Arkansas Department of Health

Hepatitis C Epidemiologic Profile 2014

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ACKNOWLEDGMENTS

The author sincerely thanks Dirk T. Haselow, MD, PhD, Nathaniel Smith, MD, MPH, Joseph Bates, MD, MS, Stephanie Williams, BSN, NP, Donnie Smith, MA, J. Gary Wheeler, MD, MPS, Kellye McCartney, Naveen Patil, MD, MHSA, Ralph Wilmoth, MPH, MPA, and Arrie Morris, MPH from the Arkansas Department of Health for their guidance and assistance during the design, completion, and writing of this report.

The author would like to thank the following organizations for their contributions to this project:

- Arkansas Department of Health: Howraa Al-Mousawi, PhD, Betty Bohanna, Lynda Lehing, Chris Fisher, Abby Holt, MPH, Paul Johnson, Shalini Manjanatha, Theressia Mitchell, CTR RHIT, John Senner, PhD, and Namvar Zohoori, MD, PhD, MPH.
- Association of State and Territorial Health Officials: Elizabeth Ruebush, MPH and Catherine Cairns, MPH for providing funding to support this project and oversight to ensure its successful completion.
- Centers for Disease Control and Prevention: Monina Klevens, DDS, MPH and Elizabeth Hughes, DrPH for providing technical and analytical assistance.
- Centers for Disease Control and Prevention (CDC)/Council of State and Territorial Epidemiologists (CSTE) Applied Epidemiology Fellowship.
- University of Arkansas for Medical Sciences, College of Public Health Interns: Mohammad Umair Azam, MPH, Alexandria Beebe, Dylan Burks, MPH, Michael J.E. Grier, MPH, Taylor Quattlebaum, and Ewelina Sulek, MPH.

The author would also like to thank the following persons, who participated as stakeholders to guide the development of this profile: Glen Baker, MD (Arkansas Public Health Laboratory), Appathurai Balamurugan, MD, MPH (Arkansas Department of Health), Ryan Bariola, MD (University of Arkansas for Medical Sciences), Deborah Buzzell, Elizabeth Childers, PhD, MPH (Division of Behavioral Health Services, Department of Human Services), Quynhchau Doan, RPH, PhD (AbbVie), Mauricio Garcia-Saenz-De-Selicia, MD (University of Arkansas for Medical Sciences), Pamela Ford (Arkansas Medicaid), Lynn Frazier, MSNc, APRN, CNP (Liver Wellness Center), B. Matt Garner, MD (St. Bernards Medical Center), Susan Garner, RN (St. Bernards Medical Center), Linda Gladden, RN (Arkansas Department of Health), William Golden, MD (Arkansas Medicaid), Selestria Guy, MHRM (Arkansas Department of Health), Peggy Healy, LCSW, LPN (University of Arkansas for Medical Sciences), Anita Joshi (Arkansas Foundation for Medical Care), Jill Johnson, PharmD, BCPS (University of Arkansas for Medical Sciences), Marcus Kirby (BriovaRx), Victoria McCoy, APRN (St. Bernards Medical Center), J. Dan Moore, MD (ARCare), Latoya Morgan, Fred Morton (AbbVie), Kesha O'Reilly (Gilead), Tony Orr (Gilead), Deborah Patton, Estelita Quimosing, MD (Jefferson Comprehensive Care System, Inc), Dean Rieger, MD (Arkansas Department of Corrections), José Romero, MD, FAAP (Arkansas Children's Hospital), Lisa Seidel, RN (Arkansas Department of Health), James Shelton, MD (Arkansas Department of Corrections), Jenny Sims (Arkansas Medicaid), David Stegall (Arkansas Department of Health), Ron Spillers, Ava Titsworth (Catar Clinic), Tiffany Vance (Arkansas Department of Health), Keyur Vyas, MD (University of Arkansas for Medical Sciences).

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ABBREVIATIONS

ADH: Arkansas Department of Health
AIDS: Acquired Immune Deficiency Syndrome
ALT: Alanine Aminotransferase
ARCHES: Arkansas Cardiovascular Health Examination Survey
ASTHO: Association of State and Territorial Health Officials
CDC: Centers for Disease Control and Prevention
CLD: Chronic Liver Diseases
CLIA: Clinical Laboratory Improvement Amendments
CME: Continuing Medical Education
CNE: Continuing Nursing Education
CSTE: Council of State and Territorial Epidemiologists
DNA: Deoxyribonucleic Acid
ED: Emergency Department
eHARS: Enhanced HIV/AIDS Reporting System
FDA: Food and Drug Administration
HBV: Hepatitis B virus
HCV: Hepatitis C virus
HIV: Human Immunodeficiency Virus
ICD-9-CM: *International Classification of Diseases, Ninth Revision, Clinical Modification*
ICD-10: *International Classification of Diseases, Tenth Revision*
IDU: Injection Drug Use
IgG: Immunoglobulin G
IgM: Immunoglobulin M
IU/mL: International Units per Milliliter
MSM: Men who have Sex with Men
NEDSS: National Electronic Disease Surveillance System
NHANES: National Health and Nutrition Examination Survey
NSDUH: National Survey on Drug Use and Health
PWID: Persons who Inject Drugs
RNA: Ribonucleic Acid
SVR: Sustained Virologic Response
SAMHSA: Substance Abuse and Mental Health Services Administration
TIP: Treatment Improvement Protocol
US: United States
USPSTF: United States Preventive Services Task Force
WHO: World Health Organization

KEY TERMS AND DEFINITIONS

- Acquired Immune Deficiency Syndrome (AIDS): Severe damage to the immune system that can occur following infection with the Human Immunodeficiency Virus (HIV).
- Acute Hepatitis C Virus Infection: A phase of hepatitis C virus (HCV) infection occurring within the first 6 months and characterized by symptoms such as yellowing of the skin or eyes, abdominal pain, vomiting, nausea, diarrhea, malaise, grey-colored stools, dark urine, or other symptoms.
- Ascites: Fluid retention of the peritoneal cavity.
- Baby Boomer: Person born in the years 1945 – 1965.
- Chronic Hepatitis C Virus Infection: A phase of hepatitis C virus (HCV) infection occurring after the first 6 months of infection acquisition, whereby the virus infects the cells of the liver in a long-term form of infection that can last several years to decades while the virus attacks the cells of the liver.
- Cirrhosis: Scarring of the liver resulting in liver function impairment that can be caused by infection, alcohol or drug use, or other causes.
- Current Hepatitis C Virus Infection: Infection with hepatitis C virus (HCV) whereby ribonucleic acid from the virus is present in the blood.
- Epidemiology: Study of the distribution of diseases or health conditions and factors influencing their occurrence.
- Esophageal Varices: Abnormally large veins in the esophagus that develop as blood flows from the liver into smaller veins of the body because blood flow has been restricted from veins flowing out of the liver.
- Hepatic Encephalopathy: Altered mental status resulting from the liver's inability to remove waste from the blood, leading to a buildup of substances such as ammonia.
- Hepatitis C Virus: An enveloped, single-stranded ribonucleic acid (RNA) virus in the family Flaviviridae and genus *Hepacivirus* that infects humans.
- Hepatitis B Virus: A double-stranded deoxyribonucleic acid (DNA) virus in the family Hepadnaviridae and genus *Orthohepadnavirus* that infects humans.
- Hepatocellular Carcinoma: Liver cancer.
- Hepatocyte: Cell of the liver attacked by hepatitis B virus and hepatitis C virus.
- Human Immunodeficiency Virus (HIV): A single-stranded ribonucleic acid (RNA) retrovirus in the family Retroviridae, genus *Lentivirus* that attacks cells of the immune system, potentially leading to Acquired Immune Deficiency Syndrome (AIDS) in humans.
- Immunoglobulin M (IgM): An antibody particle produced by the immune system that helps to fight infections. Presence of IgM antibodies against some bacteria or viruses can indicate a recently acquired infection as IgM is the first antibody produced after exposure to an antigen.
- Immunoglobulin G (IgG): An antibody particle produced by the immune system that helps to fight infections. Presence of IgG antibodies against some bacteria or viruses can indicate past or present infection.
- Incidence: Number of new infections.
- Intrahepatic Bile Duct: Bile ducts within the liver that allow bile, a product of the liver that helps in the breakdown of fats during digestion, to flow out of the liver.

- Jaundice: Yellowing of the skin.
- Malaise: Feeling of weakness or illness.
- Morbidity: Burden of illness.
- Mortality: Burden of death.
- Nucleic Acid: Molecules formed by nucleotides that encode amino acid sequences used to form proteins. Types of nucleic acids include ribonucleic acid (RNA) and deoxyribonucleic acid (DNA).
- Past or Present Hepatitis C Virus Infection: Infection with hepatitis C virus (HCV) whereby Immunoglobulin G (IgG) antibodies against HCV are present in the bloodstream and HCV ribonucleic acid may or may not be present.
- Percutaneous: Puncture of the skin.
- Prevalence: Persons living with a disease, regardless of the time of diagnosis.
- Scleral Icterus: Yellowing of the eyes.
- Seroprevalence: Number of persons with serologic blood markers (antibodies) indicative of a disease or condition.
- Signal to Cut-Off Ratio: A numeric test result provided with some hepatitis C virus (HCV) immunoglobulin G (IgG) antibody results that indicates the likelihood of a true positive result for HCV antibodies.
- Sustained Virologic Response: Absence of hepatitis C virus (HCV) ribonucleic acid in blood for 24 weeks after completion of antiviral treatment.
- Transfusion: Transfer of fluid, such as blood, into a vein or artery.
- Vertical Transmission: Transmission from mother to child during pregnancy or childbirth.

EXECUTIVE SUMMARY

Hepatitis C virus (HCV) infection is the most common bloodborne infection in the United States (US)[1]. Recognizing that HCV is increasingly important in Arkansas, the Arkansas Department of Health (ADH) created a statewide hepatitis C epidemiologic profile to better understand the burden of HCV in Arkansas and bring attention to the need for improvements in HCV prevention, testing, surveillance, and treatment availability.

HCV infection is a growing cause of illness and deaths among Arkansans. Approximately 1.8% of adult Arkansans, or nearly 38,000 persons, have been infected with HCV. The primary transmission mode of HCV is percutaneous exposure to blood from an infected person, although HCV is also transmitted sexually. The Centers for Disease Control and Prevention (CDC) estimate that 45% – 85% of persons with HCV are unaware of their infection[2].

The majority of persons newly infected with HCV experience no symptoms; however, symptoms of acute hepatitis present in 20% – 30% of cases. Symptoms include jaundice, scleral icterus, nausea, vomiting, and abdominal pain. Approximately 75% – 85% of persons infected with HCV develop chronic infection[2]. Appropriately deemed "the silent killer," HCV replicates in the hepatocytes and destroys liver function over decades of asymptomatic infection. According to the CDC, 60% – 70% of chronically infected persons develop chronic liver disease, up to 20% of persons develop cirrhosis, and up to 5% die from liver diseases related to HCV[3]. Currently, HCV is the leading cause of liver cancer and the leading indication for liver transplant in the United States[2].

The facts and figures herein include analyses of multiple data sources to describe HCV-related morbidity and mortality in Arkansas. While approximately 1.8% of adult Arkansans have been infected with HCV, baby boomers, or persons born 1945 – 1965, represent a generation of persons heavily burdened by HCV, as approximately 3.6% of Arkansan baby boomers have been infected. Persons who have ever injected drugs have the highest HCV seroprevalence, at approximately 33.7%. Many Arkansans are now beginning to experience HCV-related morbidity and mortality, which has increased over the last decade. HCV contributed to at least 4,141 inpatient hospitalizations and 3,073 emergency room visits in 2012. Hospitalizations for HCV are increasing alongside complications related to HCV, such as cirrhosis and liver cancer. Over one-quarter of hospitalizations related to cirrhosis, esophageal varices, and hepatic encephalopathy during 2004 – 2012 also documented HCV infection. Deaths related to HCV have also increased over the past several years, with HCV contributing to the death of at least 1,538 Arkansans during 1999 – 2012. HCV-related morbidity and mortality will continue to climb if Arkansans are not connected to life-saving HCV testing and treatment.

A commitment to understanding and reducing illness and death from HCV among Arkansans is part of the Arkansas Department of Health's mission to protect the health of all Arkansans. Describing HCV in Arkansas is a first step towards building targeted strategies to reduce HCV incidence and prevent morbidity and mortality among persons suffering from chronic HCV infection. Recognition of this silent killer will help Arkansas combat HCV, a curable illness, through prevention, screening, and treatment.

INTRODUCTION

Hepatitis C Virus (HCV) infection is the most common bloodborne infection in the US[1]. The primary transmission mode of HCV is percutaneous exposure to blood from an infected person, although HCV is also transmitted sexually. Groups at highest risk for acquiring HCV are injection drug users and persons who received blood transfusions before screening of blood, blood products, and organ donations began in 1992[4]. Recently, persons born in the years 1945 – 1965 have been recommended for HCV screening as rates of HCV are five times higher among this group than other birth cohorts[4].

Once a person is infected, HCV attacks the hepatocytes, or cells of the liver. Approximately 15% – 25% of persons infected with HCV will clear the virus on their own. The remaining 75% – 85% develop chronic HCV infection[2]. During chronic HCV infection, persons often remain asymptomatic for decades while HCV damages the hepatocytes, or cells of the liver. Among persons ever infected with HCV, 60% – 70% will develop chronic liver disease, 5% – 20% will develop cirrhosis, and 1% – 5% will die of cirrhosis or hepatocellular carcinoma (i.e. liver cancer)[3]. This life threatening infection is estimated to affect approximately 2.7 million persons in the United States[5] and at least 1.8%, or nearly 38,000 adult Arkansans.

The Centers for Disease Control and Prevention (CDC) estimate that 45% – 85% of persons with HCV are unaware of their infection[2]. HCV infection most often causes no symptoms when a person is infected and is called the “silent killer” as chronically infected persons often remain asymptomatic until severe liver damage develops up to decades after acquiring infection. Treatment options to cure persons infected with HCV have recently improved and are projected to improve over the next year, transitioning from injectable interferon-based regimens with multiple severe side effects to well-tolerated, all-oral regimens.

To enhance the recognition of HCV in Arkansas, the Arkansas Department of Health applied for and was awarded a grant from the Association of State and Territorial Health Officials (ASTHO) to create a state hepatitis C epidemiologic profile. What follows is a compilation of information on the burden of HCV and HCV-related illnesses and deaths among Arkansans using data collected at the state and national level. Further, an overview of testing recommendations, surveillance efforts, and national strategies, plans, and goals is provided. Finally, selected educational materials and training opportunities for both physicians and patients are provided.

BURDEN OF HEPATITIS C VIRUS INFECTION

Describing the burden of HCV in the United States and in Arkansas is key to understanding how Arkansans are affected by HCV and what transmission modes drive the occurrence of new infections. This section will highlight the prevalence (number of persons living with) and incidence (number of new infections) of HCV in the United States and in Arkansas.

Prevalence

Several data sources estimate the prevalence of HCV in the United States. Data from the National Health and Nutrition Examination Survey (NHANES), performed during 2003 – 2010, showed that the prevalence of HCV antibody, indicative of either past or present infection with HCV, was 1.3% (Table 1)[5]. This study also tested participants for HCV ribonucleic acid in blood samples to estimate the prevalence of current infection with HCV and determined that approximately 1% of the US population was living with a current HCV infection. Although NHANES provides a nationwide estimate of the burden of HCV, it has several limitations, including that persons who were institutionalized were excluded from the study. HCV prevalence has been demonstrated to be higher among incarcerated persons than non-incarcerated persons[6], and their exclusion from the study likely leads to an underestimation of the true prevalence in the US population.

The Arkansas Cardiovascular Health Examination Survey (ARCHES), a cross-sectional, representative survey of non-institutionalized Arkansans aged 18 years or older[7], was conducted in 2006 – 2008. While the primary goal of this study was to examine cardiovascular risk factors, it contributes important information regarding HCV prevalence in Arkansas. Subjects who participated were asked to provide blood samples, which were tested for presence of HCV antibodies. A detailed description of methods used to analyze ARCHES data and relevant limitations are included in Appendix A.

Testing demonstrated that 1.8% of Arkansans had a past or present infection with HCV (Table 1). Limitations of this study include the exclusion of institutionalized persons, such as persons incarcerated at the time of participant selection, people who did not speak English, people with cognitive, psychiatric, or developmental disorders, and persons without an address, such as those who were homeless at the time of participant recruitment. This study also tested only for the presence of HCV antibodies, indicative of either past or present infection. Assuming that approximately 80% (range: 75% – 85%) of persons who are infected with HCV develop a chronic HCV infection[8], the prevalence estimate for current HCV infection in Arkansas according to the ARCHES study would be 1.4%. These limitations, like with the NHANES study, likely result in an underestimation of the prevalence of HCV in Arkansas.

Logistic regression models were created to identify risk factors for HCV infection among persons in the ARCHES study. Multiple logistic regression models revealed that having an income less than $10,000 per year, ever injecting drugs, or having a sex partner who was used injection drugs or who was infected with HCV increased the likelihood of having HCV infection (Table 2). Of note, the type of sex a participant had with an HCV-infected or injection drug using person was not specified; however, the type of sex may have influenced the participant's risk for acquiring HCV as sexual practices that damage mucosal membranes or expose persons to blood are associated with a higher likelihood of sexual HCV transmission than other types of sex[9]. Other predictors, including race, ethnicity, completing less than a high school education, being born during the years 1945 – 1965, sex, and insurance status were not significantly predictive of HCV status in univariate logistic regression models.

Table 1. Prevalence Estimates of Hepatitis C Virus (HCV) Infection — Arkansas						
Population	Years of Study	Prevalence of Past or Present HCV Infection (95% Confidence Interval)*	Estimated Number in Population with Past or Present HCV Infection	Prevalence or Estimate of Current HCV Infection (95% Confidence Interval)†	Estimated Number in Population with Current Infection	Data Source
United States	2003 – 2010	1.3% (1.2% – 1.5%)	3.6 million (3.0 – 4.2 million)	1.0% (0.8% – 1.2%)	2.7 million (2.2 – 3.2 million)	National Health and Nutrition Examination Survey (NHANES)[5]
Arkansas	2006 – 2008	1.8% (0.9% – 2.6%)	37,709 (20,349 – 55,069)	1.4% (0.7% – 2.1%)	30,167 (16,279 – 44,055)	Arkansas Cardiovascular Health Examination Survey (ARCHES)[7]

*Past or Present HCV infection was detected by reactivity to an antibody test for HCV.
†Current HCV infection was detected by presence of a quantifiable viral load of HCV ribonucleic acid in the NHANES study. Prevalence of current HCV infection was estimated for the ARCHES study by assuming that current infection would occur among 80% of past or present infections (range: 75% - 85%)[8].

Table 2. Risk Factors for Hepatitis C Virus Infection in Arkansas from the ARCHES Study				
Variable	Unadjusted Odds Ratio	95% Confidence Interval	Adjusted Odds Ratio	95% Confidence Interval
Annual Income <$10,000	4.7	(1.5 – 14.7)	5.3	(1.6 – 18.1)
Ever injected drugs	38.7	(9.8 – 153.0)	24.4	(6.5 – 91.7)
Ever had sex with an injection drug user or someone with HCV	19.6	(6.2 – 61.7)	11.4	(3.7 – 35.3)
Had a blood transfusion before 1992	1.4	(0.4 – 4.7)	-	-
Born 1945 – 1965	5.9	(1.9 – 18.2)	-	-
Black race (reference = non-black)	1.5	(0.5 – 4.1)	-	-
Hispanic ethnicity	2.8	(0.3 – 22.3)	-	-
Education less than high school	1.8	(0.6 – 5.3)	-	-
Sex (reference = Male)	0.9	(0.3 – 2.3)	-	-
No Health Insurance (reference = insured)	2.8	(0.97 – 7.9)	-	-
Age	1.0	(0.99 – 1.02)	-	-

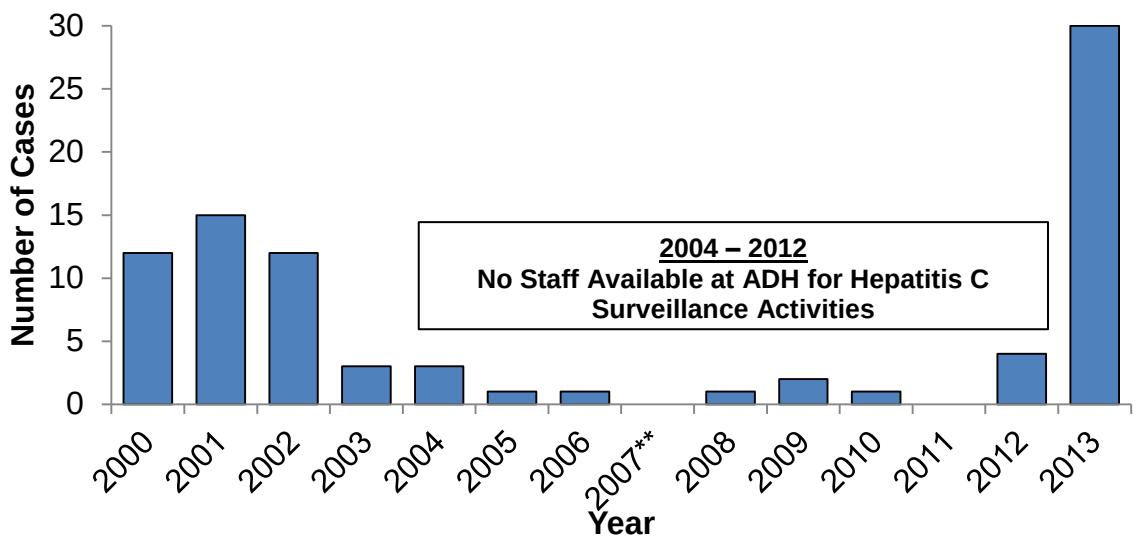
Incidence

The incidence of HCV, or number of new infections, in Arkansas is monitored by conducting surveillance for acute HCV. Public health surveillance for acute HCV infection is limited for many reasons. First, only 20% – 30% of persons develop symptoms of acute hepatitis, such as jaundice, scleral icterus, nausea, vomiting, diarrhea, abdominal pain, malaise, fatigue, grey-colored stools, or other symptoms of acute hepatitis[10]. Furthermore, many people do not seek care to determine the cause of their symptoms or are not tested for HCV even if they present to a healthcare provider, who might consider alternative reasons for these symptoms, such as liver failure, cirrhosis, cancer, gallstones, drug reaction, or other reasons. Additionally, many diseases of public health importance are under-reported to the appropriate public health entity, despite the fact that any positive HCV laboratory result performed on any Arkansan is reportable to ADH by regulation[11,12]. Even when HCV testing is reported to ADH, there is no single laboratory test that can distinguish between acute and chronic HCV infection. Laboratory results must be accompanied by morbidity reports detailing symptoms of acute hepatitis and liver function testing results or documentation of seroconversion to meet the acute HCV case definition[13]. Additionally, ADH is not currently funded for viral hepatitis surveillance from any state or federal entity. Together, these limitations result in a diminished ability to detect acute HCV cases through public health surveillance.

With these limitations in mind, ADH has continued to conduct limited surveillance and follow-up for acute HCV. Activities involve the completion of a standardized case report form documenting symptoms of acute HCV, liver function testing results, and risk factors to characterize the transmission of HCV in Arkansas. A detailed description of methods used to collect and analyze HCV surveillance data and relevant limitations are included in Appendix A. Through surveillance efforts, 30 acute HCV cases were identified in 2013 (Figure 1). Of these, 27 (90.0%) were white race and 17 (56.7%) were male. The age distribution of cases is shown in Table 3. An increase in the number of acute HCV cases detected through surveillance in 2013 should not be interpreted as a true increase as it likely reflects increased surveillance efforts achieved through development of a new ADH HCV surveillance program. Because all cases are not investigated to determine acute versus chronic status, the number of cases investigated by ADH staff is an underestimate of the true number of acute HCV cases in Arkansas.

Using methodology developed by CDC, the true number of acute cases can be estimated using surveillance data[14]. This methodology accounts for the marked under-detection of cases via public health surveillance due to the absence of symptoms in the majority of HCV cases, the fact that some persons do not get tested for HCV despite their development of symptoms, and underreporting to public health entities. The methodology entails multiplying the number of cases detected through surveillance by a correction factor of 13.4[14]. Given a case-load of 30 cases detected via public health surveillance in 2013 multiplied by a correction factor of 13.4, it is thought that at least 402 cases of HCV were newly acquired in the year 2013. Of note, this number is still believed to be an underestimate given that more cases would have been detected by public health surveillance if staff were available to investigate all reports and definitively determine their acute versus chronic status.

Figure 1. Acute Hepatitis C — Arkansas, 2000 – 2013*



*Case count data was accessed from Centers for Disease Control and Prevention (CDC) Atlas tool for years 2000-2008 (Accessed from: http://www.cdc.gov/NCHHSTP/Atlas/). Data from 2009-2013 was accessed from case count data stored in the Arkansas National Electronic Disease Surveillance System (NEDSS).
**Case count data from 2007 was unavailable from either source.

Table 3. Characteristics of Acute Hepatitis C Cases — Arkansas, 2013

Characteristic	Number of Cases (%)
Total	30 (100.0)
Age (Years)	
<30	10 (33.3)
30 – 34	10 (33.3)
35 – 54	5 (16.7)
55+	5 (16.7)
Sex	
Female	13 (43.3)
Male	17 (56.7)
Race	
White	27 (90.0)
Other	3 (10.0)
Symptoms of Acute HCV	
Yes	30 (100.0)
No	0 (0.0)
Jaundice	
Yes	16 (53.3)
No	10 (33.3)
Unknown	4 (13.3)

Alanine Aminotransferase Level		
≥400 IU/mL	29	(96.7)
<400 IU/mL	1	(3.3)
Injection Drug Use in 2 Weeks – 6 Months Before Symptom Onset		
Yes	9	(30.0)
No	7	(23.3)
Unknown	14	(46.7)
Lifetime Injection Drug Use		
Yes	16	(53.3)
No	4	(13.3)
Unknown	10	(33.3)
Abbreviations: IU/mL: International Units per Milliliter.		

HCV Surveillance Among Arkansans Under 30 Years of Age

Over the past several years, an alarming trend of increasing HCV infection rates among young persons aged 15 – 30 years in the US has been documented by several states, including, but not limited to, Massachusetts, New York, Indiana, and Wisconsin[15–20]. Infected young persons are mostly white and living in suburban and rural areas of the US[21,22]. The emergence of HCV has been attributed to the transition to heroin or prescription opioid injection after initiation of nonmedical use of prescription opioids or painkillers[21–23]. Surveillance data from Indiana and New York has demonstrated clusters of HCV among young injection drug users[18,19]. Furthermore, in Massachusetts, the number of newly reported cases in 2012 aged 15 – 30 years exceeded the number of newly reported cases in the baby boomer population born 1945 – 1965 according to 2012 surveillance data[17]. Interviews with HCV-positive persons aged 18 – 24 years and reported in Massachusetts during 2012 revealed that the most commonly used drugs were oxycodone, heroin, hallucinogens, alcohol, and marijuana. Among the reported and interviewed individuals, 65% reported injecting drugs and 71% of young injectors used a syringe that was previously used by another person[17].

Data from the National Survey on Drug Use and Health (NSDUH) show that Arkansas is consistently ranked as one of the states with the highest nonmedical use of prescription pain relievers in the US, especially among young persons[24]. For instance, 7.8% of Arkansans aged 12 – 17 years and 12.9% of Arkansans aged 18 – 25 years in the 2010 – 2011 survey cycle reported nonmedical use of prescription pain relievers in the past year, which ranks Arkansas as the 3rd and 8th highest state, respectively, for nonmedical use of prescription painkillers by these age groups in the entire United States[24].

With these national trends in mind, ADH implemented enhanced surveillance procedures for HCV among persons aged less than 30 years in January 2013 to characterize HCV infection in young Arkansans. Accordingly, all persons aged less than 30 years reported through mandatory notifiable disease reporting with a laboratory or physician's report of an HCV antibody or nucleic acid positive test result were investigated using standard communicable disease surveillance procedures. Specifically, for any new case reported to ADH, the physician ordering the HCV test

was faxed a case report form to gather information on laboratory testing, symptoms, risk factors, and demographics. Because ADH did not have an operational HCV registry before 2013, data accurately defining the time of diagnosis for cases could not be determined only by the year that they were reported to ADH. A detailed description of methods used to collect and analyze HCV surveillance data and relevant limitations are included in Appendix A.

Through surveillance during 2013, 853 Arkansans with HCV infection aged <30 years at the time of report were detected through HCV surveillance (Table 4). Among those reported, 248 persons were newly diagnosed with chronic HCV in 2013. An additional 429 persons were thought to be newly diagnosed with chronic HCV in 2013 but data were insufficient to confirm that the diagnosis was new. The rate of new HCV diagnosis was highest among persons aged 25 – 29 years.

Descriptive characteristics of all cases identified in 2013 in individuals aged <30 years at the time of report are shown in Table 5. In summary, a total of 853 persons with chronic HCV were reported during 2013; median age was 25 years and 56.5% were male. At the time of testing, 43.4% of persons were living in a correctional facility.

Table 4. Chronic Hepatitis C Virus (HCV) Infections Identified through Public Health Surveillance Among Persons Aged Less than 30 Years — Arkansas, 2013

Age Group (Years)	Arkansas Population[25]	Number of Cases of Newly Diagnosed HCV	Number of Cases with Undetermined Onset Year	Incidence Rate per 100,000*
<13	513,753	6	3	1.2 – 1.8
13 – 19	274,940	11	19	4.0 – 10.9
20 – 24	208,880	91	160	43.6 – 120.2
25 – 29	193,019	139	247	72.0 – 200.0
Total	1,190,592	248	429	20.8 – 56.9

*Incidence rate is presented as a range where the lower estimate includes only cases confirmed to be newly diagnosed in 2013 and the upper estimate includes all cases who were newly diagnosed or whose year of diagnosis was not determined.

Table 5. Characteristics of Arkansans Aged Less Than 30 Years with Hepatitis C Virus (HCV) Infection — 2013

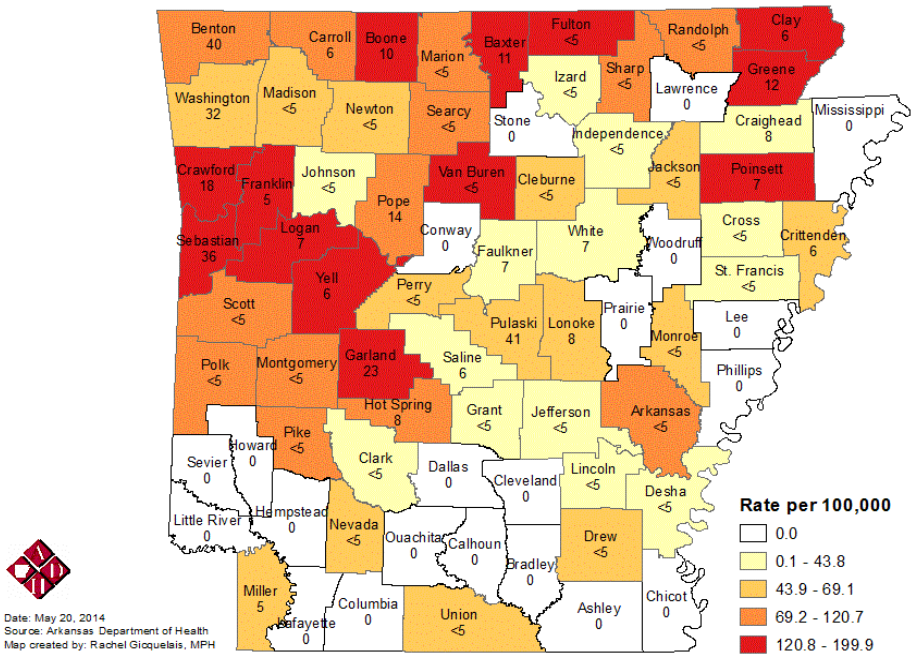
	Number of Cases	%
Total	853	100.0
Age (Years)		
<1.5	6	0.7
1.5 – 4	6	0.7
5 – 12	9	1.1
13 – 19	37	4.3
20 – 24	299	35.1
25 – 29	496	58.1

Sex			
	Female	371	43.5
	Male	482	56.5
Race			
	Black	26	3.1
	White	633	74.2
	Multi-Racial	6	0.7
	Other or Unknown	188	22.0
Reporting Source			
	Laboratory	662	77.6
	Hospital or Clinic	118	13.8
	Blood Bank	63	7.4
	Other	10	1.2
Incarceration Status at Testing			
	Incarcerated	370	43.4
	Non-Incarcerated	483	56.6
Diagnosis Year			
	2013	248	29.1
	Before 2013	176	20.6
	Undetermined	429	50.3

Using data from surveillance on each patient's county of residence or county of their physician's healthcare facility if the patient's address was unavailable, maps were created by plotting crude rates of infections among 832 persons aged 13 – 29 years. Rates are divided into quintiles in all figures below. Of note, pediatric cases of HCV among persons aged <13 years at the time of report are excluded from the analyses below as these likely represent transmission trends reflective of vertical (maternal-infant) HCV transmission. Data on these individuals is summarized in the 'Special Populations' section.

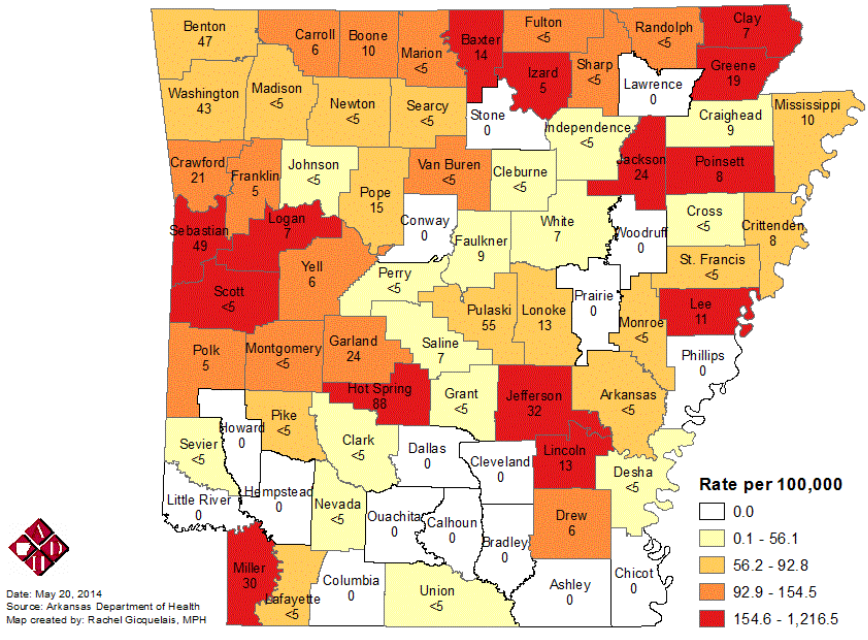
The geographic distribution of non-incarcerated cases who were newly diagnosed in 2013 or whose year of diagnosis was not determined is shown in Figure 2. High rates of infection clustered in western Arkansas among Crawford, Sebastian, Franklin, Logan, Yell, and Garland counties. Rates of infection were more than 150 cases per 100,000 persons in Logan, Baxter, and Clay counties. Notably, case counts among these areas were all fewer than 12 cases; however, the county populations were also small, resulting in high rate estimates. Figure 3 includes non-incarcerated and incarcerated cases (Figure 3), whose addresses are reported as their current detaining facility, diagnosed during 2013 or in an undetermined year. Rates of infection were above 300 cases per 100,000 persons in Hot Spring, Jackson, Lee, Lincoln, and Miller counties. Finally, Figure 4 includes all investigated cases, regardless of time of diagnosis, by county at time of the earliest received 2013 report. Notably, infection rates were highest in Hot Spring, Jackson, Lee, Lincoln, and Miller counties, which all had rates greater than 400 cases per 100,000 persons.

Figure 2. New Diagnoses* of Hepatitis C Virus Infection Among Non-Incarcerated Arkansans Aged 13 – 29 Years — Arkansas, 2013



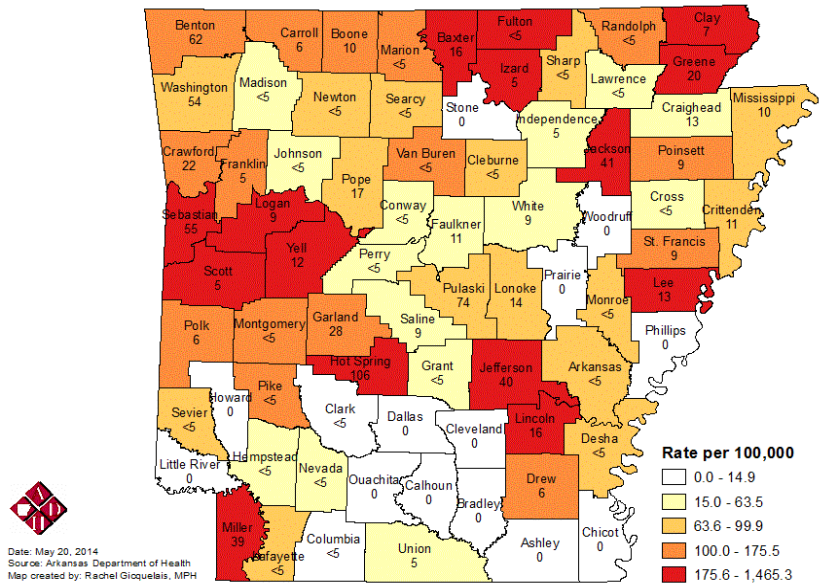
*Map includes all persons who were newly diagnosed with Hepatitis C Virus (HCV) infection during 2013 or whose diagnosis year was underdetermined.
Numbers represent HCV cases per county.

Figure 3. New Diagnoses* of Hepatitis C Virus Infection Among Incarcerated and Non-Incarcerated Arkansans Aged 13 – 29 Years — Arkansas, 2013



*Map includes all persons who were newly diagnosed with Hepatitis C Virus (HCV) infection during 2013 or whose diagnosis year was underdetermined.
Numbers represent HCV cases per county.

Figure 4. Cases of Hepatitis C Virus Infection Among Arkansans Aged 13 – 29 Years Reported During 2013



Numbers represent HCV cases per county.

Among the 832 HCV cases aged 13 – 29 years, 741 identified an ordering physician, who was asked to complete the HCV case investigation questionnaire. A total of 596 (80.4%) questionnaires were returned and characteristics of these cases are summarized in Table 6. Overall, 378 (63.4%) persons had ever injected drugs and 7 (1.2%) were coinfected with human immunodeficiency virus (HIV). Among 252 reports from persons who inject drugs (PWID) who specified drugs that were injected, 207 (82.1%) injected methamphetamine and 96 (38.1%) injected any opioid (heroin, oxycodone, hydromorphone, morphine, methadone, buprenorphine, fentanyl, hydrocodone, oxymorphone, or unspecified opioids). At least 40 (41.7%) injection opioid users injected prescription opioids.

Table 6. Characteristics of Arkansans Aged 13 – 29 Years with Hepatitis C Virus (HCV) Infection —2013

Characteristic	Number of Cases	%
Total	596	100.0
Age (Years)		
13 – 19	28	4.7
20 – 24	209	35.1
25 – 29	359	60.2
Sex		
Female	275	46.1
Male	321	53.9
Race		
White	493	82.7
Black	15	2.5
Multi-Racial	6	1.0
Other or Unknown	82	13.8

Reporting Source		
Laboratory	492	82.6
Hospital or Clinic	95	15.9
Other	9	1.5
Incarceration Status at Testing		
Incarcerated	266	44.6
Non-Incarcerated	330	55.4
Diagnosis Year		
2013	235	39.4
Before 2013	154	25.8
Undetermined	207	34.7
Ever Injected Drugs in Lifetime		
Yes	378	63.4
No	71	11.9
Unknown	147	24.7
Ever in Jail or Prison in Lifetime		
Yes	311	52.2
No	60	10.1
Unknown	225	37.8
Ever Received a Tattoo from an Unregulated Source*		
Yes	161	27.0
No	80	13.4
Unknown	355	59.6
Diagnosed with Human Immunodeficiency Virus (HIV) Infection		
Yes	7	1.2
No	428	71.8
Unknown	161	27.0
Ever been Homeless		
Yes	86	14.4
No	208	34.9
Unknown	302	50.7

*Surveillance case investigation procedures did not include questions about the receipt of tattoos from an unregulated source until April 2013. Accordingly, the data presented likely underestimates the proportion of persons receiving tattoos from an unregulated source. Tattoos received from an unregulated source included tattoos received in prisons or any other tattoos received outside of a tattoo parlor.

TESTING RECOMMENDATIONS

Testing recommendations for HCV screening involve two components: who to test and how to appropriately test for HCV. Guidelines for both of these topics were updated recently and are summarized below.

Testing for HCV should begin with consideration of the patient's risk factors for HCV and current recommendations for testing, which were updated by CDC in August 2012[2]. Table 7 presents populations currently recommended for HCV testing. Two overarching strategies for HCV testing are supported by CDC. First, all persons born in the years 1945 – 1965 should be screened once with an HCV antibody test (or routinely if risk behaviors are ongoing) in accordance with birth-cohort testing recommendations, which are recommended by both CDC

and USPSTF[2,4,26]. These recommendations were made after seroprevalence studies demonstrated that the rate of HCV infection among persons born in the years 1945 – 1965 (i.e. baby boomers) was five times higher than persons born outside of this birth cohort. The second strategy reflects a risk-based approach and identifies groups at high risk of HCV infection due their potential exposures to HCV-contaminated blood.

Once identified, persons eligible to receive HCV screening by clinicians should be tested using the most recent CDC guidelines, which were updated in May 2013[27]. The CDC testing algorithm is presented below in Figure 5 and Figure 6. In summary, persons should first be screened with an HCV antibody test. The recommended confirmatory test for positive, reactive, or indeterminate antibody results is a nucleic acid test that detects HCV ribonucleic acid (RNA). This test is important both to confirm infection and to discriminate between past and current HCV infection. Past infections will show a positive antibody result followed by a negative HCV nucleic acid test while current infections are most often positive for both HCV antibody and RNA.

Table 7. Centers for Disease Control and Prevention (CDC) Recommendations for Hepatitis C Virus (HCV) Infection Screening

Populations that should be tested for HCV[2]

- Persons born 1945 – 1965*
- Injection drug users*
- Persons who received a blood transfusion before 1992*
- Persons who received an organ transplant before 1992
- Persons who received clotting factor concentrates produced before 1987
- Persons ever receiving long-term hemodialysis
- Persons infected with Human Immunodeficiency Virus (HIV)
- Persons working in healthcare, emergency medicine, or public safety who have percutaneous exposures (such as needle sticks) or mucosal exposures to HCV-infected blood
- Children born to HCV-infected mothers
- Persons with persistently abnormal alanine aminotransferase (ALT) levels

Additional groups with undetermined need for HCV screening[26]

- Recipients of transplanted tissue (cornea, musculoskeletal, skin, ova, sperm)
- Intranasal or other non-injection illegal drug users
- Persons with tattoos or body piercings
- Persons with multiple sex partners or a history of sexually transmitted disease infection
- Long-term sex partners of persons with HCV

*Denotes concurrent recommendation for HCV screening by the United States Preventive Services Task Force (USPSTF).

Several notable points accompany these testing recommendations. First, rapid HCV tests are available and have a Clinical Laboratory Improvement Amendments (CLIA) waiver granted by the Food and Drug Administration (FDA), facilitating their use outside of traditional settings such as clinicians' offices. Second, HCV antibody tests are often accompanied by a signal to cut-off or index value, indicative of the likelihood that a specimen truly contains HCV Immunoglobulin G

(IgG) antibodies. Although the signal to cut-off or index value for many tests has an associated value at which the result will re-test positive in 95% or greater of follow-up antibody tests, confirmatory testing for HCV nucleic acid is recommended for all persons with a weakly reactive, strongly reactive, indeterminate, or intermediate HCV antibody result. HCV antibody tests without a signal to cut-off result should also always be followed by a confirmatory HCV nucleic acid test. Third, persons who disclose a significant risk event but test negative for HCV antibodies should be either screened with an HCV nucleic acid test or re-screened within 6 months for HCV antibody[27]. Finally, physicians can consider HCV nucleic acid testing for persons with immune deficiencies even if an HCV antibody result is negative or nonreactive.

Figure 5. Centers for Disease Control and Prevention (CDC) Recommendations for HCV Testing Procedures[28]

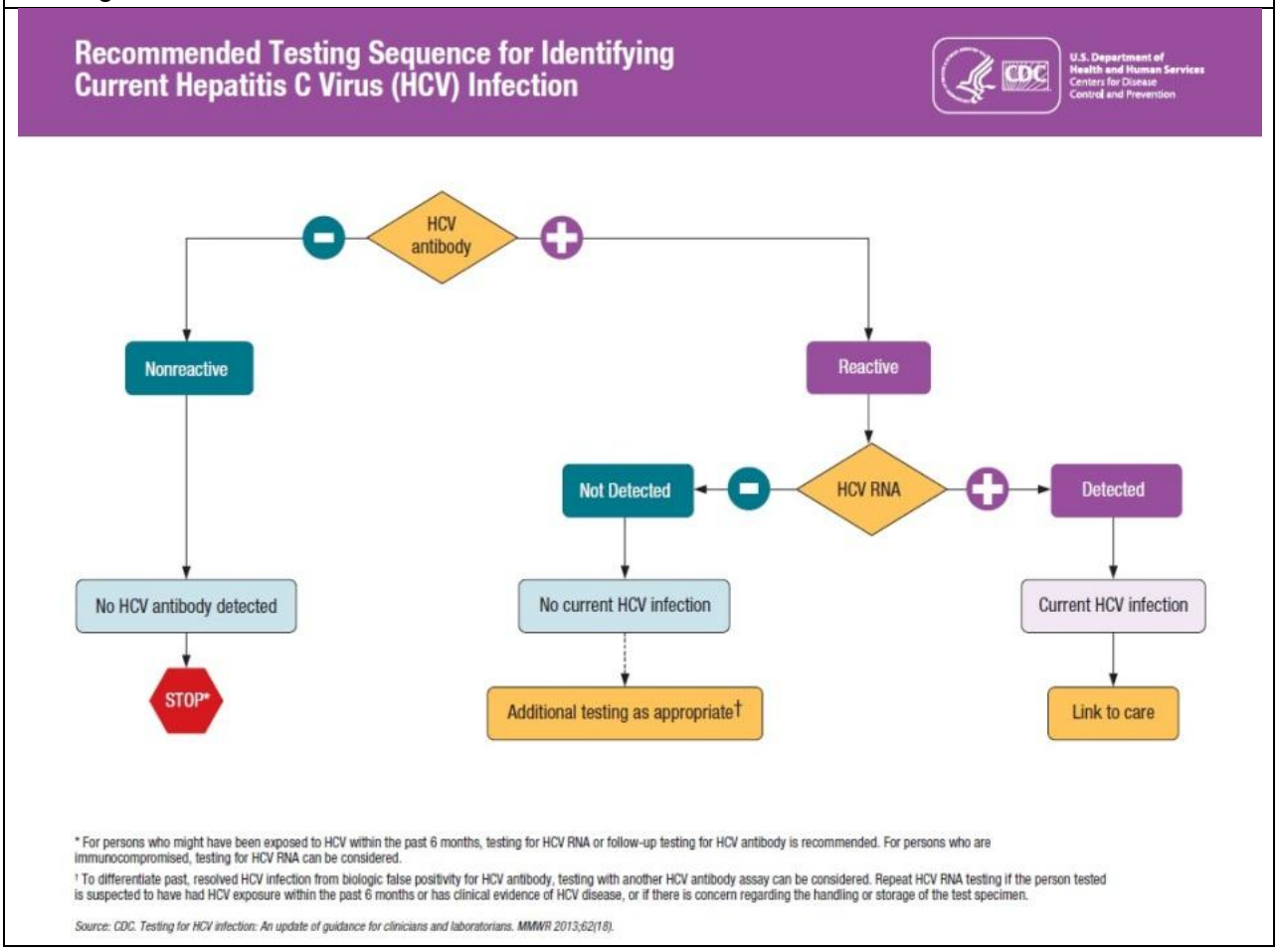
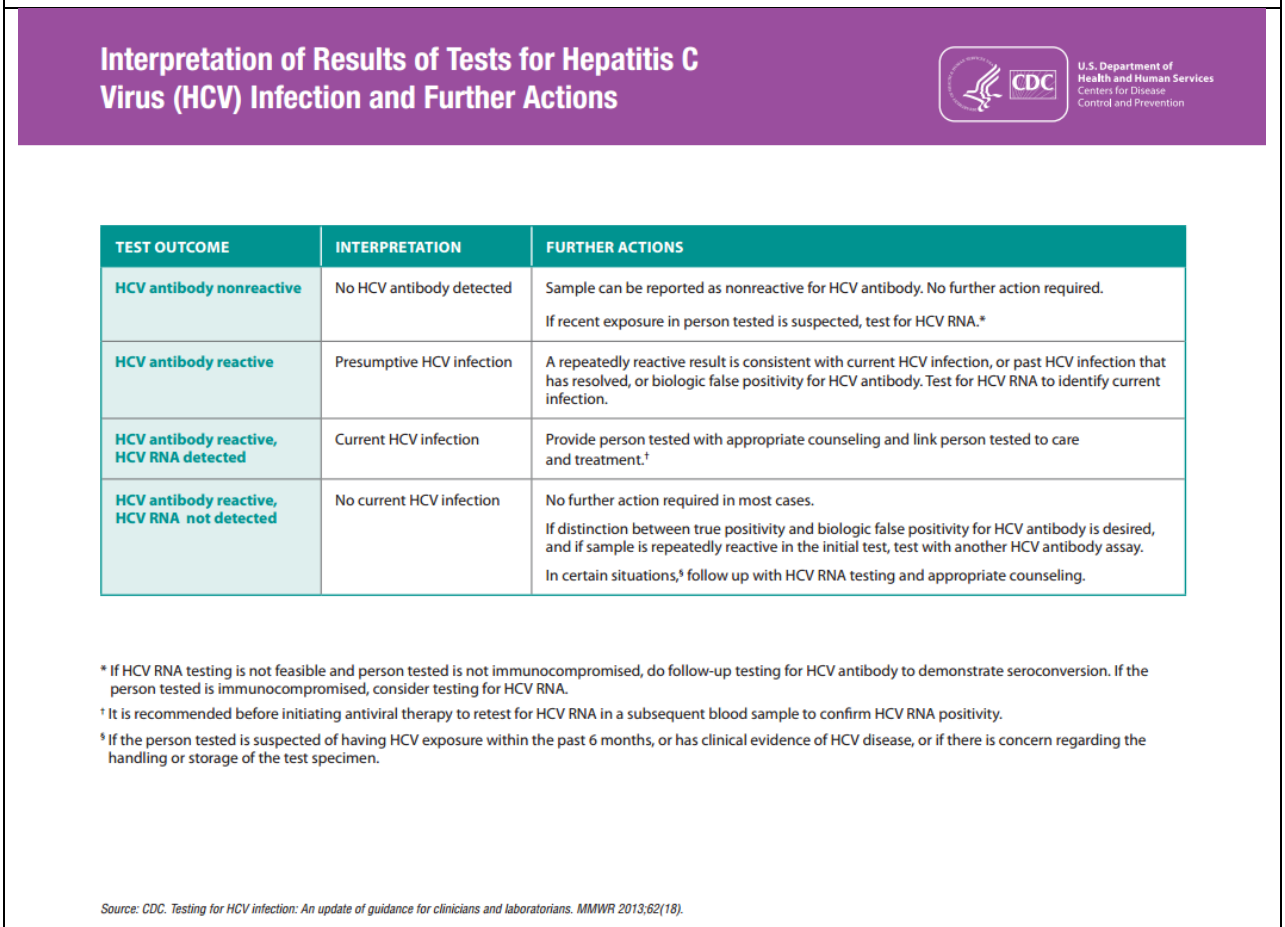


Figure 6. Centers for Disease Control and Prevention (CDC) Interpretation of HCV Testing Results[29]



Interpretation of Results of Tests for Hepatitis C Virus (HCV) Infection and Further Actions

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

TEST OUTCOME	INTERPRETATION	FURTHER ACTIONS
HCV antibody nonreactive	No HCV antibody detected	Sample can be reported as nonreactive for HCV antibody. No further action required. If recent exposure in person tested is suspected, test for HCV RNA.*
HCV antibody reactive	Presumptive HCV infection	A repeatedly reactive result is consistent with current HCV infection, or past HCV infection that has resolved, or biologic false positivity for HCV antibody. Test for HCV RNA to identify current infection.
HCV antibody reactive, HCV RNA detected	Current HCV infection	Provide person tested with appropriate counseling and link person tested to care and treatment.†
HCV antibody reactive, HCV RNA not detected	No current HCV infection	No further action required in most cases. If distinction between true positivity and biologic false positivity for HCV antibody is desired, and if sample is repeatedly reactive in the initial test, test with another HCV antibody assay. In certain situations,§ follow up with HCV RNA testing and appropriate counseling.

* If HCV RNA testing is not feasible and person tested is not immunocompromised, do follow-up testing for HCV antibody to demonstrate seroconversion. If the person tested is immunocompromised, consider testing for HCV RNA.

† It is recommended before initiating antiviral therapy to retest for HCV RNA in a subsequent blood sample to confirm HCV RNA positivity.

§ If the person tested is suspected of having HCV exposure within the past 6 months, or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.

Source: CDC. Testing for HCV infection: An update of guidance for clinicians and laboratorians. MMWR 2013;62(18).

BURDEN OF HEPATITIS C TESTING IN ARKANSAS

Prevalence calculations presented in the "Prevalence" section were applied to predict the number of Arkansans infected with HCV and the number of persons who need to be screened in Arkansas to identify all HCV-infected individuals.

CDC prevalence predictions from the NHANES study are extended to the population of Arkansas in Table 8. Overall, there are likely at least 9,771 and up to 27,684 persons with HCV-infection in Arkansas who are yet to be diagnosed.

Predictions of the number of Arkansans requiring HCV testing can also be produced from the ARCHES study. A detailed description of methods used to analyze ARCHES data and relevant limitations are included in Appendix A. Given the prevalence of HCV among groups recommended for screening, a total of 926,396 Arkansans would be recommended for screening according to the ARCHES study (Table 9). Notably, sex partners of injection drug users were included in this calculation, despite their identification as a group "of uncertain need[26]" for screening as ARCHES participants with this risk factor were significantly more likely to have HCV than persons who did not have a sex partner with HCV infection or who injected drugs (Table 2). Screening of 926,396 individuals would identify 33,075 (95% Confidence

Interval: 20,349 – 55,069), or 87.7% of the total number of infected persons in Arkansas. Many of these persons may have already been screened; however, if 45% – 85% of persons are unaware of their HCV status, we estimate that 9,157 to 46,809 persons may be unaware that they are living with HCV infection.

Table 8. Prevalence of HCV in Arkansas from the National Health and Nutrition Examination Survey (NHANES)

HCV Risk Group	US (%)[5]	No. US (million)[5]	No. Arkansans
Chronic HCV (Total Population)	0.8 – 1.2	2.2 – 3.2	21,713 – 32,569*
Positive HCV-Antibody (Total Population)	1.2 – 1.5	3.0 – 4.2	32,569 – 40,711*
Chronic HCV Infection Among Persons Born 1945 – 1965	2.1 – 3.2	1.7 – 2.6	16,372 – 24,948†
Persons Unaware of Chronic HCV Infection†	45 – 85	1.0 – 2.7	9,771 – 27,684*

*Calculated assuming a total population of persons aged 6 years or older in Arkansas (2012) of 2,714,096 persons[25].
†Calculated assuming a total population of persons born 1945 – 1965 and aged 47 – 67 during 2012 of 779,668 persons[25].

Table 9. Past or Present HCV Infection Prevalence and Screening Estimates from the ARCHES Study — Arkansas

Screening Group*	Predicted HCV Prevalence (95% CI)*	Number of HCV Positive Arkansans	% of Arkansas Adult Population (95% CI)*	Number of Arkansans in Recommended Screening Group
Total Population	1.8 (0.9 – 2.6)	37,709	-	-
Baby Boomers (Born 1945 – 1965)	3.6 (1.8 – 5.5)	29,203	37.5 (34.0 – 41.0)	866,205
PWID	33.7 (16.2 – 51.2)	10,323	1.4 (0.5 – 2.3)	30,635
Sex Partner with HCV Infection or Sex with PWID†	19.8 (2.4 – 37.3)	11,746	2.8 (1.6 – 3.9)	59,211
Transfusion Before 1992	2.4 (1.1 – 3.6)	4,410	8.7 (6.9 – 10.4)	185,980
Total Screening Population§	3.6 (1.9 – 5.3)	33,075	43.2 (39.3 – 47.1)	926,396

Abbreviations: ARCHES: Arkansas Cardiovascular Health Examination Survey; CI: Confidence Interval; HCV: Hepatitis C Virus; PWID: Persons who Inject Drugs
*Persons missing risk factor information were assumed to not have the risk factor.
†The predicted prevalence of HCV-infection in persons reporting sex with an injection drug user but who also answered 'no' when asked if they were injection drug users themselves was 8.6% (0.0 – 21.6).
§The total screening population includes the predicted population of Arkansans reporting injection drug use, sex with an injection drug user, transfusion before 1992, and/or persons born during 1945 – 1965.

MORBIDITY

Infection with HCV is often recognized late as roughly 70% – 80% of infections are initially asymptomatic. In 20% – 30% of new infections, persons experience acute HCV, which manifests with symptoms of jaundice, nausea, vomiting, abdominal pain, grey-colored stools, joint pain, and other symptoms within 14 – 180 days after infection[10]. Among persons infected with HCV, 75% – 85% become chronically infected, whereby the virus remains in the bloodstream, often for decades, causing little or no symptoms[10]. HCV-infected individuals, who may not know they are infected or to incorporate risk-reducing activities, are able to transmit the virus to others during anytime at which they have a current HCV infection. In approximately 60% – 70% of chronically infected persons, HCV infection leads to liver disease if untreated[30]. Chronic infection with HCV leads to cirrhosis in 5% – 20% of persons and death from liver cancer or cirrhosis in 1% – 5% of persons[30]. This section highlights the burden of illnesses caused by HCV infections among Arkansans using several data sources, including inpatient hospitalizations, emergency department visits, and cancer registry data in Arkansas. Please refer to Appendix A for a detailed description of these data sources, methods used in analysis, and limitations.

Inpatient Hospitalizations

Hospitalizations with *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes indicative of diseases of interest were identified by querying all diagnosis and injury fields for inpatient hospitalizations occurring in Arkansas during 2004 – 2012. Hospitalization year was assigned by the year of discharge from an inpatient hospitalization. Of 3,790,636 hospitalizations, 3,604,442 were among persons with an address in Arkansas or whose address was unknown and are included in the analyses presented. Hospitalizations with ICD-9-CM procedure codes indicative of procedures of interest were identified by querying all procedure fields for inpatient hospitalizations occurring in Arkansas during 2004 – 2012.

Methods for analysis were adopted from Ly et al[31]. Crude rates were calculated by dividing the number of hospitalizations per year by estimates of the corresponding Arkansas population[25]. Age-adjusted rates are directly standardized to the age distribution of the 2000 United States population to enhance comparability to national studies[32] and 95% confidence intervals were calculated using methods to estimate variance from the Poisson distribution[33]. The Cochran-Armitage trend test was used to test the statistical significance in trends over time of the proportion of total hospitalizations documenting a particular condition while least squares linear regression was used to calculate the change in age-adjusted hospitalization rates per year. A detailed description of methods used to analyze data and relevant limitations are included in Appendix A. Table 10 shows the total number of hospitalizations per year among residents of Arkansas. Descriptive statistics of all inpatient hospitalizations among Arkansans are shown in table 10.

Table 10. Inpatient Hospitalizations — Arkansas, 2004 – 2012	
Year	Number of Inpatient Hospitalizations
2004	408,047
2005	408,061
2006	409,365
2007	408,365
2008	405,546
2009	398,126
2010	391,452
2011	389,635
2012	385,845
Total	3,604,442

Table 11a. Descriptive Characteristics of Inpatient Hospitalizations — Arkansas, 2004 – 2012		
Characteristic	No.	%
Total	3,604,442	100.0
Sex		
Male	1,457,089	40.4
Female	2,147,229	59.6
Unknown	124	<0.1
Age (Years)		
<5	431,158	12.0
5 – 9	32,579	0.9
10 – 14	48,335	1.3
15 – 19	120,179	3.3
20 – 24	181,771	5.0
25 – 29	177,449	4.9
30 – 34	151,813	4.2
35 – 39	134,923	3.7
40 – 44	147,821	4.1
45 – 49	179,891	5.0
50 – 54	199,637	5.5
55 – 59	214,431	5.9
60 – 64	229,239	6.4
65 – 69	261,874	7.3
70 – 74	266,663	7.4
75 – 79	269,309	7.5
80 – 84	250,946	7.0
85+	306,411	8.5
Unknown	13	<0.1
Race		
American Indian or Alaskan Native	7,920	0.2
Asian or Pacific Islander	18,629	0.5
Black	555,656	15.4
White	2,954,332	82.0
Other	52,232	1.5
Unknown	15,673	0.4

Ethnicity			
	Hispanic	95,847	2.7
	Non-Hispanic	3,496,808	97.0
	Unknown	11,787	0.3
Type of Admission			
	Emergency	1,222,721	33.9
	Urgent	827,875	23.0
	Elective	1,220,021	33.9
	Newborn	325,762	9.0
	Trauma	4,039	0.1
	Unknown	4,024	0.1
Payer Source			
	Self-Pay	245,832	6.8
	Worker's Compensation	10,087	0.3
	Medicare	1,583,969	43.9
	Medicaid	750,967	20.8
	Other Federal Programs, DHS, or Managed Assistance	7,228	0.2
	Private Insurance	904,306	25.1
	Free (Medically Indigent)	8,496	0.2
	Other	91,607	2.5
	Unknown	1,950	0.1

Table 11b. Descriptive Characteristics of Inpatient Hospitalizations — Arkansas, 2004 – 2012

Variable	Mean (95% Confidence Interval)		Median	Number of Observations Missing Value
Patient Age (Years)	49.5	(49.5 – 49.6)	54	13
Visit Cost ($US)	20,517	(20,440 – 20,595)	11,365	0
Length of Stay (Days)	5.2	(5.1 – 5.2)	3	36

Hospitalizations for Hepatitis C, Hepatitis B, and HIV

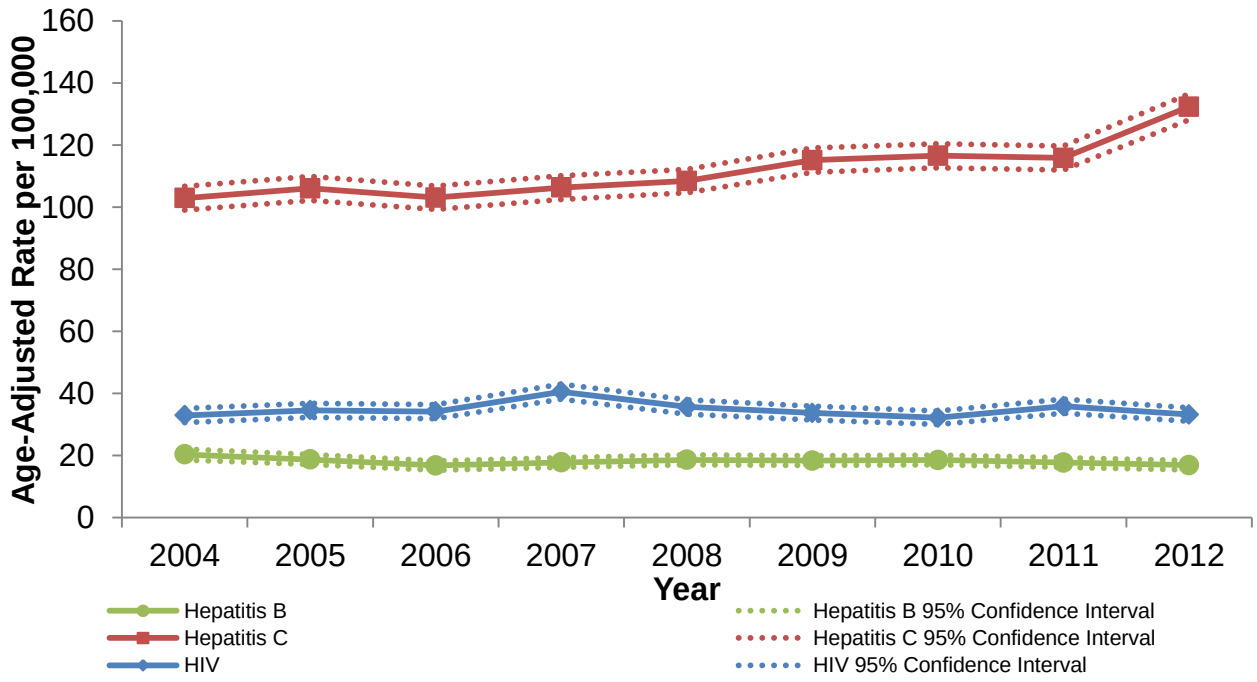
Rates of inpatient hospitalizations documenting HBV, HCV, and HIV are shown in Table 12 and Figure 7. There was a statistically significant increase in the proportion of total hospitalizations each year that documented HCV. Least squares linear regression demonstrated an increase of 3.0 hospitalizations per 100,000 persons per year. Notably, hospitalization rates noting comparable bloodborne infections, such as HBV and HIV, were much lower than for HCV. There were 936 inpatient hospitalizations documenting HIV in 2012 and 524 documenting HBV compared to 4,141 for HCV. Tests for change in the proportion of hospitalizations each year documenting HIV and HBV increased statistically during 2004 to 2012 (data not shown). Linear regression models did not demonstrate a statistically significant change in the age-adjusted rate of hospitalizations related to HBV or HIV over time (data not shown).

Table 12. Inpatient Hospitalizations Documenting Diagnoses of Hepatitis C Virus (HCV) Infection — Arkansas, 2004 – 2012

Year	Number (%) of Hospitalizations Documenting HCV[1]	Crude Hospitalization Rate per 100,000 Arkansans	Age-Adjusted Rate per 100,000 Arkansans (95% Confidence Interval)
2004	2,837 (0.7)	103.2	102.9 (99.1 – 106.8)
2005	2,991 (0.7)	107.5	106.1 (102.3 – 109.9)
2006	2,962 (0.7)	105.0	103.1 (99.3 – 106.9)
2007	3,095 (0.8)	108.6	106.4 (102.6 – 110.1)
2008	3,227 (0.8)	112.3	108.4 (104.6 – 112.2)
2009	3,447 (0.9)	119.0	115.1 (111.1 – 119.0)
2010	3,576 (0.9)	122.6	116.6 (112.7 – 120.5)
2011	3,605 (0.9)	122.7	115.8 (111.9 – 119.7)
2012	4,141 (1.1)	140.4	132.3 (128.2 – 136.5)
Total	29,881 (0.8)	N/A	N/A
Trend Statistics	PC: 0.0122* SC: 0.0121* CA: <0.0001* (Increasing)	N/A	ROC: 3.0 per 100,000 Persons (p= 0.0013)*

Abbreviations: CA: Cochran-Armitage Trend Test p-value; CI: Confidence Interval; HCV: Hepatitis C Virus; PC: Pearson Correlation Coefficient; ROC: Rate of Change; SC: Spearman Correlation Coefficient.
* Denotes statistically significant result at 95% confidence level (α ≤0.05).
[1] Hospitalizations documenting hepatitis C include ICD-9-CM codes for acute, chronic, or unspecified hepatitis C (07041, 07044, 07054, 07059, 07070, 07071, or V0262).

Figure 7. Inpatient Hospitalizations Documenting Diagnoses of Hepatitis B, Hepatitis C, and Human Immunodeficiency Virus (HIV) — Arkansas 2004 – 2012



*Hospitalizations documenting hepatitis B include inpatient hospitalizations with ICD-9-CM codes for acute, chronic, or unspecified hepatitis B (07020, 07021, 07022, 07023, 07030, 07031, 07032, 07033, or V0261). Hospitalizations documenting hepatitis C include ICD-9-CM codes for acute, chronic, or unspecified hepatitis C (07041, 07044, 07054, 07059, 07070, 07071, or V0262). Hospitalizations documenting HIV include inpatient hospitalizations with ICD-9-CM codes 042, 07953, 79571, or V08.

Descriptive statistics among hospitalizations documenting HCV infection are presented in Table 13a and Table 13b. Overall, most hospitalizations were among males compared to females. Persons aged 50 – 54 years followed by persons aged 45 – 49 years experienced the highest number of hospitalizations documenting HCV infection. The average age of persons hospitalized was 50.2 years. Hospitalizations occurred most commonly among white, non-hispanic Arkansans. The majority of admissions were emergency admissions and the payer source was most commonly Medicare. Hospitalizations cost an average of $25,015 and lasted an average of 5.7 days.

The principal diagnosis for an inpatient hospitalization is defined as "the condition established after study to be chiefly responsible for occasioning the admission of the patient for care"[34]. Table 14 presents hospitalizations where the principal diagnosis was acute, chronic, or unspecified HCV infection, which is in contrast to Table 12 above, which presents hospitalizations where HCV was documented in any of the 22 fields able to capture diagnoses or injuries assigned during inpatient hospitalizations. Table 14 documents a markedly lower number of hospitalizations for HCV compared to the results of querying all diagnosis codes. Only 4.4% (1,312 hospitalizations) of the total 29,881 hospitalizations documenting HCV had HCV as the principal diagnosis. This may suggest that physicians do not commonly admit patients primarily for their HCV infection or that HCV is documented as a finding during the inpatient hospitalization.

Table 13a. Descriptive Characteristics of Inpatient Hospitalizations Documenting Diagnoses of Hepatitis C Virus Infection — Arkansas, 2004 – 2012

Characteristic	No.	%
Total	29,881	100.0
Sex		
Male	17,061	57.1
Female	12,820	42.9
Age (Years)		
0 – 9	15	0.1
10 – 14	10	<0.1
15 – 19	90	0.3
20 – 24	392	1.3
25 – 29	860	2.9
30 – 34	1,254	4.2
35 – 39	1,927	6.5
40 – 44	3,444	11.5
45 – 49	5,774	19.3
50 – 54	6,631	22.2
55 – 59	4,575	15.3
60 – 64	2,199	7.4
65 – 69	1,126	3.8
70 – 74	638	2.1
75 – 79	471	1.6
80 – 84	299	1.0
85+	176	0.6

Race			
	American Indian or Alaskan Native	30	0.1
	Asian or Pacific Islander	95	0.3
	Black	4,655	15.6
	White	24,654	82.5
	Other	235	0.8
	Unknown	212	0.7
Ethnicity			
	Hispanic	320	1.1
	Non-Hispanic	29,513	98.8
	Unknown	48	0.2
Type of Admission			
	Emergency	15,222	50.9
	Urgent	7,706	25.8
	Elective	6,818	22.8
	Trauma	87	0.3
	Unknown or Newborn	48	0.2
Payer Source			
	Self-Pay	4,886	16.4
	Worker's Compensation	49	0.2
	Medicare	11,330	37.9
	Medicaid	7,715	25.8
	Other Federal Programs, DHS, or Managed Assistance	75	0.3
	Private Insurance	5,088	17.0
	Free (Medically Indigent)	129	0.4
	Other	602	2.0
	Unknown	7	<0.1

Table 13b. Descriptive Characteristics of Inpatient Hospitalizations Documenting Diagnoses of Hepatitis C Virus Infection — Arkansas, 2004 – 2012

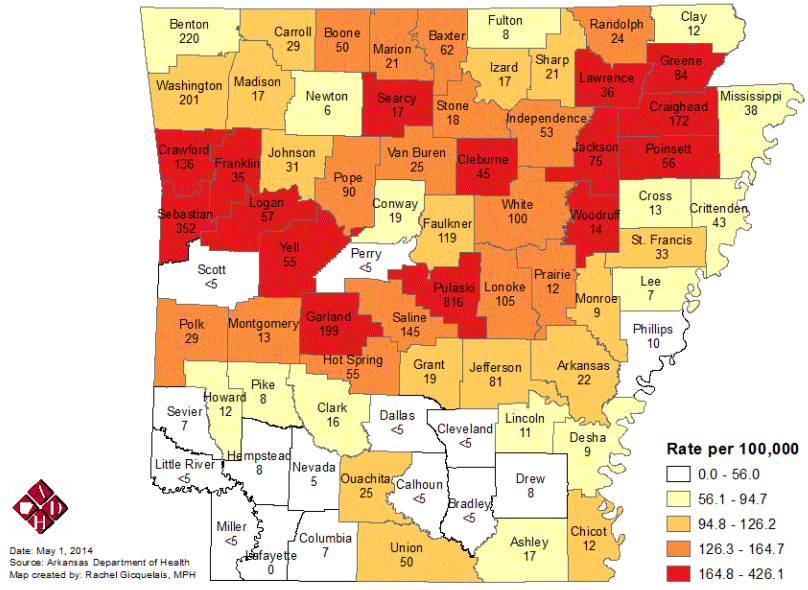
Variable	Mean (95% Confidence Interval)		Median	Number of Observations Missing Value
Patient Age (Years)	50.2	(50.1 – 50.4)	50	0
Visit Cost ($US)	25,015	(24,594 – 25,435)	14,423	0
Length of Stay (Days)	5.7	(5.6 – 5.8)	4	0

Table 14. Principal Diagnoses for Hepatitis C Virus Infection — Arkansas, 2004 – 2012

Year	Number of Hospitalizations	% of Total Hospitalizations
2004	111	0.03
2005	100	0.02
2006	92	0.02
2007	96	0.02
2008	137	0.03
2009	157	0.04
2010	164	0.04
2011	197	0.05
2012	258	0.07
Total	1,312	0.04

The geographic distribution of hospitalizations documenting HCV infections are presented in Figure 8. Crude rates of hospitalizations for each county were calculated using information on each patient's county of residence. Hospitalizations among persons whose addresses were unknown are excluded from maps. Notably, rates of hospitalizations for HCV were above 230 per 100,000 persons among residents of Jackson, Sebastian, Logan, Yell, and Poinsett counties. A cluster of high rates of hospitalizations is present among several counties in western Arkansas, including Crawford, Sebastian, Franklin, Logan, Yell, and Garland counties while a second cluster appears among Greene, Lawrence, Craighead, Jackson, Poinsett, and Woodruff counties.

Figure 8. Inpatient Hospitalizations Documenting Diagnoses of Hepatitis C Virus Infection — Arkansas, 2012



Numbers represent hospitalizations per county.

Table 15 shows concurrent diagnoses recorded during inpatient hospitalizations among persons with HCV. As time progressed from 2004 to 2012, a decreasing proportion of persons with HCV had coinfection with HBV while there was no change in the proportion with HIV. Among persons with HCV, the proportion of persons also documenting malignant neoplasms of the liver, gallbladder, or biliary tract, cirrhosis, chronic liver disease, or drug overdose related to use of opiate drugs increased over time. Notably, in 2012, over one-quarter of inpatient hospitalizations among persons with HCV documented cirrhosis. Additionally, over one-third of inpatient hospitalizations among persons with HCV documented chronic liver diseases, which include malignant neoplasms of the liver, intrahepatic bile ducts, gallbladder, extrahepatic bile ducts, ampulla of vater, or biliary tract, esophageal varices with or without bleeding, acute and subacute necrosis of the liver, alcoholic fatty liver, hepatitis, cirrhosis, or other unspecified alcoholic liver damage, chronic hepatitis, nonalcoholic cirrhosis, biliary cirrhosis, nonalcoholic liver disease, liver abscess, portal pyemia, hepatic encephalopathy, portal hypertension, hepatorenal syndrome, other sequelae of chronic liver disease, chronic passive congestion of the liver, unspecified viral hepatitis, unspecified hepatitis, hepatic infarction, hepatopulmonary

syndrome, other or unspecified disorders of the liver, portal vein thrombosis, hepatomegaly, malignant or other ascites, history of malignant neoplasm of the liver, history of liver transplant, or liver transplant complications.

Table 15. Comorbid Conditions Among Inpatient Hospitalizations Documenting Diagnoses of Hepatitis C Virus (HCV) Infection — Arkansas, 2004 – 2012

Year	HIV[1]		HBV[2]		Malignant Neoplasms of the Liver, Gallbladder, or Biliary Tract[3]		Alcoholic, Nonalcoholic, or Biliary Cirrhosis[4]		Chronic Liver Diseases[5]		Opiate-Related Drug Overdose[6]	
	N	%	N	%	N	%	N	%	N	%	N	%
2004	102	3.6	166	5.9	62	2.2	705	24.9	904	31.9	18	0.6
2005	93	3.1	172	5.8	57	1.9	725	24.3	922	30.8	19	0.6
2006	73	2.5	142	4.8	44	1.5	758	25.6	923	31.2	37	1.3
2007	103	3.3	147	4.8	68	2.2	723	23.4	902	29.2	28	0.9
2008	104	3.2	163	5.1	73	2.3	752	23.3	1,004	31.1	52	1.6
2009	112	3.3	177	5.1	95	2.8	851	24.7	1,121	32.5	45	1.3
2010	118	3.3	134	3.8	90	2.5	978	27.4	1,261	35.3	50	1.4
2011	102	2.8	154	4.3	103	2.9	993	27.5	1,295	35.9	46	1.3
2012	103	2.5	122	3.0	125	3.0	1,092	26.4	1,438	34.7	54	1.3
Total	910	3.1	1,377	4.6	717	2.4	7,577	25.4	9,770	32.7	349	1.2
Trend Statistics	PC: -0.01 SC: -0.0103 CA: 0.0843 (None)		PC: -0.0378* SC: -0.0382* CA: <0.0001* (Decreasing)		PC: 0.0254* SC: 0.0256* CA: <0.0001* (Increasing)		PC: 0.0216* SC: 0.0221* CA: 0.0002* (Increasing)		PC: 0.0364* SC: 0.037* CA: <0.0001* (Increasing)		PC: 0.02* SC: 0.0194* CA: 0.0005* (Increasing)	

Trend Statistic Abbreviations: CA: Cochran-Armitage Trend Test; PC: Pearson Correlation Coefficient; SC: Spearman Correlation Coefficient.

* Denotes statistically significant result at 95% confidence level (α ≤0.05).

[1] Hospitalizations for Human Immunodeficiency Virus (HIV) were indicated by the following ICD-9-CM codes: 042, 07953, 79571, or V08.

[2] Hospitalizations for Hepatitis B Virus (HBV) were indicated by the following ICD-9-CM codes: 07020, 07021, 07022, 07023, 07030, 07031, 07032, 07033, or V0261.

[3] Hospitalizations for malignant neoplasms were indicated by the following ICD-9-CM codes: 1550, 1551, 1552, 1560, 1561, 1562, 1568, or 1569.

[4] Hospitalizations for cirrhosis were indicated by the following ICD-9-CM codes: 5712, 5715, or 5716.

[5] Hospitalizations for chronic liver diseases were indicated by the following ICD-9-CM codes: malignant neoplasms of the liver, intrahepatic bile ducts, gallbladder, extrahepatic bile ducts, ampulla of vater, or biliary tract (1550-1569), esophageal varices with or without bleeding (4560-45621), acute and subacute necrosis of the liver (570), alcoholic fatty liver, hepatitis, cirrhosis, or other unspecified alcoholic liver damage (5710-5713), chronic hepatitis (57140-57149), nonalcoholic cirrhosis (5715), biliary cirrhosis (5716), nonalcoholic liver disease (5718-5719), liver abscess (5720), portal pyemia (5721), hepatic encephalopathy (5722), portal hypertension (5723), hepatorenal syndrome (5724), other sequelae of chronic liver disease (5728), chronic passive congestion of the liver (5730), unspecified viral hepatitis (5731), unspecified hepatitis (5733), hepatic infarction (5734), hepatopulmonary syndrome (5735), other or unspecified disorders of the liver (5738, 5739), portal vein thrombosis (452), hepatomegaly (7891), malignant or other ascites (78951, 78959), personal history of malignant neoplasm of the liver (V1007), history of liver transplant or liver transplant complications (V427, 99682).

[6] Hospitalizations for opiate-related drug overdoses were indicated by the following ICD-9-CM codes: poisoning by opium, heroin, methadone, or other opiates or related narcotics (96500, 96501, 96502, or 96509), accidental poisoning by heroin, methadone, or other opiates and related narcotics (E8500, E8501, or E8502), or adverse effects from therapeutic use of heroin, methadone, or other opiates and related narcotics (E9350, E9351, or E9352).

Because multiple hospitalizations per patient can and do occur, these analyses were repeated restricting data to only one hospitalization per year per person. Briefly, hospital discharge datasets for each year of service were de-duplicated using personal identifiers, such as social security number, patient name, and patient date of birth. In Table 16, the earliest hospitalization occurring in each year is presented for each patient. If a person had an HCV diagnosis documented in any record, the earliest record containing the HCV diagnosis was kept over any other hospitalizations not documenting HCV.

Results showed similar trends to Table 12. The number of individuals hospitalized for HCV increased over time, from 1,777 in 2004 to 2,692 in 2012, representing a statistically significant increase in the proportion of all individuals hospitalized during the time period. Further, linear regression of the age-adjusted hospitalizations rates demonstrated a statistically significant increase of 2.1 individuals hospitalized per 100,000 persons per year. Because trends were similar to those presented above, further analyses are available by request but not further discussed in the epidemiologic profile.

Table 16. Individuals Hospitalized with Diagnoses of Hepatitis C Virus (HCV) Infection Documented in Hospital Discharge Data — Arkansas, 2004 – 2012

Year	Number (%) of Hospitalizations Documenting HCV[1]	Crude Hospitalization Rate per 100,000 Arkansans	Age-Adjusted Rate per 100,000 Arkansans (95% Confidence Interval)
2004	1,777 (0.7)	64.6	64.8 (61.8 – 67.9)
2005	1,961 (0.8)	70.5	69.9 (66.8 – 73.0)
2006	1,998 (0.8)	70.8	69.7 (66.6 – 72.8)
2007	2,095 (0.8)	73.5	72.2 (69.0 – 75.3)
2008	2,185 (0.9)	76.0	73.6 (70.5 – 76.7)
2009	2,304 (0.9)	79.5	76.9 (73.7 – 80.0)
2010	2,358 (1.0)	80.9	77.2 (74.1 – 80.4)
2011	2,369 (1.0)	80.6	76.3 (73.2 – 79.5)
2012	2,692 (1.1)	91.3	86.3 (82.9 – 89.6)
Total	19,739 (0.9)	N/A	N/A
Trend Statistics	PC: 0.0104* SC: 0.0104* CA: <0.0001* (Increasing)	N/A	ROC: 2.1 per 100,000 Persons (p= 0.0002)*

Abbreviations: CA: Cochran-Armitage Trend Test; CI: Confidence Interval; HCV: Hepatitis C Virus; PC: Pearson Correlation Coefficient; ROC: Rate of Change; SC: Spearman Correlation Coefficient.
* Denotes statistically significant result at 95% confidence level (α ≤0.05).
[1] Hospitalizations documenting hepatitis C include ICD-9-CM codes for acute, chronic, or unspecified hepatitis C (07041, 07044, 07054, 07059, 07070, 07071, or V0262).

Hospitalizations for Chronic Liver Diseases

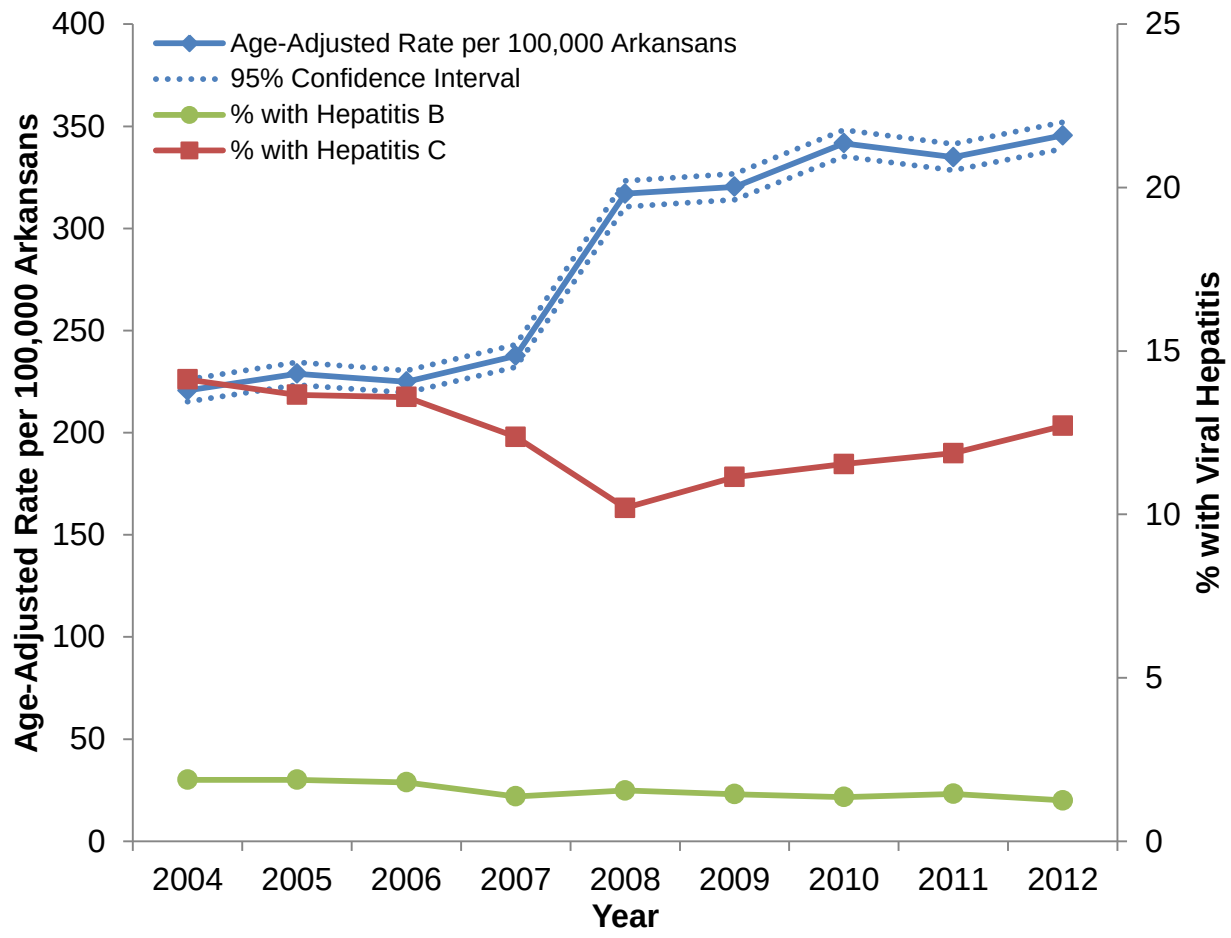
Rates of inpatient hospitalizations documenting several chronic liver diseases were examined to characterize the overall burden of liver-related conditions (Table 17, Figure 9). Overall, the number of inpatient hospitalizations documenting chronic liver diseases nearly doubled from 2004 – 2012, with 6,396 hospitalizations in 2004 to 11,317 hospitalizations in 2012. Least squares linear regression models of the age-adjusted rates demonstrated an increase of 18.9 hospitalizations per 100,000 Arkansans per year over 2004 – 2012 (p-value = 0.0003). Further, the percentage of persons with HCV documented as a diagnosis during their hospitalization ranged from 14.1% in 2004, decreased to 10.2% in 2008, and steadily increased each year thereafter to 12.7% in 2012. The percentage of persons with HBV documented as a diagnosis remained relatively constant, declining from 1.9% in 2004 to 1.3% in 2012.

Table 17. Inpatient Hospitalizations Documenting Diagnoses of Chronic Liver Diseases (CLD)[1] — Arkansas, 2004 – 2012

Year	Number (%) of Hospitalizations Documenting CLD	Crude Hospitalization Rate per 100,000 Arkansans	Age-Adjusted Rate per 100,000 Arkansans (95% CI)	Number (%) with HCV Infection
2004	6,396 (1.6)	232.6	220.6 (215.2-226.1)	904 (14.1)
2005	6,751 (1.7)	242.7	228.9 (223.4-234.4)	922 (13.7)
2006	6,792 (1.7)	240.7	225.0 (219.6-230.4)	923 (13.6)
2007	7,292 (1.8)	256.0	237.6 (232.1-243.2)	902 (12.4)
2008	9,840 (2.4)	342.3	317.0 (310.7-323.4)	1,004 (10.2)
2009	10,064 (2.5)	347.4	320.3 (314.0-326.7)	1,121 (11.1)
2010	10,924 (2.8)	374.6	341.6 (335.1-348.2)	1,261 (11.5)
2011	10,912 (2.8)	371.3	334.8 (328.4-341.2)	1,295 (11.9)
2012	11,317 (2.9)	383.7	345.5 (339.0-352.0)	1,438 (12.7)
Total	80,288 (2.2)	N/A	N/A	9,770 (12.2)
Trend Statistics	PC: 0.0346* SC: 0.0347* CA: <0.0001* (Increasing)	N/A	ROC: 18.9 per 100,000 persons (p=0.0003)*	PC: -0.0168* SC: -0.0139* CA: <0.0001* (Decreasing)

Abbreviations: CA: Cochran-Armitage Trend Test; CI: Confidence Interval; CLD: Chronic Liver Diseases; PC: Pearson Correlation Coefficient; ROC: Rate of Change; SC: Spearman Correlation Coefficient.
* Denotes statistically significant result at 95% confidence level (α ≤0.05).
[1] Liver diseases include inpatient hospitalizations with ICD-9-CM codes for malignant neoplasms of the liver, intrahepatic bile ducts, gallbladder, extrahepatic bile ducts, ampulla of vater, or biliary tract (1550 - 1569), esophageal varices with or without bleeding (4560 - 45621), acute and subacute necrosis of the liver (570), alcoholic fatty liver, hepatitis, cirrhosis, or other unspecified alcoholic liver damage (5710 - 5713), chronic hepatitis (57140 - 57149), nonalcoholic cirrhosis (5715), biliary cirrhosis (5716), nonalcoholic liver disease (5718 - 5719), liver abscess (5720), portal pyemia (5721), hepatic encephalopathy (5722), portal hypertension (5723), hepatorenal syndrome (5724), other sequelae of chronic liver disease (5728), chronic passive congestion of the liver (5730), unspecified viral hepatitis (5731), unspecified hepatitis (5733), hepatic infarction (5734), hepatopulmonary syndrome (5735), other or unspecified disorders of the liver (5738, 5739), portal vein thrombosis (452), hepatomegaly (7891), malignant or other ascites (78951, 78959), personal history of malignant neoplasm of the liver (V1007), history of liver transplant or liver transplant complications (V427, 99682).

Figure 9. Inpatient Hospitalizations Documenting Diagnoses of Chronic Liver Diseases — Arkansas, 2004 – 2012



*Liver diseases include inpatient hospitalizations with ICD-9-CM codes for malignant neoplasms of the liver, intrahepatic bile ducts, gallbladder, extrahepatic bile ducts, ampulla of vater, or biliary tract (1550 - 1569), esophageal varices with or without bleeding (4560 - 45621), acute and subacute necrosis of the liver (570), alcoholic fatty liver, hepatitis, cirrhosis, or other unspecified alcoholic liver damage (5710 - 5713), chronic hepatitis (57140 - 57149), nonalcoholic cirrhosis (5715), biliary cirrhosis (5716), nonalcoholic liver disease (5718 - 5719), liver abscess (5720), portal pyemia (5721), hepatic encephalopathy (5722), portal hypertension (5723), hepatorenal syndrome (5724), other sequelae of chronic liver disease (5728), chronic passive congestion of the liver (5730), unspecified viral hepatitis (5731), unspecified hepatitis (5733), hepatic infarction (5734), hepatopulmonary syndrome (5735), other or unspecified disorders of the liver (5738, 5739), portal vein thrombosis (452), hepatomegaly (7891), malignant or other ascites (78951, 78959), personal history of malignant neoplasm of the liver (V1007), history of liver transplant or liver transplant complications (V427, 99682).

Descriptive statistics among hospitalizations documenting chronic liver diseases are presented in Table 18. Overall, most hospitalizations were among males compared to females. Persons aged 50 – 54 years, followed by persons aged 55 – 59 years, experienced the highest number of hospitalizations documenting chronic liver diseases. The average age of persons hospitalized was 58.0 years. Hospitalizations occurred most commonly among white, non-hispanic Arkansans. The majority of admissions were emergency admissions and the payer source was most commonly Medicare. Hospitalizations cost an average of $35,206.03 and lasted an average of 6.9 days.

Table 18a. Descriptive Characteristics of Inpatient Hospitalizations Documenting Diagnoses of Chronic Liver Diseases — Arkansas, 2004 – 2012

Characteristic		No.	%
Total		80,288	100.0
Sex			
	Male	41,628	51.9
	Female	38,660	48.2
Age (Years)			
	0 – 9	708	0.89
	10 – 14	170	0.2
	15 – 19	489	0.6
	20 – 24	867	1.1
	25 – 29	1,424	1.8
	30 – 34	2,088	2.6
	35 – 39	3,260	4.1
	40 – 44	5,179	6.5
	45 – 49	8,189	10.2
	50 – 54	10,487	13.1
	55 – 59	10,417	13.0
	60 – 64	8,967	11.2
	65 – 69	8,147	10.2
	70 – 74	7,045	8.8
	75 – 79	5,564	6.9
	80 – 84	3,820	4.8
	85+	3,467	4.3
Race			
	American Indian or Alaskan Native	110	0.14
	Asian or Pacific Islander	365	0.45
	Black	10,251	12.8
	White	68,279	85.0
	Other	915	1.1
	Unknown	368	0.46
Ethnicity			
	Hispanic	1,299	1.6
	Non-Hispanic	78,788	98.1
	Unknown	201	0.3

Type of Admission			
	Emergency	39,345	49.0
	Urgent	19,554	24.4
	Elective	21,157	26.4
	Newborn	50	0.1
	Trauma	103	0.1
	Unknown	79	0.1
Payer Source			
	Self-Pay	8,846	11.0
	Worker's Compensation	64	0.1
	Medicare	39,861	49.7
	Medicaid	11,038	13.8
	Other Federal Programs, DHS, or Managed Assistance	202	0.3
	Private Insurance	17,806	22.2
	Free (Medically Indigent)	79	0.1
	Other	2,387	3.0
	Unknown	5	<0.1

Table 18b. Descriptive Characteristics of Inpatient Hospitalizations Documenting Diagnoses of Chronic Liver Diseases — Arkansas, 2004 – 2012

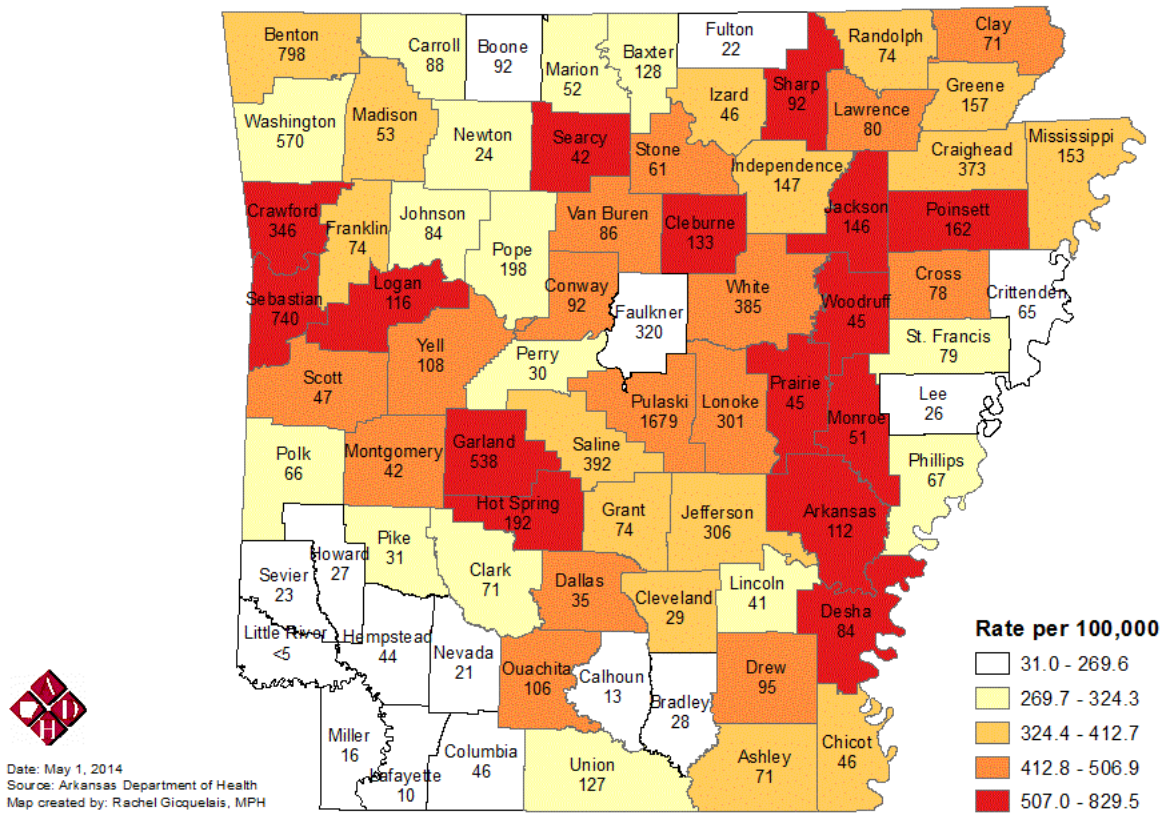
Variable	Mean (95% Confidence Interval)		Median	Number of Observations Missing Value
Patient Age (Years)	58.0	(57.9 – 58.1)	58	0
Visit Cost ($US)	35,206	(34,751 – 35,661)	18,704	0
Length of Stay (Days)	6.9	(6.8 – 6.9)	4	0

The principal diagnosis for an inpatient hospitalization is defined as “the condition established after study to be chiefly responsible for occasioning the admission of the patient for care.”[34] Table 19 presents hospitalizations where the principal diagnosis was a chronic liver disease, which is in contrast to Table 17 above, which presents hospitalizations where chronic liver diseases were documented in any of the 22 fields able to capture diagnoses assigned during inpatient hospitalizations. Table 19 documents a markedly lower number of hospitalizations for chronic liver diseases compared to the results of querying all diagnosis codes. Only 19.8% (15,895 hospitalizations) of the total 80,288 hospitalizations documenting chronic liver diseases had a chronic liver disease as the admitting diagnosis. This may suggest that physicians do not commonly admit patients primarily for chronic liver diseases or that it is documented as a finding established during the inpatient hospitalization.

Table 19. Principal Diagnoses for Chronic Liver Diseases — Arkansas, 2004 – 2012		
Year	Number of Hospitalizations	% of Total Hospitalizations
2004	1,627	0.4
2005	1,654	0.4
2006	1,758	0.4
2007	1,670	0.4
2008	1,746	0.4
2009	1,751	0.4
2010	1,844	0.5
2011	1,897	0.5
2012	1,948	0.5
Total	15,895	0.4

The geographic distribution of hospitalizations for chronic liver disease in 2012 was plotted according to the patient's county of residence. Persons who had no address in hospitalization records were excluded from maps. Figure 10 shows rates of inpatient hospitalizations for chronic liver diseases in Arkansas. Hospitalization rates were greater than 600 per 100,000 persons among Jackson, Desha, Poinsett, Monroe, and Woodruff counties.

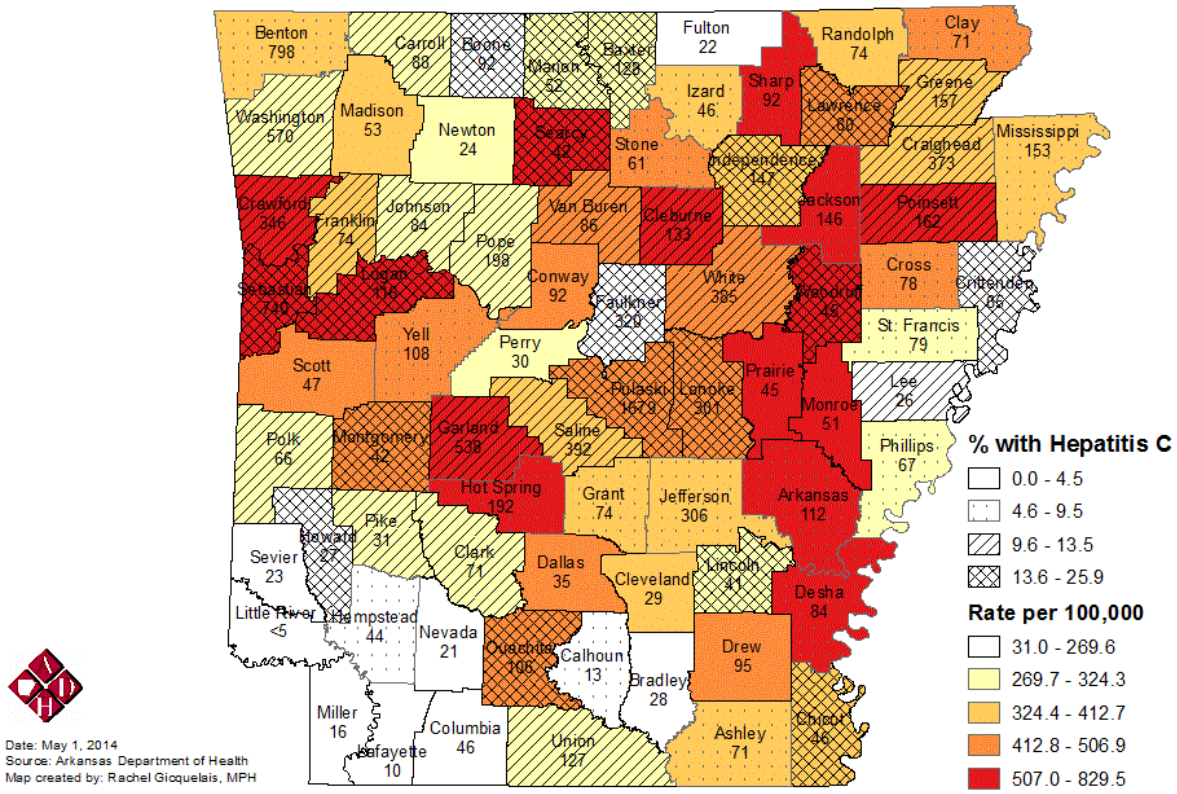
Figure 10. Inpatient Hospitalizations Documenting Diagnoses of Chronic Liver Diseases — Arkansas, 2012



Numbers represent hospitalizations per county.

HCV status among inpatient hospitalizations for chronic liver diseases by county is shown in Figure 11. Over 20% of inpatient hospitalizations for chronic liver diseases had HCV listed as a diagnosis code among hospitalizations of persons living in Howard, Searcy, Lawrence, Faulkner, Marion, and Logan counties.

Figure 11. Hepatitis C Virus Infection Among Inpatient Hospitalizations Documenting Diagnoses of Chronic Liver Diseases — Arkansas, 2012



Numbers represent hospitalizations documenting chronic liver diseases per county.

During 2004 – 2012, there were a total of 80,288 inpatient hospitalizations documenting chronic liver diseases among patients. The types of liver diseases documented are shown in Table 20. The most common type of chronic liver disease documented was cirrhosis, which was listed as a diagnosis in 37.1% of hospitalizations documenting any chronic liver disease. Notably, over one-quarter of persons with esophageal varices or any type of cirrhosis had HCV also documented in their inpatient hospitalization record. Further, nearly 18% of persons with liver diseases related to alcohol use had HCV, despite recommendations that persons diagnosed with HCV should abstain from alcohol use, as use of alcohol can accelerate the progression of liver damage and development of chronic liver diseases[2].

Table 20. Types of Chronic Liver Diseases (CLD) and Infection with Hepatitis C Virus (HCV) Among Inpatient Hospitalizations — Arkansas, 2004 – 2012

Type of Liver Disease	Number of Hospitalizations (% of Total CLD Hospitalizations)	Number (%) of CLD Hospitalizations Documenting HCV Infection
Alcoholic, Nonalcoholic, or Biliary Cirrhosis[1]	29,803 (37.1)	7,577 (25.4)
Fatty Liver, Hepatitis, Cirrhosis, or Unspecified Liver Damaged Caused by Alcohol[2]	16,777 (20.9)	3,006 (17.9)
Malignant or Other Ascites[3]	15,806 (19.7)	2,138 (13.5)
Esophageal Varices (Bleeding or Non-Bleeding)[4]	5,792 (7.2)	1,628 (28.1)
Malignant Neoplasms of the Liver, Gallbladder, or Biliary Tract[5]	4,751 (5.9)	717 (15.1)
Hepatorenal Syndrome[6]	1,014 (1.3)	209 (20.6)
Total Chronic Liver Diseases[7]	80,288* (100.0)	9,770 (12.2)

*Sum of rows will not add to total hospitalizations for all chronic liver diseases because patients can have more than one condition and all conditions included in total chronic liver diseases are not listed in table.

[1] Includes ICD-9-CM codes for alcoholic cirrhosis (5712), nonalcoholic cirrhosis (5715), or biliary cirrhosis (5716)

[2] Includes ICD-9-CM codes for alcoholic fatty liver (5710), acute alcoholic hepatitis (5711), alcoholic cirrhosis of the liver (5712), or unspecified alcoholic liver damage (5713).

[3] Includes ICD-9-CM codes for malignant ascites (78951) or other ascites (78959).

[4] Includes ICD-9-CM code for esophageal varices with bleeding (4560), without bleeding (4561), in diseases classified elsewhere with bleeding (45620), or in diseases classified elsewhere without bleeding (45621).

[5] Includes ICD-9-CM codes for malignant neoplasms of the liver (1550, 1552), intrahepatic bile ducts (1551), gallbladder (1560), extrahepatic bile ducts (1561), ampulla of vater (1562), gallbladder and extrahepatic bile ducts (1568), or unspecified site in the biliary tract (1569).

[6] Includes ICD-9-CM code for hepatorenal syndrome (5724).

[7] Includes the following ICD-9-CM codes: malignant neoplasms of the liver, intrahepatic bile ducts, gallbladder, extrahepatic bile ducts, ampulla of vater, or biliary tract (1550 - 1569), esophageal varices with or without bleeding (4560 - 45621), acute and subacute necrosis of the liver (570), alcoholic fatty liver, hepatitis, cirrhosis, or other unspecified alcoholic liver damage (5710 - 5713), chronic hepatitis (57140 - 57149), nonalcoholic cirrhosis (5715), biliary cirrhosis (5716), nonalcoholic liver disease (5718 - 5719), liver abscess (5720), portal pyemia (5721), hepatic encephalopathy (5722), portal hypertension (5723), hepatorenal syndrome (5724), other sequelae of chronic liver disease (5728), chronic passive congestion of the liver (5730), unspecified viral hepatitis (5731), unspecified hepatitis (5733), hepatic infarction (5734), hepatopulmonary syndrome (5735), other or unspecified disorders of the liver (5738, 5739), portal vein thrombosis (452), hepatomegaly (7891), malignant or other ascites (78951, 78959), personal history of malignant neoplasm of the liver (V1007), history of liver transplant or liver transplant complications (V427, 99682).

Because multiple hospitalizations per patient can and do occur, these analyses were repeated restricting data to only one hospitalization per year per person. Briefly, hospital discharge datasets for each year of service were de-duplicated using personal identifiers, such as social security number, patient name, and patient date of birth. For the analysis in Table 21, the earliest hospitalization occurring in each year is presented for each patient. If a person had any liver disease diagnosis documented in any record, the earliest record containing the liver disease diagnosis was retained over any other hospitalizations not documenting liver diseases.

Table 21. Individuals Hospitalized with Diagnoses of Chronic Liver Diseases (CLD)[1] Documented in Hospital Discharge Data — Arkansas, 2004 – 2012

Year	Number (%) of Hospitalizations Documenting CLD	Crude Hospitalization Rate per 100,000 Arkansans	Age-Adjusted Rate per 100,000 Arkansans (95% CI)	Number (%) with HCV Infection
2004	4,435 (1.8)	161.3	153.6 (149.0 – 158.1)	451 (10.2)
2005	4,750 (1.9)	170.8	161.7 (157.0 – 166.3)	498 (10.5)
2006	4,797 (1.9)	170.0	159.5 (154.9 – 164.0)	484 (10.1)
2007	5,161 (2.1)	181.2	168.8 (164.2 – 173.5)	509 (9.9)
2008	7,182 (2.8)	249.8	232.1 (226.6 – 237.5)	561 (7.8)
2009	7,276 (2.9)	251.2	232.3 (226.9 – 237.7)	615 (8.5)
2010	7,748 (3.1)	265.7	243.4 (237.8 – 248.9)	684 (8.8)
2011	7,742 (3.1)	263.5	238.8 (233.4 – 244.2)	707 (9.1)
2012	8,077 (3.2)	273.9	247.1 (241.5 – 252.6)	776 (9.6)
Total	57,168 (2.5)	N/A	N/A N/A	5,285 (9.2)
Trend Statistics	PC: 0.034* SC: 0.034* CA: <0.0001* (Increasing)	N/A	ROC: 13.9 per 100,000 persons (p=0.0004)*	PC: -0.0117* SC: -0.0097* CA: 0.0051* (Decreasing)

Abbreviations: CA: Cochran-Armitage Trend Test; CI: Confidence Interval; CLD: Chronic Liver Diseases; PC: Pearson Correlation Coefficient; ROC: Rate of Change; SC: Spearman Correlation Coefficient.
* Denotes statistically significant result at 95% confidence level (α ≤0.05).
[1] Liver diseases include inpatient hospitalizations with ICD-9-CM codes for malignant neoplasms of the liver, intrahepatic bile ducts, gallbladder, extrahepatic bile ducts, ampulla of vater, or biliary tract (1550 - 1569), esophageal varices with or without bleeding (4560 - 45621), acute and subacute necrosis of the liver (570), alcoholic fatty liver, hepatitis, cirrhosis, or other unspecified alcoholic liver damage (5710 - 5713), chronic hepatitis (57140 - 57149), nonalcoholic cirrhosis (5715), biliary cirrhosis (5716), nonalcoholic liver disease (5718 - 5719), liver abscess (5720), portal pyemia (5721), hepatic encephalopathy (5722), portal hypertension (5723), hepatorenal syndrome (5724), other sequelae of chronic liver disease (5728), chronic passive congestion of the liver (5730), unspecified viral hepatitis (5731), unspecified hepatitis (5733), hepatic infarction (5734), hepatopulmonary syndrome (5735), other or unspecified disorders of the liver (5738, 5739), portal vein thrombosis (452), hepatomegaly (7891), malignant or other ascites (78951, 78959), personal history of malignant neoplasm of the liver (V1007), history of liver transplant or liver transplant complications (V427, 99682).

Results showed similar trends to Table 17. The number of individuals hospitalized for liver diseases increased over time, from 4,435 in 2004 to 8,077 in 2012, representing a statistically significant increase in the proportion of total individuals hospitalized during the time period. Further, linear regression of the age-adjusted hospitalization rates demonstrated a statistically significant increase of 13.9 individuals hospitalized per 100,000 persons per year. Overall, 9.2% of individuals hospitalized with liver diseases also had HCV documented in the inpatient record, a slightly lower estimate compared to the 12.2% with HCV presented in Table 17, which includes all hospitalizations. This may be because persons with HCV are more likely to be hospitalized multiple times, thus over-representing hospitalizations for HCV when all hospitalizations were analyzed. Because trends were similar to those presented above, additional analyses using de-duplicated data are available by request but not further presented in the epidemiologic profile.

Hospitalizations for Cirrhosis

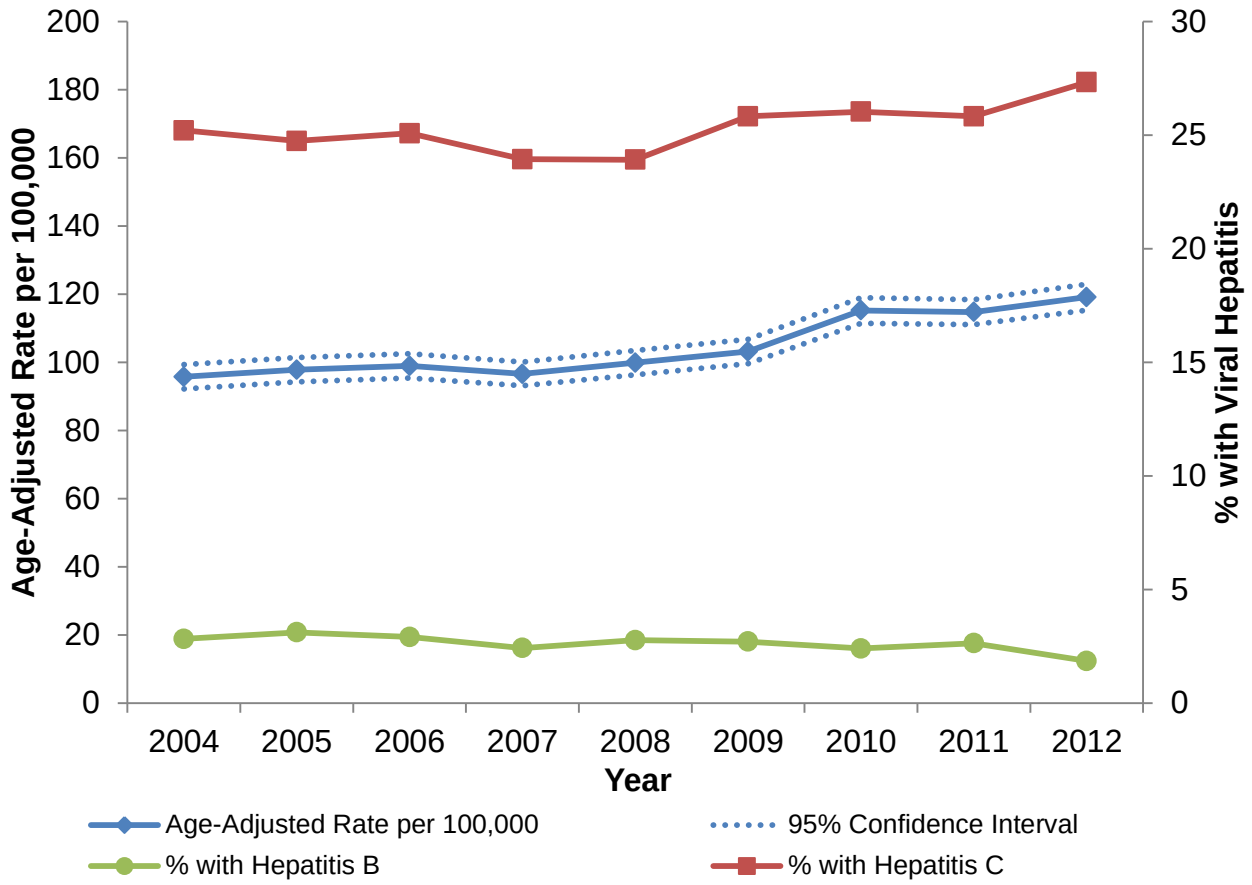
Cirrhosis, or scarring of the liver, results in impairments in liver function and occurs in up to 20% of persons infected with HCV[2]. Rates of inpatient hospitalizations documenting ICD-9-CM codes for cirrhosis are shown in Table 22 and Figure 12, accompanied by the percentage of these hospitalizations that document infection with either HBV or HCV. The number and proportion of hospitalizations per year listing cirrhosis as a diagnosis increased over time. Linear regression of cirrhosis rates predicted an increase of 3.1 hospitalizations per 100,000 Arkansans per year. Over one-quarter (27.3%) of hospitalizations for cirrhosis documented HCV infection in 2012, compared with 1.9% documenting HBV in 2012. There was a statistically significant increase in the proportion of hospitalizations documenting HCV among persons hospitalized for cirrhosis during 2004 – 2012.

Table 22. Inpatient Hospitalizations Documenting Diagnoses of Cirrhosis[1] — Arkansas, 2004 – 2012

Year	Number (%) of Hospitalizations Documenting Cirrhosis	Crude Hospitalization Rate per 100,000 Arkansans	Age-Adjusted Rate per 100,000 Arkansans (95% Confidence Interval)	Number (%) with HCV
2004	2,797 (0.7)	101.7	95.8 (92.2 –99.3)	705 (25.2)
2005	2,930 (0.7)	105.4	97.8 (94.3 – 101.4)	725 (24.7)
2006	3,022 (0.7)	107.1	98.9 (95.4 – 102.5)	758 (25.1)
2007	3,020 (0.7)	106.0	96.6 (93.1 – 100.1)	723 (23.9)
2008	3,144 (0.8)	109.4	99.9 (96.3 – 103.4)	752 (23.9)
2009	3,294 (0.8)	113.7	103.2 (99.6 – 106.8)	851 (25.8)
2010	3,757 (1.0)	128.8	115.2 (111.5 – 119.0)	978 (26.0)
2011	3,844 (1.0)	130.8	114.7 (111.0 – 118.4)	993 (25.8)
2012	3,995 (1.0)	135.5	119.1 (115.3 – 122.9)	1,092 (27.3)
Total	29,803 (0.8)	N/A	N/A	7,577 (25.4)
Trend Statistics	PC: 0.0129* SC: 0.0129* CA: <0.0001* (Increasing)	N/A	ROC: 3.1 per 100,000 persons (p=0.0006)*	PC: 0.0167* SC: 0.0173* CA: 0.004* (Increasing)

Abbreviations: CA: Cochran-Armitage Trend Test; CI: Confidence Interval; HCV: Hepatitis C Virus; PC: Pearson Correlation Coefficient; ROC: Rate of Change; SC: Spearman Correlation Coefficient.
* Denotes statistically significant result at 95% confidence level ($\alpha \leq 0.05$).
[1] Cirrhosis includes inpatient hospitalizations with ICD-9-CM codes 5712 (alcoholic cirrhosis of the liver), 5715 (cirrhosis of the liver without mention of alcohol), or 5716 (biliary cirrhosis).

Figure 12. Inpatient Hospitalizations Documenting Diagnoses of Cirrhosis — Arkansas 2004 – 2012



*Cirrhosis includes inpatient hospitalizations with ICD-9-CM codes 5712 (alcoholic cirrhosis of the liver), 5715 (cirrhosis of the liver without mention of alcohol), or 5716 (biliary cirrhosis).

Descriptive statistics among hospitalizations documenting cirrhosis are presented in Table 23. Overall, most hospitalizations were among males compared to females. Persons aged 50 – 54 years followed by persons aged 55 – 59 years experienced the highest number of hospitalizations documenting cirrhosis. The average age of persons hospitalized was 58.6 years. Hospitalizations occurred most commonly among white, non-hispanic Arkansans. The majority of admissions were emergency admissions and the payer source was most commonly Medicare. Hospitalizations cost an average of $27,122.26 and lasted an average of 6.1 days.

Table 23a. Descriptive Characteristics of Inpatient Hospitalizations Documenting Diagnoses of Cirrhosis — Arkansas, 2004 – 2012

Characteristic	No.	%
Total	29,803	100.0
Sex		
Male	16,954	56.9
Female	12,849	43.1

Age (Years)			
	0 – 9	14	<0.1
	10 – 14	5	<0.1
	15 – 19	28	0.1
	20 – 24	83	0.3
	25 – 29	147	0.5
	30 – 34	332	1.1
	35 – 39	958	3.2
	40 – 44	1,863	6.3
	45 – 49	3,588	12.0
	50 – 54	5,022	16.9
	55 – 59	4,795	16.1
	60 – 64	3,692	12.4
	65 – 69	3,160	10.6
	70 – 74	2,511	8.4
	75 – 79	1,809	6.1
	80 – 84	978	3.3
	85+	818	2.7
Race			
	American Indian or Alaskan Native	52	0.2
	Asian or Pacific Islander	120	0.4
	Black	2,970	10.0
	White	26,230	88.0
	Other	286	1.0
	Unknown	145	0.5
Ethnicity			
	Hispanic	405	1.4
	Non-Hispanic	29,346	98.5
	Unknown	52	0.2
Type of Admission			
	Emergency	15,317	51.4
	Urgent	7,409	24.9
	Elective	7,006	23.5
	Newborn	0	0.0
	Trauma	42	0.1
	Unknown	29	0.1
Payer Source			
	Self-Pay	3,149	10.6
	Worker's Compensation	19	0.1
	Medicare	15,318	51.4
	Medicaid	5,106	17.1
	Other Federal Programs, DHS, or Managed Assistance	78	0.3
	Private Insurance	5,375	18.0
	Free (Medically Indigent) or Unknown	23	0.1
	Other	735	2.5

Table 23b. Descriptive Characteristics of Inpatient Hospitalizations Documenting Diagnoses of Cirrhosis — Arkansas, 2004 – 2012				
Variable	Mean (95% Confidence Interval)		Median	Number of Observations Missing Value
Patient Age (Years)	58.6	(58.5 – 58.7)	57	0
Visit Cost ($US)	27,122	(26,708 – 27,537)	16,399	0
Length of Stay (Days)	6.1	(6.0 – 6.2)	4	0

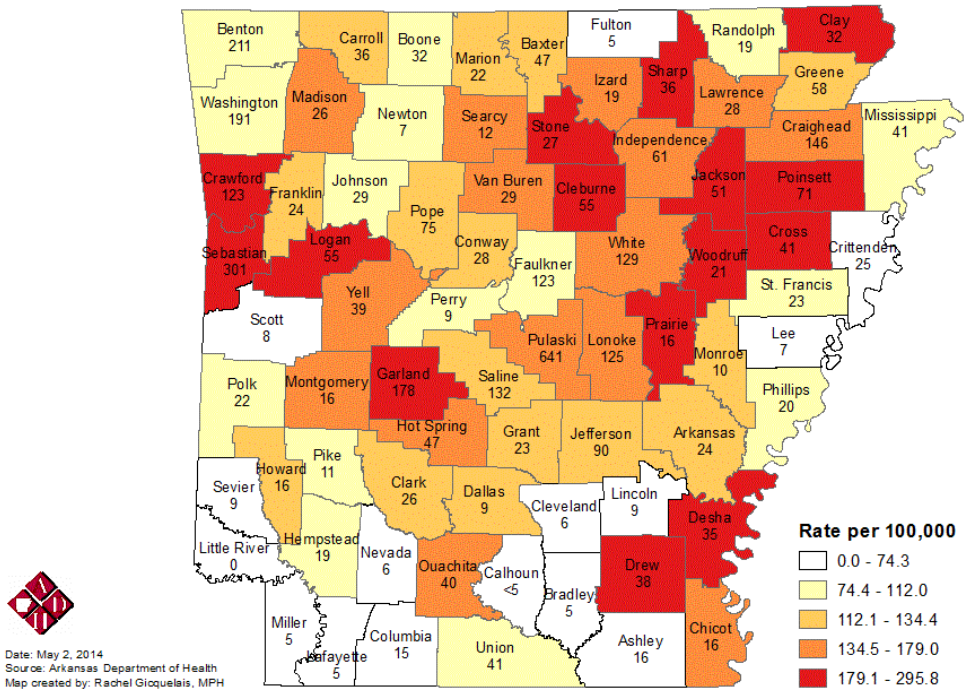
The principal diagnosis for an inpatient hospitalization is defined as "the condition established after study to be chiefly responsible for occasioning the admission of the patient for care."[34] Table 24 presents hospitalizations where the principal diagnosis was cirrhosis, which is in contrast to Table 22 above, which presents hospitalizations where cirrhosis was documented in any of the 22 fields able to capture diagnoses or injuries assigned during inpatient hospitalizations. Table 24 documents a markedly lower number of hospitalizations for cirrhosis compared to the results of querying all diagnosis codes. Only 18.5% (5,507 hospitalizations) of the total 29,803 hospitalizations documenting cirrhosis had cirrhosis as the admitting diagnosis. This may suggest that physicians do not commonly admit patients primarily for cirrhosis and that the diagnosis is documented as a finding established during the inpatient hospitalization.

Table 24. Principal Diagnoses for Cirrhosis — Arkansas, 2004 – 2012		
Year	Number of Hospitalizations	% of Total Hospitalizations
2004	619	0.2
2005	653	0.2
2006	718	0.2
2007	631	0.2
2008	562	0.1
2009	582	0.2
2010	612	0.2
2011	566	0.2
2012	564	0.2
Total	5,507	0.2

Crude hospitalization rates for cirrhosis were plotted by county of patient residence for all hospitalizations in 2012 among persons living in Arkansas with address information included in hospitalization data. Hospitalization rates for cirrhosis exceeded 250 per 100,000 persons in Woodruff, Poinsett, Jackson, Desha, and Logan counties (Figure 13).

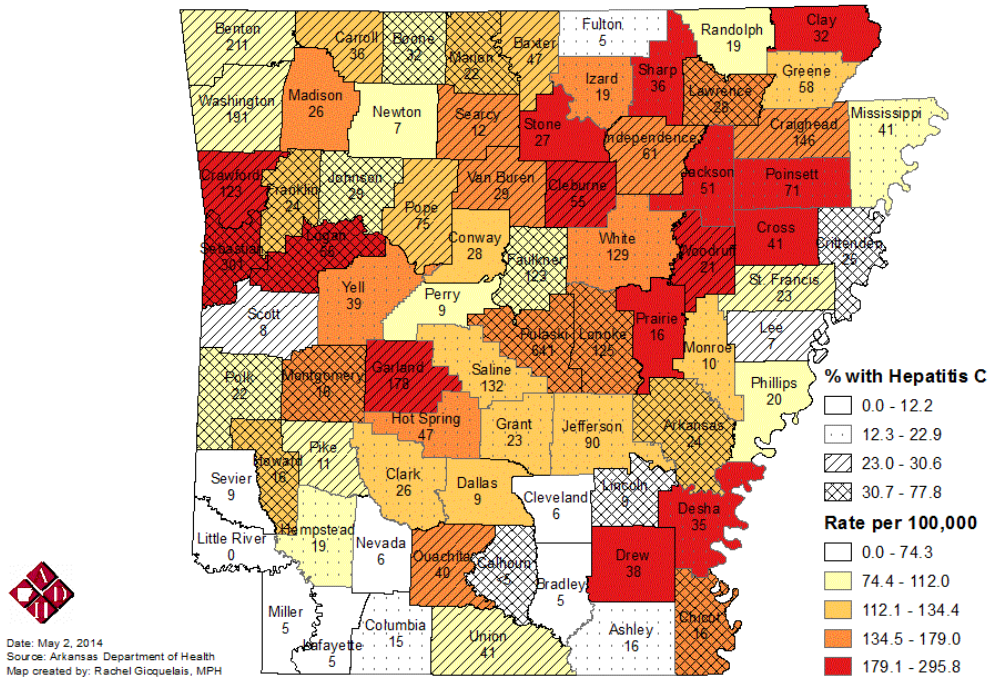
HCV status among hospitalizations for cirrhosis was plotted in Figure 14 by county of patient residence. More than half of persons hospitalized for cirrhosis also had HCV documented in their inpatient hospitalization record in Chicot, Lawrence, and Lincoln counties.

Figure 13. Inpatient Hospitalizations Documenting Diagnoses of Cirrhosis — Arkansas, 2012



Numbers represent hospitalizations per county.

Figure 14. Hepatitis C Virus Infection Among Inpatient Hospitalizations Documenting Diagnoses of Cirrhosis — Arkansas, 2012



Numbers represent hospitalizations documenting cirrhosis per county.

Several types of cirrhosis are noted among inpatient hospitalization records, including liver cirrhosis related to alcohol consumption, liver cirrhosis unrelated to alcohol, biliary cirrhosis, or presence of more than one of the aforementioned types. Table 25 shows the number of hospitalizations during the period 2004 – 2012 for each type of cirrhosis, along with the percentage with HCV infection also documented. The majority of hospitalizations for cirrhosis were cirrhosis of the liver unrelated to alcohol (17,123 hospitalizations). Of these, over one-quarter also documented HCV as a diagnosis. Among 11,628 hospitalizations for alcoholic cirrhosis, 22.4% had HCV. Persons with HCV are recommended to abstain from alcohol consumption, as alcohol use is likely to speed the progression of liver damage and the development of cirrhosis[2].

Table 25. Types of Cirrhosis and Infection with Hepatitis C Virus (HCV) Documented in Inpatient Hospitalizations — Arkansas, 2004 – 2012

Type of Cirrhosis	Number (%) of Hospitalizations for Cirrhosis	Number (%) with HCV
Alcoholic Cirrhosis of the Liver[1]	11,628 (39.0)	2,606 (22.4)
Cirrhosis of the Liver without Mention of Alcohol[2]	17,123 (57.5)	4,842 (28.3)
Biliary Cirrhosis[3]	678 (2.3)	16 (2.4)
Multiple Types of Cirrhosis[4]	374 (1.3)	113 (30.2)
Total	29,803 (100.0)	7,577 (25.4)

[1] Alcoholic cirrhosis of the liver includes inpatient hospitalizations with ICD-9-CM code 5712.
[2] Cirrhosis of the liver without mention of alcohol includes inpatient hospitalizations with ICD-9-CM code 5715.
[3] Biliary cirrhosis includes inpatient hospitalizations with ICD-9-CM code 5716.
[4] Hospitalizations with multiple types of cirrhosis includes hospitalizations with more than one of the following ICD-9-CM codes: 5712, 5715, and 5716.

Because multiple hospitalizations per patient can and do occur, these analyses were repeated restricting data to only one hospitalization per year per person. Briefly, hospital discharge datasets for each year of service were de-duplicated using personal identifiers, such as social security number, patient name, and patient date of birth. In Table 26, the earliest hospitalization occurring in each year is presented for each patient. If a person had a cirrhosis diagnosis documented in any record, the earliest record containing the cirrhosis diagnosis was retained over any other hospitalizations not documenting cirrhosis.

Results showed similar trends to Table 22. The number of individuals hospitalized for cirrhosis increased over time, from 1,635 in 2004 to 2,352 in 2012, representing a statistically significant increase in the proportion of all individuals hospitalized during the time period. Further, linear regression of the age-adjusted hospitalizations rates demonstrated a statistically significant increase of 1.8 individuals hospitalized per 100,000 persons per year. Overall, 23.6% of individuals hospitalized with cirrhosis also had HCV also documented in the inpatient record, similar to the estimate of 25.4% with HCV presented in Table 22 using all hospitalizations.

Because trends were similar to those presented above, additional analyses using de-duplicated data are available by request but not further presented in the epidemiologic profile.

Table 26. Individuals Hospitalized with Diagnoses of Cirrhosis[1] Documented in Hospital Discharge Data — Arkansas, 2004 – 2012

Year	Number (%) of Hospitalizations Documenting Cirrhosis	Crude Hospitalization Rate per 100,000 Arkansans	Age-Adjusted Rate per 100,000 Arkansans (95% CI)	Number (%) with HCV
2004	1,635 (0.7)	59.5	56.1 (53.4 – 58.8)	369 (22.6)
2005	1,729 (0.7)	62.2	57.8 (55.1 – 60.5)	397 (23.0)
2006	1,791 (0.7)	63.5	58.5 (55.8 – 61.3)	405 (22.6)
2007	1,771 (0.7)	62.2	56.6 (53.9 – 59.2)	409 (23.1)
2008	1,900 (0.8)	66.1	60.2 (57.4 – 62.9)	426 (22.4)
2009	1,994 (0.8)	68.8	62.2 (59.4 – 65.0)	489 (24.5)
2010	2,201 (0.9)	75.5	67.3 (64.4 – 70.1)	540 (24.5)
2011	2,301 (0.9)	78.3	68.5 (65.7 – 71.4)	548 (23.8)
2012	2,352 (0.9)	79.8	69.6 (66.7 – 72.5)	582 (24.7)
Total	17,674 (0.8)	N/A	N/A	4,165 (23.6)
Trend Statistics	PC: 0.0107* SC: 0.0107* CA: <0.0001* (Increasing)	N/A	ROC: 1.8 per 100,000 persons (p=0.0002)*	PC: 0.017* SC: 0.017* CA: 0.024* (Increasing)

Abbreviations: CA: Cochran-Armitage Trend Test; CI: Confidence Interval; HCV: Hepatitis C Virus; PC: Pearson Correlation Coefficient; ROC: Rate of Change; SC: Spearman Correlation Coefficient.
* Denotes statistically significant result at 95% confidence level (α ≤0.05).
[1] Cirrhosis includes inpatient hospitalizations with ICD-9-CM codes 5712 (alcoholic cirrhosis of the liver), 5715 (cirrhosis of the liver without mention of alcohol), or 5716 (biliary cirrhosis).

Hospitalizations for Alcohol Related Liver-Related Conditions

Consumption of alcohol is known to speed the progression to developing cirrhosis and other chronic liver diseases among persons infected with viral hepatitis[2]. The CDC recommends that persons diagnosed with viral hepatitis infection be evaluated for alcohol use and receive intervention to facilitate their abstinence from alcohol use when necessary[2]. Inpatient hospitalization data was used to query liver diseases related to the consumption of alcohol and evaluated the percentage of persons with concurrent diagnoses for HBV and HCV.

From 2004 – 2012, the proportion of hospitalizations documenting liver diseases related to alcohol use increased (Table 27). Linear regression of hospitalization rates demonstrated an increase of 0.9 hospitalizations per 100,000 Arkansans per year. During the time period, 17.9% (range: 15.9% – 19.0%) of hospitalizations for alcohol-related liver diseases also documented infection with HCV. Persons diagnosed with HCV are recommended to abstain from alcohol use; however, these data do not show whether the person knew previously about their HCV infection or knew about recommendations for abstaining from alcohol. Nonetheless, these data suggest that both diagnosis of HCV and education about recommendations to abstain from alcohol should be priorities in Arkansas.

Table 27. Inpatient Hospitalizations Documenting Diagnoses of Alcohol-Related Liver Diseases[1] — Arkansas, 2004 – 2012

Year	Number (%) of Hospitalizations Documenting Alcohol-Related Liver Diseases	Crude Hospitalization Rate per 100,000 Arkansans	Age-Adjusted Rate per 100,000 Arkansans (95% Confidence Interval)	Number (%) with HCV
2004	1,646 (0.4)	59.9	57.9 (55.1 – 60.7)	281 (17.1)
2005	1,692 (0.4)	60.8	57.9 (55.2 – 60.7)	294 (17.4)
2006	1,791 (0.4)	63.5	59.6 (56.8 – 62.3)	336 (18.8)
2007	1,735 (0.4)	60.9	56.8 (54.1 – 59.5)	276 (15.9)
2008	1,909 (0.5)	66.4	62.1 (59.2 – 64.9)	337 (17.7)
2009	1,887 (0.5)	65.1	61.4 (58.6 – 64.3)	352 (18.7)
2010	2,105 (0.5)	72.2	67.4 (64.5 – 70.3)	378 (18.0)
2011	1,984 (0.5)	67.5	61.5 (58.7 – 64.2)	366 (18.5)
2012	2,028 (0.5)	68.8	63.9 (61.1 – 66.8)	386 (19.0)
Total	16,777 (0.5)	N/A	N/A	3,006 (17.9)
Trend Statistics	PC: 0.0064* SC: 0.0064* CA: <0.0001 (Increasing)*	N/A	ROC: 0.9 per 100,000 persons (p=0.0198)*	PC: 0.0137 SC: 0.0138 CA: 0.077 (None)

Abbreviations: CA: Cochran-Armitage Trend Test; CI: Confidence Interval; HCV: Hepatitis C Virus; PC: Pearson Correlation Coefficient; ROC: Rate of Change; SC: Spearman Correlation Coefficient.
* Denotes statistically significant result at 95% confidence level (α ≤0.05).
[1] Alcohol-Related Liver Diseases include inpatient hospitalizations with ICD-9-CM codes 5710 (alcoholic fatty liver), 5711 (acute alcoholic hepatitis), 5712 (alcoholic cirrhosis of the liver), or 5713 (unspecified alcoholic liver damage).

Hospitalizations for Complications of Chronic Viral Hepatitis

Ascites, or fluid retention in the peritoneal cavity, is a complication among persons infected with viral hepatitis, and occurs when the liver and its blood vessels become damaged, preventing blood flow and forcing fluid into the space between the abdomen's lining and organs[35]. Ascites occurs among approximately half of persons with compensated cirrhosis[35]. Once ascites develops, persons have an increased risk of death and need to be evaluated for a liver transplant[35]. Inpatient hospitalization data was used to query hospitalizations documenting ascites. Notably, less than five ascites diagnoses per year were listed for years 2004 – 2006 (data not shown). Results of this analysis showed that the proportion of hospitalizations documenting ascites increased over time (Table 28). Linear regression of ascites hospitalization rates showed that during 2007 – 2012, rates increased by 13.9 hospitalizations per 100,000 persons per year. Additionally, the proportion of hospitalizations also documenting HCV infection increased over time.

Esophageal varices are another complication of viral hepatitis. When persons with liver damage, such as cirrhosis, have restricted blood flow from the veins of the liver, esophageal varices, or abnormally large veins in the esophagus, can develop, as blood from the liver flows into smaller veins in this area of the body. Because these smaller veins are enlarged, they are susceptible to leakage or bursting, which can lead to bleeding problems for the patient that can become life threatening[36]. Inpatient hospitalization data was used to query hospitalizations documenting esophageal varices. Results of this analysis showed that the proportion of hospitalizations documenting esophageal varices increased over time (Table 29). Linear regression of hospitalization rates for esophageal varices showed that during 2004 – 2012, rates increased by

1.0 hospitalization per 100,000 persons per year. During the time period, 28.1% (range: 23.8% – 30.9%) of hospitalizations documenting esophageal varices also documented HCV infection.

Table 28. Inpatient Hospitalizations Documenting Diagnoses of Ascites[1] — Arkansas, 2007 – 2012

Year	Number (%) of Hospitalizations Documenting Ascites	Crude Hospitalization Rate per 100,000 Arkansans	Age-Adjusted Rate per 100,000 Arkansans (95% CI)	Number (%) HCV
2007	596 (0.2)	20.9	19.2 (17.7 – 20.8)	65 (10.9)
2008	2,713 (0.7)	94.4	86.4 (83.1 – 89.7)	334 (12.3)
2009	2,805 (0.7)	96.8	88.1 (84.8 – 91.4)	401 (14.3)
2010	3,174 (0.8)	108.9	98.0 (94.5 – 101.4)	454 (14.3)
2011	3,266 (0.8)	111.1	98.5 (95.0 – 101.9)	410 (12.6)
2012	3,251 (0.8)	110.2	97.9 (94.5 – 101.4)	474 (14.6)
Total	15,806 (0.4)	N/A	N/A	2,138 (13.5)
Trend Statistics	PC: 0.0525* SC: 0.0526* CA: <0.0001* (Increasing)	N/A	ROC: 13.9 per 100,000 persons (p=0.0064)*	PC: 0.0159* SC: 0.0149 CA: 0.045* (Increasing)

Abbreviations: CA: Cochran-Armitage Trend Test; CI: Confidence Interval; HCV: Hepatitis C Virus; PC: Pearson Correlation Coefficient; ROC: Rate of Change; SC: Spearman Correlation Coefficient.
* Denotes statistically significant result at 95% confidence level (α ≤0.05).
[1] Ascites diagnoses include inpatient hospitalizations with ICD-9-CM codes 78951 (malignant ascites) and 78959 (other ascites).

Table 29. Inpatient Hospitalizations Documenting Diagnoses of Esophageal Varices[1] — Arkansas, 2004 – 2012

Year	Number (%) of Hospitalizations Documenting Esophageal Varices	Crude Hospitalization Rate per 100,000 Arkansans	Age-Adjusted Rate per 100,000 Arkansans (95% CI)	Number (%) with HCV
2004	534 (0.1)	19.4	18.3 (16.8 – 19.9)	149 (27.9)
2005	538 (0.1)	19.3	18.4 (16.9 – 20.0)	156 (29.0)
2006	504 (0.1)	17.9	16.6 (15.2 – 18.1)	153 (30.4)
2007	526 (0.1)	18.5	17.3 (15.8 – 18.8)	125 (23.8)
2008	666 (0.2)	23.2	21.1 (19.5 – 22.8)	187 (28.1)
2009	685 (0.2)	23.6	21.6 (19.9 – 23.2)	194 (28.3)
2010	748 (0.2)	25.7	23.1 (21.5 – 24.8)	231 (30.9)
2011	787 (0.2)	26.8	23.9 (22.2 – 25.6)	202 (25.7)
2012	804 (0.2)	27.3	24.3 (22.5 – 26.0)	231 (28.7)
Total	5,792 (0.2)	N/A	N/A	1,628 (28.1)
Trend Statistics	PC: 0.0075* SC: 0.0075* CA: <0.0001* (Increasing)	N/A	ROC: 1.0 per 100,000 persons (p=0.0011)*	PC: -0.0007 SC: -0.0003 CA: 0.9603 (None)

Abbreviations: CA: Cochran-Armitage Trend Test; CI: Confidence Interval; HCV: Hepatitis C Virus; PC: Pearson Correlation Coefficient; ROC: Rate of Change; SC: Spearman Correlation Coefficient.
* Denotes statistically significant result at 95% confidence level (α ≤0.05).
[1] Hospitalizations documenting esophageal varices include inpatient hospitalizations with ICD-9-CM codes 4560 (esophageal varices with bleeding), 4561 (esophageal varices without bleeding), 45620 (esophageal varices in diseases classified elsewhere [cirrhosis or portal hypertension], with bleeding), and 45621 (esophageal varices in diseases classified elsewhere [cirrhosis or portal hypertension], without bleeding).

Hepatic encephalopathy is a third complication that can develop from liver damage related to viral hepatitis. Hepatic encephalopathy occurs when the liver is no longer able to remove waste from the blood, resulting in a buildup of substances, such as ammonia, and manifesting through an altered mental status[37]. Inpatient hospitalization data was used to query for hospitalizations documenting hepatic encephalopathy. Results of this analysis showed that the proportion of hospitalizations documenting hepatic encephalopathy increased over time (Table 30). Linear regression of hepatic encephalopathy hospitalization rates showed that during 2004 – 2012, rates increased by 2.1 hospitalizations per 100,000 persons per year. During the time period, 25.6% (range: 21.8% – 30.5%) of hospitalizations documenting esophageal varices also documented infection with HCV.

Table 30. Inpatient Hospitalizations Documenting Diagnoses of Hepatic Encephalopathy[1] — Arkansas, 2004 – 2012

Year	Number (%) of Hospitalizations Documenting Hepatic Encephalopathy	Crude Hospitalization Rate per 100,000 Arkansans	Age-Adjusted Rate per 100,000 Arkansans (95% Confidence Interval)	Number (%) with HCV
2004	711 (0.2)	25.9	24.2 (22.4 – 26.0)	217 (30.5)
2005	748 (0.2)	26.9	24.7 (22.9 – 26.5)	213 (28.5)
2006	786 (0.2)	27.9	25.8 (24.0 – 27.6)	201 (25.6)
2007	842 (0.2)	29.6	26.9 (25.1 – 28.8)	221 (26.3)
2008	859 (0.2)	29.9	27.0 (25.2 – 28.9)	189 (22.0)
2009	936 (0.2)	32.3	29.0 (27.1 – 30.9)	204 (21.8)
2010	1,084 (0.3)	37.2	33.1 (31.1 – 35.1)	264 (24.4)
2011	1,259 (0.3)	42.8	37.3 (35.2 – 39.4)	327 (26.0)
2012	1,431 (0.4)	48.5	42.3 (40.1 – 44.5)	383 (26.8)
Total	8,656 (0.2)	N/A	N/A	2,219 (25.6)
Trend Statistics	PC: 0.0122* SC: 0.0122* CA: <0.0001* (Increasing)	N/A	ROC: 2.1 per 100,000 persons (p=0.0003)*	PC: -0.0196 SC: -0.0148 CA: 0.068 (None)

Abbreviations: CA: Cochran-Armitage Trend Test; CI: Confidence Interval; HCV: Hepatitis C Virus; PC: Pearson Correlation Coefficient; ROC: Rate of Change; SC: Spearman Correlation Coefficient.
* Denotes statistically significant result at 95% confidence level (α ≤0.05).
[1] Hospitalizations documenting hepatic encephalopathy include inpatient hospitalizations with ICD-9-CM codes 0700 (viral hepatitis A with hepatic coma), 07020 – 07023 (viral hepatitis B with hepatic coma [acute and chronic, with and without hepatitis delta]), 07040 – 07049 (other specified viral hepatitis with hepatic coma [acute hepatitis C, hepatitis D without hepatitis B, hepatitis E, chronic hepatitis C, or other]), 0706 (unspecified viral hepatitis with hepatic coma), 07071 (unspecified viral hepatitis C with hepatic coma), and 5722 (hepatic coma [hepatic encephalopathy, hepatocerebral intoxication, portal-systemic encephalopathy]).

Emergency Department Visits

Emergency department (ED) visits became reportable to ADH in 2012. ED visits with *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes indicative of diseases of interest were identified by querying all diagnosis and injury fields for ED visits occurring in Arkansas during 2012. A detailed description of methods used to analyzed ED visit data and relevant limitations are included in Appendix A. Of 1,074,772 ED visits, 1,015,815 were among persons with an address in Arkansas or whose address was unknown and were

included in the analyses presented. ED visits with ICD-9-CM procedure codes indicative of procedures of interest were identified by querying all procedure fields for ED visits occurring in Arkansas during 2012.

Among 1,015,815 ED visits occurring among Arkansans in 2012, most were among females, persons aged <5 years, and persons of white race and non-hispanic ethnicity (Table 31). Most visits were emergency related and Medicaid was the most common payer source. On average, persons visiting EDs were aged nearly 35 years and the average cost of each visit was $1,706.

Table 31a. Descriptive Characteristics of Emergency Department Visits — Arkansas, 2012			
Characteristic		No.	%
Total		1,015,815	100.0
Sex			
	Male	435,998	42.9
	Female	579,813	57.1
	Unknown	4	<0.1
Age (Years)			
	<5	109,055	10.7
	5 – 9	50,966	5.0
	10 – 14	44,830	4.4
	15 – 19	69,965	6.9
	20 – 24	98,524	9.7
	25 – 29	93,395	9.2
	30 – 34	86,211	8.5
	35 – 39	71,571	7.1
	40 – 44	64,950	6.4
	45 – 49	63,328	6.2
	50 – 54	56,801	5.6
	55 – 59	44,450	4.4
	60 – 64	34,530	3.4
	65 – 69	31,760	3.1
	70 – 74	26,804	2.6
	75 – 79	23,326	2.3
	80 – 84	20,198	2.0
	85+	25,151	2.5
Race			
	American Indian or Alaskan Native	2,343	0.2
	Asian or Pacific Islander	5,490	0.5
	Black	232,350	22.9
	White	742,501	73.1
	Other	32,279	3.2
	Unknown	852	0.1
Ethnicity			
	Hispanic	32,899	3.2
	Non-Hispanic	982,438	96.7
	Unknown	478	0.1

Type of Visit			
	Emergency	804,574	79.2
	Urgent	84,865	8.4
	Elective	21,806	2.2
	Newborn	31	<0.1
	Trauma	5,783	0.6
	Unknown	98,756	9.7
Payer Source			
	Self-Pay	263,047	25.9
	Worker's Compensation	10,609	1.0
	Medicare	191,266	18.8
	Medicaid	278,655	27.4
	Other Federal Programs, DHS, or Managed Assistance	4,269	0.4
	Private Insurance	219,454	21.6
	Free (Medically Indigent)	56	0.0
	Other	47,196	4.7
	Unknown	1,263	0.1

Table 31b. Descriptive Characteristics of Emergency Department Visits — Arkansas, 2012

Variable	Mean (95% Confidence Interval)		Median	Number of Observations Missing Value
Patient Age (Years)	34.9	(34.8 – 34.9)	32	0
Visit Cost ($US)	1,706	(1,701 – 1,711)	934	0

Numbers, rates, and comorbidities among emergency department visits in 2012 are shown in Table 32. Of note, the number of emergency department visits for acute, chronic, or unspecified HCV was 13 times greater than the number for HBV and 1.8 times greater than the number for HIV. Additionally, over one-third of persons with HBV documented in their emergency visit also had HCV. Nearly one-quarter of persons visiting the emergency room for cirrhosis had HCV.

Table 32. Diagnoses Listed in Emergency Department Visit Discharge Data — Arkansas, 2012

Diagnosis	Number (%) of Visits	Crude Hospitalization Rate per 100,000	Age-Adjusted Rate of Hospitalization per 100,000 (95% Confidence Interval)	Number (%) with Hepatitis B Virus (HBV) Infection	Number (%) with Hepatitis C Virus (HCV) Infection
Ascites[1]	632 (0.1)	21.4	19.3 (17.8 – 20.8)	7 (1.1)	115 (18.2)
Alcohol-Related Liver Damage[2]	282 (<0.1)	9.6	9.2 (8.1 – 10.3)	<5 (<1.8)	26 (9.2)
Cirrhosis[3]	1,328 (0.1)	45.0	41.5 (39.2 – 43.8)	20 (1.5)	327 (24.6)
Chronic Liver Diseases[4]	4,974 (0.5)	168.7	161.7 (157.1 – 166.3)	35 (0.7)	478 (9.6)
Esophageal Varices[5]	98 (<0.1)	3.3	3.1 (2.5 – 3.7)	0 (0.0)	21 (21.4)
Hepatic Encephalopathy[6]	154 (<0.1)	5.2	4.7 (3.9 – 5.5)	5 (3.3)	29 (18.8)

HBV[7]	236 (<0.1)	8.0	8.2 (7.1 – 9.2)	236 (100)	79 (33.5)
HCV[8]	3,073 (0.3)	104.2	105.7 (101.9 – 109.5)	79 (2.6)	3,073 (100)
HIV[9]	1,725 (0.2)	58.5	63.5 (60.5 – 66.5)	14 (0.2)	115 (6.7)
Malignant Neoplasms of the Liver, Biliary Tract, and Gallbladder[10]	216 (<0.1)	7.3	6.3 (5.4 – 7.1)	<5 (<2.3)	22 (10.2)
Opiate-Related Drug Overdose[11]	651 (0.1)	22.1	22.2 (20.5 – 23.9)	0 (0.0)	8 (1.2)

[1] Emergency department visits for ascites were indicated by the following ICD-9-CM codes: 78951 (malignant ascites) and 78959 (other ascites).
[2] Emergency department visits for alcohol-related liver by the following ICD-9-CM codes: 5710 (alcoholic fatty liver), 5711 (acute alcoholic hepatitis), 5712 (alcoholic cirrhosis of the liver), or 5713 (unspecified alcoholic liver damage).
[3] Emergency department visits for alcoholic, nonalcoholic, or biliary cirrhosis were indicated by the following ICD-9-CM codes: 5712, 5715, or 5716.
[4] Emergency department visits for chronic liver diseases were indicated by the following ICD-9-CM codes: malignant neoplasms of the liver, intrahepatic bile ducts, gallbladder, extrahepatic bile ducts, ampulla of vater, or biliary tract (1550 - 1569), esophageal varices with or without bleeding (4560 - 45621), acute and subacute necrosis of the liver (570), alcoholic fatty liver, hepatitis, cirrhosis, or other unspecified alcoholic liver damage (5710 - 5713), chronic hepatitis (57140 - 57149), nonalcoholic cirrhosis (5715), biliary cirrhosis (5716), nonalcoholic liver disease (5718 - 5719), liver abscess (5720), portal pyemia (5721), hepatic encephalopathy (5722), portal hypertension (5723), hepatorenal syndrome (5724), other sequelae of chronic liver disease (5728), chronic passive congestion of the liver (5730), unspecified viral hepatitis (5731), unspecified hepatitis (5733), hepatic infarction (5734), hepatopulmonary syndrome (5735), other or unspecified disorders of the liver (5738, 5739), portal vein thrombosis (452), hepatomegaly (7891), malignant or other ascites (78951, 78959), personal history of malignant neoplasm of the liver (V1007), history of liver transplant or liver transplant complications (V427, 99682).
[5] Emergency department visits for esophageal varices were indicated by the following ICD-9-CM codes: 4560 (esophageal varices with bleeding), 4561 (esophageal varices without bleeding), 45620 (esophageal varices in diseases classified elsewhere [cirrhosis or portal hypertension], with bleeding), and 45621 (esophageal varices in diseases classified elsewhere [cirrhosis or portal hypertension], without bleeding).
[6] Emergency department visits for hepatic encephalopathy were indicated by the following ICD-9-CM codes: 0700 (viral hepatitis A with hepatic coma), 07020 – 07023 (viral hepatitis B with hepatic coma [acute and chronic, with and without hepatitis delta]), 07040 – 07049 (other specified viral hepatitis with hepatic coma [acute hepatitis C, hepatitis D without hepatitis B, hepatitis E, chronic hepatitis C, or other]), 0706 (unspecified viral hepatitis with hepatic coma), 07071 (unspecified viral hepatitis C with hepatic coma), and 5722 (hepatic coma [hepatic encephalopathy, hepatocerebral intoxication, portal-systemic encephalopathy]).
[7] Emergency department visits for Hepatitis B Virus (HBV) were indicated by the following ICD-9-CM codes: 07020, 07021, 07022, 07023, 07030, 07031, 07032, 07033, or V0261.
[8] Emergency department visits for acute, chronic, or unspecified Hepatitis C Virus (HCV) were indicated by the following ICD-9-CM codes: 07041, 07044, 07051, 07054, 07059, 07070, 07071, or V0262.
[9] Emergency department visits for Human Immunodeficiency Virus (HIV) were indicated by the following ICD-9-CM codes: 042, 07953, 79571, or V08.
[10] Emergency department visits for cancers were indicated by the following ICD-9-CM codes: 1550, 1551, 1552, 1560, 1561, 1562, 1568, or 1569.
[11] Emergency department visits for opiate-related drug overdoses were indicated by the following ICD-9-CM codes: poisoning by opium, heroin, methadone, or other opiates or related narcotics (96500, 96501, 96502, or 96509), accidental poisoning by heroin, methadone, or other opiates and related narcotics (E8500, E8501, or E8502), or adverse effects attributable to the therapeutic use of heroin, methadone, or other opiates and related narcotics (E9350, E9351, or E9352).

Emergency Department Visits for Hepatitis C Virus (HCV) Infection

Descriptive characteristics of the 3,073 ED visits listing HCV as a diagnosis are presented in Table 33. Of these, HCV was the principal diagnosis in 65 (2.1%) ED visits. The majority of visits were among males and patients aged 50 – 54 years. Most patients were white race and non-hispanic ethnicity. Additionally, most ED visits were emergency-related and the majority of patients paid via a self-pay mechanism. The average visit cost was $2,653.

Table 33a. Descriptive Characteristics of Emergency Department Visits Documenting Diagnoses of Hepatitis C Virus (HCV) Infection — Arkansas, 2012

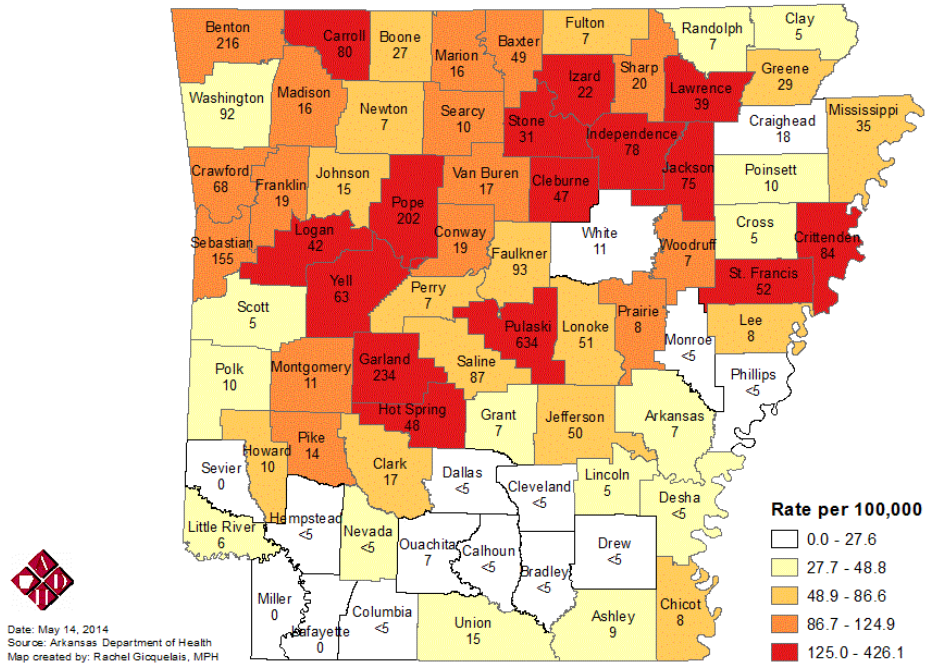
Characteristic		No.	%
Total		3,073	100.0
Sex			
	Male	1,628	53.0
	Female	1,445	47.0
Age (Years)			
	<20	20	0.7
	20 – 24	64	2.1
	25 – 29	210	6.8
	30 – 34	305	9.9
	35 – 39	309	10.1
	40 – 44	344	11.2
	45 – 49	499	16.2
	50 – 54	666	21.7
	55 – 59	381	12.4
	60 – 64	179	5.8
	65 – 69	51	1.7
	70 – 74	17	0.6
	75 – 79	15	0.5
	80 – 84	6	0.2
	85+	7	0.2
Race			
	American Indian or Alaskan Native	6	0.2
	Black	377	12.3
	White	2,638	85.8
	Other or Unknown	52	1.7
Ethnicity			
	Hispanic	35	1.1
	Non-Hispanic	3,038	98.9
Type of Admission			
	Emergency	2,430	79.1
	Urgent	199	6.5
	Elective	29	0.9
	Trauma	44	1.4
	Unknown	371	12.1

Payer Source			
	Self-Pay	986	32.1
	Worker's Compensation	7	0.2
	Medicare	822	26.8
	Medicaid	830	27.0
	Other Federal Programs, DHS, or Managed Assistance	22	0.7
	Private Insurance	287	9.3
	Free (Medically Indigent) or Unknown	10	0.3
	Other	109	3.6

Table 33b. Descriptive Characteristics of Emergency Department Visits Documenting Diagnoses of Hepatitis C Virus (HCV) Infection — Arkansas, 2012				
Variable	Mean (95% Confidence Interval)		Median	Number of Observations Missing Value
Patient Age (Years)	45.9	(45.5 – 46.3)	48	0
Visit Cost ($US)	2,653	(2,534 – 2,771)	1,651	0

County of residence for persons living in Arkansas with an address available in the emergency discharge data is shown in Figure 15. Rates of emergency department visits for HCV exceeded 200 per 100,000 persons in Independence, Lawrence, Garland, Stone, Yell, Carroll, Pope, and Jackson counties. Notably, a cluster of counties with high rates of emergency department visits occurred among counties in northeastern Arkansas.

Figure 15. Emergency Department Visits Documenting Diagnoses of Hepatitis C Virus Infection — Arkansas, 2012



Numbers represent hospitalizations per county.

Emergency Department Visits for Chronic Liver Diseases

Descriptive characteristics of the 4,974 ED visits listing one or more of several chronic liver diseases as a diagnosis are presented in Table 34. Of these, a chronic liver disease was the principal diagnosis in 696 (14.0%) ED visits. The majority of visits were among females and patients aged 50 – 54 years (average: 51.4). Most patients were white race and non-hispanic ethnicity. Additionally, most ED visits were emergency-related and the majority of patients used Medicare to pay the cost of their visit. The average visit cost was $4,298.

Table 34a. Descriptive Characteristics of Emergency Department Visits Documenting Diagnoses of Chronic Liver Diseases — Arkansas, 2012

Characteristic		No.	%
Total		4,974	100.0
Sex			
	Male	2,374	47.7
	Female	2,600	52.3
Age (Years)			
	<5	14	0.3
	5 – 9	7	0.1
	10 – 14	15	0.3
	15 – 19	53	1.1
	20 – 24	129	2.6
	25 – 29	243	4.9
	30 – 34	261	5.3
	35 – 39	363	7.3
	40 – 44	465	9.4
	45 – 49	589	11.8
	50 – 54	798	16.0
	55 – 59	649	13.1
	60 – 64	455	9.2
	65 – 69	328	6.6
	70 – 74	251	5.1
	75 – 79	145	2.9
	80 – 84	106	2.1
	85+	103	2.1
Race			
	American Indian or Alaskan Native	15	0.3
	Asian or Pacific Islander	24	0.5
	Black	644	13.0
	White	4,168	83.8
	Other	119	2.4
	Unknown	4	0.1
Ethnicity			
	Hispanic	111	2.2
	Non-Hispanic	4,860	97.7
	Unknown	3	0.1

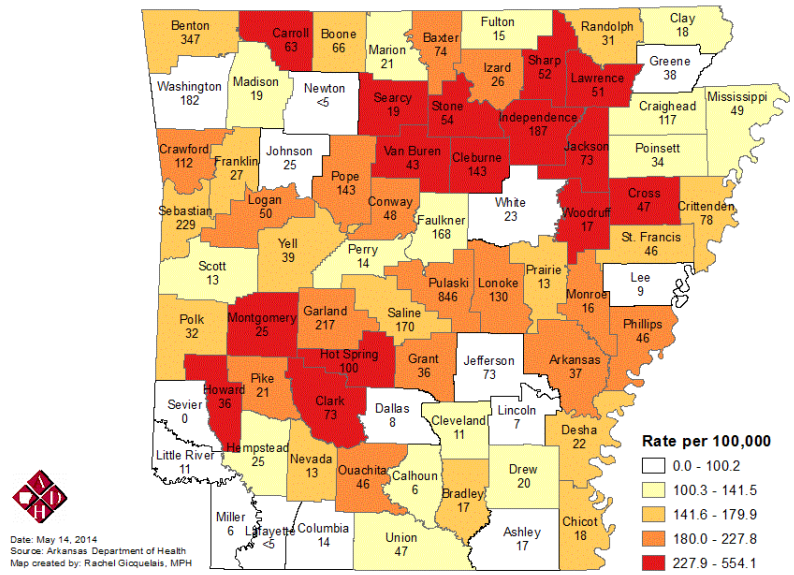
Type of Admission			
	Emergency	3,332	67.0
	Urgent	433	8.7
	Elective	86	1.7
	Trauma	21	0.4
	Unknown	1,102	22.2
Payer Source			
	Self-Pay	933	18.8
	Worker's Compensation	12	0.2
	Medicare	1,824	36.7
	Medicaid	831	16.7
	Other Federal Programs, DHS, or Managed Assistance	49	1.0
	Private Insurance	1,069	21.5
	Free (Medically Indigent)	0	0.0
	Other	252	5.1
	Unknown	4	0.1

Table 34b. Descriptive Characteristics of Emergency Department Visits Documenting Diagnoses of Chronic Liver Diseases — Arkansas, 2012

Variable	Mean (95% Confidence Interval)		Median	Number of Observations Missing Value
Patient Age (Years)	51.4	(50.9 – 51.8)	52	0
Visit Cost ($US)	4,298	(4,188 – 4,409)	3,055	0

Rates of emergency department visits for chronic liver diseases exceeded 300 per 100,000 persons in Sharp, Clark, Jackson, Stone, Independence, and Cleburne counties (Figure 16). Notably, a cluster of counties with high rates of emergency department visits occurred among counties in northeastern to north-central Arkansas.

Figure 16. Emergency Department Visits Documenting Diagnoses of Chronic Liver Diseases — Arkansas, 2012



Numbers represent hospitalizations per county.

Emergency Department Visits for Cirrhosis

Descriptive characteristics of the 1,328 ED visits listing cirrhosis as a diagnosis are presented in Table 35. Of these, cirrhosis was the principal diagnosis in 122 (9.2%) visits. The majority of visits were among males and patients aged 50 – 54 years (average: 54.2). Most patients were white race and non-hispanic ethnicity. Additionally, most ED visits were emergency-related and the majority of patients used Medicare to pay the cost of their visit. The average visit cost was $3,191.

Table 35a. Descriptive Characteristics of Emergency Department Visits Documenting Diagnoses of Cirrhosis — Arkansas, 2012

Characteristic		No.	%
Total		1,328	100.0
Sex			
	Male	711	53.5
	Female	617	46.5
Age (Years)			
	<25	10	0.8
	25 – 29	27	2.0
	30 – 34	33	2.5
	35 – 39	49	3.7
	40 – 44	115	8.7
	45 – 49	169	12.7
	50 – 54	335	25.2
	55 – 59	220	16.6
	60 – 64	140	10.5
	65 – 69	94	7.1
	70 – 74	64	4.8
	75 – 79	33	2.5
	80 – 84	21	1.6
	85+	18	1.4
Race			
	American Indian or Alaskan Native	10	0.8
	Asian or Pacific Islander	6	0.5
	Black	144	10.8
	White	1,139	85.8
	Other	28	2.1
	Unknown	1	0.1
Ethnicity			
	Hispanic	28	2.1
	Non-Hispanic	1,299	97.8
	Unknown	1	0.1
Type of Admission			
	Emergency	1,033	77.8
	Urgent	115	8.7
	Elective	32	2.4
	Trauma	6	0.5
	Unknown	142	10.7

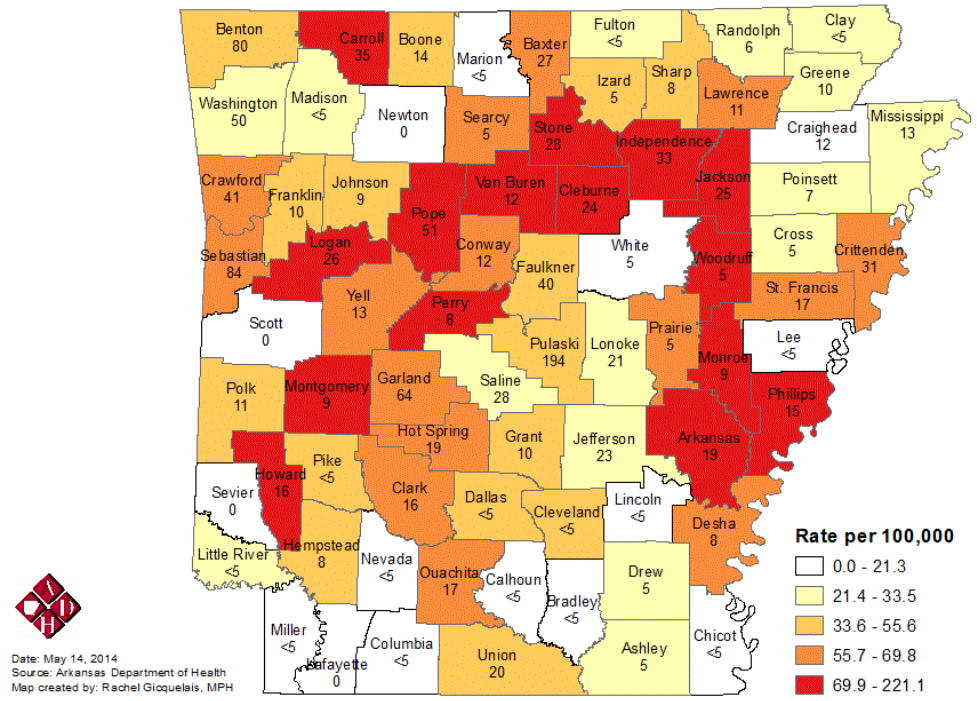
Payer Source			
	Self-Pay	201	15.1
	Worker's Compensation	2	0.2
	Medicare	574	43.2
	Medicaid	295	22.2
	Other Federal Programs, DHS, or Managed Assistance	9	0.7
	Private Insurance	189	14.2
	Other (including Worker's Compensation)	59	4.4
	Unknown	1	0.1

Table 35b. Descriptive Characteristics of Emergency Department Visits Documenting Diagnoses of Cirrhosis — Arkansas, 2012

Variable	Mean (95% Confidence Interval)		Median	Number of Observations Missing Value
Patient Age (Years)	54.2	(53.6 – 54.8)	53.5	0
Visit Cost ($US)	3,191	(3,022 – 3,359)	2,240	0

Rates of emergency department visits for cirrhosis exceeded 100 per 100,000 persons in Arkansas, Monroe, Howard, Logan, Carroll, Jackson, and Stone counties (Figure 17). Notably, a cluster of counties with high rates of emergency department visits occurred among counties in north-central Arkansas.

Figure 17. Emergency Department Visits Documenting Diagnoses of Cirrhosis — Arkansas, 2012



Numbers represent hospitalizations per county.

Liver and Intrahepatic Bile Duct Cancers

Liver and intrahepatic bile duct cancers are recorded by the Arkansas Central Cancer Registry. A detailed description of the data source, methods used in analyses, and limitations are included in Appendix A. The number of liver and intrahepatic bile duct cancers diagnosed among Arkansans each year and percentage with HBV or HCV are presented in Table 36 and Figure 18. Of note, the number of cases presented in Table 36 excludes veterans due to federal laws that restrict the use of veteran information, while the age-adjusted rate per 100,000 persons is inclusive of cases among veterans in Arkansas. Percentages of cases with HBV and HCV represent the proportion of cases among non-veterans with documented HBV or HCV in the cancer registry.

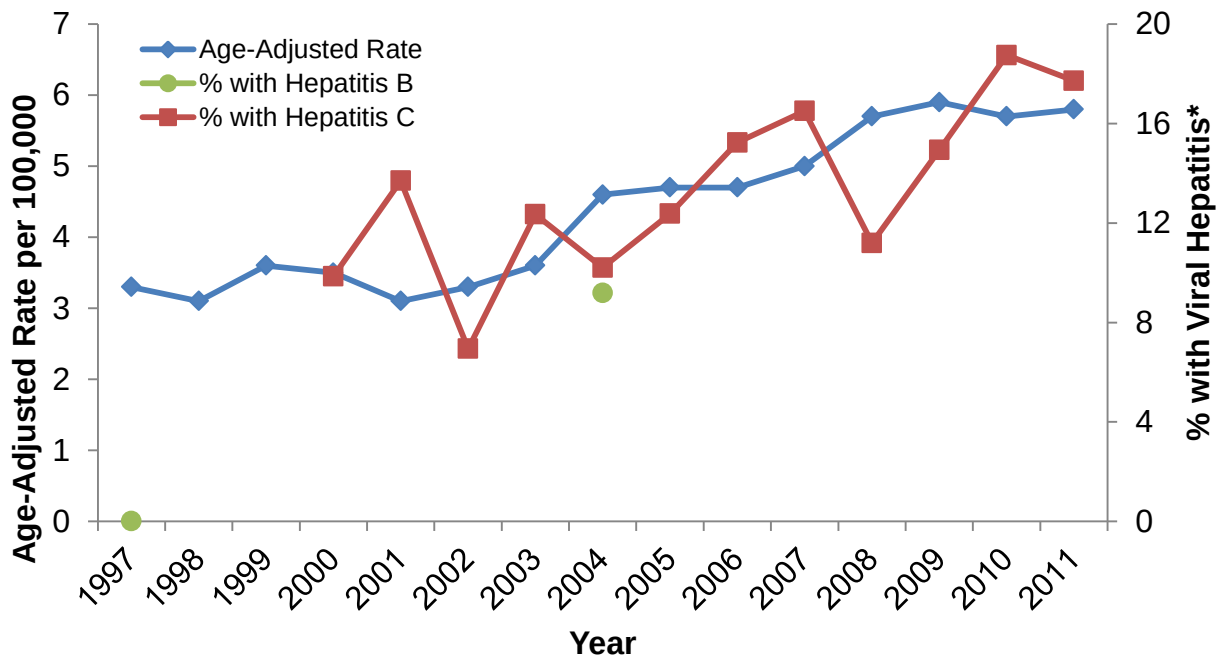
Linear regression of the age-adjusted rate of liver and intrahepatic bile duct cancers demonstrated an increase of 0.16 cancers per 100,000 persons per year (p-value<0.0001) when veterans were excluded (Table 36). Among all cases (including veterans), linear regression demonstrated an increase of 0.23 cases of liver and intrahepatic bile duct cancers per 100,000 persons per year. HBV and HCV status are not recorded in standard data fields in the cancer registry; however, HBV or HCV status is often recorded in text fields during the data abstraction process. From 1997 – 2011, the percentage of cases with HCV documented generally increased from year to year, with some variability, from <6.8% in 1997 to a maximum of 18.8% in 2010. Linear regression of the age-adjusted rate of liver and intrahepatic bile duct cancers documenting HCV demonstrated an increase of 0.05 cancers per 100,000 persons per year (p-value <0.0001). The number of cases with HBV; however, was notably lower than those with HCV and for many years, was lower than the reportable number of cases (≥5 cases). Notably, calculations of the number and percentage of cases with HBV and HCV status are likely underestimated here due to the inability to record HBV or HCV status in standard data fields, causing abstractors to record HBV or HCV status using several non-standardized methods in text fields and perhaps not always recording them during record abstraction. The trend, which suggests that the number of cases of liver and intrahepatic bile duct cancers is increasing, as is the percentage of cases with HCV, is likely representative of the overall trend even with the limitations in data.

Descriptive characteristics of the 1,505 persons with liver and intrahepatic bile duct cancers are presented in Table 37. Over two-thirds of cases were among males. The most common age group at diagnosis was 70 – 74 years while the average age was 64.7 years. Most patients were white race. Nearly one-third of patients had previously or were currently using alcohol and 43.0% were currently or had previously used tobacco products. Among 1,505 cases, 1,262 were documented as deceased in the cancer registry. The average age at death among persons who died was 66.4 years. Further, the average length of time between diagnosis and time of death was less than one year among deceased individuals (mean: 232.2 days, median: 91 days). Nationally, HCV infection is known to contribute to the development of half or more of all cases of hepatocellular carcinoma and survival from hepatocellular carcinoma is low[2].

Table 36. Liver and Intrahepatic Bile Duct Cancers — Arkansas, 1997 – 2011					
Year	Number of Cases	Age-Adjusted Rate per 100,000 (Excluding Veterans)	Age-Adjusted Rate per 100,000 (Including Veterans)[†]	Number (%) with Hepatitis B Virus (HBV)	Number (%) with Hepatitis C Virus (HCV)
1997	73	2.8	3.3	0 (0.0)	<5 (-)[§]
1998	66	2.4	3.1	<5 (-)[§]	<5 (-)[§]
1999	76	2.9	3.6	<5 (-)[§]	<5 (-)[§]
2000	71	2.6	3.5	<5 (-)[§]	7 (9.9)
2001	73	2.7	3.1	<5 (-)[§]	10 (13.7)
2002	72	2.7	3.3	<5 (-)[§]	5 (6.9)
2003	81	3.0	3.6	<5 (-)[§]	10 (12.3)
2004	98	3.3	4.6	9 (9.2)	10 (10.2)
2005	97	3.4	4.7	<5 (-)[§]	12 (12.4)
2006	105	3.5	4.7	<5 (-)[§]	16 (15.2)
2007	103	3.5	5.0	<5 (-)[§]	17 (16.5)
2008	134	4.4	5.7	<5 (-)[§]	15 (11.2)
2009	154	4.8	5.9	<5 (-)[§]	23 (14.9)
2010	144	4.5	5.7	<5 (-)[§]	27 (18.8)
2011	158	4.8	5.8	<5 (-)[§]	28 (17.7)
Total	1,505	N/A	N/A	43 (2.9)	189 (12.6)
Trend Statistics	N/A	ROC: 0.16 per 100,000 persons (p<0.0001)*	ROC: 0.23 per 100,000 persons (p<0.0001)*	PC: -0.0181 SC: -0.0269 CA: 0.4817 (None)	PC: 0.1214* SC: 0.1194* CA: <0.0001* (Increasing)

Abbreviations: CA: Cochran-Armitage Trend Test; CI: Confidence Interval; CLD: Chronic Liver Diseases; PC: Pearson Correlation Coefficient; ROC: Rate of Change; SC: Spearman Correlation Coefficient.
* Denotes statistically significant result at 95% confidence level (α ≤0.05).
[†] Denotes only column of data inclusive of cancer cases among veterans in Arkansas.
[§] Counts and percentages for events occurring at a frequency of <5 cases are suppressed.

Figure 18. Liver and Intrahepatic Bile Duct Cancers — Arkansas, 1997 – 2011



*Percentages with viral hepatitis were calculated among cancers with a primary site of the liver or intrahepatic bile duct among non-veteran Arkansans. Cases among veterans in Arkansas are included in age-adjusted rate calculations only. Data for cases occurring at a frequency of <5 are suppressed. Source: Arkansas Cancer Registry. Link: http://www.cancer-rates.info/ar/index.php.

Table 37a. Descriptive Characteristics of Persons with Liver and Intrahepatic Bile Duct Cancers — Arkansas, 1997 – 2011

Characteristic	No.	%
Total	1,505	100.0
Sex		
Male	1,022	67.9
Female	483	32.1
Age (Years)		
<19	20	1.3
20 – 24	7	0.5
25 – 29	8	0.5
30 – 34	11	0.7
35 – 39	20	1.3
40 – 44	28	1.9
45 – 49	81	5.4
50 – 54	168	11.2
55 – 59	181	12.0
60 – 64	182	12.1
65 – 69	185	12.3
70 – 74	205	13.6
75 – 79	188	12.5
80 – 84	115	7.6
85+	106	7.0

Race		
Asian or Pacific Islander	35	2.3
Black	189	12.6
White	1,266	84.1
Other (Including American Indian or Alaskan Native) or Unknown	15	1.0
Vital Status (as of Last Contact)		
Alive	243	16.2
Deceased	1,262	83.9
Family History of Cancer		
Yes	432	28.7
No	390	25.9
Unknown	683	45.4
Alcohol Use (at Diagnosis)		
No History of Alcohol Use	478	31.8
Current Use of Alcohol	267	17.7
Past History of Alcohol Use	184	12.2
Unknown	576	38.3
Tobacco Use History (at Diagnosis)		
Never Used	351	23.3
Cigarette Smoker	340	22.6
Cigar/Pipe Smoker	8	0.5
Snuff/Chew/Smokeless	14	0.9
Combination Use	5	0.3
Previous Use	281	18.7
Unknown	506	33.6

Table 37b. Descriptive Characteristics of Persons with Liver and Intrahepatic Bile Duct Cancers — Arkansas, 1997 – 2011

Variable	Mean (95% Confidence Interval)		Median	Number of Cases Included in Calculation
Patient Age at Diagnosis (Years)	64.7	(64.0 – 65.5)	66	1,505
Patient's Age at Death (Years)	66.4	(65.6 – 67.2)	68	1,261*
Length of Time from Diagnosis to Death (Days)	232.2	(211.1 – 253.3)	91	1,261*

*One patient was documented as deceased; however, the date of death was unknown.

Underlying causes of death listed for 1% or more of deaths among decedents with liver or intrahepatic bile duct cancer are listed in Table 38. Overall, 1,262 persons were listed as deceased in the cancer registry. The underlying cause of death was known for 1,114 persons, of whom the cause was related liver or bile duct cancer, illness, or dysfunction or viral hepatitis among 915 persons. Therefore, at least 72.5% of deaths among persons known to have liver or intrahepatic bile duct cancers were caused by conditions related to the liver or bile duct.

Table 38. Underlying Causes of Death Among Decedents with Liver and Intrahepatic Bile Duct Cancers — Arkansas, 1997 – 2011			
Underlying Cause	ICD-10 or ICD-9 Code	Number of Deaths	% of Total Deaths
Malignant neoplasm of liver, not specified as primary or secondary	C229	425	33.7
Liver cell carcinoma	C220	267	21.2
Death certificate unavailable	7777	83	6.6
Intrahepatic bile duct carcinoma	C221	70	5.5
State death certificate available but underlying cause not coded	7797	65	5.2
Primary malignant neoplasm of the liver	1550	35	2.8
Malignant neoplasm of unspecified part of bronchus or lung	C349	26	2.1
Secondary malignant neoplasm of the liver and intrahepatic bile duct	C787	26	2.1
Malignant neoplasm without specification of site	C80	26	2.1
Malignant neoplasm of the liver (not specified as primary or secondary)	1552	19	1.5
Unspecified malignant neoplasm of the pancreas	C259	17	1.3
Malignant neoplasm of the extrahepatic bile duct	C240	15	1.2
Other and unspecified cirrhosis of liver	K746	12	1.0
Total Deaths Attributable to Liver-Related or Bile Duct Cancer or Illness*	See Footnotes*	915	72.5
Total Deaths	N/A	1,262	100.0
*Persons categorized as having a liver or bile duct related cause of death included persons with the following ICD-9 codes: 1550, 1551, 1552, and 5715 and persons with the following ICD-10 codes: B169, B171, B181, B182, C220, C221, C222, C223, C229, C240, C249, C787, D376, K703, K729, K741, K746, K759, and K769.			

Liver Failure Requiring Transplant

HCV infection is the leading reason for liver transplant surgery in the United States[38]. In Arkansas, the University of Arkansas for Medical Sciences began performing liver transplant surgeries in 2005. Inpatient hospitalization procedure codes were queried for inpatient hospitalizations involving liver transplants among Arkansans. The number of procedures performed on Arkansans ranged from 14 in 2005 to a maximum of 29 in 2009 (Table 39, Figure

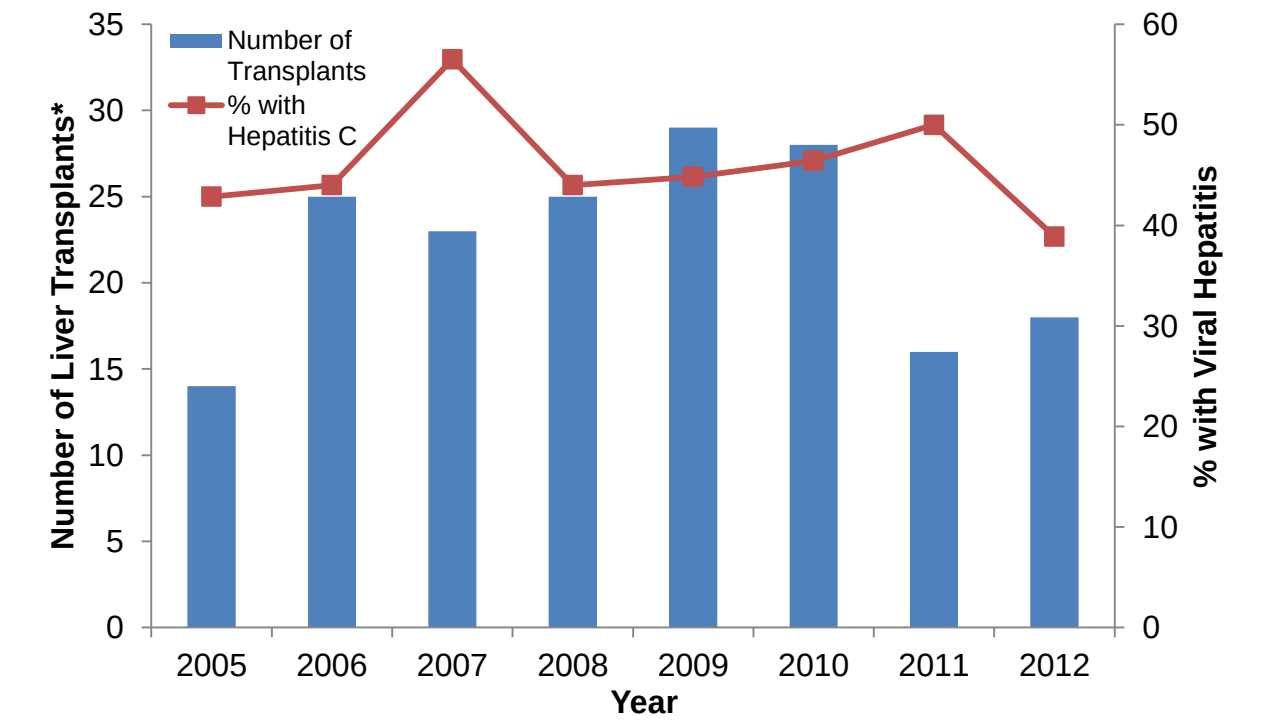
19). The proportion of liver transplants with HCV documented in the inpatient hospitalization record corresponding to their liver transplant surgery ranged from 38.9% in 2012 to a maximum of 56.5% in 2007. The proportion of surgeries documenting HBV infection was substantially lower, with all years documenting HBV infection in less than 5 transplant surgeries per year for a total of 11 surgeries.

Table 39. Number of Liver Transplant Surgeries and Infection with HBV or HCV — Arkansas, 2005 – 2012

Year	Number of Liver Transplants	Number (%) with HBV	Number (%) with HCV
2005	14	<5 (*)	6 (42.9)
2006	25	<5 (*)	11 (44.0)
2007	23	<5 (*)	13 (56.5)
2008	25	<5 (*)	11 (44.0)
2009	29	<5 (*)	13 (44.8)
2010	28	<5 (*)	13 (46.4)
2011	16	<5 (*)	8 (50.0)
2012	18	<5 (*)	7 (38.9)
Total	178	11 (6.2)	82 (46.1)

*Counts and percentages for events occurring at a frequency of <5 cases are suppressed.
Liver Transplants include inpatient hospitalizations with ICD9 procedure codes 5051 (auxiliary liver transplant) or 5059 (other transplant of liver).

Figure 19. Liver Transplants — Arkansas, 2005 – 2012



*Liver Transplants include inpatient hospitalizations with ICD9 procedure codes 5051 (auxiliary liver transplant) or 5059 (other transplant of liver).

MORTALITY

HCV is recognized as a rapidly growing cause of mortality in the US. Nationwide, the number of deaths caused by HCV per year has surpassed the number of deaths caused by HIV per year[31]. Approximately 1% – 5% of people with HCV infection will die from liver disease occurring as a result of HCV[2].

Data from deaths occurring among residents of the state of Arkansas from 1999 to 2012 were queried to determine the number and rate of death attributable to HCV. Methods for analysis were adapted from Ly et al[31]. In all analyses presented, the multiple causes of death, which include the immediate cause (the final disease or condition resulting in death), the underlying cause (disease or injury that initiated the events resulting in death), and up to two other causes within the chain of events leading to death listed in Part I of the death certificate along with any significant conditions contributing to death listed in Part II of the death certificate are referred to all together as the cause or contributing condition to death. A description of the data, methods used in analysis, and limitations are included in Appendix A.

During 1999 – 2012, there were a total of 398,123 deaths documented among Arkansas residents (Table 40). Most decedents were male and aged 85 years or more at the time of death (mean age = 71.5 years). The number of deaths per year was relatively constant over the time period (range: 27,536 – 29,841). Most decedents were of white race and non-hispanic ethnicity, died while hospitalized, and completed a high school education. Approximately 1% of decedents were born outside of the United States and nearly one-quarter of decedents were veterans who served in the United States military.

Table 40a. Descriptive Characteristics of Decedents — Arkansas, 1999 – 2012

Characteristic	No.	%
Total	398,123	100.0
Sex		
Male	200,401	50.3
Female	197,707	49.7
Unknown	15	<0.1
Age at Death (Years)		
<5	5,327	1.3
5 – 9	523	0.1
10 – 14	655	0.2
15 – 19	2,353	0.6
20 – 24	3,437	0.9
25 – 29	3,573	0.9
30 – 34	4,090	1.0
35 – 39	5,454	1.4
40 – 44	8,382	2.1
45 – 49	12,532	3.2
50 – 54	17,359	4.4
55 – 59	22,060	5.5
60 – 64	27,350	6.9
65 – 69	32,957	8.3
70 – 74	39,930	10.0

	75 – 79	49,304	12.4
	80 – 84	56,783	14.3
	85+	106,040	26.6
	Unknown	14	<0.1
Year of Death			
	1999	27,936	7.0
	2000	28,189	7.1
	2001	27,704	7.0
	2002	28,460	7.2
	2003	27,871	7.0
	2004	27,536	6.9
	2005	28,042	7.0
	2006	27,876	7.0
	2007	28,190	7.1
	2008	29,299	7.4
	2009	28,698	7.2
	2010	28,841	7.2
	2011	29,640	7.4
	2012	29,841	7.5
Race			
	American Indian or Alaskan Native	755	0.2
	Asian or Pacific Islander	865	0.2
	Black	53,195	13.4
	White	336,116	84.4
	Other	606	0.2
	Unknown	6,586	1.7
Ethnicity			
	Hispanic	3,027	0.8
	Non-Hispanic	394,915	99.2
	Unknown	181	0.1
Location of Death			
	Inpatient	162,312	40.8
	Emergency Room/Outpatient	31,827	8.0
	Dead on Arrival	2,325	0.6
	Nursing Home	68,346	17.2
	Home or Residence	102,588	25.8
	Hospice	13,862	3.5
	Other	16,496	4.1
	Unknown	367	0.1
Education Level			
	8th Grade or Less	95,574	24.0
	9th Grade through 11th Grade, No Diploma	59,739	15.0
	High School Completed	144,326	36.3
	College Credit or Beyond	85,874	21.6
	Unknown	12,610	3.2
Born Outside of the United States			
	Yes	5,690	1.4
	No	390,647	98.1
	Unknown	1,786	0.5

Veteran		
Yes	94,970	23.9
No	294,113	73.9
Unknown	9,040	2.3

Table 40b. Descriptive Characteristics of Decedents — Arkansas, 1999 – 2012				
Variable	Mean (95% Confidence Interval)		Median	Number of Observations Missing Value
Age at Death (Years)	71.5	(71.48 – 71.59)	76	14

Mortality Related to HCV Infection

Table 41 shows the number of deaths documenting HCV infection as a cause or contributing condition to death. The number of deaths attributable to HCV ranged from a minimum of 56 in 1999 to a maximum of 160 in 2011. Least squares linear regression models of the age-adjusted mortality rates per 100,000 Arkansans demonstrated a statistically significant increase of 0.15 deaths per 100,000 Arkansans per year (p-value <0.0001). A recently released study by Mahajan et al.[39] showed that HCV is often excluded as a cause or contributing condition to death on death certificates despite its contribution to the events leading to death. Therefore, the figures presented here should be interpreted as the minimum number of deaths related to HCV.

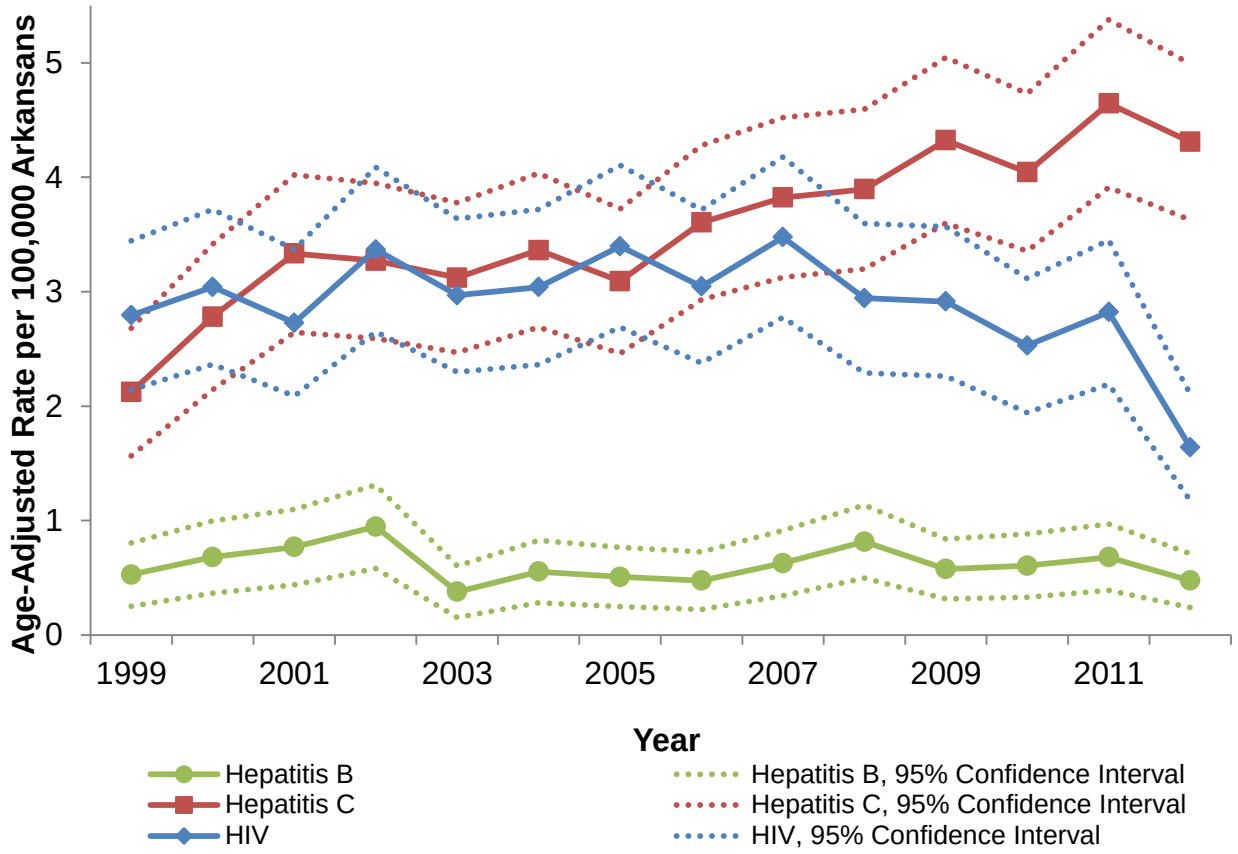
Figure 20 depicts the age-adjusted mortality rate for HBV, HCV, and HIV. The mortality rate attributable to HCV infection increased from 1999 to 2012, while the mortality rate attributable to HIV decreased. In a study by Ly et al.[31] using this methodology for all deaths occurring in the United States, the mortality rate of HCV surpassed the mortality rate of HIV in 2007. Figure 20 shows that the mortality rate of HCV in Arkansas surpassed the mortality rate due to HIV in 2001, 2003, 2004, and 2006 – 2012. Interestingly, there was not a statistically significant difference in the mortality rate of HCV and the mortality rate of HIV until after 2009. Since 2009, the mortality rate attributable to HIV has remained lower than the mortality rate attributable to HCV.

During 1999 – 2012, there were a total of 1,538 deaths documenting HCV as a cause or contributing condition to death among Arkansas residents (Table 42). Most decedents were male and aged 50 – 54 years at the time of death (mean age = 55.9 years). Most decedents were of white race and non-hispanic ethnicity, died while hospitalized, and completed a high school education. Nearly 2% of decedents were born outside of the United States and more than one-quarter of decedents were veterans who served in the United States military.

Table 41. Deaths Documenting Hepatitis C Virus (HCV) Infection as a Cause or Contributing Condition to Death — Arkansas, 1999 – 2012			
Year	Number (%) of Deaths Documenting HCV	Crude Mortality Rate per 100,000 Arkansans	Age-Adjusted Mortality Rate per 100,000 Arkansans (95% CI)
1999	56 (0.2)	2.1	2.1 (1.6 – 2.7)
2000	74 (0.3)	2.8	2.8 (2.2 – 3.4)
2001	91 (0.3)	3.4	3.3 (2.7 – 4.0)
2002	90 (0.3)	3.3	3.3 (2.6 – 4.0)
2003	88 (0.3)	3.2	3.1 (2.5 – 3.8)
2004	97 (0.4)	3.5	3.4 (2.7 – 4.0)
2005	93 (0.3)	3.3	3.1 (2.5 – 3.7)
2006	112 (0.4)	4.0	3.6 (2.9 – 4.3)
2007	118 (0.4)	4.1	3.8 (3.1 – 4.5)
2008	123 (0.4)	4.3	3.9 (3.2 – 4.6)
2009	141 (0.5)	4.9	4.3 (3.6 – 5.1)
2010	137 0.5)	4.7	4.0 (3.4 – 4.7)
2011	160 (0.5)	5.4	4.7 (3.9 – 5.4)
2012	158 (0.5)	5.4	4.3 (3.6 – 5.0)
Total	1,538 (0.4)	N/A	N/A
Trend Statistics	PC: 0.0012* SC: 0.0153* CA: <0.0001* (Increasing)	N/A	ROC: 0.15 per 100,000 Persons (p-value: <0.0001)*

Abbreviations: CA: Cochran-Armitage Trend Test; CI: Confidence Interval; HCV: Hepatitis C Virus; PC: Pearson Correlation Coefficient; ROC: Rate of Change; SC: Spearman Correlation Coefficient.
* Denotes statistically significant result at 95% confidence level ($\alpha \leq 0.05$).
Death certificates indicative of hepatitis C infection included certificates with ICD-10 codes B171 or B182.

Figure 20. Deaths Documenting Hepatitis B, Hepatitis C, or HIV as a Cause or Contributing Condition to Death — Arkansas, 1999 – 2012



Deaths certificates indicative of hepatitis B virus infection included death certificates with ICD-10 codes B160, B161, B162, B169, B170, B180, or B181. Death certificates indicative of hepatitis C infection included certificates with ICD-10 codes B171 or B182. Deaths certificates indicative of Human Immunodeficiency Virus (HIV) infection included certificates with ICD-10 codes B200 - B24 and R75.

Table 42a. Descriptive Characteristics of Decedents with Hepatitis C Virus (HCV) Infection Documented as a Cause or Contributing Condition to Death – Arkansas, 1999 – 2012

Characteristic		No.	%
Total		1,538	100.0
Sex			
	Male	1,102	71.7
	Female	436	28.4
Age at Death (Years)			
	<5	0	0.0
	5 – 9	0	0.0
	10 – 14	0	0.0
	15 – 19	1	0.1
	20 – 24	5	0.3
	25 – 29	4	0.3
	30 – 34	11	0.7
	35 – 39	30	2.0

	40 – 44	115	7.5
	45 – 49	261	17.0
	50 – 54	348	22.6
	55 – 59	303	19.7
	60 – 64	183	11.9
	65 – 69	94	6.1
	70 – 74	75	4.9
	75 – 79	57	3.7
	80 – 84	28	1.8
	85+	23	1.5
Race			
	Asian or Pacific Islander	7	0.5
	Black	237	15.4
	White	1,243	80.8
	Other (Including American Indian or Alaskan Native)	5	0.3
	Unknown	46	3.0
Ethnicity			
	Hispanic	18	1.2
	Non-Hispanic	1,517	98.6
	Unknown	3	0.2
Location of Death			
	Inpatient	822	53.5
	Emergency Room/Outpatient	76	4.9
	Dead on Arrival	5	0.3
	Nursing Home	119	7.7
	Home or Residence	364	23.7
	Hospice	98	6.4
	Other	54	3.5
Education Level			
	8th Grade or Less	132	8.6
	9th Grade through 11th Grade, No Diploma	285	18.5
	High School Completed	686	44.6
	College Credit or Beyond	371	24.1
	Unknown	64	4.2
Born Outside of the United States			
	Yes	29	1.9
	No	1,496	97.3
	Unknown	13	0.9
Veteran			
	Yes	432	28.1
	No	1,021	66.4
	Unknown	85	5.5

Table 42b. Descriptive Characteristics of Decedents with Hepatitis C Virus (HCV) Infection Documented as a Cause or Contributing Condition to Death — Arkansas, 1999 – 2012				
Variable	Mean (95% Confidence Interval)		Median	Number of Observations Missing Value
Age at Death (Years)	55.9	(55.3 – 56.4)	54	0

Table 43 shows other causes or contributing conditions to death among persons dying of HCV in Arkansas. Diseases of the liver were documented in nearly two-thirds of deaths among persons dying of HCV in Arkansas.

Table 43. Causes and Contributing Conditions to Death Among Decedents with Hepatitis C Virus (HCV) Infection Documented as a Cause or Contributing Condition to Death — Arkansas, 1999 – 2012		
Cause or Contributing Condition to Death	Number of Deaths	% of Total HCV-Related Deaths
Liver Diseases[1]	983	63.9
Malignant Neoplasms of the Liver and Intrahepatic Bile Duct[2]	200	13.0
HBV[3]	77	5.0
HIV[4]	39	2.5

[1] ICD-10 codes for liver diseases include codes for malignant neoplasms of the liver and intrahepatic bile ducts (C220 – C229), portal vein thrombosis (I81), esophageal varices with or without bleeding (I850, I859), alcoholic liver disease, toxic liver disease, hepatic failure, chronic hepatitis, liver fibrosis or cirrhosis, other inflammatory liver diseases, and other diseases of the liver (K70 – K76), hepatomegaly (R160, R162), and ascites (R18).
[2] ICD-10 codes for malignant neoplasms of the liver and intrahepatic bile duct include codes C220, C221, C222, C223, C24, C227, and C229.
[3] ICD-10 codes for Hepatitis B Virus (HBV) infection include codes for acute or chronic HBV (B160, B161, B162, B169, B170, B180, and B181).
[4] ICD-10 codes for Human Immunodeficiency Virus (HIV) infection include codes B20 – B24 and R75.

Underlying causes of death were queried for all 1,538 mortality records documenting HCV. The underlying cause is describable as the condition that most likely caused the succession of events leading to death. Aside from HCV being listed as the underlying cause of death, persons dying with HCV were most likely to die from malignant neoplasms of the liver or liver cell carcinoma, cirrhosis, or HBV (Table 44).

Table 44. Underlying Causes of Death Among Decedents with Hepatitis C Virus (HCV) Infection Documented as a Cause or Contributing Condition to Death — Arkansas, 1999 – 2012			
Underlying Cause	ICD-10 Code	Number of Deaths	% of Total HCV Related Deaths
Chronic viral hepatitis C	B182	435	28.3
Acute hepatitis C	B171	218	14.2
Malignant neoplasm of liver, not specified as primary or secondary	C229	93	6.1

Liver cell carcinoma	C220	83	5.4
Other and unspecified cirrhosis of liver	K746	71	4.6
Alcoholic cirrhosis of liver	K703	64	4.2
Acute hepatitis B without delta-agent and without hepatic coma	B169	29	1.9
ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction	I219	29	1.9
Atherosclerotic heart disease of native coronary artery	I251	25	1.6
sepsis NOS	A419	24	1.6
Malignant neoplasm of unspecified part of bronchus or lung	C349	24	1.6
Chronic obstructive pulmonary disease, unspecified	J449	22	1.4
Unspecified diabetes mellitus without (mention of) complication	E149	20	1.3
HIV disease resulting in other viral infections	B203	15	1.0
HIV disease resulting in multiple infections	B207	10	0.7
Malignant neoplasm without specification of site	C80	10	0.7
Alcoholic liver disease, unspecified	K709	10	0.7

Mortality Related to Liver Diseases

Causes or contributing conditions to death listed on death certificates were queried for a variety of liver diseases, including those documented by the following ICD-10 mortality codes: C220 – C229 (malignant neoplasms of the liver and intrahepatic bile ducts), I81 (portal vein thrombosis), I850 and I859 (esophageal varices), K70 – K76 (alcoholic liver disease [fatty liver, hepatitis, fibrosis, sclerosis, cirrhosis, hepatic failure, or unspecified liver disease], toxic liver disease, hepatic failure, chronic hepatitis, fibrosis or cirrhosis of the liver or biliary tract, inflammatory liver diseases [abscess of the liver, phlebitis of the portal vein, nonspecific reactive hepatitis, granulomatous hepatitis, autoimmune hepatitis, or other inflammatory liver diseases], or other diseases of the liver [fatty change of the liver, chronic pass congestion of the liver, central hemorrhagic liver necrosis, liver infarction, peliosis hepatitis, hepatic veno-occlusive disease, portal hypertension, hepatorenal syndrome, or other diseases of the liver]), R160 and R162 (hepatomegaly), and R18 (ascites).

From 1999 – 2012, 12,292 mortality records listed at least one liver disease as a cause or contributing condition to death (Table 45). There was a statistically significant increasing trend in

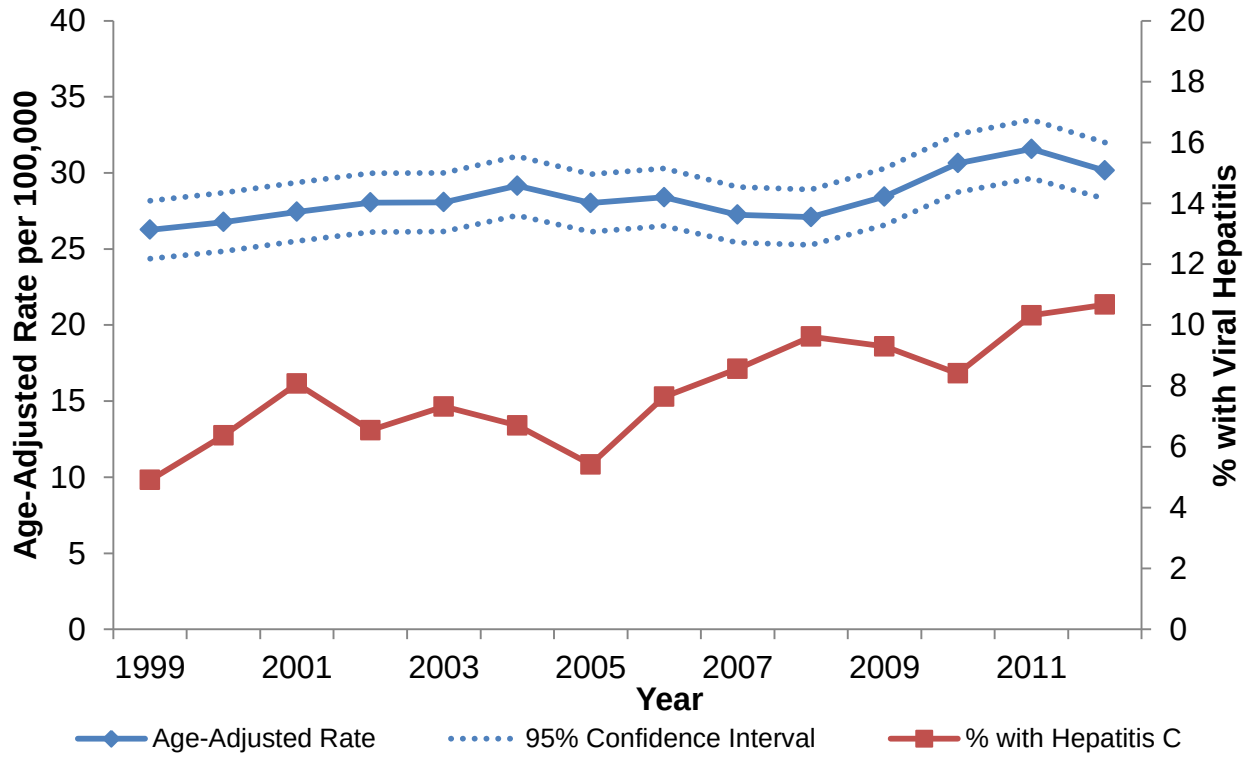
both the proportion of liver diseases listed as a cause of death per year (Cochran-Armitage trend test p-value: <0.0001, increasing trend) and the proportion of deaths also mentioning HCV as a cause or contributing condition to death (Cochran-Armitage trend test p-value: <0.0001, increasing trend). Age-adjusted rates and percentages of mortality records listing HCV as a cause or contributing condition to death are depicted in Figure 21. Least squares linear regression of the age-adjusted mortality rates attributable to liver diseases demonstrated an increase of 0.3 deaths per 100,000 Arkansans per year (p-value = 0.002).

Table 45. Deaths Documenting Liver Diseases as a Cause or Contributing to Death — Arkansas, 1999 – 2012

Year	Number (%) of Deaths Documenting Liver Diseases[1]	Crude Mortality Rate per 100,000 Arkansans	Age-Adjusted Rate per 100,000 Arkansans (95% CI)	Number (%) with HCV Infection
1999	733 (2.6)	27.6	26.3 (24.4 – 28.2)	36 (4.9)
2000	754 (2.7)	28.2	26.8 (24.9 – 28.7)	48 (6.4)
2001	781 (2.8)	29.0	27.4 (25.5 – 29.4)	63 (8.1)
2002	811 (2.9)	30.0	28.1 (26.1 – 30.0)	53 (6.5)
2003	820 (2.9)	30.1	28.1 (26.1 – 30.0)	60 (7.3)
2004	866 (3.1)	31.5	29.2 (27.2 – 31.1)	58 (6.7)
2005	849 (3.0)	30.5	28.0 (26.1 – 29.9)	46 (5.4)
2006	877 (3.2)	31.1	28.4 (26.5 – 30.3)	67 (7.6)
2007	864 (3.1)	30.3	27.2 (25.4 – 29.1)	74 (8.6)
2008	863 (3.0)	30.0	27.1 (25.3 – 28.9)	83 (9.6)
2009	925 (3.2)	31.9	28.4 (26.6 – 30.3)	86 (9.3)
2010	1,023 (3.6)	35.1	30.6 (28.7 – 32.5)	86 (8.4)
2011	1,076 (3.6)	36.6	31.6 (29.7 – 33.5)	111 (10.3)
2012	1,050 (3.5)	35.6	30.2 (28.3 – 32.0)	112 (10.7)
Total	12,292 (3.1)	N/A	N/A	983 (8.0)
Trend Statistics	PC: 0.0161* SC: 0.0161* CA: <0.0001* (Increasing)	N/A	ROC: 0.3 per 100,000 persons (p=0.002)*	PC: 0.0532* SC: 0.0535* CA: <0.0001* (Increasing)

Abbreviations: CA: Cochran-Armitage Trend Test; CI: Confidence Interval; HCV: Hepatitis C Virus; PC: Pearson Correlation Coefficient; ROC: Rate of Change; SC: Spearman Correlation Coefficient.
* Denotes statistically significant result at 95% confidence level (α ≤0.05).
[1] ICD-10 codes for liver diseases include codes for malignant neoplasms of the liver and intrahepatic bile ducts (C220 – C229), portal vein thrombosis (I81), esophageal varices with or without bleeding (I850, I859), alcoholic liver disease, toxic liver disease, hepatic failure, chronic hepatitis, liver fibrosis or cirrhosis, other inflammatory liver diseases, and other diseases of the liver (K70 – K76), hepatomegaly (R160, R162), and ascites (R18).

Figure 21. Deaths Documenting Liver Diseases as a Cause or Contributing Condition to Death — Arkansas, 1999 – 2012



Death certificates indicative of liver diseases include death certificates listing ICD-10 codes for malignant neoplasms of the liver and intrahepatic bile ducts (C220 – C229), portal vein thrombosis (I81), esophageal varices with or without bleeding (I850, I859), alcoholic liver disease, toxic liver disease, hepatic failure, chronic hepatitis, liver fibrosis or cirrhosis, other inflammatory liver diseases, and other diseases of the liver (K70 – K76), hepatomegaly (R160, R162), and ascites (R18).Death certificates indicative of HCV infection included certificates with ICD-10 codes B171 or B182.

Descriptive characteristics of the 12,292 deaths documenting liver diseases as a cause or contributing condition to death among Arkansas residents (Table 46). Most decedents were male and aged 55 – 59 years at the time of death (mean age = 62.9 years). Most decedents were of white race and non-hispanic ethnicity, died while hospitalized, and completed a high school education. More than 2% of decedents were born outside of the United States and approximately one-quarter of decedents were veterans who served in the United States military.

Table 46a. Descriptive Characteristics of Decedents with Liver Diseases Listed as a Cause or Contributing Cause to Death — Arkansas, 1999 – 2012

Characteristic	No.	%
Total	12,292	100.0
Sex		
Male	7,579	61.7
Female	4,712	38.3
Unknown	1	<0.1
Age (Years)		
<5	74	0.6
5 – 14	10	0.1

	15 – 19	19	0.2
	20 – 24	27	0.2
	25 – 29	54	0.4
	30 – 34	126	1.0
	35 – 39	230	1.9
	40 – 44	520	4.2
	45 – 49	1,064	8.7
	50 – 54	1,510	12.3
	55 – 59	1,628	13.2
	60 – 64	1,498	12.2
	65 – 69	1,338	10.9
	70 – 74	1,274	10.4
	75 – 79	1,186	9.7
	80 – 84	871	7.1
	85+	863	7.0
Race			
	American Indian or Alaskan Native	43	0.4
	Asian or Pacific Islander	63	0.5
	Black	1,524	12.4
	White	10,358	84.3
	Other	34	0.3
	Unknown	270	2.2
Ethnicity			
	Hispanic	145	1.2
	Non-Hispanic	12,139	98.8
	Unknown	8	<0.1
Location of Death			
	Inpatient	6,670	54.3
	Emergency Room/Outpatient	356	2.9
	Dead on Arrival	23	0.2
	Nursing Home	1,104	9.0
	Home or Residence	3,221	26.2
	Hospice	669	5.4
	Other	243	2.0
	Unknown	6	0.1
Education Level			
	8th Grade or Less	1,918	15.6
	9th Grade through 11th Grade, No Diploma	1,956	15.9
	High School Completed	4,996	40.6
	College Credit or Beyond	3,085	25.1
	Unknown	337	2.7
Born Outside of the United States			
	Yes	256	2.1
	No	11,965	97.3
	Unknown	71	0.6
Veteran			
	Yes	3,157	25.7
	No	8,694	70.7
	Unknown	441	3.6

Table 46b. Descriptive Characteristics of Decedents with Liver Diseases Listed as a Cause or Contributing Cause to Death — Arkansas, 1999 – 2012				
Variable	Mean (95% Confidence Interval)		Median	Number of Observations Missing Value
Age at Death (Years)	62.9	(62.6 – 63.1)	62	0

POPULATIONS DISPROPORTIONATELY AFFECTED BY VIRAL HEPATITIS

Incarcerated Arkansans

Incarcerated persons are known to be disproportionately affected by viral hepatitis. Varan et al. estimated that 17.4% (range: 9.6% – 41.1%) of persons living in state correctional facilities in 2006 had HCV infection based on data from 12 states[6].

During 2013, all laboratory reports received from the Arkansas Department of Corrections or Federal Correctional Facilities in Arkansas were electronically recorded in NEDSS. Although some cases may have gone unreported, HCV surveillance data from 2013 captured 1,943 persons who tested positive for HCV antibodies or HCV ribonucleic acid while incarcerated. Descriptive characteristics of these persons are shown in Table 47. Calculation of the prevalence of HCV in Arkansas state correctional facilities is not possible using this data as only positive laboratory results are reported. The majority of cases were males and aged 30 – 34 years at the time of testing. Race is not consistently reported, but the majority of cases with a known race were white. Additionally, 31 individuals were coinfected with HIV as they were documented in the Arkansas Department of Health's electronic registry, the enhanced HIV/AIDS Reporting System (eHARS). Risk information is unavailable for most cases as case investigation only occurs for persons aged <30 years at the time of report. A summary of risk factors among all persons aged <30 years can be found in Tables 4 – 6.

Table 47. Characteristics of Persons Incarcerated at the Time of Hepatitis C Virus (HCV) Testing and Reported to Public Health Surveillance — Arkansas, 2013		
	Number of Cases	%
Total	1,943	100.0
Age (Years)		
18 – 19	5	0.3
20 – 24	115	5.9
25 – 29	258	13.3
30 – 34	345	17.8
35 – 39	295	15.2
40 – 44	265	13.6
45 – 49	252	13.0
50 – 54	239	12.3
55 – 59	120	6.2
60 – 64	32	1.7
65+	17	0.9

Sex		
Female	450	23.2
Male	1,493	76.8
Race		
American Indian or Alaskan Native	6	0.3
Black	120	6.2
White	874	45.0
Multi-Racial	5	0.3
Other or Unknown	938	48.3
Diagnosed with Human Immunodeficiency Virus (HIV) Infection		
Yes	31	1.6
No	281	14.5
Unknown	1,631	83.9
Ever Injected Drugs		
Yes	258	13.3
No	40	2.1
Unknown	1,645	84.7

In addition to surveillance data collected by ADH, the Arkansas Department of Corrections tracks HCV diagnoses and treatments. The Health Services Report presents an overview of services provided in the Arkansas Department of Corrections (ADC) and the Arkansas Department of Community Corrections (ACC)[40]. In 2012, ADC and ACC facilities had an average monthly inmate population of 14,266 persons. A total of 3,721 chronic care clinic encounters among 1,130 enrollees were documented in 2012 for conditions including hepatitis A, B, and C and chronic liver failure[40]. Additionally, at least 375 new HCV cases were diagnosed by ADC or ACC in 2012[40]. By comparison, there were only 328 chronic care clinic encounters among 97 enrollees for HIV in 2012[40].

Veterans

Veterans are disproportionately affected by viral hepatitis compared with the civilian population. The prevalence of current HCV infection among veterans in the year 2011 was estimated to be 6.2%, compared to just 1.0% nationally during the years 2003 – 2010[5,41]. Additionally, 8.4% of veterans have HCV antibodies in their blood, demonstrating past or present infection[41]. While prevalence among the overall veteran population was higher than prevalence of HCV in the civilian population, prevalence among veterans born 1945 – 1965 was further elevated at 10.3%, with 13.5% having past or present HCV infection[41]. Studies of HCV prevalence among racial and ethnic groups demonstrated that 17.2% of persons born 1945 – 1965 of black race had a current HCV infection in 2011 (20.5% with past or present infection) and that 11.7% of persons born 1945 – 1965 of hispanic ethnicity had a current HCV infection in 2011 (17.7% with past or present infection)[41]. The prevalence of current and past or present HCV infection was higher among male veterans than female veterans, regardless of age[41].

Among Arkansans dying from 1999 – 2012 who had HCV listed as a cause or contributing to death on their death certificate, 28.1% were veterans (Table 42a). Additionally, 25.7% of persons listing any of several liver diseases as a cause or contributing cause to death on their death certificate were veterans (Table 46a).

A report produced by the Department of Veterans Affairs in 2008 noted that the prevalence of HCV among veterans was approximately double the prevalence among non-veterans[42]. The majority of veterans with chronic HCV were white, non-hispanic males and aged 50 – 59 years during 2008[42]. At the regional level, Arkansas is part of the South Central VA Health Care Network, a Veterans Integrated Service Network including all or part of seven other states (Texas, Oklahoma, Missouri, Mississippi, Louisiana, Alabama, and Florida). This region served the largest number of veterans with chronic HCV in 2008, with 14,019 veterans in the region documented with chronic HCV[42]. In 2008, 596 veterans were receiving HCV antivirals and 2,977 had ever received HCV antivirals[42].

Baby Boomers

The CDC and USPSTF recommend that all baby boomers be screened with an HCV antibody test[2,4]. Additionally, persons with a positive antibody test should receive confirmatory testing with an HCV ribonucleic acid test. If positive, they should receive a screening and intervention as appropriate to facilitate abstinence from alcohol use and immunizations against hepatitis A and B viruses[2].

Nationally, the prevalence of HCV among baby boomers, or persons born during the years 1945 – 1965 is five-fold higher than the prevalence of HCV among other groups[2]. In Arkansas, the prevalence of past or present infection with HCV among baby boomers was 3.6% compared to a prevalence of only 0.6% among non-baby boomers, demonstrated from results of the ARCHES study. This represents a prevalence 6-fold greater among baby boomers in Arkansas than non-baby boomers. Numerically, baby boomers represented 29,203, or 77.4%, of the total 37,709 predicted infections.

Baby boomers also represented 20,749, or 69.4% of all inpatient hospitalizations during 2004 – 2012 that documented HCV as a diagnosis. Baby boomers also represented 1,666, or 54.2% of all emergency department visits during 2012 that listed HCV as a diagnosis. Further, baby boomers received 136, or 76.4% of all liver transplants among Arkansans during 2005 – 2012 and represented 525 (34.9%) of a total of 1,505 cases of liver and intrahepatic bile duct cancers documented in the Arkansas Central Cancer Registry during 1997 – 2011. HCV was listed as a cause or contributing condition to death among 1,132 baby boomers, representing 73.6% of all death documenting HCV as a cause or contributing condition to death. Additionally, 5,227 baby boomers listed one of several liver diseases as a cause or contributing condition to death on death certificates, representing 42.5% of all deaths documenting liver diseases as a cause or contributing condition to death.

Persons who Inject Drugs

Injection drug use (IDU) is the primary risk factor for HCV. In Arkansas, data from the ARCHES study demonstrated that HCV infects approximately 33.7% of persons who inject drugs (PWID), the highest prevalence among any risk group assessed among ARCHES participants. Nationally, the prevalence of HCV may be as high 72% among PWID[43].

Inpatient hospitalization data was queried to determine rates of hospitalizations indicative of opiate-related drug overdose. Overall, the number of inpatient hospitalizations for opiate overdoses increased from 2004 – 2012, with 1,024 hospitalizations in 2004 to 1,697 hospitalizations in 2012 (Table 48). Least squares linear regression models of the age-adjusted rates demonstrated an increase of 2.5 hospitalizations per 100,000 Arkansans per year over 2004 – 2012 (Figure 22). There was a statistically significant increasing trend in the proportion of overdose-related hospitalizations documenting HCV infection from 2004 – 2012.

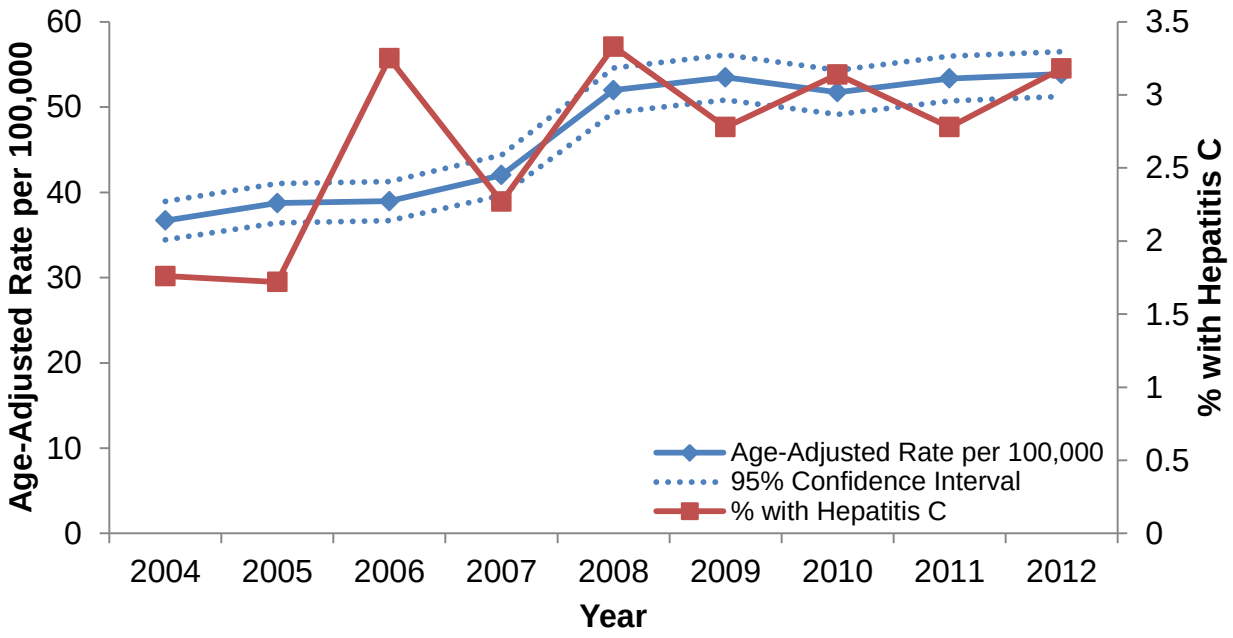
Maps of crude hospitalization rates related to opiate drug overdoses were created using information on each patient's county of residence. Counties with rates exceeding 100 per 100,000 persons included Poinsett, Sharp, Union, and Crawford counties (Figure 23). These counties may be indicative of areas in Arkansas with high levels of drug use that could potentially facilitate the transmission of HCV.

Table 48. Hospitalizations Documenting Diagnoses of Poisoning, Accidental Poisoning, or Adverse Effects from Use of Heroin, Methadone, and Other Opiates* — Arkansas, 2004 – 2012

Year	Number (%) of Hospitalizations Documenting Opiate-Related Overdoses	Crude Hospitalization Rate per 100,000 Arkansans	Age-Adjusted Rate per 100,000 Arkansans (95% CI)	Number (%) with HCV Infection
2004	1,024 (0.3)	37.2	36.7 (34.4 – 38.9)	18 (1.8)
2005	1,103 (0.3)	39.7	38.7 (36.4 – 41.0)	19 (1.7)
2006	1,139 (0.3)	40.4	39.0 (36.7 – 41.3)	37 (3.3)
2007	1,236 (0.3)	43.4	42.0 (39.6 – 44.4)	28 (2.3)
2008	1,560 (0.4)	54.3	52.0 (49.4 – 54.6)	52 (3.3)
2009	1,620 (0.4)	55.9	53.5 (50.8 – 56.1)	45 (2.8)
2010	1,590 (0.4)	54.5	51.7 (49.2 – 54.3)	50 (3.1)
2011	1,654 (0.4)	56.3	53.4 (50.7 – 56.0)	46 (2.8)
2012	1,697 (0.4)	57.5	53.9 (51.3 – 56.5)	54 (3.2)
Total	12,623 (0.4)	N/A	N/A	349 (2.8)
Trend Statistics	PC: 0.0115* SC: 0.0115* CA: <0.0001* (Increasing)	N/A	ROC: 2.5 per 100,000 persons (p=0.0004)*	PC: 0.0126* SC: 0.0204* CA: 0.0152* (Increasing)

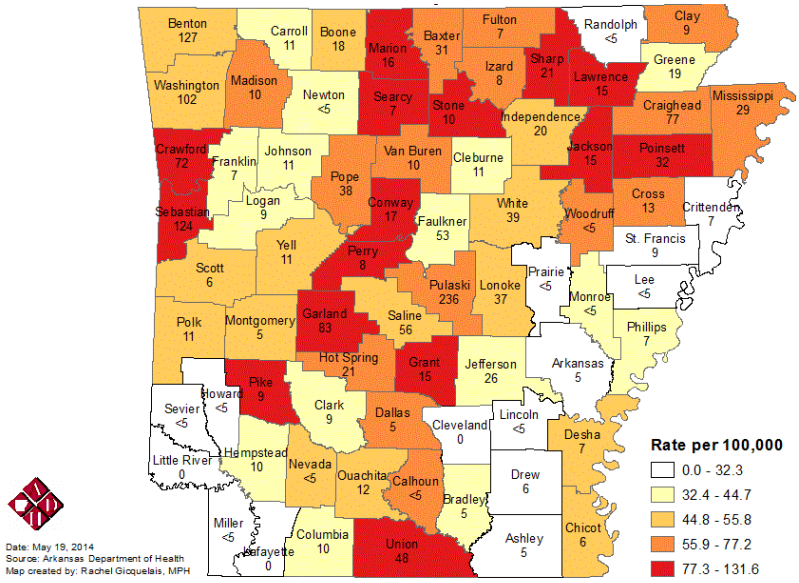
Abbreviations: CA: Cochran-Armitage Trend Test; CI: Confidence Interval; HCV: Hepatitis C Virus; PC: Pearson Correlation Coefficient; ROC: Rate of Change; SC: Spearman Correlation Coefficient.
* Denotes statistically significant result at 95% confidence level ($\alpha \leq 0.05$).
[1] Hospitalizations for opiate-related drug overdoses were indicated by the following ICD-9-CM codes: poisoning by opium, heroin, methadone, or other opiates or related narcotics (96500, 96501, 96502, or 96509), accidental poisoning by heroin, methadone, or other opiates and related narcotics (E8500, E8501, or E8502), or adverse effects attributable to the therapeutic use of heroin, methadone, or other opiates and related narcotics (E9350, E9351, or E9352).

Figure 22. Inpatient Hospitalizations Documenting Diagnoses of Poisoning, Accidental Poisoning, or Adverse Effects from Use of Heroin, Methadone, and Other Opiates — Arkansas, 2004 – 2012



*Rate calculations include inpatient hospitalizations with ICD9 codes 96500 - 96509 (poisoning by opium, heroin, methadone, or other opiates and related narcotics), codes E8500 - E8502 (accidental poisoning by heroin, methadone, or other opiates and related narcotics), or E9350 - E9352 (heroin, methadone, or other opiates and related narcotics causing adverse effects in therapeutic use).

Figure 23. Inpatient Hospitalizations Documenting Diagnoses of Poisoning, Accidental Poisoning, or Adverse Effects from Use of Heroin, Methadone, and Other Opiates — Arkansas, 2012



Numbers represent hospitalizations per county.

HIV-Infected Arkansans

All persons with HIV infection are recommended to be screened for HCV at least once, or routinely if risk behaviors are ongoing[2]. An estimated 25% of persons with HIV-infection are coinfected with HCV[44]. Among HIV-infected injection drug users, prevalence of HCV is approximately 50% – 90%[44]. As of May 1, 2014, there were approximately 6,025 persons living in Arkansas with HIV infection who were documented in ADH's enhanced HIV/AIDS Reporting System (eHARS), a national registry that compiles data on HIV-infected persons in the United States. Among 6,025 persons living with HIV-infection in Arkansas as of May 1, 2014, at least 1,506 (25%) are likely also infected with HCV.

Although surveillance for chronic HCV is limited and vastly under-documents the estimated 37,709 persons with HCV-infection in Arkansas, ADH conducted a registry match to identify individuals with HIV/HCV coinfection. Datasets from the HIV registry (eHARS) and HCV registry (NEDSS) registry were matched using Link Plus software, a probabilistic matching tool that uses identifiable information, such as name, date of birth, sex, and other characteristics, to identify individuals existent in two separate registries.

Matching of the HCV and HIV registries during May 2014 identified 95 HIV/HCV coinfected individuals, whose characteristics are summarized in Table 49. Among cases, most were male, white race, and diagnosed with HIV-infection at ages 30 – 34 or <25 years. Most detected matches were diagnosed during the years 2000 – 2009 and were aged 50 – 54 years as of January 1, 2014. Over half were previously diagnosed with Acquired Immune Deficiency Syndrome (AIDS). Finally, the primary risk factor was injection drug use (IDU), with 40 (42.1%) cases documented to have ever injected drugs. Notably, 39 (41.1%) cases were men who have sex with men (MSM).

Table 49. Characteristics of Persons with Human Immunodeficiency Virus (HIV) Infection and Hepatitis C Virus (HCV) Infection Identified by Matching HIV and HCV Surveillance Registries — Arkansas

Characteristic	Number	%
Estimated HIV/HCV Positive Arkansans	1,506	N/A
Total HIV/HCV Coinfections Detected via Registry Linkage	95	100.0
Sex		
Female	27	28.4
Male	68	71.6
Year of HIV Diagnosis		
1980 – 1989	9	9.5
1990 – 1999	26	27.4
2000 – 2009	39	41.1
2010 – 2014	19	20.0
Unknown	2	2.1
Age at HIV Diagnosis (Years)		
<25	18	18.9
25 – 29	14	14.7
30 – 34	18	18.9
35 – 39	14	14.7

40 – 44	11	11.6
45 – 49	9	9.5
≥50	9	9.5
Unknown	2	2.1
Current Age (as of January 1, 2014)		
20 – 24	2	2.1
25 – 29	10	10.6
30 – 34	6	6.4
35 – 39	5	5.3
40 – 44	15	16.0
45 – 49	16	17.0
50 – 54	20	21.3
55 – 59	14	14.7
≥60	6	6.3
Not Applicable, Patient Deceased	1	1.0
Race		
White	53	54.7
Black	32	33.7
Other or Unknown	11	11.6
HIV or AIDS Status		
AIDS	51	53.7
HIV (Non-AIDS)	42	44.2
Unknown	2	2.1
Risk Factor		
Men who have Sex with Men (MSM)	28	29.5
Injection Drug Use (IDU)	29	30.5
MSM/IDU	11	11.6
Heterosexual	15	15.8
Unknown	12	12.6

In addition to surveillance data, HIV is also documented in the hospital discharge and death certificate data using ICD-9-CM and ICD-10 codes, respectively. During 2004 – 2012, there were 8,406 hospitalizations documenting HIV, of which, 910 (10.8%) also documented HCV as a diagnosis (Table 50). Additionally, 3.1% of the 29,881 hospitalizations documenting HCV as a diagnosis also documented HIV infection. In 2012, there were 1,725 emergency department visits documenting HIV as a diagnosis. Of these, 115 (6.7%) also had HCV documented while 3.7% of the 3,073 emergency department visits documenting HCV also listed HIV. Finally, 1,019 deaths documented HIV-infection during 1999 – 2012, of which 39 (3.6%) also documented HCV infection as a cause or contributing condition to death. Of the 1,538 death listing HCV as a cause or contributing condition to death, 2.5% also documented HIV.

Table 50. Inpatient Hospitalizations, Emergency Department Visits, and Deaths Among HIV/HCV Coinfected Arkansans					
Data Source (Years)	Number Listing Hepatitis C Virus (HCV) Infection	Number Listing Human Immunodeficiency Virus (HIV) Infection	Number Listing HCV and HIV	% of HCV also Listing HIV	% of HIV also Listing HCV
Inpatient Hospitalization (2004 – 2012)[1]	29,881	8,406	910	3.1	10.8
Emergency Department (2012)[2]	3,073	1,725	115	3.7	6.7
Death Certificate (1999 – 2012)[3]	1,538	1,019	39	2.5	3.6

[1] Hospitalizations documenting hepatitis C include ICD-9-CM codes for acute, chronic, or unspecified hepatitis C (07041, 07044, 07054, 07059, 07070, 07071, or V0262). Hospitalizations documenting HIV include inpatient hospitalizations with ICD-9-CM codes 042, 07953, 79571, or V08.
[2] Emergency department visits for acute, chronic, or unspecified Hepatitis C Virus (HCV) were indicated by the following ICD-9-CM codes: 07041, 07044, 07051, 07054, 07059, 07070, 07071, or V0262. Emergency department visits for Human Immunodeficiency Virus (HIV) were indicated by the following ICD-9-CM codes: 042, 07953, 79571, or V08.
[3] Death certificates indicative of hepatitis C infection included certificates with ICD-10 codes B171 or B182. Deaths certificates indicative of Human Immunodeficiency Virus (HIV) infection included certificates with ICD-10 codes B200 - B24 and R75.

Children Born to HCV-Infected Mothers

Children born to HCV-infected mothers are recommended to be tested for HCV-infection[2]. Vertical transmission of HCV is the most common cause of childhood HCV infection and occurs when HCV is transmitted from mother to child. Approximately 3% – 10% of births to HCV-infected women result in HCV infection of the infant[45]. Although much is unknown about why or how transmission occurs, prolonged rupture of membranes may increase the risk of transmission[45]. Nationwide, an estimated 40,000 children are born to HCV-positive women and are therefore at risk of HCV-infection and require testing[45].

In Arkansas, the majority of infants born to HCV-infected mothers are referred to Arkansas Children's Hospital, where follow-up with the Pediatric Infectious Disease Clinic allows physicians specialized in HCV-related pediatric guidelines to evaluate and follow infants over time to determine if maternal to infant HCV transmission occurred.

HCV surveillance among all persons aged <18 years at the time of report began in 2013 and characteristics of cases are described in Table 51. Infants aged <18 months are only considered to be HCV-infected if they have evidence of a positive nucleic acid test. Data from 2013 showed that 24 infants were reported to surveillance as suspect HCV cases because they had at least one positive HCV test for HCV antibody or nucleic acid. The majority (20, 83.3%) were born to an HCV-infected mother while risk information for the remaining 4 infants was not obtainable.

Among infants reported, 6 were classified as confirmed cases (Table 51), whereby a positive HCV nucleic acid test was documented within the first 18 months of life. Although 12 infants were classified as non-cases, 6 additional infants were not tested with a nucleic acid test and these infants will remain suspect until further testing results are reported.

A total of 6 cases were reported among persons aged 1.5 – 4 years at the time of report, 5 (83.3%) were confirmed to have been born to an HCV-infected mother while risk factor information for one child was undetermined. Among 35 children older than 4 years at the time of report, 9 (25.7%) were confirmed to have been born to an HCV-infected mother. Notably, 6 cases (17.1%), all of whom were aged 13 – 18 years, reported injection drug use.

Table 51. Characteristics of Pediatric Hepatitis C Virus (HCV) Infections — Arkansas, 2013

Characteristic	Number	%
Total	47	100.0
Sex		
Female	26	55.3
Male	21	44.7
Year of HCV Diagnosis		
2006 – 2009	5	10.6
2010 – 2012	12	25.5
2013	13	27.7
Undetermined	17	36.2
Age (Years)		
<1.5	6	12.8
1.5 – 4	6	12.8
5 – 12	9	19.2
13 – 18	26	55.3
Race		
White	40	85.1
Other or Unknown	7	14.9
Born to an HCV-Infected Mother		
Yes	20	42.6
No	7	14.9
Unknown	20	42.6
History of Lifetime Injection Drug Use		
Yes	6	12.8
No or Unknown	41	87.2

Using data on 2012 singlet and multiple birth rates in Arkansas[46], the prevalence of HCV from the ARCHES study of approximately 0.6% – 1.8% (HCV prevalence exclusive and inclusive of baby boomers), and the assumption that vertical transmission of HCV occurs in approximately 5% of births, it is likely that approximately 213 – 640 women infected with HCV gave birth in Arkansas in 2012 and birthed approximately 220 – 661 infants. This may have resulted in 11 – 33 perinatal HCV infections in 2012. Assuming that births in 2013 were similar to 2012, the numbers of infants reported to ADH HCV surveillance only represents 6 transmission events, approximately 18.2% – 54.5% of the expected 11 – 33 vertically transmitted infections.

ARKANSAS DEPARTMENT OF HEALTH INITIATIVES AND RESOURCES

Hepatitis C Testing

Screening for HCV will be available at all ADH's 98 Local Health Units in the coming months. A list of local health units is available online at: http://www.healthy.arkansas.gov/programsServices/localPublicHealthOffices/Pages/huList.aspx.

HCV screening services are available to all persons at-risk of HCV. These groups include:

- Persons born 1945 – 1965
- Persons who have ever injected drugs or used intranasal drugs
- Persons who have received a blood transfusion or organ transplant before 1992
- Persons who have received clotting factor concentrates produced before 1997
- Persons living with HIV or AIDS
- Children born to HCV-infected mothers
- Persons ever receiving long-term hemodialysis treatment
- Persons with alanine aminotransferase (ALT) levels that are persistently abnormal
- Persons who received blood from an HCV-infected donor
- Persons with exposures in health care, emergency medicine, or public safety settings that involve needle sticks or other mucosal exposures to HCV-infected blood
- Persons who have ever received tattoos from an unregulated source
- Persons who have ever been incarcerated
- Long-term sexual partners of persons with HCV

To assess your risk of HCV and determine if screening is necessary, you can take a free, online, 5-minute risk assessment at this link: http://www.cdc.gov/hepatitis/riskassessment/start.html.

In addition to the Arkansas Department of Health, healthcare providers throughout Arkansas provide screening for HCV. Patients who choose to use the Arkansas Department of Health for HCV testing services will receive an antibody screening test for HCV. If positive, referral for confirmatory screening and treatment will be provided.

Hepatitis C Treatment

Treatment options for HCV infection have recently expanded to include new, more effective regimens with higher cure rates. Before 2013, HCV infection was treated with up to 48 weeks of pegylated interferon, an injectable drug associated with numerous, debilitating side effects, plus ribavirin. Successful treatment for HCV is determined by sustained virologic response (SVR), which means undetectable viral load for at least 6 months after completion of therapy and is functionally equivalent to cure. For these older treatment regimens, SVR was achieved for fewer than 70% of patients.

Recent treatment developments have revitalized the ability to control the HCV epidemic. Two new drugs, sofosbuvir and simeprevir, were approved for HCV treatment in late 2013. These

drugs bring the promise of more effective treatment, fewer side effects, and shorter, all-oral treatment regimens that eliminate the need for pegylated interferon in some patients. Further, several new drugs have shown promise in stage II clinical trials and could be available by late 2014 or 2015. While the cost of new HCV drugs is currently very expensive, providers and insurers can help determine what regimens may be available and if medication assistance programs can cover a portion of the cost. Nonetheless, persons who have never been evaluated for HCV treatment or who have been unable to complete treatment in the past may wish to consult with a provider to evaluate treatment options.

Although the Arkansas Department of Health (ADH) does not currently provide treatment for HCV, every effort will be made to connect patients seeking treatment with a provider. Please contact the ADH Viral Hepatitis Prevention Coordinator for a list of providers taking on HCV patients. You can reach contact the prevention coordinator at (501) 661-2408.

For more information on current treatments and treatment guidelines, please consult the American Association for the Study of Liver Diseases at the following link: http://www.hcvguidelines.org/.

Hepatitis C Surveillance

The Hepatitis C Surveillance Program at the Arkansas Department of Health receives notifiable disease reports of persons testing positive for HCV antibodies or ribonucleic acid. A registry for HCV was developed in 2013 to track persons infected with HCV and cases are investigated using standard case investigation forms to collect information about risk factors, demographics, and historical HCV data on all patients. While limited resources challenge data entry and case investigation for all reported cases, surveillance for several special populations currently occurs and is expanding as resources for HCV surveillance grow. Much of the data from the first year of data collection (2013) is presented in the epidemiologic profile. Please contact the Arkansas Department of Health STI/HIV/Hepatitis C/Tuberculosis section at phone number (501) 661-2408 if you have questions or data requests involving HCV.

CURRENT RECOMMENDATIONS: PRIMARY PREVENTION OF VIRAL HEPATITIS

Risk Reduction for Persons Who Inject Drugs

Persons who inject drugs (PWID) are at high risk of acquiring viral hepatitis. In Arkansas, the prevalence of past or present HCV infection among PWID is 33.7% (range: 16.2% – 51.2%), demonstrated by the ARCHES study (Table 9); however, studies conducted throughout the United States have shown that the prevalence of HCV among this population could be as high as 72%[43]. HCV is most often transmitted when users share injection equipment, such as needles and syringes. The World Health Organization (WHO) has recommended the following strategies to reduce transmission of viral hepatitis and HIV among PWID[43]:

1. Needle and syringe programs
2. Opioid substitution therapy or drug dependence treatment
3. HIV testing, counseling and antiretroviral therapy

4. Sexually transmitted infection prevention and treatment, including provision of condoms to PWID and their sexual partners
5. Education and information for PWID and their sexual partners
6. Vaccination, diagnosis, and treatment of viral hepatitis
7. Prevention, diagnosis, and treatment of tuberculosis

In addition to the strategies above, specific recommendations to decrease the prevalence of viral hepatitis include:

1. Offer PWID the rapid HBV vaccine regimen
2. Offer PWID incentives to increase uptake of the HBV vaccine regimen
3. Provide low dead-space syringes in needle and syringe programs that limit the amount of blood remaining in syringes after injection
4. Provide peer interventions among PWID to reduce the incidence of viral hepatitis, whereby peers of PWID provide information and services, rather than psychosocial interventions for PWID to reduce viral hepatitis incidence, whereby health professionals (and not peers) provide information and services

The Harm Reduction Action Coalition has produced a safety manual for PWID, which outlines how to safely inject drugs and prevent transmission of HIV and viral hepatitis[47]. This resource can be accessed online at the following link: http://harmreduction.org/wp-content/uploads/2011/12/getting-off-right.pdf.

The Substance Abuse and Mental Health Services Administration (SAMHSA) has produced a Treatment Improvement Protocol (TIP) to aid providers in addressing viral hepatitis among patients who are substance users. *TIP 53: Addressing Viral Hepatitis in People with Substance Use Disorders* is available for download or can be ordered online for free at the following link: http://store.samhsa.gov/product/TIP-53-Addressing-Viral-Hepatitis-in-People-With-Substance-Use-Disorders/SMA11-4656. In addition, a *Quick Guide for Clinicians and Administrators* based on *TIP 53* is available at the following link: http://store.samhsa.gov/product/Addressing-Viral-Hepatitis-in-People-With-Substance-Use-Disorders/SMA13-4794.

Prevention of Healthcare-Associated Viral Hepatitis Transmission

Outbreaks of HBV and HCV-associated with noncompliance with infection control procedures and improper use of healthcare equipment, such as glucose monitors, fingerstick devices, endoscopes, medications, hemodialysis equipment, and syringes have occurred recently in both inpatient and outpatient facilities among patients and healthcare workers in the United States[48]. Preventing healthcare-associated HBV and HCV transmission is a national priority[49]. Upon identification of a case in a person without traditional risk factors, especially when the infection likely occurred recently or is suspected to be an acute case, healthcare providers should consider recent exposures to healthcare and contact the Arkansas Department of Health immediately if healthcare-associated transmission is suspected (phone number: (501) 661-2408). Providers and other persons providing clinical care can find more information at the following websites:

- CDC Injection Safety Page (Providers): http://www.cdc.gov/injectionsafety/providers.html
- CDC Injection Safety Page (Patients): http://www.cdc.gov/injectionsafety/patients.html
- One and Only One Campaign: http://www.oneandonlycampaign.org/
- CDC Healthcare Infection Control Practices Advisory Committee (HICPAC): http://www.cdc.gov/hicpac/index.html
- HICPAC Guidelines and Publications: http://www.cdc.gov/hicpac/pubs.html
- CDC-Reported Viral Hepatitis Outbreaks in Healthcare Settings: http://www.cdc.gov/hepatitis/Outbreaks/index.htm
- Healthcare-Associated Infections and Hepatitis: http://www.cdc.gov/HAI/organisms/hepatitis.html

PREVENTION OF COMPLICATIONS RELATED TO VIRAL HEPATITIS

Immunizations

Persons with HCV infection are recommended to be immunized against hepatitis A and B[2]. Preventing hepatitis A and B infections in persons with HCV through vaccination is important as coinfection can speed a person's progression to permanent liver damage. Please consult a primary care provider to obtain these immunizations.

Alcohol Use

Persons infected with HCV are recommended to abstain from using alcohol as alcohol consumption can speed a person's progression to permanent liver damage[2]. Upon diagnosing a person with HCV, providers should assess a patient's current level of alcohol use, provide recommendations for the patient to abstain from alcohol, and facilitate a patient's connection to a substance abuse treatment program when necessary[2].

NATIONAL RECOMMENDATIONS AND GOALS FOR VIRAL HEPATITIS

Healthy People 2020

Healthy People 2020 sets 10-year objectives related to health for the United States across several topic areas, including infectious diseases[50] and substance abuse[51]. Relevant objectives related to reducing HCV incidence and improving awareness of HCV infections along with goals related to substance abuse are summarized below. Notably, objectives related to increasing immunizations against HBV for high-risk populations, such as people who inject drugs and men who have sex with men, are outlined in objective IID-15; however, these objectives are descriptive and do not have baseline and target goals set as of the writing of this report[50].

Table 52. Healthy People 2020 Objectives Related to Hepatitis C Virus Infection			
Objective	Title	Baseline (Year(s))	2020 Target
IID-26	Reduce new hepatitis C infections	0.28 new cases per 100,000 (2007)	0.25 new cases per 100,000 persons
IID-27	Increase the proportion of persons aware they have a hepatitis C infection	49% of persons in the National Health and Nutrition Examination Survey with HCV were aware of their infection before HCV testing (2002 – 2007)	60% of infected persons aware of their HCV infection
SA-7	Increase the number of admissions to substance abuse treatment for injection drug use	254,278 admissions to treatment programs (2006)	279,706 admissions
SA-19	Reduce the past-year nonmedical use of prescription drugs	6.1% of persons aged ≥12 years used pain relievers, tranquilizers, stimulants, or sedatives nonmedically in the past year (2008)	5.5% past-year nonmedical use of pain relievers, tranquilizers, stimulants, or sedatives among persons aged ≥12 years

Department of Health and Human Services

The US Department of Health and Human Services (DHHS) outlines national recommendations and strategies for the years 2014 – 2016 to reduce the burden of viral hepatitis in its report entitled *Combating the Silent Epidemic of Viral Hepatitis: Action Plan for the Prevention, Care and Treatment of Viral Hepatitis*, which was released in April 2014 and is available online at the following link: http://aids.gov/pdf/viral-hepatitis-action-plan.pdf. This document updates DHHS' first action plan for viral hepatitis, which was released in 2011 and outlined national goals for the years 2011 – 2013[52]. The overarching goals of the action plan are to:

- "Increase the proportion of persons who are aware of their hepatitis B virus (HBV) infection from 33% to 66%"[49]
- "Increase the proportion of persons who are aware of their hepatitis C virus (HCV) infection from 45% to 66%"[49]
- "Reduce the number of new cases of HCV infection by 25%"[49]
- "Eliminate mother-to-child transmission of HBV"[49]

The action plan outlines six areas to achieve these goals:

1. "Educating Providers and Communities to Reduce Health Disparities"[49]
2. "Improving Testing, Care, and Treatment to Prevent Liver Disease and Cancer"[49]
3. "Strengthening Surveillance to Detect Viral Hepatitis Transmission and Disease"[49]
4. "Eliminating Transmission of Vaccine-Preventable Viral Hepatitis"[49]
5. "Reducing Viral Hepatitis Caused by Drug Use Behaviors"[49]
6. "Protecting Patients and Workers from Health Care-Associated Viral Hepatitis"[49]

More information about national priorities and plans to achieve them can be found at the following links:

- Full action plan: http://aids.gov/pdf/viral-hepatitis-action-plan.pdf
- Fact Sheet with Summary: http://aids.gov/pdf/2014-vhap-at-a-glance.pdf

Centers for Disease Control and Prevention

The Centers for Disease Control and Prevention (CDC) recently updated guidelines regarding HCV testing. Please see the "Testing Recommendations" section for more information. In addition to testing recommendations, CDC provides a variety of fact sheets, answers to frequently asked questions, materials available for download or ordering (such as posters, infographics, and fact sheets), provider and patient education resources, and other information. Visit http://www.cdc.gov/hepatitis/ for more information.

United States Preventive Services Task Force

The United States Preventive Services Task Force (USPSTF) reviews scientific evidence and produces recommendation statements pertaining to numerous preventive health services. Recommendations are given grades, and grades of A and B represent recommendations for services that have a net benefit. Accordingly, under the Affordable Care Act, preventive health services given a grade A or B by the USPSTF are provided at no cost to patients by their insurance providers.

During 2013, the USPSTF reviewed the scientific evidence for recommendations for HCV screening. HCV screening for all persons born 1945 – 1965, persons who inject drugs, and persons who received a blood transfusion before 1992 was given a grade B recommendation[4]. Accordingly, HCV testing among these groups has been added to the list of preventive health services covered at no cost by the Centers for Medicare & Medicaid Services[53].

PROVIDER EDUCATION RESOURCES

A list of selected training courses, fact sheets, infographics, and other materials is provided below; however, it is not meant to be comprehensive of all available materials.

Continuing Medical Education (CME), Continuing Nursing Education (CNE) Courses, and other online courses (All courses are offered free of charge and completed online)

- Hepatitis Web Study (University of Washington, Free CME/CNE): http://depts.washington.edu/hepstudy/
- Hepatitis C Online Course (University of Washington, Free CME/CNE): http://www.hepatitisc.uw.edu/alternate
- ACT-First Liver-Learning for Primary Care Providers (American Association for the Study of Liver Diseases, Free CME/CNE): http://www.aasld.org/LiverLearning%C2%AE/Pages/LiverProgramforPrimaryCareProviders.aspx

- CDC Recommendations for Persons Born 1945 – 1965 (Medscape, Free CME/CNE): http://www.medscape.org/viewarticle/769593
- CDC Viral Hepatitis Serology Online Training: http://www.cdc.gov/hepatitis/Resources/Professionals/Training/Serology/training.htm
- Know Hepatitis (University of Alabama at Birmingham – National Training Center for Integrated Hepatitis HIV/STD Prevention Services: http://www.knowhepatitis.org/
- Overview of training courses and other opportunities: http://www.cdc.gov/hepatitis/Resources/Professionals/TrainingResources.htm

CDC Tools for Health Professionals

- ABCs of Hepatitis: http://www.cdc.gov/hepatitis/Resources/Professionals/PDFs/ABCTable.pdf
- Testing for HCV: http://www.cdc.gov/hepatitis/HCV/PDFs/hcv_flow.pdf
- Interpretation of Test Results: http://www.cdc.gov/hepatitis/HCV/PDFs/hcv_graph.pdf
- Recommended Groups to Test for HCV: http://www.cdc.gov/mmwr/pdf/rr/rr6104.pdf
- Updated Testing Recommendations for Clinicians and Laboratorians: http://www.cdc.gov/mmwr/pdf/wk/mm62e0507a2.pdf
- Overview of Tools: http://www.cdc.gov/hepatitis/Resources/HealthProfessionalTools.htm
- HCV Testing Fact Sheet: http://www.cdc.gov/nchhstp/newsroom/docs/HCV-Testing-Recs.pdf
- HCV Testing Infographic: http://www.cdc.gov/nchhstp/newsroom/2013/HepC-Infographic2013.html?s_cid=nchhstp-nr-ham-003
- HCV Vital Signs Fact Sheet: http://www.cdc.gov/vitalsigns/pdf/2013-05-vitalsigns.pdf

Other Tools for Health Professionals

- *Addressing Viral Hepatitis in People with Substance Use Disorders* (TIP 53, Substance Abuse and Mental Health Services Administration): http://store.samhsa.gov/product/TIP-53-Addressing-Viral-Hepatitis-in-People-With-Substance-Use-Disorders/SMA11-4656
- *Quick Guide for Clinicians and Administrators Based on TIP 53, Addressing Viral Hepatitis in People with Substance Use Disorders* (Substance Abuse and Mental Health Services Administration): http://store.samhsa.gov/product/Addressing-Viral-Hepatitis-in-People-With-Substance-Use-Disorders/SMA13-4794

PATIENT EDUCATION RESOURCES

A list of selected websites with patient education materials, including fact sheets, infographics, and other materials is provided below; however, it is not meant to be comprehensive of all available materials.

Viral Hepatitis Risk Assessment: Find out if you're at risk for HCV with this 5-minute, online quiz.

- http://www.cdc.gov/hepatitis/RiskAssessment/index.htm

Websites with Patient Education Materials Available to Download or View:

- Hepatitis C Information for the Public: http://www.cdc.gov/hepatitis/C/index.htm
- Hepatitis C Information for the Public Patient Education Resources: http://www.cdc.gov/hepatitis/C/PatientEduC.htm#cdc
- CDC Viral Hepatitis Resource Center: http://www.cdc.gov/hepatitis/Resources/PatientEdMaterials.htm
- Know Hepatitis: http://www.cdc.gov/KnowMoreHepatitis/?s_cid=bb-dvh-yb-006
- Faces of Hepatitis: http://www.viralhepatitisaction.org/faces
- Viral Hepatitis Information from the Department of Veterans Affairs: http://www.hepatitis.va.gov/patient/index.asp
- CDC Publication Ordering Page: http://wwwn.cdc.gov/pubs/CDCInfoOnDemand.aspx?ProgramID=46
- Know More Hepatitis Campaign Resources: http://www.cdc.gov/knowmorehepatitis/CampaignResources.htm
- Hepatitis C Testing Infographic: http://www.cdc.gov/nchhstp/newsroom/2013/HepC-Infographic2013.html?s_cid=nchhstp-nr-ham-003
- HCV Information and Testing Infographic (Baby Boomers): http://www.cdc.gov/knowmorehepatitis/Media/PDFs/Infographic-Paths.pdf

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APPENDIX A: DESCRIPTION OF DATA SOURCES, METHODS, AND LIMITATIONS

Arkansas Cardiovascular Health Examination Survey (ARCHES)

The Arkansas Cardiovascular Health Examination Survey (ARCHES), a cross-sectional, representative survey of non-institutionalized Arkansans aged 18 years or older, was conducted in 2006 – 2008[7]. While the primary goal of this study was to examine cardiovascular risk factors, it contributes important information regarding HCV prevalence in Arkansas. Subjects who participated were asked to provide blood samples, which were tested for presence of HCV antibodies. Nucleic acid testing for HCV was not part of this study. Participants also completed a series of survey questions, which included risk factors for HCV, demographics, and other questions. Sampling design and survey participants are described further in a paper by Zohoori et al[7].

Among 1,383 participants in the ARCHES study, 1,159 were tested for HCV antibodies. Survey results were re-weighted before analysis to calculate final weights after excluding persons not tested for HCV. The sampling weight was calculated based on the 2007 population of Arkansas and assigned each person included in the sample a weight so that the entire survey could be analyzed to represent the population of Arkansas in 2007. Analysis of ARCHES results was completed using the survey procedures in SAS 9.3 (SAS Institute, Cary, NC), which accounts for the sampling stratum and primary sampling units along with the sampling weight. Prevalence calculations were completed using frequency tables while risk factors for HCV were analyzed by building a logistic regression model using a backwards selection technique to select covariates for a final model.

Limitations of this study include the exclusion of institutionalized persons, such as persons incarcerated at the time of participant selection, people who did not speak English, people with cognitive, psychiatric, or developmental disorders, and persons without an address, such as those who were homeless at the time of participant recruitment. This study also tested only for the presence of HCV antibodies, indicative of either past or present infection. Finally, the type of sex was not specified among persons reporting sex with a person who injected drugs or HCV-infected person. Estimates of the prevalence of HCV and odds of acquiring HCV associated with this group may reflect participants reporting vaginal, oral, or anal sex; however, the type of sex may have influenced the risk of HCV transmission[9].

Arkansas Central Cancer Registry

Healthcare providers who diagnose or treat cancers in the state of Arkansas are mandated by regulation to report cases to the Arkansas Central Cancer Registry, which collects data on all cases of cancer diagnosed among Arkansans. For the purposes of this project, a Microsoft Access database was obtained from the Arkansas Central Cancer Registry containing cancer cases meeting the following specifications:

- Primary site of the liver or intrahepatic bile duct
- Diagnosed among a non-veteran during 1997 – 2011
- Histology codes 8000-9049, 9056 – 9139, 9141 – 9589[54]
- Behavior codes indicative of invasive cancer

Cases among veterans were not obtainable for analyses; however, age-adjusted rates of liver and intrahepatic are presented in Table 36 and were queried from the Arkansas Central Cancer Registry's online system, located at http://www.cancer-rates.info/ar/index.php. Data was further restricted to contain only one recorded cancer per person per year because cancer of the liver or intrahepatic bile duct could reoccur over time.

Within the cancer registry, several text fields are available for abstractors to list key information about treatment, infections, or other relevant illnesses. While HBV and HCV are not required to be tested for or recorded within the Arkansas Central Cancer Registry, these diagnoses are sometimes recorded within three text fields. To identify cases with HBV and HCV listed, SAS 9.3 software was used to search three text fields for key words indicative of HBV or HCV infection. After identifying cases of HBV or HCV, indicator variables were created to note and compile frequency statistics on cases.

For all non-veteran data, SAS 9.3 was used to calculate rates of liver and intrahepatic bile duct cancers, along with the percentage infected with HBV or HCV. Briefly, crude rates were calculated by dividing the number of cases by the population of Arkansas for each year of analysis. Age-adjusted rates were calculated by direct standardization of crude rates to the 2000 standard US population and 95% confidence intervals were calculated using methods to estimate variance from the Poisson distribution via methods adapted from *Healthy People 2010*[32,55]. Further, methods from Ly et al. were adapted to assess change over time in age-adjusted rates using linear regression and in the percentage of total cases documenting HBV or HCV using the Cochran-Armitage test for trend. Pearson and Spearman correlation coefficients are also presented to demonstrate the direction of trends among the percentages of cases documenting HBV or HCV over time, whereby positive coefficients indicate an increasing trend and negative coefficients indicate a decreasing trend. Regression or trend statistics were considered statistically significant at the 95% confidence level ($\alpha \leq 0.05$). Frequency tables and figures were created using Microsoft Excel. Notably, events occurring at a frequency of less than five cases are not reportable by ADH policy. Data are suppressed or collapsed into larger categories in these instances.

There are several limitations to the analyses presented. First, HBV and HCV status are not reliably recorded in text fields. There is no standard field to record HBV or HCV status within records for persons with liver or intrahepatic bile duct cancers. Therefore, the percentage of cases with HBV or HCV likely under-represents the true percentage of cases with these infections. Second, veterans were excluded from all analyses requiring individual records to be queried, including analyses attempting to identify persons with HBV or HCV. Because the prevalence of viral hepatitis has been documented to be higher among veterans than among civilians, the percentage of cases with HBV or HCV is again an under-estimate.

Arkansas Hepatitis C Surveillance Data (Acute and Chronic)

As a state-reportable disease, any positive laboratory result for HCV is mandated by regulation to be reported to ADH by laboratories, physicians, or other sources[11,12]. In 2013, ADH expanded its hepatitis C surveillance program, which is managed by the STI/HIV/Hepatitis C/Tuberculosis

Section. The following types of reports were electronically recorded in the National Electronic Disease Surveillance System (NEDSS):

- Persons suspected of having acute HCV due to the presence of symptoms of acute hepatitis or an alanine aminotransferase (ALT) level ≥400 IU/mL
- Persons aged <30 years
- Persons incarcerated in a state or federal correctional facility in Arkansas
- Persons received via electronic laboratory reporting who were born in the years 1945 – 1965 (beginning January 1, 2014)
- Any person on a document containing any person meeting the specifications above

Once electronically entered, persons suspected to be acute HCV were assigned to ADH Communicable Disease Nurse Specialists (CDNS), who contacted the patient and reporting physician to determine if persons met the acute case definition[13]. Briefly, to be considered an acute HCV case during 2013, cases had to have demonstrated seroconversion to a positive antibody result for HCV within 6 months of a negative test or meet the following criteria:

- Presence of jaundice (or scleral icterus) or ALT ≥400 IU/mL
- Discrete onset of symptoms of acute HCV (abdominal pain, nausea, vomiting, malaise, headache, fever, grey-colored stools, dark urine, or other symptoms)
- Sufficient HCV laboratory results to indicate infection, which could include one or more of the following: positive antibody with signal to cut-off indicative of a true positive result in ≥95% of follow-up tests, positive nucleic acid test (qualitative, quantitative, or genotype), or positive recombinant immunoblot assay
- If done, negative results for Immunoglobulin M (IgM) antibody to hepatitis A virus and IgM antibody to hepatitis B virus core antigen

Once electronically entered, the reporting physician listed on the earliest report received on or after January 1, 2013 was contacted and asked to complete a standardized case investigation form for all persons aged <30 years and suspected to have chronic HCV infection. Physicians were asked to provide demographic information, diagnosis dates, signs and symptoms necessary to identify potential cases of acute HCV, HCV risk factors, and reasons prompting testing. Cases suspected to be chronic HCV among persons aged ≥30 years were not able to be investigated by surveillance staff in 2013. Upon receipt of follow-up forms, cases were considered confirmed if they met the following case definition[56]:

- Sufficient HCV laboratory results to indicate infection, which could include one or more of the following: positive antibody with signal to cut-off indicative of a true positive result in ≥95% of follow-up tests, positive nucleic acid test (qualitative, quantitative, or genotype), or positive recombinant immunoblot assay (for persons aged <18 months at the time of testing, only a positive nucleic acid test is considered sufficient)
- Does not meet the definition for acute HCV infection[13]

Notably, many cases are unable to be confirmed by this definition. Cases identified as suspect due to the presence of any positive laboratory test (including an antibody test without a signal to

cut-off indicative of a true positive result in ≥95% of follow-up tests or lacking a signal to cut-off result) or inability to exclude acute HCV infection due to lack of information on symptoms or liver enzymes are included in tables and figures in the epidemiologic profile. Cases with only negative HCV results reported or determined to have false-positive results are not included in data presented in the epidemiologic profile.

Data collected in NEDSS on acute and chronic HCV cases identified during 2013 was analyzed using SAS 9.3. Specifically, sections above present analyses of several groups including acute HCV, chronic HCV among persons <30 years, pediatric HCV, persons incarcerated at the time of HCV testing during, and HCV/HIV coinfected persons. Frequency tables and figures were created using Microsoft Excel. Notably, events occurring at a frequency of less than five cases are not reportable by ADH policy. Data are suppressed or collapsed into larger categories in these instances. Maps were created using ArcGIS software (ESRI, Redlands, CA) by plotting crude rates and number of cases in each county according to the patient's address or the healthcare facility address of the reporting physician if patient's address was unavailable. Persons incarcerated at the time of HCV testing were counted as cases of the county of their detaining facility.

Several limitations accompany both the acute and chronic HCV data. First, HCV surveillance data is not meant to represent all persons diagnosed with HCV living in Arkansas as only certain groups, as outlined above, are electronically recorded in NEDSS. Additionally, surveillance began during 2013, so data from previous years is unavailable. Because historical data is unavailable, confirming certain characteristics of cases, such as the date of diagnosis, is reliant only on physician report, which for HCV, may be incorrect if the patient was diagnosed by another provider on a separate occasion. In addition to these limitations, HCV and other reportable diseases are often under-reported to public health entities, despite that they are mandated to be reported to ADH by regulation[11]. These limitations indicate that HCV surveillance data likely underestimate the true number of acute and chronic HCV cases.

Arkansas Hospital Discharge Data System (Inpatient and Emergency Department)

All hospitals licensed in the state of Arkansas are required to report inpatient hospitalizations and emergency department visits to the Arkansas Hospital Discharge Data System. Detailed guidelines for data submission to the Hospital Discharge Data System can be found at the following link: http://www.healthy.arkansas.gov/programsServices/healthStatistics/Pages/HospitalDischarge.aspx. Datasets for all inpatient hospitalizations occurring during the years 2004 – 2012 and all emergency department (ED) visits occurring during the year 2012 were obtained from the Health Statistics Branch at the Arkansas Department of Health. Notably, these data include hospitalizations or ED visits occurring among persons without a permanent residence in Arkansas. SAS 9.3 was used to exclude persons with an address outside of Arkansas. Persons missing address information were assumed to live in Arkansas.

SAS 9.3 was used to query each of 11 ICD-9-CM codes for datasets documenting discharges for the years 2004 – 2007 and 22 ICD-9-CM codes for datasets documenting discharges for the

years 2008 – 2012. These fields represented all diagnosis and external cause of injury codes for each of these years and include the principal diagnosis, or "the condition established after study to be chiefly responsible for occasioning the admission of the patient for care"[34] and the admitting diagnosis, or "the ICD diagnosis code provided at the time of admission as stated by the physician"[34]. All diagnosis and external cause of injury codes were coded using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM). Each section presented above lists ICD-9-CM codes queried in data tables and figures.

SAS 9.3 was used in all analyses. Crude hospitalization or ED visit rates were calculated by dividing the number of cases by the population of Arkansas for each year of analysis. Age-adjusted rates were calculated by direct standardization of crude rates to the 2000 standard US population and 95% confidence intervals were calculated using methods to estimate variance from the Poisson distribution via methods adapted from *Healthy People 2010*[32,55]. Further, methods from Ly et al. were adapted to assess change over time in age-adjusted rates using linear regression and in the percentage of total hospitalizations documenting conditions of interest using the Cochran-Armitage test for trend for the inpatient hospitalization data. Pearson and Spearman correction coefficients are also presented to demonstrate the direction of trends among percentages of cases documenting conditions of interest over time, whereby positive coefficients indicate an increasing trend and negative coefficients indicate a decreasing trend. Regression or trend statistics were considered statistically significant at the 95% confidence level ($\alpha \leq 0.05$). Frequency tables and figures were created using Microsoft Excel. Notably, events occurring at a frequency of less than five cases are not reportable by ADH policy. Data are suppressed or collapsed into larger categories in these instances. Maps were created using ArcGIS software (ESRI, Redlands, CA).

Persons who are hospitalized as inpatients can be hospitalized more than once per year and are documented as separate records in hospital discharge data. De-duplication of inpatient hospitalization data was performed using SAS 9.3 for each year of discharge data and was repeated for each condition or group of conditions of interest (i.e. HCV, chronic liver diseases, and cirrhosis) to obtain datasets containing one hospitalization per patient per year. Briefly, datasets for each year were de-duplicated using one of two strategies dependent on the availability of social security number. First, persons with valid social security numbers documented in hospitalizations were de-duplicated by retaining the earliest hospitalization occurring in each discharge year. If a patient had an ICD-9-CM code documenting the condition or group of conditions of interest for each de-duplication cycle, the earliest hospitalization documenting the condition of interest was retained over hospitalizations that occurred earlier in the discharge year but that did not document the condition of interest. For patients missing social security number information, hospitalizations documenting matching information for the following data elements were considered to be the same person: date of birth, first four letters of the last name, and first two letters of the first name. Again, the earliest hospitalization documenting the condition of interest was retained over hospitalizations that occurred earlier in the discharge year but that did not document the condition of interest. For patients missing social security number or date of birth, first name or last name, hospitalization records were retained for analysis and not subject to de-duplication. Data were analyzed as described above

using datasets restricting inpatient hospitalizations to document only one hospitalization per person per year.

There are several limitations to the analyses presented. First, the percentage of persons with HCV documented in inpatient hospitalization or ED visit data should be interpreted as the minimum percentage of persons with HCV who are hospitalized as these hospitalizations only represent hospitalizations where HCV testing was performed or noted as a diagnosis. Some hospitalizations of HCV-infected persons may not have identified or recorded their HCV infection. Second, because identifying information regarding social security number was used when possible to de-duplicate datasets and restrict the inpatient dataset for each year of hospital discharge data to contain only one record per person and name and date of birth was used for hospitalizations without social security number, there is the potential that de-duplication did not identify all individuals who were the same. For instance, if a person was hospitalized with their social security number documented in some hospitalizations and without in others, they may exist in the de-duplicated dataset up to two times. Further, because a shortened version of name and date of birth was used to de-duplicate some records, there is the potential for false matches to be identified and for persons who are not duplicates to be removed as duplicates. There is also the potential that persons not subject to de-duplication due to missing data on social security number and name or date of birth were not removed as duplicate records as they were not compared to other records where their name was listed. Resources to de-duplicate were limited to the information available and documented in hospitalization data, therefore this strategy of de-duplication was at a level sophisticated enough to remove most duplicate hospitalizations without the propensity for false matches in a large proportion of individuals.

Arkansas Vital Records: Death Certificates

The Health Statistics Branch at ADH retains death certificate data for deaths occurring among Arkansans since 1881. For the purposes of this project, a SAS dataset containing death certificate data on all Arkansans who died during the years 1999 – 2012 was obtained. SAS 9.3 was used to query multiple cause of death codes. Multiple cause of death codes represent all causes of death listed on parts I and II of death certificates. In all analyses presented, the multiple causes of death are referred to as the cause or contributing condition to death and include the immediate cause (the final disease or condition resulting in death), the underlying cause (disease or injury that initiated the events resulting in death), and up to two other causes within the chain of events leading to death listed in Part I of the death certificate along with any significant conditions contributing to death listed in Part II of the death certificate. Further, several analyses present data only on the underlying cause of death, and are indicated as such in the titles of figures and tables. All causes or conditions contributing to death are coded using the *International Classification of Diseases, Tenth Revision* (ICD-10). Each section presented above lists ICD-10 codes queried in data tables and figures.

Crude mortality rates were calculated by dividing the number of cases by the population of Arkansas for each year of analysis. Age-adjusted rates were calculated by direct standardization of crude rates to the 2000 standard U.S. population and 95% confidence

intervals were calculated using methods to estimate variance from the Poisson distribution via methods adapted from *Healthy People 2010*[32,55]. Further, methods from Ly et al. were adapted to assess change over time in age-adjusted rates using linear regression and in the percentage of total deaths documenting conditions of interest using the Cochran-Armitage test for trend. Pearson and Spearman correction coefficients are also presented to demonstrate the direction of trends among percentages of deaths documenting conditions of interest over time, whereby positive coefficients indicate an increasing trend and negative coefficients indicate a decreasing trend. Regression and trend statistics were considered statistically significant at the 95% confidence level ($\alpha \leq 0.05$). Frequency tables and figures were created using Microsoft Excel. Notably, events occurring at a frequency of less than five cases are not reportable by ADH policy. Data are suppressed or collapsed into larger categories in these instances.

Several limitations apply to analyses using death certificate data. First, HCV is known to be under-reported on death certificates[39]. A recent study by Mahajan et al. demonstrated that HCV was documented on only 19% of death certificates of persons known to have HCV-infection who died of any cause and only increased to documentation on 30% of death certificates when persons died of a liver disease that was likely related to HCV-infection[39]. The analyses presented likely represent only a fraction of the total number of HCV-related deaths. Many persons dying of HCV-related causes may also have undiagnosed HCV-infection, since HCV is known to be diagnosed in only 45% – 85% of persons living with infection[2]. Finally, causes of death listed on death certificates may not fully represent all causes related to an individual's death as they are often completed by persons using limited information to complete death certificates and with little training on how to complete them[57].

Electronic HIV/AIDS Reporting System (eHARS)

Data from the Electronic HIV/AIDS Reporting System (eHARS) contains information on all persons ever diagnosed with HIV-infection in the state of Arkansas and was used to identify persons living with HIV and HCV coinfection. On May 1, 2014, a dataset of all persons ever diagnosed with HIV in the state of Arkansas was obtained from the STI/HIV/Hepatitis C/Tuberculosis Section at the Arkansas Department of Health. Individuals with confirmed HIV-infection (i.e. diagnosed with adult HIV or AIDS or pediatric HIV or AIDS with a definitive or presumptive-positive HIV-positive laboratory test result and an eHARS record flagged as active, warning, or missing some fields[58]), and who had at least a last name on file in eHARS were eligible to be matched to an HCV dataset from NEDSS containing persons with acute or chronic HCV also obtained on May 1, 2014. Persons electronically recorded in NEDSS with HCV infection are discussed above in the Arkansas Hepatitis C Surveillance Data section of Appendix A.

Link Plus software, a probabilistic matching tool created by CDC's National Program of Cancer Registries was used to identify HIV/HCV coinfected individuals documented in the HIV and HCV registries. Link Plus analyzes datasets from two registries and assigns scores that indicate the probability of a true match, with higher scores indicative of an increasingly high likelihood that matches represent the same person listed among the two datasets. A dataset containing 9,390 HIV-infected and 4,851 HCV-infected persons were matched using Link Plus. Matches were

identified by Link Plus using information on each person's name and date of birth. Matches scoring above 14 were accepted. Potential matches scoring between 10 – <14 were reviewed manually and accepted if at least one of the following criteria matched: address, race, sex, or middle name and the match could not be disproven by internet search of the person's name. Potential matches scoring 2 – <10 were reviewed using procedures for potential matches scoring 10 – <14 if any of the following criteria were met: same first letter of first name, same first two letters of last name, same month, day, or year of birth, or same month or day of birth if month and day were potentially switched in one registry.

A total of 95 matches were identified (81 scored >14 and all were accepted, 34 scored 10 – <14 and 12 were accepted, 205 scored 2 – <10 and none were accepted, and 2 were identified as HIV-positive in the HCV registry but did not match to a record in eHARS). SAS 9.3 was used to analyze and create frequency tables of coinfected individuals.

Several limitations apply to this analysis. First, because the HCV-registry does not contain information on every Arkansan living with HCV-infection, the 95 HIV/HCV coinfected persons identified in this analysis vastly under-estimate the total number of persons. Because the prevalence of HCV among HIV-infected persons is known to be approximately 25%[44] and approximately 6,025 persons were documented in eHARS as living with HIV-infection in Arkansas as of the time of this analysis (May 1, 2014), an estimated 1,506 persons are living with HIV/HCV coinfection in Arkansas. This analysis therefore represents only 6.3% of coinfected persons. Further, eHARS serves as the most complete data source documenting all HIV-infected persons in Arkansas; however, it likely underestimates the true number of Arkansans living with HIV-infection due to under-reporting by physicians and laboratories. Additionally, an estimated 15.8% of persons with HIV-infection in the US at the end of 2010 were unaware of their infection[59], meaning that there are likely Arkansans with undiagnosed HIV who are not documented in eHARS or included in the calculations presented.