The effect of surgeon emotional support on treatment choice for low-risk thyroid cancer: a randomized hypothetical choice experiment

Protocol Number: UW21090

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Principal Investigator*: Corrine Voils, PhD

Sponsor: National Cancer Institute

Grant Title: Impact of Emotions on Treatment Decisions About Low-Risk Thyroid Cancer

Grant Number: K08CA230204

Funded by: National Cancer Institute

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Contents

STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Council on Harmonisation Good Clinical Practice (ICH GCP) and the following:

United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812).

National Institutes of Health (NIH)-funded investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of NIH-funded clinical trials have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the IRB for review and approval. Approval of both the protocol and the consent form(s) must be obtained before any participant is consented. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. All changes to the consent form(s) will be IRB approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent, using a previously approved consent form.

INVESTIGATOR'S SIGNATURE

The signature below constitutes the approval of this protocol and provides the necessary assurances that this study will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable US federal regulations and ICH guidelines.

Principal Investigator or Clinical Site Investigator:

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Signed:_____ Date: _____

1 PROTOCOL SUMMARY

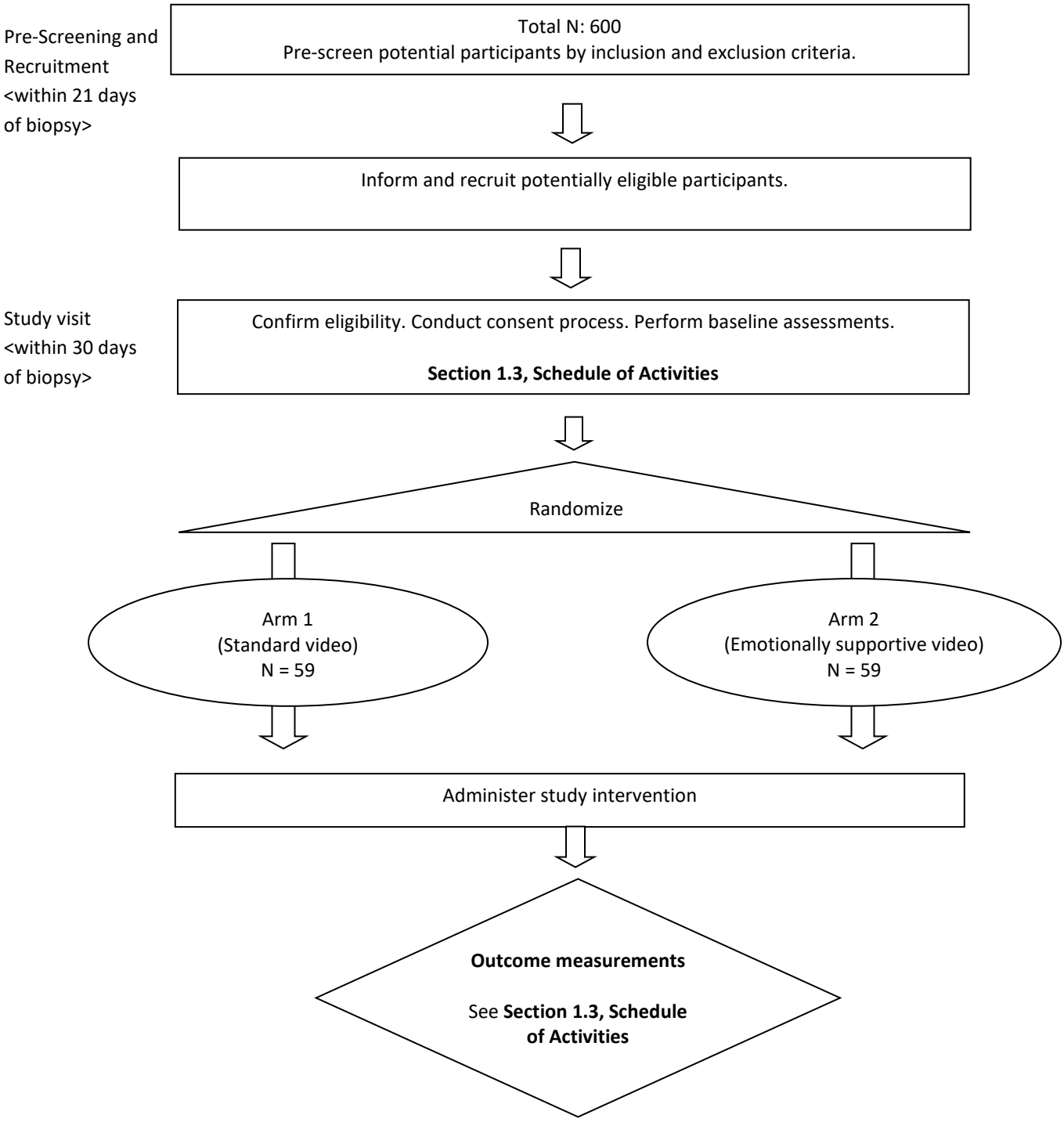
1.1 SYNOPSIS

Title:	The effect of surgeon emotional support on treatment choice for low-risk thyroid cancer: a randomized hypothetical choice experiment
Grant Number:	K08CA230204

Study Description:	In this study, we will test the extent to which emotionally supportive communication from a surgeon is associated with patient preference for total thyroidectomy. We will conduct a hypothetical choice experiment with "analogue" patients, defined as those with a benign thyroid nodule not requiring surgery. We will collect baseline measures, then randomize participants to watch a video simulation of a patient-surgeon discussion about treatment options for low-risk thyroid cancer with or without emotionally supportive statements. We hypothesize that increased emotionally supportive communication by the surgeon will decrease the likelihood of patients choosing total thyroidectomy, reduce anxiety and thyroid cancer fear, and increase decisional confidence, perceived physician empathy, trust in physician, and information recall.
Objectives*:	Primary Objective: Test the extent to which emotionally supportive communication by a surgeon is associated with patient preference for total thyroidectomy. Secondary Objectives: Test the extent to which emotionally supportive communication by surgeons is associated with anxiety, thyroid cancer fear, perceived empathy, physician trust, and decisional confidence. Tertiary/Exploratory Objectives: Test the extent to which emotionally supportive communication by a surgeon is associated with information recall.
Endpoints*:	Primary Endpoint: Hypothetical treatment choice immediately after watching the video intervention Secondary Endpoints: state anxiety, thyroid cancer fear, decisional confidence, perceived physician empathy, physician trust immediately after watching the video intervention Tertiary Endpoint: information recall immediately after watching the video intervention
Study Population:	118 adults with benign thyroid nodules who were seen at a UW Health clinic for a fine needle biopsy and do not need surgery
Phase* or Stage:	N/A
Description of Sites/Facilities Enrolling Participants:	Single-site study at University of Wisconsin-Madison, including biopsy clinics at UW Health at the American Center, 1 South Park, and UW Hospital & Clinics
Description of Study Intervention/Experimental Manipulation:	Participants will be randomized to watch one of two 6-minute videos depicting a surgeon-patient discussion about treatment options for low-risk thyroid cancer. The dialogue in the videos is the same except one contains emotionally supportive language.
Study Duration*:	36 months

Participant Duration:	Participants will be recruited for the study within 21 days of their thyroid nodule biopsy. Their one-time study session will occur within 30 days of their biopsy and will last up to 60 minutes.

1.3 SCHEMA


Pre-Screening and Recruitment <within 21 days of biopsy>
Total N: 600
Pre-screen potential participants by inclusion and exclusion criteria.
Inform and recruit potentially eligible participants.
Study visit <within 30 days of biopsy>
Confirm eligibility. Conduct consent process. Perform baseline assessments.
Section 1.3, Schedule of Activities
Randomize
Arm 1
(Standard video)
N = 59
Arm 2
(Emotionally supportive video)
N = 59
Administer study intervention
Outcome measurements
See Section 1.3, Schedule of Activities

1.3 SCHEDULE OF ACTIVITIES

	Screening & recruitment (within 21 days of biopsy)	Study participation (single study session will be completed within 30 days of biopsy)
EMR Review Eligibility	X	
Participant recruitment	X	
Eligibility confirmation		X
Consent		X
Demographics		X
Clinical history		X
Thyroid cancer fear		X
State Anxiety		X
Stratified Randomization		X
Video intervention		X
Outcome Evaluation		
Treatment choice		X
State anxiety		X
Thyroid cancer fear		X
Decisional confidence		X
Perceived physician empathy		X
Physician trust		X
Information recall		X
Adverse Events Reporting		X

2 INTRODUCTION

2.1 STUDY RATIONALE

Thyroid cancer incidence has increased significantly due to incidental detection of small, low-risk cancers.[1–10] The majority of these patients undergo total thyroidectomy, even though hemi-thyroidectomy has comparable long-term outcomes.[11–13] Compared to hemi-thyroidectomy, total thyroidectomy has greater potential for serious long-term, permanent adverse harms.[3,10,14–20] Because both treatment options have equivalent recurrence and survival, total thyroidectomy is considered overtreatment, as the potential harms outweigh the oncologic benefit.[5,12,21–23,24]

Data suggest that despite near 100% survival, patients with low-risk thyroid cancer experience fear and anxiety in response to their diagnosis and a desire to "get the cancer out" to achieve peace of mind.[25–29] This reaction combined with lack of emotional support likely contribute greatly to preference for total thyroidectomy. To reduce overtreatment of these low-risk cancers, this study seeks to understand the effect of emotionally supportive language from surgeons on patients' treatment decisions.

This study involves a hypothetical choice experiment with "analogue" patients, defined as those with a benign, ≤4 cm thyroid nodule not requiring surgery. After obtaining baseline measures of demographics, thyroid history, state anxiety, and cancer fear, we will randomize participants to watch a video simulation of a patient-surgeon discussion about treatment options for low-risk thyroid cancer with or without emotionally supportive statements. Afterward, participants will complete post-test measures regarding which treatment they would choose if they were the patient in the video, state anxiety, cancer fear, decisional confidence, reactions to the video including perception of physician empathy and level of trust, and information recall. We will compare outcomes by study arm. We hypothesize that increased emotionally supportive communication by the surgeon will decrease the likelihood of patients choosing total thyroidectomy, reduce anxiety and thyroid cancer fear, and increase decisional confidence, perceived physician empathy, trust in physician, and information recall.

2.2 BACKGROUND

In the last four decades, thyroid cancer diagnoses have increased significantly, primarily due to low-risk cancers with a very low mortality.[1–3,12] Most patients with these low-risk thyroid cancers undergo total thyroidectomy, a riskier surgical approach that represents overtreatment for many because it does not improve survival compared to less extensive options.[12,14,21,23] Overtreatment with total thyroidectomy can result in harms such as difficulty speaking, swallowing, regulating calcium, and significant fatigue.[17–20,30–36] Patients must also take life-long thyroid hormone replacement, which is associated with adverse cognitive and bone-related outcomes.[17,19,20,30]

Preference for total thyroidectomy is difficult to explain with models of rational decision-making. Rational models of decision-making would predict that patients would prefer hemi-thyroidectomy which has equivalent oncologic outcomes, but reduced risk of harms compared to total thyroidectomy. However, most patients with low-risk thyroid cancer undergo total thyroidectomy. Therefore, alternative explanations are needed to explain why patients prefer the riskier treatment option.

Our preliminary findings indicate that patients with low-risk thyroid cancer experience strong negative emotions, such as fear and anxiety, that may affect their treatment preference. Emotions are known to play a role in treatment and screening decisions in patients with other malignancies, such as breast or prostate cancer, leading to unwanted, unnecessary, or overly extensive care.[25,26,37–40] Therefore, the ***hypothesis*** of this line of investigation is that emotions influence patients' treatment decisions about low-risk thyroid cancer, leading to decisions that over treat.

Previous studies using patient-physician simulation have demonstrated that emotionally supportive statements from a physician can reduce patient anxiety, increase patient trust, and increase information recall.[41–45] The results have been successfully translated back into clinical practice for the development of effective physician-based interventions.[42–44,46]

For this study, we hypothesize that increased emotionally supportive communication by the surgeon will decrease the likelihood of patients choosing total thyroidectomy, reduce anxiety, decrease thyroid cancer fear, and increase decisional confidence, perceived empathy, trust in the surgeon, and recall. The results will provide new evidence about how emotions influence cancer-related decisions and help elucidate the effect of responding to emotional reactions to thyroid cancer diagnosis on treatment choice.

2.3 RISK/BENEFIT ASSESSMENT

2.3.1 KNOWN POTENTIAL RISKS

This study meets the criteria for minimal risk, as the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life. There are known potential risks for participants: in addition to potential loss of confidentiality, there is potential for psychological stress from taking a survey that asks them to imagine they have been diagnosed with cancer. Similar studies have been performed in patients without a cancer diagnosis with no known adverse outcomes.

2.3.2 KNOWN POTENTIAL BENEFITS

Participants are not expected to benefit directly from participating in this study. Participation in this research study may benefit other patients and surgeons in the future by helping us learn more about how emotionally supportive communication by surgeons might affect treatment decisions for low-risk thyroid cancer. This will eventually help our research team to develop, test, and implement interventions that reduce healthcare costs and decrease unnecessary harms, improving quality of life for patients with thyroid cancer by helping them avoid riskier surgery. We also anticipate that our findings will translate to other malignancies and inform the development of tools that improve our ability to reduce overtreatment of patients with other cancers.

2.3.3 ASSESSMENT OF POTENTIAL RISKS AND BENEFITS

This study presents minimal risks to participants, as the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life. The risks of this study are outweighed by the benefits as the study poses minimal risk to participants. In the future, a better understanding of factors that impact cancer fear may benefit patients. As such, participants benefit by knowing that they are helping future cancer patients.

Participants will be informed that participation is voluntary and they may skip questions they do not want to answer and/or decline to compete the study. They will be reminded to contact their provider if they experience emotional distress.

Multiple steps have been incorporated to reduce the likelihood of a breach in confidentiality. Furthermore, if a breach in confidentiality occurs, it will not negatively impact these participants because the data collected are not sensitive or stigmatizing in any way.

Study investigators and staff will be alert for any potential harms to participants, including breaches of confidentiality. Any breach of confidentiality will be immediately reported to the principal investigator and the UW-Madison Minimal Risk IRB, and the UW-Madison HIPAA Privacy and Security Officers. The risk of breach of confidentiality is low because adequate provisions are in place to ensure that breach of confidentiality will not occur, as described in **section 10.1.3**.

3 OBJECTIVES AND ENDPOINTS

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary		
Test the extent to which increased emotionally supportive communication by surgeons is associated with patient preference for total thyroidectomy.	We will measure which treatment participants would choose if they were the patient with thyroid cancer in the video (total thyroidectomy or hemithyroidectomy) immediately after they finish watching the video.	Treatment choice is the primary endpoint because prior studies in different populations indicate increased emotional support can influence medical choices. Emotionally supportive communication is most likely to impact patient preference in the short-term, as the treatment decision is being made.
Secondary		
Test the extent to which increased emotionally supportive communication by surgeons is associated with anxiety, thyroid cancer fear, perceived empathy, trust, and decisional confidence.	We will measure these endpoints immediately after participants finish watching the video, using the State Trait Anxiety Inventory brief, an adapted Cancer Fear Scale an adapted Trust in Physician Scale, an adapted Jefferson Scale of Patient's Perceptions of Physician's Empathy, and decisional confidence using a single-item 10-point Likert scale.	These secondary endpoints were selected because they represent potential emotion-related outcomes in the treatment decision-making process. Prior studies indicate the increased emotionally supportive communication can influence these outcomes in other medical settings.
Tertiary/Exploratory		
Test the extent to which increased emotionally supportive communication by surgeons is associated with information recall.	We will assess information recall immediately after participants finish watching the video with 5 multiple choice questions that ask about information relayed in both intervention videos.	Published data suggest that heightened emotional states can inhibit information processing and recall. Response to this heightened state with increased emotional support may improve recall.

4 STUDY DESIGN

4.1 OVERALL DESIGN

In this single-site, two-arm, between-subjects hypothetical choice experiment, we will test the extent to which increased emotionally supportive communication by surgeons is associated with patient preference for total thyroidectomy. We will use “analogue” patients, defined as those with a benign thyroid nodule, ≤4 cm not requiring surgery. We will randomize these patients to watch a video simulation of a patient-surgeon discussion about treatment options for low-risk thyroid cancer with or without emotionally supportive statements. We hypothesize that increased emotionally supportive communication by the surgeon will decrease the likelihood of patients choosing total thyroidectomy, reduce anxiety and thyroid cancer fear, and increase decisional confidence, trust in physician, perceived physician empathy, and information recall. This study will provide new evidence about how emotions influence cancer-related decisions. This knowledge is necessary for the design of effective interventions that attend to both emotions and cognition in decision-making. We expect this comprehensive strategy to reduce overtreatment and morbidity in patients with small, low-risk thyroid and other low-risk cancers.

Potentially eligible patients will arrive to clinic, undergo needle biopsy of their thyroid nodule, and receive a study brochure. Cytology results are automatically released to patients via MyChart and the ordering physician calls the patient within 24-48 hours with their results. Once a benign diagnosis and eligibility is confirmed via chart review, we will approach patients and enroll interested participants within 30 days of their diagnosis. Patients will complete the study in one sitting on a computer or tablet in their own home by accessing a Qualtrics link at a time that is convenient for them. They will confirm their eligibility through screening questions and then proceed to the information page with consent language. If they have questions about the information page, they are directed to contact the study team before indicating consent. Once they indicate consent they will proceed to the pre-intervention survey (administered prior to randomization) which will include demographics (sex assigned at birth, age, race, ethnicity, education, personal cancer history, clinical history regarding their recent biopsy, and baseline measures including the STAI-6 and thyroid cancer fear scale. [47,48] Participants will then get randomized by Qualtrics to a study arm. After viewing the video, they will complete measures including the STAI-6, an adapted cancer fear scale, manipulation check, physician empathy scale, trust in physician scale, a 5-question information recall questionnaire about the treatment options discussed in the video, and the following questions: (1) “If you were the patient in the video, which treatment option would you choose for yourself?” and (2) “How confident do you feel that you would be choosing the best treatment option for you?” on a 10-point scale [not at all confident to completely confident].[47–50] Our primary outcome is treatment choice: total or hemi-thyroidectomy. We chose the STAI-6 because of its predictive validity in assessing changes induced by hypothetical choice experiments in patients with cancer.[41,45] Our post-intervention measures are further described in **Section 8.1.** Participation is expected to take less than 30 minutes to complete.

Intervention: We have created two videos using rigorous methods described by van Vleit et al. for creating internally and externally valid videos that manipulate affective communication. [51] The videos are 5-6 minutes in length and portray a conversation between a patient and surgeon during which the surgeon discusses: the diagnosis, prognosis, available treatment options, benefits and harms of the options, and need for decision making. The surgeon speaks for the majority of the simulated visit and discusses total and hemi-thyroidectomy. The scripts are identical between arms except for the addition of emotionally supportive statements and

gestures in the intervention script. This study design using simulated patient-provider conversations that manipulate affective communication in analogue patients has been employed by others and successfully translated back into clinical practice for the development of effective physician-based interventions.[42–44,46]

Randomization: Participants will be stratified based on sex. Males are more likely to undergo less extensive treatment.[12] After completion of consent and the pre-intervention survey that includes demographics, Qualtrics will direct participants into two separate survey branches: males and females. Qualtrics will randomize participants 1:1 to a video within each branch. They will then proceed to the post-intervention measures. Study staff will not know participants' arm assignment.

4.2 SCIENTIFIC RATIONALE FOR STUDY DESIGN

Use of analogue patients (i.e. patients with benign thyroid nodules that do not need surgery) is necessary because this type of controlled experiment is not feasible in clinical practice and may affect patients' treatment course.

4.3 JUSTIFICATION FOR INTERVENTION

The 5-6 minute video intervention will be delivered while patients are completing the study on a computer or tablet in their own home. We have chosen this mode of delivery because it is not feasible to deliver the intervention on the same day as the thyroid nodule biopsy. Final cytology results are not available on the same day; we do not want to over burden patients on the day of their appointment; and we want to allow a short washout period from time of biopsy to time of study participation.

4.4 END-OF-STUDY DEFINITION

A participant is considered to have completed the study if they have completed the baseline assessment, the intervention, and the follow-up assessments.

5 STUDY POPULATION

5.1 INCLUSION CRITERIA

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

Determined during EMR screening

1. Aged 18 or older
2. Seen in a UW Health Clinic for FNA (fine needle aspiration) of a thyroid nodule in the last 30 days
3. Thyroid nodule measures ≤4 centimeters
4. Benign thyroid nodule biopsy result
5. Able to speak and read English
6. Access to internet

Determined/reconfirmed during pre-study screening on Qualtrics

1. Seen in a UW Health Clinic for FNA (fine needle aspiration) of a thyroid nodule in the last 30 days

5.2 EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this study:

Determined during EMR screening

1. Additional thyroid nodule biopsy results that are not benign
2. History of thyroid cancer
3. History of thyroid surgery
4. Has seen a surgeon about thyroid or parathyroid surgery
5. Has a referral to see a surgeon about thyroid surgery
6. Deaf
7. Blind
8. Vulnerable populations such as prisoners

Reconfirmed during pre-study screening on Qualtrics

1. History of thyroid cancer
2. History of thyroid surgery
3. Has seen a surgeon about thyroid or parathyroid surgery
4. Plans to see a surgeon about thyroid surgery

5.3 LIFESTYLE CONSIDERATIONS

N/A

5.4 SCREEN FAILURES

N/A

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

We will enroll 118 patients 18 years of age and older who are seen in a UW Health Clinic for a fine needle aspiration (FNA) of a thyroid nodule and receive benign pathology results. About 70% of FNAs at UW are benign, however not all patients with benign FNAs will meet other inclusion criteria. We anticipate screening approximately 600 patients in order to reach 118 participants.

Study staff will mail letters endorsed by the physicians in UW biopsy clinics at UW Hospital, The American Center, and/or 1 South Park to all patients with upcoming thyroid nodule biopsy appointments. The letters will inform patients that they may be eligible for a study and the study team will contact them if they are eligible, unless they opt out of study communications. Once potentially eligible patients are at their biopsy appointment, they will hear about the study again as endocrinologists, radiologists, ultrasound technologists, or clinic staff such as medical assistants will give all patients who are getting thyroid nodule biopsies a study brochure. They will again tell the patient a study team member will contact them if they are eligible for the study, unless they opt out of study communications by contacting the study team. Study posters may also be posted in biopsy clinic rooms to remind clinic staff of eligibility criteria and tell patients about the study.

Study staff with UW Health electronic health record (Health Link) access may search clinic schedules, Launchpad pathology records, and/or patient list templates (e.g. reporting workbench reports, reports of targeted EHR searches set up by Clinical and Health Informatics Institute [CHI2]) made available to them as part of their research access to Health Link to mail letters, check biopsy results, and help identify participants for study enrollment. After a patient has a biopsy and receives a brochure, a member of the study team will verify eligibility criteria in Health Link and log eligibility results in a tracking document. If the patient is eligible, a member of the study team will contact the patient via phone, mail, and MyChart (if available, through CHI2) to recruit them for the study. If we are unable to reach the patient during our first phone and mail contact attempt, we may make up to three more contact attempts if necessary. All attempts to contact patients will be logged in a tracking document.

We have designed study procedures including consent, baseline measures, intervention, and outcome measures to all take place in less than 30 minutes on one day, therefore we anticipate attrition will be low. We will be available by phone or email to answer questions that may arise during participation.

Participant Incentive:
All participants will receive a $40 check, cash, or gift card for completing the study.

6 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S)

6.1 STUDY INTERVENTION(S) OR EXPERIMENTAL MANIPULATION(S) ADMINISTRATION

6.1.1 STUDY INTERVENTION OR EXPERIMENTAL MANIPULATION DESCRIPTION

We have created two videos using rigorous methods described by van Vleit et al. for creating internally and externally valid videos that manipulate affective communication.[51] The videos are 5-6 minutes in length and portray a conversation between a patient and surgeon during which the surgeon discusses: the diagnosis, prognosis, available treatment options, benefits and harms of the options, and need for decision making. The surgeon speaks for the majority of the simulated visit and discusses total and hemi-thyroidectomy. The scripts are identical between arms except for the addition of emotionally supportive statements and gestures in the intervention script. This study design using simulated patient-provider conversations that manipulate affective communication in analogue patients has been employed by others and successfully translated back into clinical practice for the development of effective physician-based interventions.[42–44,46]

6.1.2 ADMINISTRATION AND/OR DOSING

The study intervention, i.e. video viewing, will last 5-6 minutes and will be administered once via Qualtrics online.

6.2 FIDELITY

6.2.1 INTERVENTIONIST TRAINING AND TRACKING

N/A

6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND BLINDING

After completion of consent and the pre-intervention survey that includes demographics, Qualtrics will direct participants into two separate survey branches: males and females. Qualtrics will randomize participants 1:1 to a video within each branch. They will then proceed to the post-intervention measures. Study staff will not know participants' arm assignment.

6.4 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION ADHERENCE

In order to create common conditions for participants to the extent possible, participants will be instructed to complete the study in one sitting, on a tablet or computer, in a quiet place where they can concentrate. After the intervention, they will be asked to rate how fully they were able to concentrate on the video while it played.

6.5 CONCOMITANT THERAPY

N/A

6.5.1 RESCUE THERAPY

N/A

7 STUDY INTERVENTION/EXPERIMENTAL MANIPULATION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

N/A

7.2 LOST TO FOLLOW-UP

A randomized participant will be considered lost to follow-up if they fail to complete outcome measures. Participants who provide consent, are randomized, receive the study intervention, and subsequently withdraw will be considered randomized and will be analyzed in the arm assigned, consistent with intent-to-treat principles. Participants who provide consent but are not randomized and do not receive the study intervention will be replaced.

7.3 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

A participant will be considered lost to follow-up if they fail to complete the study after providing consent and study staff are unable to contact the participant after at least 3 attempts. Participants may withdraw from participation in the study at any time.

8 STUDY ASSESSMENTS AND PROCEDURES

8.1 ENDPOINT AND OTHER NON-SAFETY ASSESSMENTS

Screening and eligibility assessments: Study staff with UW Health electronic health record (Health Link) access will identify biopsy patients and verify eligibility criteria in Health Link within 21 days of biopsy. If the patient appears to be eligible, a member of the study team will contact the patient via phone and mail (and

MyChart, if available through CHI2) to recruit them for the study. Patients will be provided a link to the study on Qualtrics, where they can answer questions to verify their eligibility criteria and proceed to participation if eligible. Eligibility criteria verified at each screening stage is described in **sections 5.1 and 5.2**. Reasons for screening patients out will be documented at each step of the process. Age and sex of eligible patients will be retained for all eligible patients, including those who decline to participate, to assess any bias between respondents and non-respondents.

Study data: Data will be collected virtually. Mode of data collection will not have adverse effects on our ability to test our study hypotheses. All study measurements will be entered by the participant into Qualtrics.

Baseline demographic and clinical characteristics: We will collect age, sex assigned at birth, clinical history of their thyroid, ethnicity, race, highest educational level attained, anxiety, and level of thyroid cancer fear.

Primary and secondary outcomes:

Type	Name	Timing of Measure	Brief description
Primary	Treatment choice	Post-intervention	We will assess patients' hypothetical treatment choice after the intervention. We will ask: "If you were the patient in the video and had recently been diagnosed with thyroid cancer, which of the two treatment options would you choose, knowing what you know right now?" Answers will include: removal of the entire thyroid, removal of half of the thyroid.
Secondary	Decision confidence	Post-intervention	We will assess patients' confidence in their treatment choice after the intervention. We will ask: "How confident do you feel that you are choosing the best treatment option for you?" Answers will range from 1 (not at all confident) to 10 (completely confident).
N/A	Manipulation check	Post-intervention	We will assess patients' engagement with the video with 5 items. Questions will ask about concentration and the extent to which the patient could identify with various aspects of the video. Response options are on a 7-point Likert scale ranging from 'completely disagree' [1] to 'completely agree' [7].
Secondary	Anxiety – STAI Brief	Baseline and Post-intervention	This 6-question, quantitative instrument was designed to assess state anxiety.[47] Response options are on a 4-point Likert scale ranging from 'not at all' [1] to 'very much' [4]. Scores are totaled with a potential range of 6 to 24. We chose the STAI-6 because of its predictive validity in assessing changes induced by hypothetical choice experiments in patients with cancer.[41,45]
Secondary	Thyroid Cancer Fear (*adapted*)	Baseline and Post-intervention	This 8-question quantitative instrument was originally designed to assess fear of breast cancer in patients undergoing cancer screening.[48] Items are rated on a 5-point scale from strongly disagree [1] to strongly agree [5]. We will adapt the measure to assess participants' fear of thyroid cancer. The score ranges from 8 to 40. For the original scale, low fear was defined as a total score of 8 to 15, moderate fear as a score of 16 to 23, and high fear as a score of 24 to 40.
Secondary	Jefferson Scale of Patient's Perceptions of Physician	Post-intervention	This 5-question quantitative instrument assesses patient perceptions of physician empathy.[52] Minor adaptations in wording were made to fit the video scenario. Response options are on a 7-point Likert scale ranging from

	Empathy (*adapted*)		'strongly disagree' [1] to 'strongly agree' [7]. Items are summed, with a max score of 35, and higher values indicating a perception of more empathy.
Secondary	Trust in Physician Scale (*adapted*)	Post-intervention	This 5-question quantitative instrument assesses patient trust in a physician.[49] Response options are on a 5-point Likert scale ranging from 'strongly disagree' [1] to 'strongly agree' [5]. Responses are summed and scores are on a scale of 5 to 25, with higher values indicating more trust.
Tertiary	Information recall (*adapted*)	Post-intervention	This 5-question quantitative instrument assesses participants' level of recall of information in the video intervention. Questions were modeled after Decision Quality Instruments designed by Karen Sepucha, PhD, and colleagues at the MGH Health Decision Sciences Center.[53,54] Because our questions are novel, our exploratory analysis will be determined based on distribution and variability of results. Potential analyses include assigning participants a score based on how many answers are correct out of 5 and dichotomizing into "low" knowledge versus "high" knowledge, and/or comparing mean and median scores for the five questions across the two treatment groups.[54]

8.2 SAFETY ASSESSMENTS

N/A

8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

The current study will pose minimal risk to the participants. Participants will be made aware of the risks and benefits which they may incur from participating and will have time to ask questions. Further, they will be told their participation is voluntary and may leave the study at any time at no harm to them. Although no problems or adverse events are expected, any study related adverse events will be documented and reported to the local IRB per institutional policy. The PI is responsible for ensuring the safety of the participants and their data. All data collected will be used for research purposes only and only the study team members will have access to their information. Data will be protected as described previously and any noncompliance will be reported immediately.

8.3.1 DEFINITION OF ADVERSE EVENTS

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION/EXPERIMENTAL MANIPULATION

8.3.3.3 EXPECTEDNESS

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

8.3.5 ADVERSE EVENT REPORTING

8.3.6 SERIOUS ADVERSE EVENT REPORTING

8.3.7 REPORTING EVENTS TO PARTICIPANTS

8.3.8 EVENTS OF SPECIAL INTEREST

8.3.9 REPORTING OF PREGNANCY

8.4 UNANTICIPATED PROBLEMS

8.4.1 DEFINITION OF UNANTICIPATED PROBLEMS

This protocol uses the definition of Unanticipated Problems as defined by the Office for Human Research Protections (OHRP). OHRP considers unanticipated problems involving risks to participants or others to include, in general, any incident, experience, or outcome that meets **all** of the following criteria:

- Unexpected in terms of nature, severity, or frequency given (a) the research procedures that are described in the protocol-related documents, such as the Institutional Review Board (IRB)-approved research protocol and informed consent document; and (b) the characteristics of the participant population being studied;
- Related or possibly related to participation in the research ("possibly related" means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

8.4.2 UNANTICIPATED PROBLEMS REPORTING

The principal investigator will report unanticipated problems (UPs) to the reviewing Institutional Review Board (IRB). The UP report will include the following information:

- Protocol identifying information: protocol title and number, PI's name, and the IRB project number
- A detailed description of the event, incident, experience, or outcome
- An explanation of the basis for determining that the event, incident, experience, or outcome represents an UP
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UP

To satisfy the requirement for prompt reporting, UPs will be reported using the following timeline:

- Any UP will be reported to the IRB and to the funding agency within 14 business days of the investigator becoming aware of the problem
- All UPs should be reported to appropriate institutional officials (as required by an institution's written reporting procedures), the supporting agency head (or designee), and the Office for Human Research Protections (OHRP) within 14 business days of the IRB's receipt of the report of the problem from the investigator

8.4.3 REPORTING UNANTICIPATED PROBLEMS TO PARTICIPANTS

N/A

9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

Primary Endpoint: We hypothesize that emotionally supportive communication will decrease patient preference for total thyroidectomy immediately after watching the video.

Secondary Endpoints: We hypothesize that emotionally supportive communication will decrease anxiety and thyroid cancer fear and increase trust, perceived empathy, and decisional confidence immediately after watching the video.

Tertiary/exploratory: We hypothesize that emotionally supportive communication will increase information recall immediately after watching the video.

9.2 SAMPLE SIZE DETERMINATION

We assume based on existing data that the proportion of participants choosing total thyroidectomy will be 0.89 and estimate the sample size needed for 90% power to detect a proportion lower than 89%. With a sample of n=59 in each group, we will be able to detect risk differences of -25% and medium effect sizes of -0.60 with 90% power using a 2-sided test (chi square for binary outcome) with Type I error rate alpha= 0.05. The UW Thyroid Nodule Biopsy clinic performs over 500 biopsies annually, of which approximately 70% are benign. The UW Radiology clinic performs 400 biopsies per year on patients with benign thyroid nodules.

We anticipate missing data will be very low as the study is expected to be completed in one sitting.

9.3 POPULATIONS FOR ANALYSES

We will perform a two-group intent to treat analysis based on the intervention randomization.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

For descriptive statistics, categorical and continuous data will be presented as percentages, means with standard deviations, median, and range. For inferential tests, we will use 2-sided tests with Type I error rate alpha=0.05 for statistical significance. Covariates are specified below. Checks for assumptions of normality will be performed. If data are not normal, nonparametric tests will be used.

9.4.2 ANALYSIS OF THE PRIMARY ENDPOINT(S)

The primary endpoint, treatment choice, is a binary scale. It will be measured once immediately after the intervention.

We will calculate distributional characteristics and perform a two-group intent to treat analysis for this binary endpoint using conditional logistic regression to account for stratification by sex. The Type I error rate alpha= 0.05.

9.4.3 ANALYSIS OF THE SECONDARY ENDPOINT(S)

We will calculate distributional characteristics and perform a two-group intent to treat analysis for continuous or ordinal endpoints using 2-sided t-tests or analysis of variance (ANOVA) with Type I error rate alpha= 0.05, and risk differences or mean differences with confidence intervals for quantification and estimation of effect.

Secondary endpoint	**Dependent on primary endpoint?**	**Repeated measure?**	**Scale**	**Statistical procedures**
Decision confidence	No	No	Continuous	2-sided t-tests
Anxiety – STAI Brief	No	Yes: Pre and Post	Continuous	2-sided t-tests
Thyroid Cancer Fear	No	Yes: Pre and Post	Continuous and Ordinal	2-sided t-tests and ANOVA
Patient Perception of Physician Empathy	No	No	Continuous	2-sided t-tests
Trust in Physician	No	No	Continuous	2-sided t-tests
Information recall	No	No	Continuous	2-sided t-tests

9.4.4 SAFETY ANALYSES

N/A

9.4.5 BASELINE DESCRIPTIVE STATISTICS

We will describe baseline characteristics such as age, sex, race, state anxiety, thyroid cancer fear, and clinical history such as hypothyroidism overall and by treatment arm, consistent with CONSORT checklist criteria.

9.4.6 PLANNED INTERIM ANALYSES

N/A

9.4.7 SUB-GROUP ANALYSES

For the primary endpoint, we will determine whether differences exist in response to the intervention by age, sex, race/ethnicity, and level of education. Prior data suggests disparities may exist in treatment received for actual patients with thyroid cancer and these characteristics. We will also determine if differences exist by clinical characteristics, such as hypothyroidism, thyroid-related symptoms, personal history of cancer, nodule characteristics, time of diagnosis, and medical use tendencies, again based on the published literature in patients with thyroid or other low-risk cancers.

9.4.8 TABULATION OF INDIVIDUAL PARTICIPANT DATA

Individual participant data will not be listed by measure and time point.

9.4.9 EXPLORATORY ANALYSES

We will explore the association of the secondary outcomes of decision confidence, anxiety, and thyroid cancer fear on the primary outcome: treatment choice. We will also perform sub-group analysis for the secondary end points by age, sex, race/ethnicity, level of education, hypothyroidism, thyroid-related symptoms, personal history of cancer, nodule characteristics, time of diagnosis, and medical use tendencies.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

All potential participants (i.e. adults getting thyroid nodule biopsies) will receive a letter with a URL for uwchoices.org, and an informational brochure about the study. Potential participants who are confirmed to be eligible will be given a link to complete the study on Qualtrics. After passing eligibility screening questions, they will see an information page describing the study intervention, study procedures, and risks. The information page will tell participants to contact the study team with any additional questions about the study.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

This clinical trial is a hypothetical choice experiment that presents no more than minimal risk of harm to subjects. It involves no procedures for which written consent is normally required outside of the research context. Therefore we will have a waiver of signed consent and present an information page to participants on Qualtrics. Participants will be asked to contact the study team with any questions before proceeding to the study. At the end of the information page on Qualtrics, participants will told that clicking to the next page indicates their consent to participate in the study.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to investigator, funding agency, and regulatory authorities. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform the Institutional Review Board (IRB), and sponsor/funding agency and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Insufficient compliance of study staff to the protocol (i.e., significant protocol violations)

- Data that are not sufficiently complete and/or evaluable

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the funding agency, sponsor, IRB, or other relevant regulatory or oversight bodies (OHRP, DSMB).

10.1.3 CONFIDENTIALITY AND PRIVACY

All research activities will be conducted in as private a setting as possible.

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the funding agency. This confidentiality is extended to the data being collected as part of this study. Data that could be used to identify a specific study participant will be held in strict confidence within the research team.

To ensure confidentiality, study data will only be accessed by personnel on the research team. Only the minimum amount of information that is necessary to achieve the aims of the research will be collected. All information obtained and associated data files will be confidential and will be kept in a locked file in a locked office or on a secure, password-protected server within the Department of Surgery network, which is protected by a firewall that ensures the privacy of the network. Any paper records will be kept in a locked cabinet in a locked office that only study staff have access to. Access to the information is limited to the study team, all of whom have completed the requisite human subjects/Health Insurance Portability and Accountability Act (HIPAA) training and have been given valid access to electronic medical records.

Patient information is limited to the minimum necessary to screen for eligibility, recruit patients, and mail participant incentives. The study participant's contact information will be securely stored for internal use during the study. We will also use names, MRNs, and dates/times of appointments. Identifying information will be separated from study data. Once the study is complete, all PHI will be destroyed. At the end of the study, all records will continue to be kept in a secure location for 7 years or longer.

Confidentiality will be protected further by: 1) using a participant log form that contains only the minimum necessary protected health information (PHI) concerning participants and storing this log on a secure password-protected server; 2) coding data collection forms with a consecutive participant number that is not derived from any participant personal identifiers and linking that data collection form to the participant log; 3) storing the participant log and data collection forms separately; and 4) not sharing PHI with anyone outside the research team. It is highly likely that these measures will result in avoidance of breach of confidentiality outside of the research. In addition, the data to be collected are not sensitive to participants.

Survey data will be stored on a secure Department of Surgery server. Data will be shared with Drs. Susan Pitt and Megan Haymart at the University of Michigan to assist with analysis. The data will not include identifiable information or the keycode. This information will be shared using the secure server file transfer service maintained by the UW Department of Surgery at t.surgery.wisc.edu. This is a secure, password-protected system and files transferred through it are automatically deleted from the service 7 days after upload.

It is NIH policy that the results and accomplishments of the activities that it funds should be made available to the public. The PI will ensure all mechanisms used to share data will include proper plans and safeguards for

the protection of privacy, confidentiality, and security for data dissemination and reuse (e.g., all data will be thoroughly de-identified and will not be traceable to a specific study participant). Plans for archiving and long-term preservation of the data will be implemented, as appropriate.

10.1.4 FUTURE USE OF STORED SPECIMENS AND DATA

Data collected for this study will be analyzed and stored at the University of Wisconsin. After the study is completed, the de-identified, archived data may be transmitted to and stored at a data repository for use by other researchers including those outside of the study. Permission to transmit data to a data repository will be included in the informed consent.

We will obtain IRB approval for any future research projects that might use data from this study.

10.1.5 KEY ROLES AND STUDY GOVERNANCE

Principal Investigator
Corrine Voils, PhD, Professor of Surgery
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608-262-9636
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Participants will be given information for reporting study misconduct. The following language will be included on the information page preceding the study: *"If you have any questions about your rights as a research subject or have complaints about the research study or study team, contact UW Health Patient Relations at 608-263-8009. The Patient Relations Representatives work with research subjects to address concerns about research participation and assist in resolving problems."*

10.1.6 SAFETY OVERSIGHT

The current study will pose minimal risk to the participants. Participants will be made aware of the risks and benefits which they may incur from participating and will have time to ask questions. Further, they will be told their participation is voluntary and may leave the study at any time at no harm to them.

The PI will be directly responsible for identifying and reporting all adverse events to the IRBs and funding agency as appropriate. Study staff will report any adverse event or unanticipated problem to the PIs immediately. The PIs will report any serious, unexpected, and study-related adverse event or unanticipated problem to the local University of Wisconsin (UW) Minimal Risk IRB according to the institution's requirements. The IRB will review all adverse events during continuing review, which will likely occur annually. Given that our intervention is a hypothetical choice experiment for patients who have benign thyroid nodules, rather than a clinical intervention, we do not anticipate any problems.

We will use the UW's Institute for Clinical and Translational Research's (ICTR) Data Monitoring Committee (DMC). ICTR is UW's NIH Clinical and Translational Science Award and provides extensive research support.

The ICTR DMC will ensure appropriate measures are in place to promote subject safety, research integrity, and compliance with federal regulations and local policies.

The UW ICTR DMC is comprised of experienced members (core plus ad hoc) with expertise required to oversee this study. The DMC members will review protocol-specific reports created by statisticians using data provided by the study team. These standard reports will include an overview of study objectives, a review of actual and projected accrual rates, an evaluation of patient demographics for balance of randomization, and a summary of the number and seriousness of adverse events. Source documents may be reviewed to allow the DMC to independently judge whether the overall integrity and conduct of the protocol remain acceptable based on data provided and reported by the PI. The DMC will make recommendations to the Principal Investigator that could include actions of continuation, modification, suspension, or termination.

In providing oversight for the conduct of this study, the ICTR DMC will meet with the PI prior to data collection, after the first few participants have been enrolled, and at least biannually thereafter to review enrollment and adverse events. Additional meetings will be scheduled as determined by the DMC or as requested by the PI. Because this study is minimal risk, there are no planned interim analyses or predefined stopping points due to futility, efficacy, or harms. We will submit all reportable events to the DMC and the UW Minimal Risk IRB in accordance with their reporting guidelines.

10.1.7 CLINICAL MONITORING

N/A

10.1.8 QUALITY ASSURANCE AND QUALITY CONTROL

The study team will perform internal quality management of study conduct, data collection, documentation and completion. Quality control (QC) procedures will be implemented as follows:

Screening and recruitment data will originate in the EHR (see **Section 10.1.9, Data Handling and Record Keeping**) and will ultimately be entered into the study database in REDCap. To ensure accuracy, site staff will compare a representative sample of source data against the database, targeting key data points in that review.

Protocol Deviations – The study team will review protocol deviations on an ongoing basis and will implement corrective actions when the quantity or nature of deviations are deemed to be at a level of concern.

Should independent monitoring become necessary, the PI will provide direct access to source data/documents, and reports for the purpose of monitoring and auditing by the funding agency, and inspection by local and regulatory authorities.

10.1.9 DATA HANDLING AND RECORD KEEPING

10.1.9.1 DATA COLLECTION AND MANAGEMENT RESPONSIBILITIES

Data collection will be the responsibility of the clinical trial staff under the supervision of the principal investigator. The investigator will be responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

For this study there will be no hardcopies of data, study visit worksheets, or CRFs. As the study is completed by participants online in Qualtrics, all data for baseline measures and outcome measures will be entered into Qualtrics by the study participants themselves.

Screening and recruitment data will be recorded by study staff in REDCap (Research Electronic Data Capture), a 21 CFR Part 11-compliant data capture system provided by the Department of Surgery at UW-Madison. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data relevant to screening and recruitment will be entered directly from the EMR.

REDCap and Qualtrics both provide export procedures for seamless data downloads to Excel and common statistical packages (SPSS, SAS, Stata, R).

10.9.1.2 STUDY RECORDS RETENTION

Study documents will be retained for a minimum of 3 years after the date of Federal Financial Report (FFR) submission. These documents should be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the funding agency, if applicable. It is the responsibility of the funding agency to inform the investigator when these documents no longer need to be retained.

10.1.10 PROTOCOL DEVIATIONS

This protocol defines a protocol deviation as any noncompliance with the clinical trial protocol or International Council on Harmonisation Good Clinical Practice (ICH GCP) requirements. The noncompliance may be either on the part of the participant, the investigator, or the study staff. As a result of deviations, corrective actions will be developed and implemented promptly.

These practices are consistent with ICH GCP:

- Section 4.5 Compliance with Protocol, subsections 4.5.1, 4.5.2, and 4.5.3
- Section 5.1 Quality Assurance and Quality Control, subsection 5.1.1
- Section 5.20 Noncompliance, subsections 5.20.1, and 5.20.2.

It will be the responsibility of the principal investigator to use continuous vigilance to identify and report deviations within 14 working days of identification of the protocol deviation, or within 14 working days of the scheduled protocol-required activity. All deviations will be addressed in the screening and recruitment database, and reported to National Cancer Institute Program Official. Protocol deviations will be sent to the reviewing Institutional Review Board (IRB) per their policies. The principal investigator will be responsible for knowing and adhering to the reviewing IRB requirements.

10.1.11 PUBLICATION AND DATA SHARING POLICY

This study will be conducted in accordance with the following publication and data sharing policies and regulations:

National Institutes of Health (NIH) Public Access Policy, which ensures that the public has access to the published results of NIH funded research. It requires scientists to submit final peer-reviewed journal manuscripts that arise from NIH funds to the digital archive PubMed Central upon acceptance for publication.

This study will comply with the *NIH Data Sharing Policy and Policy on the Dissemination of NIH-Funded Clinical Trial Information* and the *Clinical Trials Registration and Results Information Submission* rule. As such, this trial will be registered at ClinicalTrials.gov, and results information from this trial will be submitted to ClinicalTrials.gov. In addition, every attempt will be made to publish results in peer-reviewed journals. Data from this study may be requested from other researchers after the completion of the primary endpoint by contacting Susan Pitt and/or accessing a data repository. Considerations for ensuring confidentiality of these shared data are described in Section 10.1.3.

10.1.12 CONFLICT OF INTEREST POLICY

The independence of this study from any actual or perceived influence, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed and managed. Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial. The study leadership in conjunction with the National Cancer Institute has established policies and procedures for all study group members to disclose all conflicts of interest and will establish a mechanism for the management of all reported dualities of interest.

10.2 ADDITIONAL CONSIDERATIONS

N/A

10.3 ABBREVIATIONS AND SPECIAL TERMS

AE	Adverse Event
CFR	Code of Federal Regulations
CONSORT	Consolidated Standards of Reporting Trials
CRF	Case Report Form
DSMB	Data Safety Monitoring Board
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
ICH	International Council on Harmonisation
IRB	Institutional Review Board
NCT	National Clinical Trial
NIH	National Institutes of Health
OHRP	Office for Human Research Protections
PI	Principal Investigator

QC	Quality Control
SAE	Serious Adverse Event
UP	Unanticipated Problem
US	United States

10.4 PROTOCOL AMENDMENT HISTORY

*The table below is intended to capture changes of IRB-approved versions of the protocol, including a description of the change and rationale. A **Summary of Changes** table for the current amendment is located in the **Protocol Title Page**.*

Version	Date	Description of Change	Brief Rationale
2	Nov 8, 2021	Added 1 South Park as a potential clinic from which to recruit	Flexibility to recruit from all UW biopsy clinics if needed

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