Clinical Study Protocol

A COMMUNICATION -BASED STUDY FOCUSED ON ASSESSING AND IMPROVING HEPATITIS C SCREENING RATES, AS WELL AS TREATMENT RATES IN ARIZONA AS A STEP TOWARDS DISEASE ERADICATION

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Study Sponsor & Investigator:	Shahid Habib, MD Liver Institute PLLC 5295 E Knight Dr. Tucson, AZ 85712 United States of America
Study Related Phone Numbers:	Office – 520-382-5972 Research & 24hr – 520-822-4361

LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation:	Definition:
AA	Alcoholics Anonymous
AE	Adverse Event
ADHS	Arizona Department of Health Services
CDC	Center for Disease Control
ELISA	Enzyme-linked Immunosorbent Assay
FAQ	Frequently Asked Questions
GCP	Good Clinical Practices
HCC	Hepatocellular Carcinoma (liver cancer)
HCV	Hepatitis C Virus
IBM	International Business Machines Corporation
ICH	International Conference on Harmonization
IEC	Independent Ethics Committee
IRB	Institutional Review Board
NA	Narcotics Anonymous
NHANES	National Health and Nutrition Examination Survey
PCR	Polymerase Chain Reaction
PHI	Protected Health Information
Hep C Antibody Screening	A test used to screen for hepatitis C by identifying antibodies the body makes in response to HCV infection.

Hep C RNA Test	A more accurate test used for diagnosing hepatitis C by measuring the number of HCV genetic material (viral RNA).
Cirrhosis	Degenerative liver disease characterized by fibrosis and scarring of the liver tissue and is caused by various chronic conditions affecting the liver.
HIV	Human Immunodeficiency Virus: HIV is also transmitted through blood contact and carry the same risk factors as HCV, therefore the two may happen simultaneously.

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Clinical Study Protocol Synopsis

Title:	A Communication-Based Study Focused on Assessing and Improving Hepatitis C Screening Rates, as well as Treatment Rates in Arizona as a Step Towards Disease Eradication
Site Location:	Liver Institute PLLC 5295 E Knight Dr Tucson, AZ 85712 United States of America
Objective:	To eradicate the prevalence of hepatitis C in Arizona through improving awareness, increasing population screening rates, and providing linkage to care.
Introduction:	The World Health Organization has set a goal of Hepatitis C (HCV) eradication by 2030 and this study's focus is to assist in accomplishing this goal. The utility of modern technology such as texting, emails, and phone calls in eradication of a communicable disease has not been studied and validated.
Hypothesis:	The utilization of modern technology such as texting, emails, and phone calls will expedite population-based HCV screening. Digital coding of these screened subjects will help to connect individuals with care. Moreover, the utility of digital technology such as telemedicine would increase the rate of HCV treatment. Taken together, modern technology will expedite the process of HCV eradication.
Research Aim:	The aim of this study is to assess the HCV screening rate in Arizona by identification of potential HCV patients/subjects through different methods of communication – text message, email, social media, radio, newspaper ads, and flyers.
Research Gaps:	Currently, patients are screened by a primary care physician based upon presentation including liver function tests, abnormal liver imaging, or disclosed high risk behavior. Although the Center for Disease Control (CDC) has recommended universal screening of "baby boomers", adherence to this recommendation is poor in the primary care setting. With the current rate of screening for HCV infection, eradication of HCV

infection by 2030 as per WHO recommendations is not an achievable timeline in the United States.

Methods: The study will focus on various methods of communication to reach the population of Arizona from the most prevalent counties to lowest prevalence. The study is organized into phases focusing on the various communication methods beginning with direct communication through mass text messages and mass emails followed by indirect communication through social media (YouTube, Facebook), newspaper, radio, Alcoholics Anonymous meetings, Narcotics Anonymous meetings, and homeless shelters. Each phase will consist of four cycles of a monthly intervention period in which communication will be active and a two-month gap that will be used to assess effectiveness of the communication method. Subjects will receive information on HCV, contact information for the study coordinator at the Liver Institute PLLC to address questions or concerns, and a code that will allow them to receive a free HCV screening test at their local Sonora Quest Lab. This code can be used at the time of receipt or a few months later, whenever the subject is ready for testing. This timeline allows to enhance subject compliance. The results from Sonora Quest Lab will be transmitted to the study coordinator at the Liver Institute PLLC and depending on the subject's insurance status will link the subject to a treatment center. Ideally it will be their primary care physician but if the subject does not have one then it will be the closest treatment center. Alternatively, the Liver Institute PLLC is also equipped to provide telemedicine appointments to evaluate the subject and provide treatment depending on insurance status. Those that are uninsured will be provided with available options for treatment. All subjects will receive information on the disease to reduce transmission and encourage friends/family to get tested. This study will function on a version of the test-and-treat approach to help reduce the spread of HCV in the Arizona population.

Results: The study will allow us to obtain diagnostic rates for each communication method as well as the number of HCV positive individuals that are linked to care for treatment. By comparing diagnostic rates between communication methods, we can identify the most successful method to utilize for a bigger subject outreach. Additionally, by determining the rates of HCV positive individuals linked to care, we can identify deficits in the treatment of screened individuals. These components taken together will allow us to evaluate the overall success of our study.

Conclusion: The United States is well behind the overall goal of HCV eradication by 2030. To successfully facilitate completion of this goal, a new process of HCV screening and linkage to treatment is necessary. We propose a study

	focused on evaluating various methods of modern communication to increase the HCV screening rate in Arizona and link these individuals to treatment centers based on their insurance status. With the design of this study, we can evaluate the most successful method of communication and address the gaps in linking positive HCV individuals to treatment. Overall, the aggressive nature of our study is a step in the process to accomplish the goal of HCV eradication.
Principal Investigator:	Shahid Habib, MD & PI
Sub-Investigators:	Kristine Gradisher, MS (Physiology), Clinical Research Coordinator, & Sub-I Julie Piittmann, FNPC & Sub-I
IRB Number:	Pending
Protocol Date:	Pending

1.0 Introduction

1.1 Disease Background

CDC statistics from 2013 indicate that deaths due to hepatitis C (HCV) surpassed the number of deaths due to 60 other infectious diseases combined, including HIV and tuberculosis[3]. HCV is an ever-growing public health issue that continues to be the cause of mortality in millions. Additionally, prevalence of the disease is constantly increasing due to the initial asymptomatic phase and infectious nature of the disease[3]. Approximately 60-80% of people with the virus will develop chronic HCV infection, characterized by a lifelong illness with serious life-threatening complications such as cirrhosis, and hepatocellular carcinoma[15]. The risk of disease progression increases with concurrent heavy alcohol consumption, ingestion of hepatoxic medications or supplements, and presence of poorly managed insulin resistance, iron overload, or other comorbid conditions such as end stage renal disease[4].

With current effective and well-tolerated antiviral oral therapies, 95% of patients can be effectively treated[15]. However, their benefit will be unremarkable if efforts to improve rates of diagnosis and treatment remain the same[2]. Many barriers continue to prevent control and eradication of the disease. These include identifying HCV carriers, connecting to treatment and prevention. Most people infected with the virus are asymptomatic and therefore are unaware of their infection while still being able to transmit it to others. The only way to diagnose the disease in this case is to get tested. Therefore, nationwide screening is required if the future public health burden of hepatitis C is to be ameliorated[16].

1.2 Scientific Rational: Eradication of HCV in Arizona

HCV related malignancies are among the leading causes of mortality in comparison to death from all other causes in Arizona, especially in the middle-age population (Figure 1). The World Health Organization (WHO) set several recommendations with the goal of eradicating HCV by 2030 and several developed countries have taken the initiative to meet these goals[17]. The United States on the other hand is significantly lagging to achieve this target. With the current rate of screening, diagnosis, and treatment, it will take several decades to meet the goals of eradication. There is an urgent need to take aggressive action.

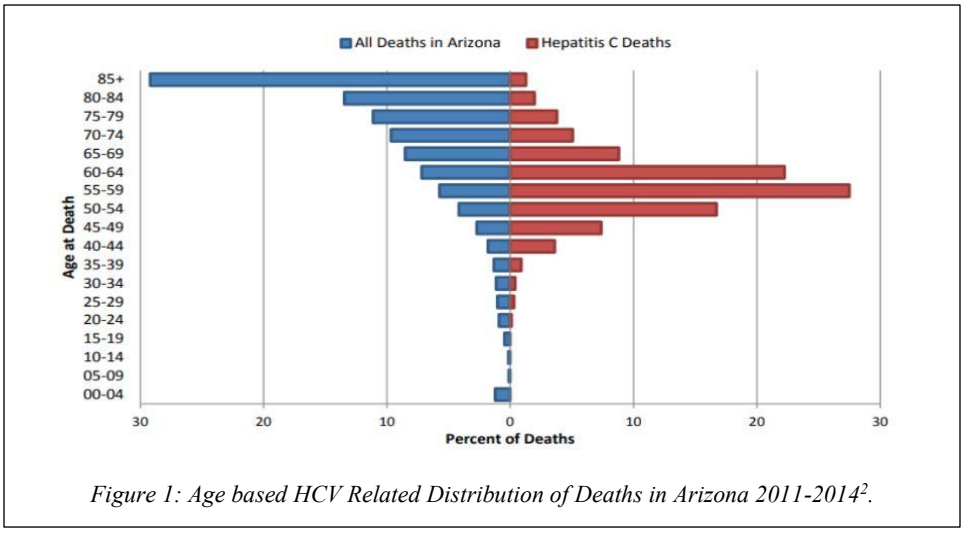

Figure 1: Age based HCV Related Distribution of Deaths in Arizona 2011-2014[2].

According to the Institute of Medicine (IOM), 75-90% of HCV positive individuals in the United are unaware of their infection[10]. Current HCV standards encourage screening to only those who are thought to be at risk including injection-drug users, baby boomers, persons with known HCV exposure, HIV infection and patients with signs/symptoms of liver disease[7, 2]. However, these standards leave millions undiagnosed, hence the increasing trends of HCV[1, 6]. According to the results of the NHANES questionnaire (Figure 2), the primary reason for lack of treatment is lack of diagnosis[16].

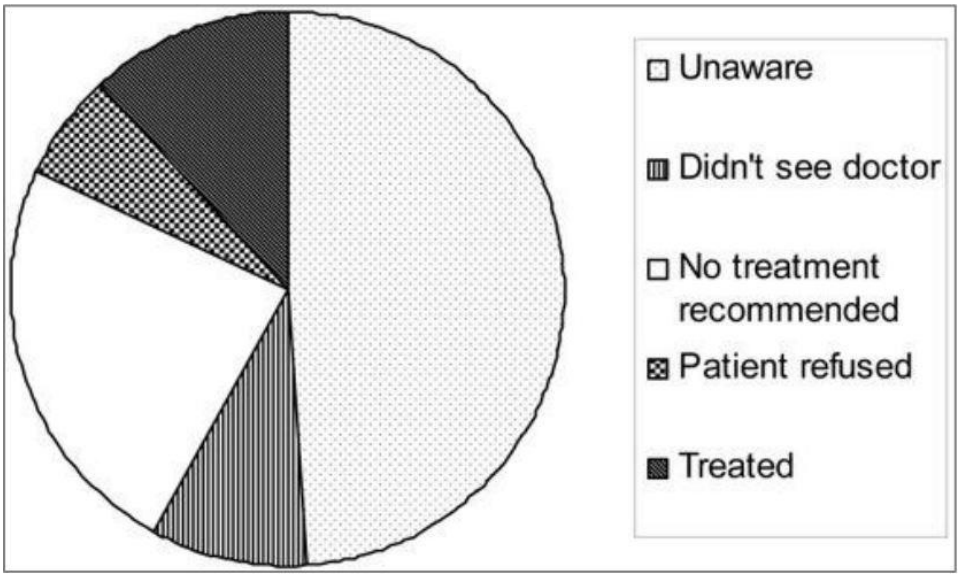

Figure 2: NHANES Hepatitis C Follow-Up Questionnaire Results (n=133)[16].

For each new acute HCV case that is reported in the United States, the CDC estimates there are approximately 13.9 actual new HCV cases (reported and unreported)[15]. This high ratio (total estimated cases to actual reported cases) is primarily a result of the large proportion of individuals with acute HCV who have asymptomatic or minimally symptomatic infection. Therefore, many may continue to transmit the disease to others but find it unnecessary to seek medical care.

1.3 Current Standards: Outreach, Screening, and Therapies

- Currently, there is no standard model of public hepatitis C education and screening promotion. Although approaches like newspaper or media advertisement were used in the past, their benefit remains unknown. On the contrary, there are published reports evaluating the benefit of media campaigns on awareness of breast and cervical cancer screenings. Evaluating the benefit of this project is quite challenging, a meta-analysis revealed short term response of 4% to mass education on improving awareness for mammogram and pelvic examination for breast and cervical cancers, respectively[14]. There are no prior studies to estimate the response to HCV screening education in the mass population.
- Current standards encourage HCV screening for individuals considered to be at risk. This includes baby boomers, individuals exposed to infected blood or illicit

drug users. However, these standards do not take into consideration the transmission of disease and other possible causes, leaving millions undiagnosed.

- There are a variety of tests that can detect the presence of Hepatitis C Virus, one of which utilizes anti-HCV ELISA test and is confirmed by HCV PCR. Additional methods include imaging studies and liver biopsies.
- Current standards of treatment include several antiviral medicines that effectively cure the disease in most cases. The course of treatment typically takes 12-24 weeks based on the genotype of disease, extent of liver damage and whether the patient was treated for hepatitis C in the past. In addition to antiviral therapy, complications like cirrhosis and subsequent complications can also be treated using different medical procedures or medicines to prevent risk of liver failure, portal hypertension and liver cancer[13].
- The Arizona Department of Public Health lags three year on their data compilation and reporting. Most recent data available for review is from 2016.

1.4 Research Hypotheses

1. We hypothesize that aggressive approach to increased awareness of the entire population while providing effective links to care will promote higher screening rates and therefore increase diagnosis rates.
2. We hypothesize that providing screening with no charges would ultimately be a cost-effective and time-efficient approach towards eradication of the disease. It will facilitate the process and invite more of the population to get screened with resultant increase in the rates of diagnosis and therefore higher treatment rates.
3. We hypothesize that creating a central system to link the identified HCV patients to a facility that could provide effective treatment with their insurance plans would help eradicate HCV in a timely and cost-efficient manner.
4. We hypothesize that an aggressive educational and treatment approach would minimize onset of new HCV infection in the future.

2.0 Objectives and Endpoints

2.1 Objectives

- To evaluate the net benefit of an aggressive approach utilizing modern day tools to reach the total population of Arizona at both an individual and population level.
- To evaluate the magnitude of increase in diagnosis rates of Hepatitis C with aggressive outreach to eradicate the disease in the state.
- To evaluate the benefit of utilizing a central system that links identified individuals to a treatment center based upon insurance status.

2.2 Endpoints

Primary Endpoints:

- Patients screened
- Patients treated

Secondary Endpoints:

- Rate of diagnosed HCV+ individuals
- Rate of patients undergoing treatment
- Increased awareness
- Identify challenges in terms of identification

3.0 Investigational Plan

3.1 Study Design

- This is a prospective study performed over a 45-month period. The principal design plan will follow Figure 3 below.

- The study design is based on HCV prevalence order, which was determined based on statistical data from the Arizona Department of Health Services and rate of Hepatitis C per 100,000 (Figure 4). High prevalence counties (123+ cases per 100,000) including La Paz, Mohave, and Yavapai with a total targeted population of 391,999 individuals. Medium-prevalence Counties (101-123 cases per 100,000) are Coconino, Gila, Greenlee, Maricopa, Pima and Pinal with total targeted population of 4,724,421. Low-prevalence counties (<101 per 100,000) including Apache, Cochise, Graham, Navajo, Santa Cruz, and Yuma with a population of 490,388.

- For the initial 9 months the study will utilize direct communication methods (email and text messages) to reach high prevalence areas (Month 1-6), medium prevalence areas (Months 7- 12), and low prevalence areas (Month 13-18).

- The second phase of the study will utilize indirect communication methods (Newspapers and Radio advertisements) and similarly target areas of high prevalence (Month 12-24), medium prevalence (Month 25-30) and low prevalence (Month 31-36).

- The third and last phase is detected for shelter visits and homeless education in high prevalence areas (Month 37-39), mid-prevalence areas (Month 40-42) and low prevalence areas (Month 43- 45).

- This program will follow a streamline cascade of care with three complementary, consecutive portions: Patient education during intervention periods, connection to appropriate care and treatment during gap periods (Figure 3).

- The person responsible for conducting and implementing the project will be the program coordinator. The coordinator will be responsible for responding to calls or emails regarding the study in reference to the FAQ in Appendix 8.3. One hour daily, 5 days per week will be dedicated to answering emails and responding to voice messages or calls. The number of hours will be adjusted according to project performance and needs.

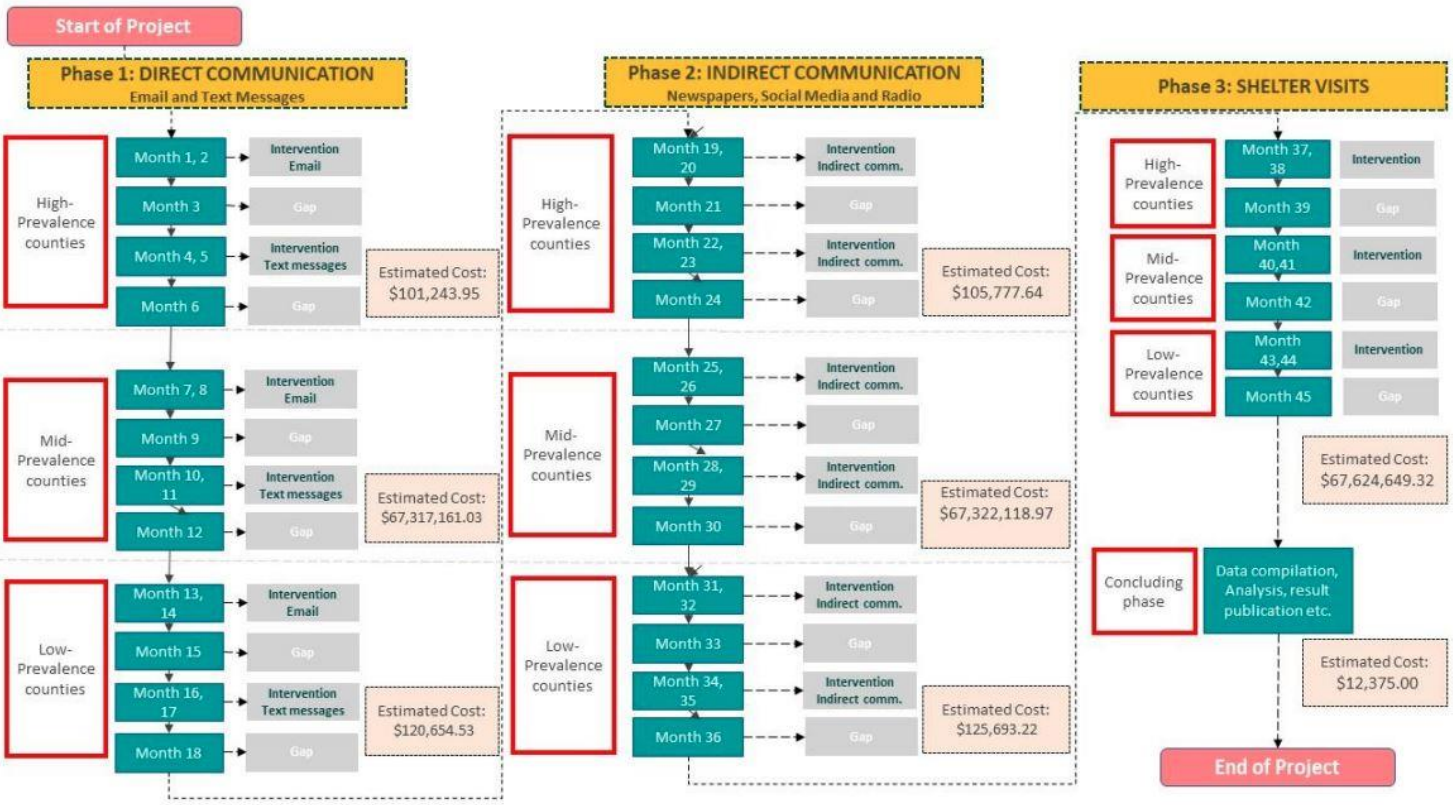

Figure 3: Study Protocol

Phase 1: Direct Communication

1. Direct Customized Email Messages

Email messages are customizable and tailored to individual people. The expected response rate as compared to similar healthcare content is about 2%, 112,136 of our targeted group.

a. Generating Email List

Email listings of Arizona residents will be obtained from National Data Group and mass emails will be sent through sendgrid.com.

b. Frequency and Resources

Emails will be sent out daily during intervention periods of 2 months followed by a 1-month gap for two rounds for each of the different prevalence groups. A project coordinator at the Liver Institute PLLC will assure expectations and targeted numbers are met.

c. Email Content

The email content will follow the template in Appendix 8.1, including an introduction of the program coordinator, introduction to the project as well as brief background information on

the disease and its risk factors (Appendix 8.6). It will also include the steps that need to be taken and contact information to answer any questions.

d. Progress Monitoring

Updates will be obtained from the carrier company as documented proof of the number of emails sent. Information will also be collected on how many emails were rejected and how many were opened. This information will then be used to guide adjustments of upcoming steps if expected response rates are not reached.

2. Direct Text Messages

Response rates to text messages are similar to that of emails at about 2% or 112,136 of the targeted population.

a. Generating Phone List

A list of Arizona residents phone numbers will be generated by National Data Group and messages will be sent to the targeted population through Verizon wireless.

b. Frequency and Resources

Text messaging will similarly follow the protocol described in Figure 3. Messages will be sent daily during the intervention period for 2-month followed by a 1-month gap for two rounds for each of the different prevalence groups.

c. Text Content

The text content will follow the template in Appendix 8.2. The message will be brief in comparison to the email content. It will include an introduction of the program coordinator, introduction to the project, the steps that need to be taken to get screened and a link to more information and background on the disease. It will additionally include contact information to answer any questions or connect to screening and treatment resources.

d. Progress Monitoring

Updates will be obtained from the carrier companies as to how many messages were sent daily and how many were rejected. This information will then be used to guide further changes or alterations if expected response rates are not reached.

Phase 2: Indirect Communication

1. Newspapers, Advertisement Content, and Duration

Newspaper advertisements are assumed to generate a response rate of 2% or 112,136 of the targeted population. However, according to the local newspaper statistics, the response rate is expected to be higher.

a. Newspapers

The most common local newspaper in Arizona is The Arizona Republic. Both newspapers are well-rounded, published daily or weekly and readily available to the public. This newspaper serves all counties in Arizona, making it efficient and more accessible to all members of the population.

- The Arizona Republic – Best Life
  According to republicmedia.com, "Best Life" is the section inside the Arizona Republic dedicated for active, healthy adults and include preventative health tips and postings. This section is published weekly on Mondays and typically generates 46% response rate from the reader population.
- The Arizona Republic – Overview
  Since the previous section focuses on health-conscious individuals, another post will be published in the overview section, which is distributed daily. According to republicmedia.com, this section reaches 1.1. million adults weekly in the Phoenix area, 32% of local residents. Advertising through the Arizona Republic is therefore likely to generate the expected response rate and reach the majority of our targeted population.

b. Duration and Monitoring
   - The hepatitis C newspaper advertisement will run similarly to other communication methods during the intervention periods; in 2-month intervals followed by 1-month gap for two rounds for each of the different prevalence groups.
   - Data collection and monitoring will be based on screening numbers during the gap periods. The project coordinator will be responsible for communicating with the magazine to make adjustments as needed.

c. Advertisement Content
   - The content of the newspaper advertisement will be an infographic designed to present background information on the disease, a brief explanation of the program and its rationale and next steps that need to be taken.
   - The infographic will be designed by the program coordinator to display the information in a simple and clear format to comply with the newspaper's requirements.

2. Social Media

The third approach aimed to target the remaining 33%; 835,414 is social media: including radio and YouTube advertisements. This method is expected to generate a response rate of about 2%.

a. YouTube

- Type of Advertisement

Bumper advertisements are only six seconds and play before videos. Since our target population consists of the entire population of Arizona, the ad will be constricted by location to only appear to viewers from the State of Arizona.

- Resources and Content

Since TrueView video has longer duration than bumper ads, it will be more detailed and include a combination of project introduction and rationale along with contact information and links to more information. The bumper ad on the other hand is limited to 6 seconds and will therefore be more concise. Both videos will provide links for more information and connections to screening locations and communication methods to answer any questions in relation to the study.

- Frequency and Implementation

The YouTube advertisement will similarly run for 2-month intervals followed by a 1-month gap for two rounds for each of the different prevalence groups. The frequency will be determined in accordance with agent feedback and adjusted according to performance thereafter.

- Monitoring

By utilizing a Google AdWords account, we will monitor our TrueView ad performance and views. This information can be used to optimize and to adjust throughout the duration of the study if needed.

b. Radio

- Resources

Radio advertising is one of the powerful means of communication that can reach a large audience from all age groups. The project will therefore employ widely known radio stations in the State of Arizona, one of which is iHeartRadio.

- Content

The content will be like that used in other methods of outreach and will include a brief introduction to the project and its rationale as well as contact information to the project coordinator to answer any questions or inquiries.

- Duration and Frequency

The radio advertisement will run in accordance with the other forms of advertising, during intervention periods for 2 months followed by a 1-month gap for two rounds for each of the different prevalence groups. The ads will run 5-7 time per week. The timing will be determined based on feedback from an advertising specialist from iHeartRadio and will be during programs dedicated to the older Arizona population of 40+ years of age.

- Monitoring

The radio advertisements will be monitored through regular performance updates of the frequency the advertisements were played over the duration of the study, what time they were played and how many were the expected number of listeners. These updates will guide any mid-study adjustments to the design if needed.

Phase 3: Conferences and Shelter Visits

The final method is educational conferences and visits to homeless shelters and NA/AA meetings. With approximately 0.64% of the population being homeless and 67% of HCV cases with a history of intravenous drug use[1], conference visits are expected to reach the remaining population.

a. Approaches

The first method of reaching this group is through educational visits to homeless shelters and NA/AA meetings in Arizona. There are 22 homeless shelters in the Phoenix area and 14 in Tucson.

b. Conference Visits Frequency

The shelter and NA/AA visits will be conducted during the intervention periods of the study with an anticipated average of three visits per shelter.

c. Monitoring

To monitor the progress of this step the number of attendees to each conference meeting will be recorded. The impact on the other hand will be measured through the screening and test results during the gab period.

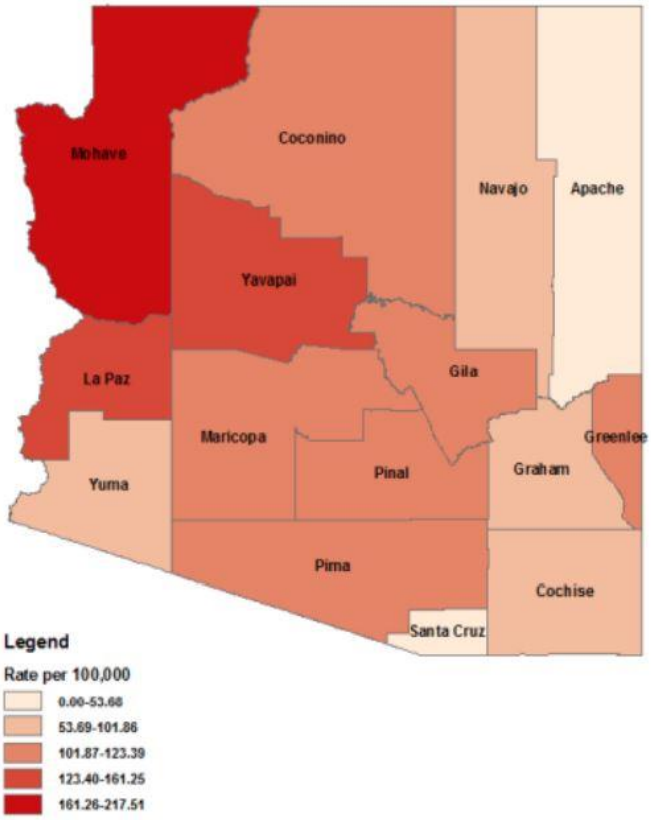

Figure 4: Average Annual Rate of Hepatitis C by County, 2002-2008. Retrieved from ADHS[1].

3.2 Subjects

The targeted study population consists of the entire Arizona population 15+ years of age. According to the ADHS 2017 vital statistics, this age range makes up 80% of the population and a total of 5,606,808 people. The targeted population is divided and ordered as below based on two parameters: known hepatitis C prevalence rates and risk, and the optimal method of communication.

1. Adults (45+)

Baby boomers are 5 times more likely to have hepatitis C than adults from any other age group[4]. According to AZ DHS population statistics, this group makes up 51% of the targeted population; 2,864,689 people. We hypothesize that older people are not exposed to social media as adolescents and young adults are. Therefore, it is important to utilize Email, direct text messages and newspaper outreach to reach this population.

2. Nasal and Injection Drug Users

Another extremely high-risk subgroup is nasal and injection drug users. Figure 5 below shows the rate of HCV positive antibody tests compared to the percentage tested categorized by risk factors. The results indicate 88% of the HCV positive clients had history of nasal drug use compared to 69% amongst all clients[1]. We believe reaching out to this community would be an essential step in diminishing hepatitis C. To reach out to this group we plan on distributing pamphlets to treatment and rehabilitation entities.

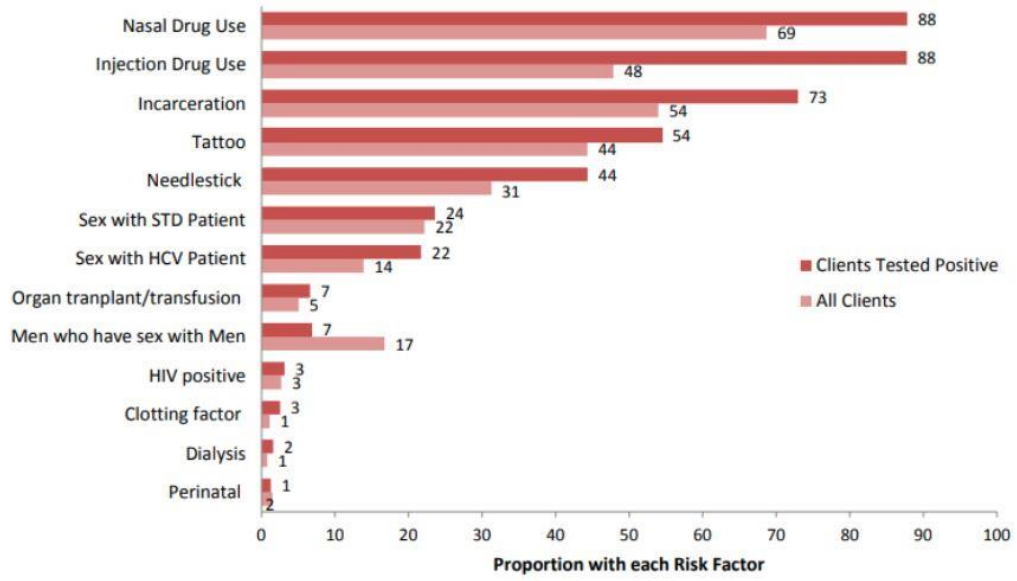

Figure 5: Risk factors for all clients who had a positive HCV result compared to all clients tested[9].

3. Homeless

Another high-risk subgroup likely to develop infectious diseases is the homeless. According to Phoenix Rescue Mission, there are over 36,000 homeless people in Arizona, 71% of which are in Maricopa county[8]. In addition to their lack of awareness, this group likely do not have access to healthcare or healthy living environments, making them even more prone to fatal viruses and diseases. The most appropriate method to reach this subgroup would be through homeless shelter visits.

4. Adults (20-44)

This age groups makes up about 40% of the targeted population; 2,273,230 people. This group is likely exposed to social media as well as newspapers and direct communication methods such as email and text messages.

5. Millennials / Adolescents (<19 years of age)

We believe this age group, consisting of 8% of the targeted population; 468,889 people, would be equally responsive to social media and directed Emails and text messages. With the growing impact social media has on this category, it has more potential of engaging them than any other means of communication would.

3.3 Educational Outreach

The systemized approach that will be taken in this study will target all patients repeatedly through a series of methods starting with individuals of higher risk, priority and expected response rate. Outreach program will follow AZ HCV prevalence map (Figure 4), starting from high prevalence counties with 123 or more Hepatitis C cases per 100,000, medium prevalence areas with 101-123 cases per 100,000 and finally low prevalence counties with less than 101 cases per 100,000[1].

3.4 Population Screening

- Screening Promotion

A time limited screening test promotion code, specific to educational outreach methods, will be obtained from Sonora Quest Laboratories and advertised in both direct and indirect communication methods of the educational program. Interested individuals would be required to present a specific promotional code and sign the Informed Consent Form.

- Screening Locations

Screening will take place in all branches of Sonora Quest Laboratories over the state of Arizona. Patients will have the opportunity to present at any of the locations and get free screening regardless of their insurance coverage or whether they are considered at risk or not.

- Informed Consents

The study, expectations and rights will be explained to patients. Informed consents will be obtained electronically by the screening team to perform anti- HCV test, to share personal information and test result with Liver Institute study investigator team, and to agree to discuss treatment options if HCV test become positive. Consents will be sent to the Liver Institute PLLC where they will be stored in an encrypted electronic data capture system as per Western Institutional Review Board (WIRB) guidelines.

- Clinical Parameters

Demographics data and contact information will be recorded for each patient in Sonora Quest Laboratories data system as per their guidelines. Clinical and relevant history pertaining to hepatitis C including diabetes and existing conditions will be collected by study team from HCV positive individuals.

- Screening

Screening will be conducted by members of the Sonora Quest Laboratories with ELISA IV antibody test with reflex to HCV PCR test to confirm the diagnosis. Patients will be contacted with their test results by a member of the research team, as well as by Sonora Quest.

3.5 Links to Care: Treatment of HCV Infection

- In case of a positive test results, the project coordinator will communicate with the patients for treatment options.
- Patients with HCV+ screening results will be contacted during the gap periods by the program coordinator, who will link these patients to treatment and care.
- Project coordinator will identify HCV care provider for each HCV positive patient depending upon patient's insurance status.
- Project coordinator will help and facilitate assistance program applications to patients without insurance.
- The screening process is shown in Figure 6.

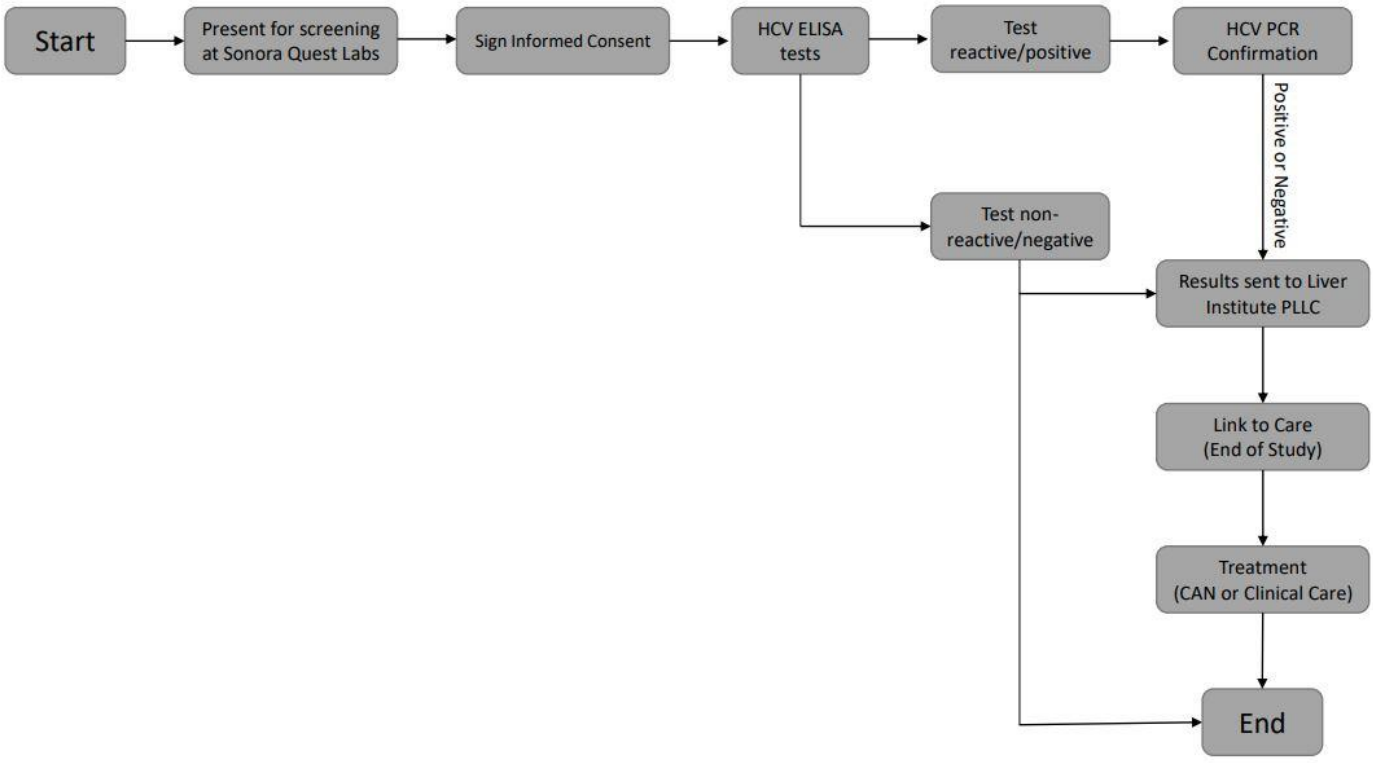

Figure 6: Hepatitis C Outreach Program Methodology.

4.0 Selection and Withdrawal of Subjects

4.1 Inclusion Criteria

- Subjects must sign the consent to screen and take part in the study.
- Subjects must be at least 15 years of age.

4.2 Exclusion Criteria

- Patients will only be enrolled once
- Patients who do not meet the inclusion criteria
- Patients with a current HCV diagnosis
- Patients who underwent a liver transplant

4.3 Withdrawal of Patients

- Patients who do not wish to participate in the study can withdraw at any time.

5.0 Data Management and Analysis

5.1 Data Entry and Management

- Data will be entered into the electronic data capture system utilized by the Liver Institute PLLC.
- Data and results will be entered within a week after they are collected during the mid-study and end-of-study data collection phases.
- Data will be de-identified prior to analysis

5.2 Data Analysis

- A statistician will overlook and conduct final data analysis
- Data will be analyzed for trends at the end of the study
- Analysis will be completed using IBM SPSS statistics version 24

5.3 Results

- Assuming similar response as obtained for breast cancer or cervical cancer projects, we expect 4% of the targeted population to respond.
- Based on the prior data, we computed the trend of increase in number of new HCV patients added per year to the pool of diagnosed cohort.
- According to mapping hep C[11], the total number of Antibody screening tests performed in 2016 is 53,580, or 4,465 per month, which is expected to be like current rates of 2019.
- We estimate that similar number of subjects will come for self-screening
- We expected to, at minimum, double the number of screenings to 8,930 tests per month, which will be evaluated after each intervention period as defined in Figure 3. This increase will correlate with the increase in diagnosis rates per 100,000 from 776 to at least 1,552. These numbers will be used as measures of success for the project.
- Assuming the current rate of 5.2% positive HCV tests holds, we expect at least 464 people to be HCV+ per month from the 8,930 people screened.
- From the total number of HCV positive individuals, only 26.1% in Arizona get treatment, which correlates with 120 people per month from the screened population or total of 1440 by the end of the study. Considering there are multiple challenges to treatment and complete eradication, the goal of the study is to promote treatment for those with access to healthcare; expecting to increase treatment rate to about 30%.
- Statistical data and trends of HCV prevalence over previous years, obtained from the Arizona Department of Public Health, will be compared with the study outcomes to assess the success rate of the study. we expect the number of screened individuals to double and the diagnosis rate to remain at 5.2%. A measure of success is therefore defined as 8,930 or more screening tests performed per month.

- The proposed intervention aims to increase the rate of diagnosed individuals to identify more of the HCV infected population as predicted by Yahia BR, et al (Figure 7)[18]. By increasing the number of screened individuals, we predict a 4.0% increase in addition to the current 50% diagnosed and aware.

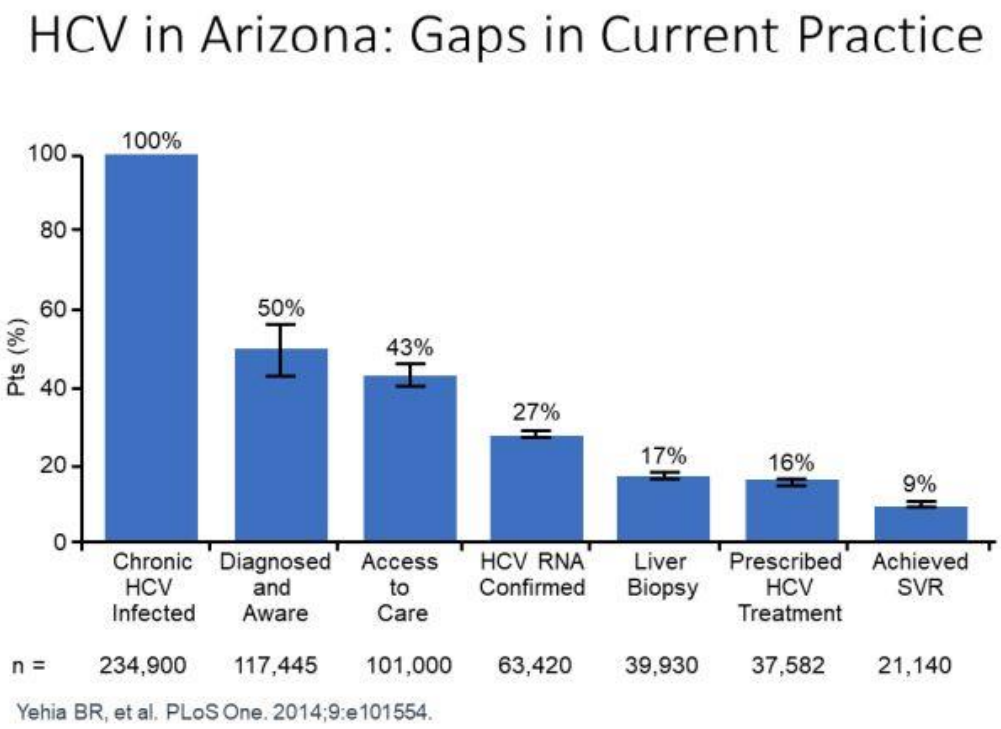

Figure 7: HCV Expected and current screening and treatment rates. Treatment cascade created by Yahia BR, et al. Graph was modified to display 2015, cumulative number of reported cases of Hepatitis C in Arizona[1, 18].

6.0 Legal and Ethical Considerations

The Principal Investigator and the study staff are responsible for conducting this study in accordance with the applicable principles which have their origins in the Declaration of Helsinki, ICH, GCPs, and all other applicable laws and regulations.

6.1 Institutional Review Board / Independent Ethics Committee (IRB/IEC) Approval

- This protocol, the Informed Consent, relevant supporting information, and all types of subject recruitment or advertisement information must be approved by the appropriate IRB/IEC before the study is initiated. Any amendments to the protocol must also be approved, where necessary, by the IRB/IEC prior to implementing changes in the study. The IRB/IEC used must comply with current regulations and GCP.
- The investigator's responsibilities regarding the IRB/IEC are as follows:
    - Obtaining IRB/IEC approval of the protocol, informed consent, and any advertisements to recruit subjects prior to their use.
    - Obtaining IRB/IEC approval for any protocol amendments and Informed Consent revisions before implementing the changes.
    - Providing the IRB/IEC with any required information before and during the study.
    - Submitting progress reports to the IRB/IEC as required.
    - Notifying the IRB/IEC within 10 days (unless required sooner by IRB/IEC) of all serious and unexpected AEs related to the study medications that are reported to you by the Sponsor. The investigator is responsible for updating the IRB/IEC on the progress of the study and of any changes made to the protocol at least once a year or at regular intervals as required by the IRB/IEC. The investigator must also keep the IRB/IEC informed of any AEs, according to the IRB/IEC policy.

6.2 Subject Information and Informed Consents

- Informed consent (per 21 CFR, Part50) and Health Insurance Portability and Accountability Act of 1996 authorization (per 45 CFR, Part 164) will be obtained from each subject and their caregiver prior to conducting/ obtaining any study-related assessments including the discontinuation of any study prohibited medications. An informed consent document that includes both information about the study and the consent from will be prepared and given to the subject. The document must be in a language understandable to the subject and must specify who informed the subject.
- The investigator's draft Informed Consent must be reviewed by the Liver Institute, prior to IRB/IEC submission for approval.
- If, during the study, the subject's protected health information (PHI) is to be used or disclosed in a manner that is inconsistent with the Informed Consent, the investigator must obtain a new authorization from the subject or a waiver of authorization from the IRB/IEC or privacy board, as applicable. If the Informed Consent is amended during the study, the investigator must follow all applicable regulatory requirements pertaining to

approval of the amended Informed Consent by the IRB/IEC and use of the amended form (including for ongoing subjects).

- The Informed Consent documents the study-specific information the investigator provides to the subject and the subject's agreement to participate.

6.3 Confidentiality

- Anonymity of subjects participating in this study will be maintained. Every effort will be made to maintain the confidentiality of documents that identify the subjects by name (e.g., signed informed consent document and patient data).
- The investigator and other study site personnel will keep confidential any information related to this study and all data and records generated in the course of conducting the study, and will not use the information, data, or records for any purpose other than conducting the study. These restrictions do not apply to:
    1. Information which becomes publicly available through no fault of the investigator or study site personnel
    2. Information which it is necessary to disclose in confidence to an IRB/EC solely for the evaluation of the study

       or
    3. Study results which may be published. If a written contract for the conduct of the study which includes confidentiality provisions inconsistent with this statement is executed, that contract's confidentiality provisions shall apply rather than this statement.

6.4 Record Retention

- Essential documents as described above should be retained for one of the following time periods: At least 2 years after conclusion of the study.

6.5 Publication Policy

- Institution and the investigator shall have the right, consistent with academic standards, to publish or present the results of the study, provided such publication or presentation does not disclose confidential information.

6.6 Financial Support

- This study is funded by the Liver Institute PLLC.

7.0 Discussion and Expected Challenges

- Several challenges stand in the way towards complete Hepatitis C eradication. In addition to lack of public awareness leading to low screening percentage, only about 26.1% of the HCV+ population receive treatment.
- During the gap periods of the study the project coordinator will communicate with patients and providers to facilitate the process of treatment. However, several challenges like insurance and access to healthcare might not be inevitable, making it unlikely to increase the treatment rate significantly. On the other hand, the total number is expected to proportionally increase with the number of screened individuals.
- Increasing the public awareness will likely result in a sustained increase in screening rates and gradual improvement in treatment availability and access. Therefore, and through utilizing more efforts the treatment rates can be expected to increase over the upcoming years, moving closer towards our goal of HCV eradication.

8.0 Appendix

8.1 Email Message Template

"Dear Patient Name,

My name is coordinator name, and I am the coordinator of a Hepatitis C Outreach program designed to increase awareness and promote screening of all the Arizona population for a goal of improved total community health.

Hepatitis C is a widespread, possibly asymptomatic disease affecting millions of the population and could result in severe liver damage and even mortality if left untreated. While historically people with risk factors are screened, these standards left millions undiagnosed and therefore contributed to making it an epidemic. We encourage you to go over the attached infographic for more information on hepatitis C.

To avoid complications of this treatable condition, we have collaborated with Sonora Quest Laboratories in the state of Arizona to provide screening services, free of charge, to all individuals in the state. If needed, our research team will contact you for further links to care and treatment. We ask you to please use the promotional code at any Sonora Quest to get your Hepatitis C screening. click on the link below to select your preferred Sonora Quest and schedule an appointment.

'Link'

Best regards,

'Attached infographic'

Contact Information"

8.2 Text Message Template

"We are reaching out to you regarding our Hepatitis C eradication program. Hepatitis C is widespread, possibly asymptomatic disease and, if left untreated, could result in serious liver damage. Our goal is to increase awareness and promote screening of all individuals residing in Arizona. If interested, use the code below to get free screening at any Sonora Quest labs."

8.3 FAQ Section

1. Is hepatitis C curable?
    a. Yes. With current and evolving antiviral treatments and liver transplants, 95% of hepatitis C cases are treated.
2. Does it cause any complications?
    a. Hepatitis C is a progressive infection and can lead to cirrhosis (scarring of the liver tissue), liver cancer and liver failure.
3. Is hepatitis C fatal?

   a. Hepatitis C can be fatal if left untreated as it can lead to cirrhosis, HCC (liver cancer), and several other complications.
4. Am I at risk?
   a. You are considered at risk if you:
      i. Were born between 1945 and 1965.
      ii. Had a blood transfusion or organ transplant before the year of 1992
      iii. Received clotting factors prior to 1987
      iv. Received hemodialysis for a long period of time
      v. Were born to a mother with hepatitis C
      vi. Have piercings or tattoos
      vii. Have a risky sex life
      viii. Have injected or inhaled illicit drugs
      ix. Have HIV (Human Immunodeficiency Virus)
      x. Work in healthcare and have been exposed to infected blood
5. Where can I get screened?
   a. Screening will be provided at any of our collaborating pharmacies in the State of Arizona.
6. What will be the next step if I test positive?
   a. In case the antibody test is positive, further testing will be done and you will be linked to specialists for treatment.
7. Can I get screened if I do not have insurance?
   a. Yes. Screening will be provided free of charge at any of our collaborating pharmacies.
8. Are there any lifestyle changes I need to follow in case of Hepatitis C diagnosis?
   a. Some lifestyle changes that could slow the progression of Hepatitis C are to stop drinking alcohol, avoid medications that can cause liver damage including some herbal supplements and over-the-counter drugs.

8.4 Abbvie Infographic

- Available at the following link: AbbVie Breaking Barriers Infographic_Global 031918

8.5 Resources Needed and Time Allocations

8.6 Investigator's Agreement and Signature

I have read the attached protocol: A Communication-Based Study Focused on Assessing and Improving Hepatitis C Screening Rates, as well as Treatment Rates in Arizona as a Step Towards Disease Eradication and agree to abide by all provisions set forth therein.

I agree to comply with the International Council for Harmonization Guidelines for Good Clinical Practices, and the laws, rules, regulations, and guidelines of the community, country, state, or locality relating to the conduct of the clinical study.

I also agree that persons debarred from conducting or working on clinical studies by any court or regulatory agency will not be allowed to conduct or work on studies for the sponsor or a partnership in which the sponsor is involved. I will immediately disclose it in writing to the sponsor if any person who is involved in the study is debarred, or if any proceeding for debarment is pending, or, to the best of my knowledge, threatened.

This document contains confidential information of the sponsor, which must not be disclosed to anyone other than the recipient study staffs and members of the IRB. I agree to ensure this information will not be used for any purpose other than the evaluation or conduct of clinical investigation without prior written consent of the sponsor (Liver Institute PLLC.)

Recoverable Signature

X Shahid Habib

Shahid Habib
MD, Principal Investigator
Signed by: 514635c7-6bc0-499a-a3c3-2f50de45918d

8.7 Signature of Sub-Investigators

To the best of my knowledge, this report accurately describes the planned conduct of the study.

Study Title: A Communication-Based Study Focused on Assessing and Improving Hepatitis C Screening Rates, as well as Treatment Rates in Arizona as a Step Towards Disease Eradication

Protocol Number: LI-HEPC-AZ

Protocol Version: Version 1.0

Kristine Gradisher, MS (Physiology), Clinical Research Coordinator, Sub-Investigator

Recoverable Signature

X Kristine Gradisher

Kristine Gradisher
MS (Physiology), Clinical Research Coordinato...
Signed by: 514635c7-6bc0-499a-a3c3-2f50de45918d

Julie Piittmann, FNPC, Sub-Investigator

Recoverable Signature

X Julie Piittmann

Julie Piittmann
FNPC, Sub-I
Signed by: 514635c7-6bc0-499a-a3c3-2f50de45918d

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