PROTOCOL TITLE: Targeted Melanoma Detection with Skin Self-Examination During COVID-19 Restricted Physician Access

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STUDY SUMMARY:

The purpose and overarching aim of this study is to reduce melanoma mortality by improving early detection of melanoma with skin self-examination among people who self-identify as being at risk. Self-management of melanoma detection with skin self-examination (SSE) depends on ready access to dermatologists when a concerning mole is detected. In March 2020, the Illinois stay at home order (COVID-19) removed ready physician access and prohibited non-essential health care. Additionally, there was uncertainty about when regularly scheduled health care would resume. This submission seeks to explore the feasibility of at-home non-invasive mole self-sampling for those with a concerning mole with the intention of providing recommendations about the need for the mole to be biopsied.

OBJECTIVES:

Aim 1: To assess the effectiveness of targeted melanoma detection (TMD) with SSE education delivered remotely to women who had a screening mammogram. The effect of TMD with SSE education on a) SSE performance, b) identification of concerning moles, c) time between noticing a concerning mole, requesting a mole self-sampling kit and receiving health care, and d) SSE sustainability in comparison with controls will be assessed among women served by Northwestern Medicine in one rural community and one metropolitan community. Health care providers' (HCPs) clinical/pathologic assessment of concerning moles will be identified in the Northwestern Medicine electronic health record (EHR) system.

Exploratory Aim: To assess the feasibility of self-sampling concerning moles for gene assay. Self-sampling kits will be sent to women who identify concerning moles and chose to perform self-sampling rather than watch the mole for change in a month. The blinded samples will be sent to DermTech, Inc., a CLIA laboratory, for analysis and the results reported directly to the PI. The PI will give the results to the participant, make a recommendation about the need to obtain a biopsy of the mole, offer to provide a referral to local HCPs, and send the laboratory results to the HCP selected by the participant. Anxiety/cancer worry will be assessed monthly to compare a) baseline measures, b) initial SSE and c) monitoring concerning moles for change.

Knowledge gained from this study may be helpful to other health care systems serving at-risk women and their families in locations with limited access to physicians, especially dermatologists.

BACKGROUND:

Early detection of melanoma remains a crucial component of effective treatment to reduce the mortality and morbidity of melanoma and the costs of melanoma care. In the United States (US), melanoma incidence has increased by 270% between 1973 and 2002 and is projected to continue rising in the US with doubling of newly diagnosed cases by 2030.[1,2] Melanoma is the sixth most common cause of cancer in women in the US (fifth in men). There will be an estimated 100,350 new cases and 6,850 deaths in 2020.[11] Melanoma predominantly occurs in non-Hispanic Whites with a history of unprotected occupational or recreational sun exposure; however, indoor tanning by

women as adolescents and young adults contributes to the rising incidence.[12,13] People with a history of 10 or more indoor tanning sessions in their lifetime,[14] a personal or family history of melanoma, and a history of sunburn,[15,16] are at risk to develop melanoma. When people with skin of color, such as Hispanics, develop melanoma they are twice as likely to present with late stage disease, thus, fatality is greater.[11] Prognosis is dependent on melanoma stage. For early stage melanoma, the 5-year survival is 98%, but for metastatic disease (late stage), the 5-year survival is 25%.[17] Until we effectively address self-management for early detection of melanoma among at-risk people, patients will present late in the disease process incurring significant mortality, morbidity and health care costs. Early detection of melanoma with SSE, which relies on the person promptly presenting for health care, can improve patient experience, costs of care, and survival. A case can be made for patient self-management by informed, confident patients, who appropriately seek health care for concerning moles identified with partner assisted SSE.

Since most melanomas are visible on the surface of the skin at a curable phase in their evolution, people can perform screening at home with the help of a partner. The annual prevalence of self-reported SSE in the general community ranges from 8 to 21%.[20] Women perform more SSE than men.[7] Women self-detect more than half of melanomas and melanomas detected by women had better prognosis than those detected by men because they were identified at an earlier stage.[8] The American Academy of Dermatology recognized that 6-50% of melanomas were self-detected;[21,22] therefore, the Academy encourages self-advocacy thorough routine SSE and regular skin cancer screening for at-risk patients.[23] In a 20 year follow-up case control study of people newly diagnosed with melanoma in 1987-89, skin awareness was associated independently with a decreased risk of melanoma death (HR=0.46, 95% CI=0.28-0.75, p<0.01).[24] Currently, the median delay in diagnosis, is ~27 months.[25] Reports suggest melanomas get about 0.12 mm deeper per month with attendant increasing disease stage.[26] A 27-month delay in diagnosis may result in a 0.12 mm deep melanoma (Stage 1A) becoming a 3.24 mm melanoma (Stage 2B with greater risk of metastasis). Time to presentation for care is a key determinant of the patient outcome. Compared with other cancers, melanoma has the longest delays measured as the median time to patient presentation. One goal of this research is to reduce the time from a woman first noticing a “new or changing mole” to examination by a doctor.

<u>Leveraging the Mammogram Screening Encounter.</u>
In the US, women age 50 and older develop the habit of having regular screening mammograms.[27] From 50-59 years of age is also when melanoma incidence in women increases.[28] In Illinois, screening mammograms may be scheduled without a physician’s order, thus, women who do not have regular care with HCPs may obtain mammograms. One of the innovations of our proposed study, as described below, is using the screening mammography encounter as an opportunity to educate women of all races and ethnicities at the point in their lives when melanoma is most likely to develop. In our pilot feasibility research, we leveraged mammogram screening encounters to reach women, who were not aware of their melanoma risk.[4] Women, who are the nexus of familial communication of health information and social support in their own homes and

make 80% of all health care decisions for the family, shared the SSE brochure with relatives.[4,6,29,30]

The *long-term goal* of this research is to reduce melanoma mortality by improving self-management of early detection of melanoma. Reduced mortality cannot be proven without effective structured melanoma SSE with partner assistance. One way to achieve partner-assisted SSE is to deliver a uniform self-management program to women who self-identify as at-risk, perform SSE and seek appointments with HCPs for concerning moles. In the absence of ready physician access due to COVID-19, we will test the feasibility of at-home mole self-sampling with a non-invasive adhesive patch used to acquire surface cells of the mole. Our *primary objective,* assessing effectiveness of a SSE education with partner assistance among at-risk women, extends the evidence-based SSE intervention developed among melanoma survivors and their skin check partners (R01CA154908)[6] and delivers the program to women who had a screening mammogram, which demonstrated the individuals' commitment to health promotion and cancer screening.

STUDY ENDPOINTS:

Aim 1

Primary outcome:

Effectiveness of TMD with SSE will be defined as SSE performance. Further measures of fidelity will be assessed by:

a) extent of body checked,

b) recruitment of a skin check partner,

c) time between noticing a concerning mole, requesting a mole self-sampling kit, and seeking HCP care for a concerning mole, and

d) SSE sustained by monthly performance over 4 months.

Secondary Outcome:

The effect of TMD with SSE on seeking health care comparing intervention vs control groups for:

a) inappropriate HCP appointments and skin biopsies for benign conditions, and

b) appropriate HCP appointments for the clinical diagnosis of atypical (dysplastic nevus) or rule out melanoma and biopsy performed.

Exploratory Aim

Proof-of-concept Outcome:

Research participants will self-sample concerning moles using a kit currently used in physician offices to obtain a sample (DermTech, Inc). DermTech, Inc. will perform analysis on up to 100 specimens and send the report to the PI. This report will include gene assay results or indicate if there are too few cells for analysis, which may reflect lack of self-sampling competency. If the initial sample has too few cells for analysis, then the instructions will be reviewed by telephone with the participant and an additional sample will be obtained. Time to initiation of mole self-sampling after identifying a concerning mole, number of kits returned for analysis, and adequate number of cells acquired will be assessed. Correlation with monthly SSE anxiety will be done.

STUDY INTERVENTIONS:
Contact information for potential subjects, who will be women who had a screening mammogram from January 2, 2019 until February 28, 2020, will be obtained from the Northwestern Medicine Electronic Data Warehouse (EDW). Based on our experience, women with a history of breast cancer will be excluded because the focus of their health care is on treatment of breast cancer. Subjects will be emailed a recruitment email explaining the research study regarding skin cancer prevention and skin self-examinations. Subjects will receive a link to the online REDCap program that offers electronic consent, randomization, and self-reported surveys. After remotely enrolling in the study, and completing the baseline questionnaire, the subjects will be randomized 1:1 between intervention and control arms. Intervention arm participants will receive the SSE brochure. The SSE brochure discusses basic information about melanoma, how to identify a melanoma, the importance of a skin check partner, and gives a diary for tracking monthly changes in moles via a provided scorecard. The provided postcard maybe printed by the woman and affixed to a location in their homes to capture their attention and remind participants to perform SSE. Subjects will invite a skin check partner to help score the border, color, and diameter of a new and/or concerning mole(s) using a provided scoring system for their 4 months of study participation. While a skin check partner will be beneficial to perform SSE, a skin check partner is not an absolute requirement to participate in this research. The scoring system uses a scale of 1-3 (1= normal, 2= unsure, 3= not normal). In the brochure, color examples of normal and abnormal features illustrate the scoring rules. The decision rules about seeking health care are based on the cumulative score of three features of the mole: 3 = benign, stop checking the mole; 4-7 = check the mole in one month; 8-9 = make an appointment with a doctor to have the mole checked in about 2-3 weeks, which is the standard of care for evolving moles. In the absence of physician access (COVD-19), the decision rules used in our prior research will be modified to:
8-9= perform mole self-sampling to determine if the mole needs to be biopsied.

Subjects in the intervention arm will monitor new and concerning moles for 4 months by doing monthly skin checks and partner-assisted skin checks (if applicable), record the scores on a scorecard provided in their SSE brochure, and complete the monthly online survey, which asks about changes in mole scores and potential anxiety associated with evolving moles. Subjects will also receive a monthly text message to their personal phone with SSE reminders.

If the subject indicates on their monthly survey or by communicating with the study team, in the form of an email and/or call, that the score of their mole has increased, three options on how to proceed will be offered to the subject. The three choices are as follows: a) continue monthly checking the mole for change, b) receive the mole self-sampling kit to obtain genetic analysis to guide the decision to seek health care, or c) seek an appointment with an HCP.

The mole self-sampling kit contains the materials, directions and a Fed Express or USPS Express mail envelop to overnight the kit to the DermTech laboratory.

Participants may request a kit by email or telephone call to the research team, who will send the kit by Fed Express or USPS Express mail. Within 3-5 business days, the DermTech laboratory will provide the results of the gene analysis online to the PI, Dr. Robinson, who will inform the participant with a written report stating:
a) the mole is benign, and nothing further is needed or
b) the mole needs to be biopsied.

If the initial sample has too few cells for analysis, then the participant will be invited to obtain another sample, instructions will be reviewed by telephone or by Facetime with the participant and an additional sample will be obtained.

Participants requiring a skin biopsy will be referred to a local HCP. The research team will develop a participant navigation system for triage to a local HCP, including surgical oncologists, dermatologists, and family practitioners. This triage system will be used to refer participants to schedule an appointment for the skin biopsy within 2-3 weeks. The genetic analysis of the mole will be provided in a letter to the HCP selected by the participant.

In our prior research, women have checked moles of family members, especially the male spouse. We will extend the opportunity for the women enrolled in the study to sample the concerning moles of their skin check partner. If throughout the 4 months of the intervention arm's active engagement in skin self-examinations, participants indicate that they found a concerning mole on their skin check partner while performing a partner skin exam, an opportunity for the mole of the partner to be self-sampled (or sampled by the participant) will be offered. For mole self-sampling to occur, the subject would first be asked eligibility questions to ensure they are over the age of 18. Once the age is established, the partner will be required to sign an electronic consent form, indicating what information will be collected and what information will be shared with them and their HCP.

Participants who have selected the self-sampling kit will be invited to participate in a structured telephone exit interview. The exit interview will seek to obtain feedback from the participant on the process of self-sampling and gain feedback on study materials.

PROCEDURES INVOLVED:
Enrollment to intervention or control arms, randomization, will be automated in REDCap using a specific formula generated by the performed Northwestern University's Department of Preventative Medicine statistical team. The randomization of subjects who had screening mammograms at Northwestern Medicine Kishwaukee Community Hospital Breast Center and Northwestern Medicine Lynn Sage Comprehensive Breast Center will continue until about 500 women are enrolled from each location. De-identified data will be reviewed by the study's statistical team to ensure there is an equal distribution of subjects at each site in both the intervention and control arm.

In the intervention arm (Group 2), the participant will receive the SSE brochure and SSE postcard after consenting online and completing baseline assessments. Upon request,

a printed brochure will be mailed. Participants will receive monthly reminders via email and text messaged to their personal phone to perform SSE, to encourage engagement and retention. In addition, a monthly REDCap survey will be sent to the subject's email. This monthly survey will include goal setting and reminders to engage a skin check partner to help check skin in hard to see areas and to assist with the monitoring of any concerning moles and new moles. Tracking of specific details and changes of concerning and new moles will be documented on the provided scorecard in the brochure. If the score of the mole increases, which is indicated on the monthly survey or via email and/or phone, three options on how to proceed with the concerning mole will be provided to the subject.
-Option 1 is to continue monitoring the mole monthly for change.
-Option 2 will be to perform mole self-sampling with the kit to collect a sample of surface cells of the concerning mole with four adhesive patches for gene analysis to help decide about seeking further health care for biopsy of the mole. Of note, physician collected samples tested for *LINC* and *PRAME* gene mutations differentiated melanoma and melanoma in situ from benign moles and were confirmed histologically with 91% accuracy.
-Option 3 will be to seek an appointment with a health care provider.

If mole self-sampling is selected, the kit with the subject number as ID (blinded for personal identifying information), directions, and postage for the kit to be sent to the company that created this self-sampling kit, DermTech, will be provided. Upon completing the mole self-sampling and mailing the specimen to the DermTech laboratory, it will take 3-5 days for the results to be provided to the PI, Dr. Robinson, in the form of a secure online portal. The subject will not obtain their gene test results from the DermTech laboratory. Dr. Robinson will provide written test results to the participant with the option of discussing the results with a telephone call. A referral will be made to the HCP to perform a skin biopsy if needed. The DermTech self-sampling kit is approved for use but requires ordering by a licensed HCP, who will be Dr. Robinson, the PI.

If the option to see the HCP is selected, the research team will assist with locating one and will remind the subject that the HCP may not be available for some time. The study team will not cover the cost of seeing the HCP or cost of treatment recommended by the HCP. The non-payments details are explicitly stated in the consent document.

If the mole(s) requires a biopsy and/or treatment, the EHR will be reviewed to identify diagnosis codes of the mole and review HCP notes.

If throughout the 4 months of active engagement in skin self-examinations, a participant in the intervention arm indicates that they found a concerning mole on their skin check partner while performing a partner skin exam, an opportunity for the concerning mole of the partner to be self-sampled will be offered. For the self-sampling to occur, the subject (the skin check partner) would first be asked eligibility questions to ensure they are over the age of 18 and meet basic eligibility criteria. Once eligibility is established, the partner will be sent an electronic consent form, via REDCap, and complete and sign the form,

indicating they understand what is expected of them as a research participant and the information that was presented to them in the consent document. The same process will be followed for the skin check partner as is in place for the research subject.

Controls (Group 1) will receive a healthy lifestyle brochure and a healthy lifestyle postcard after consenting online and completing baseline assessments. After enrolling in the study, a baseline survey will populate in REDCap, and the subject will be able to download a healthy lifestyle brochure and the postcard reminder. Upon request, the brochure will be mailed. Each month, the subject will receive an email to complete the monthly survey and will receive healthy lifestyle text messages to their mobile phone. The survey they receive will mirror the survey of the SSE intervention arm; therefore, awareness of SSE will be expected to increase, and SSE may be initiated among controls. If a subject indicates that they have found a concerning mole on their monthly survey, the subject will be advised to reach out to their health care provider for further assessment. After completing the final monthly survey, controls will be offered the SSE brochure.

Intervention participants who have selected the mole self-sampling kit will be invited to participate in a structured telephone exit interview. The exit interview will seek to obtain feedback from the participant on the process of mole self-sampling and gain feedback on study materials. Subjects will be asked, at time of consent, if the study team has permission to audio record the exit interview for purposes of data analysis. Subjects may opt out of the audio-recording portion of the study. The researcher will not share these recordings with anyone outside of the immediate study team. The recordings will remain in locked file cabinets and on computers with restricted and password protected access.

Anxiety will be assessed on monthly surveys. If enhanced anxiety regarding a concerning mole is indicated, a referral for psychological support will be made my PI, Dr. June Robinson.

Out of the 500 women enrolled at each location, it is expected that 140 of the 1000 (14%) enrolled will identify a concerning mole.[4]

DATA AND SPECIMEN BANKING:
See Data Management. Specimens will not be banked.

SHARING RESULTS WITH PARTICIPANTS:
Results of the gene analysis from the cells captured by the adhesive patches will be provided to the PI, Dr. June Robinson. Dr. Robinson will then inform the participant, in the form of a written report, if the mole is benign and nothing further needs to be done or if the mole needs to be biopsied. If requested, Dr. Robinson will discuss the report with participants. Participants requiring a skin biopsy will be referred to a local HCP, who will receive the genetic analysis of the mole via fax from Dr. Robinson. At the conclusion of the study, all participants will receive an email summary of the results.

The same process of sharing results applies to participants and their skin check partners who have a concerning mole to self-sample.

STUDY TIMELINES:
Subjects, both intervention and controls will be engaged with the research for 4 months. After 4 months of active engagement, follow-up communication will only occur via telephone or email to answer any incomplete questions on surveys or any questions that arise from evaluating the EHR of HCP visits regarding the concerning mole(s). All communication will be documented in the subject's file as a progress note.

In order to complete this research before the end of the grant (March 2021), we need to have IRB approval in early May, which will allow EDW to build the lists of eligible subjects. Then we will enroll subjects remotely in June-August 2020 and follow them for 4 months with online surveys (Oct-Dec 2020). Finally, the EHR of HCP visits will be reviewed about 3-4 months after the completion of the last online survey. This additional period of EHR review (Feb 2021- March 2021) gives subjects time to obtain an appointment with their HCP and have a biopsy, if needed.

INCLUSION AND EXCLUSION CRITERIA:
Inclusion Criteria:
- Adult women (aged 18 and older) having a screening mammogram with no upper age limit, who had a screening mammogram from January 1, 2019 to February 28, 2020.
- Able to read English
- Vision enough to read a newspaper
- Self-perception of their potential melanoma risk
- Willing to perform SSE with a skin check partner
- Willing to complete monthly surveys for 4 months and receive monthly text messages to personal mobile phone
- Have home Internet access and smartphone with data plan
- Have access to Federal Express or US Postal Service Express Mail to send mole self-sampling kits
- Willing to allow the research team access to their electronic health record to abstract physician assessment of concerning moles, biopsy results and treatment
- Willing to provide up-to-date email address, mailing address and telephone number

Inclusion criteria of skin check partner to have mole self-sampled
- Male or female over the age of 18 years
- Able to read English
- Vision enough to read a newspaper

Exclusion criteria
- Women under the age of 18 years

- Women overburdened with other co-morbid diseases, medical treatments (e.g., chemotherapy), or cognitive impairment (e.g., by a stroke) as determined by the PI.
- Previous participation in SSE research previously which may be a confounding variable in data analysis

Exclusion criteria of skin check partner to have mole self-sampled
- Male or female under the age of 18
- Unable to read English

VULNERABLE POPULATIONS:
This study will not include the participation of vulnerable populations

PARTICIPANT POPULATIONS:

Accrual Number:	Category/ Group:	Consented: Maximum Number to be Consented or Reviewed/Collected /Screened	Enrolled: Number to Complete the Study or Needed to Address the Research Question
Northwestern Medicine: Prentice Women's Breast Center	Women ≥ 18 years old	500	400
Northwestern Medicine: Kishwaukee Breast Center	Women ≥ 18 years old	500	400
Total:		1000	800

RECRUITMENT METHODS:
Recruitment for this study will use the Northwestern Medicine Electronic Data Warehouse (EDW) to obtain contact information of women, over the age of 18, who have had a screening mammogram.

Women, who completed their screening mammogram, will be sent a general recruitment email using the secure data collection method, REDCap. This email will allow women to click on a link that generates an interest email. If interested, an eligibility questionnaire will populate using REDCap branching logic. If a woman is eligible, based on the inclusion criteria, the consent form will populate. If no response to the email is received, a second email will be sent in 5 days. If participants do not respond to the initial and follow-up email, we will follow-up by phone.

COMPENSATION FOR PARTICIPATION IN RESEARCH ACTIVITIES:
Research subjects will be compensated with a $20 Amazon electronic gift card for completing the baseline survey and a $15 Amazon electronic gift card for each completed monthly survey for 4 months ($80 paid after completing the final survey). The total amount a research subject can receive for participation in this research study is $100 in the form of Amazon electronic gift cards.

RISKS TO PARTICIPANTS:
The potential risks to participants are expected to be minimal if they occur.

Subjects will be participating in an intervention that may enhance their awareness of their risk of developing skin cancer. All study participants will be provided with an email address and phone number to contact study staff in the event they have concerns. If a subject indicates they have a concerning mole, they will be provided with three options on how to address the mole. The research team will be in communication with the subject to ensure there are no questions or concerns regarding next steps. Because of the potential for the intervention to help the subject identify melanoma at a stage of development with the best prognosis, we feel that the potential benefits, in reduced morbidity and mortality, to the subject outweigh the risk of potential enhanced anxiety in discovering a suspicious mole. If subjects report high levels of anxiety, then a referral for psychological support would be made. We do not believe that subjects in this study will be exposed to any risk of physical or psychological harm as a result of either the intervention or research processes. Our measures do not assess individuals at risk of immediately harming themselves (e.g. suicide); therefore, we will not have to screen the data to potentially intervene with individuals who may be a risk to themselves.

POTENTIAL BENEFITS TO PARTICIPANTS:
Because of the potential for the intervention to help the subject improve their ability to detect melanomas in the early and potentially curable phase, they will reduce their risk of death from melanoma. We feel that the potential benefits in reduced morbidity and mortality to the subject outweigh the risk of potential enhanced anxiety in discovering that they are at risk to develop another melanoma. If subjects report high levels of anxiety, then a referral for psychological support would be made.

DATA MANAGEMENT AND CONFIDENTIALITY:
Data Management and Quality Control
Data will be collected via REDCap and by EHR data abstraction to populate the database. The subject number identifies the specimen on the case report form for gene sampling of moles. All databases are encrypted and stored on study specific servers at Northwestern University. Forms and database architecture will be set up during study preparation and launch. Only authorized study personnel can access these servers. Our data manager maintains data integrity and does fidelity checks and performs regular data checking for accuracy and completeness in coordination with the PI.

Design, Analysis, and Power Calculation with Target Enrollment Justification

For the RCT, participants will be randomly assigned to receive the SSE intervention or control (healthy lifestyle) in a 1:1 ratio. This will result in approximately 500 participants in each group. The primary analysis will be intent to treat, with data imputed one of two ways. First, we will run a “worse-case scenario” where all drop- outs will be assumed to not be performing SSE. Second, we will create 5 imputed data sets for missing data based on all available data and analyze with PROC MIANALYZE to obtain valid statistical inferences. From previous work, we expect at least 60% retention at 4 months.

We will use GLMM with a logit link to test if the intervention affects the rate of SSE, while adjusting for the repeated measures within individuals over the first 4 months. Using these repeated measures, and assuming an autocorrelation of 0.9, a total sample of 1000 would enable us to detect an increase from 80% of SSE in the control group to 86.3% in the intervention group. Assuming only 10% discordance, a sample of 500 control women provides 80% power to detect an increase of 7%, while the remaining 3% cease SSE. Additional fidelity measures in Aim 2 will be combined to score an overall standardized fidelity score at each time. If the mean fidelity score is 80%, a sample of 500 women provide enough information to produce a 95% Confidence interval with a width of 0.09. The sample for 500 intervention women provides 80% power to detect declining fidelity or sustainability of monthly SSEs as a standardized slope of 0.13. The secondary outcome of seeking HCP appointments for a necessary mole will be analyzed with generalized linear models, as described above, but considering the outcome as “any HCP appointment” during the study time frame. Previous data suggests that approximately 14% of women should contact HCP for an appointment, and our sample of 1000 women provides 80% power to detect a baseline rate in the control group as small as 21%.

Plans for securing the data is in the “provisions to protect the privacy interests of participants” section of the protocol.

PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF PARTICIPANTS:

All subjects are encouraged and will be encouraged throughout the course of their participation in the research study to contact the PI, Dr. Robinson at Northwestern, to report complaints or adverse events. A telephone number and email address will be provided to subjects to contact Dr. Robinson if they have any concerns or increased anxiety, or if they become worried about developing skin cancer. Instructions for reporting adverse events and complaints are included in the consent documents and on all contact, information provided to subjects through the course of the study. Any significant adverse events will be reported to NIH in addition to the local IRB, in compliance with federal regulations. Our measures do not assess individuals at risk of immediately harming themselves (e.g., suicide); therefore, we will not have to screen the data to potentially intervene with individuals who may be a risk to themselves. Dr. Robinson has been a board-certified physician for over three decades and has conducted an NCI funded R01 of a similar nature. We will notify the Northwestern University IRB, our project officers, and NCI within 24-48 hours of any serious adverse

event. We will provide an annual report to the NCI Project Officer summarizing all adverse events, should any arise.

PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF PARTICIPANTS:
This research includes provisions for protecting the privacy of research subjects. Study interactions will take place in person, through electronic collection data forms using REDCap, with a paper-based on the case report form for gene sampling of moles that used a subject number to identify the specimen, and by telephone. The research team will make every effort to address the questions and concerns of potential and current subjects. Steps will be taken to ensure that the subjects feel at ease throughout the entire process. To reduce the sense of intrusiveness a subject may experience in response to survey questions, subjects will be informed that they may decline to provide any information they do not wish to disclose. The information being collected is limited to only the minimum amount of data necessary to accomplish the research purposes.

The research team will be permitted to access study-related, subject-reported information and the EHR of subjects who have a visit with a health care provider for a concerning mole. The EHR of skin check partners will not be accessed. The database that will house this data will only have de-identified data. A unique subject number will replace the use of names in the database. Our systems are guarded against outside entry by Northwestern's own firewall supporting 128-bit encryption. This level of encryption provides the highest level of protection against hackers, computer break-ins, etc. All data is de-identified. Only experienced research team members will work on this study and will have receive training that includes an emphasis upon the importance of confidentiality of information, and all personnel on the project will complete the required NIH training in the protection of human research participants. Physical copies of collected data forms will be retained in separate locked file cabinets and on computers with restricted and password-protected access, without links to the master code list. All data based on the research will be reported in aggregate form. No individual respondents will be identified. Electronic data will be maintained in a study-specific database on the server of the Department of Dermatology at the Feinberg School of Medicine. Paper-based files will be kept in a locked cabinet in a locked room within the Northwestern University Department of Dermatology research offices. Identifiable data will be kept separate from the case report forms and source documents. Data gathered as a result of this study are available to inspection on request by the Food and Drug Administration or other government regulatory agency auditors, and the Northwestern University Institutional Review Board (IRB).

Only approved research personnel will have access to the stored data. The PI is ultimately responsible for the receipt and transmission of the data. As per the Department of Dermatology protocol, data will be retained indefinitely after the completion of the study. All data and other information in this study will be maintained confidentially.

ECONOMIC BURDEN TO PARTICIPANTS:

Taking part in this research study will not lead to any costs for subjects unless the option of seeing an HCP for a new or concerning mole is selecting. This research will not cover the cost of a copayment for seeing the HCP or any cost of treatment or care provided by the HCP. No monetary or non-monetary (gift cards, coupon codes) forms of reimbursement options will be provided to subjects for health care resulting from finding a concerning mole. This information is explicitly stated in the consent document.

CONSENT PROCESS:
Participants will be required to answer eligibility questions prior to obtaining access to the online consent form (REDCap). A question on the eligibility criteria will ask participants if they feel comfortable reading and completing the consent process electronically. Question regarding the research will be invited and answered by telephone as needed. If a participant indicates she would like to participate in the research study, the consent document will be completed electronically and the participant will complete the following survey items electronically, as they will be sent to the participant's email.

The electronic consent process will use the secure data collection platform, REDCap. Participants will have questions asking them if they would like to speak to a research team member before signing the consent form. Questions will also be in place to ensure that the subject is comfortable with what is required of them if they agree to participate in the research and that they understand the information. If they indicate no to either of the questions, the consent form will generate an option for a phone number to be collected for a study team member to contact the potential subject to review the information. These steps are put in place to ensure each subject is comfortable with the information in the consent form, before being enrolled in the study.

PROTECTED HEALTH INFORMATION:
This research study involves the use of Protected Health Information. A HIPAA Authorization will be obtained from all subjects. This Authorization will be included in the consent document. Subjects who do not authorize the use of their PHI will have the alternative of not participating in this study. Information to be obtained from EDW by access to EHR data is indicated below:

- Name
- Geographic Subdivisions
- Dates and Age
- Telephone numbers
- Email address
- Medical Record Numbers
- Most recent mammography screening appointment information (date of screening mammogram and location of screening mammogram)

The EHR will be reviewed by the PI for:

- Health care provider notes from visit pertaining to a concerning mole (date of visit, notes from visit, diagnosis code of mole, plan of treatment and/or treatment)

HIPAA Authorization will not be obtained from skin check partners, as the study team will not be viewing their EHR.

QUALIFICATIONS TO CONDUCT RESEARCH AND RESOURCES AVAILABLE:
Dr. Robinson has been a board-certified physician for over three decades and has conducted an NCI funded R01 and R21 of a similar nature. We will notify the Northwestern University IRB, our project officers, and NCI within 24-48 hours of any serious adverse event. All research assistants have CITI documents on file. Other resources. Lynn Sage Breast Center completes approximately 90,000 screening mammograms each year and Kishwaukee Hospital completes approximately 7,000 screening mammograms/year; therefore, there are adequate numbers of potential subjects to be identified by the EDW search. Dr. Robinson has full-time research staff and voluntary medical students who fully support this research study at 100% effort. Dr. Robinson also has weekly meetings with research staff to address any questions regarding the protocol, questions from research subjects, or study related procedures.

MULTI-SITE RESEARCH:
NA

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