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A Comparison of Two Hepatitis C Virus Surveillance Systems in Hamilton County, TN

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A Comparison of Two Hepatitis C Virus Surveillance Systems in Hamilton County, TN

By Randall Van Dolson, RN

Background: Hepatitis C virus (HCV) surveillance is difficult to perform, partly due to the asymptomatic nature of many chronic infections and requirement of multiple confirmatory laboratory tests. As the literature reflects this difficulty, I sought to describe and demonstrate significant differences between populations identified of two different HCV surveillance systems in order to identify strengths and weaknesses of each system and inform development of future systems.

Methods: Two datasets were used in this analysis. The first included HCV RNA-positive cases from Hamilton County, TN from June 1, 2016 – October 31, 2016 collected by Tennessee Department of Health's (TDOH) Global Health Outbreak Surveillance Technology (GHOST) surveillance pilot and the TDOH-based National Electronic Disease Surveillance System (NEDSS) Based System (NBS). The second included l data from the U.S. Census at the Zip Code Tabulation Area (ZCTA) level to provide population-level descriptive variables of the HCV RNA-positive cases. ArcMap was used to create two custom variables that estimated the distance between case and health department. ZCTA-specific variables were categorized at or above and below the median. The two custom variables were categorized into quintiles. Cross tabulation analyses were performed between 74 HCV RNA-positive cases and ZCTA variables.

Results: Both systems identified similar numbers of cases for many of the variables, including educational attainment, employment status, veteran status, disability, private insurance coverage, citizenship status, urban/rural status, Black race, American Indian/Alaska Native race, Asian race, and distance from health departments. Differences between the two systems occurred. GHOST identified more cases at or above the median White population, more cases below the median Hispanic population, and nearly twice as many cases above the median household income than NBS. More cases below the median White population and more cases above the median Hispanic population were identified by NBS.

Conclusion: Both systems are similar in whom they identify and how they identify positive cases, revealing that both opt-out targeting and routine reporting of positive cases are targeting similar populations. The exceptions encourage further investigation into each surveillance system's gaps. Future directions can include more robust analyses with larger populations and geographical areas to better assess strengths and weaknesses of these surveillance systems.

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I. Introduction

Viral hepatitis is a major threat to the health of individuals worldwide and is an increasing concern for public health internationally and domestically. Globally, it is estimated that 1.4 million deaths per year are due to acute hepatitis infections and its sequelae, including hepatocellular carcinoma and cirrhosis, and its burden of disease rivals that of HIV, tuberculosis, and malaria (1). Most of these cases are due to hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, which are distinct viruses but similar in that they affect the liver. In the United States, millions are estimated to have chronic viral hepatitis and it is projected that more than 320,000 Americans will die from complications of infection in the next decades (2). Since 2012, more infectious disease deaths in the U.S. are attributable to HCV infection than all other reportable infectious diseases combined (2).

Hepatitis C virus can cause both an acute and chronic disease, with severity ranging from a mild to serious, long-term illness resulting in liver failure and death (3, 4). It is estimated that 19,659 individuals died in 2014 from HCV but many contend that underreporting likely affected these figures (2).

Since HCV's identification in the early 1990s, medical treatments to cure the infections have slowly progressed in therapeutic efficacy. Within the past few years, there has been a breakthrough in treatment with the advent of direct-acting antivirals (DAAs), which can substantially reduce viral load and provide a cure. However, the asymptomatic and silent nature of HCV infection, the ubiquity of risk factors and multiple modes of

transmission, the high cost of treatment, and generally weak surveillance systems combine to make HCV infection a serious public health problem.

Much has been published on HCV's epidemiology, risk factors, and disease manifestation. Nonetheless, there is a noticeable lack of literature regarding the status and benefits of surveillance systems to identify HCV cases. What literature is available recognizes the importance of surveillance in identifying and mitigating HCV infections, but also reveals the challenge of monitoring HCV infections through such systems (6). In response, the purpose of this thesis is to describe and demonstrate significant differences in two distinct surveillance systems in Hamilton County, Tennessee in the hope of illuminating the strengths and weaknesses of these two systems. This study hopes to provide insight into the development of future surveillance systems, which would better identify HCV cases.

II. Background

Molecular Epidemiology

The hepatitis C virus is a single-stranded, positive polarity, enveloped RNA virus in the Flaviviridae family of the type species of the genus *Hepacivirus* (7, 8). It was identified in 1989 as the main cause of non-A non-B (NANB) hepatitis (9, 10). Other causes of NANB can include autoimmune disease or hepatitis E virus (HEV) (11, 12). The HCV RNA genome codes for a single polyprotein which is divided into three structural proteins (C, E1, E2) and seven nonstructural proteins (p7, NS2, NS3, NS4A,

NS4B, NS5A, and NS5B) (8, 13). NS5B is the RNA polymerase required for viral replication (14).

Experts disagree on how many HCV genotypes, or strains, exist. Messina et al., Preciado et al., and Petruzziello et al. contend there are seven major genotype classes (15, 8, 16). Lingala et al. recognize six major genotypes (18). The disagreement over HCV genotype 7 may stem from its recent identification and rarity. For example, Murphy et al. performed a nucleotide sequence analysis of the NS5B region from 8,479 HCV RNA-positive individuals in Quebec, Canada to identify genotypes (13). Through this analysis, HCV genotype 7 was identified in four individuals from the Democratic Republic of the Congo (19).

Hepatitis C virus is distributed geographically based on its genotype (15, 8). Genotype 1 is the most prevalent in the world and in developed countries, accounting for approximately 46% of all cases (15, 18). Genotype 3 is found in approximately 30% of global cases and is endemic to the Indian subcontinent (15, 8). Genotypes 2, 4, and 6 are found in approximately 23% of all cases, with genotype 2 endemic to West Africa, genotype 4 endemic in Egypt and Central Africa (and found mainly throughout Africa), and genotype 6 endemic in Asia (18, 8). Genotype 5 is found in the majority of the remaining cases (~1%), mainly in Africa (8). Only a handful of cases are comprised of genotype 7, originating from the Democratic Republic of the Congo (19, 13).

Petruzziello et al. have slightly different results from other reported global studies due to including countries previous excluded and because their data were combined with other global or continental reports (16). Of all anti-HCV adult cases, they report that

genotype 1 is found in 49.1%, genotype 3 in 17.9%, genotype 4 in 16.8%, genotype 2 in 11.0%, genotype 5 in 2.0%, and genotype 6 in 1.4% (16).

The distribution of HCV genotypes is also determined by its subtypes, often revealing historical and developmental factors. Subtypes 1a, 1b, 2a, and 3a, collectively referred to as "epidemic subtypes" are found globally and especially in high-income countries (15, 16). It is likely that these subtypes were distributed via certain modes of transmission, including blood transfusion and drug abuse (15, 16). Other subtypes are considered endemic subtypes because they have not spread as widely around the world as the epidemic subtypes but have remained confined to specific regions for a longer duration, such as West Africa, Southern Asia, Central Africa, and Southeastern Asia (15, 16). Additionally, the global genetic variation of HCV is most likely influenced by trends in human movement, such as the Atlantic Slave Trade (15, 16).

In their analysis using data from the Chronic Hepatitis Cohort Study (CHeCS), Gordon et. al. show that there is considerable genotype and subtype variation within the U.S. when adjusting for age and race (20). Among four healthcare systems analyzed, Detroit, Michigan and Honolulu, Hawaii had a higher proportion of genotype 1a and genotype 3 compared to Dansville, Pennsylvania and Portland, Oregon. Detroit also had a higher probability of genotype 1b and Portland had a higher probability of genotype 2b and genotype 6 (20).

These authors also show a variation in genotype and subtype distribution among race and age. When adjusted for age, African American patients had a higher probability of genotype 1a and genotype 1b, Whites had a higher probability of genotype 2b and 3,

and Asians and others exclusively had genotype 6 and a higher probability of genotype 4 (20). When adjusted for race and geographic distribution, genotype 1a had the highest proportion among all decades. Genotype 1b decreased in younger ages, while genotypes 1a, 3, and 4 increased in younger ages (20).

The various genotypes and subtypes have implications in the development of treatment and may also have a role in disease progression. Messina et al. state that length of treatment, cure rates, and need to combine interferon and ribavirin with DAA medications partly rely on genotype and subtype (15). The development of a hepatitis C vaccine also depends on an understanding of genotypes and subtypes (15). Seeff suggests that little evidence exists that viral genotype (in addition to viral concentration) is associated with disease progression (10). Lingala et al. state that the association between HCV genotype and disease progression is unclear but suggest that HCV genotype 3 may be associated with increased fibrosis, either directly or indirectly through its association with steatosis (18). Preciado et al. affirm this, suggesting that HCV genotypes are associated with the pathological progression of HCV-related disease, specifically that genotype 1 is associated with a myriad of risks and that genotype 3 is associated with increased fibrosis and steatosis (8). Overall, the authors agree to some degree that understanding of HCV genotypes and subtypes is important to understand disease progression and response to therapy (8, 18, 15).

Acute Infection

Acute HCV infection is defined as the first 6 months of infection. During this period, spontaneous resolution of the infection without treatment is possible, occurring in

15% to 45% of infected individuals (18). Most individuals with acute infection are asymptomatic, with roughly 20% presenting with jaundice (18). Typical symptoms are like those of other viral hepatitis infections and are, thus, not ideal ways to identify HCV infection. Symptoms include nausea, vomiting, abdominal pain, flulike symptoms, and jaundice, among others (18). One of the main challenges of HCV surveillance is that most infected individuals are asymptomatic and, as a result, do not seek immediate medical care (2).

If identified, it is possible to treat acute HCV. Historically, this was done with interferon (IFN) or IFN with ribavirin (RBV), in order to decrease the risk of progressing to chronic HCV (9). Additionally, pegylated interferon (PEG IFN) with or without RBV for 24 weeks or longer has been shown to increase viral clearance (9). However, it is currently debatable if treating acute HCV infection with PEG IFN and RBV is optimal given associated risks and side effects. Especially with the increase in use of DAAs which are well tolerated and have minimal side effects, it may be prudent to use them if the individual progresses to chronic HCV and then treat with DAAs, since DAAs are currently only licensed for treatment of chronic HCV (21).

The nature of acute HCV infection in the U.S. has changed dramatically. An increase in acute HCV cases in suburban eastern and midwestern U.S. states associated with an increase in injection drug use was observed between 2010-2013 (18). Van Handel et al., in their seminal study on Scott County, Indiana, support this, stating that between 2006-2012, acute HCV rates increased, especially east of the Mississippi River and in central Appalachia (23). Additionally, the demographics have changed. Where HCV used

to be diagnosed more in males, non-Hispanic Blacks, and individuals between the ages of 40-49 years, as of publication, the authors state acute infections were equally diagnosed among both genders and are mainly in White, non-Hispanics at a younger age (23).

Chronic Infection

Chronic HCV infection is defined as detectable HCV RNA in the blood after 6 months of an acute infection (18). Approximately 130 – 150 million people are chronically infected worldwide, and these numbers are increasing every year (1). According to the World Health Organization, roughly 399,000 people die each year from HCV infection complications, including cirrhosis and hepatocellular carcinoma (4). In the U.S., there are estimated to be between 2.0 – 2.8 million chronic HCV cases (5). Throughout the Western world, chronic HCV infections is the main cause of end-stage liver disease, hepatocellular carcinoma, and liver-related deaths (9). Lingala et al. states that 55% to 85% of acute HCV individuals will progress to chronic HCV infection (18).

According to the CDC, of those with chronic HCV infection, 60% to 70% will progress to chronic liver disease, 5% to 20% will develop cirrhosis over 20 to 30 years, and 1% to 5% will die from liver disease (17). However, Westbrook et al. suggest that the progression to cirrhosis can vary, ranging from 2% to 51% over 22 years (9). Regardless, most individuals with chronic HCV infection will not show symptoms of infections and will remain undiagnosed until they present with symptoms of chronic liver disease or are identified through blood donation or from recognition of elevated alanine aminotransferase (ALT) levels (2, 9). Due to this insidious progression, it is important to screen individuals at high risk of exposure to identify those with HCV infection (2).

Certain factors affect the progression of chronic HCV. Host factors include age at infection, gender, race, obesity, steatosis, insulin resistance/diabetes, genetics, ALT levels, and exercise. Viral factors include HCV RNA level, HCV quasispecies/genotype, and co-infection with other viruses including HBV and HIV. Environmental factors include alcohol use, smoking, cannabis, caffeine, and herbals (10, 18).

Modes of Transmission

As HCV is mainly bloodborne, risk factors include behaviors that put one at risk of exposure to infected blood. Transmission of HCV occurs primarily through percutaneous exposure to infected blood, including intravenous drug use (IVDU), receipt of blood or blood/organ products, needlestick injuries, and birth to an HCV-infected mother (17). Less frequently, transmission can occur through non-percutaneous routes of exposure to infected blood, including use of personal items that are contaminated with HCV (toothbrushes, shaving razors, and earrings, for example), and sex with an HCV-infected individual (17).

Intravenous Drug Use

The most common method of acquiring HCV infection is through intravenous drug use (IVDU) and one of the largest populations of HCV in the world are people who inject drugs (PWID) (4, 24). Roughly 70% of all new acute case of HCV infection are attributed to PWID (2). In the U.S., transmission via IVDU most frequently occurs in White, young, nonurban persons (2, 25). Transmission among this population is primarily with the HCV 3a genotype and may represent a second HCV epidemic primarily driven

by the current opioid epidemic that is separate from the older population infected via blood transfusions or an unknown source (26).

Roughly 10 million active PWID are infected with HCV worldwide, which corresponds to about 67% of the global HCV prevalence (27). Stone et al. states a lower number, suggesting that injection drug use is associated with 40% of global HCV burden (28). Former PWID are a large reservoir of HCV infection (27). Some countries have a HCV prevalence of 90% among PWID (27). China, the U.S., and Russia have the highest number of PWID with HCV (27).

The main route of transmission of HCV in PWID is through the sharing of needles and other drug equipment and paraphernalia, which may include syringes, filters, cookers, and water (24, 27). However, Thibault et al. state that HCV RNA was often found on syringe pools and, particularly, swabs, compared to used filters, water vials, and cups (29). Additionally, transmission via these objects is compounded by how long HCV can remain viable on a surface and by the nature of exposure. HCV is persistent and the length with which it can remain viable on a surface varies from days to roughly four weeks on a surface at room temperature (3, 24, 27).

In addition to the persistence of HCV on surfaces, such as drug equipment, the methods used to clean drug equipment is implicated in HCV transmission. Binka et al. performed a study on the effectiveness of various methods of disinfection of syringes contaminated with HCV. They found that many PWID clean their syringes with cola, wine, beer, and vodka, in addition to methods promoted by harm reduction programs such as bleach, rubbing alcohol, and dishwashing detergent when new equipment is

unavailable (24). Their results reveal that bleach is most effective at disinfection after one rinse, and that other diluted household products such as rubbing alcohol, kitchen sink detergent, and hydrogen peroxide were effective in disinfection after one rinse (24). Water, beer (5% ethanol), and 20% ethanol were ineffective and not recommended as disinfection methods (24).

Such issues underscore the barriers present in the treatment of HCV among PWID. Despite the prevalence and availability of DAAs and other advances in treatment and recommendations, treatment uptake remains as low as 1-2% per year (27). Factors potentially responsible for this include low awareness among the public, IVDU, providers, and lawmakers, including increased awareness of the need to test and screen at-risk individuals; stigmatization; and, the cost of treatment and lack of universal access to such treatments. (24, 27, 30).

Receipt of Blood and Organ Products

Transmission of HCV in the U.S. through the receipt of blood products, such as blood donations and organs, is now rare due to widespread HCV screening measures in blood products established in 1992 (17). The CDC estimates that the current risk of acquiring HCV infection via transfused blood or blood products is low at 1 per 2 million units transfused due to advanced screening tests for HCV in blood banks (17). In their 2010 Guidance for Industry, the U.S. Food and Drug Administration supports this, indicating that from 2007-2008, the residual risk of acquiring HCV through screened blood and blood component donations was approximately 1 in 1,149,000 donations prior to utilizing nucleic acid testing (NAT) (31). It can be assumed that the risk is even

smaller with the adoption of NAT since then. In fact, the last case of transmission of HCV due to receipt of blood products was in 1994 (32).

However, though the probability of being exposed to HCV through the receipt of blood and organ products is currently rare in the developed world, many individuals in developed countries were exposed to HCV infected blood and organ products prior to routine screening of the blood supply. Furthermore, screening of blood and organ products, as well as certain infection control policies, are not universally held worldwide and those in developing countries are at risk of HCV infection through the blood supply. Globally, it is still important to identify, manage, and treat populations who were, and may continue to be, exposed to HCV through the receipt of blood and organ products.

One of the reasons the CDC promotes HCV screening for Baby Boomers (individuals born from 1945 – 1965) is because they are five times as likely to have HCV compared with other adults and may have been exposed to HCV via exposure to blood and organ products prior to the adoption of widespread HCV screening of these products, among other risk factors (33). Transfusion-associated hepatitis has been well-recognized for decades (34). Engle et al. attempted to use more modern, sensitive screening tests to analyze the viral markers of a virgin collection of blood that had been frozen for around 50 years. The authors determined that the donor carrier rate for HCV was 3%, compared to a current rate of 0.032% and that hepatitis B virus (HBV) and HCV were more prevalent than realized at the time (34). Selvarajah et al. state that nearly 25% of blood recipients in the U.S. were infected with HCV as demonstrated through retrospective studies from the 1960s and 1970s (35). Because of the prevalence of HCV in the blood

supply prior to 1992, it is important that those alive prior to the adoption of widespread HCV screening be tested to determine if they are infected.

Compared to developed countries, HCV transmission via blood transfusions is currently a serious problem in developing countries. From 2001-2002, the WHO reported that six million blood units were not screened for certain bloodborne infections, including HCV (56). This number is not sufficient to stop the current HCV epidemic (32). In its 2016 Global Status Report on Blood Safety and Availability, the WHO concluded that transmission of HCV via blood products is a problem in low- and middle-income countries (36).

The reason for the persistent spread of HCV via blood transfusion on a global basis is primarily based on socio-economic factors and include the following: the majority of blood donors are first-time donors in developing countries; developing countries lack appropriate regulations and systems to assure that enzyme immunoassay (EIA) testing is appropriately performed; NAT testing can reduce the long window period present with EIA testing but many countries lack the resources to support training and costs associated with NAT testing; poverty; lack of infrastructure; and, frequent electricity failure (24, 35).

Occupational Exposure

The risk of HCV acquisition after a percutaneous exposure is roughly 1.8% - 1.9% (37, 38). In their review, Hughes et al. state that there is no recommendation for

postexposure prophylaxis for HCV exposure and evidence to support using DAAs for postexposure prophylaxis for HCV exposure is lacking (38).

Risk of Hepatitis C Virus Infection in Pediatrics

With the decline of HCV risk via blood transfusion, HCV infection in children is primarily caused by vertical transmission (39). Specifically, vertical transmission is causative in developed countries and horizontal transmission in low- to middle-income countries (40). Worldwide, approximately 60,000 babies with HCV infection are born each year (41). Of the estimated 130 – 150 million people with chronic HCV infection globally, 11 million are less than 15 years of age (40).

There are unique effects of HCV infection in children. HCV infection in children can lead to accelerated development of certain liver disease, including an increased risk of end-stage liver disease later in life and the development of fibrosis and cirrhosis in childhood (40). Additionally, HCV infection in children may be associated with early cognitive impairment and high caregiver stress (40). Factors that increase the development of decompensated liver disease in HCV infected children include the presence of genotype 1a infection, steatosis at liver biopsy, viral co-infections (including HIV and HBV), presence of liver-kidney microsomal type-1, cancer, hematological diseases with iron overload, and vertical transmission (40).

The estimated risk of vertical transmission is 4.3% in a mother with a detectable HCV RNA level (39). Factors that increase the risk of vertical transmission include maternal viral load of 600,000 IU/mL or higher, co-infection with HIV (2-3x increase,

though risk is normalized to that of monoinfected mothers when HIV is controlled), prolonged rupture of membranes, placement of fetal scalp monitors, exposure to contaminated maternal blood, fetal anoxia at time of delivery, length of labor, gender of newborn, and amniocentesis (39, 41). Choosing cesarean section to reduce vertical transmission is controversial, with most expert bodies acknowledging that election cesarean section is not recommended for prevention of vertical transmission or that vaginal and cesarean deliveries are similar in infection rates (41, 42). However, Sokal et al imply that elective cesarean in patients with high viral load and/or HIV co-infection is associated with a reduction of transmission (40).

Khaderi et al. admit that the specific period when transmission occurs between mother and child is unknown, but states that data points to transmission likely occurring *in utero* than during the perinatal stage (39). However, Floreani A et al. state that the majority of transmission occurs during the perinatal period (40-50% compared to at least 33% *in utero*), and that postpartum transmission is uncommon (43). Additionally, they propose that the detection of HCV RNA in newborn serum in the first 24 hours of life suggests infection is possible during the early intrauterine period (43).

Transmission via Personal Items

Some studies propose an association between personal care items and spread of HCV. Yang et al state that at the time of their publication, data from their literature view can neither confirm nor deny the risk of HCV transmission associated with personal care/multiuse items and personal care services such as nail salons and barbershops (44). Though theoretically possible, transmission through these media are understudied and

under-documented, especially since the majority of studies included in their literature review were conducted in Asia, South America, and Europe (44).

In a cross-sectional survey of 196 Japanese psychiatric patients with HCV and HBV markers and 400 age- and sex-matched controls, Sawayama et al. demonstrated that razor sharing was a statistically significant independent risk factor (OR = 4.90, 95% CI = 1.29-18.86) in HCV transmission (45). In response to the general recommendation for positive HCV individuals to not share toothbrushes and other personal care items, Lock et al. suggest a theoretical risk of infection by sharing toothbrushes by demonstrating HCV RNA contamination of toothbrushes (46). Additionally, in a very small study of nine heterosexual couples, the sharing of personal hygiene items was a confounding variable in sexual transmission of HCV (47).

Sexual Transmission

HCV is not typically transmitted sexually among heterosexual monogamous partners (48). The majority of recent literature appears to focus on HCV transmission in homosexual and/or MSM sexual contact. It is possible that HCV can be sexually transmitted by mucosal exposure to infected blood and serum-derived fluids, but such transmission inefficient compared to sexual transmission of HBV and HIV (48).

However, sexual transmission of HCV among heterosexual couples is possible. A cross-sectional study consisting of 500 anti-HCV positive, HIV negative subjects and their long-term heterosexual partners indicated a maximum incidence rate of HCV sexual transmission of roughly 1 per 190,000 sexual contacts with no specific practices

associated with HCV positivity (48). Another study concluded that male-to-female sexual transmission of HCV is likely, though the authors admit the confounding factor of shared personal hygiene items (49). Additionally, there is a distinction between the impact of certain sexual behaviors on sexual transmission of HCV compared to specific sexual acts. Hershow et al. suggests that certain sexual behaviors are significant risk factors for HCV infection, such as sexual partners who are PWID, STDs, paying for sex, long-term living with an HCV positive partner, and multiple partners (50). However, Terrault et al. state that data does not show that certain sexual practices increase the risk of transmission (48). Yet, having multiple partners increase the risk of HCV transmission (49, 50, 51, 52). Overall, these studies conclude that sexual transmission of HCV among monogamous heterosexual couples is possible but rare, yet certain behaviors can increase its frequency.

The majority of sexual transmission of HCV, however, appears more prevalent in the homosexual community, specifically in the men who have sex with men (MSM) population (53). Since 2000, there has been an increase of acute HCV in HIV-positive MSM via the mucosal route rather than the established parental route of transmission (54). The results of a case-control study by the CDC of 74 HIV positive MSM with no history of IVDU indicate that high-risk sexual behavior is implicated with HCV acquisition (55). High-risk sexual behavior among this population may also include "chemsex" and associated drugs which may be injected, and which have recently been increasingly reported among the MSM population (56). However, van de Laar et al. provide examples that HIV positive status among this population is not required for sexual transmission of HCV, and that HIV negative MSM with other factors including

ulcerative STIs, those who practice rough sex, and HCV positive partners should be screened (57). Additionally, MSM status is a risk for HIV and HCV co-infection (58, 59).

High-Risk Groups

Aside from the high-risk groups associated with certain modes of transmission as previously stated, HCV disproportionately affects specific population groups. These groups include Baby Boomers, American Indians and Alaskan Natives, African Americans, people in correctional facilities, veterans, and homeless individuals (2). It is important to note that in terms of high-risk racial/ethnic groups, there is disagreement on the size of the effect of HCV infection in Asians/Pacific Islanders.

Baby Boomers

Individuals born between 1945-1965, also known as Baby Boomers, comprise approximately 75% of chronic HCV infections in the U.S. (2). Since 2012, the CDC has recommended that all individuals within this birth cohort be screened once for HCV regardless of past risk factors (60). The prevalence of anti-HCV within this birth cohort is approximately 3.25% - 3.5% and reflects both the chronic nature of HCV infection and the high incidence of infection during the 1970s and 1980s (60, 61). This birth cohort is five times more likely to have HCV infection than other adults (33). Additionally, although those within this birth cohort represent roughly 27% of the U.S. population, they account for approximately 70% - 73% of all HCV-related deaths and are at highest risk for hepatocellular carcinoma and other HCV-related morbidities (60, 61).

Despite the CDC's and U.S. Preventive Services Task Force's (USPSTF) recommendation to screen all Baby Boomers for HCV infection, there is debate regarding the necessity and effectiveness of this recommendation. In a series of pro/con editorials in response to the question, "Should family physicians routinely screen for hepatitis C?", Dr. Kenneth Lin writes that one-time screening may not be as beneficial and as wise a recommendation as the CDC and USPSTF and suggests that HCV treatment be targeted toward those at higher risk of HCV-related complications rather than treating everyone that tests positive (62). His position is based on two reasons. First, treatment is expensive. Full courses of HCV treatments can be just shy of $100,000, at the time of the author's remarks, and such treatments may not be cost-effective with the risk of overwhelming the budgets of private and public payers (62). Additionally, seven percent of all Medicare drug spending is on HCV treatment and, as the Baby Boomer generation ages into the Medicare age range, spending on HCV treatment will most likely increase (62). Second, it is unknown if birth cohort screening will have the intended positive health outcomes since there is a lack of data from randomized controlled trials testing expanded HCV screening (62).

Dr. Marc Ghany argues that birth cohort screening is important for two main reasons. First, with highly effective treatments with sustained virologic response up to 90% now available, morbidity and mortality may decrease, quality of life and general well-being may improve, and viral eradication may lead to net annual savings of $2.7 billion (63). Second, even if treatment is not considered, screening HCV infection patients and informing them of their status empowers patients with health knowledge and decision-making ability; this is particularly important since many HCV infections are

asymptomatic and non-curative management techniques can be established and maintained (63).

Additionally, treating all individuals born from 1945-1965 as one unit categorized as Baby Boomers may be problematic. Gordon et al. show that there are significant HCV genotype and subtype differences between older Baby Boomers born between 1946-1955 and younger Baby Boomers born from 1956-1965. Their results show that those born between 1946-1955 were more likely to have HCV genotype 1b whereas those born between 1956-1965 were more likely to have HCV genotype 1a and genotype 3 (20).

American Indians/Alaska Natives

As a racial and ethnic group, American Indians and Alaska Natives (AI/AN) are disproportionately at higher risk for HCV infection and HCV-related mortality and have the highest rate of new HCV infections among all ethnic groups (2, 64, 65). According to the CDC, the incidence rate of acute HCV infection increased for all racial/ethnic groups, except for Asians/Pacific Islanders, from 2011-2015. However, the acute incidence rate of HCV per 100,000 population in 2015 was 1.8 for American Indians/Alaska Natives, twice that of the second highest group which was non-Hispanic Whites at 0.9 (0.3 for Hispanics and non-Hispanic Blacks, 0.1 for Asians/Pacific Islanders (66). In terms of HCV-related mortality, American Indians/Alaska Natives had a 13% increase from 2011-2015, with a rate of 12.95 deaths per 100,000 population in 2015 compared to 4.91 deaths per 100,000 population for the overall U.S. population (66).

There are many possible attributable factors for this disproportionate rate of infection and mortality. Reilley et al. offer insight into one such factor by comparing American Indians/Alaska Natives and another high-risk group, veterans, through the proxies of the Department of Veterans Affairs (VA) health care system and the Indian Health Service (IHS). The authors found a difference in available resources between the VA and its success in treating HCV patients and the difficulty the IHS has in treating its HCV population. The IHS faces a disadvantage in that it has a disproportionately smaller budget than the VA when comparing their number of patients. Additionally, though the IHS is successful in using telehealth and teleconsultation services, HCV drugs are not on the IHS formulary, and the authors suggest that the lack of drug access is the biggest obstacle that the IHS faces with HCV treatment (64). Hossain et al. showed that 18% of American Indian/Alaska Native HCV-positive patients in their study received treatment due, in part, to an inability to show up to appoints, a lack of referrals to specialists (noting that specialists are not found in American Indian/Alaska Native communities but found in urban areas), liver disease, and polysubstance abuse (67).

African Americans

The prevalence of hepatitis C antibody in African Americans is higher in comparison to other racial and ethnic groups (3, 15). The Third National Health and Nutrition Examination Survey (NHANES III) from 1988 to 1994 revealed an HCV seroprevalence of 3.2% in African Americans, compared to 1.5% in Whites (68, 69). A subsequent NHANES from 1999 to 2002 study showed that this difference continued with African Americans' HCV seroprevalence twice that of non-Hispanic Whites (68).

Additionally, this latter survey showed that HCV seroprevalence was even higher for African American men born from 1945-1965, the defined Baby Boomer population. Men born within these decades had an HCV seroprevalence of 13.6% (68). Specifically, African American men between the ages of 40-49 years had an HCV seroprevalence from 9.4% - 14%, depending on the author (68, 69). The HCV seroprevalence in non-Hispanic Whites ages 40-49 years was around 6% (68). Additionally, in a study from 2014 investigating veteran HCV prevalence and screening rates, Black male born between 1945-1965 had a higher HCV prevalence than non-Baby Boomer Black male veterans and higher HCV prevalence than screened veterans overall (70).

In addition to having a higher prevalence of HCV, African Americans may be disproportionately affected by HCV, including complications and treatment. There is disagreement on the prevalence of various HCV sequelae. Forde et al. report that certain cross-section and retrospective studies have shown that African Americans have a lower prevalence of cirrhosis compared to other groups (69).

People in Correctional Facilities

Incarceration may be a high-risk factor for HCV transmission. In their systematic review and meta-analysis, Stone et al. share that incarceration among PWID may be a contributor to HCV transmission specifically within PWID (28). Their work shows that recent incarceration was associated with a 62% increase of HCV acquisition and may be compounded in countries with high incarceration rates (28). Among persons incarcerated in the U.S. in 2015, Spaulding et al. estimated an HCV seroprevalence of 18% (71). However, they state that transmission and acquisition within a correctional setting is rare, suggesting that screening is important and that universal opt-out screening is ideal (71).

The CDC suggests that correctional facilities have a role to play in the prevention and control of viral hepatitis because many inmates continue to transmit infections once released (72). However, the CDC has recognized the difficulty in implementing such involvement, such as issues with budgets, communication issues between correctional facilities and public/private health care systems, and differing priorities (72). Crowley et al. suggest an understanding of an HCV-positive inmate's life and stressors to better meet their care needs (73).

Veterans

It is estimated that among veterans in care, 4% of the veteran population has chronic HCV infection (2). Especially at risk are Vietnam War veterans, veterans with alcohol and substance abuse, and veterans with psychiatric issues and who are experiencing homelessness (2). Despite the focus on HCV testing and care, roughly 71,000 veterans with HCV infection had yet to be treated as of October 2016, and roughly 30% - 60% proved difficult to provide care and treatment (2). Ross et al., in a 2017 article clarifying supposedly misleading conclusions from a previous study by Sarkar et al. state that the Department of Veterans Affairs are increasing veterans birth cohort HCV testing (74). Belperio et al. state that through a number of developments and improvements, including the availability of DAAs, the VA has increased treatment of HCV and decreased the number of veterans still needing to be treated (75).

Surveillance

Hepatitis C is a nationally notifiable condition (76). However, there are important barriers to the identification of HCV RNA-positive cases. Unlike many other notifiable diseases, hepatitis C requires multiple laboratory confirmatory tests. The CDC's case

definition laboratory criteria for diagnosis for acute and chronic hepatitis C is a positive hepatitis C antibody test (anti-HCV) and a positive HCV detection test, such as a positive NAT for HCV RNA or positive HCV antigen test (78, 79). For a more complete picture, the CDC's National Notifiable Diseases Surveillance System (NNDSS) hepatitis C surveillance data is supplemented with additional data from other sources (22).

Additionally, many cases of acute HCV infection are not reported because many cases are asymptomatic (22). Dr. Gottfried Hirnschall is one, of many, that describes chronic hepatitis C infection (as well as hepatitis B infection) as "silent" (79, 80, 81). Such a description is borne out of the fact that many infected people are unaware of their infection until serious liver damage occurs (79).

In *Hepatitis and Liver Cancer: A National Strategy for Prevention and Control of Hepatitis B and C*, the authors suggest several problems in the identification and surveillance of HCV. Such issues include lack of sensitive and specific case definitions for acute HCV, many cases being asymptomatic and, thus, not receiving medical care and testing, and incomplete and inaccurate reporting of chronic cases if an anti-HCV case fails to be tested for the presence of HCV RNA for various reasons (82).

Despite the issues in HCV surveillance, many systems exist to attempt to identify positive cases. The two surveillance systems analyzed in this thesis are the Tennessee Department of Health's (TDOH) GHOST surveillance pilot and the TDOH-based National Electronic Disease Surveillance System (NEDSS) Based System (NBS).

Global Health Outbreak Surveillance Technology is a cloud-based surveillance system that provides a "virtual diagnostic system intended for use in molecular surveillance and outbreak investigations rather than in research." (83). GHOST was piloted in five states: Alaska, Michigan, New Hampshire, New York, and Tennessee (84). In 2016, under the umbrella of GHOST, the TDOH performed an HCV testing pilot in three metropolitan counties from June 1, 2016 – October 31, 2016: Hamilton (Chattanooga), Knox (Knoxville), and Sullivan (Blountville). During this pilot, all visitors to specific clinics at these health departments were offered free, opt-out HCV testing. In total, 4,753 persons were tested for HCV with an 8.4% HCV Ab positivity rate, of which 74.1% were confirmed with RNA (85).

The NEDSS-Based System (NBS) is a CDC-developed information system to assist health departments in relaying reportable disease information to each other, other partners, and the CDC (86). NBS consists of roughly 3,000 public health departments monitoring approximately 120 infectious diseases (87). A core function of NBS is to facilitate reporting of specific infectious and non-infectious conditions by hospitals, laboratories, healthcare providers, etc. to health departments. Tennessee maintains its own version.

III. Methods

Study Design and Population

This study is a retrospective analysis of collected data from the TDOH GHOST surveillance pilot and the TDOH NBS. The study received IRB approval from Emory

University and the TDOH. The GHOST surveillance pilot collected HCV data from Hamilton, Sullivan, and Knox County Health Departments from June 1, 2016 – October 31, 2016. Only data from Hamilton County was used in this thesis. All clients to the Chattanooga-Hamilton County Health Department's STD and Family Planning clinics were offered free HCV testing on an opt-out basis. GHOST data was housed in a REDCap database maintained by TDOH. REDCap "is a secure web application for building and managing online surveys and databases" (90). Comparative cases were gathered from the TDOH NBS. The TDOH Data Steward provided a data set consisting of HCV cases identified from the GHOST pilot and the TDOH NBS.

Study Variables

Two data sets of variables were used in this analysis. The TDOH's dataset contains variables from both the GHOST pilot and NBS surveillance system and describes each case tested for HCV. These variables included ZIP code, date of birth (year only), race, gender, ethnicity, and HCV RNA testing results.

The second data set was created from U.S. Census data obtained via American Fact Finder and consists of descriptive variables at the Zip Code Tabulation Area (ZCTA) level. The purpose of these data is to provide population-level descriptive data to describe where HCV RNA-positive cases resided according to their self-reported address. These data included race, ethnicity, gender, socioeconomic, educational, work, and urban/rural variables.

Though HCV RNA case addresses, as found in the NBS dataset, contain ZIP codes, little U.S. Census data is available at the ZIP code level. Thus, ZCTAs were used as a replacement. ZIP codes and ZCTAs are not perfectly matched, so a ZIP code-to-ZCTA crosswalk located at https://www.udsmapper.org/zcta-crosswalk.cfm was used to match ZCTAs to case ZIP codes. Only 3 ZIP codes had non-matching ZCTAs. One ZIP code was located in Mexico and was excluded, and three others were merged with non-matching ZCTAs. All ZCTAs were randomly coded in Microsoft Excel to ensure confidentiality of case ZIP codes.

ZCTAs were used extensively in this analysis as they are more geographical in nature than ZIP codes. ZCTAs "are generalized areal representations of United States Postal Service (USPS) ZIP Code service areas" (88). In contrast, ZIP codes are not areal representations but represent mail routes (88). Additionally, ZIP codes do not contain population data (89). As a trademark of the U.S. Census Bureau (88), ZCTAs are more useful for geographical data analysis. These ZCTA data were appropriately cleaned in Microsoft Excel and SAS and coded in SAS.

Two variables were created using ArcMap. The first variable, "Distance to 3rd Street," measures the distance, in miles, between a ZCTA's geographical centroid and the Hamilton County Health Department located at 921 E. Third Street, Chattanooga, TN, 37403. The second variable, "Distance to Closest Health Department," measures the distance, in miles, between a ZCTA's geographical centroid and the closest health department, either in Hamilton County, TN or one of the other 94 counties in Tennessee.

These variables serve as proxies to estimate the distance between an HCV-positive case and a health department.

To create these variables, ZCTA shapefiles were downloaded from the U.S. Census' TIGER/Line Shapefiles website located at https://www.census.gov/geographies/mapping-files/time-series/geo/tiger-line-file.html. Once downloaded, the ZCTA shapefiles were imported into an ArcMap map and merged to create a shapefile consisting of all case-related ZCTAs. Using the ArcMap Geometry tool, the geographical centroid of each ZCTA was calculated as a XY coordinate. These XY coordinates were then entered in Google Maps as a starting point destination and all five Chattanooga-Hamilton County Health Department locations (3rd Street, Homeless, Ooltewah, Birchwood, and Sequoyah) were alternately entered as the end destination. Distance was calculated using the road system, as it is unlikely that someone travels to a health department "as the bird flies." The arrival time was set for 2:00 am to mimic empty road conditions. The first result was chosen; this was not always necessarily the shortest distance-wise but shortest temporally.

Microsoft Excel was used to create a table with these results. From here, the shortest distance was chosen for the two custom variables, "Distance to 3rd Street" and "Distance to Closest Health Department" and were added to the ZCTA dataset. For ZCTAs representing cases who reside outside of Hamilton County, TN, the closest health department in whichever county the case resided was used. The TDOH and ZCTA datasets were merged into a master dataset.

In SAS, the ZCTA-specific variables were categorized into two categories at or above the median and below the median. The two custom variables, "Distance to 3rd Street" and "Distance to Closest Health Department" were categorized into five categories calculated as quintiles. All HCV non-reactive and HCV unknown cases were dropped in order that the analyzed population consisted of only HCV RNA-reactive individuals.

IV. Analysis

A descriptive summary of both HCV cases and of the ZCTA population was performed. Cross-tabulation analysis was used to investigate relationships between cases identified by the GHOST pilot, the TDOH NBS surveillance system, and ZCTA-specific variables to determine differences between the GHOST pilot and the subset of clients in the TDOH NBS. Specifically, the cross-tabulation analysis involved the GHOST variable and various case-specific and ZCTA-specific variables. The NBS variable was not tested in order to reduce redundancy as it was assumed that if a case was not identified by GHOST (coded as GHOST = 2), then it was identified by NBS.

All statistical analyses were performed with SAS 9.4. All spatial analyses were performed with ArcMap 10.5.1.

V. Results

A descriptive summary of HCV-positive cases is shown in Table 1. Specific cross-tabulation output are available in the Appendix. Seventy-four HCV RNA cases

were included in the analysis, but one case was frequently missing certain variables and was often excluded from cross tabulation analyses.

When reviewing the results, it is important to note that for most variables, nearly twice as many cases were identified in NBS than with GHOST. To that point, the analysis results reveal both similarities and differences between the two surveillance systems; however, both surveillance systems were more similar than not.

Both systems identified similar numbers of cases for many of the variables tested by cross-tabulation analysis, including educational attainment, employment status, veteran status, disability, private insurance coverage, citizenship status, and urban/rural status. This is clearly seen in urban/rural populations with both surveillance systems identifying a large amount of cases in rural areas compared to urban areas. Additionally, both surveillance systems were nearly equal in identifying cases based on specific racial characteristics of ZCTAs, including Black, American Indian/Alaska Native, and Asian populations.

Both surveillance systems identified HCV-positive cases of similar distances from health departments. Of note, however, is that GHOST identified more cases ≤ 5.2 miles from the 3rd Street Health Department than the TDOH NBS. As far as the estimated distance of positive cases to their closest health departments, no major differences between the two surveillance systems were apparent. Overall, both surveillance systems performed similarly in identifying cases based on residential location from health departments.

Differences do occur between the two surveillance systems. White and Hispanic populations were the exception to the other racial characteristics noted above. Though close, there are differences between GHOST and the TDOH NBS in identifying cases by White population. GHOST identified more cases at or above the median White population than NBS, whereas the TDOH NBS identified slightly more cases below the median. Yet, both identified high numbers on each end of the median. Regarding the Hispanic population, more cases were identified by both surveillance systems below the median Hispanic population. However, GHOST identified slightly more cases below the median Hispanic population whereas the TDOH NBS identified slightly more cases above the median Hispanic population. Additionally, when standardized to each other, GHOST identified almost twice as many cases above the median household income than the TDOH NBS, and the TDOH NBS identified more cases below the median household income.

VI. Discussion

Overall, there are few noticeable differences between the types of cases identified by GHOST and the TDOH NBS based on cross tabulation analyses. This may suggest that both systems are similar in whom they identify and how they identify positive cases and reveal that both opt-out targeting, as seen in GHOST surveillance, and routine reporting of positive cases, as seen in TDOH NBS surveillance, are effectively targeting similar populations. The exceptions encourage further investigation into the limitations of each surveillance system.

Many results were unremarkable and reflect previously known facts about HCV acquisition. The literature shows that acute HCV infections are diagnosed equally in both men and women and in predominantly White, non-Hispanic people and the results of this analysis appear to confirm this. Additionally, the results suggest that most population variables have little effect on differences in surveillance system performance. For example, the similarities in cases identified by both surveillance systems based on many racial characteristics of ZCTAs suggest that Black, American Indian/Alaska Native, and Asian populations are as likely to receive services at health department clinics as outside the health department. Additionally, both surveillance systems identified a large amount of cases in rural areas compared to urban areas, corroborating the general understanding that many positive HCV cases are found in rural areas.

Income level may play a role in where cases are tested. Counterintuitively, it appears that those with a higher income are tested at the health department clinics and those with lower income are tested elsewhere. Income level may indicate where people are tested as seen in those with public insurance coverage. Such unexpected results of the role of income level leave more sophisticated statistical analyses to be desired.

Both surveillance systems identified positive cases of similar distances from health departments. Of note, however, is that GHOST identified more cases ≤ 5.2 miles from the 3rd Street Health Department than the TDOH NBS. This suggests that individuals closer to where HCV testing is performed on an opt-out basis may be more likely to be tested in those clinics than going elsewhere and that convenience is a factor. As far as the estimated distance of positive cases to their closest health departments, no

major differences between the two surveillance systems are apparent. Overall, both surveillance systems perform similarly in identifying cases based on location from health departments, with the exception being specific opt-out testing attracting individuals in very close proximity than further away.

There are enough limitations to this study to suggest that deeper and more sophisticated analysis is warranted for better understanding of the strengths and weaknesses of these surveillance systems. First, the results are from cross-tabulation analysis which does not allow for analysis of statistical significance. This limitation is partly due to the type and amount of data available. The small case counts cast a level of doubt on the results' significance. Thus, with a larger population and clearer denominator data, more accurate statistical significance may be illuminated through relevant statistical analyses.

Second, only clinical, socioeconomic, and population-level data were utilized to compare these two surveillance systems. No outcome variables, aside from positive case status, were available for analysis. Additionally, many of the descriptive variables were not specific to the cases but were aggregated at the ZCTA population level. ZCTAs are extremely useful for utilizing U.S. Census data. But in this analysis, they most likely served as rudimentary, yet necessary, proxies as they are not perfectly synonymous with ZIP codes and are more generalized, rather than specific, in describing cases.

An important future direction for this topic should include answers to the limitations listed above. A larger population set with appropriate variables and denominator data will lend itself to more sophisticated and robust statistical analyses. As

this thesis is limited to only Hamilton County, TN data, extending the analysis to other participating counties in the GHOST project may be important to assess not only differences between surveillance systems in the same geographical area, but also between different geographical areas.

Overall, the results of the analysis reveal that the GHOST and the TDOH NBS surveillance systems are often equal in the amount and type of cases identified. Certain types of populations stand out as indicators for differences within the two surveillance systems and deserve deeper and more thorough investigation to determine whether these variables truly represent a chasm between surveillance techniques. If so, then the development of future surveillance systems can account for and incorporate these differences to ensure that positive HCV cases are being identified in order to link them to suitable HCV care, management, and treatment. As HCV surveillance is difficult to construct and perform, the results of this thesis may serve as one tiny piece in a much larger puzzle.

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Table 1. Descriptive Summary of HCV RNA-Positive Cases

	N (%)
Race	
Black	8 (10.81)
White	35 (47.30)
Unknown	31 (41.89)
Gender	
Female	42 (56.76)
Male	32 (43.24)
Ethnicity	
Not Hispanic/Latino	36 (48.65)
Hispanic/Latino	1 (1.35)
Unknown	37 (50.00%)
Identified by GHOST	25 (33.78%)
Identified by NBS	49 (66.22%)

Appendix: SAS Cross Tabulation Output

Table of GHOST by ZCTA Hispanic Population			
GHOST	ZCTA Hispanic Population		
	1	2	Total
1	5	20	25
2	15	33	48
Total	20	53	73

Table of GHOST by ZCTA Black Population			
GHOST	ZCTA Black Population		
	1	2	Total
1	3	22	25
2	9	39	48
Total	12	61	73

Table of GHOST by ZCTA White Population			
GHOST	ZCTA White Population		
	1	2	Total
1	12	13	25
2	18	30	48
Total	30	43	73

Table of GHOST by ZCTA American Indian/Alaska Native Population			
GHOST	ZCTA American Indian/Alaska Native Population		
	1	2	Total
1	11	14	25
2	22	26	48
Total	33	40	73

Table of GHOST by ZCTA Asian Population			
GHOST	ZCTA Asian Population		
	1	2	Total
1	6	19	25
2	15	33	48
Total	21	52	73

Table of GHOST by ZCTA Other Race Population			
GHOST	ZCTA Other Race Population		
	1	2	Total
1	9	16	25
2	26	22	48
Total	35	38	73

Table of GHOST by ZCTA Citizen Population			
GHOST	ZCTA Citizen Population		
	1	2	Total
1	5	20	25
2	12	36	48
Total	17	56	73

Table of GHOST by ZCTA Non-Citizen Population			
GHOST	ZCTA Non-Citizen Population		
	1	2	Total
1	6	19	25
2	13	35	48
Total	19	54	73

Table of GHOST by ZCTA Naturalized Citizen Population			
GHOST	ZCTA Naturalized Citizen Population		
	1	2	Total
1	6	19	25
2	14	34	48
Total	20	53	73

Table of GHOST by ZCTA Household Median Income			
GHOST	ZCTA Household Median Income		
	1	2	Total
1	15	10	25
2	17	31	48
Total	32	41	73

Table of GHOST by ZCTA Less Than High School Education			
GHOST	ZCTA Less Than High School Education		
	1	2	Total
1	8	17	25
2	16	32	48
Total	24	49	73

Table of GHOST by ZCTA High School Education			
GHOST	ZCTA High School Education		
	1	2	Total
1	5	20	25
2	12	36	48
Total	17	56	73

Table of GHOST by ZCTA Some College Education			
GHOST	ZCTA Some College Education		
	1	2	Total
1	4	21	25
2	9	39	48
Total	13	60	73

Table of GHOST by ZCTA Bachelor's Degree			
GHOST	ZCTA Bachelor's Degree		
	1	2	Total
1	6	19	25
2	13	35	48
Total	19	54	73

Table of GHOST by ZCTA Employed Population			
GHOST	ZCTA Employed Population		
	1	2	Total
1	4	21	25
2	8	40	48
Total	12	61	73

Table of GHOST by ZCTA Unemployed Population			
GHOST	ZCTA Unemployed Population		
	1	2	Total
1	7	18	25
2	18	30	48
Total	25	48	73

Table of GHOST by ZCTA Veteran Population			
GHOST	ZCTA Veteran Population		
	1	2	Total
1	6	19	25
2	11	37	48
Total	17	56	73

Table of GHOST by ZCTA Non-Veteran Population			
GHOST	ZCTA Non-Veteran Population		
	1	2	Total
1	4	21	25
2	11	37	48
Total	15	58	73

Table of GHOST by ZCTA Vietnam Veteran Population			
GHOST	ZCTA Vietnam Veteran Population		
	1	2	Total
1	6	19	25
2	11	37	48
Total	17	56	73

Table of GHOST by ZCTA Urban Population (2010)			
GHOST	ZCTA Urban Population (2010)		
	1	2	Total
1	4	21	25
2	11	37	48
Total	15	58	73

Table of GHOST by ZCTA Rural Population (2010)			
GHOST	ZCTA Rural Population (2010)		
	1	2	Total
1	21	4	25
2	38	10	48
Total	59	14	73

Table of GHOST by ZCTA Disability Population			
GHOST	ZCTA Disability Population		
	1	2	Total
1	5	20	25
2	12	36	48
Total	17	56	73

Table of GHOST by ZCTA Private Insurance Coverage			
GHOST	ZCTA Private Insurance Coverage		
	1	2	Total
1	7	18	25
2	14	34	48
Total	21	52	73

Table of GHOST by ZCTA Public Insurance Coverage			
GHOST	ZCTA Public Insurance Coverage		
	1	2	Total
1	5	20	25
2	15	33	48
Total	20	53	73

Table of GHOST by Distance from 3rd Street Health Department						
GHOST	ZCTA Distance from 3rd Street Health Department					
	1	2	3	4	5	Total
1	8	7	9	0	1	25
2	11	12	22	3	0	48
Total	19	19	31	3	1	73

Table of GHOST by Distance from Closest Health Department						
GHOST	ZCTA Distance from Closest Health Department					
	1	2	3	4	5	Total
1	2	5	7	8	3	25
2	4	7	17	14	6	48
Total	6	12	24	22	9	73

Table of GHOST by ZCTA											
GHOST	ZCTA										
	BB	DD	EE	FF	II	JJ	MM	NN	OO	PP	A
1	0	0	3	0	1	1	0	0	1	2	0
2	1	2	5	3	0	3	1	1	2	2	2
Total	1	2	8	3	1	4	1	1	3	4	2

GHOST	ZCTA										
	D	E	F	G	H	M	N	O	R	S	T
1	0	3	3	0	1	1	1	0	1	3	2
2	1	1	9	1	4	0	0	2	0	5	3
Total	1	4	12	1	5	1	1	2	1	8	5

GHOST	ZCTA		
	U	Z	Total
1	1	1	25
2	1	0	49
Total	2	1	74