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Descriptive Report

Recruitment of Hard-To-Reach Populations in Randomized Controlled Trials Using Medical Students and Electronic Consents

Austin T Jones, MD, PhD, MPHTM[1]; Anadil Zakaria, MD[2]; Latha Rajan, MD, MPHTM[2,3]; Patricia J Kissinger, PhD[4]

[1]Department of Emergency Medicine, Denver Health Medical Center, Denver, Colorado, USA
[2]Tulane University School of Medicine, New Orleans, Louisiana, USA
[3]Department of Tropical Medicine, Tulane University School of Public Health and Tropical Medicine, New Orleans, Louisiana, USA
[4]Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine, New Orleans, Louisiana, USA

Corresponding Author: Austin T Jones, MD, PhD, MPHTM; email: austin.jones@denverem.org

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Abstract

Viral hepatitis is concentrated in populations with low healthcare system engagement, including non-white, rural, non-English speaking, and low socioeconomic status persons. Recruiting these participants for clinical trials has immense implications for trial feasibility and generalizability. Through the example of a trial delivering a behavioral intervention to patients with hepatitis C virus (HCV) in a network of medical student-run clinics, we describe the implementation of a student-run HCV testing program in the community and describe novel strategies to improve the recruitment of hard-to-reach participants using medical student counselors and electronic consents.

Introduction

Hepatitis C virus (HCV) claims more American lives than the next 60 reportable infectious diseases combined.[1] HCV leads to systemic immune and inflammatory pathology. In the liver, cycles of cellular damage and resulting to wound healing leads to hepatic fibrosis.[2] The predominant late-stage complications include decompensated cirrhosis and hepatocellular carcinoma (HCC). Beyond the liver, the systemic inflammatory state caused by HCV particularly accelerates arterial vascular disease.[3] Those living with chronic HCV have a higher likelihood of carotid atherosclerosis, cardiovascular mortality, and cerebrocardiovascular accidents.[4]

In 2011, HCV became a curable disease with the advent of direct-acting antivirals.[5] Despite the remarkable efficacy of direct-acting antivirals (DAAs) at achieving functional cure, there remains significant barriers in curing those with chronic HCV infection. This problem is multifactorial. There is a profound diagnostic gap as nearly 50% of those infected are unaware of their HCV status.[6] Once diagnosed, patients' access to the drug is limited by cost. While courses of newer DAAs are as low as $26,400, the range of wholesale prices extends to a maximum of $189,000.[7] The cost of HCV treatment may increase the time that patients who are underserved are living with the disease therefore increase the risk of disease sequelae.

Viral hepatitis disproportionately burdens racial and ethnic minorities, as well as individuals battling substance abuse, incarceration, and homelessness.[8] These patients cite stigma, fatalism, and a lack of knowledge regarding liver disease symptomatology as deterrents in seeking medical care.[9] The low healthcare engagement common in these populations lends difficulty to studying viral hepatitis.[10]

Informed consent is an essential component of trial participation; however, paper documentation demonstrates limitations, especially in

Table 1. Barriers to trial recruitment of persons living with hepatitis C and how barriers were addressed by utilizing medical student counselors and electronic consents.

Barrier to recruitment	Rationale
Medical Student Counselors	
Stigma against healthcare system	• Medical students have increased interest and eagerness to work with underserved populations than physicians[11,12] • Application process selected students with demonstrated experience and passion working with underserved populations, thereby reducing implicit bias • Medical handoff to well-known federally qualified health center trusted among the study population
Disease fatalism	• Counselors trained in motivational interviewing • Counseling focused on ability to reverse disease process through seeking treatment
Low health literacy of liver disease	• Counselors had medical education in the biology, pathology, and epidemiology of hepatitis C • Additional 20-hour training by state public health agency and investigators
Electronic Consents	
Multiple enrollment sites needed to achieve sample size	• All electronic consents stored in HIPAA-compliant server updating enrollment in real time • Circumvented need for counselors to safeguard and track hard-copy consents
Field data collection	• Able to enroll at venues frequented by patient population using smart phones • Reduced cost of buying and maintaining computers at each recruitment site
Difficulty re-contacting participant	• Prevented submissions with missing information or inaccurate dates • Avoided incorrect consent forms that would void enrollment and necessitate re-contacting patient for form correction

HIPAA: Health Insurance Portability and Accountability Act.

resource-poor environments common to these patient populations. Paper forms are susceptible to missing information that could void enrolment. Researchers expend time collecting, replenishing, and moving paper consents that impedes the flow of both clinic and trial enrollment. Hardcopy consents must also be properly secured and archived for future audit. Time, security, and logistical barriers surrounding paper documentation reduce trials' ability to enroll participants who are underserved in low-resource settings.

Ease of recruitment has broad implications for clinical trial feasibility and generalizability. Challenging recruitment increases operating costs and the enrollment timeline. These barriers also threaten achievement of the sample size, thereby jeopardizing study power and ability to answer the research question. Widening the gap between the target and study populations limits generalizability and impacts the interpretation of trial results. Strategies are needed to reduce barriers in engaging and recruiting hard-to-reach populations for viral hepatitis trials.

We herein describe a clinical trial in a network of student-run clinics enrolling patients living with hepatitis C virus (HCV) and unique strategies—including medical students and electronic consents—that aided in the recruitment of this hard-to-reach population (Table 1).

Methods

Establishment of the HCV screening program

Founded in 2015 by medical students at Tulane University School of Medicine, Acacia New Orleans Louisiana (NOLA) is a student-run screening program for HCV in New Orleans, Louisiana (LA). An unmet need was identified among the high-risk population served by these clinics. Prior to 2015, testing for human immunodeficiency virus (HIV) was being performed, however, incidence of HIV was low. Tulane medical students recognized the profound burden of HCV in New Orleans as well as the underserved population with HCV risk factors seeking care at student clinic. At

the time, no such HCV testing services existed among Tulane community clinics. The organization partnered with the New Orleans Office of Public Health, who provided the necessary training and testing kits for HCV testing. Medical student counselors performed point of care testing, HCV counseling, and referred HCV seropositive patients to care at a single federally qualified health center (FQHC) for further treatment of HCV. These services included ribonucleic acid (RNA) confirmation, fibrosis staging, and direct acting antiviral therapy, and in addition, management of the sequalae of HCV infection. The program begam with simple tracking of demographic information and positivity rates. The program expanded in size and capacity by earning a Frontlines of Communities in the Unites States (FOCUS) grant from Gilead Sciences. This granted funded the program in increasing the volume of HCV point of care testing, as well as hiring of social workers, patient navigators, and research managers. Equipped with the resources and personnel to begin collecting follow up data, the program realized that linkage to care rates could be improved. The authors hypothesized that augmenting the counseling patients received would improve rates of patients seeking care for HCV.

Trial

A multi-site, single blinded, parallel arm randomized controlled trial was conducted. Enhanced counseling with HCV-associated cardiovascular disease risks was tested against Centers for Disease Control and Prevention (CDC) standard of care HCV counseling. Enrollees were referred to a single FQHC, well-known and trusted among the underserved community. The primary outcome was linkage to care. The trial was conducted in an HCV screening and linkage to care program in a network of student-run clinics. The trial was approved by the Tulane University Institutional Review Board and registered at clinicaltrials.gov as study NCT03402334.

Medical students

HCV screening, counseling, and trial recruitment were conducted by medical students. Counselor training consisted of an intensive 16-hour group session over two days administered in conjunction with state public health officials and trial investigators. These counselors were trained and certified by the Louisiana Office of Public Health. This training involved CDC standard-of-care HCV counseling and how to operate the point-of-care HCV test. Counselors were also training in motivational interviewing and ethical consent. Trainees were observed for four hours of counseling, recruitment, and testing prior to working independently. In total, each counselor received at minimum 20 hours of training prior to recruiting for the trial.

Patients were recruited during HCV testing appointments at eight community venues in New Orleans, LA. Enrollment sites included community food pantries, homeless shelters, and drug rehabilitation facilities. HCV screening occurred at pre-designated and consistent times each week, most often in the evenings. Counselors tested and counseled patients in a private, on-site room. During the 20 minutes in which the HCV test was running, counselors recruited patients to enroll in the trial. The student volunteers were provided service hours for training and testing that qualified for graduation requirements set by the university. No financial compensation was provided.

Electronic consents

Our trial used electronic consents (e-consents) on counselors' smartphones. E-consents have also been demonstrated effective in populations of low health literacy.[13] Qualtrics (Qualtrics, 2019, Provo, Utah), a Health Insurance Portability and Accountability Act (HIPAA)-compliant survey platform was used to collect informed consent and HIPAA authorization. The participant provided a digital signature using their finger. An electronic timestamp was recorded upon submission of the e-consent forms to the Qualtrics server.

Randomization was also conducted by the Qualtrics survey platform. Patients were assigned to the intervention and control groups using simple randomization in a 1:1 ratio. A Qualtrics prompt notified the counselor of the participant's assignment. For participants assigned to the intervention group, the prompt contained a video file with the enhanced counseling intervention to be played at the conclusion of the counselor's CDC standard of care counseling. For those

randomized to the control group, a prompt alerted the counselor to this assignment, instructing the counselor to provide only CDC standard of care counseling.

Results

In 17 months of recruitment, 513 patients were assessed for eligibility and 231 were consented to participate. In total, 223 patients (43.5%) were randomized and engaged with the trial. This was on average 11.6 participants per recruiter.

Medical students

We found that medical students served as a qualified population to conduct HCV testing and counseling, and more broadly, recruit patients for clinical trials. Health professional students are an underutilized resource for public health interventions. Equipped with several years of higher education, medical students have a significant education in the sciences. The counselors' extensive education in the biology, pathology, and epidemiology of hepatitis C decreased training and improved their ability reduce barriers in health literacy experienced by the population. These students lent high value to cost compared to healthcare professionals who have completed their training.

Beyond their knowledge base, we found that medical students displayed empathy for marginalized HCV populations essential to counsel trial participants on behavioral change. Compared to resident and attending physicians, medical students have demonstrated increased empathy and positive attitudes for patients who are underserved.[12] First- and second-year medical students also have demonstrated higher interest in working with the complex psychosocial issues and understanding the lives of this patient population.[12] This association is multi-factorial. Medical students have more time and availability to participate in patient outreach, compared to practicing physicians and residents. Burnout and workload are more common more senior physicians than trainees. Similarly, implicit bias training become more prevalent in medical student education. As volunteers, counselors' participation was driven by a desire to benefit the community. Counselors underwent a competitive application process and were selected by having demonstrated prior experience working with underserved populations. This combination selected a cohort of empathetic volunteers that minimized implicit bias for the study population. The medical students' attitudes and perspectives were ideally suited to overcome participants' disease fatalism and healthcare stigma.

In addition to the value students provided the trial, counselors also benefited from participation. All students received certification in counseling and testing by the state public health agency. Counselors learned ethical consent practices translatable to their future clinical careers. Students also developed counseling and motivational interviewing skills often lacking in traditional medical education. Medical students' exposure to persons experiencing homelessness and psychiatric illnesses in student-run clinics has been associated with decreased stigma towards vulnerable populations.[14] Working with these populations in medical training may protect future physicians from developing biases that would negatively impact care delivery.

Given a combination of their high education, low cost, and resounding empathy, leveraging this medical student population was essential to conducting a low-resource randomized clinical trial in an underserved population.

Electronic consents

We found smartphone e-consents to be a practical, safe, and effective means to enroll hard-to-reach participants in a clinical trial. Using personal smartphones obviated the need to spend modest study resources on purchasing tablets or site computers. As counselors were familiar with their smartphones, this reduced the time to train personnel on new devices. E-consents were automatically uploaded to a HIPAA complaint server and study data was continuously updated in the cloud without delay. The e-consent circumvented the need for counselors to safeguard and track hard-copy consent paperwork across the eight study sites, likely improving participant confidentiality. Being electronic, force response features flagged inaccuracies in dates and prevented submission with missing information. Both scenarios could have voided enrollment and would have been difficult to rectify for a

difficult-to-reach population without reliable contact information.

E-consents were particularly advantageous to consent and enroll patients in the 20-minute time span of the HCV rapid test. Reducing consent time maximized the time spent on patient counseling and education. Consistent with prior findings, we believe the interactive interface of the e-consent improved participants' ability to comprehend and retain information.[15] E-consents likely removed barriers to participation and improved equitable access to research participation in our underserved HCV population. E-consents were extremely practical for use in our low-resource, student-operated clinics and facilitated the counseling intervention to occur in the short window of HCV point-of-care testing.

Discussion

Medical students and e-consents were useful strategies to conduct a low-resource community intervention for a difficult-to-reach population. Our electronic consent facilitated recruitment, lowered capital costs, and improved participant confidentiality. The strategies of this trial have broad implications for expanding infectious disease surveillance and other United States Public Health Service screening programs in low resource settings.

While medical students and e-consents improved trial feasibility and recruitment, limitations to the study are noted. Testing occurred in two-hour time slots per clinic per week. Increasing testing availability was limited by personnel constraints. Recruitment was performed among patients seeking testing; resources did not exist to advertise testing in New Orleans.

This is the first known trial implemented and administered by medical students, an educated and low-cost workforce with high empathy for underserved populations. Enrolling hard-to-reach populations imposes greater time and resource costs, ultimately threatening study power and generalizability. Researchers recruiting these hard-to-reach populations should employ design strategies to facilitate recruitment.

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