Treating Nicotine Addiction in Caregivers of Children at American Family Children's Hospital

PI: Brian Williams, MD

10/27/2023

SCIENTIFIC PROTOCOL

Treating Nicotine Addiction in Caregivers of Children
at American Family Children's Hospital

Protocol Number: 2023-0727
Principal Investigator: Brian Williams, MD
Funding Source: UW Department of Pediatrics Faculty R&D Grant

Protocol Version History

Protocol Version	Version Date	Summary of Revisions Made	Rationale
1.0	06/30/2023	Initial version	
2.0	10/27/2023	Revision #1	Clarify Informed Consent, simplify payment structure, simplify contacting participants, simplify survey questions

REMINDER: update the Table of Contents before considering the document or draft final. To update the Table of Contents, right click anywhere below and then select "Update Field."

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1.0 STATEMENT OF COMPLIANCE

I confirm that I have read this protocol. I will comply with the IRB-approved protocol, and applicable regulations, guidelines, laws, and institutional policies.

I agree to ensure that all staff members involved in the conduct of this study are informed about their obligations in meeting the above commitment.

Name	Signature	Date
Brian Williams, MD		5/22/2023
Principal investigator		

2.0 LIST OF ABBREVIATIONS

AE	Adverse Event
AFCH	American Family Children's Hospital
CTRI	Center for Tobacco Research and Intervention
DSMB	Data & Safety Monitoring Board
DSMC	Data & Safety Monitoring Committee
DSMP	Data & Safety Monitoring Plan
EHR	Electronic Health Record
FDA	Food and Drug Administration
HIPAA	Health Insurance Portability and Accountability Act
ICTR	Institute for Clinical and Translational Research
IRB	Institutional Review Board
NIH	National Institutes of Health
NRT	Nicotine Replacement Therapy
PHI	Protected Health Information
PI	Principal Investigator
REDCap	Research Electronic Data Capture
SAE	Serious Adverse Event
TSE	Tobacco Smoke Exposure
UW-CTRI	University of Wisconsin – Center for Tobacco Research and Intervention

3.0 STUDY SUMMARY

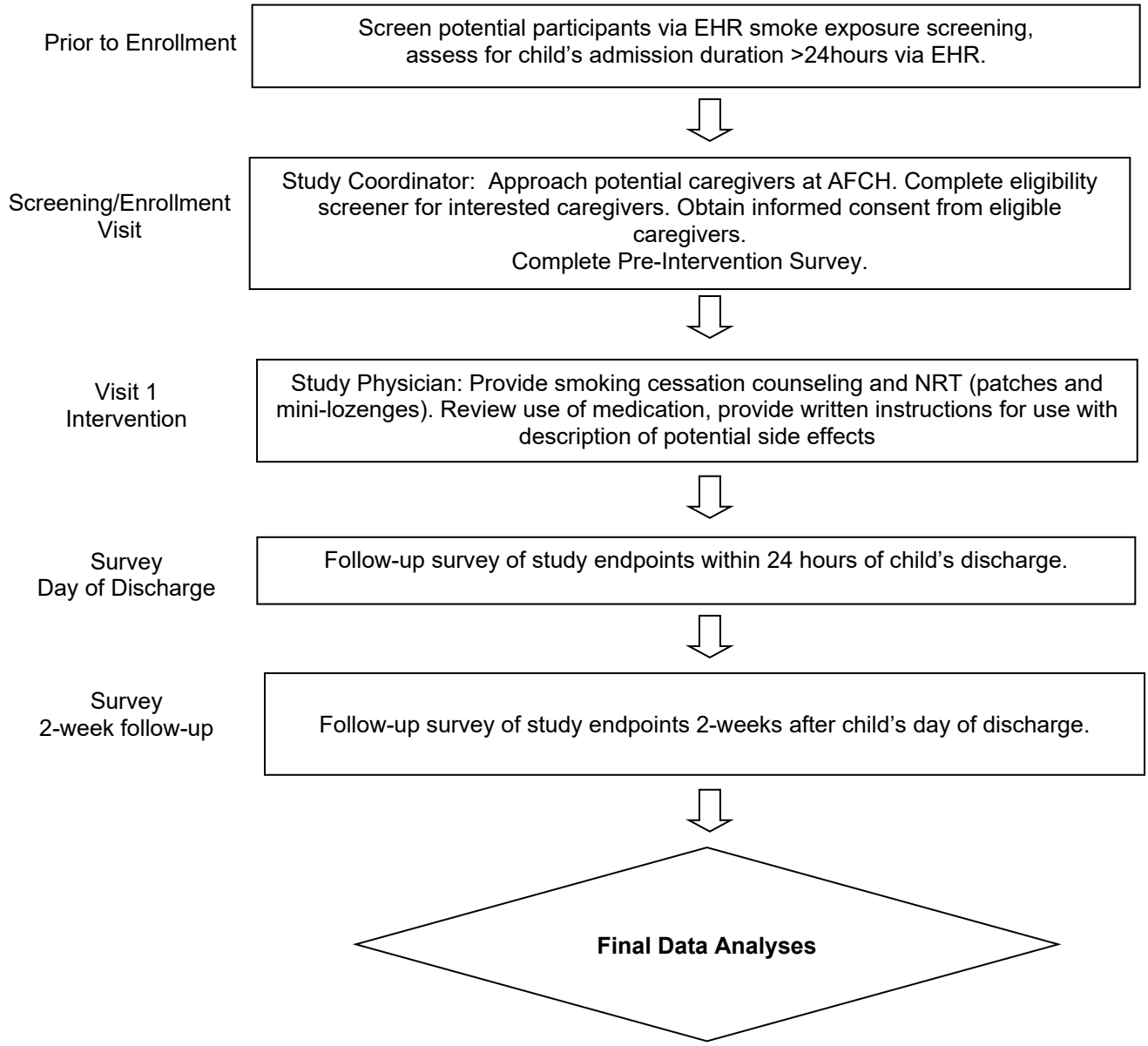
3.1 Synopsis

Full Title	Treating Nicotine Addiction in Caregivers of Children at American Family Children's Hospital
Short Title	Treating Caregivers who smoke at AFCH
Protocol Number	2023-0727
ClinicalTrials.gov Identifier & Summary	ClinicalTrials.gov ID: NCT06051474 Summary: This study is being done to assess the feasibility and acceptability of providing NRT and counseling to caregivers who smoke while their child is hospitalized. We hypothesize that 50% of eligible caregivers will enroll in the program, use NRT, and recommend program implementation. We will also examine how smoking behavior changes for participants who enroll in the study.
Number of Site(s)	This study is being done at 1 clinical site, American Family Children's Hospital in Madison, WI on the inpatient med-surg (non-ICU) units.
Phase	Feasibility
Main Inclusion Criteria	• Adults who identify as the primary caregiver during their child's hospitalization. • Smoke ≥5 cigarettes per day • Willing to use NRT during child's hospitalization
Main Exclusion Criteria	• Currently using smoking cessation medication (bupropion, varenicline, nicotine replacement therapy [NRT]) • Contraindication to NRT (pregnancy, myocardial infarct in past 2 weeks)

Objective(s)	Primary Objective • To evaluate the feasibility and acceptability of a smoking intervention (NRT and cessation counseling) for caregivers of children admitted at American Family Children's Hospital (AFCH). Secondary Objectives • To evaluate effects of a smoking intervention on additional key outcomes, such as the number of cigarettes a caregiver smokes per day while their child is hospitalized, number of times they leave the bedside to smoke per day, and changes in self-efficacy and interest in quitting pre- and post-intervention.
Endpoints	Primary Endpoint • Feasibility will be measured by 1) enrollment in study (N of eligible who enroll/N of eligible who are invited to enroll) and 2) NRT use (N who use NRT/N enrolled in study). • Acceptability will be measured using Likert scales assessing participants likelihood to recommend program implementation. Secondary Endpoints • Change in cigarettes smoked per day at day of discharge and 2 weeks post-discharge, compared to pre-intervention • Number of times participant left bedside/day to smoke compared to pre-intervention prediction • Changes in self-efficacy score at day of discharge and 2 weeks post-discharge, compared to pre-intervention • Change in interest in quitting at day of discharge and 2 weeks post-discharge, compared to pre-intervention
Study Design	This is an open label, 2-week single center study assessing the feasibility, acceptability, and preliminary efficacy of NRT and counseling in parents who smoke while their child is hospitalized.
FDA Regulatory Overview	The protocol uses nicotine replacement therapy (NRT). NRT is an FDA-approved, over-the-counter medication. The use of the medication falls under IND Exemptions "Lawfully Marketed Drugs (21 CFR 312.2(b)(1)) or Biologics"
Study Intervention	Adults will receive a 2-week supply of nicotine patches to place on skin (14mg or 21mg; dosing depending on tobacco use per package insert) and oral nicotine mini-lozenges (2mg, 4mg, dosing depending on tobacco use per package insert). All participants will also receive a single smoking cessation counseling session with a physician. Surveys will be completed pre-intervention, within 24 hours of hospital discharge, and 2-weeks after hospital discharge.
Total Number of Subjects	A total of 50 subjects will be recruited for the study.
Study Population	Adults of all genders and races/ethnicities, aged ≥18 years, who smoke ≥5 cigarettes per day and are the primary caregiver of a hospitalized child at AFCH.
Statistical Methodology	Basic descriptive statistics will be used to assess feasibility (percentage enrolled, percentage using NRT) and acceptability (likelihood to recommend program implementation). General linear modeling will be used to assess key smoking outcomes.
Estimated Subject Duration	The duration of the study for each subject will vary, based on duration of hospitalization, but will last approximately 2-3 weeks, on average.
Estimated Enrollment	Study enrollment and follow-up will occur over 6 months with the total expected duration of the trial to be 8 months.

Period & Study Duration	

3.2 Schematic of Study Design



4.0 KEY ROLES

The following is a list of all key personnel and roles:

Principal Investigator	**Brian Williams, MD** Assistant Professor of Pediatrics and Medicine UW-School of Medicine and Public Health 600 Highland Ave, H4/418 MC 4108 Madison, WI 53792 608-262-9364 bswillia@medicine.wisc.edu
Participating Site(s)	American Family Children's Hospital 1675 Highland Ave. Madison, WI 53792
Medical Monitor	Brian Williams, MD Assistant Professor of Pediatrics and Medicine UW-School of Medicine and Public Health 600 Highland Ave, H4/418 MC 4108 Madison, WI 53792 608-262-9364 bswillia@medicine.wisc.edu
Local Laboratory Services	N/A
Central Laboratory Services	N/A
Data and Safety Monitoring Board	UW-CTRI DSMB Dr. James Clearly, Dr James Sosman, Dr. Burke Richmond
Funding Sponsor	UW-SMPH, Department of Pediatrics 600 Highland Avenue, MC 4108 608-263-8558 Rebecca.bound@wisc.edu
NIH Point of Contact	N/A
Biostatistician	Megan Piper, PhD Professor of Medicine UW-School of Medicine and Public Health 1930 Monroe St, Madison, WI, 53711-2059 608-265-5472 mep@ctri.wisc.edu
Data Coordinating Center	UW-Center for Tobacco Research and Intervention 1930 Monroe St #200, Madison, WI 53711 608-262-8673 jlmatthews@ctri.wisc.edu
Clinical Coordinating Center	N/A

5.0 INTRODUCTION

5.1 Background: Pediatric Tobacco Smoke Exposure

Cigarette smoking is the number one preventable cause of death in the US and worldwide[1]. Smoking is particularly problematic for caregivers of children as tobacco smoke exposure (TSE) can adversely affect the health of the exposed child in addition to the caregiver. Children exposed to tobacco smoke are known to be sick more frequently[2] and have more severe outcomes in cases of asthma[3], pneumonia[4], bronchiolitis[5], and influenza[6]. Furthermore, children with TSE can have lower academic performance[7] and are at higher risk of becoming smokers themselves[8]. It is estimated that 38% of children aged 3-11 experience TSE[9]. Thus, finding effective interventions to decrease pediatric TSE can have a huge impact on the health of a child.

The hospitalization of a child is a stressful time for caregivers. In caregivers who smoke, this stress can be compounded by nicotine withdrawal (anxiety, irritability, difficulty concentrating) while their child is hospitalized. The need to smoke during a child's hospitalization to prevent withdrawal and cope with stress limits a caregiver's time at the bedside, can lead to a caregiver missing rounds or treatment, and their return to the bedside after smoking can expose the child and hospital staff to third-hand smoke. Thus, a child's hospitalization could be a 'teachable moment' for caregivers who smoke and presents an opportunity to intervene and decrease the negative effects of caregiver smoking.

5.2 Current Standard of Care

For caregivers who smoke in the pediatric setting, there is a lack of data on how to effectively intervene, no existing standard of care, and interventions with adults who smoke in the pediatric setting are rare.

The current standard of care for treating adult smokers is by combination therapy of both an FDA-approved smoking cessation medications and behavioral counseling[10]. FDA approved medications include NRT, Bupropion, and Varenicline. NRT in the form of patches, gum, and lozenges are available over the counter. Given the high volume of evidence supporting NRT and counseling for treatment of smoking[10], along with the low-risk profile of NRT, we chose these two interventions for our study. This approach (NRT + Counseling) is similar to what a participant would receive if they were to call the Wisconsin Tobacco Quit Line.

5.3 Study Intervention: NRT and Behavioral Counseling

Nicotine Replacement Therapy: NRT is a well-established medicine, and standard of care, for the treatment of smoking cessation[10]. We will be using NRT patches and mini-lozenges which are both available over the counter. Patches are worn for 24 hours at a time and provide a steady state of nicotine to reduce cravings. NRT mini-lozenges will also be used on an as needed basis by participants to treat urges to smoke. Patches come in 7mg, 14mg, and 21mg formulations. Dosing will be based on the package insert, with the number of cigarettes smoked per day determining patch dosing (>10 cigarettes per day = 21mg patch, <10 cigarettes per day = 14mg patch). Participants with a latex allergy will only be offered mini-lozenges. Mini-lozenges come in 2mg and 4mg formulations. Dosing will be based on the package insert which recommends 2mg mini-lozenges for individuals who smoke their first cigarette >30 minutes after waking up and 4mg mini-lozenges for individuals who smoke their first cigarette ≤30 minutes of waking up.

Behavioral Counseling: Counseling for smoking cessation is also a well-established, evidence-based treatment for smoking cessation[11]. Counseling sessions will last approximately 20 minutes and will focus on 3 objectives: 1) review participants' motivation for smoking and for quitting and 2) use the information on participants' motives to provide tailored education regarding a) benefits of quitting smoking to the caregiver and the child, b) strategies to reduce nicotine withdrawal symptoms/urges to smoke during the hospitalization, and c) benefits of smoke-free home and car rules; and 3) review smoking cessation resources.

5.4 Rationale

Intervening with caregivers who smoke offers an opportunity to improve the health of both the caregiver who smokes and the child who is exposed to tobacco smoke. The pediatric hospital setting offers a "teachable moment" where caregivers may be more motivated to change their smoking behavior. Due to the lack of data on how to effectively intervene with caregivers who smoke in the pediatric hospital, this study will provide data on the feasibility and acceptability of providing a standard of care smoking cessation intervention to participants. It will also provide some basic data on treatment outcomes that will be used to estimate sample sizes for future, definitive treatment interventions.

6.0 STUDY OBJECTIVES AND ENDPOINTS

Objectives	Endpoints
Primary	
To evaluate the feasibility and acceptability of a smoking intervention (NRT and cessation counseling) for caregivers of children admitted at American Family Children's Hospital (AFCH).	Feasibility will be measured by 1) enrollment in study (N of eligible who enroll/N of eligible who are invited to enroll) and 2) NRT use (N who use NRT/N enrolled in study). Acceptability will be measured using Likert scales assessing participants likelihood to recommend program implementation.
Secondary	
To evaluate effects of a smoking intervention on additional key outcomes, such as the number of cigarettes a caregiver smokes per day while their child is hospitalized, number of times they leave the bedside to smoke per day, and changes in self-efficacy and interest in quitting pre- and post-intervention.	Change in cigarettes smoked per day at day of discharge and 2 weeks post-discharge, compared to pre-intervention. Number of times participant left bedside/day to smoke compared to pre-intervention prediction. Changes in self-efficacy score at day of discharge and 2 weeks post-discharge, compared to pre-intervention. Change in interest in quitting at day of discharge and 2 weeks post-discharge, compared to pre-intervention.

7.0 STUDY DESIGN

7.1 General Design

This feasibility, single site, prospective, open-label study will assess the feasibility and acceptability of providing NRT and counseling to adult caregivers who smoke while their child is hospitalized. Additionally, the study will assess preliminary outcomes of the intervention on key smoking outcomes (changes in the number of cigarettes a caregiver smokes per day while their child is hospitalized, number of times they leave the bedside to smoke per day, and changes in self-efficacy and interest in quitting from pre- to post-intervention). Subject accrual will occur over 6 months with the total duration of the trial expected to be 8 months.

Following the completion of screening and informed consent, eligible subjects will complete a pre-intervention survey. They will then have 1 visit with the study physician during which they will receive counseling on smoking cessation as well as a 2-week supply of nicotine patches and mini-lozenges. Within 24 hours of their child's discharge, they will complete a second survey describing use of NRT during the child's hospitalization, leaving the bedside to smoke, acceptability of the intervention, and changes in smoking behavior and quit interest/efficacy. At 2 weeks post-discharge, subjects will again complete a follow-up survey to assess smoking behavior, NRT use, quit interest/efficacy, and implementation of smoke-free home/car rules.

If a participant's child remains hospitalized at 2 weeks, they will be offered an additional 2 weeks of NRT.

7.2 End of Study Definition

The end of the study is defined as the date of completion of any final follow-up activity or data collection described in the protocol.

8.0 SUBJECT SELECTION

8.1 Inclusion & Exclusion Criteria

Eligibility will be determined by inclusion and exclusion criteria below. Inclusion and exclusion criteria will be assessed prior to informed consent to minimize burden on potential study participants' time. Criteria will only be reviewed with potential participants who's child screens positive for tobacco smoke exposure.

Inclusion Criteria
1. Hospitalized child will have a 'yes' response to the screening question, "Does anyone in your household smoke"
2. Hospitalized child is expected to be admitted for >24 hours
3. Caregiver is at least 18 years of age
4. Participant self-identifies as the primary caregiver of the hospitalized child during the hospitalization (not limited to one caregiver per child)
5. Participant smokes ≥5 cigarettes per day
6. Participant is willing and able to use NRT
7. Participant is not currently pregnant, trying to get pregnant, or breastfeeding and willing to use acceptable birth control for duration of medication use
8. Participant is willing to comply with all study procedures and be available for the duration of the study

Exclusion Criteria
1. Contraindication to NRT use (pregnancy, myocardial infarction in past 2 weeks)
2. Previous reaction to the nicotine patch or mini-lozenge that prevented them from continuing to use it
3. Allergy to Adhesive Tape
4. Current Diagnosis of congestive heart failure, stomach ulcers, seizure disorder, or diabetes.
5. Diagnosis of stroke in the past year
6. Diagnosis of and/or treatment for schizophrenia, other psychotic disorders, or bipolar disorder within the last 5 years
7. High Blood Pressure not controlled with medication
8. Current use of smoking cessation medications (any NRT, bupropion, varenicline)
9. Caregiver's child is being cared for by PI (Dr. Brian Williams)
10. Need for an interpreter

8.2 Vulnerable Populations

No vulnerable populations will participate in this research.

8.3 Lifestyle Considerations

N/A

8.4 Subject Identification

8.4.1 Electronic Health Record (EHR) Query

To identify potential caregivers in the hospital who smoke, the EHR of pediatric patients admitted to the med-surg (non-ICU) units at AFCH will be reviewed by Dr. Williams to identify which patients screened 'yes' to the question, "Does anyone in your household smoke". Dr. Williams will conduct further screening to determine if the child is expected to be admitted for >24 hours by reviewing the patient's chart and discuss expected discharge with the bedside nurse. The team will also ensure the pediatric patient is not being cared for by Dr. Williams and no interpreter is needed.

This screening protocol is similar to the approach used in prior research at AFCH. See IRB ID: 2019-0866.

8.5 Subject Recruitment

Participants in this study will be caregivers of children admitted at American Family Children's Hospital (AFCH). A total of 50 participants will be recruited from 1 site, AFCH in Madison, WI. Potential participants will be identified through the hospitalized child's EHR. Individuals from populations who are underrepresented in clinical research (e.g., racial and ethnic minorities, women, individuals from rural and underserved communities, older individuals, federally recognized nations and tribes) will be prioritized for enrollment with a goal of ensuring that all eligible individuals are given the opportunity to participate and that research findings can be generalizable to the entire population. Please note that due to the limited resources available for this pilot study, we will not have access to interpreter services but seek to address this in a larger, future study.

Given the specific population being recruited (individuals who smoke and are the primary caregivers of a hospitalized child) no additional specific recruitment strategies will be employed.

8.6 Remuneration and Retention Strategies

Strategies for retention include:

- Participants will receive a reimbursement of $20 for each completed study survey (pre-intervention, within 24 hours of hospitalized child's discharge, 2 weeks post-discharge) for a maximum total of $60. The reimbursement will be provided as cash for the pre-intervention and as a $20 gift card (emailed to participant) for surveys completed on day of discharge and 2-weeks after discharge from the hospital. If a participant does not have a valid email-address, we would mail them a gift card to their home address.

8.7 Early Termination and Withdrawal

Subjects are free to withdraw from participation in the study at any time upon request.

The Principal Investigator (PI) may discontinue or withdraw a subject from the study for the following reasons at his discretion:

- Pregnancy
- If any clinical adverse event (AE) or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the subject

Given the primary outcome of feasibility, subjects who sign the informed consent form and do not receive the study intervention will not be replaced. Similarly, subjects who sign the informed consent form, receive the study intervention, then subsequently withdraw, or are withdrawn or discontinued from the study, will not be replaced.

9.0 STUDY AGENT (STUDY DRUG, DEVICE, BIOLOGIC, VACCINE, ETC.) AND/OR PROCEDURAL INTERVENTION AND/OR BEHAVIORAL/SOCIAL INTERVENTION

9.1 Study Agent and Control Description

Study Product
The study product (medication) is nicotine replacement therapy (NRT) consisting of both nicotine patches and nicotine mini-lozenges. These forms of NRT are both FDA-approved medications for smoking cessation and are available over the counter for individuals ≥18 years of age. This study meets criteria for IND Exemption of a lawfully marketed drug (21 CFR 312.2(B)(1)). NRT meets the following required criteria to be listed under the IND exemption of a lawfully marketed drug: (a) the drug or biologic is lawfully marketed in the United States, (b) the research is not intended to be reported to the FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug, (c) the research is not intended to support a significant change in the advertising for the product, (d) the research does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product, and (e) the research is conducted in compliance with the marketing limitations described in 21 CFR §312.7

Participants in the study will receive a 2-week supply of both nicotine patches and nicotine mini-lozenges. Patches are worn for 24 hours at a time and are used to provide a steady state of nicotine to reduce cravings. Mini-lozenges are used on an as needed basis to treat acute cravings. The nicotine patch is dosed based on the number of cigarettes smoked per day (>10 = 21mg patch per day, <10 = 14mg patch per day). Nicotine lozenges are dosed based on how soon after waking an individual smokes the first cigarette (≤30 mins after waking = 4mg mini-lozenge, >30 minutes after waking = 2mg mini-lozenge). Participants will be provided NRT at the conclusion of their counseling session with Dr. Williams. They will be encouraged to begin using NRT at the time that it is dispersed. Recommended dosing schedules are provided (patches - apply a new patch daily, mini-lozenges – use as needed for cravings). Only participants whose child is still hospitalized 14 days after study enrollment will receive an additional 2-week supply of NRT.

Active Control: N/A
Placebo: N/A

9.1.1 Source

Nicotine patches and mini-lozenges will be ordered via standard of care institutional procedures. Neither product requires temperature control.

9.2 Study Procedural Intervention(s) Description

N/A

9.3 Study Behavioral or Social Intervention Description

Counseling Session:

Counseling sessions will last approximately 20 minutes and will focus on 3 objectives: 1) review participants' motivation for smoking and for quitting and 2) use the information on participants' motives to provide tailored education regarding a) benefits of quitting smoking to the caregiver and the child, b) strategies to reduce nicotine withdrawal symptoms/urges to smoke during the hospitalization, and c) benefits of smoke-free home and car rules; and 3) review smoking cessation resources.

9.3.1 Administration of Behavioral or Social Intervention

The behavioral intervention will be delivered in person and will consist of a single counseling session lasting approximately 20 minutes. It will be delivered by Dr. Brian Williams who is board-certified in both internal medicine and pediatrics. The intervention will occur either in the pediatric patient's room at AFCH or in a private conference room on the same floor as the child's hospital room (per caregiver preference). The intervention will occur on the same day as study enrollment.

9.3.2 Procedures for Training Interventionalists and Monitoring Intervention Fidelity

The behavioral intervention will be conducted by the PI who will document each counseling component that is covered during the session (Review participants motivation for smoking/quitting, Education, provide quit resources). If any part of the counseling session is not completed, this will be documented along with reason for not completing that component. If NRT is not accepted, this will also be documented along with reason for not accepting. Duration of counseling will be documented.

9.4 Method for Assigning to Treatment Groups

N/A

9.5 Unblinding Procedures

N/A

9.6 Study Intervention Compliance

The primary outcome of this study is feasibility. We record whether participants accept NRT and whether they complete the behavioral intervention (counseling session). Participants' use of NRT will be assessed via surveys. Given the pilot nature of this study with a focus on feasibility, we will not replace participants if they choose to not complete any part of the study intervention or withdraw completely from the study.

9.7 Concomitant Therapy

9.7.1 Permitted Concomitant Therapy

Aside from the prohibited concomitant therapy noted below, all additional medications that patients are taking will be allowed (per FDA package insert).

9.7.2 Prohibited Concomitant Therapy

Current use of any smoking cessation medications: NRT, bupropion, or varenicline.

10.0 STUDY VISITS AND PROCEDURES

10.1 Study Calendar

The procedures performed at each study visit are listed in the table below.

Procedure	Screening	Visit 1 (MD)	Within 24h of discharge	Post-Discharge
Date of Pediatric Admission	**+0-23 hours**	**+0-23 hours**	**1-14+ days**	**+14 days from discharge date**
Assess Inclusion/Exclusion Criteria	X			
Informed Consent	X			
Demographics	X			

Procedure	Screening	Visit 1 (MD)	Within 24h of discharge	Post-Discharge
Complete Survey	X		X	X
Administer Study Intervention		X		
Adverse Event Review and Evaluation			X	X

10.2 Screening and Enrollment

The Screening and Enrollment visits and procedures are described in detail below.

10.2.1 Pre-screening

Pre-screening will consist of reviewing the charts of pediatric patients admitted to AFCH in the previous 24 hours. Charts will be reviewed by the study MD who has completed HIPAA and human subjects training. Patients who are under the care of the study MD will not be reviewed. Only the nursing intake assessment in the EHR will be reviewed to identify if the admitted pediatric patient screened positive for "*Does anyone in your household smoke*". If the answer is 'no', this will be tallied but no additional information will be recorded, and the chart will be closed. If the answer is 'yes', the study physician will review the need for an interpreter as well as the History and Physical to determine if the child is likely to be admitted for an additional 24 hours. No information from the child's chart will be recorded. Hospital duration will also be reviewed with the bedside RN. If the child is expected to be admitted for >24 hours, the research coordinator will be notified to assess caregiver eligibility.

The research coordinator will approach caregivers to introduce themselves and briefly describe the study. Potentially interested participants will be screened for eligibility criteria and interest in learning more about the study (see document 'Study Invitation and Screening'). Those who are interested in learning more about the study will complete informed consent and all screening procedures as described below. Those who are not interested in learning more will have their response tallied but no additional information will be collected. The pre-screening discussion with potential participants is estimated to take less than 5 minutes.

10.2.2 Informed Consent

Overview: The informed consent process will be initiated prior to the individual's agreeing to participate in the study and continue throughout the individual's study participation. The consent form will be Institutional Review Board (IRB)-approved. To minimize the possibility of coercion or undue influence in the consent process, participants will be informed that their decision to participate or not participate will have no effect on the care their child receives. Only the caregiver who is participating in the study will be allowed to provide informed consent. The study will not enroll any individual who cannot provide their own informed consent.

Preliminarily eligible subjects will be approached in the child's hospital room. They will be invited to a separate conference room (or to stay in the child's room) for informed consent and formal screening. The screening questions will be reviewed with the participant after a brief study description. A consent waiver to ask the screening questions (prior to obtaining full consent) is being requested due to the minimal risk nature of the screening items and the desire not to waste caregivers' time with consent procedures if they are not eligible to participate. The informed consent process will be conducted following all federal and institutional regulations relating to informed consent. Informed consent will be obtained prior to conducting any study-related activities.

The informed consent process will be performed as follows:

- A video will be played by the research coordinator explaining the study, its risks and benefits, what would be required of the research subject, and alternatives to participation.

- The research coordinator will review the informed consent form and discuss the study in detail with the potential research subject.
- The subject will be asked to read and review the informed consent document.
- The subject will have the opportunity to ask questions and have all questions answered by the research coordinator and/or PI.
- The research subject will be given the opportunity to discuss it with family members, friends, clergy or others as they desire.
- The informed consent document must be signed and dated by the research subject.
- The research coordinator will review the informed consent document to ensure that all fields that require a response are completed.
- The research subject will be given a copy of an unsigned consent form. The original signed informed consent form is kept in a locked cabinet in the PI's office (which also requires a key to enter).

10.2.3 Screening Visit

During the screening visit, the research coordinator will explain the study, review inclusion/exclusion criteria, and obtain informed consent as described in section 10.2.2. If Inclusion/Exclusion criteria are not met, the reason will be recorded. Once informed consent is obtained and the participant meets all inclusion/exclusion criteria, the participant will be provided a study tablet to complete a baseline survey.

10.2.4 Enrollment

A research subject will be defined as "enrolled" in the study when they meet the following criteria:

- The subject has been consented by study staff.
- The subject and study staff have completed all screening documentation.
- The PI has verified that the subject meets all the inclusion criteria.
- The PI has verified that subject meets none of the exclusion criteria.
- The subject has scheduled a study visit.

10.2.5 Screen Failure and Re-enrollment

Individuals who do not meet the criteria for participation in this trial (screen failure) will not be rescreened during their child's hospitalization. They will be offered a referral to the Wisconsin Tobacco Quit Line.

10.3 On-Study/Follow-up Visits

After subjects have been enrolled, the visit activities and follow-up surveys are described in detail below.

10.3.1 Visit 1: Intervention - Counseling and NRT

All participants will receive a one-time visit with the study PI who also serves as the study physician. This visit will occur on the day of study enrollment, either in the patient's room or in a private conference room on the same floor as the child's hospital room – per caregiver preference. This visit will consist of a brief counseling session. Counseling sessions will last approximately 20 minutes and cover the 3 objectives of 1) review participants' motivation for smoking and for quitting and 2) use the information on participants' motives to provide tailored education regarding a) benefits of quitting smoking to the caregiver and the child, b) strategies to reduce nicotine withdrawal symptoms/urges to smoke during the hospitalization, and c) benefits of smoke-free home and car rules; and 3) review smoking cessation resources.

After the counseling session, participants will also be provided a 2-week supply of nicotine patches and nicotine mini-lozenges, along with instructions for their use. The study physician will review how to use the medication, dosing, benefits of use, and potential side effects of use. Data collected at this visit will include whether each objective of the counseling session was covered (participant motivations, education, smoking cessation resources), duration of counseling, and dose of NRT provided. If any

portion of the intervention is not completed, reasons for not completing will be documented. Participants whose child remains hospitalized 14 days after study enrollment will be offered an additional 2-week supply of both NRT patches and NRT mini-lozenges.

10.3.2 Follow-Up Number 1: Discharge Survey

Within 24 hours of discharge, participants will be contacted to complete a post-intervention survey via UW REDCap. Attempts will be made to complete the survey on a study tablet at the bedside. If we are unable to complete the survey using a study tablet, a link to the UW REDCap survey will be emailed to the participant from a secure, University of Wisconsin email and will assess NRT use during the hospitalization and likelihood that the participant would recommend program implementation in the hospital. If the survey is not completed within 48 hours, one follow-up email will be sent. If there is still no response after an additional 48 hours, we will call the participant to attempt to fill out the survey via phone. In the case that the participant does not have an email address, the survey will be mailed to them along with a pre-addressed stamped envelope. Smoking behavior during the child's hospitalization will be examined, including assessments of 1) number of cigarettes smoked per day and 2) number of times participant left the bedside to smoke per day. Participant's self-efficacy and interest in quitting smoking will be assessed, using the same questions from the pre-intervention survey, to assess for changes after the intervention. Any questions or concerns the participant has, along with changes in physical or mental health will also be assessed in this survey. Any positive response will lead to a phone call from the study physician within 24 hours. Participants will receive a $20 gift card to Amazon via email for completing the discharge survey. If an email address is not available, the gift card will be mailed to them.

10.3.3 Follow-Up Number 2: 2-Week Post-Discharge Survey

Participants will be contacted again via email 2 weeks after discharge with a link to complete the follow-up survey via UW REDCap (or mailed a copy if preferred). If the survey is not completed within 48 hours, one follow-up email will be sent. If there is still no response after an additional 48 hours, we will call the participant to attempt to fill out the survey via phone. In the case that the participant does not have an email address, the survey will be mailed to them along with a pre-addressed stamped envelope. Using similar questions as the discharge survey, we will again assess current smoking status, use of NRT post-hospitalization, self-efficacy and interest in quitting smoking, establishment of smoke-free home and car rules, and interest in ongoing smoking cessation treatment. Any questions or concerns the participant has, along with changes in physical or mental health will also be assessed in this survey. Any positive response will lead to a phone call from the study physician within 24 hours. Participants will have a $20 gift card to Amazon emailed to them within 24 hours of completing this survey. If the participant does not have an email address, the survey and gift card will be mailed to them.

Unscheduled visits will not occur for the study.

10.4 Early Termination/Withdrawal Visit

Subjects who are either withdrawn or terminated early from the study will not have any additional follow-up.

10.5 Long-Term Follow-up | Re-contacting Subjects

N/A

11.0 CORRELATIVE | SPECIAL STUDIES

[N/A]

12.0 DATA HANDLING AND RECORD KEEPING

12.1 Data Collection

12.1.1 Data Collection Forms

Standardized data collection forms (e.g., source standardized assessment forms, etc.) will be used to ensure data collected are consistent and compliant with the protocol and IRB application.

Data collection is the responsibility of study team members under the supervision of the Principal Investigator (PI). The PI is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the recorded and reported data.

All data collection will be completed electronically, ensuring legibility; any missing data will be explained. The only exception will be follow-up survey paper forms mailed to participants (if requested by participant)

Data collection forms are maintained in the subject files and retained as described in Section 12.3: Records Retention.

12.1.2 Data Management Software System(s)

Participant data (demographics, survey responses, intervention completion, AE's) will be entered into the following data management software system(s) to ensure consistent data entry and data quality: REDCap.

REDCap

The UW REDCap system is used to manage the data for this study. REDCap is a largely self-service, secure, web-based application for building and managing data collection forms. REDCap provides data management functionality by allowing the development of instrument and surveys to support data capture for research studies.

12.2 Confidentiality and Privacy

Subject confidentiality and privacy are strictly held in trust by the participating investigators, their staff, and the sponsor. Therefore, the study documentation, data, and all other information generated will be held in strict confidence. No information concerning the study, or the data, will be released to any unauthorized third party without prior written approval of the sponsor. All research activities will be conducted in as private a setting as possible.

All study staff engaged in the conduct of this project have completed training on the protection of human subjects and the Health Insurance Portability and Accountability (HIPAA) Privacy Rule. In addition, all key personnel (i.e., Principal Investigator, individuals involved in identifying/recruiting subjects, obtaining informed consent, or interacting and intervening with subjects) have undergone Good Clinical Practice (GCP) training.

Data generated through study participant survey completion using UW REDCap will be stored in secure databases under protections and procedures consistent with the guidelines and regulations of the UW School of Medicine and Public Health (UW-SMPH)..

As stated above, no data are stored on individual computer hard drives. All data are transmitted from the point of collection to the UW REDCap system through a secure, encrypted web connection. On those rare occasions when, due to a loss of internet access or computer hardware failure, data are collected in paper forms, these forms will be stored securely in a locked cabinet within the PI's locked office. Any data collected on paper will

be entered into the computer and the paper document disposed of securely. Consent forms are obtained in paper copy; these forms contain the participant's name and signature. These are retained in secure files at the PI's office, where they are securely stored.

Study staff may use e-mail, mail or phone calls to communicate with research subjects, if the subject has agreed (in the informed consent form) to using email, phone, and mail . The information contained in the email will be limited to a link to complete the study survey. Emails will be sent from secure institution-based accounts; personal, home or Gmail email or texting accounts will not be used.

12.3 Records Retention

It is the investigator's responsibility to retain study essential documents for a minimum period of 7 years following completion of the study per UW-Madison institutional policy.

12.4 Retention for Future Research: [Optional or Mandatory] Data, Image, Audio- or Video-Recording & Biospecimen Banking

Not Applicable

12.5 Protocol Deviations

A protocol deviation is any noncompliance with the clinical trial protocol. The noncompliance may be either on the part of the subject, the investigator, or the study site staff. As a result of deviations, corrective actions are to be developed by the site and implemented promptly.

It is the responsibility of the Principal Investigator and study staff to use continuous vigilance to identify and report deviations. The Principal Investigator is responsible for assessing whether the deviation constitutes noncompliance as defined by the reviewing IRB and if so, reporting it within the required time frame(s). The PI is responsible for knowing and adhering to the reviewing IRB requirements.

12.6 Publication and Data Sharing Policies

The study sponsor (UW Department of Pediatrics) does not have a specific public data sharing policy. Authorship guidelines will be strictly followed based on the publishing journal's authorship policy.

13.0 STUDY ANALYSIS

13.1 Statistical Hypotheses

- **Primary objective(s):** Our primary objective is to evaluate the feasibility and acceptability of a smoking intervention (NRT and cessation counseling) for caregivers of children admitted at American Family Children's Hospital (AFCH).

Our primary hypothesis is that more than 50% of eligible caregivers offered will enroll in the study, use NRT, and recommend program implementation in the hospital.

- **Secondary Objective(s):** Our secondary objectives are to evaluate effects of a smoking intervention on additional key outcomes, such as the number of cigarettes a caregiver smokes per day while their child is hospitalized, number of times they leave the bedside to smoke per day, and changes in self-efficacy and interest in quitting pre- and post-intervention

Our secondary hypothesis is that caregivers who participate in the intervention will be able to reduce their smoking by 50% during their child's hospitalization, will leave the bedside to smoke 50% less frequently

than they predicted, and report an increase in scores assessing self-efficacy and interest in quitting smoking after completing the study intervention.

13.2 Sample Size Justification

This is a pilot study focusing on feasibility and acceptability of a smoking cessation intervention at AFCH. The sample size of 50 will permit estimates of effect sizes but will not be powered to detect statistical differences in outcomes. Findings will be used to estimate sample sizes needed for a fully powered future trial.

We anticipate enrollment rate of 1 in 8 charts reviewed (approximately 25% of charts will have documented smoke exposure, of those we estimate 50% will enroll). This means we anticipate needing to screen 400 charts to reach our enrollment population of 50 participants.

13.3 Subject Population(s) for Analysis

The primary outcome of this study is feasibility and acceptability. See statistical methods below (Section 13.4) for details on statistical approach to our study population.

13.4 Statistical Methods

Basic cohort demographics will be evaluated using descriptive statistics. Aim 1 objectives will be achieved via descriptive statistics regarding feasibility (percentage who enrolled, percentage who used NRT) and acceptability of the interventions (likelihood to recommend program implementation). For Aim 2, comparative analyses will be used to identify differences between the baseline survey and both the discharge survey and 2-week follow-up survey regarding key outcomes: cigarettes smoked per day (pre-hospitalization vs during hospitalization and at 2-week follow-up), leaving the bedside (predicted vs actual), and pre- and post-intervention changes on self-efficacy and interest in quitting smoking. Frequency of non-smoking home and car rules will also be assessed by comparing pre-intervention and 2-week follow-up survey responses. Specifically, for Aim 2, we will use general linear modeling which will allow us to control for baseline levels of the outcome variables.

13.5 Planned Interim Analysis

Not Applicable

13.6 Handling of Missing Data

Not applicable.

14.0 RISK/BENEFIT ASSESSMENT

14.1 Known Potential Benefits to the Subjects

The potential benefits to research subjects associated with this study include the possible reduction in, or cessation of, smoking as well as reduction of withdrawal symptoms when they are not able to go outside to smoke due to their caretaking responsibilities. These potential benefits will also be provided to the participant’s informed consent and in the package inserts from the nicotine patch and mini-lozenges.

If this study is able to show a therapeutic benefit of reduced smoking in caregivers while their child is hospitalized, the community at large would benefit by the availability of a future standardized approach to all caregiver’s who smoke at AFCH while their child is hospitalized.

14.2 Known Potential Risks

The one-time counseling session could lead to adverse psychological feelings of guilt, shame, sadness, anxiety around smoking, exposing a child to tobacco smoke, and anxiety over thoughts of quitting. The use of cessation medications poses a risk of side-effects. Participants will be made aware of the common nicotine replacement side effects before they consent to participate in the study. It should be noted that the nicotine patch and nicotine mini-lozenge are available over the counter. The Food and Drug Administration (FDA) has approved using a combination of two forms of NRT (e.g., nicotine patch + nicotine mini-lozenge) for smoking cessation. These interventions have also been studied and used safely in multiple clinical trials, are used by clinicians in clinical practice, are available over-the-counter, and are reviewed in the 2008 PHS Guideline[10]. The PHS Guideline, in fact, recommends combination NRT as a particularly effective treatment. The self-assessment follow-up surveys ask about smoking behavior and any new medical or emotional symptoms. These questions may make participants feel uncomfortable.

There is always a remote, but existing, possibility that sensitive or personal information about a participant could be divulged as a function of his/her research participation. No information about illegal behavior will be collected by research staff. Finally, smoking withdrawal is associated with a number of unpleasant symptoms, such as sleep disturbance, hunger, craving, and negative mood. Most smokers have tried to quit before and are familiar with these phenomena. Though unpleasant, smoking withdrawal symptoms pose minimal health risk. Participants will be informed about the possible effects of smoking withdrawal should they decide to quit or cut down on their smoking. Individuals who elect not to participate in this research, or are eliminated due to screening failure, will be provided a referral to the Wisconsin Tobacco Quit Line.

14.2.1 Known Interventional Risks

The nicotine patch is generally well tolerated, but up to 50% of participants may have a local skin reaction, and rarely, individuals may have a more systemic allergic reaction. The nicotine patch is also known to cause vivid dreams or other sleep disturbances. If this occurs, participants are instructed to remove the patch at bedtime. The most likely side effects associated with the nicotine mini-lozenge are heartburn, hiccup, nausea, upper respiratory tract infections, coughing, and sore throat. Although most smokers have tolerance to nicotine, symptoms of acute nicotine toxicity (nausea and vomiting) are possible. Information about side effects can be found on the package insert for both products and will be provided to participants.

The risk of NRT in pregnancy is unclear. Per the package insert “If you are pregnant or breast-feeding, only use this medicine on the advice of your health care provider. Smoking can seriously harm your child. Try to stop smoking without using any nicotine replacement medicine. This medicine is believed to be safer than smoking. However, the risks to your child from this medicine are not fully known”. Pregnancy or intention to get pregnant are exclusion criteria and a voluntary statement of intent to avoid pregnancy is listed at the end of the informed consent document.

14.2.2 Other Known Study Risks

N/A

14.3 Risk/Benefit Analysis

Given the limited risks of NRT, the rigorous pre-treatment screening, and the availability of both a physician and psychologist to address any adverse effects, we believe that the potential risks involved in participating in the study are low and outweighed by the benefits to both the individual study participant and society.

15.0 DATA AND SAFETY MONITORING

Please see the Data Safety and Monitoring Plan (DSMP), which has been added to the ARROW application.

16.0 STUDY FEASIBILITY

16.1 Economic Burden to Subjects

Subjects will not have to pay for study procedures (counseling) or medications (NRT). Subjects will be responsible for any costs related to follow-up from smoking cessation such as clinic visits (including out of pocket costs) for change in mood or side effects from use of NRT. This is included in the informed consent document.

16.2 Facilities and Locations

American Family Children's Hospital: Study participants consist of caregivers of children who are admitted to a Med-Surg floor (non-ICU) at American Family Children's Hospital. The study intervention (smoking counseling and distribution of NRT) will occur in-person, either in the child's room or in a separate, private, conference room on the same floor of the child's hospital room (per caregiver preference).

16.3 Feasibility of Recruiting the Required Number of Subjects

Approximately 25% of children at AFCH are documented as having smoke exposure. We anticipate half of those will agree to participate in the study. Thus, with a sample size of 50, we anticipate we will need to screen 400 charts in order to meet our sample size of 50. On average, there are an average of 8 admissions to AFCH Med/Surg units per day, thus we anticipate being able to recruit the required sample within 3-6 months.

16.4 Principal Investigator Considerations

16.4.1 Time Devoted to Conducting the Research

Dr. Williams currently has 30% FTE devoted to clinical research via internal start-up funds. It is estimated that he will spend 1.5 hours per day on this research project (18.75% FTE) for a 3-month period (active enrollment) and 1 hour per day (12.5% FTE) on this project for an additional 3 months (data analysis, abstract/manuscript preparation). He is also currently involved in additional studies at UW-CTRI though has flexible FTE allowing for this project.

16.4.2 Process for Informing Study Teams

Prior to the commencement of research, Dr. Williams and the research coordinator will review the study protocol in detail. The research coordinator has experience in study recruitment and obtaining informed consent. We will perform mock trials of recruitment, participant screening, obtaining informed consent, and counseling sessions to ensure adherence to study protocol.

16.5 Availability of Medical or Psychological Resources

Smoking cessation has the potential for psychological consequences including increased stress, anxiety, and depression. Use of NRT is associated with side effects. Participants will have access to the study physician, should any psychological or medication side effects occur. They will also have access to Dr. Megan Piper (Co-Investigator) who is a licensed clinical psychologist, should any psychological concerns develop.

17.0 MULTI-SITE RESEARCH

Not Applicable

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Appendices

18.1 Appendix A