravings in response to situational cues (e.g., cup of coffee, meals). Behavioral techniques that focus on self-regulation and restraint have the potential to help smokeless tobacco users manage their responses to situational cues.[23] In fact, investigators found that cue extinction (which consisted of each participant identifying 2-3 situations that were associated strongly with smokeless tobacco use and breaking those associations by not chewing or dipping for 30 minutes twice a day) produced smokeless quit rates of 66% at 9 months.[24] Results of this trial should be interpreted with caution given the small sample size and lack of comparison arm. However, addressing cues is an important intervention target for an intervention. To date this strategy has been largely unexplored in the smokeless tobacco cessation literature, and our study was designed to fill this gap.

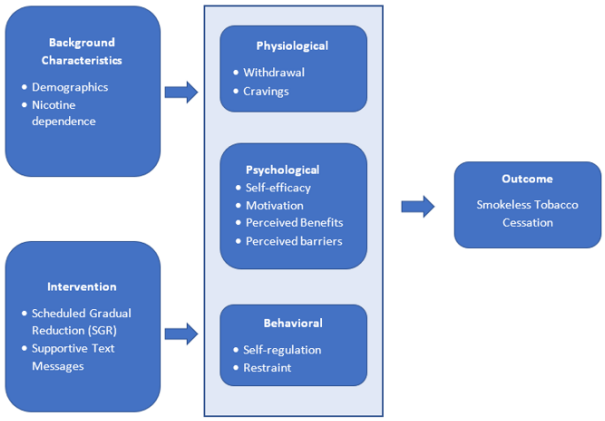
Scheduled Gradual Reduction (SGR) helps users to self-regulate and practice restraint in response to tobacco use cues and has great potential to improve cessation rates. Scheduled Gradual Reduction (SGR) may be especially efficacious in helping smokeless tobacco users to quit as it addresses self-regulation of situational cues to chew. SGR is a reduction-based cessation method that first assesses smokeless tobacco user patterns, then gradually reduces the number of chews/dips used per day by lengthening the time interval between use ending with a definitive quit date at the end of the reduction period. SGR has been minimally studied in smokeless tobacco users.[9] However, the few studies available demonstrate that SGR promotes cessation among smokeless tobacco users.[9,25] Our SGR intervention is unique compared to other smokeless tobacco cessation interventions in that it provides chewers with a specific schedule for chewing, encouraging use of chewing restraint techniques during intervals between alerts to chew. Chewing on a schedule has two important functions: (1) nicotine use is evenly spaced to manage withdrawal symptoms; and (2) it provides multiple opportunities to employ restraint, defined as conscious, chronic restriction of chewing based on set limits.[23] Evidence from studies with cigarette smokers have shown that successful use of restraint during reduction is predictive of quitting. [5] Very few interventions for smokeless tobacco users have addressed self-regulation and restraint through scheduled chewing. Our intervention provides a schedule for chewing and chewers are asked to chew only when alerted. As a result, chewing becomes unlinked from the cues (i.e., psychological, behavioral, and environmental) and smokeless users can learn how to manage cravings using restraint during the reduction period prior to quitting.

Our SGR intervention also helps participants manage withdrawal symptoms, an important determinant of cessation success through scheduled chewing that gradually reduces their tobacco use down to zero. The gradual reduction of the SGR intervention provides even spacing between nicotine self-administration leading to the down regulation of nicotine receptors over time.[26] Given nicotine dependence is a predictor of smokeless tobacco cessation and smokeless tobacco users report a similar severity of withdrawal symptoms compared to cigarette smokers,[27] addressing withdrawal symptoms during a quit attempt is critical

to success. Prior SGR intervention work in both cigarette smokers and smokeless tobacco users report reductions in withdrawal symptoms over the scheduled gradual reduction period.[7,8,9]

SGR combined with CBT support texts strengthens our intervention and will improve cessation rates compared to other evidenced-based cessation interventions in this group of tobacco users. Our SGR intervention was designed to supplement a cognitive behavioral intervention delivered via text messaging to help smokeless tobacco users quit. Past SGR studies used a combination of cognitive-behavioral telephone counseling to help smokeless tobacco users cope with quitting along with the SGR program.[8,9] We will combine the SGR program with text-based support messages to provide participants with advice and support for quitting. Our team adapted the support messages for this program from text messages developed by Dr. Herbert Severson for local health department use and are based off constructs of the Social Cognitive Theory [28] and the Health Belief Model [29] including perceived benefits, perceived susceptibility, perceived barriers, and self-efficacy. This is an important addition to the SGR program, as smokeless tobacco users need to be motivated to quit, believe that quitting will be beneficial, feel confident they can quit, and believe that barriers to quitting are surmountable. See **Figure 1**.

Figure 1: Conceptual Model



Delivering our SGR intervention via text message has great potential to increase access to cessation services and reach more rural and medically underserved smokeless tobacco users, helping to eliminate health disparities. Web-based cessation interventions for adult smokeless tobacco users have been modestly effective in reducing smokeless tobacco use, with quit rates around 12%.[30] However, many underserved Americans often lack consistent computer skills and access; therefore, they are less likely to access existing web-based interventions consistently. [2] Text messaging is a method that has strong potential to deliver cessation interventions to smokeless tobacco users given its availability, low cost, and widespread use. In addition, text messaging requires a low level of technological expertise and does not require expensive equipment or data plans.[31] A recent Cochrane review of mobile phone-based interventions for smoking cessation supports the use of mobile phone-based smoking cessation interventions in helping people to quit.[32] However, there are no available text-based interventions to help smokeless tobacco users quit. Delivery of behavioral interventions via text messaging has the potential for efficacy and widespread dissemination in underserved smokeless tobacco users, as cell phone use is widespread. Further, our pilot work supports the feasibility and acceptability of a text-based smokeless tobacco cessation approach. Thus, the potential impact and reach of a text-based intervention warrants investigation in helping underserved smokeless tobacco users quit. Our study was designed to fill this gap.

Summary. Rural and medically underserved smokeless tobacco users represent a vulnerable group for tobacco use. Despite their high risk for tobacco-related cancers, underserved smokeless tobacco users have not been widely targeted for cessation intervention trials. Text-based interventions have the potential to consistently reach many more underserved smokeless tobacco users compared to both clinic-based and web-based interventions. Our SGR intervention has the potential to increase quit rates compared to the current standard of care as our SGR intervention addresses common barriers (withdrawal symptoms and situational and environmental chewing cues) to quitting. Our pilot work supports the feasibility and acceptability of a text-based smokeless tobacco cessation intervention approach. *The proposed study has public health relevance as it will determine if our intervention performs better than standard of care and is worthy of larger scale dissemination, will add to evidenced-based cessation treatments for smokeless tobacco users and shed light on the important mechanisms of intervention effects in this understudied group of tobacco users.*

2. Innovation

The proposed project has the potential to improve the health of underserved smokeless tobacco users and will have implications for future tobacco cessation initiatives in rural and underserved communities. This project is innovative for multiple reasons.

- We propose one of the first large-scale studies using SGR aimed at an underserved group of tobacco users. Therefore, this study aims to decrease a tobacco-related health disparity by decreasing rates of use and bringing innovative interventions to those with limited access.

- Our study is innovative in that it is the first RTC to compare a text-based reduction intervention to a standard of care intervention. The results of this innovative study have public health relevance and can be used to determine if our SGR intervention should be disseminated broadly.
- Our study will explore mechanisms of cessation intervention effects to expand the limited literature in the field on this area. This information will provide valuable data on important intervention targets that can be used to inform future more targeted treatment strategies in this group of tobacco users
- Our study targets behavioral techniques that focus on self-regulation and restraint have the potential to help smokeless tobacco users manage their responses to situational cues. To date, this strategy has been largely unexplored in the smokeless tobacco cessation literature.
- Delivering SGR via text messaging is an innovative way that is a more convenient format and increases the potential reach of the intervention to more vulnerable groups of tobacco users at high risk for tobacco-related morbidity/mortality.

3. APPROACH

Research Team

Our experienced, multidisciplinary research team collaboratively developed the SGR intervention for the current study. (**Table 1**). This team obtained our initial funding for our pilot (1R15CA198841-01) and have worked together on this grant application. Collectively, our team brings a wealth of experience in designing and implementing tobacco cessation interventions and working with underserved populations.

Table 1. Study Team

Team Member	Unique contribution to project
Devon Noonan, PhD, MPH, FNP-BC Principal Investigator	Oversee all aspects of study recruitment, enrollment, implementation, and dissemination of results
Laura Fish, PhD, MPH Co-Investigator	Intervention development, implementation and interpretation of the real-time text data
Kathryn Pollak, PhD Co-Investigator	Recruitment and intervention implementation and delivery
Susan Silva, PhD Co-Investigator	Statician; Statistical analysis and quantitative methods
Leigh Ann Simmons, PhD, MFT Co-Investigator	Recruitment of rural smokeless tobacco users
Herb Severson PhD Consultant	Consult on recruitment, intervention delivery, Enough Snuff intervention and retention

Preliminary Data

Our pilot study of an SGR intervention shows promise for helping participants gradually reduce their tobacco use down to zero. We are the first to test a text-based delivered SGR intervention for rural and underserved smokeless users (1R15CA198841). Our team conducted a pilot study with 98 rural and medically underserved smokeless tobacco users to determine the feasibility and acceptability of an SGR program delivered via text message paired with text-based support messages aimed at decreasing smokeless tobacco use and promoting cessation. We recruited smokeless tobacco users primarily from social media targeting rural and underserved areas in North Carolina and four rural northern counties in South Carolina and randomized in a 2:1 fashion to either: (1) the SGR program (N=65), a text-based program aimed at reducing chewing over a four-week plus text-based support messages; or (2) text-based support messages only (N=33). Participants completed surveys at baseline and end of program to assess feasibility, acceptability, self-report and biochemically validated 7-day point prevalence of cessation. We also conducted a 6-month survey to assess self-report cessation. To determine rural status, we used Rural-Urban Continuum Codes (RUCC) designated as non-metropolitan (designated as a RUCC code of 4 or above) [33] and Medical Underserved Areas were defined using Health Resources and Services Administration (HRSA) index of Medical Underservice with a score of 62 or indicating medically underserved.[34]

We recruited 98 rural and medically underserved smokeless tobacco users in 17 months. We moved to a solely social media recruitment approach as clinic recruitment did not work well. With social media, we recruited 70 smokeless tobacco users over one year (averaging about 5-6 per month). We retained 70% of the study sample. Sensitivity analyses revealed no differences between completers and non-completers on key demographic (age, education, marital status and income) and tobacco use variables (baseline number of chews and dependence). The mean age of the sample was 35 (SD=11.7), 97% were male and 98% were Caucasian. We had solid intervention penetration. Almost all participants in both groups (96%) read all the messages they received. Over half of all participants in both groups found the intervention useful in helping them quit smokeless tobacco and over 90% would recommend it to a friend. In the SGR arm, participants responded via text to their alerts to chew the majority of the time (72% median response rate/person). At end of treatment follow-up, the SGR arm had a higher rate of self-report cessation (Intent-to-treat where missing data were coded as using smokeless: SGR= 22% vs Control=9%). As is consistent with the field, biochemical validation proved not to be feasible in this text-based intervention.

Common themes from 16 semi-structured interviews at end of program with SGR participants revealed that many thought the program was too short and “if it was just a couple more weeks I probably could have quit”

and “I will be honest it will probably take more than 4 weeks because it was just too hard some of the drops”. Participants also commented that the SGR program helped them manage cravings and helped them to not take chew when they were feeling the urge…” I had confidence that I could wait it out and I would get an alert to chew soon”. Participants also found support messages that talked about health effects and money saved from quitting very beneficial. Further, SGR participants noted that stopping the support messages on the quit day or last day of reduction was like “dropping them off a cliff” with no support when they needed it most.

We completed self-report follow-up assessments with all participants at 6-months to determine the sustainability of our intervention effects and found that cessation rates did not significantly differ between the two treatment arms (Intent-to-treat: SGR=22% vs Control=21%). We believe due to the high level of missing data and the intent to treat analysis we did not show a difference between interventions and these results need to be interpreted with caution. However, it is noteworthy that 75% of SGR participants who were quit at end of treatment remained quit at 6-months speaking to the sustainability of the SGR intervention. These results support the need to add an additional assessment at 3-months to determine the more proximal time to quitting.

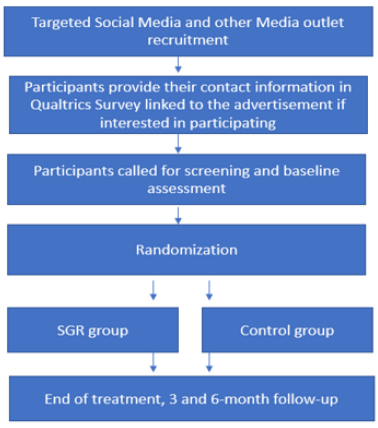
Table 2. Lessons Learned from Pilot and Changes made to Proposal

Areas for Improvement	Changes for Current Proposal
Length of time for accrual of our sample	Clinic recruitment was not feasible in our pilot. Once we switched to a social media recruitment approach, at the suggestion of Dr. Severson our metrics improved significantly. We plan to recruit solely using media outlets (including social media) and will expand our targeted recruitment area to increase reach. Dr. Severson will consult on recruitment in the current study.
4-week reduction period was too short for many smokeless tobacco users	We will extend our reduction period to 6 weeks.
30% attrition rate	High attrition rates (as high as 60%) have been reported in other low touch smokeless tobacco use cessation trials; therefore, we plan to institute text-based check-ins with our participants every 3-4 weeks after the intervention period to increase engagement.
No support after reduction or quit day in SGR group	We will start support messages 2 weeks before the quit date and extend them to 4 weeks after the quit date.

Strengths of our pilot work include strong evidence of feasibility and acceptability of the intervention. The SGR group had an excellent response rate to the SGR texts (72%), showing that smokeless tobacco users will interact with our intervention. Further, our self-report quit rates were promising and much higher in the SGR group (22% vs 9%, Cohen’s *d* equivalent=0.55, medium effect) in the short term, and these quit rates were sustained in the SGR group at 6-months; most chewers who quit at end of treatment remained quit at 6-months (75%). After critically evaluating our pilot work, we found areas for improvement for the current study (see **Table 2**). **Thus, our pilot work found that a text-based SGR intervention is both feasible and acceptable among underserved smokeless tobacco users and warrants further testing. For the current study we have included an evidenced-based control condition to determine if our SGR intervention improves quit rates compared to an available evidenced-based cessation intervention. Results of this study will inform future treatment strategies in this population of tobacco users.**

Overall Strategy

Figure 2: Consort Diagram



We will recruit smokeless tobacco users (N=500) and randomize them to receive the SGR intervention (N=250) or the Enough Snuff intervention (N=250). We will conduct phone-based or smart phone-based assessments with participants at baseline prior to randomization, end of treatment, 3 and 6-month follow-up after intervention completion. The primary outcome will be self-reported 7-day point smokeless tobacco use at 6-months (yes/no). We will biochemically confirm a subset of participants who report quitting via saliva samples using NicAlert test Strips (20% of sample who report quitting split between intervention and control group). NicAlert strips can be used with all tobacco types and have been used with smokeless tobacco users.[35] We will randomly select these participants at end of program, 3 and 6-month survey time points as to not confound intervention results. We will conduct a supplemental analysis to compare self-report and biochemically confirmed quit results. The secondary aims are to assess: 1) the efficacy of the text-based SGR intervention compared to the control intervention on changes in withdrawal, craving, self-regulation and restraint across the 6-month period and 2) explore whether changes in withdrawal, craving, self-regulation and restraint mediate intervention effects on self-reported cessation at 6 months post-intervention **(Figure 2)**. We will follow participants regardless of whether they complete or adhere to the intervention.

Design Considerations. We chose our control comparator using guidance from the *Pragmatic Model for Compartive selection in Health Related Behavioral Trials*.[36] The main goal of our trial is to compare our new SGR intervention to a well established evidenced-based alternative like the Enough Snuff Intervention. We decided against adding nicotine replacement therapy or varenicline for smokeless tobacco users. A recent

Cochrane review found that the quality of evidence for NRT among smokeless tobacco users is low.[37] Varenicline has shown efficacy in the short term for smokeless tobacco cessation, however this is based on a recent meta-analysis that contained only three published trials. [38] Further, varenicline has increased exclusion criteria, side effects and low adherence levels in smokeless tobacco users.[36] Our goal is to have a trial that has the broadest inclusion criteria to reach the largest number of underserved smokeless tobacco users possible.

We also decided against biochemical verification of cessation in this study given that we found it was not feasible in our pilot. Other smokeless tobacco cessation studies also use self-report cessation as the primary outcome.[37,39] Much like these studies, our study is community-based and has comparable demand characteristics as both arms are interactive. Thus, according to the SRNT Subcommittee on Biochemical Verification (2000) guidelines,[40] biochemical verification is not feasible or warranted as there is no reason to believe that one treatment will group will lie or give false information relative to another treatment group in this study. However, to further assess feasibility for future work we will biochemically confirm via saliva samples using NicAlert test strips. Twenty percent of the sample who report quitting (split between intervention and control group) of participants will be randomly selected at end of treatment, 3 and 6-month survey time points as to not confound intervention results. We will conduct an analysis to compare self-report and biochemically confirmed quit results overall and by each treatment group.

We chose our primary outcome follow-up time-point at 6 months for several reasons. First, most comparable behavioral smokeless tobacco trials have used 6-months as the primary outcome[37,39] therefore we can easily compare our results to these previous trials. Further relapse following cessation usually occurs within six months, with no significant changes from 6 to 12 months.[41] A 6-month rather than a 12-month follow-up also allows for more rapid decisions on treatment efficacy.[42]

Study Setting and Sample. We will leverage successful recruitment strategies from our pilot study, our previous work, and work of our consultant Dr. Herbert Severson, who has recruited smokeless tobacco users via social media for several cessation studies. Further, we now will work with Kevin Danaher Consulting to aid in recruitment (**See Letter of Support and Recruitment and Retention Plan**). This is the same recruitment consultant firm that Dr. Severson has worked with to recruit thousands of smokeless tobacco users to treatment trials. We will recruit nationally, specifically targeting states with high smokeless tobacco use rates (**Table 3**). We will recruit from the Rural and Medically Underserved Areas in these states. Rural status will be determined by Rural-Urban Commuting Codes (RUCC) designated as non-metropolitan (designated as a RUCC code of 4 or above) [33] and Medical Underserved Areas as designated by Health Resources and Services Administration (HRSA) by an index of Medical Underservice of 62 or less.[34] We will recruit participants and verify upon screening that each participant county address has a 4 or higher RUCC code and/or has an IMU of 62 or lower. This is easily done by having participants provide their zip code. A large percentage of the counties in the states we are specifically targeting are rural (**Table 4**) and >75% of the counties are medically underserved. Most rural counties also qualify as medically underserved counties. However, many non-rural counties are also designated as medically underserved and would benefit from our intervention given the lack of medical providers and high poverty rates in these counties.[10]

Table 3. Smokeless Tobacco Population Pool

State	Total % Smokeless Tobacco Users	Male % Smokeless Tobacco Users
Wyoming	9.1	16.9
West Virginia	8.5	17.1
Mississippi	7.5	13.1
Montana	7.4	13.4
Oklahoma	6.7	13.9
Kentucky	6.7	12.4

Table 4. Rural Counties

State	% Rural Counties
Wyoming	91
Montana	69
Mississippi	79
Oklahoma	76
Kentucky	70
West Virginia	60

We plan to recruit all participants for the current study using social media and other media advertisement outlets (i.e., Facebook, Instagram, Google Ads). As we did in our pilot, we will create an advertising profile for the study targeted to our study population (e.g., smokeless tobacco users (chewer/dipper), over age 18, profiled for tobacco use) for rural and medically underserved counties in the U.S. The advertisement briefly describes the study and links to a project-specific landing page that includes project branding (e.g., study logo, name, and Duke University association), a simple contact form with name, phone number, email and two simple baseline questions (e.g., “Do you use smokeless tobacco (chew/dip) every day and use at least one or more tins/cans per week or more?” and “Please provide your zip code”). After they enter their information, a member of the study team can call to collect more information to determine if they meet the criteria for participation in the study. Targeting rural and medically underserved counties in North Carolina and four rural counties in South Carolina for our pilot study, we were able to recruit 70 smokeless tobacco users in one year

(approximately 5-6 per month) using these methods. Data from our targeted marketing profiles show Facebook and Instagram ads reached 15,147 people total over 30 days resulting in 22,055 ad views and 121 link clicks per month with a monthly advertisement budget of $200. To increase our recruitment numbers for the current study we plan to: 1) target rural and medically underserved counties nationally with high smokeless tobacco use rates; 2) increase our Facebook budget and work with Kevin Danaher recruitment consulting firm to manage our media platforms and 3) change ad messaging, demographic targeting and geographic targeting weekly to ensure we are recruiting a diverse sample. Even if we estimate similar, very conservative recruitment metrics as seen in our pilot, given our increased reach with national recruitment we anticipate we can recruit at least 168 participants a year (or 14 per month) from our proposed (social) media recruitment methods. Given our 3-year recruitment time frame, we anticipate having ample time to achieve the target enrollment of participants for this study.

Inclusion criteria will include: 1) 18 years of age and older, 2) Have used smokeless tobacco for the last year, currently (past 30 days) uses smokeless tobacco daily, and use of at least one or more tins/cans per week 3) Have an address in a rural census tract defined by a RUCC code of 4-10 and/or an IMU of 62 or lower; 4) Interested in participating in a cessation program; and 5) Have access to a cell phone with unlimited texting ability. **Exclusion criteria** include: 1) Non-English speaking; 2) Have smoked cigarettes or used any other tobacco product in the past 30 days (i.e., dual user); and 3) Currently participating in a smokeless tobacco cessation study. We are excluding dual users (those who use both cigarettes and smokeless tobacco) who plan to continue to smoke cigarettes. It is too challenging to promote scheduled gradual reduction when participants use more than smokeless tobacco. We will track how many participants are not eligible for this study because they do not meet this eligibility requirement. We did not exclude anyone from our pilot for not having his or her own cell phone or for using multiple tobacco products.

Recruitment and Data Collection. Advertisements for the study will be placed on Facebook, Instagram and Google Ads. For example, Facebook users will be shown an advertisement that shows a quit smokeless tobacco related image and quit smokeless tobacco related messaging (**Figure 3)**. Users who click on that advertisement will then be taken to a project-specific landing page that includes project branding (e.g., study logo, name, and Duke University association), a simple contact form with name, phone number, email and simple baseline question (e.g., “Do you use smokeless tobacco (chew/dip) every day and use at least one or more tins/cans per week or more?” and “Please provide your zip code”). Research staff will call these participants to screen them for eligibility and set up a baseline/enrollment phone visit where informed consent will be obtained and baseline study measures collected. All participants will be asked to provide the three best contact methods and times to reach them and contact information of two people the study staff could contact should they have issues reaching the participant. Follow-up assessments will be conducted over the phone or a smartphone option will be available for survey completion at the end of treatment, 3 and 6-months post-intervention. Study data collectors will be blinded to study arm. Our two research assistants will document who randomized each participant and will not conduct the follow-up assessment with those participants. We will obtain follow-up data on all participants regardless of adherence or completion of treatment. The follow-up rate in our pilot study was >70%, and we will use similar strategies to obtain follow-up data. To increase this follow-up rate, we also will maintain regular contact with participants in-between the end of program 3 and 6-month follow-up using cards, e-mails, and study updates summarizing study results. We will also use a graded compensation for surveys with $10 for baseline $15 for end of program, $20 for 3 months and $25 for 6-month follow-up. Participants will receive a bonus of $25 for completing all assessments.

Figure 3. Facebook Ad

Randomization. The target sample will be eligible and enrolled participants randomized to either the SGR (N=250) or control (N=250) intervention group. Computerized randomization will be used to deliver a permuted block randomization with block sizes of four that will be used to randomly assign participants to one of the two intervention groups. The randomization scheme generated by the study statistician will be administered using the REDCap system.

Interventions:

SGR Intervention Group. We will send those in the SGR intervention group a 6-week text-based scheduled gradual reduction intervention and 6 weeks of support text-messages. Typical SGR interventions have lasted for 4 weeks. We have increased our program to 6 weeks based on feedback from our pilot.

SGR program: The SGR program will occur over a six-week period to reduce frequency of smokeless tobacco use to zero by program completion. On the baseline survey, we will ask participants to report their typical wake and sleep times to determine average waking hours per day. During Week 1 of the program, we will ask participants to use smokeless tobacco according to their usual habit and text "s" before they chew. The purpose of this is to have participants self-monitor their behavior and become more aware of their smokeless tobacco use habit. At the completion of week one, the average number of times they chewed per day will be calculated and texted to participants, who will be asked to confirm the average number of chews per day. This will confirm that we are basing our reduction on the correct number of chews/dips, as under- or overestimating the number of chews/dips in our reduction schedule could impact quitting success. For example, if we underestimate the amount of smokeless tobacco use at baseline and base our reduction on this, the reduction schedule may be too difficult for participants and lead to failure.

For the reduction schedule we will use an algorithm similar to that of Cinciripini [7 8] and colleagues as well as Jerome and colleagues,[9] which involves taking the average number of chews or dips per day and reducing this number by 1/3 each week by progressively lengthening the interval between chewing/dipping and lengthening the time to first chew. The program ends at the end of Week 6 with a reduction to zero chews/dips (quit day). During the reduction period (Weeks 2-6), we will ask participants to only chew when they receive a text message telling them to do so. We also will ask them to only keep chew or dip in their mouth for 30 minutes and then remove it as smokeless tobacco users may try to compensate for fewer dips by leaving their current dip in longer. We will ask them to respond to the aforementioned text with an "s" when they chew. They will be asked to respond within 30 minutes of receiving the message; reminder texts will be sent if responses are not received within 30 minutes to bolster adherence and stress the importance of following the schedule in order to successfully quit. We also will ask them to text us if they chew at different times than when we text them. We will also text participants at the end of each day and ask how many times they chewed that day and compare that to what they texted to us during the day. This will help us to learn when participants are not following the schedule. Should participants indicate they are regularly chewing off-schedule, we will continue the intervention but contact the participants through automated SMS messages to reassess their smokeless tobacco use patterns and adjust their schedule as needed. **Table 5** provides a sample SGR schedule.

Table 5. SGR schedule for a participant who chews 8 times a day and has 16.5 waking hours.

Week 1	8 dips or chews/day	Self monitoring week
Week 2	6 dips or chews/day	1 dip/chew every 2hr and 45 minutes
Week 3	4 dips or chews/day	1 dip/chew every 4 hr and 10 minutes
Week 4	3 dips of chews/day	1 dip/chew every 5 hrs
Week 5	2 dips or chews/day	1 dip/chew every 7 hrs and 30 min
Week 6	1 dips or chews/day	1 dip/chew every 11 hrs and 20 min
QUIT DAY		

Table 6. Example Text Messages Developed for Smokeless Tobacco Cessation

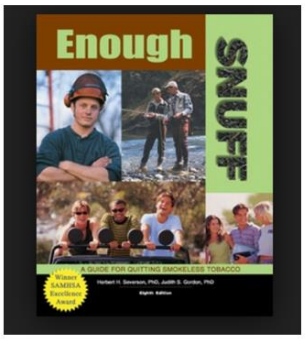
Content	Example	Number of Characters
Benefits of Quitting (Pre-Quit)	Oral cancer kills one person every hour. Many are young and otherwise healthy chewers. Now is the time to quit.	112
Motivation (Pre-Quit)	Quitting saves money. Write down the things you will do with the money you spend on chew. Put it somewhere to keep you on track.	128
Tempting Situations (Post-Quit)	Your body knows when to expect to chew. If you fool it by changing your routine, you may get fewer cravings.	109

Support Messages: SGR group participants will receive text-based support messages three times per day over six weeks. They will start receiving these messages 2 weeks before their quit date (e.g. last day of reduction) and will continue to receive these support messages for 4-weeks post quit date or reduction to zero chews. This will prevent the SGR group from getting an intolerable number of messages during their reduction period. The messages are based on constructs of Social Cognitive Theory[28] and the Health Belief Model. [29] Messages were developed from our pilot work and work from our consultant Dr. Herbert Severson. We interviewed 21 smokeless tobacco users (5 pre- pilot intervention and 16 post- pilot intervention) to obtain feedback on our messages, including readability, and gather information on what type of messages would be helpful when quitting. We found that messages around money and the health effects of chewing/dipping were most effective, so we have increased the number of these messages in the current study. Messages contain information on the health effects of chewers, benefits and barriers of quitting, making a quit plan, self-efficacy and motivation, and dealing with cravings, relapse and cost-savings **(Table 6).** Much like commonly available cessation interventions like smokefree.TXT and Dipfree.TXT, pre-quit messages will focus on health benefits of quitting, building confidence, and making a quit plan. Post-quit messages will focus on dealing with cravings and urges and relapse prevention. The text-based system with have interactive capabilities, can text the word CRAVE if they are having a craving and will receive a message to help them deal with the craving. Participants can also text the word SLIP if they have a slip after their quit date and will receive a message to get them back on track. Finally. participants can text MOOD if they need a positive message to boost their mood (**Table 7**).

Table 7. Example of Interactive text messages	
Content	**Example Message**
CRAVE	When you have an urge to chew ride it out by taking five deep breaths. It will go away, but don't fool yourself into thinking you can have just one dip. (*160 characters*)
MOOD	Talk and do things with other people, even if you don't feel up for it. This will increase your mood. (*100 characters*)
SLIP	Having a slip does not mean you can't quit. It does not mean you can't quit for good. You can do it! (*100 characters*)

Control Intervention Group (Enough Snuff Cessation Booklet and Motivational Text Messages)

Figure 4: Enough Snuff Cessation Booklet



Original Enough Snuff Intervention: The Enough Snuff Intervention is a self-help cessation booklet paired with two brief motivational phone counseling calls that occur one week after the cessation booklet is sent and the week of the set quit date. The first call focuses on increasing motivation for quitting (e.g. reasons for quitting), setting a quit date, and choosing a quit method. The second call focuses on dealing with tough situations when quitting and following through on quit plans. The Enough Snuff program has been shown to be efficacious in promoting smokeless tobacco cessation with quit rates ranging from 16-18% [43,44] and is an intervention endorsed by the NCI in their Research-Tested Intervention Programs (RTIPs).[45] For the current study we are delivering the program as follows:

Enough Snuff Cessation Booklet: We will provide all control participants with the Enough Snuff Cessation Booklet developed by our consultant Dr. Herbert Severson. The manual is organized around four key steps to quitting: 1) evaluating readiness and motivation to quit; 2) setting a quit date and selecting a quit plan; 3) dealing with withdrawal symptoms; and 4) maintaining quit status. We will send all participants a link to the manual via text-message as well as mailed a hard-copy of the booklet.

Motivational Text-Messages: To deliver the most equivalent intervention to the original *Enough Snuff* Program, we will send participants motivational text messages that map to the content of the phone counseling sessions. One week after the cessation booklet is sent we will text participants twice a week for the next 5 weeks. We will model the messages after the phone content and messages will focus on: motivation to quit (Week 1), setting a quit date (Week 2), picking a quit plan (Week 3), motivation to follow-through with plan (Week 4) and dealing with tough situations when quitting (Week 5). Messages will refer to the Enough Snuff booklet ask for a response from participants (See **Table 8**). We chose to send text messages to participants instead of phone calls as texting is consistent with our mode of contact with participants, less expensive, expands our reach, and is highly acceptable according to our pilot work.

Table 8. Example Text Messages Mapped from Enough Snuff Support Phone Calls

Content	Example	Number of Characters
Motivation	Make a list of your reasons for quitting. Text us one reason why you are quitting.	67
Quit Date	Setting a quit date increases your chances of quitting. Pick a date in the next two weeks and give quitting a try. What will be your quit date?	116
Quit Plan	Having a quit plan is important. Think about your plan. Text Y if you have a quit plan.	70
Following Quit Plan	Don't forget your quit plan! Text Y if you have a quit plan. Is your quit plan working to help you reach your goals?	93
Dealing with Tough Situations	Don't temp yourself- take everything out of your home, care and workplace that reminds you of chewing. What will you remove?	104

Intervention Delivery. *Mosio* will manage the technical aspects of the SGR computer-based program, the support messages and the motivational messages in the control group. *Mosio* will provide the two-way text messaging platform that we will use for this study. This platform allows to communicate with participants, collect data and contact participants via mobile text-messaging for follow-up. This is the same company and program our team successfully used as the texting platform for our pilot and was approved by our Information Security Office. The **Participant interface** with the intervention will be entirely through SMS messaging. Outbound messages from the intervention to participant will pass through an SMS gateway that queues each message, delivers it to the cell provider (which passes to the participant's phone), and returns delivery status (success or failure) to the intervention application. Inbound messages from participants to the intervention, such as a reply indicating whether they chewed, will be queued at the gateway and retrieved each minute by the application. **Study staff interface** with the intervention through a web-based dashboard and email messages from the application. Through the dashboard, staff will see aggregate information and can identify individual participants by criteria such as SGR status and drill down to their detailed data. Manual outbound SMS messages can be delivered from the dashboard using templates or freeform (for example, to respond to a participant who has requested help via SMS).

Measures

Outcomes and Mediators

Self-report smokeless tobacco cessation will be assessed at the end of treatment, 3 and 6-months post-intervention. **Self-report smokeless tobacco cessation at month 6 will be the primary outcome**. Secondary outcomes, which will be subsequently evaluated as mediators of the intervention effects, will be assessed at baseline, end of treatment, and 3 and 6-months post-intervention.

Primary Outcome: Smokeless Tobacco Cessation Outcome. Self-reported abstinence from tobacco use will be collected at end of treatment, 3 and 6-months post-intervention. We will measure 7-day point prevalence abstinence by asking participants, “In the past 7 days, have you used smokeless tobacco (chew or dip)?” This binary outcome will be dichotomized as 0=no and 1=yes. We will also randomly select a 20% (10% in control and 10% in intervention arm) of those who report quitting at the end of treatment, 3 and 6 months to biochemically confirm cessation using saliva cotinine strips. NicAlert Semiquantitative test strips will be used and a 10 ng/ml cutoff will indicate exposure. Biochemically validated cessation at each of these assessment points will be coded as 0=no and 1=yes.

Mediator: Craving. We will assess craving using the Smokeless Tobacco Evaluation Questionnaire (STEQ) based on the Cigarette Evaluation Questionnaire (mCEQ) modified for ST users.[46] The STEQ is a 12-item scale assessing the degree to which participants experience the reinforcing effects of smokeless tobacco on a 7-point Likert scale. The scale has five domains: chewing satisfaction, psychological reward, enjoyment of sensations in cheek/gum, craving reduction, and aversion.

Mediator: Withdrawal. We will assess withdrawal using the self-report seven item Minnosota Nicotine Withdrawal Scale[47] as has been used in other smokeless tobacco cessation trials assessing withdrawal. This seven-item scale measures withdrawal symptoms (i.e., irritability, anxiety, difficulty concentrating, restlessness, increased appetite or weight gain, depression, and insomnia) and measured on an ordinal scale (0= not present) to 4 (severe). A total score ranging from 0 to 28 will be derived to measure severity of withdrawal symptoms, with higher total scores representing greater withdrawal. Internal consistency of the scales are reported to be between α= 0.76-0.91.

Mediator: Self-regulation. We will assess self-regulation using the Short-form Self-Regulation Questionnaire, which is a 31 item self-report survey measuring the ability to regulate behavior and achieve goals.[48] Participants indicate the extent to which they agree with each item using a 5-point Likert scale: 1 (Strongly Disagree), 2 (Somewhat Disagree), 3 (Neutral), 4 (Somewhat Agree), and 5 (Strongly Agree). The measure has a total scale computed by summing the items, with higher total scores indicating increased self-regulation. Internal consistency of the scale is reported to be α=0.92.

Mediator: Restraint. We will measure restraint using a modified version of the Smoking Restraint Questionnaire[49] for smokeless tobacco by replacing all smoking references with smokeless tobacco. The Smoking Restraint Questionnaire is a four-item survey. The two binary questions of the questionnaire are scored 1 (No) and 5 (Yes). The two multiple-choice items are scored from 1 to 5. Total smokeless tobacco restraint is calculated as the sum of the four items. The minimum possible score is 4 and the maximum possible score is 20, with higher total scores indicating higher levels of restraint. Internal consistency of the scale is reported to be α=0.74.

Sample Characteristics : Baseline sociodemographic and clinical measures will be collected to describe the characteristics of the total sample and intervention arms. Many of these measures are potential important moderators or mediators of intervention effects that will be explored after the specific aims are fully examined.

- Demographics and Relevant Biological Variables. We will assess age, sex, race, education, marital status, and socio-economic status (SES) at baseline using measures adapted from our prior research.
- Smokeless and other Tobacco Use History. At baseline, participants will be asked about their tobacco use habit including: number of chews/dips per day, number of quit attempts in the past year, age of chewing/dipping initiation and past use of other tobacco products including electronic cigarettes.
- Nicotine Replacement Therapy (NRT) Use: We will ask participants at all follow-up time points if they have used any NRT including the patch, gum or lozenge.
- Nicotine Addiction. We will assess nicotine addiction at all time-points using the Severson Smokeless Tobacco Dependence Scale-Short Form (SSTDS). The SSTDS is a validated questionnaire has eight items with a range of scores from 0-19 with higher scores being most addicted to nicotine.[47]
- Self-efficacy. At all time-points we will measure self-efficacy using a similar 9 item scale to the Temptations scale. We will adapt the scale by switching out smoking with chewing/dipping. Sample items read, "How

confident are you that you would not chew in the following situations: when you are very angry about something or someone, when you feel you need a lift, etc." (1=Not at all confident and 5=Extremely confident).

- Alcohol Use Disorder Identification Test (AUDIT-3). At all time-points we will use the AUDIT, a 3 item self-report scale that measures risky drinking, as this may influence quit rates. [50]

Process Measures: Process measures that could impact outcomes will be collected at baseline, during intervention administration, at the end of treatment, 3 and 6 month follow-up.

- Adherence (Intervention Group). Adherence to the SGR intervention will be calculated two ways. First, we will measure time to response from the SGR message. Second, we will create a categorical variable (0=respond in more than 30 minutes, 1=respond after 30 minutes. If a participant responds to less than half of chewing/dipping prompts in one day, we will exclude this day from the adherence analysis examining whether overall adherence predicts quit rate and/or smokeless reduction in the SGR group.
- Adherence (Control Group). Participants will be asked at all follow-up time points how often they read the cessation booklet using a using a 5-point Likert scale (1 = none, 2 = some, 3 = most, 4 = the entire guide, and 5 = the entire guide more than once). [44]
- Satisfaction with Intervention. Participants in both arms will be asked at end of treatment survey 1) "How useful was the intervention in helping you to quit smokeless tobacco?" (Not at all useful=1, Extremely useful =5) and 2) "Would you recommend the program to a friend?" (Definitely would not recommend=1, Definitely would recommend=5).