Fall 1-5-2018

A Systematic Analysis of Hepatitis C Virus Screening Trends and Linkage to Care Program in the United States

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Abstract

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By

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Hepatitis C is a common blood borne infection in the United States; currently this infection is a primary public health concern. The World Health Organization estimates about 150 million carriers of chronic HCV; more than 350,000 deaths each year are attributed to Hepatitis C virus(HCV) related hepatic diseases such as chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma. The population subgroup commonly known as baby boomers have five times the risk of HCV than other groups (CDC 2015). It is therefore imperative to encourage testing among all vulnerable populations including the baby boomers. Evidence suggests underuse of HCV testing services, despite the recommendations of testing by the United States Centers for Disease Control and Prevention. Identifying the major predictors of HCV testing can be used to explain testing behaviors and possibly develop future HCV testing initiatives. The linkage to care for Hepatitis C infection which is an important component of the Hepatitis C cascade of care will also be evaluated and possible recommendations for future research will be explored. This research describes results of systematic analysis of Hepatitis C virus screening trends and linkage to care Program in the United States. The main finding is that despite the evidence based recommendations, the reported screening rates for Hepatitis C virus are still sub-optimal, also most testing centers still do not have an effective linkage to care system. Implementation of national guidelines for HCV screening,

establishing high yield screening centers and using linkage care providers will help reduce the HCV-related disease burden and ultimately improve health outcomes.

A Systematic Analysis of Hepatitis C Virus Screening Trends and Linkage to Care Program in the United States.

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A Thesis Submitted to the Graduate Faculty of Georgia State University in Partial Fulfillment of the Requirements for the Degree

MASTER OF PUBLIC HEALTH

ATLANTA, GEORGIA 30303

Abbreviations

AA-African Americans

HCV- Hepatitis C Virus

LTC – Linkage to care

HIV – Human Immunodeficiency Virus

PWID- People who inject drugs

Emergency Department -ED.

CDC- Center for Disease Control and Prevention

APPROVAL PAGE

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Acknowledgements

I would like to express thanks and immense gratitude to my parents Dr. and Mrs. J. Nwosu for supporting my dreams and encouraging me to pursue my career goals. Special thanks to my committee chair, Dr. Ike Okosun for investing his time, expertise and knowledge in me and being a valuable mentor; I appreciate your devotion, patience and constructive criticisms. I also thank my committee member, Kenya Kirkendoll RN, MSN, MPH; thank you so much for your time and immense contributions to all my research projects. Finally, thank you Nnenna and Gozie Azih for your patience and prayers.

Author's Statement Page

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Chapter I

Introduction

Hepatitis C virus is a small, enveloped, single-stranded RNA virus classified as a member of the Hepacivirus genus within the Flaviviridae family (Lindenbach et al., 2013). Chronic Hepatitis C remains a major source of morbidity and mortality; globally chronic Hepatitis C affects about 70 million people (Blach et al., 2017)). In the United States, it is expected that HCV-related mortality will surpass HIV-related mortality in the coming years (Deuffic-Burban,2010). Approximately half of adults with Hepatitis C in the United States do not know their infection status, and most persons who know they are positive for HCV antibodies fail to receive care (Kugelmas et al., 2017). Prior to 2012, the Centers for Disease Control and Prevention (CDC) recommended that HCV screening be based on risk factors such as injected drug use, long-term hemodialysis, or receipt of a blood transfusion prior to July 1992. In 2012, the CDC expanded its screening guidelines to recommend one-time HCV screening for all persons born between 1945 and 1965 (Smith et al.,2012). From 2012, CDC has recommended that persons born during 1945–1965 receive one-time HCV testing. Approximately 75% of all HCV infections in the United States and 73% of HCV-associated mortality occur in baby boomers; persons born during 1945–1965 placing this birth cohort at increased risk for liver cancer and other HCV-related liver disease (Bureau of Hepatitis Health Care 2012). The US Centers for Disease Control and Prevention and US Preventive Services Task Force (USPSTF) recommends a one-time hepatitis C virus screening for adults born between 1945 and 1965 (a birth cohort known as “baby boomers”) (Smith et al., 2012). The reported ranges for screening among this cohort vary but in general are estimated to be less than 30%, even after implementing interventions specifically aimed at increasing HCV screening among baby boomers (Adebajo et al.,2015; Allison et al 2016). Despite these evidence-based

recommendation, uptake of one-time universal HCV screening among baby boomers remains low. Many states in the US are gradually trying to increase HCV screening rates for baby boomers and other people at risk for HCV infection. For example, to increase the number of persons tested for HCV and to ensure timely diagnosis and linkage to care, in 2014, New York enacted a Hepatitis C testing law that requires health care providers to offer HCV antibody screening to all persons born during 1945–1965 who are receiving services in primary care settings or as hospital inpatients, and to refer persons with positive HCV antibody tests for follow-up health care, including an HCV diagnostic test (HCV RNA) (Smith et al., 2012). Potentially curative interferon based treatments have been available for more than 15 years, but less than 15% of those infected had been treated. HCV cure is associated with reduced morbidity and mortality (Simmons et al., 2015; Singal et.al.2010). Availability of well-tolerated, short-course (8–12 weeks), interferon-free, direct-acting antiviral (DAA) drugs with cure rates approaching 95% is expected to be a game changer in preventing progressive liver disease (Smith et al., 2015; Smith & Lim, 2015). However, for these drugs to have major population-level impact on morbidity and mortality, screening efforts must reach undiagnosed individuals, also diagnosed individuals must be linked with care and people remain engaged with care to be assessed for and receive treatment. In recent years, new therapeutic approaches have rendered chronic HCV treatable, with reversal of liver disease (Dultz,2015). With the availability of these new drugs, HCV could be eliminated within the next 15–20 years. Yet, this would require a collaborative effort of improving screening techniques, treating existing cases, and preventing new infections (Gower et al 2014). Timely diagnosis and treatment will help reduce existing HCV infections from metamorphosing into end stage liver diseases; these would only be possible with prompt screening.

Chapter II

Epidemiology of Hepatitis C

2.1 Brief Global Epidemiology

Hepatitis C virus (HCV) is a single strained RNA formerly identified as a putative viral hepatitis occurring after transfusion of blood products or intravenous drug use. It is a leading cause of liver-related mortality worldwide and was estimated to have caused 333,000 deaths in 1990, 499,000 in 2010, and 704,000 in 2013 (WHO facts sheet 2016; Lozano et al.,2012). After the discovery of the HCV in 1989 and its linkage to non-A, non-B hepatitis, HCV was first thought to be an infection of minor importance, affecting selected drug user and blood product recipient populations in developed countries (Lavanchy,2011). More than 20 years later, it is now well established that HCV is of global importance, affecting all countries, leading to a major global health problem that requires widespread active interventions for its prevention and control (Lavanchy,2011). Acute HCV infection results in chronic carriage in 70%–80% of cases, and 20%–25% of those with persistent infection will develop liver disease that may manifest as cirrhosis, liver failure, or hepatocellular carcinoma (Burke 2010). The acute infection culminates in chronicity which can lasts for years and if not diagnosed and treated can result in chronic liver diseases or carcinoma Within developed countries many of those affected are people who inject drugs (PWID); they comprise the largest affected group (Degenhardt et al., 2016). Within Europe the sero-prevalence increased with age with a peak prevalence occurring in 55–64-year-old patients; Southern and Eastern Europeans have the highest peak prevalence (Mohd et al.,2013). A systematic review of 4901 studies from 87 countries which included unpublished reports, and excluded older studies generated substantially lower estimates of global HCV antibody prevalence at 110 million cases (95% CI 92-149 million) and an HCV viremic population of 80 million people (95% CI 64-103

million) (Gower et al.2014. However, even in a relatively homogenous setting such as Western Europe, prevalence of viremic HCV infection may range between 0.4% (Austria, Cyprus, Germany, Denmark, France, UK) to 1.5% (Israel, Italy) (Mohd et al.,2013).

2.2 Epidemiology of Hepatitis C in the United States.

In the United States, an estimated 1.3% of adults are positive for hepatitis C virus (HCV) antibody (Gower et al.,2014). Over the past decade, the overall incidence of hepatitis C has been relatively stable; however in 2011, a rise in new HCV infections was noted among white adolescents and young adults with a history of injection drug use and prescription opioid use (Hagan & Shinazi 2013). A dramatic recent increase in the annual incidence of HCV-related hepatocellular carcinoma is expected to peak in 2019 also HCV-related deaths are anticipated to rise until 2022(Asrani,2014). Previous research on chronic hepatitis C infection in the US show that men are more likely to be infected compared with women and a higher prevalence among racial and ethnic minority populations compared with whites (Denniston et al.,2013). The prevalence of chronic HCV infections is still rising because people that get infected are unaware of their status and the disease progresses to a chronic state. The prevalence is higher in certain populations, such as African American and persons born between 1945 and 1965 (baby boomers). Hepatitis C–related liver disease has been the leading cause of death among blacks 45-64 years old (CDC, 2014). African Americans had the highest mortality rates from HCV in the United Sates from 2004 to 2008, at 6.5 to 7.8 deaths per 100,000 persons and died from HCV 78.9% more often than whites(CDC,2014); this disparity in HCV mortality rates increased between 2008 to 2010(Bailey et al., 2013). In more recent years, American Indian and Alaskan Natives had the highest incidence of Hepatitis C infection (Razavi,2014; Hagan,2013). For HCV infection, much interest has recently been given to BB screening, most infections for this birth cohort occurred by blood transfusion in

the late 1980s, before blood products were systematically screened for HCV (Deltenre 2016). Most patients who received blood products before this time frame were most susceptible to infection (Deltenre,2016). Blacks, who comprise approximately 12% of the population, have 22% of the chronic hepatitis C (Denniston et al 2013). Contributing factors include that blacks are both less likely to clear hepatitis C virus infection spontaneously and had lower rates of response to interferon-based treatments (Mir et al.,2012).

Suryaprasad et al., (2014) examined data from a national surveillance and supplemental case follow-up at selected jurisdictions to describe the US epidemiology of hepatitis C virus (HCV) infection among young persons (aged ≤30 years). According to the national surveillance data, the number of cases of acute hepatitis C declined rapidly from 1992 to 2003 but has increased since 2006, especially among PWID (CDC 2011). This increase has coincided with numerous HCV outbreaks among PWID in nonurban communities, frequently associated with injection or prior misuse of prescription opioids (Havens 2013). During 2006–2012, 7169 cases of acute hepatitis C were reported to CDC. Of 7077 cases with reported age, 44% were aged ≤30 years; of these, approximately 1% were aged ≤5 years. In 2012, 49% of all US cases were aged ≤30 years, vs 36% in 2006. From 2006 to 2012, reported cases in young persons were predominantly white (93%) and non-Hispanic (92%), and as likely to be female (50%) as male. Among all ages and specifically among ages≤30 years, the average annual incidence was significantly greater in 2011–2012 than in 2006–2010. This reflects a worrisome increase in HCV infection among young PWID in the United States. The incidence of reported acute hepatitis C among young persons has significantly increased during 2006–2012, with annual increases >2 times greater in nonurban compared to urban jurisdiction (Suryaprasad et al.,2014).

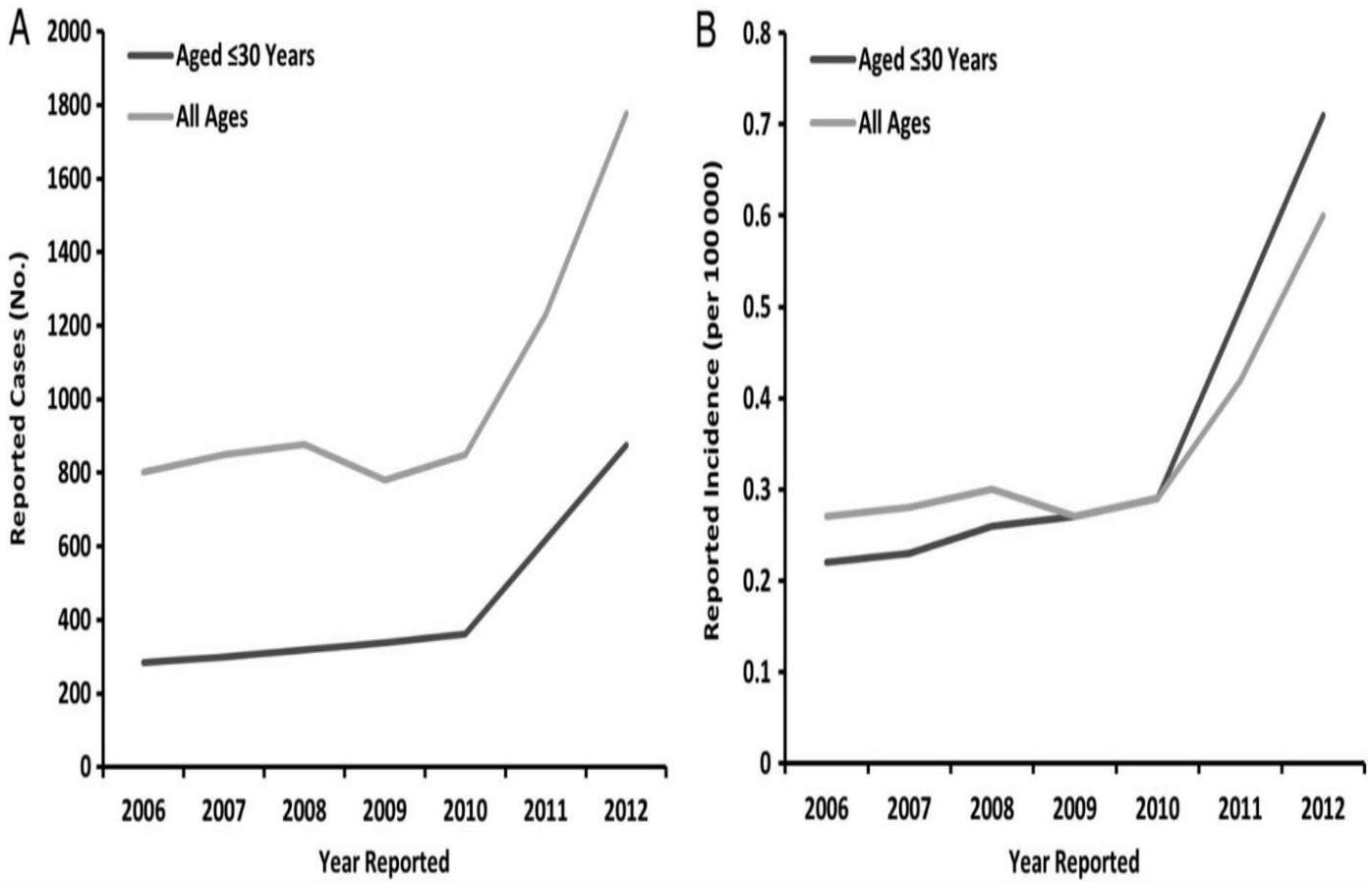

Figure 1.

Number of cases (A) and incidence (B) of acute hepatitis C reported to CDC by year among young persons and all persons, United States, 2006–2012. Abbreviation: CDC, Centers for Disease Control and Prevention. From: Emerging Epidemic of Hepatitis C Virus Infections among Young Nonurban Persons Who Inject Drugs in the United States, 2006–2012. (Source: Clinical Infect Dis. 2014; Oxford University Press on behalf of the Infectious Diseases Society of America 2014)

2.3. HCV Transmission and Reinfection

HCV is predominantly transmitted via the parenteral route, primarily with direct exposure to blood and/or derivatives. Until the early 1990s, blood transfusion was the main mode of HCV dissemination. However, with the introduction of serological screening techniques for HCV antibodies (anti-HCV) and the more recent finding of HCV RNA in blood bank specimens in several countries, viral exposure through blood transfusion has been drastically reduced (Teles et al.,2017). Populations at risk of acute hepatitis C are: patients who received blood transfusions, blood products or anti D immunoglobulin in pregnancy prior to 1990, before routine screening of blood products for HCV, intravenous drug users and intra nasal cocaine users, patients with tattoos or body piercings, heath care workers, dialysis patients, and those partaking in high risk sexual activities. Other routes of HCV transmission include high-risk behaviors: people who inject drugs (PWID). sharing needles & syringes and other equipment are responsible for a significant proportion of infections among young adults at global level (Suryaprasadet al.,2014, Negro et al., 2014). Other predictors of HCV infection, such as invasive medical procedures, tattooing/body piercing, and sharing sharp personal care objects, seem to increase the risk of virus transmission (Tohme et al.,2012; Wahab et al.,2014). Today, most cases of HCV are associated with sharing syringes and contaminated needles, therefore, injection drug users are the principal carriers of the viral agent (Dultz et al 2015); studies involving non-injection drug users have shown a higher prevalence of HCV in this group than that of the general population (Belaunzarán-Zamudio et al 2017). The risk of reinfection remains a possibility after clearance of acute hepatitis C. People who inject drugs (PWID) represent a priority population, given the high prevalence and incidence of HCV infection observed among PWID (Morris et al 2013).

Acute hepatitis C infection presents clinically as a mild illness non-specific flu-like symptom and typically unrecognized and thus, it is only infrequently diagnosed in clinical practice, particularly in those who progress to chronic hepatitis. The infection progresses after six months of persistence of HCV RNA within the blood to a chronic illness; the transition from acute to chronic hepatitis C is usually sub-clinical (Westbrook et al.,2014). Chronic hepatitis is the most common outcome, usually characterized by raised serum aminotransferases and may lead to fibrosis and cirrhosis in the liver; thus, chronicity is the major complication of acute hepatitis C infection (Westbrook et al.,2014). It is not uncommon for patients to remain undiagnosed with hepatitis C until they present with the complications of end stage liver disease. Decompensated liver disease is estimated to currently be present in 11.7% of persons with cirrhosis and that number is expected to rise through 2030(Asrani,2014). Once cirrhosis is established the disease progression remains unpredictable, cirrhosis can remain indolent for many years in some patients whilst progressing in others to hepatocellular carcinoma, hepatic decompensation and death (Westbrook et al.,2014).

There is also a common trend of co-infection with HIV Infection and Hepatitis C infection; given similar modes of acquisition through sharing of needles/syringes and other injecting equipment, HIV infection is a major co-morbidity among PWID with HCV infection (Platt el al 2016). HCV infection is a principal source of morbidity and mortality for people living with HIV infection (PLWH) (CDC,2014). The prevalence of HCV in the general U.S. population is approximately 1.0% to 1.5% (Smith et al., 2012), but for PLWH, the rate of HCV co-infection is as high as 25% (CDC, 2014). HIV-HCV co-infection is associated with decreased antiretroviral effectiveness, thereby increasing the risk for HIV virologic failure (Hua et al., 2013). The resulting immune suppression is, in turn, correlates with accelerated progression to hepatitis-related advanced liver disease and death (CDC, 2014; Kim et al.,2013; Kirk et. al.,2013). The relative risk for hospital

stays and emergency department visits may be more than 1.5 times higher for HIV-HCV co-infected persons compared to HIV mono-infected persons (Linas et al., 2011). Therefore, screening for hepatitis C antibodies is strongly recommended in HIV positive individuals or following spontaneous or treatment-induced resolution because of the substantial incidence of HCV in this group of people.

Chapter III

Literature Review

3.1 Methods

This literature review will be conducted as part of a broader literature search analyzing evidence-based research articles on Hepatitis C screening trends and linkage to care in different regions in the United Sates; the disparities in screening and linkage to care in different health care settings among a diverse population will also be examined. The criteria for selecting research articles for this paper include: recent articles (publications in the last 10 years), published in English language, representing diverse population cohorts including the baby boomers, a broad spectrum of healthcare settings and research conducted in the United States. The main electronic databases accessed for relevant literature include: Medline via PubMed, Medline via Ovid, EBSCO, Science Direct, and Web of Science. The papers identified from the literature search were screened and analyzed for sufficient of data on Hepatitis C screening and linkage to care in the United States. A detailed hand search was also conducted to check the reference lists of all included papers, and citation searches of key included papers.

3.2 Review of Hepatitis C Screening Trends

As new therapies promise opportunity for HCV cure, the public health agenda has placed emphasis on improving HCV screening and engagement in care. (Holmberg et al.,2013). The United States Preventive Services Task Force has made a “B” level recommendation that all individuals born between 1945 and 1965 be screened for HCV infection at least once. Screening practices, however, typically vary by geographic region, and even between individual practices (Johnson et al.,2010).

Unlike the Hepatitis B virus (HBV) infection, there is no conclusive evidence for protective immunity against HCV, therefore, the likelihood of a prophylactic vaccine is slim. To identify and proactively treat HCV infections, comprehensive screening of at-risk populations should be undertaken (Medici et al.,2015). Anti-HCV antibody enzyme-linked immunosorbent assay (ELISA) testing followed by confirmatory polymerase chain reaction testing has been found to accurately detect chronic HCV infection (Coughlin et al.,2015). The CDC recommends that providers should simply screen by age alone; not by deciding whether to test only after asking members of that birth cohort if they ever received a blood transfusion, used injectable drugs, subjected themselves to tattoo needles of dubious sterility, and so on. This new screening guideline arose from an exhaustive literature search indicating that the rate of chronic HCV infection in baby boomers is 5 times higher than for adults born in other years (Smith et al.,2012). An estimated 3.25% of baby boomers are HCV positive and most do not know that they are infected (Smith et al.,2012). The CDC has recommended that HCV screening be done using HCV antibody tests that have been approved by the US Food and Drug Administration (CDC,2013). Such tests are either laboratory-based assays ordered by health care providers or assays performed at the site of patient care. Increased accessibility of point-of-care tests means that they have the potential to increase the number of individuals who know their infection status. However, even among those who know they are anti-HCV–positive, barriers to confirming the diagnosis and receiving treatment are considerable, and the majority fail to receive care (McGowan et al.,2012; Patel et al.,2016.)

Linas et al (2014) used data from Kaiser Permanente Mid-Atlantic States (KPMAS), a large integrated health care system that serves a broad array of patients in the Maryland, Virginia, and Washington, DC area to study HCV screening frequency, as well as temporal trends in screening practice. They investigated rates of screening stratified by age and sex, trends in screening over

time, the proportion of patients who had ever been screened for HCV, provider type of those ordering HCV antibody test (HCV Ab), patient-level factors associated with ever being screened, and the test positivity rate. Their study showed that 15.8% were screened for HCV at least once during follow-up, adult primary care (44.2%) and obstetrics and gynecology providers (31.7%) performed most of screening. Of those born between 1945 and 1964, 14.4% were ever screened for HCV; 16.4% of women and 15.0% of men were ever screened. For subjects with histories of illicit injection and non-injection drug use, 67.4% and 31.6%, respectively, were ever screened for HCV. Of those with documented history of never using illicit drugs, 19.9% were ever screened, while of those with missing drug use history, 10.9% were screened. The 60-month cumulative incidence of screening was 11.5% for males and 12.2% for females 11.9% for in total. The 60-month cumulative incidence of screening was highest among females born 1985-1994 (24.6%) and lowest among females born before 1944 (5.5%). At all-time points, the cumulative incidence of screening was highest among those born between 1985 and 1994, and it decreased monotonically with older age. This study showed that among patients attending a large US integrated health care system, only 15.8% had ever been tested for HCV with serum antibody; for the baby boomers 14.4% were ever screened for HCV. Testing rates were significantly higher in high-risk groups such as injection drug users, those infected with HIV or HBV although even in these highest-risk populations, substantial numbers of patients were never screened.

3.3 Hepatitis C Virus Screening and Linkage to Care

The National Research Council in 2010 compared the Hepatitis C linkage of care to that of those living with human immunodeficiency virus (HIV) infection who follow a treatment cascade consisting of diagnosis, linkage to care, retention in care, and treatment. They stated that people with HCV infection should pursue the same objectives to improve their disease outcomes.

Individuals with HCV infection need to be diagnosed by HCV antibody and HCV ribonucleic acid (RNA) testing to confirm chronic infection, followed by linkage to care with a provider who can prescribe HCV therapy to achieve sustained virologic response (SVR) and provide other means to decrease the risk of disease progression. Following its recommendation for one-time hepatitis C virus (HCV) testing of baby boomers, CDC implemented the Hepatitis Testing and Linkage to Care (HepC-TLC) initiative to conduct birth cohort hepatitis testing in U.S. health-care settings. The CDC's HepC-TLC provided an opportunity to assess the implementation of BBs testing recommendations. This initiative explored methods for identifying people infected with HCV, including birth-cohort testing, and ways to link chronically infected people to care. In order for HCV screening to have the highest impact, however, screening needs to be linked with subsequent care after test results are available. Prior estimates from outpatient and emergency room settings have shown that 30%-50% of persons who test positive for HCV antibody (anti-HCV) never receive confirmatory HCV RNA testing, and among those with a confirmed diagnosis of HCV infection, only a minority of about 35% are referred to specialty care (Reau,2014; Yehia et al.,2014). Tohme et al (2013) examined the rates and determinants of HCV testing, infection, and linkage to care among US racial/ethnic minorities using data from the 2009-2010 Racial and Ethnic Approaches to Community Health Across the US Risk Factor Survey (n=53,896 minority adults). Overall, only 19% of respondents were tested for HCV, including about 60% of those reporting a risk factor. College-educated, non-Hispanic blacks and Asians had lower odds of HCV infection than those who did not finish high school. Among those who were infected, 44.4% were currently being followed by a physician and 41.9% had taken HCV medications. The authors concluded that HCV testing and linkage to care among racial/ethnic minorities in the United Sates are suboptimal

and that further HCV testing and prevention activities should be directed toward racial/ethnic minorities, especially those of low socioeconomic status (Tohme et al., 2013).

3.4 Linkage to care in different healthcare settings

The HCV current estimates suggest that only between 10–50 % of HCV infected patients in the US are currently diagnosed (McGowan et al.,2012). This is partly due to health care providers' lack of enthusiasm about the previous anti-HCV treatment regimens and their substantial side effect profile. Additionally, the recommended risk-based screening has not been effective in identifying infected patients (Cohn et al.,2015). Implementing HCV screening and linkage to care in healthcare settings is essential in bridging the health outcome gaps in the Hep-C cascade of care. With the current all-oral second generation direct-acting antiviral agents, over 95 % of treated patients can achieve sustained viral response (SVR) of HCV infection with an excellent safety profile (Gulab et al.,2015; Lawitz et al.,2013). With therapies achieving SVR in >90 % of patients, targeted testing and link to care for infected persons are expected to reduce HCV-related morbidity and mortality (Cohn et al.,2015).

Systematic emergency department screening of baby boomers has revealed HCV-antibody (Ab) prevalence rates between 11.1% and 13.7%, with disproportionately high prevalence among uninsured and underinsured persons (Galbraith et al.,2015; Kelen et al.,2012). Franco et al., (2016) conducted a retrospective cohort study to examine the rates of HepC-TLC after HCV screening of newly diagnosed baby boomers in an Emergency Department (ED) at the University of Alabama, Birmingham. The study's objective was to measure linkage to care(LTC) based on actual attendance to HCV clinics, analyze the failure rates of linkage to HCV care in a cohort of BBs and determine factors associated with LTC failure. They also looked at other demographic variables associated with LTC and the role of competing medical priorities, lack of access to care. The

authors had previously described a high prevalence of unrecognized HCV in an ED setting; they now wanted to extrapolate their findings to assess care linkage. HCV testing was offered to baby boomers unaware of their status; a trained linkage coordinator obtained referrals for positive cases, patient demographics, and clinic visits data. Linkage to care was defined as an HCV clinic visit within the hospital system; for LTC the linkage coordinator promoted HCV education and awareness. The results from their analysis showed that: mean age was 57.3 years (SD = 4.8); 70% were male and 61% were African Americans, that the odds of LTC failure were significantly higher for white males (aOR)2.57; 95% CI , 1.03–6.38) and uninsured individuals (aOR,5.16;95% CI, 1.43–18.63) and lower for patients with cirrhosis (aOR,0.36; 95% CI, 0.14–0.92) and access to primary care (aOR, 0.20; 95%CI, 0.10–0.41). This study showed that 4371 baby boomers were screened from September 2013 to June 2014, of whom 473 tested positive for HCV-Ab (11%). The HCV-positive baby boomers comprised mostly of aging, non-married, African American males living in inner-city, low income areas. The researchers concluded that only 1 in 3 of the studied cohort of baby boomers with newly diagnosed HCV in the ED were linked to HCV care. They found that the "no show phenomenon" to HCV care and the potential role played by demographic and clinical factors, was somewhat analogous to the linkage to care associated with HIV. They also noted that their cohort was largely composed of vulnerable minorities with frequent comorbid conditions, the subjects that had of access to care (attendance to specialty or primary care, and insurance) had more chances of a successful HepC-LTC. It was also observed that most of the patients who screened positive did not link to care in their referral system, 25% of patients who achieved HepC-LTC did so in the first 6 months of follow up; this finding was consistent with the findings of another study in which 23% of individuals (baby boomers and intravenous drug users) successfully attended HCV care visit within 6 months of ED diagnosis

(White et al.,2016). Male gender (white males in this study) was an independent predictor associated with lack of attendance to HCV clinics, HCV viremia was detected in 332 (83%) of which 221(66%) patients were referred and notified of appointments to any outpatient care within campus and 211 (64%) used any outpatient care within campus. It was also noted that African Americans (AAs) had slightly higher prevalence of HCV clinic attendance compared with whites (38% vs 31%), although not statistically significant (OR, 0.72; 95% CI, 0.45–1.15). The higher HCV clinical attendance observed in AAs was attributed to expansion of the HCV care access to inner-city minorities as opposed to the whites who predominantly live in the suburbs. One major limitation of this study was conducting their research exclusively in the university healthcare system; other clinics near Birmingham City and surrounding suburbs were not represented in this study.

Screening of baby boomers will help reduce the prevalence of HCV related liver diseases in that birth cohort. Zobair et al (2016) implemented a pilot screening project in five gastroenterology practices to identify baby boomers infected with HCV and to test the feasibility of screening and linking patients to care in a specialized practice setting. They screened 2,000 individuals in five gastroenterology centers located close to large metropolitan areas on the East Coast (3 Northeast, 1 Mid-Atlantic and 1 Southeast). These sites were large clinical practices within metropolitan areas that had familiarity with standard preventative screening procedures (e.g., colon cancer screening). For their study, the primary endpoint of this study was the percentage of individuals with a positive HCV-Ab. The secondary endpoints were the percentages of HCV Ab-positive patients who underwent confirmatory testing and were linked to care, and health related quality of life information (HRQL) scores at baseline and at follow-up. Study results showed that HCV RNA testing was done in 90 % of HCV-antibody positive individuals, and 44.4 % were found to be HCV

RNA-positive, 100 % of whom were counseled and linked to care by establishing an appointment regarding their HCV. This study shows that the outcome of screening and then linkage for the BBs may depend on the clinical setting; even though gastroenterology practices appeared to have a low prevalence of HCV the linkage to care occurred universally. They recommended maximizing both the yield of HCV screening and linkage to care with appropriate providers for identifying and successfully treating patients infected with HCV. One limitation of this study was selection bias; the patient referrals to a gastroenterology practice most likely would have insurance coverage thereby excluding uninsured individuals who are known to have high prevalence. The results may not be extrapolated to the general US population where a lot of individuals still do not have health insurance. Birth cohort testing proved to be more cost-effective, especially when most of the cohort was tested and enough HCV-infected persons were treated to offset the costs of screening (Asrani,2014).

Another study was done by Falade-Nwulia et al., in 2017 examining the capacity of public health clinics to provide HCV clinical services and the rates of and factors associated with linkage to care at two public health clinics in Baltimore City. They conducted a cross-sectional study on a cohort of patients receiving STI care at the Baltimore City Health Department (BCHD) STI clinics, Baltimore, Maryland from June 2013 through April 2014. They cited in their paper that Baltimore had a high burden of HCV infection with a reported prevalence of 10% among persons attending STI clinics who denied injection drug use, 18% in persons attending emergency departments, and 60–90% among persons who inject drugs. Patient demographics and clinical such as past and current injection/non-injection drug and alcohol use and linkage to care efforts were obtained from the clinic electronic medical record system. They defined linkage to care by (1) primary HCV care, repeated attendance at the STI clinic to receive HCV RNA results, HCV counseling, and referral

to HCV specialist and (2) specialty HCV care, attendance at first tertiary HCV specialist appointment. They stated that their study, to the best of their knowledge was the first to report the impact of on-site patient navigation services on increasing rates of HCV linkage to care in public health clinic settings. Descriptive statistics characterized the study population with respect to demographics and risk behaviors, logistic regression was used to assess factors associated with HCV infection and specialist linkage to care. The results of this study showed that from June 24, 2013 to April 15, 2014, 2681 patients were screened for HCV infection;(70%) of patients were offered a free rapid HCV test regardless of HCV risk factor or prior HCV testing history. Overall, 189 (7%) were anti-HCV positive, of whom 185 (98%) received follow-up HCV RNA testing, with 155 (84%) testing RNA positive. Of 155 RNA positive individuals, 138 (89%) returned to the STI clinic for HCV RNA results and initial HCV care including counseling regarding transmission and harm reduction for alcohol, and 132 (85%) were referred to a specialist for HCV care. With provision of patient navigation services, 81(52%) attended an offsite HCV specialist appointment. It may be possible that the screening rates in this cohort of patients were high since they had co-existing infections; only 70% were offered a free HCV test. Since this was an STI clinic, all the clinic attendees should have been offered a HCV test.

California Castrejón et al (2017) evaluated a large health system-wide HCV screening and linkage to care program for the baby boomers, persons born between 1945 and 1965. The objective of this study was to report on the implementation of the program and to evaluate its impact on HCV screening and linkage to care for patients seen in the outpatient University of California, Los Angeles (UCLA) healthcare system setting. After obtaining IRB approval, a HCV screening clinical decision support (CDS) tool was added to the routine health maintenance reminder in the EHR, for patients born between 1945 and 1965. A linkage coordinator was responsible for patient

follow up and linkage to care for HCV positive patients. For analysis, they compared HCV testing in the year prior (August 2014–July 2015) to the year after (August 2015–July 2016). HCV-related care outcomes was compared among patients with reactive HCV antibody testing, including HCV ribonucleic acid (RNA) testing, HCV RNA positivity, and linkage to HCV specialty care. The researchers observed that Hepatitis C virus antibody screening increased for all demographic groups by 145% (from 5676 patients tested to 13 930 tested) after introduction of the CDS intervention. It was also noted that addition of an HCV care coordinator increased follow-up HCV RNA testing for HCV antibody positive patients from 83% to 95%. Ninety-four percent of HCV RNA positive patients were linked to care after implementing the CDS tool. They concluded that the EHR CDS tool and care coordination markedly increased the number of baby boomers screened for HCV, rates of follow-up HCV RNA testing, and linkage to specialty HCV care for patients with chronic HCV infection (Casterton et al.,2017). The results from the last four reviewed articles show that the usage of a linkage coordinator increase the rates of follow up and post screening referral to specialty care. The HEPC-LTC is very important in all health care settings not only in specialized patient settings.

Pharmacists and other healthcare professionals should also be to conduct routine screenings for HCV; these would include nurses, nurse practitioners, and physician assistants. HCV screenings are not routinely conducted by community pharmacists, yet several studies describe how they may be able to improve patient access to clinical services and enhance chronic disease state management through the use of point-of-care tests (POCs) (Kehrer. Et al 2016; Darin et al 2015, Weidle et al 2014). In a large study, retail pharmacy staff members administered more than 1500 human immunodeficiency virus POCTs and demonstrated the feasibility of conducting this POCT in a community setting (Weidle et al 2014). Pharmacist-initiated HCV screening in a community

pharmacy can assist with identifying patients at risk for HCV infection and provide patients with linkage to care in the health system (Isho et al.,2017).

Chapter IV

Discussion and Conclusion

4.1 Discussion

Hepatitis C virus (HCV) is the most common blood borne infection in the United States; an estimated 5.2 million people are infected (Chap et al 2011). It is estimated that 50% of people living with chronic HCV in the United States are undiagnosed, and fewer than 40% of HCV-infected Americans are linked to medical care for their condition (Yehia et al 2014). Chronic Hepatitis C infection when left untreated progresses to chronic liver diseases, liver cirrhosis or hepatocellular carcinoma or even death. The economic burden of illnesses, hospitalization, absenteeism or deaths due to Chronic Hepatitis C infection can be enormous both in terms of direct and indirect costs associated with management of HCV-related diseases. Without changes to screening, diagnosing and treatment paradigms, over the next 20 years, the total medical costs for individuals with HCV infection are expected to more than double, from $30 billion to over $85 billion (Razavi et al 2013). The cost of birth cohort testing (approximately US$2 billion to test 66 million people) and treatment (approximately $26 billion to treat an expected 551,000 people over 10 years) is considerable (Asrani 2014).

Since the 2012 CDC Hep-C recommendation the screening rates have increased but is still sub-optimal; most individuals infected with Hep-C are still unaware of their sero-status. Despite evidence-based recommendation, uptake of one-time universal HCV screening among baby boomers remains low. The reported ranges for screening among this cohort vary but in general are estimated to be <30%, even after implementing interventions specifically aimed at increasing HCV screening among baby boomers (Adebajo 2015, Sanchez 2017). In a setting of high HCV infection

prevalence and low screening rates the health outcome would be sub-optimal. Screening alone would not bridge the gap in health outcomes; linkage to care is an important ancillary tool in the Hep-C LTC continuum of care. Current national and international guidelines for the management of HCV infection recommend that screening for HCV infection should be performed in individuals with well-known risk factors (risk-based screening) or individuals within a certain age group (birth cohort screening).(Fretz et al 2013).

Screening rates are determined by a lot of factors: disease prevalence, availability of screening centers, lack of transportation, health insurance and health care provider recommendations (or lack of). African Americans are disproportionally affected by HCV with higher prevalence of infection, higher liver-related morbidity and mortality, and underrepresentation in cohorts undergoing HCV treatment compared with whites (Wise et al, 2008). As the group with the lowest income in the United States (Saab et al 2014) African Americans also have the highest hepatitis C prevalence at 22% (Pyrsopoulos et al 2005; Trooskin et al 2007). Increasing screening rates in African American baby boomers will improve the quality of life of individuals living with Hep-C infection. Establishing screening programs and EHR –based alert systems in hospitals and use of linkage coordination will help reduce the low screening rates. There is a need for HCV screening programs for both general and at-risk populations, including intravenous drug users, people with a history of using blood products or unsafe injections, those with piercings and tattoos, prisoners, and homeless people. Lack of knowledge and awareness about HCV are observed among healthcare providers, policy makers, the public, and at-risk population (Waheed et al 2015). In 2010, the Institute of Medicine indicated that the lack of knowledge and awareness about viral hepatitis and insufficient understanding about the extent of this public health problem impeded efforts to prevent and control HCV. Ward et al. (2012) cited lack of public and provider awareness as a major cause

of inadequate public health and health-care resource allocation for HCV. There is insufficient understanding about the seriousness of this public health problem, so inadequate public resources are allocated for the prevention and control of HCV (Waheed 2015). Health care provider awareness and recommendations also affects Hep C- screening rates and linkage to care. Retail pharmacies can also serve as centers of Hep-C screening for at-risk populations in a community; phlebotomists and pharmacists could work together in providing screening thereby reducing the number of seropositive persons who are unaware of their status. Adequately trained linkage coordinators or counsellors could also help with post screening counseling and active linkage to care for people with chronic HCV infection. Local health department should offer screening especially in STD clinic, county jail, and drug recovery/rehabilitation centers to cater to a diverse population of at-risk individuals.

4.2 Recommendations and Policy Implications

Health care professionals can assist with these recommendations and perform HCV screening in inpatient, ambulatory care, and community settings (Isho et al 2017). Primary care physicians are often the point of entry into the US healthcare system; therefore, they are essential to identifying at-risk individuals, providing screening, and making the necessary referrals to specialists (Hu et al., 2011). Still, in a survey of general practitioners (GPs), 42% reported that they lacked confidence in interpreting HCV serology; in addition, 89% of GPs also identified language difficulties as the main barrier to treatment among the immigrant population (Guirgis et al.,2012).

There is a need for additional efforts to provide continuing professional education about developments in HCV linkage to and to increase community awareness about the availability of improved therapies for hepatitis C (Coughlin,2015). In terms of patient-related costs, screening and care may be expensive for patients with no health insurance; most individuals would defer

screening if they feel they cannot afford to continue receiving care or treatment. Local health departments should able to offer the first one time recommended screening especially for the baby boomers. Policymakers should consider a comprehensive HCV care program like the Ryan White HIV/AIDS Program; this will provide primary medical care and essential support services for people who are uninsured or underinsured. Currently, Medicare Part B may cover a one-time hepatitis C screening test for baby boomers ordered by a physician and sometimes may cover a confirmatory test if the person is a high risk patient.

Health policy advocates should lobby for expansion and revision of this coverage to include confirmatory test and specialty care. Public health practitioners should develop strategies to expand health care coverage for people living g with drugs, prisoners, homeless individuals and other at-risk groups. All health care systems should be encouraged to implement HCV screening, counseling, and linkage to care in to their electronic medical systems to ensure a continuum of care beyond screening. Effective screening programs are also recommended to include culturally sensitive educational outreach efforts to promote awareness, screening, and vaccination and should also include a counseling component with connections to healthcare services and follow-up care (Hu et al., 2011; Rein et al 2010).

4.3 Conclusion

Despite the availability of the Direct Acting Antiretrovirals (DAA) and evidence based screening recommendations, chronic hepatitis C infection is currently still a national public health concern. The importance of increasing the screening rates nationwide cannot be overemphasized since a considerable proportion of the at-risk population, the baby boomers are still not aware of their status. Current all-oral therapies have the highest cure rates in history (Kohli et al 2014). For these treatments to achieve their full potential, more undiagnosed chronic HCV patients must be

identified with improved screening (Miller et al 2017). Prolonged infection whish can result in chronic liver disease or in severe cases hepatocellular carcinoma can amount to huge health care costs. Recent studies demonstrating that birth cohort screening in the primary care setting was cost-effective were largely contingent on the linkage to care (treatment) and the better rates of SVR with newer antiviral drugs(Rein et al 2012). Screening as recommended and early treatment with DAA options will eliminate the infection and decrease the likelihood of progression and burden of disease. Health care providers should consider disparities and incorporate culturally sensitive educational outreach efforts to promote awareness, screening with a counseling component to bridge the gap. Ensuring a continuum of care for people living with chronic Hepatitis C infection requires prompt screening and linkage to care: this will eliminate the gap in the care cascade from screening point to a physician visit. The ideal integral process would be identifying high yield screening centers, incorporating linkage care providers who would educate and follow up screened individuals up till the point of successful treatment.

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