

Hepatitis C Screening and Linkage to Care in an Urban Emergency Department

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Abstract

Background: Hepatitis C virus (HCV) is a major cause of chronic liver disease and is the most common chronic bloodborne pathogen in the United States. The Emergency Department (ED) is potentially a high-yield site in healthcare to reach patients at risk for HCV infection. If the current rates of identification remain constant, it is estimated the HCV-related morbidity and mortality will quadruple over the next decade. The present study aims to determine the effectiveness of an automated ED-based HCV testing and HCV linkage-to-care model, evaluate the Best Practice Advisory (BPA) utilization and increase screening rates of HCV.

Methods: An automated HCV screening protocol was implemented into the electronic medical record (EMR) at Henry Ford Hospital. This system screens patients born from 1945 through 1965 and/or those with a history of intravenous drug use, two identified risk factors for HCV. A best practice advisory (BPA) notifies providers to order an HCV antibody (Ab) test for patients with an ordered complete blood count (CBC) and have at least one risk factor. If the HCV Ab test is positive, the provider is prompted to order an HCV ribonucleic acid (RNA) test. Team members follow up with patients until they attend their first visit with Henry Ford Hospital Hepatology Clinic. Data was collected for the first five months before and five months after the implementation (March 2018 through December 2018).

Results: In the first five months before the automated screening program was implemented, only 360 HCV Ab tests were performed and only 5.8% were positive. Approximately 72 HCV Ab tests were performed each month. A total of 4 patients received the HCV RNA test and 3 were connected to care. In the five months after implementation, 4,075 HCV Ab tests were performed, 10.4% resulting positive. An average of 815 HCV Ab tests were performed per month (an increase of more than 11-fold). A total of 215 patients received RNA testing and 63 RNA positive patients were connected to care.

Conclusion: An automated HCV testing system can be successfully implemented in an ED setting. Additionally, this model places the responsibility of patient follow-up onto non-clinical staff and can be employed in diverse medical settings. These protocols not only can potentially prevent one of the major causes of chronic liver disease and cirrhosis in the U.S. but could also prove effective to screen and test for other infectious diseases.

INTRODUCTION

The hepatitis C virus (HCV) is one of the major causes of chronic liver disease and cirrhosis (Wilkins, Akhtar, Gititu, Jalluri, & Ramirez, 2015). In the United States, it is the most common chronic bloodborne pathogen affecting almost 2% of the population (U.S. Preventive Services Task Force, 2016). Globally, it is estimated that 71 million people are living with a chronic hepatitis infection and many of these people are unaware of their infection status (Sidlow & Msaouel, 2015; World Health Organization [WHO], 2017). Almost 400,000 people worldwide die each year from HCV due to the complications of cirrhosis or hepatocellular carcinomas (WHO, 2017). If the current rates of identification remain constant, it is estimated the HCV-related morbidity and mortality will quadruple over the next decade as more and more people remain undiagnosed and may unknowingly spread the disease to others (Sidlow & Msaouel, 2015). It has been reported that between 1-12% of eligible adults are tested for HCV (Linas, Hu, Barter, & Horberg, M., 2014). WHO has established a goal reduce new viral hepatitis infections by 90% and reduce death due to HCV by 65% by 2030 (WHO, 2017). HCV is a major public health problem and if the screening methods are improved and increased, then we will be one step closer to ridding the world of this devastating disease.

The Frontlines of Communities in the United States (FOCUS) program was created in 2010 to develop screening, diagnosis, and linkage-to-care practices that follow screening guidelines set by the Centers for Disease Control (CDC) (Sanchez *et al.*, 2014). FOCUS originally began to address human immunodeficiency virus (HIV), but expanded to HCV in 2014 (Sanchez *et al.*, 2014). In March 2018, Henry Ford Hospital (HFH) in Detroit, Michigan became a part of the FOCUS program by implementing the practices into the Emergency Department (ED). The FOCUS project is a quality improvement project which is designed to align the

screening practices in the ED with the CDC guidelines and develop a linkage-to-care practice in the ED. The ED is potentially a high-yield healthcare site to reach patients at risk for HCV infection. As a part of this partnership, HFH implemented an automated electronic medical record (EMR) screening system to screen and test at-risk patients for HCV.

As the EMR-based screening system was being built, manual screeners were already working in the ED to identify patients at risk for HIV and concurrently were screening patients also at risk for HCV. Only two FOCUS team members were screening for HCV during this time (a period of five months). This manual screening method was an inefficient system and the implementation of an EMR screening system was hoped to increase screening and connection to care rates.

The FOCUS project aims to determine the effectiveness of an automated ED-based HCV testing and HCV linkage-to-care model, evaluate the Best Practice Advisory (BPA) utilization and increase screening rates of HCV.

BACKGROUND

Transmission

Exposure to HCV-infected blood is the primary cause of HCV (Chen & Morgan, 2006). In the past, the most common method of transmission was through blood transfusion (Mehta, Carey, Alkhouri, & O'Shea, 2017). Before 1992, there was not a test sensitive enough to test for HCV in the blood banks (CDC, 2014). Now, blood donations are screened for liver disease and donors answer risk factor questions (Shepard, Finelli, Alter, 2005). Once the testing was developed and implemented, there was a reduced risk of transmission to less than 1 per 2 million units of blood (Mehta, 2017). Presently, the most common way to transmit this virus in the

developed world is intravenous (IV) drug use (Shepard, 2005). Sharing needles, syringes, or other equipment for drug use causes the spread of the virus between IV drug users (CDC, 2018). For those who are long-term IV drug users (6 years or more), the prevalence of HCV is between 64-94%, an extremely high infection rate (Shepard, 2005). Other methods of transmission occur much less frequently compared to repeated activities like IV drug use (Shepard, 2005). HCV can be transmitted from an infected mother to child in about 5-10% of pregnancies, but this is more likely to occur for mothers that are also infected with HIV (Mehta, 2017). HCV can also be transmitted through needle-stick injuries in health-care workers, but the average transmission rate is about 0.5% (Mehta, 2017; Shepard, 2005). HCV is also transmitted sexually, but it is unlikely to be a major method of HCV transmission (Shepard, 2005). Finally, other groups who are at risk are those receiving tattoos, those infected with HIV, and men who have sex with men (CDC, 2018).

Screening Methods

The CDC recommends HCV testing for: current or former IV drug users (whether they injected drugs once or many times), those born from 1945 through 1965, recipients of blood transfusions before 1992, healthcare workers after needlesticks from an HCV-infected individual, people with HIV, and children born to mothers with HCV (CDC, 2018). The American Association for the Study of Liver Diseases recommends annual HCV screening for IV drug users and men who have sex with men (Wilkins, 2015).

Diagnosis of HCV is a two-step process. HCV antibodies must be identified and there must be a demonstration of a viral load (Mehta, 2017). The most common test for HCV antibodies is an enzyme-linked immunosorbent assay (ELISA) (Mehta, 2017). This test has a

95% sensitivity and specificity for HCV and can detect antibodies from 4 to 10 weeks post-infection (Mehta, 2017). If a patient is positive, they may have an active infection or have had a previous infection that has resolved (Mehta, 2017). To confirm whether the infection is active, an HCV ribonucleic acid (RNA) by polymerase chain reaction (PCR) must be completed which will determine the viral load and genotype (Mehta, 2017; Wilkins, 2015). The PCR will amplify the sequences in the conserved 5' noncoding region of the virus to create products that are detected and counted to determine the amount of viral RNA in the serum (Mayo Clinic Laboratories, 2018). The PCR test can detect HCV RNA 2-3 weeks post-infection (Mehta, 2017). This test will not define disease progression or severity, it is used to provide a baseline value prior to treatment to compare to the viral load after therapy is complete (Mehta, 2017). Those who test HCV-antibody positive, but HCV RNA negative, are not considered to have an infection (Wilkins, 2015).

The HCV antibody (Ab) test can read as a false negative in patients that have not established high enough antibody levels to be detected by the ELISA test (Mehta, 2017). This can occur in individuals who are tested before 4 to 10-weeks post-infection (before there are enough antibodies for the ELISA to detect them) or in immunocompromised patients, like those with HIV who cannot produce an antibody level measurable by the test (Mehta, 2017). If there is clinical suspicion that the patient in either of case has HCV, the RNA level should be checked to confirm if there is infection (Mehta, 2017).

Acute vs. Chronic Infection and their Symptoms

Acute HCV is usually asymptomatic (Mehta, 2017). Acute infections are rarely diagnosed because they are asymptomatic and only 20-30% of individuals who develop an acute

infection have clinical symptoms (Chen & Morgan, 2006). If symptoms do occur, the infected person usually has mild flu-like symptoms (Mehta, 2017). Other symptoms that may occur are: weight loss, muscle or joint pain, nausea, malaise, dark yellow urine, fever, clay-colored stools, loss of appetite, abdominal pain, vomiting, and jaundice (CDC, 2018; Mehta, 2017). If there are symptoms, they can occur anywhere from 2 to 24 weeks after exposure to HCV (Mehta, 2017). Serum alanine aminotransferase (ALT) levels will increase 2-8 weeks after an acute infection begins, signifying necrosis of hepatocytes (Chen & Morgan, 2006). During the first few weeks of infection, the level of HCV RNA will increase rapidly, then peak (Chen & Morgan, 2006). Next, the levels of the virus and ALT levels will decline (Chen & Morgan, 2006). In 50% of acute infection cases, individuals will clear the HCV infection spontaneously, so there are cases where treatment is deferred while waiting to see if infection will clear on its own (Mehta, 2017). The RNA levels need to be monitored for at least 3 months before treatment begins to evaluate if the infection clears spontaneously since there is no value in early treatment (Mehta, 2017). However, studies suggest clearance is more likely in younger individuals and those who present with symptoms (especially jaundice) (Mehta, 2017). Acute HCV infections that resolve are not associated with long-term liver damage (Westbrook & Dusheiko, 2014).

Chronic HCV is defined as the presence of the HCV RNA for at least 6 months after acute infection (Chen & Morgan, 2006). Chronic HCV also usually does not exhibit symptoms and if they do appear, they are very common symptoms such as chronic fatigue and depression (CDC, 2018). Normally, the finding of abnormal ALT levels leads to more specific testing for HCV (Mehta, 2017). The aminotransferase levels reflect the amount of hepatocellular injury of the liver, however they can fluctuate and are not the most reliable marker of severity (Mehta, 2017). Chronic HCV infection can lead to end-stage liver disease, hepatocellular carcinoma and

eventually lead to a liver-related death (Westbrook & Dusheiko, 2014). The chronic infection progresses slowly and can lead to cirrhosis (Westbrook & Dusheiko, 2014). There are many infected people that are not diagnosed with HCV until they reach this advanced stage and exhibit signs of end-stage liver disease (also known as decompensated cirrhosis) (Westbrook & Dusheiko, 2014). Decompensated cirrhosis shows symptoms of cirrhosis such as jaundice or hepatic encephalopathy (Thornton, 2018). Unlike an acute infection, chronic HCV leads to extreme liver damage which may eventually lead to a liver-related death.

Societal Issues Associated with Hepatitis C

There is an incredible economic burden associated with treating HCV. The cost of treating HCV is currently the primary barrier to receiving treatment (Mehta, 2017). In September 2016, Epclusa cost \$1,068 per pill bringing the total for a 12-week course of this medication to \$89,712 (Mehta, 2017). Harvoni is even more expensive costing \$1,350 per pill totaling to \$113,400 for one course of treatment (Mehta, 2017). Most patients are not able to afford this high cost of treatment. The expense of this medication has fallen to the insurance companies. Insurers have a “triage strategy” which attempts to help patients with more advanced disease receive payment for treatment (Mehta, 2017). Authorization of payment is based on the stage of fibrosis (liver scarring), risk of progression of the disease, an increased risk of transmission, those with HIV or hepatitis B virus (HBV), and decompensated cirrhosis (Mehta, 2017). Most insurance companies require the patient to provide a negative drug test before they agree to pay for the medication (Mehta, 2017). Some insurers may not agree to pay because of a missed doctor appointments or other history of noncompliance, insufficient social support, or having a history of drug abuse (Mehta, 2017). With the strict compliance requirement, few patients

diagnosed with HCV will be covered by insurance for treatment causing less people to be treated and an increase of new infections.

Like HIV, HCV also has a social stigma. With HCV, many people may assume that an infected individual is an active, illicit drug user, but that is not always true. In some cases, a person may have used IV drugs one time, or may have received contaminated blood products (Wilkins, 2015). Because many of those diagnosed with HCV have a history of IV drug use, they are blamed for acquiring the disease and viewed as “unworthy” individuals (Marinho & Barreira, 2013). Also, since HCV is a blood-borne disease, it is associated with HIV, which also has a social stigma (Marinho & Barreira, 2013). Furthermore, these patients can feel marginalized and alienated from their family and friends due to their diagnosis (Marinho & Barreira, 2013). This social stigma of this diagnosis can prevent people from being tested for HCV in fear of societal judgment. If people are fearful of being tested, undiagnosed HCV will continue to rise, resulting in an increase in the disease being unknowingly spread between people.

The Hepatitis C Virus

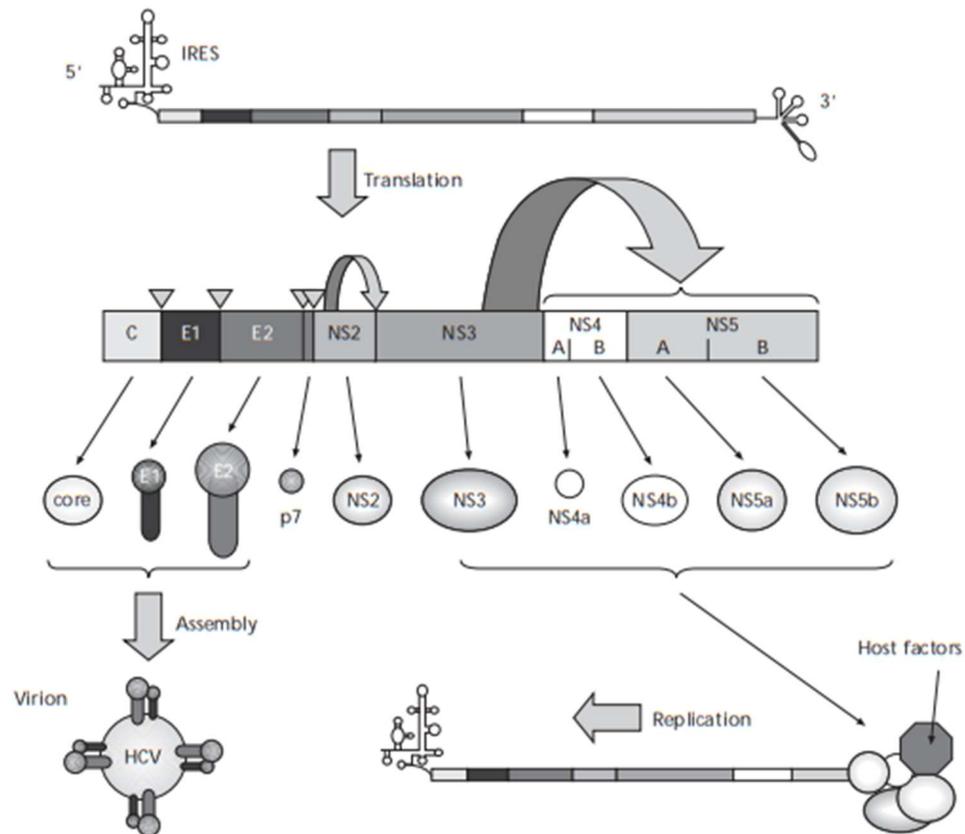
HCV belongs to the Flaviviridae family and the genus hepacivirus (Irshad, 2013; Mehta, 2017). HCV is an enveloped, single-stranded, positive-sense RNA virus that has a genome of around 9.6-kb (Irshad, 2013). The virus has an open reading frame of 9033-9099 nucleotides surrounded by 5' and 3' conserved non-coding regions at each end (Irshad, 2013). HCV codes for about 3000 amino acids that go on to form structural proteins (core and envelope (E1 and E2)) and non-structural proteins (NS1/p7, NS2, NS3, NS4A, NS4B, NS5A, and NS5B) (Irshad, 2013) (Figure 1). E1 and E2 code for the outer surface proteins that are involved in the entry into the hepatocytes; these are also two of the most variable regions along with NS1 (Irshad, 2013).

NS5B codes for the RNA-dependent RNA polymerase (Irshad, 2013). The lack of proofreading by RNA polymerase may alter its detection by the immune system and its sensitivity to interferon anti-viral activity (Irshad, 2013).

Between the different genotypes of HCV, the virus varies by about 30-35% (Irshad, 2013). The genotypes also vary by region, type 1 and 2 are found around the world while genotype 3 has a high prevalence in India (Irshad, 2013). Though they are different genotypes, they have similar transmission patterns and disease development (Irshad, 2013).

Figure 1

Structure of HCV genome and viral proteins
(Moriishi & Matsuura, 2003)



Long-Term Effects

Since chronic HCV usually does not exhibit symptoms, infected individuals may not be aware they have HCV (CDC, 2018). If a person is unaware of their infection status, HCV will go untreated and the inflamed liver will begin to scar (American Liver Foundation [ALF], 2017). The hepatocytes are continually destroyed by the immune system and replaced by fibrosis, scar tissue which develops in the place of once healthy liver tissue (ALF, 2017; Mehta, 2017). The scar tissue is not able to function as healthy liver tissue, therefore, preventing blood from flowing through the liver (ALF, 2017). Over time, more scar tissue continues to build, and the healthy liver must work even harder to make up for the unhealthy tissue (ALF, 2017). There are many factors that increase an infected individual's risk for fibrosis: being infected at an older age, male gender, alcohol consumption (more than 50g/day), obesity, co-infection with HIV or HBV, or genetic factors of the host (Westbrook & Dusheiko, 2014). The degree of fibrosis is assessed by a liver biopsy (Mehta, 2017). When scar tissue replaces the healthy tissue and the liver begins to break down, the fibrosis becomes cirrhosis (ALF, 2017; National Institute of Diabetes and Digestive and Kidney Diseases [NIDDK], 2017). This progression to cirrhosis usually does not have any associated symptoms (Chen & Morgan, 2006). There is less healthy liver tissue and the liver cannot function normally (ALF, 2017; NIDDK, 2017). The scar tissue will block the blood flow and the liver begins to fail (NIDDK, 2017). Over a 20-year period, HCV can lead to cirrhosis in about 20% of infected people (Mehta, 2017). Cirrhosis may cause little pain for many years—the disease progression cannot be predicted, so some people may experience liver decompensation much faster (Westbrook & Dusheiko, 2014). Liver cirrhosis can also lead to hepatocellular carcinoma and liver-related death (Westbrook & Dusheiko, 2014).

There is some evidence to variability in HCV pathology. Hepatic steatosis, or fatty liver, has a strong association with HCV infection (Irshad, 2013). There have been experimental studies on animal models that demonstrate HCV-core protein promoting the liver steatosis (Irshad, 2013). Though steatosis is seen in all HCV genotypes, it seems to appear more prominently in those with an HCV-genotype 3 infection (Irshad, 2013). When studied, patients with the genotype-3 infection had a high correlation of steatosis, HCV replication, and the presence of the HCV core (Irshad, 2013). Other studies have found that HCV-genotype 3 interferes with the very low-density lipoproteins and increases secretion (Irshad, 2013). The core proteins of a genotype 3 infections promote fat buildup in the liver more prominently than other HCV genotype infections (Irshad, 2013).

Treatment of Hepatitis C: Past, Present, and Future

In 1991, the FDA approved alpha interferon as the first treatment for HCV, which at the time was also an effective treatment for HBV (Fisher, 1991). Alpha interferon's side effects are flu-like symptoms (Fisher, 1991). When introduced, this drug was given three times a week for six months (a total dose of three million units) (Fisher, 1991). This course of treatment cost \$2,400 (Fisher, 1991). During clinical trials, alpha interferon improved liver function in more than half of the subjects and many of the subjects had symptomatic improvement (Fisher, 1991). Alpha interferon was given in combination with ribavirin (a drug that inhibits viral RNA polymerase), however, this course of treatment was not effective in 50% of treated patients when placed on the market for HCV (Guo, Bichko, & Seeger, 2001; Wilkins, 2015).

There are currently ten FDA-approved direct-acting drugs for the treatment of HCV (Mehta, 2017). The most successful strategy for curing HCV is to combine two or more drugs

that target different steps in viral replication (Mehta, 2017). The current first-line therapy for HCV is sofosbuvir in combination with ledipasvir (Harvoni) or velpatasvir (Epclusa) (Mehta, 2017). Harvoni was approved by the FDA in October 2014 (Wilkins, 2015). This combination therapy is 90 mg of ledipasvir, a NS5A inhibitor, and 400 mg of sofosbuvir, a NS5B inhibitor (Gilead, 2014; Mehta, 2017). This is a once-daily dose that treats HCV genotypes 1,4,5, and 6 (Mehta, 2017). Harvoni provides very high cure rates and eliminated the need for interferon and ribavirin (drugs which are challenging to tolerate) (Gilead, 2014). The most common side effects of Harvoni are fatigue, headache, nausea, diarrhea, and insomnia (Gilead, 2014)

In June 2016, the FDA approved the drug Epclusa, another combination therapy of 400mg of sofosbuvir and 100mg of velpatasvir, which is also a NS5A inhibitor (Food & Drug Administration, 2016; Gilead, 2016; Mehta, 2017). Like Harvoni, Epclusa is also a one-daily dose, however this combination therapy can be used to treat all genotypes for HCV (Mehta, 2017). The most common side effects are headache and fatigue (Gilead, 2016). Both Harvoni and Epclusa produce cure rates of 95-100% after 12 to 24 weeks of treatment (Mehta, 2017). Furthermore, both combination therapies can be used while a patient has cirrhosis (Mehta, 2017).

Sofosbuvir is a nucleotide pro-drug (Mehta, 2017). It is a faulty substrate for the RNA-dependent viral nonstructural protein NS5B RNA polymerases (Mehta, 2017). Sofosbuvir is incorporated into the viral RNA and terminates viral synthesis of the non-structural protein NS5B and disrupts the replication of HCV, thus leading to viral death. (Mehta, 2017).

Ledipasvir is a NS5A inhibitor and its exact mechanism is unknown (Gritsenko & Hughes, 2015). It is suggested that ledipasvir inhibits the hyperphosphorylation of NS5A that is required to produce HCV (Gritsenko & Hughes, 2015). If NS5A is not hyperphosphorylated, the protein will be defective and viral replication will stop. In another speculated mechanism, this

NS5A inhibitor may cause defective viral assembly because ledipasvir will redistribute the sub-cellular localization of the protein NS5A (Gritsenko & Hughes, 2015). If the viral assembly stops, HCV cannot replicate. Velpatasvir is another inhibitor of the NS5A protein (Bonaventura & Maontecuccio, 2016). The protein plays a role in virus replication and when it is inhibited by velpatasvir, HCV can no longer replicate (Bonaventura & Montecuccio, 2016). When NS5A and NS5B inhibitors are used together, the therapy will have a synergistic effect, meaning it will have a greater therapeutic effect than only one inhibitor (Gritsenko & Hughes, 2015). If the treatment is successful, there will be an absence of HCV in the blood 12 or more weeks after therapy ends (Mehta, 2017).

The ideal treatment for HCV would be highly effective, easy to administer, have few side effects, lack significant drug-drug interactions, not need treatment monitoring, and have a low cost (Mehta, 2017). The current treatments for HCV achieve all the attributes except for the low cost (Mehta, 2017). Future treatments for HCV would include a drug that is at a lower cost so that everyone infected will be able to receive treatment for HCV. The cost of the medication is currently the greatest barrier to widespread treatment (Mehta, 2017). On September 24, 2018, Gilead Sciences (the company that makes Epclusa and Harvoni) announced their plans to launch generic versions of their drugs through a new company, Asegua Therapeutics. These authorized generics will be at a list price of \$24,000 which is significantly lower than the cost of Epclusa in 2016 at \$89,000 (Gilead, 2018; Mehta, 2017). The President and Chief Executive Officer, John Milligan, PhD, said that the generic versions are currently the best solution to quickly produce a lower priced alternative without disruption to the healthcare system (Gilead, 2018). While the drug is still expensive, Gilead's goal is to lower drug prices as to not deter anyone from being

treated (Gilead, 2018). This could result in the drug being available to more patients and lead to a path to eliminate new HCV infections and a cure for those currently infected.

METHODS

Overview

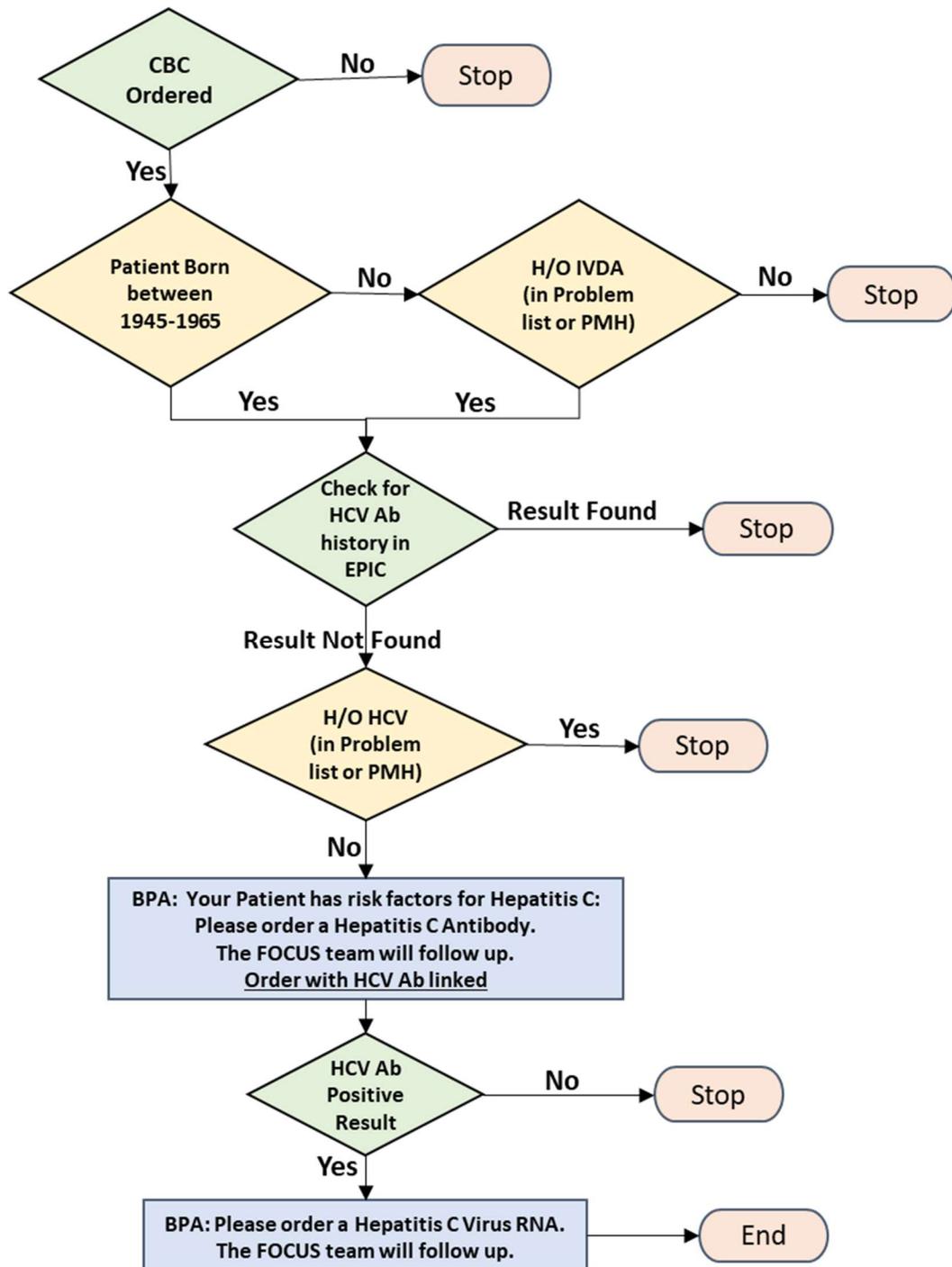
The FOCUS project was submitted to and approved by the Institutional Review Board at HFH. The data was collected from ED patients from March through December of 2018. Any identifiable patient information is kept in a shared drive that can only be accessed by the research team at HFH. The information is kept behind a secure firewall. All information that is sent to FOCUS is de-identified and each patient is given a unique client ID which is not connected to any of a patient's personal information.

Screening for HCV

The FOCUS project implemented an automated EMR-based HCV screening system. The HFH EMR, EPIC®, identifies patients born from 1945 through 1965 and/or those with a history of IV drug use. These criteria were selected based on their alignment with screening guidelines set by the CDC. The EMR alerts the provider of identified patients with a complete blood count (CBC) ordered using a Best Practice Advisory (BPA). The automated BPA encourages providers to order an HCV Ab test for those patients who: 1) meet at least one of the identified risk factors, 2) have a CBC ordered, and 3) do not have a previous HCV Ab history in EPIC® (Figure 2).

Figure 2

BPA Flowchart: EPIC® automatically alerts providers to order an HCV Ab test for patients born from 1945 through 1965 and/or have a history of IV drug abuse (IVDA). The BPA alerts the provider when they are ordering blood tests for the patient. If the result is positive, the BPA alerts the provider to order an HCV RNA test.



Linking the Patient to Care

All HCV Ab results are sent in an EPIC®-generated report to the FOCUS team. Team members are assigned patients from the report and are responsible for linking patients to care.

For each patient, the FOCUS team assesses the patient's chart to determine their HCV status. Information to be noted is HCV Ab result, whether an HCV RNA test was ordered and results were received, previous history and/or treatment of HCV, if the ED provider spoke with the patient about HCV status, or if the patient has already made an appointment with an appropriate physician to care for HCV.

Patients with a positive HCV Ab result will be contacted by a FOCUS team member via phone call to evaluate if the patient is interested in further HCV testing. Figure 3 has an example script for a team member to contact a patient. Patients interested in receiving further testing will have their information sent to one of the FOCUS team doctors to order an HCV RNA test. Once the test has been ordered, FOCUS team members will contact the patient to inform them to go to an HFH lab for the blood draw.

FOCUS team members will continue to evaluate the patient's chart until the patient has completed their blood test and the results are posted. If the patient's results are positive, the FOCUS team will contact the patient again to connect the patient to care. During this phone call, patients will be informed that their HCV test was abnormal, and the FOCUS team will evaluate

Figure 3. Example script of phone call for patient in need of HCV RNA testing

“Hello, I am looking to speak with Mr./Ms. [insert patient’s name]. My name is [insert first name] and I am calling from Henry Ford Hospital. I would like to speak with you about a lab result you received when you came to the hospital recently. Do you have time to talk for a few minutes? Great. When you came to the emergency department, you were tested for Hepatitis C. Are you familiar with Hepatitis C? Hepatitis C is a virus that causes liver inflammation. When you were tested for Hepatitis C, you received an abnormal result. We would like to know if you would be willing to come in for further testing. Since you are willing to come back, I will contact the physician to put in the order for the test. When the order is approved by the physician, I will give you a call back to let you know when you can come in for the blood test. I will give you another call in a few days—thank you.”

if the patient is interested in being connected to a physician to discuss the results of the HCV test (Figure 4). If the patient is interested, the team member will contact a doctor on the FOCUS team to inform them a patient is interested in being linked to care. The doctor will contact the Hepatology clinic and give them the patient's information. The Hepatology clinic will contact the patient within a few days to set up an appointment. The FOCUS team member will verify the scheduled date for the Hepatology appointment. After the appointment, the FOCUS team will again check the patient's chart to assess whether the patient has attended their first appointment. If they attend their appointment, they are marked as connected to care.

After three attempts at contacting a patient with no response, the patient is marked as a loss of follow-up.

Measurements

Demographics- Demographic data was collected only on patients that had a positive HCV Ab test. Demographic data included birthdate, sex, race, and ethnicity. This data was collected from the patient's EMR.

Drug Use History- Drug use history was collected from the EMR. This data could be reflected from self-report or if the physician documented drug use. Drug use history only

Figure 4. *Example script of phone call for a patient who needs to be connected to care*

“Hello, I am looking to speak with Mr./Ms. [insert patient's name]. My name is [insert first name] and I am calling from Henry Ford Hospital. I have previously contacted you about having an abnormal Hepatitis C result. You came back and received confirmatory testing and have received another abnormal lab result. I would like to get you connected with a doctor to discuss the results. If you are interested, I will give the Hepatology clinic your information and they will reach out to you to schedule an appointment. At the appointment, you will be able to discuss your results with a doctor. Are you interested in being connected with a doctor? Wonderful. I will give the clinic your information and they should give you a call within a few days—thank you.”

included IV drug use. This data was only collected on those that did not fall under the birth cohort of 1945-1965.

Laboratory Tests- Laboratory tests included HCV Ab and HCV RNA. Most of the tests were processed at the HFH Laboratory.

RESULTS

Demographics

From March 2018 through December 2018, 471 patients received a positive HCV Ab test and their demographic information was collected (Table 1). The racial composition was 77.9% African American/Black, 18.5% white, 0.6% other, and 3.0% unreported or unknown.

In terms of ethnicity, 1.9% of HCV Ab positive patients were Hispanic, 94.7% were non-Hispanic, and 3.4% were unreported or unknown.

The cohort was 64.3% male and 35.7% female.

About 82.8% of patients are included in the date of birth cohort of 1945-1965. Those that were not included in the birth cohort had drug use data collected. Of the 81 patients that were not included in the birth cohort, 46.9% had a history of intravenous drug use in their EMR, in 8.6% of those patient's charts it was explicitly stated that those patients did not ever use IV drugs, and 44.4% of those patients did not have this information included in their EMR.

Table 1
Demographic Information on HCV Ab Positive Patients

HCV Antibody Positive Patients' Demographics			
Race	African American/Black	367	77.9%
	White	87	18.5%
	Other	3	0.6%
	Not Reported or Unknown	14	3.0%
Ethnicity	Hispanic	9	1.9%
	Non-Hispanic	446	94.7%
	Not Reported or Unknown	16	3.4%
Gender	Male	303	64.3%
	Female	168	35.7%
Date of Birth Cohort	1945-1965	390	82.8%
IVDA Hx (Non-Baby Boomer)	Yes	38	8.6%
	No	7	1.5%
	Not Reported or Unknown	36	7.6%

Before BPA Implementation

During the five months before the BPA was implemented (March through July 2018), 360 HCV Ab tests were performed in the ED (averaging 72 tests per month) and 21 (5.8%) received a positive result (Table 2). Only 4 (19.0%) patients had HCV RNA tests performed, all of which were positive. A total of 3 (75.0%) patients were linked to care before BPA implementation.

After BPA Implementation

In the first five months after BPA implementation (August through December 2018), 4075 HCV Ab tests were performed in the ED (averaging 815 tests per month). There were 423 (10.4%) patients that received a positive result. Of those patients with a positive HCV Ab test,

215 (50.8%) received the HCV RNA test and 139 (64.7%) had a positive result. Over the five months after BPA implementation, a total of 63 (45.3%) patients were connected to care.

Pre/Post-BPA Implementation Comparison

After implementing the automated EMR-based screening protocol in August 2018, the number of HCV Ab tests performed in the ED increased from an average of 72 tests per month to 815 tests per month—an increase of more than 11-fold. The number of HCV RNA test increased by nearly 54-fold from an average of 0.8 per month to 43 HCV RNA tests per month.

Table 2
A comparison of the Pre/Post-BPA Implementation results

Pre/Post-BPA Implementation Comparison			
	Pre-BPA (March-July)	Post-BPA (August-December)	Fold Increases
Number of Ab Test	360	4075	11.3
Average Number of Ab Tests Per Month	72	815	11.3
Number of Positive Ab Tests	21	423	20.1
Number of RNA Tests	4	215	53.8
Average Number of RNA Tests Performed Per Month	0.8	43	53.8
Number of Positive RNA Tests	4	139	34.8
Number of Patients Linked to Care	3	63	21.0
Average Number of Patients Linked to Care Per Month	0.6	12.6	21.0

Cumulative HCV Screening and Connection to Care Rates

Approximately 100,000 patients are seen in the HFH ED each year which equates to the ED treating approximately 83,333 patients between the months of March and December (Henry Ford Hospital, 2019). In total, 4,435 patients received an HCV Ab test during their ED visit—so, approximately 5.3% of the HFH ED was screened during this 10-month period (Table 3). Of the 4,435 tested in the ED, 444 (10.0%) had a positive result. Approximately half (49.3%) of those patients received an HCV RNA test, confirming 143 patients with an active HCV infection, making the positive RNA rate 65.3%. A total of 66 (46.2%) patients were connected to care.

Table 3

The cumulative results of HCV Ab, HCV RNA, and linkage to care rates by month.

Final Report of HCV Testing and Linkage to Care (March-December 2018)					
Date (MM/YY)	HCV Antibody Tests	Positive HCV Antibody Tests	HCV RNA Tests	Positive HCV RNA Tests	Patients Linked to Care
03/18	83	3	1	1	1
04/18	65	6	0	0	0
05/18	47	8	2	2	1
06/18	74	4	1	1	1
07/18	91	0	0	0	0
08/18	649	41	10	6	1
09/18	813	157	58	37	16
10/18	971	90	56	35	15
11/18	881	78	52	33	17
12/18	761	57	39	28	14
Totals	4435	444	219	143	66

Figure 5 illustrates the HCV Ab and RNA screening rates from March 2018 through December 2018. Figure 6 displays the HCV Ab and RNA positive results and the linkage to care rates from March 2018 through December 2018.

Figure 5
HCV Ab screening rates and HCV RNA test rates March through December 2018

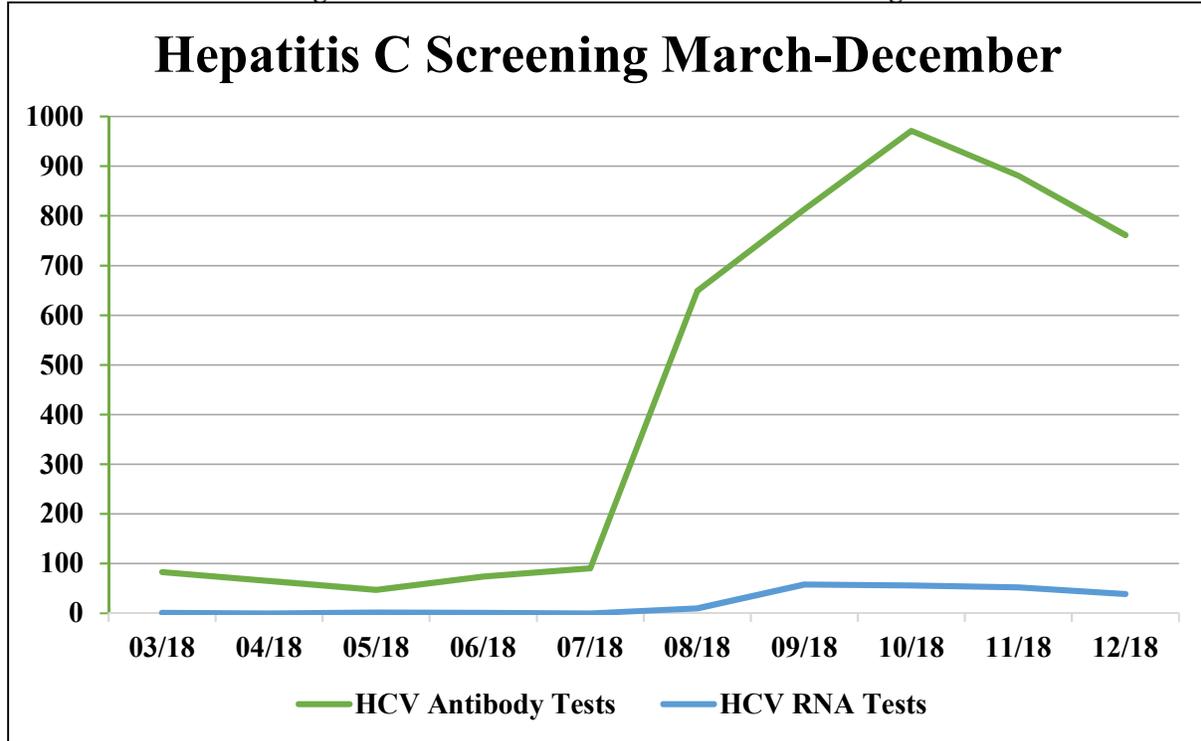
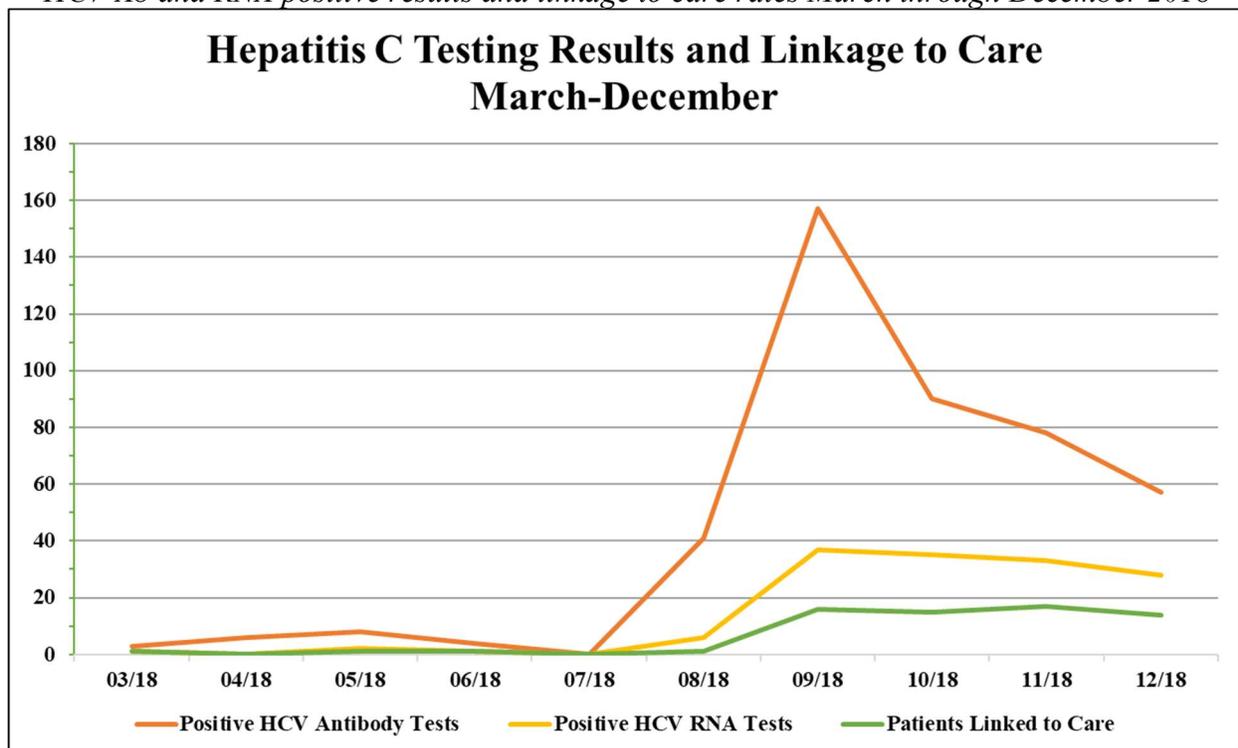


Figure 6
HCV Ab and RNA positive results and linkage to care rates March through December 2018



DISCUSSION

The majority of HCV Ab positive patients are African American/Black. This is consistent with the demographics of HFH in Detroit, as most of the patients are African American/Black. Before the automated EMR-based screening protocol was in place (March to July 2018), screening and linkage to care rates were very low. Only 72 HCV Ab tests were performed per month on average and in the five months before the protocol was implemented only 3 patients were connected to care.

The EMR screening protocol was rolled out mid-August 2018. Immediately, the testing rates increased to 649 tests per month in August alone, while only a total of 360 HCV Ab tests were performed in the previous five months combined. However, the number of HCV Ab tests in August was lower than the number of tests during the months of September through December because providers did not always add the HCV Ab test to the patient's orders. Informational meetings were held to educate the healthcare providers about FOCUS and by September, the HCV Ab tests began to rise to an average of 815 tests per month.

In order to keep up with the volume of patients on the HCV report, the staff for the FOCUS project was doubled. The additional staff also helped increase the rates of RNA testing (because many patients needed to be contacted to return for HCV RNA testing), so the RNA testing rates increased from 0.8 per month to 43 per month post-BPA. Both the increase in HCV Ab testing and additional staff allowed for the average number of patients linked to care to increase from 0.6 to 12.6 per month.

There was a decrease in the incidence of positive HCV RNA tests from 100% to 64.7% and a decrease in the frequency of connection patients to care from 75% to 45.3%. These reductions are due to the higher rate of RNA testing after BPA implementation.

Overall, HCV Ab tests increased by 11-fold, HCV RNA tests increased by 54-fold, and connection to care rates increased by 21-fold.

Limitations

One limitation to the FOCUS project is that demographic information was not collected on all the individuals that had HCV Ab test performed. The demographic information, especially gender, is difficult to analyze without complete demographic information for all patients with the antibody test. The results cannot differentiate if more men were tested for HCV than women or if more men had a positive result.

There are a few limitations that prevent the team from providing more patients with a connection to the Hepatology clinic. First, many patients at HFH provide unreliable contact information. This greatly impedes follow up with the patients. In addition, the patient population of HFH has significant economic and social barriers that prohibit them from returning for outpatient testing or a clinic visit. Finally, the FOCUS team is still relatively small compared to the number of patients received each week and their abilities to connect patients to care are limited by time, as they also have other obligations as research assistants.

Future Directions

The RNA testing rate (49.3% of eligible patients) was lower than expected. To increase the rate, RNA reflex testing began in January 2019 to automatically order an RNA test when a patients HCV Ab test yielded a positive result. The addition of the reflex testing will allow more people to receive the test while they are in the ED and the team will not have to ask the patients

to come back for an HCV RNA blood test. It is expected that the reflex testing will help the team connect more patients to care.

In addition, to increase chances of contacting the patients, the research team plans to develop a system to contact patients via mail. If after three attempts to contact the patient by phone is unsuccessful, they will be sent a letter. This effort may also help increase the linkage to care rate.

CONCLUSIONS

Overall, an automated HCV testing system can be successfully implemented into an ED setting. Compared to manual screening, this is a valid and effective screening method based on criteria set by the CDC. Additionally, this model places the responsibility of patient follow-up onto non-clinical staff and can be employed in diverse medical settings. The usage of a BPA system was extremely successful as the number of HCV Ab tests greatly increased after this system was implemented. The World Health Organization set a goal to reduce new viral hepatitis infections by 90% and reduce deaths due to infection by 65% by the year 2030—this model can help meet that goal (WHO, 2017). As the FOCUS project continues, more patients will be screened for HCV and it is the hope that actively screening and following up with patients will positively impact the incidence of HCV-related morbidity and mortality in the future. Furthermore, this screening and linkage to care model can not only potentially prevent one of the major causes of chronic liver disease and cirrhosis in the U.S. but could also prove effective to screen and test for other infectious diseases and in other healthcare settings.

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