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Attribution of the Causes of Death in People Infected with HIV and/or Hepatitis C in Connecticut, 2003-2007

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Attribution of the Causes of Death in People Infected with HIV and/or Hepatitis C in Connecticut, 2003-2007

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Abstract

Introduction: This study examined the causes of death in Connecticut residents who were infected with hepatitis C and/or HIV/AIDS and died between 2003 and 2007. Disease surveillance and mortality data can provide important public health information that may be used to develop important public health programs, policies, or legislation. Underreporting of diseases in mortality data may lead to reduced public health funding.

Background: Hepatitis C and HIV/AIDS are two potentially fatal infectious diseases that have been reportable in Connecticut since 1994 and 1981, respectively. Mortality data in Connecticut contain information about the causes of death in a deceased individual, which may or may not encompass all actual causes.

Methods: The hepatitis C and HIV/AIDS databases were matched to death data from 2003 to 2007 using Link Plus, electronic matching software from the CDC. The match resulted in three de-identified databases: deceased hepatitis C cases, deceased HIV/AIDS cases, and deceased co-infected cases. Primary and underlying causes of death were examined.

Results: HIV disease was the primary cause of death in more than half of HIV/AIDS and co-infected cases while chronic hepatitis C was the primary cause of death in 6.7% of hepatitis C cases. In hepatitis C cases where the primary cause of death was liver disease, hepatitis C was listed as an underlying cause of death in 6.2% of those cases. Similar findings were shown in HIV/AIDS cases when major cardiovascular disease was the primary cause of death.

Conclusions: HIV/AIDS and hepatitis C are underreported on death certificates in Connecticut, especially when the person died of a condition possibly related to their infection. Hepatitis C was underreported more often than HIV/AIDS. Increased HIV and hepatitis C screening for at-risk persons, comprehensive prevention programs, education about the importance of death certificates and how to complete them, and data sharing between agency programs may help to reduce underreporting in mortality data.

Introduction

The Connecticut Department of Public Health and other state agencies collect many kinds of health-related data, which provide important information for state and federal policy-making. This information can be used to determine the burden of disease in a community, to tailor prevention programs, or to apply for state or federal funding, among other things. Disease surveillance and mortality data are two specific types of data that are collected and that can provide valuable information regarding the health of Connecticut's citizens. Hepatitis C and HIV/AIDS are long-standing reportable diseases in Connecticut. Hepatitis C is the number one bloodborne pathogen in the United States and can lead to chronic liver disease. HIV/AIDS is a well known and potentially fatal infectious disease that disproportionately affects minorities, injection drug users, and men who have sex with men.

Causes of death listed on death certificates may or may not encompass important underlying medical conditions. Underreporting or inaccurate reporting of the mortality of hepatitis C or HIV/AIDS cases could affect perceptions about their severity. If deaths that are actually related to hepatitis C or HIV/AIDS are not reported in mortality data, this may negatively impact prevention programs or funding sources and lead people to believe that the disease is less of a burden in their community. While it would be difficult, as part of this study, to assess whether or not the causes of death listed are accurate without a medical record review, it should be possible to hypothesize about underreporting that may exist on death certificates in Connecticut.

The primary aim of this study is to identify the causes of death in persons reported to be infected with hepatitis C and/or HIV/AIDS in Connecticut. Deaths must have occurred in Connecticut residents between 2003 and 2007. A secondary aim of this study is to develop a working hypothesis regarding underreporting of hepatitis C and/or HIV/AIDS on death certificates and to assess possible program and policy implications of this problem.

Study Hypotheses:

- Hypothesis 1: Hepatitis C and HIV/AIDS will be underreported on death certificates, even when the person suffered from a disease that was probably related to their infection.
- Hypothesis 2: Hepatitis C underreporting will be greater than HIV/AIDS underreporting.

Background

Hepatitis C

Hepatitis C is the most common bloodborne pathogen in the United States with an estimated 3.2 million people chronically infected nationwide.[1] The hepatitis C virus (HCV) causes inflammation of the liver, which can be acute or chronic. The Centers for Disease Control and Prevention (CDC) estimate that 75-85% of people infected with hepatitis C will become chronically infected, whereas the remaining people will clear virus from their system, although they will retain hepatitis C antibodies. Chronic HCV infection places people at higher risk for chronic liver disease, cirrhosis, and liver cancer and is currently the leading cause of liver transplants in the United States.[2]

Hepatitis C is transmitted primarily via percutaneous exposures to infected blood. The prevalence of antibodies to HCV (anti-HCV) is high among people who report a history of injection drug use, even if their last use was years ago.[1] Prior to 1992 there were no effective screening techniques to detect hepatitis C in the blood supply. Consequently, people who received blood transfusions prior to 1992 or clotting factor concentrates before 1987 have a higher prevalence of anti-HCV.[3]

Transmission of hepatitis C in a healthcare setting is not currently common, but has been reported. Healthcare workers may be at a higher risk for hepatitis C due to possible blood exposures at work. A needlestick exposure to HCV-positive blood poses a risk of HCV infection of about 1.8%, compared to 0.3% for HIV-positive blood or 6 to 30% for hepatitis B-positive blood.[4] Although the widespread use of standard precautions and infection control practices has made the likelihood of getting

HCV from a medical/dental procedure, hemodialysis, or other healthcare setting a rare occurrence, outbreaks have been reported.[5] These outbreaks were primarily associated with improper handling of injection equipment or medications, or re-use of syringes between patients.

HCV is not efficiently transmitted via sexual exposures, although certain sex practices may make transmission more likely (e.g. sexual practices that involve blood). The CDC does not currently recommend that people in a long-term monogamous relationship change their sex practices if one person is HCV positive.[3] However, a lifetime history of multiple sex partners may place a person at higher risk for HCV.[1]

Hepatitis C poses many challenges for detection and treatment. One challenge is that up to 60-70% of people with acute HCV infection are asymptomatic. Additionally, when they occur, symptoms of HCV are usually non-specific, such as fatigue, anorexia, abdominal pain, nausea, or vomiting.[3] Consequently, HCV infection can go undetected in a person for many years because individuals may have non-specific or no symptoms at all. This puts a person at risk for developing chronic liver disease and also increases the likelihood of transmitting the virus to others.

Unlike hepatitis A and B, there is no vaccine for hepatitis C. Although treatment options are available, they vary in efficacy and the side effects and cost can deter people from completing the entire regimen. The most common treatment is interferon with ribavirin, but treatment can cost $20,000 to $30,000 per year.[6] The most common HCV genotype in the U.S. in genotype 1 and it is also one of the hardest to treat.[2,6] Treatment for genotype 1 is effective at inducing a sustained

virologic response (no HCV RNA detectable in the blood 24 weeks after treatment ends) in only 50% of cases.[3]

Although hepatitis C primarily affects the liver, there are other medical conditions that have been linked to HCV infection. There is a strong association between HCV infection and essential mixed cryoglobulinemia, which can cause nerve and kidney disease; porphyria cutanea tarda, which can cause photosensitivity and skin blistering; and glomerulonephritis, a type of kidney disease where part of the kidney becomes damaged.[7] Hepatitis C is also significantly associated with albuminuria, which can be an indicator of kidney damage.[8] A study of data from the Veteran's Administration, which has the largest HCV screening program in the U.S., indicated that HCV positive patients were less likely to have chronic kidney disease at baseline, but at a greater risk to develop treated end-stage renal disease over time, which was defined as renal therapy with hemodialysis or kidney transplantation.[9] Another study found that HCV positive patients are also at increased risk for death, heart failure hospitalizations, and cardiovascular events.[10] Other conditions that may be associated with HCV infection include diabetes mellitus and non-Hodgkins lymphoma.[2]

Chronic hepatitis C infection is projected to place a large burden on the American healthcare system. Up to 20% of chronic HCV positive individuals will develop cirrhosis in their lifetime. Other liver complications may also develop, such as decompensated liver disease or hepatocellular carcinoma (HCC).[6] Currently, HCV infection causes an estimated 8,000 to 12,000 deaths per year and costs more than $600 million annually.[3,11] Mathematical modeling has projected that for the time

period of 2010 to 2019 there will be 165,900 deaths from HCV-related chronic liver disease and 27,200 deaths from HCV-related HCC. The direct cost to treat HCV-related disease during the same time period will be between $6.5 and $13.6 billion.[12] This dramatic increase will likely be due to the fact that most individuals currently infected with HCV were born between 1945 and 1964 and a large portion were infected through drug experimentation in the 1960s and 1970s.[1,6] Since HCV can take twenty to thirty years to lead to serious illness, the burden of HCV-related disease will continue to rise as these baby boomers age. Many HCV positive individuals are also uninsured or underinsured.[13,14] This means that Medicaid and Medicare bear a majority of the healthcare costs for HCV.

Hepatitis C is a prevalent public health problem in Connecticut. Both laboratories and physicians are required to report to the Department of Public Health (DPH) (DPH regulation 19a-36-A1 to 19a-36-A24). The hepatitis C registry at DPH contains records of HCV positive test results from 1994 through the present, with the exception of 1997-1998 when HCV was removed from the list of laboratory reportable significant findings.[15] There have been 24,834 confirmed hepatitis C cases reported to the DPH through December 31, 2008 and 1,247 deaths (5.0%). Deaths were obtained from matching State Vital Records Office death data to the hepatitis C database or occasionally from provider report. The rate of hepatitis C is higher in males, who represent 63% of cases, and in people between the ages of 40 and 59.[16]

HIV/AIDS

Human immunodeficiency virus (HIV) attacks the immune system. It is a serious, chronic disease that may progress to acquired immunodeficiency syndrome (AIDS), which is characterized by low white-blood cell counts and/or opportunistic infections and greatly increased risk of death.[17] People who have HIV/AIDS are more susceptible to infections, cancers, and other diseases because of their immunocompromised status. An estimated 1.1 million people in the U.S. are infected with HIV.[18]

HIV is primarily found in the blood, semen, or vaginal fluids of an infected person. Therefore, sexual contact with an infected person or contact with an infected person's blood (e.g. through contaminated injection equipment or blood transfusions prior to effective blood supply screening) puts people at risk for acquiring HIV. Additionally, HIV may be spread perinatally from a mother to her newborn, or after birth through breastfeeding.[17] Like hepatitis C, HIV is often asymptomatic for many years, and the CDC estimates that nearly one quarter of people in the U.S. who are HIV positive do not know it.[18] As a result, some people are not diagnosed until they develop AIDS and have symptoms of an opportunistic infection or cancer, representing lost opportunities for secondary prevention efforts and treatment.

The HIV epidemic has changed over the years. AIDS was first described as a syndrome present in young gay men, however, injection drug users, transfusion and blood product recipients, female sex workers, and female partners of bisexual men were also identified as at risk. Currently, HIV disproportionately affects blacks and Hispanics.[18] Young people are also at an increased risk for HIV due to a variety of

factors: earlier sexual debut, more sexual partners over a lifetime, high sexually transmitted disease (STD) rates among youth aged 13 to 19, and substance abuse.[19]

As a result of all of this, the CDC revised its testing recommendations for HIV in 2006.[20] Prior to this recommendation, HIV testing in most states was performed on an opt-in basis, where a person would either have to request or be offered the test, often undergo specific pre-test counseling, and give specific informed consent (either written or oral, depending on the state). The new recommendations eliminate the separate written consent and prevention counseling. They also recommend that HIV testing be performed on an opt-out basis, meaning that HIV testing would be performed unless the patient refuses. While state laws supersede the CDC recommendations, several states have modified their laws to reflect the new recommendations. As of July 1, 2009, Connecticut eliminated separate written consent from the general statutes for HIV testing.[21]

Because HIV compromises a person's immune system, a variety of infections, diseases, or conditions may occur as a person progresses to AIDS. Common conditions include recurrent bacterial infections, pneumocystis carinii pneumonia (PCP), Kaposi sarcoma, lymphomas, tuberculosis, HIV encephalopathy, toxoplasmosis of the brain, and wasting syndrome.[22] Since the advent of highly active antiretroviral therapy (HAART) in the 1990s, people receiving treatment are living longer with HIV and delaying progression to AIDS. While some drug resistance has occurred, in general, HAART has been highly effective in adding years of life and preventing a variety of opportunistic infections.[23,24]

People who are infected with HIV may be at higher risk for hepatitis C infection. Because both diseases are transmitted via percutaneous blood exposure, injection drug users are at the highest risk of being co-infected. Anywhere from 50 to 90% of HIV positive injection drug users are also infected with hepatitis C.[25] Co-infection with HIV and HCV can lead to a variety of health problems. One study showed that HIV/HCV co-infected individuals had two times the risk of developing an AIDS-defining illness when compared to HIV-positive individuals who were not co-infected. If cirrhosis was also present, there were even higher rates of certain AIDS-related illnesses.[26]

HIV/AIDS is a reportable disease in Connecticut. AIDS cases were made reportable in Connecticut in 1981, and HIV in adults were made reportable in 2002. In 2006, viral load results for HIV were made reportable.[27] From the beginning of public reporting until December 31, 2008 there have been 18,862 HIV/AIDS cases reported in Connecticut, with 8,699 deaths (46.1%). Deaths were obtained from matching State Vital Records Office death data to the HIV/AIDS database or occasionally from provider report. Nearly three-quarters of cases were diagnosed with HIV/AIDS between the ages of 30 and 49 and 66% are male. The most common risk factors identified among reported cases were injection drug use (IDU, 45%) and men who have sex with men (MSM, 22%).[28] In 2007, Connecticut was ranked 9th in the nation for its AIDS rate, at 15.1 cases per 100,000 people.[29] However, the rate of AIDS cases in a state can be a poor indicator of the level of HIV infection, due to varying levels of HAART use and thus, time to disease progression, among populations.

A match of Connecticut's HIV and hepatitis C registries was performed in 2009 at the DPH.[30] A risk factor or mode of transmission was known for 90% of HIV/AIDS cases, but for only 4% of hepatitis C cases. Hepatitis C cases were less likely to include information on mode of transmission because there was no statewide program to conduct follow-up on reported cases until 2008. The match used data from both registries from 1994 to 2007, resulting in 2,345 co-infected cases. This represented 24% of the HIV registry and 5% of the hepatitis C registry. Three-quarters of the cases had a risk of IDU. Furthermore, 47% of the HIV-positive IDU cases also were co-infected with hepatitis C, consistent with findings from other studies.[25]

These results underscore the need for public health intervention for populations at risk for both hepatitis C and HIV. They also highlight the importance of data sharing and collaboration between public health programs within state agencies. Although not easily accomplished in some states due to confidentiality constraints, matching between disease registries or from disease registries to vital statistics data may yield important information. The data matching of the HIV and hepatitis C registries done at DPH showed that co-infected persons are most likely to be IDUs. This implies that an increase in programs tailored to the IDU population, such as syringe exchange programs (SEPs), enhanced drug treatment, or educational prevention programs, may be necessary.

Mortality data

Mortality data are an important source of information about demographic, geographic, and disease information. The data can be used to describe mortality trends and life expectancy and can be an indicator of the burden of disease in a community. Mortality data are also necessary for identifying where public health prevention and education are needed and for enhancing surveillance systems.[31]

Connecticut law requires health care providers to complete a death certificate for all deaths and to report deaths with the certificate to the Department of Public Health, State Vital Records Office (CT General Statutes, chapter 93, section 7-62b). The death certificate is first filed in the town where the death occurred and then forwarded to the State Vital Records Office at DPH. This office maintains a registry of all births, deaths, fetal deaths, marriages, and civil unions in the state since July 1, 1897.[32] The attending physician or advanced practiced registered nurse must complete the medical portion of the death certificate at the time of death. Funeral directors or embalmers must complete an additional demographic section of the death certificate. However, the accuracy of mandatory reporters may be questionable. Depending on where the person died and how, a provider who was not the person's primary care provider – such as a medical examiner, pathologist, etc. – may complete the medical portion. Information on the death certificate must include, but is not limited to, the person's full name, date of birth and death, place of birth and death, race, education, primary cause of death, and up to 20 contributing causes of death.[33]

Mortality data are then reported nationally to the National Vital Statistics System, a division of the CDC. At the CDC, the raw data are coded into multiple-

cause-of-death data. This data coding is important because what is written on the actual death certificate may differ slightly from the death data that are sent back to the states. The actual death certificate codes are called *entity axis codes*, which are a direct transcription from the raw data on the death certificates. The *record axis* is a cleaned version of the *entity axis*. Data cleaning the *entity axis* may entail eliminating duplicate conditions or causes that violate logic (e.g. prostate cancer in a female) or combining related conditions for efficiency.[11] Studies have shown that in co-infected people HIV and hepatitis C are often combined into a single code for HIV in the *record axis*, despite being listed separately on the *entity axis*.[11] Therefore, if the *record axis* is used for mortality studies, this could lead to the underreporting of the burden of hepatitis C.

Current mortality data for HIV-infected people in Connecticut show that approximately one-third of known HIV-infected individuals had a primary cause of death that was not listed as HIV/AIDS.[34] This is consistent with New York City's findings as well.[35] It is possible that in these cases the actual causes of death were unrelated to HIV, such as accidental injuries. However, these deaths may also have been related to HIV, but the underlying HIV infection was not noted on the death certificate. For example, deaths from HIV opportunistic infections or cancers might have been attributed the proximate cause, such as the infection or cancer, but not to HIV. If this is the case, HIV may be underreported in mortality data.

Studies of hepatitis C mortality data have shown that there may already be significant underreporting of this disease on death certificates. While chronic liver disease (CLD) is a well recognized cause of death, persons dying of CLD may have

underlying viral hepatitis that goes unnoted on the death certificate. One study from 2008 in California found that only 64% of hepatitis C-related CLD cases had hepatitis C or viral hepatitis listed on the death certificate.[36] Additionally, other studies have shown that hepatitis C infection may place patients at greater risk for developing end-stage renal disease or coronary heart disease.[8,9,10] These diseases may be listed as the cause of death on the death certificate with no mention of hepatitis C infection, when hepatitis C may actually have contributed to the person's death.

The causes of death listed on death certificates provide critical information on the health status of a population. Being able to accurately identify causes of death (both primary and underlying) at the population level may lead to changes in public health prevention programs, policies, or perhaps most importantly, changes in funding. When the causes of death listed on the death certificate do not encompass the true underlying conditions, those conditions will be underreported. Funding at the federal and state level is often tied to the burden of disease in a community. If a disease or condition is not perceived to be a public health burden, then funding may not be allocated, which leads to a negative impact on public health programs.

This study is the first to compare the causes of death, and potential underreporting of disease, in hepatitis C and/or HIV-infected individuals in Connecticut from 2003-2007. The purpose of this study was to identify how often HIV/AIDS and/or hepatitis C were potentially underreported on death certificates in Connecticut residents over a five-year period. Previous studies have shown that there is already an underreporting of hepatitis C in other states and potentially an underreporting of HIV/AIDS as well.[34,35,36] If these diseases are underreported,

Connecticut may potentially be losing federal and/or state funding for HIV/AIDS and/or hepatitis C programs, research, or treatment.

Methods

Data sources

Data for this study were obtained from the Connecticut Department of Public Health. DPH maintains extensive surveillance databases for reportable diseases and conditions as well as vital statistics information. Death data came from the Office of Vital Records and contained information from death certificates of all Connecticut residents who died between 2003 and 2007 with selected variables: last name, first name, date of birth, sex, year of death, age at death, town of residence, county of residence, race/ethnicity, and all causes of death. These data were the final data, containing *record axis* codes that DPH uses for publications, meaning that the original data, containing *entity axis* codes, had been sent to CDC to be analyzed, cleaned, re-coded as necessary (see page 12) and then sent back to Connecticut.

The HIV/AIDS and hepatitis C data came from the HIV/AIDS and Viral Hepatitis Surveillance Program and contained all records in both registries with the following variables: last name, first name, date of birth, sex, town of residence when diagnosed, county of residence when diagnosed, race/ethnicity, death date (if any), and risk factor for infection. Case information comes from laboratory reports, physicians, and occasionally the patients themselves. While all HIV/AIDS cases must be entered into the electronic database with a race/ethnicity, hepatitis C cases are entered primarily on laboratory reports, which generally do not contain race or ethnicity information. Information such as race/ethnicity, risk factors, and reasons for testing usually come from follow-up forms mailed to providers or from medical record reviews. Prior to 2008, follow-up was limited to a few counties. Statewide follow-up

of all newly reported positive hepatitis C laboratory reports began in 2008. Therefore, risk and race/ethnicity information in the hepatitis C database are not as complete as in the HIV/AIDS database.

This study was approved by the University of Connecticut's Institutional Review Board and the Connecticut Department of Public Health's Human Investigations Committee.

Preparing the data for matching

Both the HIV/AIDS and hepatitis C datasets contained all records in the registries up to the time of retrieval. To make the registries more comparable, cases were selected that were reported from the beginning of each registry up through December 31, 2008. Due to the possibility of false positives in people reported with only positive anti-HCV tests, cases were selected in the hepatitis C registry that met the 2005 case definition for a past or present hepatitis C infection: a positive anti-HCV verified by a more specific assay, HCV RIBA positive, nucleic acid test for HCV RNA positive, a report of an HCV genotype, or anti-HCV positive with a high signal-to-cutoff ratio.[37] This ensured that people in the resulting dataset were true positives for hepatitis C.

Each registry has the capability to record an individual's risk for infection. Risk information is gathered from follow-up forms sent to providers, medical record reviews, or less frequently, patient interview. The HIV/AIDS data contained this information as a risk-rank scenario. If an individual had more than one risk, only the highest ranked risk behavior was reported. The hepatitis C registry, on the other hand,

had each individual risk as either "yes," "no," "unknown," or "missing" (blank). To make this more comparable to the HIV/AIDS risks, the hepatitis C risks were ranked and risk categories with fewer numbers were combined. The order of the risk ranking was: injection drug use (IDU), sexual contact of a person with hepatitis C, household contact of a person with hepatitis C, receipt of a blood/organ product (organ or blood transfusion prior to 1992 or clotting factor concentrate prior to 1987), street drugs, other (containing all other risk categories), and unknown.

Additionally, two race categories were combined in the hepatitis C dataset, Asian and Pacific Islander, as Pacific Islander was only added as a separate race category in 2007.

Matching the disease datasets to the death dataset

Matching was performed using Link Plus, version 2.0.[38] Link Plus allows a user to match two delimited or fixed-width datasets after defining key variables and choosing a cutoff value. Link Plus then automatically assigns each matched pair a cutoff value based on the likelihood that they are a match – the higher the score, the more likely they are a true match.

The HIV/AIDS and hepatitis C datasets were exported as tab delimited datasets for use in the match. Next, the blocking and matching variables were defined. Blocking variables chosen and their phonetic systems were: last name (soundex), first name (soundex), and birthdate. The matching variables and their matching methods were: last name (last name), first name (first name), birthdate (date), and sex (exact).

An initial cutoff value of 10.0 was chosen for each match (HIV/AIDS to death and hepatitis C to death) and the resulting matches were manually reviewed. Matches with cutoff values from 10.0 to 14.9 matched on last name and/or first name and/or birthdate and/or sex but not all four. On closer inspection, the birthdates were drastically different and the names were common names. A higher cutoff value of 15.0 was chosen and the matches were re-run. The resulting matches were then manually reviewed for spelling mishaps (e.g. Vazquez versus Vasquez, etc.) and birthdate transpositions (e.g. 01/11/1950 and 11/01/1950) to yield the final matches. This process was then repeated to match the deceased HIV/AIDS cases to the deceased hepatitis C cases to identify deceased co-infected cases. A cutoff value of 10.0 was chosen and all resulting matches were exact matches because the names and birthdates were matched based on death certificate data. The co-infected cases were then manually removed from the deceased HIV/AIDS and deceased hepatitis C datasets to yield three datasets: deceased cases reported to have HIV/AIDS, deceased cases reported to have hepatitis C, and deceased cases reported to be co-infected with HIV/AIDS and hepatitis C. At this point, the three datasets were de-identified by removing last name, first name, and birthdates to produce the final three datasets.

Analysis

All data were analyzed using univariate and bivariate descriptive statistics. Univariate statistics were used to describe the demographic characteristics of the datasets as well as frequencies among causes of death. Bivariate statistics were used to compare how often hepatitis C or HIV disease were listed as causes of death in

conjunction with other diseases or conditions. Data were analyzed using SAS version 9.2 (SAS, Inc., Cary, NC).

The cause of death codes in the datasets were International Classification of Disease (ICD) 10 codes. On the death certificates there can be one primary cause of death and up to 20 underlying causes of death. To capture causes that may be of interest to either HIV/AIDS or hepatitis C infections, the 113 causes of death from the CDC National Center for Health Statistics were used to develop a classification system for each cause of death.[39] Death from HIV and AIDS opportunistic infections and diseases were grouped together according to the ICD-10 codes. The individual viral hepatitis codes were left separate. Possible indicators of liver disease were also separated: liver cancer, alcoholic liver disease, hepatic failure, and other liver disease and/or cirrhosis. The remaining causes of death were either classified according to the 113 causes of death from CDC or collapsed into an "other cause" category (Appendix I).

To determine whether hepatitis C was mentioned on death certificates when a form of liver disease was a cause of death, several liver disease variables were combined (ICD-10 codes C22 and K70-K77). Several kidney disease variables were combined for the same reason (ICD-10 codes C64-C65, N00-N07, N17-N19 and N25-N27).

Results

Unmatched datasets

The unmatched HIV/AIDS dataset contained 18,862 cases reported through December 31, 2008. Males represented 70% of the cases. The majority of cases were white (36.4%), black (35.3%), or Hispanic (27.7%). The most common risk factor was IDU (45.2%) followed by MSM (21.9%) and heterosexual contact (18.4%). There were 8,699 deaths in the HIV/AIDS dataset (46.1%).

The unmatched hepatitis C dataset contained 24,834 confirmed cases (using the CDC/CSTE 2005 case definition) reported through December 31, 2008 including 1,247 cases deaths (5.0%). Two-thirds of the cases were male. Race/ethnicity was unknown for half of the cases, followed by white (28.4%), Hispanic (11.8%), and black (9.3%). Risk was unknown for 90% of cases.

The unmatched death dataset contained 145,643 cases of Connecticut residents who died between 2003 and 2007. Just over half of them were female (52.8%). The cases were evenly split between all five death years. The majority of cases were white (87%).

Matched datasets, demographics

There were 1,004 cases of HIV/AIDS, 704 cases of hepatitis C, and 144 cases of co-infection with both HIV/AIDS and hepatitis C. The co-infected cases represented 17.0% of the total hepatitis C cases and 12.5% of the total HIV/AIDS cases.

There were more than twice as many males as females in all three of the matched datasets. Black was the most common race/ethnicity in the HIV/AIDS and co-infected datasets, while white was the most common race/ethnicity in the hepatitis C dataset. The number of cases per year of death increased dramatically for both co-infected and hepatitis C cases but showed an overall decrease for HIV/AIDS cases (Table 1).

The mean age of death was higher for hepatitis C cases than for HIV/AIDS and co-infected cases. Females also died at slightly older ages in hepatitis C cases (Table 1). The mean age of death did not differ from the median age of death. Overall age of death was younger in HIV/AIDS and co-infected cases, with most cases between 30 and 49 years old (Fig. 1).

Risk was known for more than 90% of HIV/AIDS and co-infected cases, compared to less than 3% of hepatitis C cases. More than half of HIV/AIDS cases and the majority of co-infected cases had a risk of IDU. MSM and heterosexual contact were more prevalent in HIV/AIDS cases than in co-infected cases (Table 1).

Primary causes of death

Death certificates in Connecticut have one primary cause of death and up to twenty underlying causes of death, which were designated the primary cause of death, first underlying cause of death, second underlying cause of death, etc. Some institutions may call the primary cause of death the "underlying cause of death" and the underlying causes of death the "contributing cause of death" but for these research purposes they have been designated the primary and underlying causes.

The most common primary cause of death for HIV/AIDS and co-infected cases was HIV disease, representing 58.5% and 62.5% of the primary causes, respectively. The 30 to 39 year old age group had the highest percentage of HIV disease as the primary cause of death among co-infected cases (72.2%). Among HIV/AIDS cases, the 0 to 19 year old age group had the highest percentage of HIV disease as the primary cause of death; however, there were only four cases in this group. The 30 to 39 year olds were second highest (66.9%). The lowest percentage of HIV disease as the primary cause of death was in the 60 to 69 year olds for HIV/AIDS cases (46%) and the 50 to 59 year olds for co-infected cases (55.8%). The percent of HIV/AIDS cases with HIV disease as the primary cause of death decreased over the years from 63.3% in 2003 to 50.6% in 2007.

Other common primary causes of death for HIV/AIDS and co-infected cases were: major cardiovascular disease, other malignant neoplasm (excluding liver cancer, kidney cancer, and Kaposi sarcoma that was not mentioned under HIV disease), accident, and the "other cause" of death group (Table 2). The "other cause" group is a constructed category of causes that did not appear to be related to HIV/AIDS or hepatitis C. More than half of the cases with accident as their primary cause of death died of accidental poisoning by and exposure to narcotics or hallucinogens; 74% of those had a risk factor of IDU. When HIV disease was the primary cause of death, the most frequent specific ICD-10 codes were HIV disease resulting in other specified conditions, unspecified HIV disease, or HIV disease resulting in different types of infections (multiple, viral, infectious, bacterial, etc.).

Unlike HIV/AIDS and co-infected cases, no single cause of death dominated the hepatitis C data. Although major cardiovascular disease was the most common primary cause (15.6%), it was followed closely by accident, "other cause," and other malignant neoplasm. When accident was the primary cause of death, 65.1% of those cases died of accidental poisoning by and exposure to narcotics or hallucinogens, similar to HIV/AIDS and co-infected cases. When the primary cause was the "other cause" group, the top cause within that category was other ill-defined and unspecified causes of mortality (11.1%). Chronic hepatitis C ranked sixth among primary causes of death, having been listed in only 6.7% of cases (Table 2).

Accident was the most common primary cause of death among the younger age groups of hepatitis C cases (less than 50 years old), while major cardiovascular disease or cancer were the leading causes of death among the older age groups. Liver disease (alcoholic liver disease, hepatic failure, liver cancer, other chronic liver disease and cirrhosis, and other liver disease; ICD-10 codes C22 and K70-K77) as a primary cause of death was highest in the 50 to 59 year old age group (25.1%) for hepatitis C cases, compared to other age groups.

The ranking of primary causes of death changed slightly when broken down by sex. For co-infected cases, the most common primary cause was similar for both sexes. HIV disease was the most common primary cause in 61.2% of co-infected females and 63.2% of co-infected males, followed by accident in both groups. In the HIV/AIDS dataset, females had HIV disease listed as their primary cause of death slightly more often than males (61.4% versus 57.1%). Major cardiovascular disease was the second most common primary cause of death in HIV/AIDS males (10.5%)

while it was the fourth most common in HIV/AIDS females (6.3%). "Other cause" of death was ranked second for females (7.6%).

Among hepatitis C cases, major cardiovascular disease remained the most common primary cause of death for both males and females (16.1% and 14.5%, respectively). Chronic hepatitis C was ranked eighth for females (5.2%) and sixth for males (7.2%).

The proportion of cases with HIV disease as the primary cause of death differed between races. In co-infected cases, 72.4% of whites had HIV disease as their primary cause of death versus 57.7% of Hispanics. However, in HIV/AIDS cases, 62.4% of blacks had HIV disease as primary cause, whereas only 54.1% of whites did (Table 3).

Black and Hispanic hepatitis C cases' most common primary cause of death was major cardiovascular disease (17.1% and 16.7%, respectively), compared to accident for white cases (17.1%). Major cardiovascular disease was second for white cases (15.0%). Another difference between race/ethnicities in hepatitis C cases was the proportion of cases with other malignant neoplasm as a primary cause of death. It was ranked third for blacks (15.3%) and whites (12.8%) but tenth for Hispanics (3.5%). In contrast, liver cancer was more prevalent as a primary cause of death in blacks (10.8%) and Hispanics (9.7%) than in whites (5.6%).

Underlying causes of death

Up to twenty underlying causes of death can be listed on a death certificate in Connecticut. Only one-quarter of co-infected and hepatitis C cases had the first

underlying cause of death filled in, compared with 68.6% of HIV/AIDS cases. Overall, co-infected cases had up to six underlying causes of death (with only one case having six and one case having five), HIV/AIDS cases had up to seven underlying causes of death (with eight cases having seven), and hepatitis C cases had up to nine underlying causes of death (with one case having nine and two cases having eight).

The distribution for the first underlying cause of death was similar to the distribution for the primary cause of death in all three datasets. The most common first underlying cause of death was HIV disease for both co-infected and HIV/AIDS cases (54.1% and 60.1%, respectively). HIV disease was only listed as an underlying cause of death in the first three underlying cause fields for both co-infected and HIV/AIDS cases.

If HIV disease was listed as the first underlying cause of death for co-infected cases, the primary cause of death was also HIV disease in 90% of those cases. Similarly, for HIV/AIDS cases the primary cause of death was HIV disease in 87.2% of cases where the first underlying cause of death was HIV disease. HIV disease ICD-10 codes in these cases were commonly HIV disease that resulted in other specified conditions, unspecified HIV disease, or HIV disease resulting in a variety of infections that were not specifically listed.

The first underlying causes of death for hepatitis C cases were scattered, with "other cause" of death at the top (Table 4). The "other cause" ICD-10 codes were most commonly deaths due to heroin use, mental and behavioral disorders due to multiple drug use and use of other psychoactive substances, and other ill-defined and

unspecified causes of mortality. Chronic and acute hepatitis C were only mentioned in the first two underlying causes of death fields.

Hepatitis C in cases of liver disease

Any form of liver disease (alcoholic liver disease, hepatic failure, liver cancer, other chronic liver disease and cirrhosis, and other liver disease; ICD-10 codes C22 and K70-K77) was listed as a primary cause of death in 20.6% of hepatitis C cases and was listed as any cause of death in 24.0% of hepatitis C cases. When liver disease was the primary cause of death, hepatitis C was mentioned as an underlying cause of death only 6.2% of the time. If liver disease was listed anywhere on the death certificate, hepatitis C was listed 12.4% of the time. Hepatitis C was mentioned more often in males than in females with liver disease. In co-infected cases, hepatitis C was never listed as a cause of death when liver disease was the primary cause of death (Table 5).

Hepatitis C in cases of other chronic diseases

Major cardiovascular disease was the top primary cause of death in hepatitis C cases, and hepatitis C was listed as an underlying cause of death in 3.6% of those cases. If major cardiovascular disease was listed in any field as a cause of death, hepatitis C was mentioned in 5.8% of those cases, and slightly more often in males (6.3%) than in females (4.8%).

Renal disease was defined as kidney cancer (ICD-10 codes C64-C65) or nephritis, nephritic syndrome, and nephrosis (ICD-10 codes N00-N07, N17-N19, N25-N27). It was listed as a primary cause of death in 24 hepatitis C cases (3.4%). When

renal disease was a primary cause of death, hepatitis C was never mentioned as an underlying cause of death. If renal disease was listed anywhere as a cause of death (41 cases, 5.8%), hepatitis C was mentioned in 9.8% of those cases. Hepatitis C was mentioned slightly more often in females than in males when renal disease was listed anywhere as a cause of death.

HIV/AIDS in cases of other chronic diseases

Cancer (a combination of other malignant neoplasm, liver cancer, kidney cancer, and Kaposi sarcoma; ICD-10 codes C00-C97) was a primary cause of death in 8.9% of HIV/AIDS cases, and HIV disease was listed as a cause of death in 23.6% of them. However, when cancer was expanded to any cause of death, the percent of those cases with HIV disease listed increased to 34.9%. Females were more likely than males to have HIV disease listed when cancer was listed as a cause of death (Table 6A).

Major cardiovascular disease was the second primary cause of death among HIV/AIDS cases, and HIV disease was listed as a cause of death in 19.4% of those cases. When major cardiovascular disease was listed as any cause of death, the proportion of cases that also listed HIV disease as a cause of death increased to 32.6%. Females were also more likely to have HIV disease listed than males (Table 6B).

Table 1. Demographic information on deceased Connecticut residents who had HIV/AIDS, hepatitis C, or both (co-infected), 2003-2007.

	HIV/AIDS		Hepatitis C		Co-infected	
	n	%	n	%	n	%
Sex						
Female	316	31.5	193	27.4	49	34.0
Male	688	68.5	511	72.6	95	66.0
Race/ethnicity[1]						
Asian/PI	3	0.3	8	1.1	0	0.0
Black	441	43.9	111	15.8	63	43.8
Hispanic	220	21.9	114	16.2	52	36.1
Native American	4	0.4	2	0.3	0	0.0
White	318	31.7	461	65.5	29	20.1
Unknown	18	1.8	8	1.1	0	0.0
Risk[2]						
Blood products	2	0.2	4	0.6	0	0.0
Heterosexual contact[3]	137	13.7	--	--	7	4.9
IDU	592	59.0	11	1.6	126	87.5
MSM[3]	151	15.0	--	--	4	2.8
MSM/IDU[3]	25	2.5	--	--	1	0.7
Other	0	0.0	3	0.4	0	0.0
Perinatal (<13 years old)[3]	5	0.5	--	--	0	0.0
Unknown	92	9.2	686	97.4	6	4.2
Year of death						
2003	245	24.4	18	2.6	3	2.1
2004	246	24.5	50	7.1	9	6.3
2005	203	20.2	110	15.6	25	17.4
2006	150	14.9	221	31.4	40	27.8
2007	160	15.9	305	43.3	67	46.5
Age at death, in years, mean						
Both sexes	48.2		54.0		48.9	
Female	46.4		56.5		47.9	
Male	49.0		53.0		49.4	
Total (n)	1,004		704		144	

[1] Race/ethnicity as recorded on the death certificate. PI = Pacific Islander.
[2] Risk for co-infected cases is the HIV/AIDS risk.
[3] Risks unique to HIV/AIDS cases.

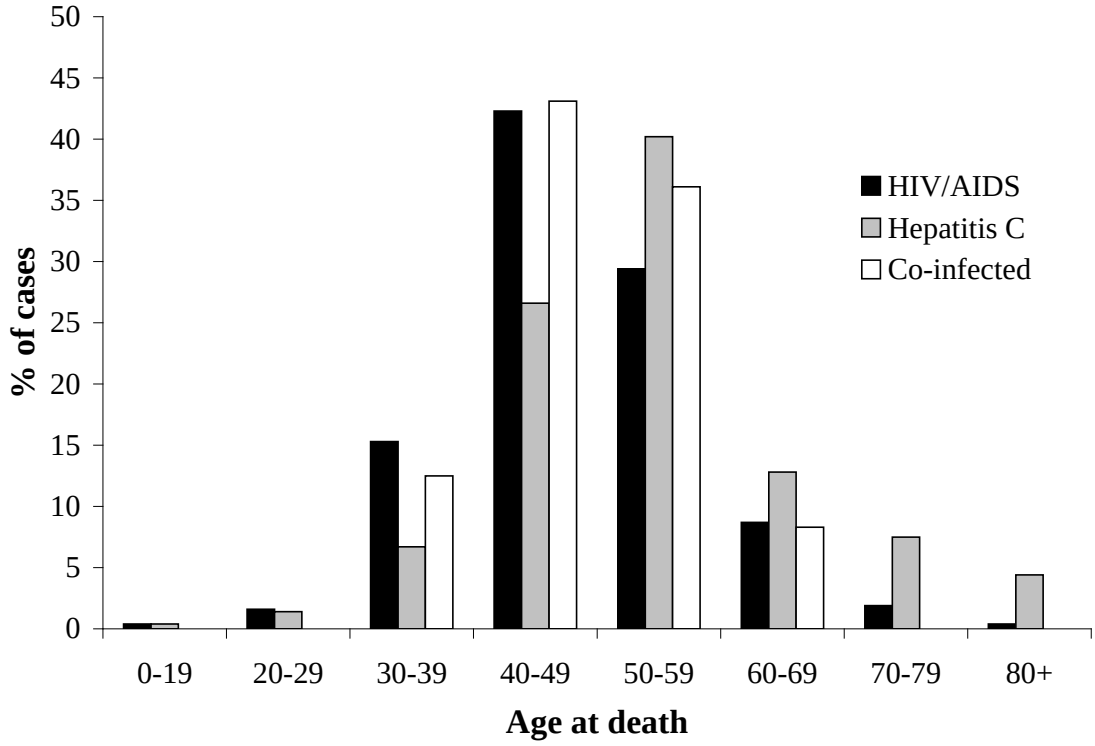

Figure 1. Age at death for persons infected with HIV/AIDS, hepatitis C, or both (co-infected), Connecticut, 2003-2007

Table 2. Top 10 primary causes of death for persons infected with HIV/AIDS, hepatitis C, or both (co-infected), Connecticut, 2003-2007.

HIV/AIDS			Hepatitis C			Co-infected		
	n	%		n	%		n	%
HIV disease	587	58.5	Major cardiovascular disease	110	15.6	HIV disease	90	62.5
Major cardiovascular disease	92	9.2	Accident	103	14.6	Accident	15	10.4
Other cause	73	7.3	Other cause	86	12.2	Other malignant neoplasm[1]	10	6.9
Other malignant neoplasm[1]	72	7.2	Other malignant neoplasm[1]	82	11.7	Major cardiovascular disease	9	6.3
Accident	50	5.0	Liver cancer	51	7.2	Other cause	5	3.5
Other infectious/parasitic disease	29	2.9	Chronic hepatitis C	47	6.7	Chronic hepatitis C	4	2.8
Chronic lower respiratory disease	17	1.7	Other CLD[2] and cirrhosis	36	5.1	Alcoholic liver disease	2	1.4
Liver cancer	15	1.5	Other infectious/parasitic disease	34	4.8	Liver cancer	2	1.4
Other CLD[2] and cirrhosis	14	1.4	Alcoholic liver disease	24	3.4	Other liver disease	2	1.4
Influenza/pneumonia	12	1.2	Other liver disease	23	3.3	Chronic lower respiratory disease	1	0.7
Total[3]	1,004			704			144	

[1] Other malignant neoplasm includes all malignant neoplasms excluding liver cancer, kidney cancer, and Kaposi sarcoma (ICD codes C00-C97).
[2] CLD = chronic liver disease.
[3] Causes do not add up to 100% because only the top 10 causes are shown.

Table 3. Percent of cases with HIV disease as the primary cause of death in persons infected with HIV/AIDS or co-infected with HIV/AIDS and hepatitis C, by race/ethnicity[1], Connecticut, 2003-2007.

	HIV/AIDS	Co-infected
	%	%
Race/ethnicity		
Black	62.4	61.9
Hispanic	57.3	57.7
White	54.1	72.4
Unknown	44.4	--

[1] Race/ethnicity as recorded on the death certificate. Asian/PI and Native American were omitted due to low sample sizes.

Table 4. Top 10 first underlying causes of death for persons infected with hepatitis C, Connecticut, 2003-2007.

	Hepatitis C	
	n	%
Other cause	44	25.3
Other infectious/parasitic disease	29	16.7
Major cardiovascular disease	28	16.1
Other malignant neoplasm	19	10.1
Chronic hepatitis C	18	10.3
Acute hepatitis C	9	5.2
Hepatic failure	6	3.5
Liver cancer	6	3.5
Diabetes	4	2.3
Acute hepatitis B	3	1.7
Total[1]	174	

[1] Causes do not add up to 100% because only the top 10 causes are shown.

Table 5. Hepatitis C as a cause of death when liver disease[1] is a cause of death, in persons A.) infected with hepatitis C, and B.) co-infected with HIV/AIDS and hepatitis C, Connecticut, 2003-2007.

A.)

	Hepatitis C					
	Both sexes		Females		Males	
	n	%	n	%	n	%
Liver disease						
As a primary cause of death	145	20.6	38	19.7	107	20.9
Mention of hepatitis C in any field[2]	9	6.2	1	2.6	8	7.5
As any cause of death	169	24.0	45	23.3	124	24.3
Mention of hepatitis C in any field[3]	21	12.4	5	11.1	16	12.9
Total	704		193		511	

B.)

	Co-infected					
	Both sexes		Females		Males	
	n	%	n	%	n	%
Liver disease						
As a primary cause of death	7	4.9	2	4.1	5	5.3
Mention of hepatitis C in any field[2]	0	0	0	0	0	0
As any cause of death	11	7.6	2	4.1	9	9.5
Mention of hepatitis C in any field[3]	1	9.1	0	0	1	11.1
Total	144		49		95	

[1] Liver disease includes ICD-10 codes C22 (liver cancer) and K70-K77 (liver disease).
[2] Number/percent of time that hepatitis C is mentioned as any cause of death when liver disease is the primary cause of death.
[3] Number/percent of time that hepatitis C is mentioned as any cause of death when liver disease is mentioned as any cause of death.

Table 6. HIV disease as a cause of death in persons infected with HIV/AIDS when A.) cancer[1] is a cause of death, and B.) major cardiovascular disease is a cause of death, Connecticut, 2003-2007.

A.)

	Cancer					
	Both sexes		Females		Males	
	n	%	n	%	n	%
Cancer						
As a primary cause of death	89	8.9	26	8.2	63	9.2
Mention of HIV/AIDS in any field[2]	21	23.6	7	26.9	14	22.2
As any cause of death	106	10.6	30	9.5	76	11.1
Mention of HIV/AIDS in any field[3]	37	34.9	11	36.7	26	34.2
Total	1,004		316		688	

B.)

	Major cardiovascular disease					
	Both sexes		Females		Males	
	n	%	n	%	n	%
Major cardiovascular disease						
As a primary cause of death	92	9.2	20	6.3	72	10.5
Mention of HIV/AIDS in any field[2]	9	9.8	2	10.0	7	9.7
As any cause of death	245	24.4	71	22.5	174	25.3
Mention of HIV/AIDS in any field[3]	112	45.7	39	54.9	73	42.0
Total	1,004		316		688	

[1] Cancer includes all malignant neoplasms (ICD codes C00-C97).
[2] Number/percent of time that HIV/AIDS is mentioned as any cause of death when A.) cancer, or B.) major cardiovascular disease is the primary cause of death.
[3] Number/percent of time that HIV/AIDS is mentioned as any cause of death when A.) cancer, or B.) major cardiovascular disease is mentioned as any cause of death.

Discussion

These results support the hypotheses that HIV/AIDS and hepatitis C are underreported on death certificates in cases where the decedent was known to be infected with either or both of these diseases. Furthermore, HIV disease was listed as a primary cause of death in known HIV/AIDS or co-infected cases more often than hepatitis C was listed in known hepatitis C cases. This is important to note because mortality data often look at the primary cause of death to determine the burden of disease in a population.

Deaths among co-infected cases

There were 144 cases of co-infection with both HIV/AIDS and hepatitis C. The number of deaths per year increased over time, but due to sample size and time constraints, statistical tests to determine whether the increase was statistically significant were not conducted. It is possible that the number of deaths increased because co-infected people may not have had access to HAART, due to the potentially toxic effects that HAART has on the liver.[40] HAART has been shown to delay progression to AIDS and can add years of life or prevent opportunistic infections.[23,24] Additionally, the percentage of cases with HIV disease as a primary cause of death was slightly higher in co-infected cases than in HIV/AIDS only cases. Co-infected cases may have a higher risk of developing AIDS-defining illnesses, which may explain the higher percentage seen here.[26] However, another study indicated that in the era of HAART, HIV co-infection with hepatitis C increases mortality but not AIDS-defining illnesses.[41] It is not known whether or not any of these cases were on

HAART and therefore it cannot be determined if co-infection increased mortality from HIV disease or mortality over time. However, the increase is worth noting and may also be related to socioeconomic status, drug use (as most co-infected cases were IDUs), or a lack of access to health services.[42]

The increase may also be a surveillance or data artifact. AIDS cases were reportable in Connecticut starting in 1981 but HIV in adults was not added until 2002, causing many HIV cases to be reported in the years afterward which were not previously reported. Additionally, the CDC guidelines on HIV testing in adults were published in 2006 and may have caused an increase in HIV testing.[20] An increasing awareness of hepatitis C and HIV co-infection among providers may have also caused an increase in testing and reporting. Expansion of enhanced hepatitis C surveillance in Connecticut from one county to three counties in 2007 may have also captured additional confirmed hepatitis C cases, which may or may not have also been co-infected with HIV.

Co-infected cases were more likely to be male than female, which is consistent with both the HIV/AIDS and hepatitis C cases. They were also more likely to have a risk of IDU, which is consistent with other findings.[25,30] Co-infection disproportionately affected blacks and Hispanics as they accounted for 43.8% and 36.1% of cases but only 6.6% and 4.3% of all deaths during that same time period. This is consistent with other findings among HIV/AIDS cases.[18] However, HIV disease was listed as a primary cause of death more often among white cases than among black or Hispanic cases, suggesting that blacks and Hispanics are dying more

often of non-HIV causes despite being disproportionately affected by HIV. It may also suggest that there are differences in identifying causes of death by race/ethnicity.

HIV disease as an underlying cause of death was often listed when HIV disease was the primary cause of death as well. When HIV disease was listed on the death certificate, it was most often listed as HIV disease that resulted in some type of infection (viral, bacterial, etc.) or as unspecified HIV disease. A listing of HIV disease that resulted in a specific infection or other disease was less common. This makes it hard to determine if co-infected cases are indeed dying of AIDS-defining illnesses at higher rates than HIV/AIDS cases.

When liver disease was the primary cause of death in co-infected cases, hepatitis C was never listed on the death certificate. Liver disease may cause an increase in mortality among co-infected patients due to progression of hepatitis C over time or exposure to potentially hepatotoxic antiretroviral therapy.[40] Again, small sample sizes make it hard to infer how often this actually occurs, but it is worth mentioning since these are cases that were known to be infected with both HIV/AIDS and hepatitis C.

It is possible that on the original death certificate, hepatitis C may have been listed as a cause of death in these co-infected cases. However, studies have shown that HIV disease and hepatitis C are often combined into a single HIV code after data cleaning.[11] The death data used for this study were the final data, as reviewed, recoded, and returned from the CDC. Therefore, without the original death certificates it is impossible to tell how often hepatitis C was originally listed.

Deaths among HIV/AIDS cases

HIV disease was the primary cause of death in two-thirds of HIV/AIDS cases, which is consistent with previous Connecticut findings.[34] Another leading cause of death was major cardiovascular disease, which has also been noted elsewhere.[35] The percentage of deaths that had a primary cause of death of HIV disease decreased over the years. Additionally, the number of HIV/AIDS cases per year of death decreased as well. HAART is known to delay progression to AIDS and to extend lifetimes, as previously stated, so it is possible that more people are receiving HAART and therefore living longer lives.[23] The decrease in HIV/AIDS cases may also be reflective of Connecticut HIV/AIDS data in general, which has also shown a decrease in the number of reported cases over the years.[27] This may be due to fewer infections, effective prevention programs, or simply that the surveillance database has identified the majority of infections that exist in Connecticut.

Similar to co-infected cases, HIV/AIDS cases were most commonly black, followed by white and Hispanic. HIV disease was also listed as a primary cause of death more often in blacks and Hispanics than in whites. These results add to previous findings that HIV/AIDS disproportionately affects minorities, because cases among blacks and Hispanics represented two-thirds of the HIV/AIDS cases, although blacks and Hispanics represented only 10.9% of the deceased population in the same time period.[18,19]

HIV disease was the primary cause of death in all four cases between the ages of 0 and 19 years old and after that was the most prevalent primary cause of death among 30 to 39 year olds. The lower percentage of HIV disease as the primary cause

of death among older cases implies that if a person lives longer with HIV/AIDS he or she may die of something unrelated to HIV. In these cases, HAART may have played a role.

Accident was a prevalent cause of death and was often related to drug overdose, as three-quarters of cases who had accident as their primary cause of death also had a risk factor of IDU. IDU is a well-known risk factor for HIV infection, and accidental drug overdoses are a prevalent problem in some locations.[42]

Underlying causes of death for HIV/AIDS cases were similar to the primary causes of death. HIV disease was listed as an underlying cause of death in the first three underlying fields and often when HIV disease was the primary cause of death as well. Unfortunately, as in co-infected cases, the specific ICD-10 codes for HIV disease were non-specific, implying that a variety of infections or unspecified HIV disease was the cause of death. It is entirely possible that the person responsible for filling out the death certificate knew that the decedent had HIV, but did not know any specifics beyond that. This would explain the lack of specific named viruses or bacterial infections. It is also possible that what was written on the death certificate was re-coded into a less specific HIV cause when the death data were sent to CDC for data cleaning. The many steps in the death certificate process make it hard to determine where HIV disease is underreported and for what reason.

Studies have shown that, in addition to AIDS-defining illnesses such as PCP and Kaposi sarcoma, people with HIV/AIDS may be at increased risk of a range of other cancers and cardiovascular disease.[43,44] In this study, major cardiovascular disease was the second most common primary cause of death among HIV/AIDS cases,

other malignant neoplasm was fourth, and liver cancer was eighth. HIV disease was listed on the death certificate 19.4% and 23.6% of the time when major cardiovascular disease or any type of cancer was the primary cause of death, respectively. This may represent an underreporting of HIV/AIDS, especially as an underlying cause of death among people known to be infected with HIV.

Deaths among hepatitis C cases

Hepatitis C cases differed from co-infected and HIV/AIDS cases in many ways. Due to differences in the history of each disease surveillance system at DPH, there were more unknown or missing demographic data for hepatitis C cases, including the person's behavioral or exposure risks for infection. Additionally, hepatitis C was not the most common primary cause of death; instead, chronic hepatitis C was the sixth most common primary cause of death. This may imply that hepatitis C is underreported as a primary cause of death. However, it may also indicate that hepatitis C is less frequently fatal than HIV disease. The higher proportion of deceased cases in the DPH HIV/AIDS database versus in the hepatitis C database supports the idea that HIV/AIDS is a more often and rapidly fatal.

The number of hepatitis C cases increased over the five-year time period. Studies have projected that the number of hepatitis C-related deaths will increase over the next decade, and the findings in this study may be a reflection of this prediction.[12] They may also have increased because of enhanced hepatitis C surveillance, better reporting over time, or an increase in hepatitis C testing in the state.

Although hepatitis C has been linked to an increased risk of cardiovascular events, cardiovascular disease is also the number one cause of death in the United States.[10,45] Therefore, it is not surprising that major cardiovascular disease is the number one cause of death among hepatitis C cases. What is surprising is that hepatitis C was listed as an underlying cause of death in only 3.6% of those cases. Similarly, renal disease is also known to be linked to hepatitis C.[7,8,9] When renal disease was listed as the primary cause of death, hepatitis C was never listed as an underlying cause of death. These two examples may indicate an underreporting of hepatitis C on death certificates. However, without more in-depth knowledge about each individual case, it is hard to tell if hepatitis C was actually related to the deaths.

The most important finding for the hepatitis C cases was how often hepatitis C was omitted as a cause of death when liver disease was a cause of death. Liver disease was listed as a primary cause of death most often in people between 50 and 59 years old, which is not surprising given that most persons with hepatitis C are among the "Baby Boomers" generation.[1] Liver disease was a primary cause of death in one-fifth of all hepatitis C cases and listed as any cause of death in one-quarter of all the cases. Hepatitis C was concurrently listed on the death certificate in only 6.2% and 12.4% of those cases, respectively. Liver disease is a known exacerbation of hepatitis C and even in cases of alcoholic liver disease hepatitis C infection may speed the progression of cirrhosis or other liver complications. This finding supports previous research that hepatitis C is underreported in cases of liver disease in a known hepatitis C positive population.[36]

Hepatitis C may be underreported for a variety of reasons. The Institute of Medicine recently released a report on viral hepatitis and liver cancer. This report indicated that a major challenge to preventing chronic hepatitis infections is the lack of awareness about hepatitis among healthcare providers and the general public, as well as insufficient surveillance systems.[46] Since hepatitis C can remain asymptomatic for decades, many patients may not be aware that they are infected or their providers may not see any reason to test them. Also, depending on who filled out the death certificate, the provider may or may not have been aware of the person's underlying hepatitis C infection. If a person presented in the emergency department with end-stage liver disease and was clearly intoxicated, the provider may attribute this death to alcoholic hepatitis and may not have known about an underlying hepatitis C infection.

Policy and program recommendations

The results from this study show that HIV and hepatitis C are underreported on death certificates. States should share data and collaborate within their own agencies whenever possible. Intra-agency data matching among public health programs can yield interesting and important findings that may give direction to public health programming or policies. Barriers to routine data matching or collaborations may include confidentiality constraints, internal or external Institutional Review Board processes, or the reliability or completeness of datasets. Further research is necessary to fully explore the implementation of data integration within state agencies.

Current hepatitis C and HIV/AIDS reporting mechanisms may not be adequate to identify the full burden of disease in Connecticut. Although laboratories and

providers are mandated to report certain findings, the information is not always complete and providers often do not initiate reporting of some diseases on their own. Emphasizing the importance, and the requirements, of provider reporting is necessary. Although laboratory reporting may capture cases of hepatitis C or HIV, it does not provide risk information, case status (chronic versus acute, or alive versus dead), or even certain demographic data, such as race/ethnicity. Surveillance systems often rely on providers for this data, whether through provider reporting or through follow-up forms or phone calls to the provider.

There are no vaccines for either HIV or hepatitis C and therefore prevention and awareness are key issues that need to be addressed at a policy level. Healthcare providers need to test at-risk patients for both diseases since many people who are infected are not aware. Additionally, providers need to obtain full risk histories from their patients that encompass all lifetime risks, not just current ones. Although a patient may say that he is not currently an injection drug user, he may have had one episode thirty years ago that might have exposed him to hepatitis C or HIV. Without a full history, his provider may not test for either disease. Similarly, patients need to be their own advocates and ask their providers to test them if they have any risk factors.

Primary and secondary prevention programs need to be aimed at those who are most likely to be at-risk or already positive. Federal funding needs to be allocated in a fair and consistent manner to states and prevention programs. The Institute of Medicine report on hepatitis B and C found that inadequate funding is allocated to viral hepatitis, as viral hepatitis programs receive a fraction of the funding that HIV/AIDS programs receive, despite having many more cases of disease. The report

also has several policy recommendations that should be adopted, including: adding hepatitis screening guidelines as a component of core preventive services for Medicare and Medicaid, expanding hepatitis C prevention programs among injection drug users, expanding funding for community health centers, and fostering relationships between health departments and correctional institutions to ensure that incarcerated persons have access to viral hepatitis services.[46]

Another way to address the underreporting on death certificates is to teach medical and nursing students how to accurately complete them. Providers need to realize the importance of accurate death certificate reporting and how that data can affect funding and prevention programs in their areas. States should emphasize that the death certificate should be filled out by the person's primary care provider whenever possible, even if that person died in a hospital emergency room.

Limitations

There are several limitations in this study. A stringent matching system was used, which likely left out several HIV/AIDS, hepatitis C, or co-infected cases from the final datasets. This was to ensure that the final datasets had the greatest likelihood of containing true matches; however, it limited the overall sample size. Sample size was also limited by choosing only hepatitis C cases that met the 2005 CDC/CSTE case definition for a confirmed past or present case of hepatitis C. This eliminated many older cases of hepatitis C that were never confirmed according to the present case definition, but that were likely true cases of hepatitis C.

Another limitation is that the data were taken from the finalized death datasets from the DPH's Office of Vital Records. While these were the most reliable death data because they had been analyzed for coding accuracy and logistics, they were not a direct transcription of what was on the death certificates. Without seeing the original death certificates, it is hard to determine any differences between what the provider listed as a cause of death and what ended up being listed as a cause of death in the final dataset. Future research could address this limitation by comparing the causes of death written on the death certificates to those coded by the CDC.

Finally, these results are limited in interpretation and cannot be literally compared to causes of death in the general population. The general population was not examined in this study and age-adjusted death rates were not used, so any generalizations beyond these datasets would be mere speculation.

Conclusion

This study examined the reported causes of death for Connecticut residents who had HIV/AIDS and/or hepatitis C and died between 2003 and 2007. The results support other studies that have indicated that HIV/AIDS and hepatitis C are underreported on death certificates. HIV disease is more likely to be reported as a primary cause of death in persons with HIV/AIDS or in co-infected persons than hepatitis C is to be reported in hepatitis C infected persons.

These results show that program and policy changes are needed at various levels. Hepatitis C is the most common bloodborne infection in the United States, yet is severely underreported on death certificates. Analyses of mortality data will therefore show a lesser burden of disease than actually exists. Even among HIV/AIDS cases there were low frequencies of HIV disease listed in cases where deaths may have been attributable to HIV disease. More funding for prevention programs, enhanced screening of at-risk persons, and stricter guidelines on death certificate completion may alleviate this underreporting.

Appendix I. ICD-10[1] cause of death groups for analysis.

Cause of death	ICD-10 code
Infectious diseases	
HIV disease	B20-B24
Viral hepatitis	
Acute hepatitis A	B15
Acute hepatitis B	B16
Acute hepatitis C	B17.1
Other acute viral hepatitis	B17, B17.0, B17.2, B17.8
Chronic hepatitis B	B18.0, B18.1
Chronic hepatitis C	B18.2
Other chronic viral hepatitis	B18.8
Chronic viral hepatitis, unspecified	B18, B18.9
Other viral hepatitis, unspecified	B19
Other infectious/parasitic disease	A00-B99 and not in above categories
Neoplasms	
Liver cancer	C22
Kaposi sarcoma, not listed in B20-B24	C46
Kidney cancer	C64-C65
Other malignant neoplasm	C00-C97 and not in above categories
Diabetes mellitus	E10-E14
Major cardiovascular disease	I00-I78
Alzheimer's disease	G30
Influenza/pneumonia	J09-J18
Chronic lower respiratory disease	J40-J47
Liver disease	
Alcoholic liver disease	K70
Hepatic failure	K72
Other chronic liver disease and cirrhosis	K73-K74
Other liver disease	K71, K75-K77
Nephritis, nephrotic syndrome, and nephrosis	N00-N07, N17-N19, N25-N27
Symptoms and signs involving the digestive system and abdomen	R10-R19
Accident	V01-X59, Y85-Y86
Intentional self-harm	X60-X84, Y87.0
Assault	X85-Y09, Y87.1
Other cause of death	All other ICD-10 codes

[1] International Classification of Diseases, 10th Revision. <http://apps.who.int/classifications/apps/icd/icd10online/>.

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