FOX CHASE CANCER CENTER
TEMPLE HEALTH

Protocol Title
LIVE-R Life: Liver Cancer Education

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1.0 Introduction

Incidence and mortality rates in liver cancer are on the rise in the U.S[1]. By 2030, liver cancer is expected to exceed breast cancer as the second leading cause of cancer death in the U.S[2]. Up to 30% of liver cancer cases are attributed to Hepatitis B (HBV) and/or Hepatitis C (HCV) viral infection, though the fraction of liver cancer cases in African American and Asian patients attributed to chronic HBV or HCV is much higher, closer to 40%-50%[3]. In Caucasians and Hispanics, HCV infection is considered a second leading cause of liver cancer, behind only diabetes and obesity[4]. In the State of Pennsylvania, racial trends in liver cancer, HBV, and HCV are similar to those in the U.S[5]. In the Temple University Health System, which serves primarily African American and other minority groups, incidence rates of liver cancer are the highest of any cancer site.

Liver cancer incidence rates could be significantly lowered by reducing rates of HCV and HBV infections[6]. Treatments with high cure rates exist for HCV, and HBV can be prevented through vaccination[7]. Further, HCV and HBV infection are often contracted through risk behaviors (i.e., sexual activity, drug use, unsanitary tattoo/nail salon practices) that could be modified through educational interventions and policies. However, rates of both liver cancer and HCV continue to rapidly increase, suggesting that available, evidence-based interventions are not reaching the most vulnerable, high risk populations. There is a disconnect between translation of findings from discovery into population impact, and the disproportionate rates of HBV, HCV, and liver cancer across racial groups suggest health inequities contribute to the growing burden of liver disease in this country.

In this study, we propose to bridge the gap between evidence and action and combat rising liver cancer rates attributed to Hepatitis B and C infection in Philadelphia by identifying neighborhoods with higher than expected rates of liver cancer and related risk factors and administering an educational intervention in those communities, working with existing community partners at Fox Chase Cancer Center. In this proposal, we will generate new methods for identifying smaller communities or geographic areas (at the census tract level) in need of liver-cancer related interventions. This is an improvement over existing studies that focus mostly on single risk factors for disease and targeting counties, which are often too large to implement public health programs[8]. By dually considering area-level measures of disparity (i.e. race/ethnicity, immigration, poverty, etc. from the U.S. Census) WITH the distribution/co-occurrence of liver cancer, HBV, and HCV, we hope to also shed light on disparities in liver cancer. We hypothesize that communities carrying the greatest burden of liver disease (liver cancer/HCV/HBV) AND health disparities, if targeted, could lead to the greatest declines in liver cancer over time. Further, community partners that work with the Fox Chase Office of Community Outreach requesting cancer education sessions via our Community Speaker's Bureau for their community programs will be approached with this new liver cancer initiative. We will begin with partner sites identified via geocoding as well as regions where we need to establish new partnerships. Partners will be informed of the project, its objectives and if interested, we will deliver the educational session about person-level liver cancer risk factors and how to reduce liver cancer risk, as well as some background on liver cancer rates and neighborhood research. We will then administer pre-post tests to participants to test knowledge, attitudes, and intentions, and will disseminate liver cancer brochures from the American Liver Cancer Foundation to relevant community groups. The use of surveillance data and the application of geospatial analytics to guide interventions that benefit populations more efficiently is a strategy that defines precision public health[9].

2.0 Objectives/Aims

Aim 1 (Similar to currently approved IRB #17-9031): Conduct a geographic scan of liver cancer and related risk factors (age, race/ethnicity) for the entire State of PA by census tract in order to dually *identify* neighborhoods in Philadelphia with greater disease/disparity burdens than expected compared to the State and to *inform* where liver cancer-related educational interventions may be most needed. *Hypothesis:* Enhanced spatial tools/metrics (that couple disease rates & area-level measures of disparity) will inform resource allocation through more precise identification/targeting of communities in need.

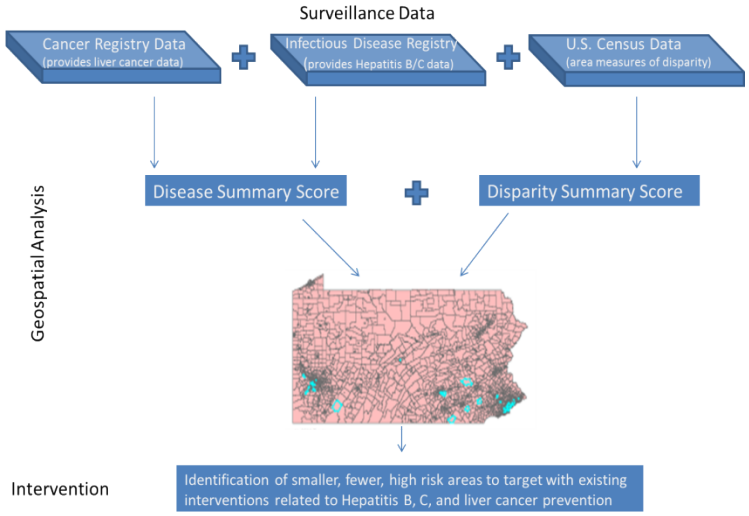
Aim 2: To identify and/or establish community partnerships in "high-risk" areas to collaborate with, delivering and evaluating educational sessions.

Impact: Our focus on geospatial, area level risk factors will provide novel insights into liver cancer disparities. We take an innovative precision public health approach where the successful primary and secondary prevention of liver cancer could be monitored in areas selected for intervention in future studies.

3.0 Background/Rationale

A. Precision Public Health Approach in Liver Cancer. As outlined in currently approved IRB 17-9031, the use of data to guide interventions that benefit populations more efficiently is a strategy referred to as precision public health. Precision public health requires primary surveillance data, rapid application of sophisticated analytics to track the geospatial distribution of disease, and the capacity to act on this information in the form of interventions. In this proposal, we plan to use surveillance data from the Pennsylvania (PA) Cancer registry, the PA and Philadelphia Infectious Disease HBV/HCV registries and the U.S. Census in order to identify fewer and smaller geographic areas that are carrying the greatest disease burden of liver cancer, as well as a high burden of determinants of health disparities. We will create new combinations of disease metrics and summary scores for determinants of disparity in order to estimate the disease/disparity burden in each census tract in Pennsylvania. In an attempt to maximize limited resources, our goal is to select the fewest number of "in need" areas, where existing educational and screening interventions are likely to have the greatest impact on decreasing liver cancer rates.

Figure 1. Precision Public Health Approach to Liver Cancer



B. Liver Cancer Statistics. The incidence rates of liver cancer have tripled over the past three decades. Due to a very poor prognosis, liver cancer is the fifth most common cause of cancer death in the United States. Hepatocellular carcinoma (HCC) is the major histological subtype, accounting for up to 80% of all cases[10]. In Pennsylvania, the incidence and mortality rates of liver cancer have been climbing each year since 2003. In our catchment area, incidence rates of liver cancer are the highest of any cancer site in the Philadelphia area. Thus, the burden of liver cancer needs to be addressed.

C. Liver Cancer and Hepatitis. Risk factors for liver cancer are largely understood, with up to 70% of liver cancer cases being attributed to modifiable factors, including drug/alcohol use, obesity, diabetes, and viral infection with Hepatitis B/C[4]. Despite these risk factors being largely addressable through early detection, vaccination, treatment, and lifestyle interventions, liver cancer continues to rise in the U.S., particularly in minority populations) [4]. Hepatitis B and C account for 32% of liver cancer cases in the U.S. In African American and Asian populations, HBV and HCV account for 40-50% of liver cancer cases, whereas in Hispanics and Caucasians, HBV and HCV account for closer to 20% of cases. In a study of Philadelphia residents between 2003-2012, individuals with HCV and HBV accounted for close to 40% of all liver cancer diagnoses. Further, HCV-infected patients were also 2.8 times more likely to have liver cancer detected before age 65 and to have an earlier age of death than individuals without HCV. For Philadelphia males and non-Hispanic blacks, HCV was more common and more often associated with liver cancer diagnosis and death at a younger age. For Asians in Philadelphia, HBV was more common and more often associated with liver cancer diagnosis and death. Given the contribution of HCV and HBV to liver cancer in our area, widespread public health actions to prevent HCV and HBV infection could have a substantial effect on the burden of liver cancer in Philadelphia. Thus, in this proposal, we focus on identifying geographic areas (census tracts) that carry the greatest burden of liver cancer, and will be creating an educational session to review risk factors for liver cancer and how to decrease risk.

D. Disparities in Liver Cancer. Beyond race/ethnicity, individual-level socioeconomic status (SES) (e.g., education, income, employment), as well as area-level SES conditions (i.e., neighborhood socioeconomic deprivation), are also believed to contribute to liver cancer[11]. Liver cancer patients are more likely to live in deprived-socioeconomic conditions, and studies show that these area-level socioeconomic associations may result from the geographic distribution of individual risk factors associated with liver cancer, such as low educational attainment. This is important because studies have shown differences in area-level determinants of disparity by race, i.e. African Americans living in neighborhoods with high poverty (but not areas with high unemployment) and Hispanics living in areas of low educational attainment have higher rates of liver disease. Further, additional determinants of disparity (beyond race/ethnicity, education, income, employment) that are dually related to health outcomes and can provide useful information for intervention development, also warrant further study. These determinants include immigration status, literacy, transportation, and housing (Table 1). In this study, we more comprehensively evaluate determinants of disparity in liver cancer. We do not plan to investigate associations between determinants of disparity and liver cancer, but will quantify the prevalence of determinants of disparity in small geographic areas (i.e. census tracts) and use that information to create an overall disparity metric or score. This new disparity metric can be referenced and used to determine 1) which areas with high rates of liver disease (liver cancer, HCV, and/or HBV) also have a high disparity score (with the hypothesis that targeting fewer areas with higher disease and disparity scores will result in maximizing limited resources); 2) what determinants (i.e. education, employment, literacy, etc) are driving the low disparity score in each area, which can inform the type of intervention/intervention materials needed for designated high risk areas(i.e. where should Spanish educational interventions be offered, etc).

E. Recommendations for the Primary and Secondary Prevention of Liver Cancer. While recommendations for liver cancer do vary, the National Comprehensive Cancer Network panel recommends screening with ultrasound and alpha fetoprotein (AFP; a liver cancer blood biomarker) testing every 6 to 12 months for patients at risk for liver cancer. At risk populations are defined as those with liver cirrhosis and hepatitis B. Liver cirrhosis can be caused by HBV

and HCV infections. Screening tests for HCV and HBV involve blood test screening for HCV and HBV antibodies. For those diagnosed with HCV, curative treatment is recommended. One problem is the majority of HBV/HCV carriers do not know they are infected. Thus, they can unknowingly spread the virus (through risk behaviors such as unsanitary needle use). Further, those with chronic HCV and/or HBV infection are often diagnosed with advanced liver disease (cirrhosis) and/or advanced liver cancer. Patients diagnosed with early stage liver cancer survive more than 5 years. However, the majority of liver cancer cases are diagnosed with advanced stage liver cancer where the average survival is less than one year. Given the contribution of HBV and HCV to liver cancer incidence, interventions that provide education about hepatitis, who is at risk, and how it is contracted, will likely have an impact on liver cancer incidence and mortality rates. The complex interactions of risk behaviors, differences in disease rates by race/ethnicity, and the impact of social environment on liver cancer suggests that community-based approaches to identifying high risk areas and high risk individuals within those areas, is warranted. We will discuss recommendations and reduction of risk behaviors in our educational session.

F. Innovation. This is the first study to apply a precision public health approach to address the growing burden of liver cancer and to engage community partners in this process.

4.0 Study Design

In line with the Precision Medicine Initiative, we propose to utilize data from existing resources, to inform liver cancer prevention using cross-sectional data for the liver cancer geospatial analysis. Intervention materials include the development of an educational module addressing risk factors, symptoms, diagnosis and treatment. The sessions will incorporate both didactic and interactive modalities. The educational module includes a slide presentation, and will be accompanied by an educational brochure that participants can take home. The information included in the educational brochure reinforces the information presented in the slide show. Prior to each session, a pre-test will be administered to establish a baseline of knowledge and to collect demographic information. Following the education session, we will administer a post-test to evaluate the initial impact and assess participants' interest and impact of neighborhood health.

4.1 Recruitment and Eligibility. Eligible participants will self-identify at scheduled community events with identified community partners. They will be able to read and understand English or Spanish, and be 18 years or older. Participants must also be Philadelphia residents, or receive healthcare at a community partner site that is located in Philadelphia. Additional demographic data such as age and racial/ethnic background will be collected on the pre-survey.

Recruitment of participants during the COVID-19 pandemic will be adjusted to adhere to stay-at-home and social distancing orders. These adjustments will include working with community partner sites to assist with the promotion of the liver study via a recruitment flyer to assist with identification of potential participants. Individuals interested in participating will contact FCCC staff directly at the number provided on the flyer or provide the partner with permission for us to contact them. We may also contact participants from a previous study that gave us permission to contact them about future research opportunities (IRB #17-8005). Per our protocol, staff will identify themselves and let them know why we are calling and how we obtained their name. Former study participants who are being re-contacted will be reminded that they gave us permission during previous study participation.

The ongoing COVID-19 pandemic has negatively impacted the research team's ability to recruit via standard methods originally proposed due the "stay-at-home" orders. Therefore, the team would like to explore the following two approaches to facilitate recruitment efforts:

1. Collaboratively working with Temple Physicians Inc., an existing partner, we have drafted an invitation letter to their patients promoting the study and requesting that interested individuals, contact the research team. No direct patient recruitment will be employed.
    a. The TPI practices have been identified and categorized according to the priority methodology presented.
2. With the approval of a Fox Chase Cancer Center Facebook Community Outreach page, we will utilize passive recruitment practices to promote the study, utilizing the approved recruitment flyer, to invite interested participants to contact the research team member listed on the recruitment flyer[12].
    a. The Community Outreach FB sites intended audience is FCCC Community Outreach partners and their networks;
    b. No direct targeting of individuals will be administered. Interested participants will call the research team listed on the approved recruitment flyer or may click a link provided in the Facebook post to be taken to an opt-in survey in REDCap. The opt-in survey responses are only accessible by the study team;
    c. No individual's personal data will be collected via FB;
    d. No individual's online activity will be collected and retained by the investigators;
    e. Online communications will be monitored to ensure no PHI is divulged.
    f. Comments posted regarding participation will be allowed as long as no specific information that might jeopardize the study is posted i.e. responses to questions;
    g. Online communications will be monitored by the Outreach team (Zambon, González, Ortiz). Any negative comments or PHI will be blocked from public view. All negative comments will be collected and if appropriate, will be reported to the IRB.

We believe these additional strategies will expand our reach, potentially benefitting our recruitment efforts. While the FB approach may garner a broader audience that our priority areas, we will continue to utilize the eligibility criteria stated, remaining focused on Philadelphia County. We will monitor and assess the overall impact of our new approaches as part of the data analysis and manuscript development.

This protocol is registered on clinicaltrials.gov, and eligible individuals who reach out to the study contact (Sorice) listed on the study profile will also be recruited.

Participants recruited during the COVID-19 pandemic will also be asked if they have reliable telephone access and if they have access to a computer; due to suspension of in-person recruitment, the study will be conducted over the telephone and/or via Zoom or a similar platform.

4.2 Aim 1 Methods: Conduct a geographic scan of liver disease rates and determinants of disparity

A. Study Population. As part of IRB 17-9031, we will use **Registry data from the Pennsylvania (PA) State Liver Cancer Registry.** This data has about 18,000 incident liver cancer cases (primarily Hepatocellular Carcinoma cases) diagnosed from 2003-2015 from the cancer registry. For each patient in the registry, we will geocode or request existing geocodes at the census tract level to represent the neighborhood in which they live. We will exclude cases missing geocodes, address information or with P.O. Box addresses.

B. Area-level Determinants of Disparity. As part of IRB 17-9031, area level determinants of disparity were selected from Year 2010 U.S. Census and the 2010-2015 American Community Survey. In this analysis, we focus primarily on race/ethnic breakdown by neighborhood (i.e. % non-Hispanic Black; %Hispanic). We also collected information on the estimated total population of each census tract, gender breakdowns and reported age ranges within each census tract to allow for stratification/adjustment. Area-level determinants of Disparity from the U.S. Census data were linked at the census tract level to the PA State Cancer Registry.

C. Database Linkage and Geocodes. Geocoding of liver cancer data was completed a part of IRB 17-9031. Geocoding is the process of assigning latitude and longitude to a point, based on street addresses, city, state and ZIP code. Geocodes are defined here in terms of Federal Information Processing Standard (FIPS codes) and will link each case to the geographic area in which they live. These codes include unique identifiers for each state (two digits), each county (3 digits), and each census tract (6-digits) in the U.S. On average, there are approximately 4,000 residents located in a single census tract; as such, census codes can serve as unique identifiers for census tract-level neighborhood characteristics[13], and household information is not easily identifiable[13]. Patient addresses, including street address, city, state, and ZIP code, are needed to create geocodes and assign individual patients to a census tract. The Pennsylvania Cancer Registry and Pennsylvania Department of Health have provided patient address for geocoding. As part of IRB 17-9031, we implemented additional protections for our geocoded study populations by employing a “false coordinate system” to decouple household addresses from individual personal data attributes. That is, we have mapped the data in such a way that the true geographic location is not stored in the GIS software. For instance, the actual position of an address might be described by the coordinates: -125.652, 24.229. The statistical tools within GIS enable us to very simply alter the true coordinate values by adding or subtracting a fixed value to all the X and Y geographic coordinates in the dataset. We intend to employ a “minimum-maximum false coordinate range” of values 1-8 — to ensure that the confidentiality of the study participants’ household addresses are, not in any way, compromised. Further, for areas or census tracts with a minimal number of patients (i.e. <6 patients), we employed geographic aggregation techniques and small area estimations to further protect confidentiality[14]. Once geocodes were created from PA Cancer Registry data, patient address information were removed and destroyed, as only geocoded, de-identified data was kept and used for analysis.

D. Liver Disease Definitions. Incidence rates of hepatocellular cancer(HCC) and early (Stage 1/2) versus late stage (Stage 3/4) HCC.

4.3 Aim 2 Methods: Identification of Community Partners and Development of Education Session

A. Identification of Community Partners. Working with long-standing community partners, the Office of Community Outreach (OCO) will isolate those located within the "high-risk" communities identified via geo-spatial analysis. Community sites may include community-based, faith-based, academic, primary care community practices or non-government organizations. Once we have worked with a set of identified partner sites, we will seek to establish additional partnership to expand our reach.

Historically, OCO networks with community partners to offer our education sessions via our community speaker's bureau. The sessions are generally one-hour long and are offered at no cost. For the purposes of this study, we will inform the partner sites that this education session is part of a pilot research project we are conducting to determine the community's understanding of the liver cancer burden in the region and to assess their interest in community health. Based on this conversation, the partner will inform us of their interest in participating.

B. Education Session. The intervention consists of a PowerPoint presentation (See Appendix B), an educational brochure, and a pre/post test (Appendix C). An OCO trained health educator will provide delivery of the session; didactic and interactive modalities will be employed to engage participants. This includes sharing liver cancer anatomical models and encouraging participants to ask questions during the Q/A period.

The module will provide participants with a general overview of cancer and will then provide liver cancer specific information. Included in the module is risk factors, symptoms, screening, and diagnosis and treatment information. The PowerPoint presentation will be accompanied by an educational brochure for participants to take home with them. Following the liver cancer information, the health educator will provide an overview of neighborhood health and what this project aspires to yield from our approach.

The PowerPoint liver module is written at a 7.3 grade level and has been vetted for accuracy by clinician Minhhuyen Nguyen, MD at Fox Chase Cancer Center. Behavioral Scientists, Shannon Lynch, Ph.D., Jennifer Reese, Ph.D. and OCO Sr. Director Evelyn Gonzalez have developed the pre/post tests. The final versions has been reviewed by the director of health communications, Stephanie Raivitch for plain language review. Once approved by IRB, OCO will proceed with translation of the documents into Spanish, using the TUHS approved vendor(s).

Because in-person education sessions cannot be held during the COVID-19 pandemic, the educational slides will be converted to a set of handouts that will be sent to the participant (along with the educational brochure). The educational intervention materials will be sent via US mail to participants who do not have reliable internet access, and those who prefer to view the materials online will be offered the choice of having them emailed or texted, or viewing them on Zoom. The health educator will call the participant to review the educational materials over the telephone (or Zoom). By default, the intervention will be conducted over the telephone and only participants who indicate that they are comfortable utilizing a web platform will be offered the intervention over Zoom (or a similar program). Zoom instructions will be given over the telephone at the time of the intervention to those who opt to receive the intervention online. For analysis purposes, intervention delivery method (pre-COVID in-person/telephone/online) will be tracked, as well as the timing of the intervention relative to consent and baseline (immediate administration, i.e., at time of consent and baseline vs. delayed administration, i.e., after materials are mailed to the participant after consent and baseline).

4.4 Study Procedures

A. Recruitment and Informed Consent. The Office of Community Outreach (OCO) has a history of working with multiple community organizations, offering free bilingual education via our community speakers bureau. During our education sessions, community partners coordinate logistics, promote our programs and invite community members to participate. Recruitment of study participants will occur working through these long-standing community partners. Partner sites will promote the study and invite participants to a session to learn more. A recruitment flyer may be used at some sites to advertise the study.

Recruitment efforts will be concentrated in census tracts with the greatest need for intervention, i.e., census tracts identified as high-risk due to socioeconomic factors linked to liver cancer (e.g., % non-Hispanic Black, household stability) and high rates of liver cancer. If no current partners are located in these high-risk census tracts, potential new partners will be identified by searching for community centers, federally qualified health centers, etc.

Individuals who attend the session will be informed about the scope of the study and invited to formally participate by the study team. Individuals interested in participating will be consented by health educator Rosa Ortiz, project manager Allison Zambon, or Co-PI Evelyn González prior to completing the pre-intervention survey. Persons not interested will be thanked for their time and excused. We anticipate recruiting between 50-100 participants, depending on the number of participating community partners and the number of education session completed. Education sessions may be conducted on a one-on-one basis or in a group, depending on the number of interested individuals present at any given session. Individuals who refuse to participate or who withdraw from the project will be treated without prejudice.

Due to the COVID-19 pandemic, in-person recruitment efforts conducted by OCO has ceased. During pandemic-related closures, all study-related activities will be conducted over the phone, online, and through US mail. Recruitment will be conducted over the telephone, and informed consent will be obtained verbally (also over the telephone). Once informed consent is obtained, an oral consent document will be sent via US mail to the participant.

B. Study Survey
Once eligibility has been confirmed, informed consent has been obtained, participants will fill out a sign-in sheet that includes their street address. If the participant agrees to be contacted about this or future research after their participation, they will also be asked to write their telephone number on this form. Because the sign-in sheet contains identifiable information, it will be kept separate from survey data and will be linked by a study ID assigned to the participant after consent. The street address data will be geocoded for neighborhood analysis. Telephone numbers will be stored in a secure database. Once geocodes are created from the street addresses, hard copies of the sign-in sheets will be destroyed. After the sign-in sheet is collected, the study survey will be administered. Once approved, the English survey will be translated into Spanish language. Once translated, a modification will be submitted.

The study “pre” survey will be administered post informed consent process and prior to the educational intervention by OCO health educators (field staff). Upon completion of the educational module, a posttest survey will be administered. All survey data will be entered in the RedCap database.

Both the pre- and post-survey will contain measures of knowledge about liver risks and prevention, self-efficacy about talking to medical professionals about neighborhood risk, as well as demographic items (e.g. gender, race/ethnicity). The post survey will include similar knowledge questions as well as additional questions specifically related to neighborhood health, including a program evaluation, outcome expectancies about learning about neighborhood health (i.e., the extent to which leaning about neighborhood health will be beneficial), and intentions to talk with clinicians about liver cancer, neighborhood health and liver cancer screening. **Primary outcomes** include pre-post changes in knowledge about liver cancer, interest in learning about neighborhood health, outcome expectancies for learning about neighborhood health, and participant intentions for talking to their doctors about liver cancer risk.

During COVID-19 closures, the survey will be administered over the telephone. Mailing and street address will be collected during recruitment, so that informed consent copies and intervention materials can be mailed to the participant.

C. Follow-up of Participants

At this juncture, we do not anticipate active follow-up of participants. However, we will include an option on the consent form for patients to be re-contacted should we determine it necessary or if we have other research opportunities.

5.0 Data Management

All study data released to Fox Chase Cancer Center (FCCC) will be kept in a study-specific, secure, password protected, REDCap database (which will be created by the FCCC Population Studies Facility or study team). REDCap (Research Electronic Data Capture; developed by Vanderbilt University in collaboration from a consortium of institutional partners) will be used for electronic data collection and study data management[15]. The REDCap system is a secure, web-based application that is flexible enough to be used for a wide variety of research studies. It offers intuitive interfaces for data entry and real time data validation. REDCap relies on a study-specific data dictionary that will be defined by the research team. REDCap supports easy data manipulation with audit trails and reporting capabilities, including automated export to common statistical packages (SPSS, SAS, Stata, R). REDCap was developed around HIPAA-Security guidelines, and all web-based information transmissions are encrypted. REDCap currently supports 500+ academic/non-profit consortium partners on six continents and over 70,000 research end-users (www.project-redcap.org). All data will be stored on a server maintained by the FCCC Information Systems and Technology Department in a secure data center. The server is backed up to tape on a daily basis and is protected from inappropriate outside access by commercial grade firewalls.

Separate secure databases will be used to a) store information which could identify participants (e.g., name, local address, contact information, etc) and b) store geocoded de-identified data from regional/state/national data resources for subsequent data linkage. Select research staff will be given access to the study REDCap database. Only research staff involved in patient recruitment/geocoding will have access to information which could identify participants. Only geocoded de-identified data will be used/released for analysis. Address information will be destroyed once geocoding is complete. All data will be destroyed seven years after study closure.

6.0 Risks to Participants

For this study, in Aim 1, we will be utilizing existing data resources under a currently approved IRB protocol #17-9031. Only geocoded (census tract level), de-identified data will be used for analysis. We will provide additional protections for our geocoded study populations as follows. If we are provided patient addresses, we will employ a "false coordinate system" to decouple household addresses from individual personal data attributes. That is, we will map the data in such a way that the true geographic location is not stored in the GIS software. For instance, the actual position of an address might be described by the coordinates: -125.652, 24.229 (see the illustration below). The statistical tools within GIS enable us to very simply alter the true coordinate values by adding or subtracting a fixed value to all the X and Y geographic coordinates in the dataset. We intend to employ a "minimum-maximum false coordinate range" of values 1-8 — to ensure that the confidentiality of the study participants' household addresses are, not in any way, compromised. Further, for areas or census tracts with a minimal number of patients (i.e. <6 patients), we will employ geographic aggregation and geomasking techniques to further protect confidentiality[14, 16] Given we are working with geocoded, de-identified registry data for analysis and employing patient protections during the collection, storage, and analysis of data, this study represents minimal risk to participants.

There is no physical risk to participants. There is a however a small risk that participant(s) may feel uncomfortable answering some questions on the survey. Participants will be informed of their options to not answer any question they are uncomfortable responding to.

The study team will make every effort to keep the information provided in the study confidential.

- All information gathered during this study will be kept in locked cabinets or in electronic databases that are password-protected.
- The study team will delete your name and other information that might identify participants, whenever possible.

Additional Protections Against Risk. Fox Chase Cancer Center (FCCC) participates in the Collaborative Institutional Training Initiative (CITI) on-line education program. In order to participate in the conduct of research, all research personnel involved with human subjects research must complete the tutorials designated as applicable to their research role. Test dates and results are on file with the FCCC Institutional Review Board Office and Human Subjects Protection Office. Investigators/staff participating in this project will complete CITI training (and have evidence of current certification on-file). In addition, all research personnel will be in compliance with the Health Insurance Portability and Accountability Act (HIPAA) and other federal/state regulations.

Every effort will be made to protect participants against risk. All participants, will be told that they do not have to answer any questions that they do not want to answer and that they have the right to withdraw from the project at any time. Data will be collected and maintained in a manner that will not jeopardize the integrity of the project, but more importantly the privacy and confidentiality of the participants.

Study processes regarding to data entry, data management are outlined in Section 5.0.

Only persons directly involved with the project will have access to data identifying individuals. No names will be stored on computer files for data analysis, and no individuals will be identified in the results of this project. Access to computer-stored information will require simultaneous

knowledge of the data format, computer language, file name, and password. We anticipate no significant risks

7.0 Potential Benefits to Participants

There may or may not be direct benefits to the participants of this project. The information learned from this project may benefit underserved populations in our Primary Service Area and will contribute to our efforts to better target prevention programs for liver disease and liver cancer.

FCCC is committed to focusing its clinical and research enterprise on vulnerable populations. The proposed local data collection will provide new, potentially "actionable" information about risk behaviors, cancer knowledge/attitudes, cancer information access/usage, and cancer screening knowledge/access/usage across the various populations served by FCCC. Data/insights gathered from the large, at risk, minority population will be of crucial importance. The proposed project will also provide the Center with a deeper understanding of knowledge/attitudes about screening testing among the populations FCCC serves, which will in turn allow us to more effectively engage them in community-based, hypothesis-driven, research initiatives moving forward.

The specific areas of health benefit to the populations served by FCCC will not be appreciated until the data are analyzed and strategies to align the Center's research initiatives with the cancer burden in the catchment area Primary Service Area, optimize cancer prevention and control efforts, and increase inclusion of minorities in clinical research/trials and biobanking research have been implemented. Nonetheless, because the proposed study poses minimal risks to participants, the potential health benefits to the populations served will likely greatly outweigh any potential risks to participants.

8.0 Provisions to Maintain the Confidentiality of Data

Research study staff and the FCCC Population Studies Facility will maintain project data in confidence according to the rules and regulations of FCCC, the ICR, the FCCC/TU IRB, and HIPAA requirements. All information which could potentially identify participants will be maintained on a separate secured database. All paper files with identifiable information will be stored under lock and key at all times. All computer systems will be password-protected against intrusion; all network-based inter-site communications of confidential information will be encrypted.

An on-going computer virus protection program is available and utilized, maintained, and audited on all computers and pathways into the system, including good practice policies, screening of data files, executable software, diskettes, text macros, downloads, and other concerns as they arise. The redundant backups described above allow for quick restoration of data in the unlikely event that a security breach (or the more likely event of a hardware failure) occurs. Patient addresses will be removed from the dataset once geocoding is complete, and only geocoded, de-identified data will be used for analysis. Identifiers will be stored separately from study data, and all identifiers and linkages will be destroyed 7 years after the completion of this study.

9.0 Costs to Participants

There is not cost associated with this project. Neither community partners nor participants will incur any costs.

10.0 Consent Process

Informed consent will be obtained from all participants prior to study participation. The informed consent form has been written at a 6.9 grade level and has been reviewed by the health communications director at Fox Chase. The health educator will read aloud the consent to participants and participants will be given time to ask questions before they sign consent forms (or indicate verbal consent). Participants with email access will be offered the opportunity to be sent the verbal consent form via email so that they may read the form along with the recruiter during the consent process. Once the individual fully understands each element of the consent, including the purpose, requirements, risks, confidentiality, right to withdraw, and contact person, the individual will be asked to provide informed consent. Eligible participants will be given a copy of the consent form for their records (either a copy of their written consent or an oral consent form). Participants who consent in person will be given a copy of the consent form at the time of consent, and those who consent verbally over the telephone will be sent a copy of the consent form via U.S. Mail. Consents will be translated into Spanish and submitted as a modification in the event we plan to enroll Spanish-speaking participants.

The informed consent process for both in-person and telephone verbal consent will be documented in detail, and research staff will date and sign the informed consent document. The original paper copy of the signed/countersigned document will stored in the participant's file, as well as uploaded into the study REDCap database.

11.0 Off-Study Criteria

Not applicable

12.0 Drugs and Devices

Not applicable

13.0 Multi-Site Research Study

Not applicable

14.0 Statistical Analysis

14.1 Spatial Analysis. The dataset for the geospatial analysis is de-identified, and geospatially aggregated to protect patient confidentiality[14]. Spatial analyses will be conducted by Fox Chase Cancer Center/Temple University using SatScan spatial scan statistics that empirically identify neighborhood clusters at the census tract level wither higher than expected rates of liver cancer [17], similar to existing protocol #17-9031. Mapping will be completed using ArcGIS 10.2 software (www.esri.com)**.**

14.2 Participant Self-Report Data. Demographics will be summarized using descriptive statistics. Statistical analysis for efficacy of the education sessions will include changes in knowledge, changes in self-efficacy, and intention. Mean differences will be calculated in self-report outcome measures at pre- and post-survey, along with standard deviations and the effect size (mean difference/SD of the differences). We will compare the pre-post differences using t-tests or Wilcoxon tests, as appropriate.

14.3 Power. The sample size calculations are based on the primary outcomes for the pre-post evaluation of the education intervention. We assume a standard effect size of 0.3-0.4 on the primary outcomes (0.3-0.4 times the standard deviation of the pre-post changes for the

measures). We therefore aim to accrue up to 100 patients (but no less than 50) to have 80% power to detect a standard effect of 0.3-0.4, with 5% two-sided type-I error.

14.4 Limitations. Modifiable area unit problem (MAUP) will be evaluated and appropriate scale, aggregation, and cluster size will be considered for geospatial analysis.

15.0 Data Safety Monitoring Plan

Not applicable

16.0 Adverse Events

Not applicable

17.0 Quality Assurance Procedures and Participant Confidentiality

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). To ensure confidentiality all records will be on encrypted, password-protected computers (See section 7).

Quality assurance procedures for administration of the educational intervention include completion of a fidelity checklist to ensure that health educators are reviewing the material in consistent and complete manner. Health educators will be asked to track whether any portion of the educational slides was not reviewed, and will document reasons for non-completion.

18.0 Participant Informed Consent

See Section 9.0.

19.0 Appendices

Appendix A: Informed Consent Form
Appendix B: PowerPoint Presentation and Educational Brochure
Appendix C: Pre/Post-Test Survey
Appendix D: Sign in Sheet

20.0 References

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