12-13-2021

HIV and HCV Outcomes Among People Who Inject Drugs: Identifying those at most risk for transmission and opportunities for prevention

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HIV and HCV Outcomes Among People Who Inject Drugs: Identifying those at most risk for transmission and opportunities for prevention

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A Dissertation Submitted to the Graduate Faculty
of Georgia State University in Patrial Fulfillment
of the
Requirements for the Degree

DOCTOR Of PHILOSOPHY IN PUBLIC HEALTH (EPIDEMIOLOGY)

ATLANTA, GEORGIA

30303

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Abstract

Introduction: Injection drug use (IDU) behavior has increased in the U.S. during the past decade largely due to the on-going opioid epidemic. People who inject drugs (PWID) have substantial risk for HIV and hepatitis C virus (HCV) infections. This dissertation consists of three studies to understand risk for HIV and HCV among PWID and people living with HIV (PLWH) in Georgia, as well as missed opportunities to address these infections.

In study 1, we constructed a retrospective longitudinal cohort using clinical encounters with patients who had probable recent IDU behavior based on diagnostic codes in electronic medical records at a metro Atlanta hospital during 2012 – 2018. We linked cohort data with HIV and HCV surveillance records from Georgia Department of Public Health (GDPH) to examine prevalence of infections at clinical discharge and incidence of infections post-clinical encounters. Nearly 4% of patients with IDU-related clinical encounters were later diagnosed with HIV, and 17% were later diagnosed with HCV, translating to incidence rates of 9.3 per 1,000 person-years and 42.9 per 1,000 person-years, respectively. Results from Poisson models indicate that patients aged 16-39 years at discharge were less likely than older patients to be later diagnosed with HCV (Adjusted Incidence Rate Ratio [IRR]=0.63, 95% Confidence Interval [CI]=0.41-0.97, p=0.04) The majority of HIV and HCV diagnoses post-discharge occurred among Black/African Americans and males. At the time of clinical discharge, 32.9% of patients had an HIV diagnosis and 28.1% of patients had an HCV diagnosis.

In study 2, we used IDU-related clinical encounters at an urban Atlanta hospital spanning January, 2012 – December, 2018 to estimate the frequency of HIV and HCV testing at clinical encounters. We also assessed associations between patient factors and testing using unadjusted and adjusted generalized estimating equations models. Of encounters eligible for HIV or HCV testing, testing occurred in 29.3% and 12.2%, respectively. Testing was less likely among Black/African American patients compared to white patients (HIV, adjusted odds ratio [AOR]=0.43, 95% CI, 0.29-0.63, *P* <0.01; HCV, AOR=0.43, 95% CI, 0.26-0.72, *P* <0.01). Testing was more likely to occur in encounters during 2016-2018 than in encounters during 2012-2013; (HIV, AOR=4.73, 95% CI, 2.72-8.23, *P* <0.01; HCV, AOR=3.74, 95% CI, 1.93-7.24, *P* <0.01) and in those requiring five days or longer hospital stays compared to those requiring less than five days or emergency department (ED) visits (HIV, AOR=3.70, 95% CI, 2.30-5.95, *P* <0.01; HCV, AOR=4.49, 95% CI, 2.78-7.25, *P* <0.01).

In study 3, we constructed a retrospective cohort of PLWH using matched GDPH HIV and HCV case surveillance data from persons diagnosed with HIV and/or HCV from January 1, 2014 – December 31, 2019. We estimated trends over time in HCV co-diagnoses among a cohort of PLWH by demographic characteristics and HIV care outcomes. From 2014 – 2019, 1,183 (3.8%) PLWH were co-diagnosed with HCV infection. During this time period, the percentage of PLWH newly co-diagnosed with HCV increased by 243%, from 7% to 24% (β = 0.03, *P* for trend <0.01) among persons born during 1980-1989, and by 900%, from 1% to 10% (β = 0.01, *P* for trend <0.01) among persons born in 1990 or later. The percentage of PLWH newly co-diagnosed with HCV increased by 42%, from 43% to 61% (β = 0.03, *P* for trend <0.01) among persons with male-to-male sexual contact (MSM).

Overall, targeted interventions for HIV/HCV prevention, diagnosis and linkage to treatment are needed to reduce incidence of new infections among high-risk groups (i.e., PWID, younger populations, PLWH and MSM). Use of novel data sources including linking surveillance and clinical data can aid in informing these strategies.

Acknowledgments

First, I would like to thank my committee members, Drs. Heather Bradley, Pascale Wortley, and Katherine Masyn for your endless support. Dr. Bradley, thank you for accepting me as one of your first students and believing in my dreams to obtain the data set wanted to answer valuable research questions. Thank you for your consistency, your advice, and the opportunity to learn from you. Dr. Wortley, thank you for your support navigating the numerous institutional review boards and your expertise using the health department data. Dr. Maysn, thank you for your statistical support and guidance throughout my dissertation.

Next, I would like to thank all the other key people that helped make this dissertation possible. Dr. Theresa Vettese, thanks for serving as the Principal Investigator and helping me obtain the data set to make this possible. Thanks for your clinical guidance throughout this dissertation. Thanks to Dr. Lesley Miller, Ami Gandhi, Rodriques Lambert and Stephen Ray for all your clinical and data support. Also, thanks to my cohort peers and the other GSU PhD graduates I've met along the way. From study sessions to accountability groups, thanks for always being available. We will forever be a small group of people who truly understand each other.

Finally, I would like to thank God, my family, friends, and coworkers who have also supported me throughout this journey. To my husband, who has made many sacrifices, I thank you for your continued support and patience. To my child, Aiden, who was born 4 days before my originally scheduled defense, I can only imagine the stress mommy has put you through, and so for that, this PhD is for you.

Author's Statement Page

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Chapter 1: Literature Review and Statement of Purpose

Introduction

The United States (U.S.) Opioid Epidemic has impacted many lives stirring a public health emergency and response. From non-fatal and fatal overdoses to Human Immunodeficiency Virus (HIV) and Hepatitis C Virus (HCV) outbreaks, the opioid epidemic has contributed to the decrease in life expectancy for Americans and refueled previously declining rates of infectious diseases. Declared a National public health emergency in October 2017, the public health response continues across America impacting both rural and urban communities. Since 1999, approximately 841,000 people have died from a drug overdose[1], and from 2013 to 2019, the rate for synthetic opioid involved deaths has increased 1,040%.[2] Weaving through this epidemic and its intersection with infectious diseases, it is important to describe this evolving epidemic from its inception.

U.S. Opioid Epidemic

To date, there have been four waves to describe the current opioid-related epidemic: 1) Prescription Wave, 2) Heroin Wave, 3) Synthetic Opioid Wave and 4) Methamphetamine/Polysubstance Wave. Beginning in the early 1990s, increases in prescription opioids and over prescribing led to increases in overdose deaths[3] igniting much of the current epidemic to date. This spiraled into the second wave starting in 2010 involving heroin,[4] a semi-synthetic opioid that is often injected, but also snorted or smoked by users contributing greatly to overdose deaths. Shortly after the semi-synthetic opioid uptick, in 2013, the third wave began with increasing rates of overdose deaths related to fentanyl, fentanyl analogs and tramadol by 71% from 2013 to 2017.[5] This was the largest increase in the rate of overdose deaths compared to heroin, natural opioids and other semisynthetic opioids such as morphine, hydrocodone, oxycodone and codeine. Now in the fourth wave of the epidemic, increases in overdose

deaths related to methamphetamine, cocaine and benzodiazepines are rising[6,7] and polysubstance use continues to increase causing more alarm for deadly combinations of drug interactions.

Responding to this epidemic has been challenging as the rate of nonfatal overdose emergency department (ED) visits continue to increase[8] and impacts from the COVID-19 pandemic taking a toll. Sweeping across America, the opioid epidemic originally impacting the mid-West, with higher rates of overdose deaths in West Virginia, Ohio, Indiana, Kentucky, Pennsylvania, and District of Columbia[9] is shifting. Increasing research demonstrates the impact the opioid epidemic is having nationally, with rising rates in metropolitan areas due to illicit opioid use.[10]

Opioid Epidemic in Georgia

The opioid epidemic has impacted Georgia equivalently. Increasing 245%, the number of opioid-related overdose deaths surged sharply from 2010 to 2017 and illicit opioids such as heroin and fentanyl were the main contributors for increases in deaths starting in 2013.[11-13] As an example of the increases in illicit use, in June 2017, Georgia responded to a cluster of 27 counterfeit Percocet cases mostly affecting younger adults, Black/African American (hereafter referred to as Black), and males in North-Central Georgia.[14] Likely due in part to the public health response in Georgia, the number of prescription-opioid related deaths decreased from 2017 to 2018; however, heroin was the only drug class to not decline.[11] In 2018, there was an 11% decline in the number of ED visits and hospitalizations due to an opioid with 5,014 ED visits, 2,345 hospitalizations, and 873 deaths. Heroin-involved overdoses also experienced declines from 2017 accounting for 1,357 ED visits, 324 hospitalizations, and 303 deaths. Impacting both urban and rural parts of Georgia, the highest numbers of heroin- and opioid-involved overdose deaths, ED visits, and hospitalizations occurred predominantly among residents in urban areas (Atlanta Metropolitan Area, Augusta, Macon, Columbus, and Savannah); however, high rates also occurred among residents in both urban and rural areas of North, South Central, and Southeast Georgia. Mostly affected by opioid-involved overdoses, white adults, aged 35–44 years were more likely to die from an

opioid-involved overdose compared to any other age group. Persons aged 25–34 years old were more likely to die from a heroin- or fentanyl-involved overdose compared to any of other age category. In terms of racial differences in the epidemic, in 2018, whites were 3.5 times more likely to die from an opioid-involved overdose, 2.5 times more likely to visit an ED for any opioid-involved overdose, and 4.8 times more likely to visit an ED for a heroin-involved overdose than Blacks. While opioid-related ED visits and overdose deaths declined, they remained unchanged for Blacks overall making this racial group more at risk for overdose.[11]

Illicit to Injection Drug Use

To combat the U.S. Opioid Epidemic many surveillance systems, studies, interventions, and policies have been implemented to curtail the number of drug-related overdoses and deaths. With rising restrictions in policies related to prescription opioids[15,16] and provider prescribing pattern changes,[17] the opioid epidemic has evolved shifting from prescription to illicit-opioid use.[18] This is noted with the significant increases in overdose deaths related to synthetic opioids such as heroin and fentanyl.[5,19] Injection is a common route of administration among persons misusing opioids and previous studies have found people abusing prescription opioids have a higher risk of transitioning to injection of opioids and heroin.[20-25] From 2004 to 2013, injection drug use (IDU) was found to increase from 11.7% to 18.1%.[26] Guarino and colleagues found youth began prescription opioid misuse around 17 years old, with 86% of youth progressing to prescription opioid misuse.[27] Sixty-four percent (64%) of these prescription opioid users transitioned to heroin injection approximately four years after their first prescription opioid misuse. It is important to note that the typical person who injects drugs (PWID) is now younger,[28] white, and resides in a rural setting;[29,30] although, recent literature suggest this epidemiologic profile is shifting to include other races and more urban settings.[31-33]

Infectious Risk associated with IDU

With increases in illicit opioid use and the estimated rise in transition to IDU, the risk for infectious diseases such as HCV, HIV, infective endocarditis (IE), central nervous systems (CNS) abscesses, and osteomyelitis increases drastically.[34] The World Health Organization estimates around 13 million people across the world inject drugs and are greater risk for HIV and HCV infection. [35] Approximately, 1.7 million PWID are infected with HIV and approximately 67% are infected with HCV. Combined, over 1.2 million are co-infected with HIV and HCV. Thus, it is important to address the risk for infectious diseases and prevent the spread among PWID. Evidence shows individuals using illicit opioids have greater risk for transitioning to injection use, more frequently injecting and overall puts them at greater risk for infectious diseases [36]. This literature review will describe the risk for each of these infectious diseases as it relates to PWID and strategies for prevention.

Human Immunodeficiency Virus Among PWID

HIV, first detected in 1981, is a virus that attacks the body's immune system by reducing the amount of CD4 T lymphocytes (CD4 cells) in the body needed to fight infections. Untreated, it can lead to acquired immunodeficiency syndrome (AIDS), once a death sentence prior to advancements of antiretroviral therapy (ART). Spread through an HIV-positive person's body fluids such as blood, semen, and vaginal fluids; the most common transmission, is through vaginal or anal sex, needles, syringes, or other injection equipment. The first published report linking HIV transmission and intravenous drug abuse was published in 1981[37,38] and over 40 years later outbreaks of HIV related to IDU continues. Once at declining rates, the opioid epidemic has contributed to the resurging numbers of HIV attributable to IDU with clusters emerging throughout the U.S. in Indiana, Massachusetts, West Virginia, and Washington.[33,39-47] In 2018, the Centers for Disease Control and Prevention (CDC) reported 37,832 new HIV diagnoses, a 11% decrease in HIV diagnoses from 2010-2017. Seven percent of these new HIV

diagnoses occurred among PWID in which four percent occurred in men and three percent occurred in women.[48] In 2015, 79% of HIV infections among PWID occurred in urban settings [49] and incidence was often higher among Blacks compared to other races.[50]

The crack cocaine epidemic of the 1980s and 1990s has many parallels with the current opioid epidemic and it is important to learn from these previous studies. During this time, crack smokers were more likely to be HIV positive compared to nonsmokers, and HIV transmission was mostly associated with having sex in exchange for drug money and men who have sex with men (MSM).[51] Also most affected by this epidemic were Blacks compared to whites.[52] Sharing injection equipment, having condomless sex and sex in exchange for money and drugs remains factors in the spread of HIV among PWID in the opioid epidemic today.[50,53,54]

Another factor related to HIV transmission among PWID is co-occurring sexual behaviors which can be difficult to distinguish between the primary route of transmission. Thus, it is necessary to examine the amount of transmission related to sexual behavior networks[40] such as condomless anal sex and heterosexual sex related numerous sexual partners.[54-56] The use of novel molecular epidemiologic methods[57] can be helpful in making these distinctions and monitor HIV trends when clusters among PWID arise.

To most effectively address and prevent further HIV outbreaks occurring in the U.S., research initiatives addressing factors related to HIV incidence, promoting use of syringe service programs (SSPs), increasing routine HIV testing, and increasing timely access to ART to reduce viral loads will be important.

Hepatitis C Virus

There are five types of viral hepatitis infections; however, the most common in the U.S. are hepatitis A, hepatitis B, and hepatitis C. Commonly found among PWID, HCV can cause inflammation of the liver

and severe infection. Occurring within the first six months of infection, acute hepatitis C is typically short-lived and often clears the body without treatment causing this disease at times to be undiagnosed, especially among asymptomatic carriers. However, chronic hepatitis C can also develop, often leading to a lifelong infection and adverse health outcomes including liver damage, cirrhosis and mortality. HCV is transmitted through needles, syringes and other injection equipment. Other less commons methods of transmission include occupational exposure, via birth, and sex while the later risk remains very low. Mostly in baby boomers born 1945 to 1965, this population was primarily infected through donated blood before screening was made available in 1992. Today, HCV is of most concern among PWID or MSM, specifically among young adults aged 20-39.[58] Thus, it is important that treatment of HCV is initiated early to prevent further transmission and adverse health outcomes. Recent advancements in direct-acting antiviral (DAA) medications now require shorter duration to cure HCV infection and can be cured with 12 weeks of starting therapy.[59,60]

Understanding the prevalence of HCV infection in the U.S. is complicated and often underreported. Reporting requirements for HCV differs across states, as they are not required to report acute and chronic cases to CDC.[61] In addition, health departments' capacity to follow-up varies, and many do not have the resources to prioritize follow-up for clinical criteria to make acute classifications resulting in vast under-reporting. In Georgia alone, approximately 23,000 (45%) of cases reported between 2012–2016 lacked enough information to classify as current or past infection and lacked resources for follow-up.[62] Onofrey and colleagues in Massachusetts found 81% of clinical cases diagnosed in a hospital or facility setting that were reported to the state health department for surveillance lacked data on clinical criteria to meet the acute infection case definition and therefore could not be counted by the CDC.[63] While the CDC estimates approximately 44,300 new infections each year, this number is often under-ascertained and under-reported.[64]

From 2013–2016, over 6 million people were estimated to have current or past HCV infection (HCV antibody positive or HCV RNA-positive),[65] with 51,094 cases occurring in Georgia from 2012–2016.[62] Mostly related to IDU, new cases of HCV occur through injection equipment sharing (i.e., needles, syringes, cookers and filters).[66] Monitoring acute HCV infection is key to understanding the increases in incidence which are mostly among young people under 40, related to IDU, and among whites and Hispanic/Latinos.[67-69] Prioritizing this group to mitigate their risk for acute HCV infection is important as previous studies have found strong associations with prescription opioid abuse and heroin use.[68,70] Additionally, educating young PWID is needed as many lack knowledge about HCV, treatment options (i.e., DAA therapies) and believe their risky IDU behaviors of sharing injection equipment and reusing needles are negligible.[71] Reducing drug injection initiation and increasing HCV treatment interventions is key. Gicquelasis and colleagues estimated that treating 3 per 100 PWID per year would reduce active HCV infection by 23.6 % and 27.3% for chronic HCV by 2030. A combination of interventions, reducing syringe sharing, injection initiation and relapse rates by 10% and increasing cessation rates by 10% could have an even greater impact in reducing acute HCV infection by 38.4% and chronic HCV by 27.7%.[72]

HIV/HCV Coinfection

Given the common routes of transmission, PWID are at increased risk for HIV and HCV coinfection presenting another set of challenges for treating both infections and leading to exacerbated risk for mortality. It is important to describe the population at greatest risk for coinfection and identify the risk factors to reduce overall morbidity and mortality. Bosh et al. conducted a study using National HIV and HCV surveillance data and found among people living with HIV (PLWH), 6.7% were coinfected with HCV, and the majority were male, Black, PWID, MSM, and their HIV diagnosis preceded their HCV diagnosis (83.6%).[73] In other studies, similar characteristics are risk factors for coinfection, with co-infection occurring mostly among MSM or PWID[74] and co-infected persons were a median age of 47.[75]

Another study linking state and local surveillance data found HIV/HCV co-infection greater among PWID, with the majority of infection among 40–49 and 50–64 which could represent chronic HCV infection.[73] This evidence demonstrates the need for more harm reduction interventions among PWID, dual testing for HIV and HCV, and substance abuse treatment to prevent secondary HCV infection. Overall, there are limited coinfection studies; however, trends demonstrate greater co-infection rates among PWID, MSM, Blacks, and persons living in high poverty neighborhoods.[76] There is a need for more studies examining trends in coinfection and the risk factors associated to address HCV and HIV prevention and treatment among these populations.

Infectious Endocarditis, Osteomyelitis, Abscesses and Soft Skin Tissue Infections

In addition to PWID being at risk for HIV and HCV, they are also at risk for other infectious bacterial diseases such as IE, osteomyelitis, CNS abscesses, and skin soft tissue infections (SSTI)[77] that are not reported to surveillance systems. Many of these infections are localized to the infection site and used among researchers as proxies to identify PWID in clinical data sets based on International Classification of Diseases (ICD), Ninth Revision (ICD-9) or Tenth (ICD-10) revision codes (Table 1).

Table 1: ICD-9-CM and ICD-10-CM Diagnosis Codes

Diagnosis	ICD-9-CM	ICD-10-CM
Infectious Endocarditis	421,421.1,421.9,424.9	I33.0,I33.9,I38,I39,B37.6
Intracranial and Intraspinal Abscesses	324,324.1,324.9	G06.0,G06.1,G06.2
Osteomyelitis	730.00,730.01,730.02,730.03 730.04,730.05,730.06,730.07 730.08,730.09,730.20,730.21 730.22,730.23,730.24,730.25 730.26,730.27,730.28,730.29	M86.10,M86.20,M86.119,M86.219 M86.229,M86.139,M86.239 M86.149,M86.249,M86.159 M86.259,M86.169,M86.269 M86.179,M86.279,M86.18,M86.28 M86.19,M86.29,M86.9

Many studies, to date, have found increases in IE hospitalizations related to prescription opioid abuse, heroin use and IDU.[34,78-82] Other studies have also examined SSTIs,[83] osteomyelitis and CNS abscesses

[34,84] and found similar associations. Following similar epidemiologic profiles as those with opioid use disorders (OUD), those infected with these diseases tend to be younger patients < 40 years old, white,[78,85] inject daily,[84] and share needles[83,84]. This dissertation will use these bloodborne pathogens as signals for IDU behavior to monitor for HIV and HCV outcomes, and this work is described in greater detail later in the purpose of the study.

Strategies to Address HIV and HCV Prevention Among People Who Inject Drugs

Understanding the epidemiologic profile of PWID at increased risk for HIV and HCV can be important to developing and implementing evidence-based interventions to prevent transmission. Much of this framework is formally addressed through The HIV National Strategic Plan for the U.S.: A Roadmap to End the Epidemic 2021-2025 and the Viral Hepatitis National Strategic Plan for the U.S.: A Roadmap to Elimination 2021-2025. The National HIV Strategic Plan was recently revised through 2025 and identifies four overarching goals: 1) prevent new HIV Infections; 2) improve HIV-related health outcomes of people living with HIV; 3) reduce HIV-related disparities and health inequities; and 4) achieve integrated and coordinated efforts that address the HIV epidemic among all partners and stakeholders.[86] Released in 2019, Ending the HIV Epidemic in the U.S. (EHE), is another initiative to address the HIV epidemic. Developed by the U.S. Department of Health and Human Services (HHS), the goal is for a 75% reduction in HIV infection by 2025 and 90% by 2030 through diagnosing early infections, treating infections rapidly to sustain viral suppression, preventing new HIV transmission through evidence-based interventions such as pre-exposure prophylaxis (PrEP) and SSPs, and responding quickly to HIV outbreaks through prevention and treatment.[87,88]

Addressing these action plans calls for swift and bold action. Bradley and colleagues project maintaining the current levels of HIV testing, and treatment will lead to increased incidence of HIV infections until and past 2030. Ambitious 95/95/95 goals (95% of PLWH will know their HIV status, 95% of all people diagnosed with HIV will receive ART, 95% of all people receiving ART will be virally suppressed),

exceeding those set in the EHE plan, would be required to reduce HIV incidence, adverting 210,500 infections by 2025 and 290,000 infections by 2030.[89] To assess their capacity to meet the demand for HIV care and support services needed to meet earlier National HIV Plan goals, the Georgia Department of Public Health (GDPH) conducted a study modeling future HIV prevalence using viral load data from Georgia's enhanced HIV/AIDS Reporting System and death rates for PLWH.[90] Models predicted achieving 90/90/80 (90% of PLWH will know their HIV status, 90% of all people diagnosed with HIV will receive ART, 80% of all people receiving ART will be virally suppressed) by 2020 would not be attainable even if doubling the rate of those being diagnosed or tripling the rates of those retained in care who were originally out of care. This speaks to the dire and complex HIV epidemic in Georgia.

Lastly, the Viral Hepatitis National Strategic Plan outlines five goals for addressing viral hepatitis in the U.S.: 1) prevent new viral hepatitis infections; 2) improve viral hepatitis-related health outcomes of people with viral hepatitis; 3) reduce viral hepatitis-related disparities and health inequities; 4) improve viral hepatitis surveillance and data usage; and 5) achieve integrated, coordinated efforts that address the viral hepatitis epidemics among all partners and stakeholders. The plan focuses on many targeted populations, including PWID, homeless individuals, MSM, PLWH, and baby boomers among other targeted populations.

Both plans specifically address HIV and HCV transmission related to PWID, identifying goals and indicators focused on increasing access to new, sterile syringes and other injection equipment to reduce infection. There is also a need to increase the percentage of PWID with diagnosed HIV infection who are virally suppressed to at least 80 percent, increasing access to viral hepatitis prevention services, reducing the number of HCV infections by at least 60%, increasing those aware of their status by 66%, and reducing the number of new HCV infections among 20–39 years old by 60%.

To effectively address morbidity and mortality rates for HIV and HCV among PWID, and meet the goals of EHE, and both National HIV and Hepatitis plans, there are many societal, community and

individual factors that contribute this paradigm. Factors such as substance misuse and abuse, access to SSPs, sharing of injection equipment, and use and adherence to medications such PrEP, ART, and DAA therapies should be considered. We must also consider other factors such as social determinants of health (SDOH) that negatively impact and increase the risk of becoming infected with HIV or HCV such as race, socioeconomic status (SES), housing status, incarceration, and access to healthcare. In rural Kentucky, Cloud and colleagues used the Risk Environment Framework to identify risk factors contributing to HCV transmission among PWID.[67] Through semi-structural qualitative interviews, they found generational poverty, low employment rates, lack of knowledge about HCV transmission, and limited harm reduction services in their area contributed to HCV transmission.

We have long known that race and ethnicity play important factors in HIV and HCV transmission risk. For example, Black PWID are more likely to live in ZIP codes with higher poverty rates, higher crime rates, and less access to substance abuse treatment compared white PWID.[91] All of these factors disproportionately affect Blacks contributing to racial/ethnic disparities in HIV-related outcomes.[92,93] Despite the opioid epidemic being commonly described as a rural, white epidemic, with the rise in illicit and polysubstance use, the epidemic also affects urban Blacks and Hispanic/Latinos at alarming rates. Given the higher rates of HIV infection among Blacks and Hispanic/Latinos, trending higher rates of HCV infection mostly among Blacks compared to other racial groups[94] and coupled with the overlapping drug-overdose epidemic, it is important to expand research to include urban population settings and be more inclusive of minority ethnic groups.

Linkage to Care through Harm Reduction and Treatment Strategies

Broadly, linkage to care can be defined as the transition from testing to medical care and treatment. Before we can link to care, we first need to identify PWID. Due to sigma related to injection behaviors, PWID are a hard-to-reach population and identification through community settings, harm reduction centers, physician practices and hospital settings is needed. Once identified, it is crucial PWID are tested

for infectious diseases and provided with the best prevention or treatment options. The CDC recommends anyone who has ever injected drugs and shared injection equipment be tested at least once in their lifetime for HCV infection[95] and HIV infection,[96] and ongoing routine testing while their risk remains, although studies have found testing within the this population to be subminimal.[50,97] After testing, PWID should be linked with the appropriate medical care resources including harm reduction services such as SSPs to prevent transmission or reinfection, access to opioid agonist therapy (OAT) to treat their substance use addiction, PrEP for those who are HIV negative, ART for those who are HIV positive, and DAA for those who are HCV RNA positive. The importance of each of these will be discussed in further detail for addressing the spread of infectious diseases among PWID.

Harm Reduction for Active PWID.

Harm reduction services allows opportunities to identify and reduce the harms associated with injection drug use and substance abuse through changing high-risk behaviors. Service such as SSPs, HIV, HCV and sexually transmitted diseases (STDs) testing and counseling, and distribution of naloxone are all examples of harm reduction services to prevent drug overdose and the spread of infectious diseases. SSPs are evidenced-based programs found to be beneficial in providing services such as access to sterile syringes and needles, testing and linkages to substance uses disorder treatment and infectious disease services.[98] Despite its effectiveness, Burnett and colleagues found among those who had injected drugs and HIV positive, only 11% had participated in distributive sharing of syringes, 10% shared other injection equipment, and 53% reported disposing needles in the trash, street, or a nonmedical waster container.[99] Additionally, researchers in Puerto Rico found sharing of injection equipment such as cookers, cotton and filters occurred more often than sharing needles contributing to their HCV infection.[100] This research identifies gaps noting PWID behaviors in sharing injection equipment and improper disposal and provides opportunities for further interventions to reduce the spread of infectious diseases through injection equipment.

While SSPs are effective, we know use of SSPs are not 100% effective or accessible due to restrictive laws in certain states or less accessible in rural areas. As a complementary tool, pharmaceutical interventions to combat HIV and HCV transmission through OAT, ART, PrEP, and DAA therapies can and should be used among PWID.

We also know that with the advancement in medications to prevent and treat HIV and HCV achieving viral suppression and preventing transmission is attainable. PrEP is 74% effective in preventing HIV if taken consistently among PWID[101] and while the effectiveness of ART among those who are HIV positive and the risk for transmitting HIV through drug injection equipment is unknown, it is likely a reduced risk for those on ART and sustaining an undetectable viral load. [102] Additionally, DAA is over 95% effective in curing HCV but uptake remains low.[103] Nonetheless, PWID adherence to taking PrEP, ART and DAA remains challenging. There are many barriers to uptake of these medications, including provider awareness and willingness to prescribe, awareness about PrEP among PWID,[104] HIV retention in care, [105] PWID forgetfulness to take their medications due to effects of drug use, and other SDOH (i.e., poverty and stigma).[106,107] Considering transmission occurs mostly among undiagnosed PWID[105] following the linkage to care continuum is important to identify, diagnose and treat these individuals.

Treatment Strategies for Substance Use

At various stages in their disorder, OAT is an evidence-based use of medications such as methadone and buprenorphine to treat OUD. These medications are highly effective in treating OUD patients and combined with counseling, Medication Assisted Treatment (MAT), has been effective in treating patient's addiction.[108] Studies have found both methadone and buprenorphine can improve HIV viral suppression, adherence to ART, and reduce mortality among persons with OUD. Extended-release naltrexone, an antagonist, can also improve HIV viral suppression among PLWH and those exiting

incarceration settings.[109] Despite OAT and MAT successes, linkage to these services upon discharge from hospitals[110,111] and PWID receiving treatment are not occurring despite the need.[99]

Conclusion

Overall, the opioid epidemic is driving current increases in HIV and HCV transmission rates related to IDU behaviors. Economically, IDU cost millions of dollars on longer hospital stays doubling the cost of admission[78,80], HIV[112] and HCV[113] treatment. Educating PWID on services such as SSPs, removing barriers to access and increasing the number SSPs in most needed areas can help reduce the spread of infectious diseases related to sharing of injection equipment. Interventions are needed to combat transition to injection drug use from other routes, reduce frequent injection among those who already inject, prevent sharing injection equipment[114,115] and initiating PWID on medications to prevent or treat HIV and HCV infections.

PWID are at greater risk for HCV, HIV and other infectious bloodborne pathogens. Monitoring trends of HCV and HIV incidence through proxies (i.e., IE, central CNS abscesses, SSTI, osteomyelitis) are viable methods for collection of data and the use of novel methods in both urban and rural settings among Blacks and Hispanic/Latinos and targeting younger populations are needed.

Purpose of Study

While the opioid epidemic in the U.S. continues to evolve and rates of HIV and HCV diagnoses continue to climb in Georgia, the number of persons with diagnosed HIV attributable to IDU increases. In most recent years, the number of HIV infections attributable to IDU has leveled off and clusters of HIV infections have been documented in Indiana, Massachusetts, West Virginia, and Washington [33,39-47]. Coinciding, acute HCV infections are steadily rising with IDU contributing to surging numbers.[116] A recent HCV/HIV vulnerability assessment ranked four Georgia counties in the top 220 most vulnerable counties experiencing or at-risk for HIV/HCV infection among PWID, increasing the odds of similar HIV and HCV outbreaks in Georgia.[30] To date, there have been limited studies identifying the impact of

HIV and HCV outcomes among PWID, specifically in Atlanta, Georgia, as a result of the opioid epidemic. This three-manuscript dissertation proposes to address these gaps in the literature, while also creating a body of literature that can be generalizable to other urban metropolitan cities in the U.S. with similar demographics.

The first study will examine prevalence of HIV and HCV infections at-discharge and incidence and hazard rates in HIV and HCV diagnoses post-clinical encounters from the ED or an inpatient hospitalization among PWID. The association of age and race/ethnicity with incidence of HIV and HCV will be estimated using a Poisson regression model. A sensitivity analysis using Cox Proportional Hazard models will be used to estimate the hazard rate ratios in HIV and HCV diagnoses associated with age, race/ethnicity, and discharge year. We will also assess characteristics associated with an HIV and HCV diagnosis at-discharge using logistic regression models. This information will improve our understanding of IDU-related hospitalizations or ED visits who are most at risk of becoming infected with HIV or HCV. It will also help close the gaps on missed opportunities to test individuals identified with IDU-related risk factors for HIV or HCV in the hospital setting and link them to care for substance use treatment and infectious disease prevention and treatment. Methods used in this analysis will include: 1) creating a dataset of IDU-related cases (IE, osteomyelitis, SSTIs) using ICD-9 and ICD-10 discharge diagnoses codes; 2) linkage of this dataset with GDPH HIV and HCV case surveillance records; 3) incidence of HIV and HCV diagnoses post-clinical encounter; 4) hazard rate ratios of HIV and HCV diagnoses post-clinical encounter and 5) the characteristics associated with being HIV or HCV diagnosed at-discharge. We hypothesize Blacks and younger age groups will be at increased risk for developing HIV or HCV post-clinical encounter compared to whites and older age groups with IDU-related risk factors.

The second study will examine the likelihood of HIV and HCV testing occurring during an IDU-related hospital encounter from 2012–2018. Secondly, the study will also determine the characteristics

associated with the likelihood of receiving testing. This information may improve our understanding if there are missed opportunities for HIV and HCV testing among PWID and identify opportunities for linkage to care and hard reduction opportunities for prevention. Methods used will include: 1) creating a dataset of IDU-related discharge cases (IE, osteomyelitis, CNS abscesses, SSTIs) using ICD-9 and ICD-10 codes; 2) linking this created dataset with GDPH HIV and HCV surveillance records to determine diagnosis status and determine who was eligible for testing; 3) using the linked dataset and generalizing estimating equations (GEE) with repeated measures to determine if eligible individuals were HIV or HCV tested at each encounter and 4) identifying if race/ethnicity and other predictors are associated with the likelihood being HIV or HCV tested during an IDU-related encounter. Previous studies have identified missed opportunities for HIV and HCV testing.[97,117-119] This study will provide estimates for HIV and HCV testing among PWID in the South at an urban hospital with opt-out and routine testing procedures. We hypothesize HIV testing will be higher compared to HCV testing given the hospital testing policies during the study-period time but will be sub-optimal overall with only 40% of encounters receiving testing. We also hypothesize testing will be lower among Blacks, compared to whites and among those without health insurance, compared to those with insurance.

The third study will examine yearly trends, from 2014–2019, in the percentage of PLWH in Georgia newly co-diagnosed with HCV. The study will also assess trends in retention and HIV viral suppression, and other characteristics among PLWH and co-diagnosed with HCV. Methods used in this study will include 1) creating a dataset with individuals co-infected with both HIV and HCV by linking HIV and HCV surveillance datasets together and 2) conducting a trend analysis in yearly HCV diagnoses from 2014–2019 among people diagnosed with HIV prior to 2014. This information may improve our understanding of HCV co-diagnoses over the recent years and which sub-populations among PLWH should be targeted to prevent subsequent HCV infection. We hypothesize trends among PLWH and newly co-diagnosed with HCV will have increased among younger adults and PWID.

Overall, this dissertation aims to increase the understanding of risk factors related to HIV and HCV transmission related to IDU by contributing a body of literature to this evolving field. These studies will inform our understanding of risk for HIV and HCV among PWID, by obtaining incidence rates in HIV and HCV diagnoses related to IDU, examining HIV and HCV testing patterns during IDU-related encounters and trends in characteristics among PLWH and newly co-diagnosed with HCV. This information can be used by clinical practitioners and public health professionals to identify PWID and other at-risk groups for HIV and HCV incidence and encourage linkage to HIV and HCV prevention and treatment.

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Chapter 2: Missed Opportunities for Prevention: Incidence of HIV and HCV Diagnoses Among a Cohort of Individuals Discharged from Hospital with Injection Drug Related Diagnoses, 2012–2019

Abstract

Background: Injection drug use (IDU) behavior has increased in the U.S. during the past decade largely due to the on-going opioid epidemic. Risk for HIV and hepatitis C virus (HCV) infections have also increased due to unsafe injection practices. We estimated incidence of HIV and HCV diagnoses among people who inject drugs (PWID) post-discharge from hospital-based clinical encounters.

Methods: We constructed a retrospective longitudinal cohort using clinical encounters with patients who had probable recent IDU behavior based on diagnostic codes in electronic medical records. Patients attended a metro Atlanta hospital during 2012 – 2018. We linked cohort data with HIV and HCV surveillance records from Georgia Department of Public Health (GDPH) to examine prevalence of infections at clinical discharge and incidence of infections post-clinical encounters.

Results: Nearly 4% of patients with IDU-related clinical encounters were later diagnosed with HIV, and 17% were later diagnosed with HCV, translating to incidence rates of 9.3 per 1,000 person-years and 42.9 per 1,000 person-years, respectively. Patients aged 16–39 years at discharge were less likely than older patients to be later diagnosed with HCV (Adjusted Incidence Rate Ratio [IRR]=0.63, 95% Confidence Interval [CI]=0.41-0.97, p=0.04). The majority of HIV and HCV diagnoses post-clinical encounter occurred among Black/African Americans and males. At discharge, 32.9% of patients had an HIV diagnosis and 28.1% of patients had an HCV diagnosis. HIV and HCV diagnoses at the time of discharge were mostly among 40–64 year-old patients, males, and Black/African Americans.

Conclusion: Targeted interventions for HIV/HCV prevention, diagnosis and linkage to treatment are needed to reduce incidence of new infections among high-risk groups. Future interventions should use novel data sources to focus on PWID in urban settings most susceptible to infection and disparities in HIV and HCV. Combining clinical and surveillance data can provide important information about how to focus such interventions.

Introduction

Injection drug use (IDU) behavior has increased during the past decade in the United States, largely due to the opioid epidemic and shifts from use of prescription to illicit opioids.[1-4] As a result, risk for bloodborne infectious diseases such as HIV and HCV has also increased. HIV and HCV infections attributable to IDU risk are resurging, and outbreak clusters have recently been detected through surveillance.[1,5-13] In 2019, 7.2% of new HIV infections were attributable to IDU risk compared to 5.8% in 2016.[14] Additionally, in 2019, 67% of HCV infections reported to surveillance were attributable to IDU risk.[15] Demographic characteristics of people who inject drugs (PWID) have also been shifting toward younger,[16] non-Hispanic white, and rural populations[17,18]although recent literature suggests IDU behavior is also increasing among urban and racial minority populations.[10,19,20]

PWID also have increased risk for other serious infections and conditions such as infective endocarditis (IE), skin soft tissue infections (SSTIs), osteomyelitis, and central nervous abscesses (CNS), which often require hospitalization. Hospitalizations due to these infections are also increasing.[21-28] IDU behavior is difficult to detect and monitor due to stigma and criminalization, so observation of these diagnoses in clinical settings may be used to classify patients as PWID for clinical care and research purposes.[29,30]

To reduce HIV and HCV transmission related to IDU behavior, it is important to identify opportunities for infectious disease prevention and screening interventions among PWID. These interventions could be effectively delivered in hospital settings for PWID who present with injection-related infectious or conditions. Understanding the probability of receiving an HIV or HCV diagnoses among PWID upon hospital discharge, and how that probability differs by patient characteristics, can shed light on missed opportunities for in-hospital screening or

prevention services. Such information may also motivate health care and public health professionals to increase delivery of screening and prevention services to patients with IDU risk; these services may include HIV and HCV testing and linkage to care, harm reduction services, and pre-exposure prophylaxis (PrEP).

In this study, we linked HIV and HCV case surveillance data from the Georgia Department of Public Health (GDPH) to hospitalization records of PWID in an urban setting to estimate incidence of HIV and HCV diagnoses among PWID after clinical discharge. We also estimated prevalence of these infections at the time of clinical discharge.

Methods

Study Design and Population

We constructed a retrospective longitudinal cohort using electronic medical record (EMR) patient data from an urban, metro Atlanta hospital spanning January 1, 2012 to December 31, 2018. We used patient encounters from the emergency department (ED) and inpatient settings to identify patients with probable, recent IDU behavior, based on having 1) at least one diagnostic code indicated for IE, Osteomyelitis, or SSTI based on International Classification of Diseases, Ninth Revision (ICD-9) or Tenth (ICD-10) Revision, and 2) an indication of a secondary substance use diagnosis (Table 1). ICD-9 and 10 codes used to identify probable IDU behavior were identified from published studies.[22,25,26,28,31-33] We limited patients in the cohort to those aged 16–64 years, and only patients' most recent IDU-related clinical encounter was included (i.e., earlier encounters were excluded for patients with multiple encounters during this time period).

Measures

Socio-demographic characteristics were categorized as follows: race/ethnicity (non-Hispanic Black/African American, non-Hispanic white, and other [e.g., Hispanic/Latino, Asian, mixed race], age at ED or hospital discharge (16–39 years old or 40–64 years old), sex (male, female), health insurance status (Medicare, Medicaid, private insurance, self-pay/uninsured, other), hospital stay type (ED visit, inpatient), length of hospital stay (0 days, 1–3 days, 4–7 days, 8+ days), repeat (i.e., more than one) IDU-related clinical encounter during study period (yes, no), IE diagnosis (yes, no), Osteomyelitis diagnosis (yes, no), SSTI diagnosis (yes, no), and discharge year (2012–2018). HIV and HCV infections at the time of ED or hospital encounter were determined based on ICD codes[22,31,34] or based on a previous case report to GDPH, which is described in the next section.

Linkage to HIV and HCV Case Surveillance Records

All retrospective cohort records were linked with HIV and HCV surveillance records to identify confirmed cases of HIV[35] or HCV[36,37] through December 31, 2019. A GDPH staff member linked the data sets based on exact matches for the following variables: first name, last name, date of birth, and sex and performed a manual review of all electronic matches.

Statistical Analysis

We used descriptive statistics to characterize the cohort of patients with ED or inpatient encounters resulting in IDU-related diagnoses (Table 1). We estimated, separately, the proportion of patients with an HIV or HCV diagnosis after their clinical encounter and compared the characteristics of patients with and without diagnoses using chi-square and global F-tests (Tables 2 and 3). We then used unadjusted and adjusted Poisson regression models to estimate, separately, incidence of post-discharge HIV and HCV diagnoses (Table 5). Adjusted models were used to assess potential differences in incidence by age and race/ethnicity. Given large

differences in person time at risk based on year of patient discharge and due to likely changes in substance use behavior and norms (i.e., changes in substances used and frequency of injection) during the study period, we conducted a sensitivity analysis using Cox Proportional Hazards models to estimate hazard rate ratios in HIV and HCV diagnoses (separately) associated with age, race/ethnicity, and discharge year (Table 1, supplemental material). Patients diagnosed with HIV or HCV at time of discharge were left censored for both Poisson and Cox models. Patients who did not have a recorded diagnosis of HIV or HCV, depending on model outcome, by December 31, 2019 were right censored. Last, we compared patients with and without HIV or HCV diagnoses at the time of discharge to understand characteristics associated with prevalent infections. We compared prevalent infections among patients within sub-groups using chi-square tests (Table 2, supplemental material) as well as logistic regression models (Tables 3 and 4, supplemental material). SAS Software 9.4 was used for all statistical analyses. Our study was reviewed and approved by Emory University, GDPH, and Georgia State University Institutional Review Boards and the local Grady Research Oversight Committee.

Results

Characteristics of Patients

A total of 857 patients had at least one IDU-related clinical encounter during January 1, 2012 – December 31, 2018 (Table 2). The majority of patients were male (67.7%), Black/African American (67.0%), and had an SSTI diagnosis (93.6%). The median age of patients was 43.8 years (Interquartile Range [IQR]=34.7-53.2). Nearly 33% of patients had a diagnosed HIV infection at the time of discharge, and 28.1% had a diagnosed HCV infection.

HIV Diagnoses Post-Clinical Encounter

Among the 575 patients without an HIV diagnosis at the time of discharge from their IDU-related clinical encounter, 22 (3.8%) were later diagnosed with HIV (before January, 2020). (Table 3). The majority of HIV diagnoses occurred among males (63.6% of infections), Black/African Americans (72.7%), and patients who were self-pay or uninsured (68.2%). The median time to HIV diagnosis was 1.59 years (IQR=0.65-2.5) (data not shown in table). There were no statistically significant associations between the characteristics of patients and being diagnosed with HIV post-clinical encounter.

HCV Diagnoses Post-Clinical Encounter

Among the 616 patients without an HCV diagnosis at the time of discharge from their IDU-related clinical encounter, 105 (17.0%) were later diagnosed with HCV (before January, 2020) (Table 4). The majority of these HCV diagnoses occurred among patients aged 40–64 years (69.5%), males (69.5%), Black/African Americans (73.3%), and patients who were self-pay or uninsured (56.2%). The mean time to HCV diagnosis was 2.0 years (IQR=0.87-3.91) (data not shown in table). Patients aged 40–64 years were more likely than younger patients to be diagnosed with HCV (p=0.01) post-clinical encounter, and patients whose clinical encounter occurred more recently were less likely than those with clinical encounters in earlier years to be diagnosed with HCV (p<0.01).

Incidence of HIV and HCV Diagnoses Post-Clinical Encounter

The incidence of HIV diagnosis post-clinical encounter was 9.3 per 1,000 person-years (Table 5). The incidence of HCV diagnosis post-clinical encounter was 42.9 per 1,000 person-years. Patients aged 16–39 years at discharge were less likely than older patients aged 40–64 years to be diagnosed with HCV (Adjusted Incidence Rate Ratio [IRR]=0.63, 95% Confidence Interval [CI]=0.41-0.97, p=0.04) after adjusting for race/ethnicity.

In Cox models adjusting for the year of discharge, patient age was negatively associated with HCV diagnosis (Adjusted Hazard Ratio [AHR]=0.63, 95% CI 0.41-0.98) (Supplementary Table 1). Hazard ratios and associated p-values from the Cox proportional hazards model were nearly identical to IRRs.

Due to the small number of HIV infections among other race/ethnicity IRRs and HRs could not be produced.

Characteristics of Patients with HIV or HCV Diagnoses at Discharge

Of the 282 patients with HIV diagnoses at the time of discharge, 71.6% were aged 40–64 years, 78.0% were male, 70.6% were Black/African American and 35.8% also had an HCV diagnosis at the time of discharge (Supplementary Table 2). Of the 241 patients with HCV diagnoses at the time of discharge, 70.1% were aged 40–64 years, 67.2% were male, 58.1% were Black/American and 41.9% had an HIV diagnosis at time of discharge (supplementary table 8). A total of 101 people (11.8%) were coinfected with HIV and HCV (data not shown in table). In multivariate analysis, older age, being male, and having diagnosed with HCV were significantly associated with having an HIV diagnosis at the time of discharge (Supplementary Table 3). In multivariate analysis, older age, and having diagnosed with HIV were significantly associated with having an HCV diagnosis at the time of discharge (Supplementary Table 4).

Discussion

During 2012 to 2019, incidence of HIV and HCV diagnoses following IDU-related clinical encounters among patients in an urban Atlanta hospital was 9.3 per 1,000 person-years and 42.9 per 1,000 person-years, respectively. The majority of post-clinical encounter HIV and HCV diagnoses occurred among Black/African Americans and males. At the time of discharge from

IDU-related clinical encounters, 282 (32.9%) patients had HIV diagnoses, 241 (28.1%) patients had HCV diagnoses, and 101 (11.8%) patients had both HIV and HCV diagnoses. Findings from this study demonstrate the importance of delivering HIV and HCV prevention strategies to PWID when they present clinically to improve long-term health outcomes and reduce incidence and transmission of these infectious diseases.

We observed potential missed opportunities for prevention, diagnosis, and early treatment of HIV and HCV in this study. Some patients with post-encounter diagnoses likely had existing infections at the time of the encounter and would have benefited from testing at encounter, facilitating earlier diagnosis and linkage to care. Others likely developed infections after their IDU-related clinical encounter. These incident infections may have been prevented by linkage to harm reduction services and substance use treatment when appropriate.

Routine HIV and HCV testing among PWID can effectively diagnose infection in the early stages and provide opportunities for rapid linkage to treatment. The Centers for Disease Control and Prevention (CDC) recommends testing PWID at least once yearly for HCV and HIV.[38,39] While HIV testing of PWID has improved in recent years;[40] missed opportunities for HIV testing still occur.[41,42] Opportunities to improve HCV testing also exist, particularly among younger people for whom IDU-behavior is increasing[28] and new HCV infections are most prevalent.[15] Early detection and treatment for HCV and HIV infections can greatly improve health outcomes and reduce onward transmission, but PWID are less likely than people in other risk groups (e.g., men who have sex with men [MSM], heterosexual) to be linked to and retained in care for these infections.[43,44] As such, when seen in clinical settings, PWID who are recently diagnosed with one of these infections, or patients previously diagnosed but not in care, should be immediately

linked to care, including treatment with direct-acting antivirals (DAA) for HCV and ART for HIV.

It may also be feasible to link PWID in clinical settings to harm reduction services including substance use treatment and syringe service programs (SSPs). Treatment of substance use disorders (e.g., medication assistance treatment [MAT]) can have substantial impacts on downstream factors including reducing HIV and HCV. However, some PWID are not ready to cease their addiction permanently. Ensuring PWID are aware and utilize other preventative and harm reduction services may have greater impact on prevention of infectious diseases than focusing on treatment of substance use disorders alone. SSPs are one effective strategy that provides PWID access to sterile syringes, condoms, and can also facilitate referrals to HIV and HCV testing and PrEP. Linkage from the hospital setting to these effective strategies can potentially reduce HIV and HCV infection and vastly reduce the cost for PWID treatment currently totaling millions of dollars.[32]

PWID are a stigmatized and hard-to-reach population. When PWID are encountered in clinical settings (e.g., hospitals, routine clinical care) offering them interventions to prevent, diagnose, and treat HIV and HCV infections is imperative. Hospitals may be particularly opportune settings for such interventions given longer patient stays. Extended hospital stays may also provide opportunities for physicians to treat patients using a holistic approach,[45,46] rather than treating infections such as HIV, HCV, or IE and conditions such as opioid use disorder (OUD) in isolation. Integrating HIV and HCV testing reminders into EMRs, particularly for patients presenting with IDU-associated conditions, may be helpful to clinicians.

Our study has limitations. First, no formal ICD-9 or ICD-10 codes exist for IDU behavior, and patients may be reluctant to share information about IDU behavior with providers. The diagnostic codes used in this study to identify IDU behavior have been previously used in research, but sensitivity and specificity of these codes for classifying PWID remains variable.[29,30] Because we were unable to manually review all medical records, it is possible the diagnostic codes used to identify IDU behavior may overestimate or underestimate IDU-related clinical encounters in this hospital. Second, in the absence of diagnostic codes in the EMR, we were limited to reported diagnoses of HIV and HCV to the GDPH. It is possible that individuals discharged from the hospital were diagnosed with HIV or HCV outside Georgia and their diagnoses were not transferred to GDPH surveillance records. In this case, post-clinical encounter incidence of infections would be underestimated.[42,47] Last, although race/ethnicity lacked evidence of an association with incidence of HIV and HCV diagnoses, this may be due to our study being under powered to detect significant differences and the majority of IDU-related cases being among Black/African American patients.

Conclusion

Our study adds to the literature describing IDU-related infections identified in Atlanta area hospitals[48] and is the first study to estimate incidence of HIV and HCV diagnoses among PWID discharged from IDU-related clinical encounters. Linking clinical data with state surveillance data when feasible can provide insight into incidence of diagnoses, longer term health outcomes (i.e., those encountered and not in HIV or HCV care) and unmet needs of people infected with HIV or HCV. There are substantial opportunities to improve integration of care for PWID and strengthen linkage to infectious disease prevention (e.g., PrEP, SSPs, harm reduction) and substance use treatment (e.g., MAT, DAA, ART) services. Further research should examine risks

for HIV and HCV transmission among PWID in urban settings most susceptible to infection and disparities in HIV and HCV care using novel data sources.

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Table 1. International Classification of Diseases, Ninth and Tenth Revisions, Codes Used to Identify Patients with Injection Drug Use Behavior

	Injection Drug Use-related Conditions	
	ICD-9 codes	ICD-10 codes
Infective Endocarditis	421,421.1,421.9,424.9	I33.0,I33.9,I38,I39,B37.6
Osteomyelitis	730.00,730.01,730.02,730.03,730.04,730.05, 730.06,730.07, 730.08,730.09, 730.20,730.21, 730.22,730.23, 730.24,730.25, 730.26,730.27, 730.28,730.29	M86.10,M86.20,M86.119,M86.219,M86.229, M86.139,M86.239,M86.149,M86.249 M86.159,M86.259,M86.169,M86.269,M86.179,M86.279,M8 6.18,M86.28,M86.19,M86.29,M86.9
Skin and Soft Tissue Infections	324,324.1,324.9, 326, 040.00,681, 681.01, 681.02, 681.1, 681.11, 681.9, 682, 682.1-682.9, 785.4, 728.86, 707.1, 707.8, 707.9, 451.0-451.9, 567.2, 569.5, 572.0, 590.1, 723.6, 729.3	G06.0, G06.1, G06.2, G09, A48, I96, K65.0-K65.9, M72.6, L02.0-L02.93, L03.0-L03.91, L97.1-L97.929, L98.8, M793, I80, K63.0, K75.0, M54.0, N10
	Substance Use Diagnoses	
	ICD-9 codes	ICD-10 codes
Opioid	304.0-304.3, 304.70-304.73, 305.5-305.53, E850.0-E850.2, 965.00, 965.01, 965.02, 965.09	F11, T40.0 -T40.4, T40.6,
Cocaine	304.20-304.23, 305.60-305.63, 970.81	F14, T40.5

Amphetamine	304.4-304.43, 305.70-305.73, 969.72	F15, T43.60, T43.62, T43.69
Sedative	304.10-304.13, 305.40-305.43,967.0,E852.8,E852.9	F13, T42.3, T42.4, T42.5, T42.6, T42.7, T42.8
Hallucinogen	304.50-304.53, 305.30-305.33,969.6	F16, T40.9
Other	304.60-304.63, 304.80-304.93, 305.90-305.93, 966	F19, T42, T43.6, T43.8, T43.9

Table 2. Characteristics of Patients at Most Recent Injection Drug Use-related Clinical Encounter, 2012–2018 (N=857)

Characteristics	Total N (%)
Total	857
Age Group, years	
16–39	331 (38.6)
40–64	526 (61.4)
Sex	
Female	285 (33.3)
Male	572 (67.7)
Race/ethnicity	
Black/African American	574 (67.0)
White	264 (30.8)
Other[a]	19 (2.2)
Infective Endocarditis Diagnosis	
Yes	26 (3.0)
No	831 (97.0)
Osteomyelitis Diagnosis	
Yes	65 (7.6)
No	792 (92.4)
Skin and Soft Tissue Infection Diagnosis	
Yes	802 (93.6)
No	55 (6.4)
Health Insurance Type	
Medicare	84 (9.8)
Medicaid	252 (29.4)
Private Insurance	34 (4.0)
Self-Pay/Uninsured	484 (56.5)
Other	3 (0.3)
Hospital Stay Type	
ED	255 (29.8)
Inpatient	602 (70.2)
HIV Positive[b]	
Yes	282 (32.9)
No	575 (67.1)
HCV Positive[b]	
Yes	241 (28.1)
No	616 (71.9)
Length of hospital stay	
0 days	154 (18.0)
1–3 days	298 (34.8)
4–7 days	211 (24.6)
8+ days	194 (22.6)
Repeat IDU-Related Encounter	
(32.9%)Yes	117 (13.7)
No	740 (86.3)
Discharge Year	
2012	105 (12.2)
2013	107 (12.5)
2014	115 (13.4)

2015	142 (16.6)
2016	117 (13.7)
2017	134 (15.6)
2018	137 (16.0)

Abbreviations: HIV, human immunodeficiency virus; HCV, hepatitis C virus; IDU, injection drug use
[a]Other includes Hispanic/Latino, Asian, and Mixed Race
[b]Based on International Classification Modification Diagnosis Code or previous report to Georgia Department of Public Health. See methods.

Table 3. Characteristics of Patients with and without HIV Diagnoses Post-IDU-related Clinical Encounters, 2012–2019 (N=575)

Characteristics	Patients with HIV Diagnosis N (%)	Patients without HIV Diagnosis N (%)	*P* value
Total, n (%)	22 (3.8)	553 (96.2)	
Age Group, years			0.54
16–39	11 (50.0)	240 (43.4)	
40–64	11 (50.0)	313 (56.6)	
Sex			0.81
Female	8 (36.4)	215 (38.9)	
Male	14 (63.6)	338 (61.1)	
Race/ethnicity			0.81
Black/African American	16 (72.7)	359 (64.9)	
White	6 (27.3)	179 (32.4)	
Other[a]	0 (0.0)	15 (2.7)	
Infective Endocarditis Diagnosis			0.38
Yes	0 (0.0)	19 (3.4)	
No	22 (100.0)	534 (96.6)	
Osteomyelitis			0.21
Yes	3 (13.6)	37 (6.7)	
No	19 (86.4)	516 (93.3)	
Skin and Soft Tissue Infection Diagnosis			0.63
Yes	20 (90.9)	517 (93.5)	
No	2 (9.1)	36 (6.5)	
Health Insurance Type			0.80
Medicare	1 (4.6)	51 (9.2)	
Medicaid	6 (27.2)	144 (26.0)	
Private Insurance	0 (0.0)	22 (4.0)	
Self-Pay/Uninsured	15 (68.2)	335 (60.6)	
Other	0 (0.0)	1 (0.2)	
Hospital Stay Type			0.16
ED	10 (45.4)	172 (31.1)	
Inpatient	12 (54.6)	381 (68.9)	
Length of hospital stay			0.15
0 days	8 (36.4)	107 (19.4)	
1–3 days	4 (18.2)	196 (35.4)	
4–7 days	4 (18.2)	129 (23.3)	
8+ days	6 (27.2)	121 (21.9)	
Repeat IDU-Related Visit			0.43
Yes	4 (18.2)	69 (12.5)	
No	18 (81.8)	484 (87.5)	
Discharge Year			0.34
2012	2 (9.1)	58 (10.5)	
2013	4 (18.2)	69 (12.5)	
2014	5 (22.7)	68 (12.3)	
2015	6 (27.2)	94 (17.0)	

2016	2 (9.1)	85 (15.4)
2017	2 (9.1)	83 (15.0)
2018	1 (4.6)	96 (17.3)

Abbreviations: HIV, human immunodeficiency virus; IDU, injection drug use
[a]Other includes Hispanic/Latino, Asian, and Mixed Race

Table 4. Characteristics of Patients with and without HCV Diagnoses Post-IDU-related Clinical Encounters, 2012–2019 (N=616)

Characteristics	Patients with HCV Diagnosis N (%)	Patients without HCV Diagnosis N (%)	*P* value
Total, n (%)	105 (17)	511 (83)	
Age Group, years			0.01
16–39	32 (30.5)	227 (44.4)	
40–64	73 (69.5)	284 (55.6)	
Sex			0.48
Female	32 (30.5)	174 (34.0)	
Male	73 (69.5)	337 (66.0)	
Race/ethnicity			0.77
Black/African American	77 (73.3)	357 (69.9)	
White	25 (23.8)	139 (27.2)	
Other[a]	3 (2.9)	15 (2.9)	
Infective Endocarditis Diagnosis			0.17
Yes	5 (4.8)	12 (2.3)	
No	100 (95.2)	499 (97.7)	
Osteomyelitis Diagnosis			0.73
Yes	7 (6.7)	39 (7.6)	
No	98 (93.3)	472 (92.4)	
Skin and Soft Tissue Infection Diagnosis			0.20
Yes	95 (90.5)	480 (93.9)	
No	10 (9.5)	31 (6.1)	
Health Insurance Type			0.93
Medicare	10 (9.5)	52 (10.1)	
Medicaid	31 (29.5)	145 (28.4)	
Private Insurance	5 (4.8)	20 (3.9)	
Self-Pay/Uninsured	59 (56.2)	291 (57.0)	
Other	0 (0.0)	3 (0.6)	
Hospital Stay Type			0.14
ED	40 (38.1)	157 (30.7)	
Inpatient	65 (61.9)	354 (69.3)	
Length of hospital stay			0.77
0 days	23 (21.9)	94 (18.4)	
1–3 days	36 (34.3)	187 (36.6)	
4–7 days	26 (24.8)	118 (23.1)	
8+ days	20 (19.0)	112 (21.9)	
Repeat IDU-Related Visit			0.59
Yes	10 (9.5)	58 (11.3)	
No	95 (90.5)	453 (88.7)	
Discharge Year			<0.01
2012	29 (27.7)	59 (11.5)	
2013	18 (17.1)	68 (13.3)	
2014	21 (20.0)	70 (13.7)	

2015	18 (17.1)	76 (14.9)
2016	7 (6.7)	73 (14.3)
2017	6 (5.7)	78 (15.3)
2018	6 (5.7)	87 (17.0)

Abbreviations: HCV, hepatitis C virus; IDU, injection drug use
[a]Other includes Hispanic/Latino, Asian, and Mixed Race

Table 5. Incidence Rates and Ratios for HIV and HCV Diagnosis Post-IDU-related Clinical Encounter, 2012–2019

	HIV Diagnosis Post-Encounter				**HCV Diagnosis Post-Encounter**			
Incidence Rate	**22/2365.59 = 9.3 per 1,000 person-years**				**105/2448.48 = 42.9 per 1,000 person-years**			
Characteristic	**Unadjusted IRR (95% CI)**	***P* value**	**Adjusted IRR* (95% CI)**	***P* value**	**Unadjusted IRR (95% CI)**	***P* value**	**Adjusted IRR* (95% CI)**	***P* value**
Age Group, years								
16–39	1.44 (0.62-3.31)	0.40	1.68 (0.70-4.02)	0.24	0.64 (0.42-0.97)	0.04	0.63 (0.41-0.97)	0.04
40–64	Reference		Reference		Reference		Reference	
Race/Ethnicity								
White	Reference		Reference		Reference		Reference	
Black	1.26 (0.49-3.22)	0.63	1.49 (0.56-3.96)	0.42	1.10 (0.70-1.73)	0.67	0.96 (0.60-1.53)	0.86
Other[a]	-	-	-	-	1.06 (0.32-3.51)	0.93	1.17 (0.35-3.88)	0.80

Abbreviations: HIV, human immunodeficiency virus; HCV, hepatitis C virus; IRR, incidence rate ratio; CI, confidence interval
*Adjusted for race/ethnicity
[a]Other includes Hispanic/Latino, Asian, and Mixed Race; IRRs could not be produced for other race/ethnicity due to small number of HIV infections.

Supplementary Table 1. Cox Proportional Hazard Rates and Ratios for HIV and HCV Diagnosis Post-IDU-Related Clinical Encounter, 2012–2019 (N=616)

	HIV Diagnosis Post-Encounter				HCV Diagnosis Post-Encounter			
	Unadjusted Hazard Ratio (95% CI)	***P* value**	**Adjusted Hazard Ratio* (95% CI)**	***P* value**	**Unadjusted Hazard Ratio (95% CI)**	***P* value**	**Adjusted Hazard Ratio* (95% CI)**	***P* value**
Characteristic								
Race/Ethnicity								
White	Reference		Reference		Reference		Reference	
Black	1.39 (0.51-3.35)	0.57	1.40 (0.53-3.71)	0.50	1.10 (0.70-1.74)	0.67	0.95 (0.59-1.51)	0.82
Other[a]	—	—	—	—	1.07 (0.32-3.55)	0.91	1.18 (0.35-3.95)	0.78
Age group, years								
16–39	1.37 (0.59-3.16)	0.46	1.69 (0.71-4.03)	0.24	0.64 (0.42-0.97)	0.04	0.63 (0.41-0.98)	0.04
40–64	Reference		Reference		Reference		Reference	
Discharge Year								
2012	Reference		Reference		Reference		Reference	
2013	3.33 (0.37-29.81)	0.28	3.56 (0.40-31.87)	0.26	0.71 (0.39-1.30)	0.27	0.69 (0.38-1.25)	0.22
2014	4.28 (0.50-36.64)	0.18	4.25 (0.50-36.42)	0.19	0.84 (0.47-1.50)	0.56	0.80 (0.45-1.43)	0.45
2015	4.14 (0.49-34.68)	0.19	4.11 (0.49-34.50)	0.19	0.84 (0.46-1.54)	0.57	0.86 (0.47-1.58)	0.62
2016	1.66 (0.15-18.52)	0.68	1.67 (0.15-18.67)	0.68	0.47 (0.20-1.10)	0.08	0.49 (0.21-1.22)	0.10
2017	1.99 (0.18-22.34)	0.58	1.89 (0.17-21.24)	0.61	0.48 (0.19-1.20)	0.12	0.69 (0.27-1.73)	0.13
2018	1.35 (0.08-22.36)	0.83	1.32 (0.08-21.82)	0.85	0.66 (0.26-1.67)	0.38	0.63 (0.41-0.98)	0.42

Abbreviations: HIV, Human Immunodeficiency Virus; HCV, hepatitis C virus; CI, confidence interval

*Adjusted for discharge year and race/ethnicity

[a]Other includes Hispanic/Latino, Asian, and Mixed Race. HRs could not be produced for other race/ethnicity due to small number of HIV infections.

Supplementary Table 2. Characteristics of Patients with and without HIV or HCV Diagnoses at Discharge from IDU-related Clinical Encounter, 2012–2018 (N=857)

Characteristics	HIV Diagnosis At Discharge N (%)	No HIV Diagnosis at Discharge N (%)	*P* value	HCV Diagnosis at Discharge N (%)	No HCV Diagnosis at Discharge N (%)	*P* value
Total, n (%)	282 (32.9)	575 (67.1)		241 (28.1)	616 (71.9)	
Age Group, years			<0.01			<0.01
16–39	80 (28.4)	251 (43.7)		72 (29.9)	259 (42.0)	
40–64	202 (71.6)	324 (56.3)		169 (70.1)	357 (58.0)	
Sex			<0.01			0.85
Female	62 (22.0)	223 (38.8)		79 (32.8)	206 (33.4)	
Male	220 (78.0)	352 (61.2)		162 (67.2)	410 (66.6)	
Race/ethnicity			0.21			<0.01
Black/African American	199 (70.6)	375 (65.2)		140 (58.1)	434 (70.5)	
White	79 (28.0)	185 (32.2)		100 (41.5)	164 (26.6)	
Other[a]	4 (1.4)	15 (2.6)		1 (0.4)	18 (2.9)	
Infective Endocarditis Diagnosis			0.51			0.45
Yes	7 (2.5)	19 (3.3)		9 (3.7)	17 (2.8)	
No	275 (97.5)	556 (96.7)		232 (96.3)	599 (97.2)	
Osteomyelitis Diagnosis			0.32			0.84
Yes	25 (8.9)	40 (7.0)		19 (7.9)	46 (7.5)	
No	257 (91.1)	535 (93.0)		222 (92.1)	570 (92.5)	
Skin and Soft Tissue Infection Diagnosis			0.74			0.65
Yes	265 (94.0)	537 (93.4)		227 (94.2)	575 (93.3)	
No	17 (6.0)	38 (6.6)		14 (5.8)	41 (6.7)	
Health Insurance Type			<0.01			0.75
Medicare	32 (11.4)	52 (9.0)		22 (9.1)	62 (10.1)	
Medicaid	102 (36.1)	150 (26.1)		76 (31.6)	176 (28.6)	
Private Insurance	12 (4.3)	22 (3.8)		9 (3.7)	25 (4.0)	
Self-Pay/Uninsured	134 (47.5)	350 (60.9)		134 (55.6)	350 (56.8)	
Other	2 (0.7)	1 (0.2)		0 (0.0)	3 (0.5)	
Hospital Stay Type			0.16			0.02
ED	73 (25.9)	182 (31.7)		58 (24.1)	197 (32.0)	
Inpatient	209 (74.1)	393 (68.3)		183 (75.9)	419 (68.0)	
HCV Positive[b]			<0.01			
Yes	101 (35.8)	140 (24.3)		—	—	
No	181 (64.2)	435 (75.7)		—	—	
HIV Positive[b]						<0.01
Yes	—	—		101 (41.9)	181 (29.4)	
No	—	—		140 (58.1)	435 (70.6)	
Length of hospital stay			0.12			0.15
0 days	39 (13.8)	115 (20.0)		37 (15.4)	117 (19.0)	
1–3 days	98 (34.8)	200 (34.8)		75 (31.1)	223 (36.2)	
4–7 days	78 (27.6)	133 (23.1)		67 (27.8)	144 (23.4)	
8+ days	67 (23.8)	127 (22.1)		62 (25.7)	132 (21.4)	

Repeat IDU-Related Visit			0.24			<0.01
Yes	44 (15.6)	73 (12.7)		49 (20.3)	68 (11.0)	
No	238 (84.4)	502 (87.3)		192 (79.7)	548 (89.0)	
Discharge Year			0.10			<0.01
2012	45 (16.0)	60 (10.4)		17 (7.0)	88 (14.3)	
2013	34 (12.0)	73 (12.7)		21 (8.7)	86 (14.0)	
2014	42 (14.9)	73 (12.7)		24 (10.0)	91 (14.8)	
2015	42 (14.9)	100 (17.4)		48 (19.9)	94 (15.2)	
2016	30 (10.6)	87 (15.1)		37 (15.4)	80 (13.0)	
2017	49 (17.4)	85 (14.8)		50 (20.8)	84 (13.6)	
2018	40 (14.2)	97 (16.9)		44 (18.2)	93 (15.1)	

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; HCV, hepatitis C virus

[a]Other includes Hispanic/Latino, Asian, and Mixed Race

[b]Based on International Classification Modification Diagnosis Code or previous report to Georgia Department of Public Health. See methods.

Supplementary Table 3. HIV Diagnosis at Discharge from IDU-related Clinical Encounter, 2012–2019 (N=857): Logistic Regression Results

Characteristics	Unadjusted Odds Ratio (95% CI)	*P* value	Adjusted Odds Ratio (95% CI)	*P* value
Age Group, years				
16–39	0.51 (0.38-0.69)	<0.01	0.61 (0.44-0.85)	<0.01
40–64	Reference		Reference	
Sex				
Female	Reference		Reference	
Male	2.25 (1.62-3.12)	<0.01	2.17 (1.55-3.03)	<0.01
Race/ethnicity				
Black/African American	1.24 (0.91-1.70)	0.13	1.21 (0.86-1.70)	0.37
White	Reference		Reference	
Other[a]	0.62 (0.20-1.94)	0.31	0.83 (0.26-2.65)	0.63
Infective Endocarditis Diagnosis				
Yes	0.75 (0.31-1.79)	0.51	—	—
No	Reference			
Osteomyelitis Diagnosis				
Yes	1.30 (0.77-2.19)	0.32	—	—
No	Reference			
Skin and Soft Tissue Infection Diagnosis				
Yes	1.10 (0.61-1.99)	0.74	—	
No	Reference			
Health Insurance Type				
Medicare	1.13 (0.49-2.59)	0.66	—	
Medicaid	1.25 (0.59-2.63)	0.89	—	
Private Insurance	Reference			
Self-Pay/Uninsured	3.67 (0.30-44.73)	0.03	—	
Other	0.70 (0.34 -1.46)	0.29	—	
Hospital Stay Type				
ED	Reference			
Inpatient	1.33 (0.96-1.82)	0.08	—	
HCV Positive[b]				
Yes	1.73 (1.27-2.36)	<0.01	1.70 (1.23-2.35)	<0.01
No	Reference		Reference	
Length of hospital stay				
0 days	Reference			
1–3 days	1.45 (0.93-2.24)	0.81	—	
4–7 days	1.73 (1.09-2.73)	0.10	—	
8+ days	1.56 (0.97-2.49)	0.43	—	
Repeat IDU-Related Visit				
Yes	1.27 (0.85-1.91)	0.24	—	
No	Reference			
Discharge Year				
2012	Reference			
2013	0.62 (0.35-1.09)	0.78	—	

2014	0.77 (0.45-1.32)	0.38	—
2015	0.56 (0.33-0.95)	0.36	—
2016	0.46 (0.26-0.81)	0.07	—
2017	0.77 (0.46-1.30)	0.34	—
2018	0.55 (0.32-0.94)	0.32	—

Abbreviations: ; HIV, human immunodeficiency virus; IDU, injection drug use; CI, confidence interval; HCV, hepatitis C virus

[a]Other includes Hispanic/Latino, Asian, and Mixed Race

[b]Based on International Classification Modification Diagnosis Code or previous report to Georgia Department of Public Health. See methods.

Supplementary Table 4. HCV Diagnosis at Discharge from IDU-related Clinical Encounter, 2012–2019 (N=857): Logistic Regression Results

Characteristics	Unadjusted Odds Ratio (95% CI)	*P* value	Adjusted Odds Ratio (95% CI)	*P* value
Age Group, years				
16–39	0.51 (0.38-0.69)	<0.01	0.49 (0.34-0.70)	<0.01
40–64	Reference		Reference	
Sex				
Female	Reference		Reference	
Male	1.03 (0.75-1.41)	0.85	0.92 (0.65-1.30)	0.64
Race/ethnicity				
Black/African American	0.53 (0.39-0.72)	0.29	0.44 (0.31-0.62)	0.61
White	Reference		Reference	
Other[a]	0.09 (0.01-0.69)	0.04	0.11 (0.01-0.87)	0.09
Infective Endocarditis Diagnosis	1.37 (0.60-3.11)	0.46	—	
Yes				
No				
Osteomyelitis Diagnosis	1.06 (0.61-1.85)	0.84	—	
Yes				
No				
Skin and Soft Tissue Infection Diagnosis	1.16 (0.62-2.16)	0.65	—	
Yes				
No				
Health Insurance Type				
Medicare	0.99 (0.40-2.43)	0.98	—	
Medicaid	1.20 (0.54-2.69)	0.98	—	
Private Insurance	Reference		—	
Self-Pay/Uninsured	1.06 (0.48-2.34)	0.98	—	
Other	—	0.98		
Hospital Stay Type				
ED	Reference		Reference	
Inpatient	1.48 (1.06-2.09)	0.02	1.36 (0.94-1.96)	0.10
HIV Positive[b]				
Yes	1.73 (1.27-2.36)	<0.01	1.70 (1.23-2.35)	<0.01
No	Reference			
Length of hospital stay				
0 days	Reference			
1–3 days	1.06 (0.68-1.67)	0.22	—	
4–7 days	1.47 (0.92-2.35)	0.18	—	
8+ days	1.49 (0.92-2.39)	0.17	—	
Repeat IDU-Related Visit				
Yes	2.06 (1.38-3.08)	<0.01	1.88 (1.23-2.89)	<0.01
No	Reference			
Discharge Year				
2012	Reference		Reference	
2013	1.26 (0.62-2.56)	0.07	1.22 (0.59-2.53)	0.05

2014	1.37 (0.69-2.71)	0.13	1.42 (0.70-2.87)	0.17
2015	2.64 (1.42-4.94)	0.04	2.86 (1.49-5.48)	0.03
2016	2.40 (1.25-4.58)	0.19	2.54 (1.30-4.97)	0.14
2017	3.08 (1.65-5.76)	<0.01	2.94 (1.54-5.64)	0.02
2018	2.45 (1.30-4.60)	0.13	2.50 (1.30-4.82)	0.14

Abbreviations: HCV, hepatitis C virus; IDU, injection drug use; CI, confidence interval; HIV, human immunodeficiency virus;

[a]Other includes Hispanic/Latino, Asian, and Mixed Race

[b]Based on International Classification Modification Diagnosis Code or previous report to Georgia Department of Public Health. See methods.

Chapter 3: HIV and HCV Testing at Each Hospital Encounter Among People Who Inject Drugs, 2012–2018 — Opportunities for Increased Testing and Prevention

Abstract

Background: People who inject drugs (PWID) have substantial risk for HIV and hepatitis C virus (HCV) infections. Clinical encounters for injection drug use (IDU)-related conditions provide opportunities for HIV and HCV testing among PWID, but such testing may not always occur. We describe the frequency of, and factors associated with, HIV and HCV testing during hospital-based clinical encounters with PWID.

Methods: IDU-related clinical encounters at an urban Atlanta hospital were abstracted from medical records spanning January, 2012–December, 2018. We estimated the frequency of HIV and HCV testing at clinical encounters. We assessed associations between patient factors and testing using unadjusted and adjusted generalized estimating equations models.

Results: Of 729 encounters eligible for HIV testing, testing occurred in 29.3%. Of 793 encounters eligible for HCV testing, testing occurred in 12.2%. Testing was less likely among Black/African Americans compared to whites (adjusted odds ratio [AOR]: HIV, AOR=0.43, 95% confidence interval [CI], 0.29-0.63, *P* <0.01); HCV, AOR=0.43, 95% CI, 0.26-0.72, *P* <0.01). Testing was more likely to occur in encounters during 2016–2018 than in encounters during 2012–2013; (HIV, AOR=4.73, 95% CI, 2.72-8.23, *P* <0.01; HCV, AOR=3.74, 95% CI, 1.93-7.24, *P* <0.01) and for five days or longer hospital stays compared to those less than five days or in emergency department (ED) visits (HIV, AOR=3.70, 95% CI, 2.30-5.95, *P* <0.01; HCV, AOR=4.49, 95% CI, 2.78-7.25, *P* <0.01).

Conclusion: When PWID are encountered in hospital settings, HIV and HCV testing should be universally offered to facilitate early diagnosis and treatment services. Strategies should aim to improve HIV and HCV testing among all PWID of all race/ethnicities and increase testing in the ED. Use of novel data sources including linking surveillance and clinical data can aid in informing these strategies.

Introduction

In 2019, 7.2% of new HIV infections and 67% of hepatitis C virus (HCV) infections were attributable to injection drug use (IDU) risk behavior.[1,2] Increases in IDU behavior related to the opioid epidemic has contributed to HIV and HCV outbreaks in the United States (U.S.).[3-7] While currently underutilized, opportunities exist to prevent HIV and HCV transmission among people who inject drugs (PWID), including evidence-based strategies such increasing access to sterile syringe services programs (SSPs)[8,9] and routine HIV and HCV testing.

The Centers for Disease Control and Prevention (CDC) recommends HIV and HCV testing for PWID at least once a year.[10,11] However, because IDU is a stigmatized and criminalized behavior, PWID may not seek medical care from providers unless medically necessary. Additionally, clinical providers may be unaware of IDU behavior even when medical care is sought. Together, these factors lead to missed opportunities for HIV and HCV testing and prevention among PWID. Undiagnosed HIV and HCV infections can be unknowingly transmitted to injection and sexual partners through syringe and other equipment sharing and risky sexual behaviors (i.e., sex in exchange for money, condomless sex).[12]

Despite CDC recommendations, several studies have documented missed opportunities for HIV and HCV testing among PWID.[13-18] Infective endocarditis (IE), osteomyelitis, and skin and soft tissue infections (SSTI) are conditions that are often indicative of IDU behavior,[19-22] and recent studies have identified increases in IDU-related hospital visits related to these conditions.[20,22,23] Clinical encounters related to these conditions thus provide opportunities to test patients for HIV and HCV and initiate treatment, reducing onward HIV and HCV transmission risk. In this study,

we estimate the frequency of, and risk factors associated with, HIV and HCV testing during IDU-related encounters at an urban hospital with opt-out and universal testing guidelines in Atlanta, Georgia. We also estimate the frequency of HIV and HCV diagnosed among patients who had missed opportunities for testing.

Methods

Study Population

We used data collected from an Atlanta metro area hospital from January 1, 2012 to December 31, 2018 to describe IDU-related patient encounters. Electronic medical records from emergency department (ED) or inpatient encounters were used to identify patients with probable recent IDU behavior based on the following: 1) at least one International Classification of Diseases, Ninth Revision, (ICD-9) or Tenth Revision, (ICD-10), diagnostic code indicated for IE, osteomyelitis, or SSTI and 2) a secondary substance use ICD-9 or ICD-10 diagnostic code (Table 1). The codes used to identify probable IDU behavior were identified from published studies.[13,20,22-26] For analytic purposes, we limited these clinical encounters to patients who were 16-64 years old.

Measures

Patient characteristics were categorized from each IDU-related encounter as follows: race/ethnicity (Black/African American, white, or other [e.g., Hispanic/Latino, Asian, mixed race]), age at discharge (16–39 or 40–64 years old), sex (male or female), health insurance status (Medicare/Medicaid, private insurance/other, or self-pay/uninsured), hospital stay type (ED visit, inpatient stay 1–4 days, or inpatient stay 5+ days), discharge year (2012–2013, 2014–2015, or 2016–2018), IE or osteomyelitis diagnosis (yes or no), and SSTI diagnosis (yes or no).

HIV and HCV Testing Frequency

In order to determine which IDU encounters were eligible for HIV and/or HCV testing, all IDU-related encounters were linked with GDPH HIV and HCV surveillance records to identify patients with confirmed cases of HIV[27] or HCV[28,29] through December 31, 2019. A staff member at GDPH conducted a match based on the following variables: first name, last name, date of birth, and sex and performed a manual review to determine final matches.

Using the linked data set, we first identified patients who were HIV or HCV diagnosed prior to their admission date. If the HIV diagnosis date occurred before the encounter admission date, the encounter was classified as ineligible for HIV testing. Encounters among patients with no recorded HIV diagnosis prior to encounter admission date were determined to be among patients at risk for new HIV diagnoses and were thus used as the denominator (risk set) for testing frequency. This same logic was applied to encounters eligible and ineligible for HCV testing based on prior HCV diagnoses.

Statistical Analysis

We created two separate data sets for analyses: 1) encounters eligible for HIV testing and 2) encounters eligible for HCV testing. We used descriptive statistics to characterize IDU-related encounters by patient characteristics associated with each encounter (Table 2). We compared the proportion of IDU-related encounters in which HIV or HCV testing occurred versus did not by patient characteristics using chi-square or global F-tests (Table 2). We used generalized estimating equations (GEE) models accounting for repeated measures (i.e., two or more IDU-related encounters for the same patient) to assess associations between patient characteristics and receipt of HIV or HCV testing during IDU-related encounters (Table 3 and 4). A log link was used in models to express associations in terms of odds ratios (ORs) and associated 95% confidence intervals (CIs). In the HCV models, hospital stay type categories were further

collapsed to 0-4 days versus 5+ days due to the small number of HCV tests conducted in ED encounters. All variables associated with testing at $P < 0.05$ in the bivariate models or associated with HIV and HCV diagnosis based on previous literature were included in multivariable GEE models. Last, using the merged clinical encounter and GDPH surveillance data, we summarized diagnostic results among patients who were HIV or HCV tested during IDU-related encounters, and among those not tested at clinical encounters, and the frequency of HIV or HCV diagnoses post-discharge reported to the GDPH by December 31, 2019.

SAS Software 9.4 was used for all statistical analyses. Our study was reviewed and approved by Emory University, GDPH, and Georgia State University Institutional Review Boards and the local Grady Research Oversight Committee.

Results

IDU-related Encounters

We identified 1069 IDU-related encounters spanning January 1, 2012 to December 31, 2018. Of the total IDU-related encounters, 729 (68.2%) were eligible for HIV testing and 793 (74.2%) were eligible for HCV testing. The remaining encounters were among patients who had previous HIV (31.8%) and/or HCV (25.8%) diagnoses. Of encounters among patients eligible for HIV testing, 221 (30.3%) were among patients with repeat IDU-related encounters and of those eligible for HCV testing 215 (27.1%) were among patients with repeat IDU-related encounters (data not shown).

HIV or HCV Testing in IDU-related Encounters

The majority of IDU-related encounters were among persons aged 40–64 years, male, Black/African American, diagnosed with an SSTI, uninsured, and admitted for inpatient stays

(Table 2). HIV testing occurred in 214 encounters (29.3% of eligible), and HCV testing occurred in 97 encounters (12.2% of eligible) (Table 2). HIV and HCV testing were less likely to occur in encounters with Black/African American patients compared those with white patients (23.5% vs. 41.7% for HIV testing; 9.6% vs. 18.1% for HCV testing). Frequency of testing also differed among encounters based on discharge year and hospital stay type, diagnosis of IE or osteomyelitis (HCV only), patient age (HIV testing only), and patient insurance type (HIV testing only).

In multivariate analysis, HIV testing was less likely to occur in encounters with Black/African American patients compared to in those with white patients (adjusted OR [AOR]=0.43, 95% CI= 0.29-0.63, *P* <0.01) and in encounters with patients with Medicare/Medicaid compared to those with self-pay/uninsured patients (AOR=0.65, 95% CI = 0.44-0.95, *P*=0.03) (Table 3). HIV testing was more likely to occur in encounters during 2014-2015 compared to encounters during 2012-2013 (AOR=5.15, 95% CI = 2.82-9.39, *P* <0.01) or 2016-2018 (AOR=4.73, 95% CI =2.72-8.23, *P* <0.01), and in encounters requiring an inpatient stay 1–4 days (AOR=2.55, 95% CI = 1.59-4.09, *P* <0.01), or inpatient stay 5 days or longer (AOR=3.70, 95% CI=2.30-5.95, *P* <0.01), compared to an ED visit.

HCV testing was less likely to occur in encounters with Black/African American patients compared to those with white patients (AOR=0.43, 95% CI = 0.26-0.72, *P* <0.01). HCV testing was more likely to occur in IDU-related encounters during 2014–2015 (AOR=2.42, 95% CI = 1.17-5.02, *P*=0.02) or 2016–2018 (AOR=3.74, 95% CI =1.93-7.24, *P* <0.01), compared to encounters during 2012–2013. HCV testing was also more likely to occur in encounters requiring hospital stays 5 days or longer (AOR=4.49, 95% CI = 2.78-7.25, *P* <0.01) compared to those requiring shorter stays.

HIV and HCV Test Results

Of the 214 IDU-related encounters in which HIV testing occurred, 213 (99.5%) tests yielded negative results, and one (0.5%) yielded a positive result (Figure 1). Of the 515 IDU-related encounters in which HIV testing did not occur, 24 (4.7%) were with patients later diagnosed with HIV (reported to GDPH before January 2020). Among patients who were not HIV tested at the time of their IDU-related encounter, the median time from discharge to HIV diagnosis was 1.67 years (Interquartile Range [IQR]=0.89-3.02) (data not shown in figure).

Of the 97 IDU-related encounters in which HCV testing occurred, 76 (78.3%) tests yielded negative results, and 21 (21.7%) yielded positive results for HCV antibody or RNA (Figure 2). Of the 696 IDU-related encounters in which HCV testing did not occur, 133 (19.1%) were with patients later diagnosed with HCV (reported to GDPH before January 2020). Among patients not HCV tested at the time of encounter, the median time from discharge to HCV diagnosis was 1.86 years (IQR=0.85-3.70) (data not shown in figure).

Discussion

Of IDU-related encounters in an Atlanta metro area hospital during 2012–2018, HIV testing occurred in just 29.3%, and HCV testing occurred in just 12.2%. Among patients not HIV or HCV tested at the time of their IDU-related encounter, 4.7% were later diagnosed with HIV and 19.1% were later diagnosed with HCV. Many patients also had repeat IDU-related encounters during this time period; 30.3% of encounters eligible for HIV testing and 27.1% of encounters eligible for HCV testing were among patients with previous encounters. These findings indicate substantial opportunities to prevent HIV and HCV transmission and improve the health of PWID through increased HIV and HCV testing among patients in clinical care.

Black/African American patients were less likely to be tested for both HIV and HCV compared to white patients. In 2018, white people accounted for 46% of HIV diagnoses among PWID, and Black/African American persons accounted for 26% of HIV diagnoses.[30] While the number of HCV and HIV diagnoses may be greater among white PWID than among Black PWID, racial disparities remain when the population-level racial distribution is taken into account. Additionally, if testing is less frequent among Black/African American PWID in other settings as we observed here, national rates of diagnoses among PWID could be underestimated for Black/African American persons compared to white persons. Black/African American persons living with HIV are more likely than white persons to be undiagnosed, have higher HIV incidence rates, and less likely to be linked to HIV care or be virally suppressed.[1,31,32] Testing all patients presenting with IDU indications for HIV and HCV regardless of race can help to address racial disparities in HIV and HCV infections and clinical outcomes.

Notably, the frequency of HIV and HCV testing in IDU-related encounters improved over time. This may be partially attributed to this hospital's implementation of routine opt-out HIV testing in the ED in 2013 and in inpatient settings in 2017. Routine opt-out HCV testing also launched in late 2012, implemented only in the primary care clinics until 2016, followed by the inpatient service in 2017. However, this screening targeted those born between 1945-1965. In April 2020, the hospital expanded from routine baby boomer screening to universal screening for all individuals aged 18–79 years in both ED and inpatient settings based on the new CDC and United States Preventive Services Task Force (USPSTF) guidelines. Of note, uninsured patients were more likely to receive HIV testing than those with Medicare/Medicaid. While Medicaid covers medically necessary HIV testing, states must opt-in to providing routine HIV screening, and unfortunately Georgia has not done so.[33]

During recent years, uptake of CDC HIV and HCV testing guidelines has improved among providers in the U.S.[34] However, our results identified many missed testing opportunities and continued needs for testing improvements in clinical settings. Our findings are consistent with other studies that have also reported missed opportunities for HIV and HCV testing among PWID at risk for HIV and HCV infection.[13,16] Developing algorithms in electronic medical records as reminders for simultaneous HIV and HCV testing may be most efficacious in the uptake of CDC's HIV and HCV testing recommendations for PWID and reduce missed opportunities for testing. Our study also found particularly low HIV and HCV testing rates in the ED. Ensuring collaboration between ED and infectious disease physicians may increase testing in the ED and result in more opportunities to diagnose and link patients to HIV and HCV care.

In our study, the median time to HIV diagnosis was 1.67 years and 1.86 years to HCV diagnosis among patients not tested at the time of IDU-related encounters, suggesting some infections may have been diagnosed earlier in the clinical setting. The availability of effective treatment for both HIV (antiretroviral therapy) and HCV (direct-acting antivirals), and the impact of treatment on long-term morbidity and mortality, makes testing and early diagnoses particularly critical. Treatment outcomes for both HIV and HCV infections are greatly improved when diagnoses are made early in infection. Additionally, clinical settings may provide ideal opportunities to link PWID to other services including pre-exposure prophylaxis (PrEP) which is up to 74% effective for HIV prevention among PWID.[35] Linkage to other services offered to PWID may include referrals to SSPs where available and medication assisted treatment (MAT) when appropriate.

This study has limitations. First, our findings are limited to information available in medical records. We do not know if individuals were recently tested in a previous setting, and hospital providers opted to not test based on CDC recommendations for testing at least once a year.

Second, we were limited to the combination of a previous diagnosis being noted in the medical record and surveillance data from GDPH in determining which IDU-related encounters were eligible for HIV or HCV testing. It is possible that individuals not residing in Georgia could have been diagnosed in another state and not transferred to Georgia's surveillance registry, although this possibility is minimal given greater than 90% of encounters had a Georgia residence. Last, there is no formal ICD-9 or ICD-10 code to identify IDU behavior. The ICD-9 and ICD-10 diagnostic codes used to classify IDU behavior are imperfect in terms of sensitivity and specificity for correctly classifying a patient as a current PWID, but previous studies have shown these codes perform relatively well in identifying PWID.[36,37]

Conclusion

Increasing HIV and HCV testing in settings where high-risk PWID present for care is critical for improving patient health and preventing onward transmission. PWID seeking clinical care for IDU-related conditions should be among the highest priority populations for testing. Strategies should focus on increased and equitable testing for PWID across racial/ethnic groups and with various insurance/payer types and should focus particularly on increasing testing in EDs. Novel data sources such as linkage of surveillance and clinical data may help hospitals and other clinical settings to identify HCV and HIV testing patterns and to ensure equitable and timely care for PWID populations.

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Table 1. International Classification of Diseases, Ninth and Tenth Revisions, Codes Used to Identify Patients with Injection Drug Use Behavior

Injection Drug Use-related Conditions		
	ICD-9 codes	ICD-10 codes
Infective Endocarditis	421,421.1,421.9,424.9	I33.0,I33.9,I38,I39,B37.6
Osteomyelitis	730.00,730.01,730.02,730.03,730.04,730.05, 730.06,730.07, 730.08,730.09, 730.20,730.21, 730.22,730.23, 730.24,730.25, 730.26,730.27, 730.28,730.29	M86.10,M86.20,M86.119,M86.219,M86.229, M86.139,M86.239,M86.149,M86.249 M86.159,M86.259,M86.169,M86.269,M86.179,M86.279,M86.18,M86.28,M86.19,M86.29,M86.9
Skin and Soft Tissue Infections	324,324.1,324.9, 326, 040.00,681, 681.01, 681.02, 681.1, 681.11, 681.9, 682, 682.1-682.9, 785.4, 728.86, 707.1, 707.8, 707.9, 451.0-451.9, 567.2, 569.5, 572.0, 590.1, 723.6, 729.3	G06.0, G06.1, G06.2, G09, A48, I96, K65.0-K65.9, M72.6, L02.0-L02.93, L03.0-L03.91, L97.1-L97.929, L98.8, M793, I80, K63.0, K75.0, M54.0, N10

Substance Use Diagnoses		
	ICD-9 codes	ICD-10 codes
Opioid	304.0-304.3, 304.70-304.73, 305.5-305.53, E850.0-E850.2, 965.00, 965.01, 965.02, 965.09	F11, T40.0 -T40.4, T40.6,
Cocaine	304.20-304.23, 305.60-305.63, 970.81	F14, T40.5

Amphetamine	304.4-304.43, 305.70-305.73, 969.72	F15, T43.60, T43.62, T43.69
Sedative	304.10-304.13, 305.40-305.43,967.0,E852.8,E852.9	F13, T42.3, T42.4, T42.5, T42.6, T42.7, T42.8
Hallucinogen	304.50-304.53, 305.30-305.33,969.6	F16, T40.9
Other	304.60-304.63, 304.80-304.93, 305.90-305.93, 966	F19, T42, T43.6, T43.8, T43.9

Table 2. Characteristics of IDU-Related Encounters Eligible for HIV and HCV Testing, 2012-2018

	HIV Testing Performed During Encounter				HCV Testing Performed During Encounter			
Characteristics	**Total Encounters n (%)**	**Yes n (%)**	**No n (%)**	***P* value**	**Total Encounters n (%)**	**Yes n (%)**	**No n (%)**	***P* value**
Total	729	214 (29.3)	515 (70.6)		793	97 (12.2)	696 (87.8)	
Age Group, years				<0.01				0.27
16–39	307 (42.1)	110 (35.8)	197 (64.2)		327 (41.2)	45 (13.8)	282 (86.2)	
40–64	422 (57.9)	104 (24.6)	318 (75.4)		466 (58.8)	52 (11.2)	414 (88.8)	
Sex				0.91				0.91
Female	302 (41.4)	88 (29.1)	214 (70.9)		290 (36.6)	61 (12.1)	442 (87.9)	
Male	427 (58.6)	126 (29.5)	301 (70.5)		503 (63.4)	36 (12.4)	254 (87.6)	
Race/ethnicity				<0.01				<0.01
Black/African American	494 (67.8)	116 (23.5)	378 (76.5)		563 (71.0)	54 (9.6)	509 (90.4)	
White	218 (29.9)	91 (41.7)	127 (58.3)		210 (26.5)	38 (18.1)	172 (81.9)	
Other[a]	17 (2.3)	7 (41.2)	10 (58.8)		20 (2.5)	5 (25.0)	15 (75.0)	
Discharge Year				<0.01				<0.01
2012–2013	171 (23.4)	18 (10.5)	153 (89.5)		234 (29.5)	13 (5.6)	221 (94.4)	
2014–2015	230 (31.6)	74 (32.2)	156 (67.8)		241 (30.4)	26 (10.8)	215 (89.2)	
2016–2018	328 (55.0)	122 (37.2)	206 (62.8)		318 (40.1)	58 (18.2)	260 (81.8)	
Infective Endocarditis/ Osteomyelitis Diagnosis								<0.05
Yes	75 (10.3)	21 (28.0)	54 (72.0)	0.79	78 (9.8)	15 (19.2)	63 (80.8)	
No	654 (89.7)	193 (29.5)	461 (70.5)		715 (90.2)	82 (11.5)	633 (88.5)	
Skin Soft Tissue Infection Diagnosis								0.03
Yes	681 (93.4)	203 (29.8)	478 (70.2)	0.31	743 (93.7)	86 (11.6)	657 (88.4)	
No	48 (6.6)	11 (22.9)	37 (77.1)		50 (6.3)	11 (22.0)	39 (78.0))	
Health Insurance Type				<0.01				0.52
Medicare/Medicaid	255 (35.0)	57 (22.4)	198 (77.6)		307 (38.7)	35 (11.4)	272 (88.6)	
Self-Pay/Uninsured	444 (60.9)	149 (33.6)	295 (66.4)		453 (57.1)	56 (12.4)	397 (87.6)	
Private Insurance/Other	30 (4.1)	8 (26.7)	22 (73.3)		33 (4.2)	6 (18.2)	27 (81.8)	
Hospital Stay Type				<0.01				<0.01
ED	237 (32.5)	41 (17.3)	196 (82.7)		253 (31.9)	1 (0.4)	252 (99.6)	
Inpatient, 1–4 days	222 (30.5)	72 (32.4)	150 (67.6)		251 (31.7)	31 (12.3)	220 (87.7)	

Inpatient, 5+ days	270 (37.0)	101 (37.4)	169 (62.6)	289 (36.4)	65 (22.5)	224 (77.5)

Abbreviations: IDU, injection drug use; HIV, human immunodeficiency virus; HCV, hepatitis C virus

[a]Other includes Hispanic/Latino, Asian, and Mixed Race

Table 3. Patient and Encounter Characteristics and HIV Testing during IDU-Related Encounters, 2012-2018: Results from Unadjusted and Adjusted GEE models.

Characteristics	Unadjusted Odds Ratios for HIV testing (95% CI)	*P* value	Adjusted Odds Ratio for HIV testing (95% CI)	*P* value
Age Group, years				
16–39	1.69 (1.22-2.33)	0.002	1.31 (0.89-1.93)	0.17
40–64	Reference		Reference	
Sex				
Female	Reference		Reference	
Male	1.02 (0.74-1.41)	0.89	1.14 (0.80-1.63)	0.46
Race/ethnicity				
Black/African American	0.42 (0.30-0.58)	<0.01	0.43 (0.29-0.63)	<0.01
White	Reference		Refence	
Other[a]	0.99 (0.39-2.53)	0.98	1.22 (0.49-3.00)	0.67
Discharge Year				
2012–2013	Reference		Reference	
2014–2015	4.03 (2.31-7.02)	<0.01	5.15 (2.82-9.39)	<0.01
2016–2018	5.03 (2.97-8.51)	<0.01	4.73 (2.72-8.23)	<0.01
Infective Endocarditis/ Osteomyelitis Diagnosis				
Yes	0.93 (0.51-1.68)	0.81	0.65 (0.29-1.45)	0.29
No	Reference		Reference	
Skin Soft Tissue Infection Diagnosis				
Yes	1.44 (0.69-3.03)	0.34	1.36 (0.49-3.81)	0.55
No	Reference		Reference	
Health Insurance Type				
Medicare/Medicaid	0.57 (0.40-0.81)	<0.01	0.65 (0.44-0.95)	0.03
Self-Pay/Uninsured	Reference		Reference	
Private Insurance/Other	0.73 (0.32-1.66)	0.45	0.49 (0.21-1.15)	0.10
Hospital Stay Type				
ED	Reference		Reference	
Inpatient, 1–4 days	2.29 (1.48-3.54)	<0.01	2.55 (1.59-4.09)	<0.01
Inpatient, 5+ days	2.86 (1.87-4.35)	<0.01	3.70 (2.30-5.95)	<0.01

Abbreviations: CI, confidence interval; HIV, human immunodeficiency virus; IDU, inject drug use

[a]Other includes Hispanic/Latino, Asian, and Mixed Race

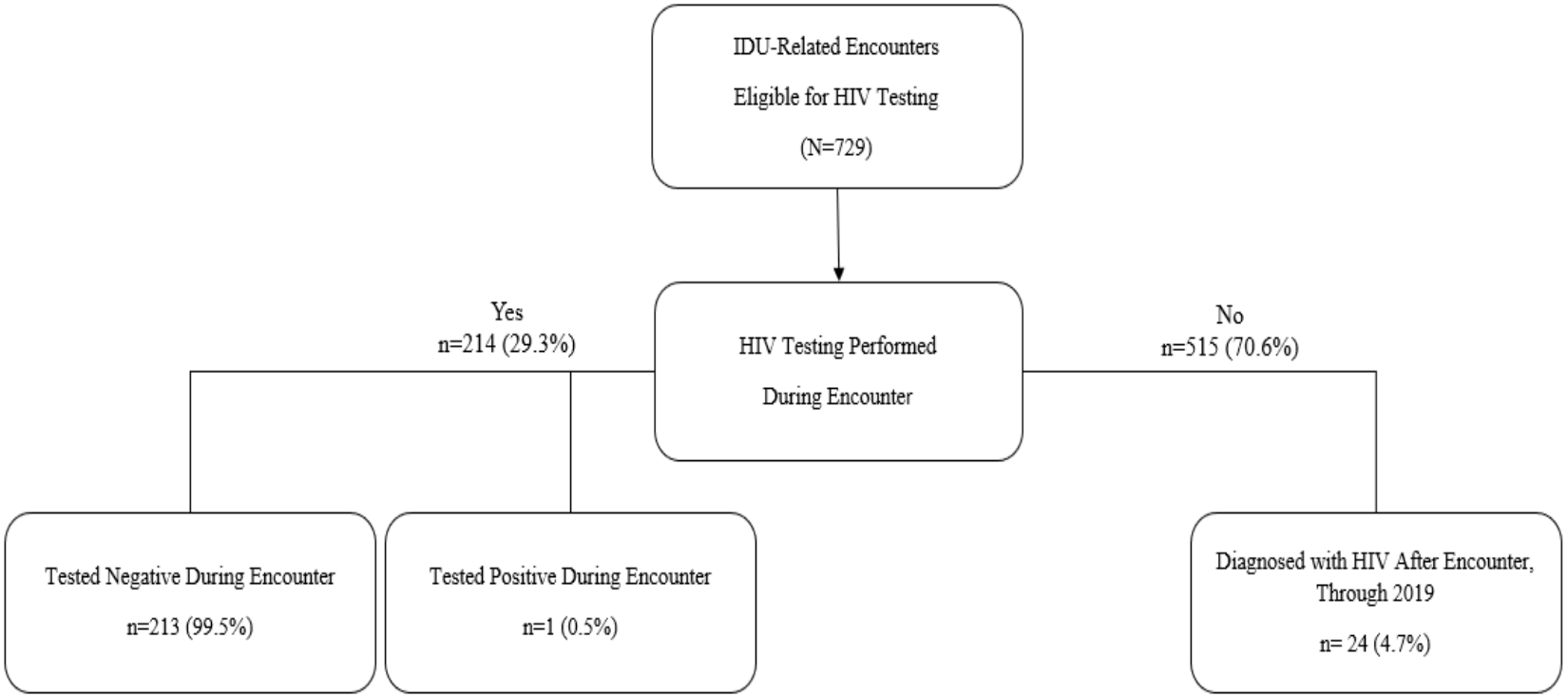
Table 4. Patient and Encounter Characteristics and HCV Testing during IDU-Related Encounters, 2012-2018: Results from Unadjusted and Adjusted GEE models.

Characteristics	Unadjusted Odds Ratio for HCV testing (95% CI)	*P* value	Adjusted Odds Ratio for HCV testing (95% CI)	*P* value
Age Group, years				
16–39	1.26 (0.83-1.92)	0.28	1.00 (0.61-1.65)	0.99
40–64	Reference		Reference	
Sex				
Female	Reference		Reference	
Male	0.98 (0.64-1.50)	0.91	1.04 (0.66-1.64)	0.87
Race/ethnicity				
Black/African American	0.48 (0.31-0.75)	<0.01	0.43 (0.26-0.72)	<0.01
White	Reference			
Other[a]	1.50 (0.51-4.46)	0.46	1.24 (0.35-4.40)	0.74
Discharge Year				
2012–2013	Reference		Reference	
2014–2015	2.06 (1.03-4.10)	0.04	2.42 (1.17-5.02)	0.02
2016–2018	3.77 (2.00-7.09)	<0.01	3.74 (1.93-7.24)	<0.01
Infective Endocarditis/ Osteomyelitis Diagnosis				
Yes	1.87 (1.04-3.36)	0.04	0.56 (0.18-1.74)	0.31
No	Reference		Reference	
Skin Soft Tissue Infection Diagnosis				
Yes	0.46 (0.23-0.91)	0.03	0.35 (0.10-1.27)	0.11
No	Reference		Reference	
Health Insurance Type				
Medicare/Medicaid	0.91 (0.59-1.41)	0.67	0.87 (0.53-1.42)	0.57
Self-Pay/Uninsured	Reference		Reference	
Private Insurance/Other	1.59 (0.65-3.90)	0.31	0.89 (0.32-2.45)	0.82
Hospital Stay Type				
0–4 days[b]	Reference		Reference	
5+ days	4.29 (2.73-6.74)	<0.01	4.49 (2.78-7.25)	<0.01

Abbreviations: CI, confidence interval; HCV, hepatitis C virus; IDU, injection drug use

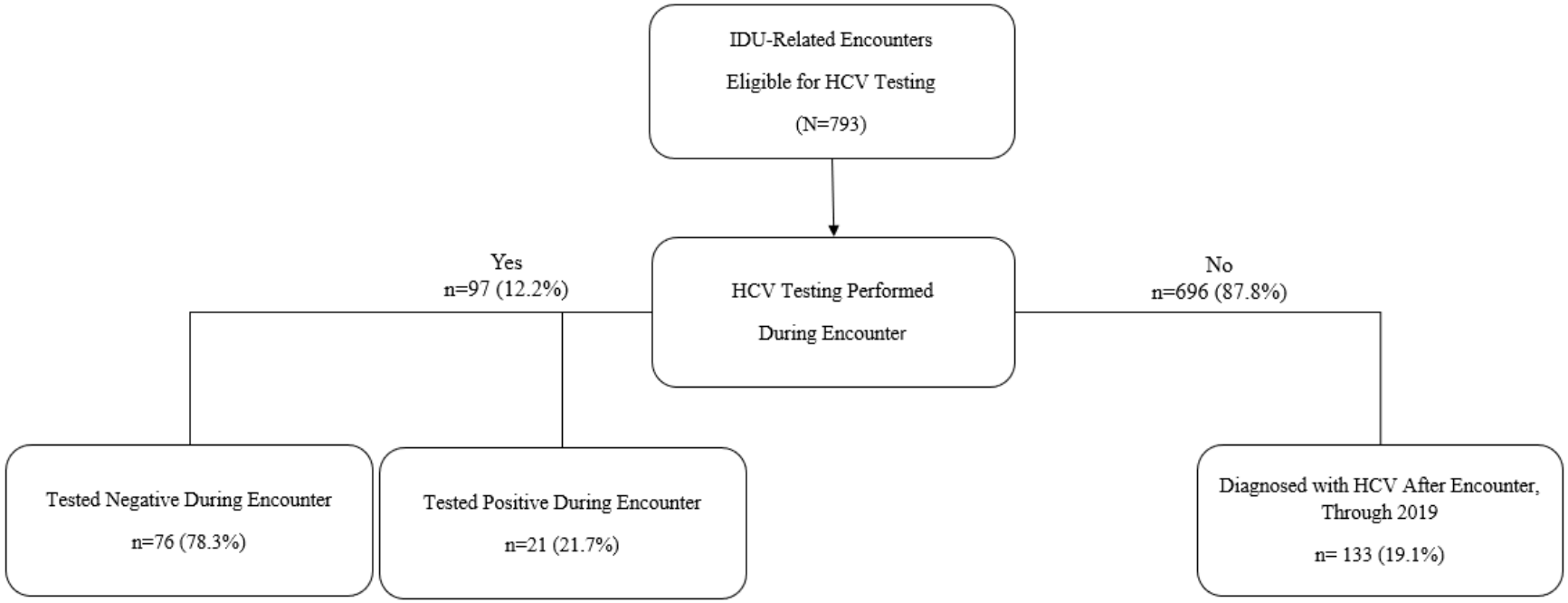
[a]Other includes Hispanic/Latino, Asian, and Mixed Race
[b]ED and Inpatient, 1-4 days levels for hospital stay type are further collapsed together for the HCV Model

Figure 1. HIV Test Results for Tests Administered in IDU-Related Encounters (2012–2018) and through 2019 for Patients not Tested in IDU-related Encounters, 2012–2019



Abbreviations: HIV, human immunodeficiency virus; IDU, injection drug use

Figure 2. HCV Test Results for Tests Administered in IDU-Related Encounters (2012–2018) and through 2019 for Patients not Tested in IDU-related Encounters, 2012–2019



Abbreviations: HCV, hepatitis C virus; IDU, injection drug use

Chapter 4: Trends in Hepatitis C Virus Among People Living with HIV in Georgia, 2014-2019

Abstract

Background: Hepatitis C Virus (HCV), if untreated, leads to poor health outcomes including liver disease and death, particularly among people living with HIV (PLWH). We describe trends over time in the percentage, characteristics, and HIV care outcomes of PLWH in Georgia who were co-diagnosed with HCV infection from 2014–2019.

Methods: We constructed a retrospective cohort of PLWH using matched HIV and HCV case surveillance data from persons diagnosed from January 1, 2014 – December 31, 2019. We estimated trends over time in HCV co-diagnoses among the cohort of PLWH by demographic characteristics and HIV care outcomes from 2014–2019 using bivariate linear regression models.

Results: From 2014–2019, 1,183 (3.8%) PLWH were diagnosed with HCV infection. During this time period, the percentage of PLWH newly co-diagnosed with HCV increased from 7% to 24% (β = 0.03, *P* for trend <0.01) among persons born during 1980–1989, and from 1% to 10% (β = 0.01, *P* for trend <0.01) among persons born in 1990 or later. The percentage of PLWH newly co-diagnosed with HCV increased from 43% to 61% (β = 0.03, *P* for trend <0.01) among persons with male-to-male sexual contact.

Conclusion: Strategies to increase prevention, diagnosis, and treatment of PLWH co-diagnosed with HCV infection are needed. Increasing routine HCV testing among PLWH and promptly treating persons with HCV infection can reduce associated poor health outcomes. PLWH who are younger, PWID or MSM should be prioritized for preventing and treating HIV/HCV co-infection.

Introduction

In 2019, approximately 1.2 million adults in the United States (U.S.) were estimated to be living with HIV, with approximately 67,000 individuals living with HIV in Georgia.[1] People living with HIV (PLWH) are at increased risk for comorbidities including hepatitis C virus (HCV) given similar transmission routes (i.e., unsafe injection practices, condomless anal sex). The prevalence of HCV coinfection among PLWH is estimated to be 2.4%[2] and is likely underestimated due to underreporting of HCV infection in the U.S.[3]

People coinfected with HIV and HCV are at increased risk for adverse health outcomes including severe liver disease[4], progression of HIV infection to late stage acquired immunodeficiency syndrome (AIDS), and mortality.[5,6] Advancements in direct-acting antiviral (DAA) therapies can effectively treat HCV infection, preventing serious liver disease complications and improving quality of life, but are costly to the healthcare system.[7] Identifying characteristics of PLWH at increased risk for HCV infection can help target HCV prevention strategies, and this is especially important because the epidemiologic profile of people with HCV infection is currently shifting. Previously affecting primarily older individuals in the "baby boomer" generation (i.e., born 1945 to 1965), HCV infections are now more prominent among younger populations, due to increasing injection drug use (IDU) associated with the opioid epidemic.[8-11] Additionally, men who have sex with men (MSM) and others who engage in condomless anal sex increasingly have risk for HCV infection.[12]

Due to geographic differences in HCV epidemics, understanding geographically-specific changes over time in the characteristics of PLWH who are co-diagnosed with HCV infection is important for informing local surveillance, prevention, and treatment strategies. Overall, there are limited HIV/HCV coinfection studies[13-15] using state surveillance data, especially in the South, describing characteristics of coinfected populations and none examining trends over time in HCV diagnoses among PLWH. This study proposes the first match of HIV and viral hepatitis surveillance data at the Georgia Department of

Public Health (GDPH) to 1) determine the percentage of PLWH who are co-diagnosed with HCV infection from 2014 to 2019 and 2) describe trends during this time in demographic characteristics and HIV care outcomes among PLWH co-diagnosed with HCV infection.

Methods

Study design

We matched HIV and HCV case surveillance data from GDPH to construct a retrospective cohort of PLWH. Using this retrospective cohort, we described trends over time in the percentage and characteristics of PLWH in Georgia who were co-diagnosed with HCV infection. The study was reviewed and approved by the institutional review boards at GDPH and Georgia State University.

Study population

Confirmed adult HIV cases[16] (greater than or equal to 13 years of age at time of diagnosis) who were diagnosed by December 31, 2013, alive through December 31, 2019, and living in Georgia through December 31, 2019 were included in the cohort. Cases with reported perinatal, hemophilia, or blood transfusion exposure were excluded (2.77%). All confirmed HCV cases[17,18] diagnosed during January 1, 2014 – December 31, 2019 were included in HCV surveillance data used for the match.

Data Linkage

HIV case records meeting inclusion criteria were matched to HCV case records in order to identify persons who were co-diagnosed with HIV and HCV infections. Linkage occurred using Registry Link Plus™ [19] by GDPH staff. Probabilistic linkage using a matching algorithm including first name, last name, and date of birth was used to match cases. The GDPH manually reviewed cases to determine final matches.

Measures

We defined HIV/HCV co-diagnosis using the following criteria: 1) diagnosed with HIV on or before December 31, 2013; 2) alive and residing in Georgia as of December 31, 2019; and 3) newly diagnosed with HCV infection between January 1, 2014 – December 31, 2019. Characteristics of persons in the cohort were drawn from HIV surveillance records, due to better completion of key variables than observed in the HCV case surveillance data. Retention in HIV care was defined as 2 or more CD4 test or viral load (VL) measures at least 3 months apart during 2019. Viral suppression was defined as VL <200 copies/ml at most recent VL measure in 2019. Additional characteristics were categorized as follows: birth year cohort based on date of birth year (<1960, 1960–1969, 1970–1979, 1980–1989, ≥ 1990), HIV year diagnosis cohort (<2000, 2000–2010, 2010+), race/ethnicity (Black/non-Hispanic, White/non-Hispanic, Hispanic/Latino, other/unknown [i.e., American Indians/Alaska Natives, Asian, Native Hawaiian/Pacific Islander, Multi-race]), transmission category (male-to-male sexual contact [MSM], injection drug use [IDU], both MSM & IDU, heterosexual contact, other/unknown), and sex at birth (male, female).

Statistical Analysis

Demographic characteristics were summarized using frequencies and medians (Table 1). The percentage of people newly co-diagnosed with HIV/HCV in each year was computed using the number of people matched to the HCV case surveillance registry as the percentage numerator and the cohort of PLWH (previously undiagnosed with HCV at the beginning of each year) as the denominator. Median time between HIV diagnosis and HCV diagnosis was calculated. Characteristics between people co-diagnosed with HIV/HCV infection compared to those diagnosed with HIV only were compared using percentages in each population sub-group and chi-square tests or global F-tests. Bivariate linear regression (ordinary least squares) was used to estimate trends over time in HCV co-diagnoses among the cohort of PLWH by demographic characteristics, retention in HIV care status, and HIV viral suppression status during 2014–2019 (Table 2). Beta-coefficients for year represent the average annual

change in the percentage of people with new HCV diagnoses. These were computed overall and by characteristics of people in the cohort. Percent change in HIV/HCV co-diagnoses from 2014 to 2019 was also estimated by cohort sub-groups. Statistical significance of chi-square or global F-tests and linear regression models was defined at the $\alpha = 0.05$ level. All statistical analyses were conducted using SAS Software 9.4.

Results

Characteristics of People HCV Diagnosed and Living with HIV

A total of 31,383 adults were diagnosed with HIV in Georgia as of December 31, 2013 and living in Georgia through December 31, 2019 (Table 1). Of these, 1,183 (3.8%) people were subsequently diagnosed with HCV between 2014 and 2019. The median age at co-diagnosis of HCV was 48 years old (Interquartile Range [IQR]: 39–57), and the median time to co-diagnosis of HCV was 13 years (IQR: 7-18). There were statistically significant differences in the characteristics of people with HIV/HCV co-diagnoses and those diagnosed with HIV only. People co-diagnosed with HIV/HCV were more likely than those diagnosed with HIV only to be retained in HIV care during 2019 (70% vs. 53%, $p<0.01$), virally suppressed (73% vs. 58%, $p <0.01$), and to have MSM (52% vs. 45%, $p<0.01$), and IDU (13% vs. 4%, $p<0.01$) risk factors.

Trends in Select Characteristics

Table 2 summarizes trends in demographic and HIV care outcomes among PLWH co-diagnosed with HCV infection by year of HCV diagnosis. Among persons born before 1960, the percentage of PLWH who were newly co-diagnosed with HCV decreased by 75% during 2014–2019, from 35% to 20% ($\beta = -0.03$, *P* for trend <0.01). Among persons born 1980–1989, the percentage PLWH who were newly co-diagnosed with HCV increased by 243% during 2014–2019, from 7% to 24% ($\beta = 0.03$, *P* for trend <0.01) and among persons born in 1990 and later increased by 900%, from 1% to 10% ($\beta = 0.01$, *P* for trend <0.01). Among male persons, the percentage of PLWH and newly co-diagnosed with HCV

increased by 9% during 2014–2019, from 79% to 86% (β = 0.02, *P* for trend =0.02) and similarly, among persons who engage in male-to-male sexual contact, increased by 42% from 43% to 61% (β = 0.03, *P* for trend <0.01). Among persons diagnosed with HIV before 2000, the percentage of PLWH and newly co-diagnosed with HCV decreased by 29% during 2014–2019, from 34% to 24% (β =-0.02, *P* for trend <0.01) and among persons diagnosed with HIV in 2010 and later increased by 44% from 18% to 26% (β = 0.02, *P* for trend =0.03). There were no statistically significant increases or decreases in HCV diagnoses among PLWH in HIV care outcomes or race/ethnicity.

Discussion

During 2014 and 2019, 3.8% of PLWH living in Georgia were newly co-diagnosed with HCV infection. Increasing trends over time in HCV diagnoses were observed among PLWH born from 1980–1990 (243% increase), born 1990 or later (900% increase), with male-to-male sexual contact (42% increase), and diagnosed with HIV in 2010 or later (44% increase). These findings support the need to prioritize HCV screening, prevention, and treatment interventions among PLWH who are younger and MSM in Georgia and states with similar HCV epidemics.

We observed increasing trends in HCV infections among young people, supporting previous research.[10,11,20,21] In 2019, 2.9 and 3.2 acute HCV cases per 100,000 people between 20–29 years old and 30–39 years old, respectively, were reported to national surveillance,[21] compared to 2.2 and 1.7 acute HCV cases per 100,000 people among these same age groups in 2014.[22] The opioid epidemic has contributed to the increases in HCV infections, especially in the Midwest and Appalachia and among younger popuations.[9] Although increases were most notable among younger populations, older populations born prior to 1960 and 1960-1969 accounted for the largest percentages of new HCV diagnoses among PLWH. Addressing prevention and treatment of recent infections among both older and younger populations may have the greatest impact on reducing future transmission. Our study is the first in South to present age-specific information on new HCV diagnoses among PLWH, and the second

in the South[14] to evaluate characteristics of people co-diagnosed with HIV/HCV infections and how they have changed over time. Combining public health HIV and HCV surveillance data with data on opioid and drug overdose hot spots may help to further identify areas where both younger and older PLWH at risk for HCV infection reside for targeted harm reduction, prevention, and treatment strategies.

Our study also found significantly increasing trends in HCV diagnoses among MSM. While most new HCV infections are attributable to unsafe IDU behavior,[8,21,23] condomless anal sex also increases risk for HCV infection among MSM,[12,24-27] making MSM another priority population for routine HCV testing. The Centers for Disease and Control and Prevention (CDC) recommends HCV testing at least once for PLWH and routinely for PWID.[28] It is likely our study found more HCV diagnoses among MSM (as a percentage of underlying infections) than among other risk groups, because MSM are more likely to be linked and retained in HIV care[29] compared to PWID and heterosexual populations. MSM may receive more routine testing and monitoring for comorbidities, including HCV, than other risk groups. However, while significant increasing trends attributable to IDU was not found, a higher percentage of PLWH and coinfected with HCV compared to HIV only was found. Future research is needed to fully understand the HCV epidemic among PLWH, MSM, and those with IDU behavior living in Georgia and other geographical regions.

We also found a statistically significant positive trend in HCV diagnoses among those diagnosed with HIV in 2010 and later. This may be partially reflecting increases in HCV diagnoses among young people but may also be attributed to better integration of care at HIV treatment clinics, including more routine testing of PLWH for comorbidities such as HCV infection. While routine HCV testing has improved since the revised CDC guidelines, there are still opportunities for improvement especially among populations disproportionally affected by HCV infection, including PLWH who experience more

adverse health outcomes (i.e., progression of chronic liver disease, complications with HIV infection) related to HCV infection.[30,31]

This is the first study that includes HIV care outcomes (e.g., retention in care and HIV viral suppression) as potential predictors of HCV co-diagnoses among PLWH. We did not detect changing trends in HCV diagnoses among PLWH by HIV retention in care and viral suppression status. However, compared to persons diagnosed with HIV only, there were higher percentages of people co-diagnosed with HIV/HCV who were retained in HIV care and virally suppressed. It is possible that either co-diagnosed persons are more engaged with the healthcare system due to comorbidities or that PLWH who are more engaged in care are more likely to have their HCV infections diagnosed. Either possibility underscores the importance of retention in care among PLWH, which improves health outcomes related to HIV and detection and management of co-morbidities such as HCV infection.[32-34]

The use of surveillance data can help guide prioritization efforts for HCV prevention, screening, and treatment interventions. According to our findings, populations that should be prioritized for screening and prevention in Georgia and states with similar HCV epidemics are younger people with risk factors and MSM. While our study did not find significant trends over time in HCV diagnoses by race/ethnicity, non-Hispanic Black persons accounted for the majority of new HCV diagnoses and continue to bear disproportionate rates of both HCV[35] and HIV[36] infections nationally, and both infections are less likely to be treated compared to non-Hispanic white persons.[37,38] Therefore, non-Hispanic Black persons should also be prioritized for HCV and HIV testing and treatment.

Our study has several limitations. First, findings rely on the last known reported address as Georgia which may underestimate retention and HIV viral suppression measures for people who may have unknowingly moved. Secondly, it should be noted these data represent only diagnosed HIV and HCV cases reported to GDPH. Many cases of HIV and HCV are undiagnosed and are not represented in these

findings. Therefore, our findings are an underestimate of the number of PLWH coinfected with HCV in Georgia during this time period. Third, because we were unable to differentiate between acute and chronic infections in these data, some HCV infections likely happened substantially earlier than the year of diagnosis. Finally, the increases in HCV diagnoses found among PLWH and MSM may be attributable to MSM being increasingly more likely to be linked and retained in HIV care[29] compared to PWID and heterosexual populations. It is possible the extent to which HCV diagnoses signal underlying burden of HCV disease is greater for MSM compared to PWID and heterosexual PLWH.

Conclusion

Strategies to increase preventing, diagnosing, and treating PLWH co-diagnosed with HCV infection are needed. Increasing routine HCV testing among PLWH and those with risk factors for HCV can have substantial impacts on health and resources required from the healthcare system. Treating PLWH infected with HCV can drastically reduce poor health outcomes including severe liver disease, progression of HIV infection, and death among PLWH. As younger populations currently have increasing HCV risk, there is an urgent need to both prevent new infections and diagnose and treat existing infections among young PLWH. Strategies to accomplish these efforts may vary by geography and will rely on routinely linking surveillance data to inform prioritization of PLWH at highest risk for HCV infection. Our study provides a methodological framework for states with similar HCV epidemics as Georgia and a model for using surveillance data to target prevention and treatment strategies.

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Table 1. Characteristics of People diagnosed with HCV and HIV compared to those diagnosed with HIV only, 2014-2019

Demographic Characteristics	People diagnosed with HIV & HCV n (%)	People diagnosed with HIV only n (%)	*P* value
Total, N (%)	1,183 (3.77)	30,200 (96.3)	
Median Age at HIV Diagnosis (IQR)	35 (27-43)	35 (26-42)	0.13
Retained in Care, 2019			
Yes	829 (70)	16,056 (53)	<0.01
No	354 (30)	14,144 (47)	
Virally Suppressed, 2019			<0.01
Yes	858 (73)	17,375 (58)	
No	325 (27)	12,825 (42)	
Birth Year Group			<0.01
<1960	325 (27)	6,078 (18)	
1960–1969	371 (31)	9,836 (31)	
1970–1979	239 (20)	7,285 (25)	
1980–1989	201 (17)	5,803 (22)	
≥1990	47 (4)	1,198 (4)	
Sex			<0.01
Male	991 (84)	22,227 (74)	
Female	192 (16)	7,973 (26)	
Race/ethnicity			0.02
White	189 (16)	5,788 (20)	
Black/African American	838 (71)	20,255 (67)	
Hispanic/Latino	70 (6)	2,075 (7)	
Other[a]	86 (7)	2,082 (7)	
HIV Transmission Category			<0.01
Male-to-male sexual contact	612 (52)	13,465 (45)	
Injection drug use	155 (13)	1,172 (4)	
Male to male sexual contact and injection drug use	91 (8)	885 (3)	
Heterosexual contact	130 (11)	4,949 (16)	
Other/Unknown[b]	195 (16)	9,729 (32)	
HIV Diagnosis Year			<0.01
<2000	330 (38)	6,733 (22)	

2000–2005	310 (26)	7,848 (26)
2006–2010	297 (25)	8,034 (27)
2010+	246 (21)	7,585 (25)

Abbreviation: HCV, Hepatitis C Virus; HIV, Human Immunodeficiency Virus; IQR, Interquartile Range

[a]Other races include American Indians/Alaska Natives, Asian, Native Hawaiian/Pacific Islander, and Multi-race

[b]Transmission categories identified as other or unknown were not statistically adjusted using multiple imputation methods; Other/Unknown includes risk factor not reported or not identified.

Table 2. Percentage of People Diagnosed with HCV and Living with HIV by Demographic Characteristics and HIV Care Outcomes, by HCV Diagnosis Year, 2014-2019

	People Diagnosed with HIV Only	People Diagnosed with HIV and HCV, By HCV Diagnosis Year								
	Total	2014	2015	2016	2017	2018	2019			
Characteristic	**n(%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**% Change, 2014-2019**	**β for trend**	***P* value for trend**
Total, N	30,200	227	193	201	205	190	167			
Retained in Care, 2019										
Yes	16,056 (53)	164 (72)	136 (70)	136 (68)	134 (65)	138 (73)	121 (72)	0	0.0004	0.96
No	14,144 (47)	63 (28)	57 (30)	65 (32)	71 (35)	52 (27)	46 (28)	0	-0.0004	0.96
Virally Suppressed, 2019										
Yes	17,375 (58)	168 (74)	143 (74)	155 (77)	140 (68)	137 (72)	115 (69)	-7	-0.0113	0.14
No	12,825 (42)	59 (26)	50 (26)	46 (23)	65 (32)	53 (28)	52 (31)	19	0.0113	0.14
Birth Year Group										
<1960	6,078 (18)	79 (35)	67 (35)	55 (27)	53 (26)	38 (20)	33 (20)	-75	-0.0345	<0.01
1960–1969	9,836 (31)	78 (34)	57 (30)	67 (33)	60 (29)	62 (33)	47 (28)	-18	-0.0075	0.34
1970–1979	7,285 (25)	51 (22)	38 (20)	39 (19)	34 (17)	46 (24)	31 (19)	-14	-0.0029	0.68
1980–1989	5,803 (22)	17 (7)	25 (13)	34 (17)	47 (23)	38 (20)	40 (24)	243	0.0321	<0.01
≥1990	1,198 (4)	2 (1)	6 (3)	6 (3)	11 (5)	6 (3)	16 (10)	900	0.0128	<0.01
Sex										
Male	22,227 (74)	179 (79)	157 (81)	170 (85)	179 (87)	162 (85)	144 (86)	9	0.0153	0.02
Female	7,973 (26)	48 (21)	36 (19)	31 (15)	26 (13)	28 (15)	23 (14)	-33	-0.0153	0.02
Race/ethnicity										
White	5,788 (20)	30 (13)	35 (18)	33 (16)	21 (10)	37 (20)	33 (20)	54	0.0085	0.18
Black/African American	20,255 (67)	163 (72)	134 (69)	149 (74)	149 (73)	130 (68)	113 (68)	-6	-0.0067	0.39
Hispanic/Latino	2,075 (7)	11 (5)	12 (6)	7 (3)	20 (10)	9 (5)	11 (7)	40	0.0032	0.42
Other[a]	2,082 (7)	23 (10)	12 (6)	12 (6)	15 (7)	14 (7)	10 (6)	-40	-0.0050	0.26
HIV Transmission Category										
Male-to-male sexual contact	13,465 (45)	97 (43)	89 (46)	112 (56)	109 (53)	103 (54)	102 (61)	42	0.0326	<0.01
Injection drug use	1,172 (4)	39 (17)	24 (12)	25 (12)	26 (13)	23 (12)	18 (11)	-35	-0.0098	0.09
Male to male sexual contact and injection drug use	885 (3)	26 (15)	15 (8)	11 (6)	16 (8)	11 (6)	12 (7)	-53	-0.0079	0.09
Heterosexual contact	4,949 (16)	29 (13)	28 (15)	20 (10)	18 (9)	21 (11)	14 (8)	-38	-0.0095	0.08

Other/Unknown[b]	9,729 (32)	36 (16)	37 (20)	33 (16)	36 (18)	32 (17)	21 (13)	-19	-0.0054	0.40
HIV Diagnosis Year										
<2000	6,733 (22)	78 (34)	57 (30)	64 (32)	45 (22)	46 (24)	40 (24)	-29	-0.0230	<0.01
2000–2005	7,848 (26)	62 (27)	45 (23)	54 (27)	55 (27)	54 (28)	40 (24)	-11	-0.0003	0.97
2006–2010	8,034 (27)	46 (20)	55 (29)	49 (24)	52 (25)	52 (27)	43 (26)	30	0.0082	0.27
2010+	7,585 (25)	41 (18)	36 (19)	34 (17)	53 (26)	38 (20)	44 (26)	44	0.0152	0.03

[a]Other races include American Indians/Alaska Natives, Asian, Native Hawaiian/Pacific Islander, and Multi-race

[b]Transmission categories identified as other or unknown were not statistically adjusted using multiple imputation methods; Other/Unknown includes risk factor not reported or not identified

Chapter 5: Dissertation Summary and Future Directions in Research

Dissertation Summary

People who inject drugs (PWID) are at risk for HIV and hepatitis C virus (HCV) infections, accounting for 7.2% of new HIV infections[1] and 67% of HCV infections, in 2019. Strategies to prevent HIV and HCV infection can be effective, if utilized. Pre-Exposure Prophylaxis (PrEP) is 74% effective in preventing HIV infection[2] and direct-acting antiviral (DAA) therapy is over 95% effective in treating HCV.[3] Use of syringe service programs (SSPs), reducing condomless sex, and increasing HIV and HCV testing are also effective in HIV and HCV prevention. Despite the effectiveness of these strategies, uptake remains low.[4-7] Thus, the three studies in this dissertation were designed to address these gaps by adding to the literature the incidence of HIV and HCV diagnoses among PWID post-clinical encounters, determining the gaps in HIV and HCV testing among PWID in a hospital setting, and examining trends in percentage of people living with HIV (PLWH) and newly co-diagnosed with HCV over the recent years. While other published studies continue to advance our knowledge in these areas, these three studies were either the first or adds to the limited knowledge particularly among PWID and coinfected infected individuals living in the South.

The first study addressed in this dissertation was innovative and the first, to our knowledge, to link HIV and HCV surveillance data to hospital records to examine HIV and HCV incidence in diagnoses among a cohort of PWID discharged from an urban hospital in the South. Findings from this study identify potential missed opportunities to prevention, diagnosis, and early treatment of HIV and HCV. Incidence rates were 9.3 and 42.9 per 1,000 person-years for HIV

and HCV, respectively. The majority of post-clinical encounter HIV and HCV diagnoses occurred among Black/African Americans and males. At the time of discharge from IDU-related clinical encounters, 282 (32.9%) patients had HIV diagnoses, 241 (28.1%) patients had HCV diagnoses, and 101 (11.8%) patients had both HIV and HCV diagnoses. There are many opportunities to decrease incidence among PWID starting with approaches when PWID are encountered in the hospital with IDU-related diagnoses. Beyond the preventative measures already discussed (i.e., PrEP, DAA, antiretroviral therapy [ART]) hospital settings can be ideal settings to increase HIV and HCV testing[8], and linkage to substance use treatment and harm reduction services.[9] These approach would substantially improve integration of care for PWID and reduce incidence in HIV and HCV infections.

Findings from the second study identified missed opportunities for HIV and HCV testing during IDU-related clinical encounters. Overall, testing improved during IDU-related encounters from 2102–2018; however, HIV testing occurred in just 29.3%, and HCV testing occurred in just 12.2%. Additionally, Blacks were less likely to be HIV and HCV tested. Early detection of HIV or HCV infection can improve HIV and HCV health outcomes. Thus, increasing testing among PWID in the hospital setting can be beneficial. More efforts and strategies should focus on universal testing in both the ED and inpatient setting and ensuring equitable testing for all race/ethnicities.

The third study presents opportunities to decrease HCV coinfection among PLWH. Among PLWH, 3.8% were newly co-diagnosed with HCV infection during 2014–2019. Increasing trends over time in HCV diagnoses were statistically significant among PLWH born 1980–1990 (243% increase), born 1990 and later (900% increase), men who have sex with men (MSM) (43% increase), and diagnosed with HIV in 2010 and later (44% increase). These findings

support the need to prioritize PLWH who are younger and MSM. Treating PLWH infected with HCV can drastically reduce poor health outcomes including severe liver disease, progression of HIV infection, and death among PLWH. The opioid epidemic has been attributed to rises in HCV infections especially in the Midwest and among younger populations.[10] However, strategies and target populations will differ by geography. Linking of surveillance data can inform these strategies locally in states.

Limitations

Each study had several limitations. The most critical limitation of this dissertation was the limitation of reported diagnoses to the Georgia Department of Public Health (GDPH). Thus, these data only represent diagnosed HIV and HCV infection. It is possible the diagnoses examined in study one and study three may be underestimated if individuals were not diagnosed by the end of our study period. For study one and study two, there is no formal ICD-9 or ICD-10 code to identify IDU behavior. The ICD-9 and ICD-10 diagnostic codes used to classify IDU behavior are imperfect in terms of sensitivity and specificity but previous studies have shown these codes perform relatively well in identifying PWID.[11,12] In each study, because we were unable to differentiate between acute and chronic infections in these data, some HCV infections likely happened substantially earlier than the year of diagnosis.

Future Research

As the opioid epidemic continues to evolve, risk for HIV and HCV infection increases. Future research can focus on creating longitudinal and experimental studies with PWID populations to further answer some of the questions addressed in this dissertation. Because PWID are heavily stigmatized, addressing healthcare needs when encountered and in a convenient and discrete way can be successful in reducing HIV and HCV infections among PWID. For HIV, PrEP is an

effective tool that can be used to prevent HIV. With advancements in injectable PrEP and rings that also incorporate birth control for women, interventions that aim to increase uptake of these tools could have significant impact. Additionally, interventions that can reduce viral load and increase viral suppression can be impactful, particularly among younger populations with cell phone access, text messaging reminders can be helpful. Studies should also help identify the barriers and facilitators to accessing PrEP, SSPs, maintaining viral suppression or accessing DAA treatment. Integrating care at SSPs by offering MAT, PrEP, ART, and DAA could also be effective in reducing barriers.

Future research should also continue routine use and linkage of HIV, HCV, overdose surveillance data and clinical data to identify prevention efforts among most at-risk populations. As the epidemic evolves it will be important to prioritize populations not just most affected currently (i.e., less than 40 years old, white)[13,14] but also where trends are evolving to other race/ethnicities (i.e., Black, Hispanic/Latino).[15] Routine linkage at health departments can help monitor these trends.

Lastly, there is a need for more public health resources and funding to prioritize surveillance and routine screening for HCV among those most at risk. Collaboration with community researchers to develop customized interventions for prevention and treatment informed by state surveillance systems can help guide recruiting populations disproportionally affected and most in need. Particularly, for HCV infection, there is a need for prevention of acute infections among PWID and younger populations and a need to make treatment of chronic infections equitable for Blacks living with HIV.

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