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Hepatitis B testing, care linkage, and vaccination coverage within a registry of hepatitis C infected patients

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ABSTRACT

Background: Hepatitis B virus (HBV) infection testing among persons with hepatitis C virus (HCV) infection is necessary to appropriately care for these patients, yet uptake of HBV testing and vaccination in this population is suboptimal.
Methods: In a retrospective cohort analysis, we describe the prevalence of hepatitis B testing, linkage to hepatitis B care, and hepatitis B vaccination in patients with HCV infection within a large urban safety-net health system. Using a registry of HCV-infected patients with patient-level electronic health record data, that included demographic, clinical, and laboratory information from 2004 to 2016 from Grady Health System in Atlanta, GA, we describe (1) The prevalence of hepatitis B testing (hepatitis B surface antigen [HBsAg], core antibody [anti-HBc], surface antibody [anti-HBs]); (2) The proportion of HBsAg-positive persons receiving HBV DNA and e-antigen (HBeAg) as indicators for linkage to hepatitis B-directed care; and (3) The proportion of persons receiving hepatitis B vaccine.
Results: Of 4224 HCV-infected patients, 3629 (86%) had test results for HBsAg and 43 (1.2%) were HBsAg-positive. Of 2342 (55%) with test results for all three HBV serological markers, median age was 60 years, 67% were male, and 83% were African-American, 789 (34%) anti-HBc positive only, 678 (29%) anti-HBc/anti-HBs positive, 190 (8.1%) anti-HBs positive only, and 642 (27%) were HBV-susceptible. Of HBsAg-positive patients, 21% received HBV DNA and 40% HBeAg testing. The proportion of HBV-susceptible patients receiving at least 1 dose of hepatitis B vaccine was 322/642 (50%).
Conclusions: In a large cohort of HCV-infected patients, we found a high prevalence of current or past HBV infection, but there were gaps in complete hepatitis B testing, hepatitis B-directed care, and hepatitis B vaccination. Strategies are needed to increase hepatitis B testing, linkage to care, and administration of the hepatitis B vaccine for HCV-infected persons in this healthcare system.

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1. Introduction

Millions of people are living with chronic viral hepatitis in the United States; about 2.4 million were living with chronic hepatitis C virus (HCV) infection in 2016, and 847,000 were living with chronic hepatitis B virus (HBV) infection in 2012 [1,2]. Chronic hepatitis B and C are leading causes of premature death from end-stage liver disease, cirrhosis and hepatocellular carcinoma in the United States [3,4]. HCV and HBV share similar modes of transmission, an estimated 1–2% of patients with HCV-infection are co-infected with HBV [5,6]. In order to identify patients who would benefit most from hepatitis B vaccination, HBV surface antibody (anti-HBs) is necessary, though one study showed only 43% of HCV-infected persons were tested [6]. Furthermore, the hepatitis

Abbreviations: HCV, hepatitis C virus; HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen; anti-HBc, hepatitis B core antibody; anti-HBs, hepatitis B surface antibody; HBeAg, hepatitis B e antigen; HBV DNA, hepatitis B viral load.

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B vaccination rate among persons with chronic liver disease was 30% in 2015 [7].

Complete HBV screening includes 3 HBV seromarkers: HBV total core antibody (anti-HBc), HBV surface antigen (HBsAg), and anti-HBs [8]. HBV status according to these seromarkers is important to understand clinical management for the patient. HBsAg-positive persons are infected with HBV and should be evaluated for antiviral treatment. Anti-HBs-positive persons can be reassured that they are immune to HBV. Anti-HBc-positive persons should receive counseling that they have been exposed to HBV previously, and a small proportion of anti-HBc-positive persons without a detectable HBsAg may have occult HBV infection [9]. Persons who are negative for all three seromarkers are susceptible. HBV vaccination is recommended for all susceptible individuals living with chronic HCV-infection [10,11]. However, prior studies have shown that receipt of hepatitis B vaccination in HCV-infected patients is low [12,13].

In HBV/HCV coinfection, cases of HBV reactivation have been reported. As a result, clinical guidelines state that all patients initiating HCV DAA therapy should receive HBV screening [10]. Because of the risk of HBV reactivation, HBsAg-positive patients should be considered for evaluation for antiviral treatment with a test for HBV DNA [10]. Guidance is not clear for persons with occult HBV infection, but it may be reasonable to also monitor them for HBV reactivation.

Grady Health System in Atlanta, GA has a primary care-based liver clinic that provides hepatitis C care and treatment to an underserved population. The Grady Liver Clinic supports routine HBV screening on all HCV-infected patients and vaccination of HCV infected patients who are susceptible to HBV infection. Using their electronic health record (EHR), a registry of HCV-infected patients was created [14]. The objective of this report is to describe the proportion of persons receiving hepatitis B testing and vaccination in a registry of HCV-infected patients within a large urban safety-net health system.

2. Methods

2.1. Study sample

Grady Memorial Hospital is Atlanta's safety-net health system where an underserved population is able to access longitudinal healthcare. Patient-level data were abstracted from Grady Health System's EHR (Epic Systems Corporation, Madison, WI) on August 24, 2016 to create a HCV patient registry in order to evaluate the HCV cure cascade. The inclusion criteria for the registry were the patient was alive and had at least one of the following laboratory test results: (1) reactive anti-HCV or (2) detectable HCV RNA (>12 IU/mL) or (3) HCV genotype result. For the purposes of this analysis, patients were considered HCV-infected if they had a detectable HCV RNA or HCV genotype result. There was no date restriction during the data abstraction, and the registry included information from May 2004 through August 2016. Demographic characteristics (age, gender, race/ethnicity, and health insurance status) and laboratory information were abstracted. Laboratory information included HBsAg, total anti-HBc, anti-HBs, HBV DNA, hepatitis B e antigen (HBeAg), HIV, and hemoglobin A1c (HgA1c). Patients were grouped into five HBV clinical statuses based on HBV serologic profile: HBsAg-positive, anti-HBc positive only, anti-HBc positive/anti-HBs positive, anti-HBs positive only, and negative for all three markers (HBV-susceptible). Information regarding date of each vaccine administration was available for hepatitis B vaccination for patients in the registry. Comorbidities were ascertained through presence on the encounter list (named condition billed for during a visit) or problem list (clinician manually enters problems in the EHR) or by laboratory data or weight measurements where available. HIV was determined by presence of a positive laboratory result, obesity (body mass index (BMI $\geq$ 30) was calculated using the most recent documented height and weight, diabetes was determined by HgA1c $\geq$ 7% or diabetes on encounter/problem list when HgA1c data was missing, and other comorbidities (alcohol abuse, chronic kidney disease, tobacco use, liver cirrhosis, depression) were determined by encounter/problem list.

2.2. Statistical analysis

First, we performed a descriptive analysis of demographic characteristics, health insurance status, and comorbidities according to each HBV clinical status; and compared each HBV clinical status to patients testing negative for all 3 HBV seromarkers. Second, we described the proportion of patients within the HBsAg-positive or anti-HBc-positive only clinical status receiving hepatitis B-directed care laboratory tests, as measured by HBV DNA or HBeAg. Third, we described the proportion receiving partial (1 or 2 doses) and complete (3 or more doses) hepatitis B vaccination for hepatitis B-susceptible patients.

All analyses were conducted with SAS version 9.4 (SAS institute, Cary, NC). Comparisons were performed using chi squared analysis with a P-value threshold of < 0.05.

2.3. Ethical considerations

The analysis was determined to be human subjects research exempt from Institutional Review Board review by the Centers for Disease Control and Prevention and the IRB at Emory University (IRB #00103807).

3. Results

Of 4224 HCV-infected patients identified in the registry, 3629 (85.9%) had test results for HBsAg and 43 (1.2%) were HBsAg-positive. Of 2342 (55.4%) with test results for all three HBV serological markers, 789 (33.7%) were anti-HBc-positive only, 678 (28.9%) were anti-HBc/anti-HBs-positive, 190 (8.1%) were anti-HBs-positive only, and 642 (27.4%) were HBV susceptible (Fig. 1). Of 2342 with complete HBV testing results, the median age was 60 years, 67% were male, and 84% were Black. Other notable demographic and clinical characteristics are described in Table 1.

Regarding laboratory tests reflecting hepatitis B-directed care of HBsAg-positive patients, 17 (40%) and 9 (21%) received HBeAg testing and HBV DNA testing, respectively (Table 2). Of anti-HBc-positive only patients, 64 (8%) and 148 (19%) received HBeAg testing or HBV DNA testing, respectively.

The proportion of HBV-susceptible patients with documentation of receipt of at least 1 dose of hepatitis B vaccine was 322 (50%), and 163 (25%) completed the three dose series (Fig. 2). Among the 1,882 with incomplete HBV seromarker testing, 467 (25%) received at least 1 dose of hepatitis B vaccine, and 222 (12%) completed the three dose series.

4. Discussion

Using a registry of 4224 HCV-infected patients receiving care in a large, urban, safety-net hospital, we found 2342 (55%) received complete hepatitis B testing with all three HBV seromarkers, and 1467 (63%) had evidence of previous HBV infection (anti-HBc-positive, either alone or in conjunction with anti-HBs). Of 43 (1.2%) with serologic evidence of current infection (HBsAg-positive), <39% of HBV/HCV co-infected patients had evidence of

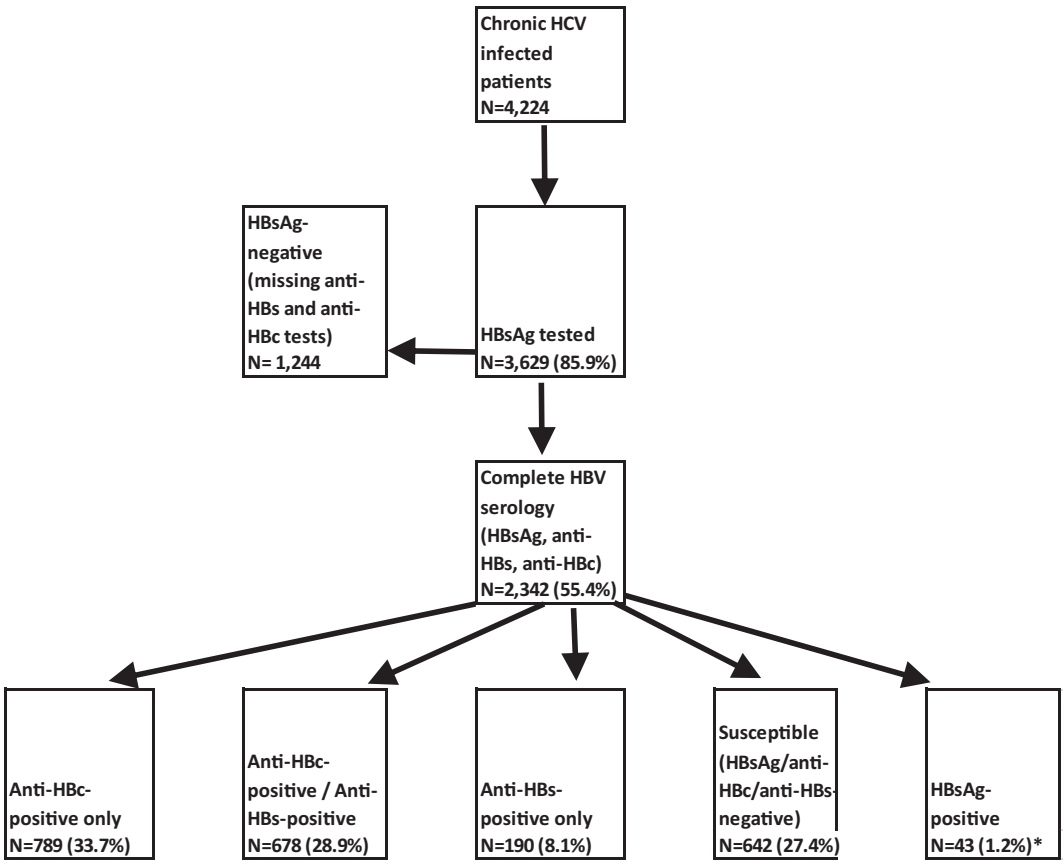

Fig. 1. Prevalence of hepatitis B serological markers among chronic HCV infected patients in Grady Health System, 2004–2016. (Footnotes: *Of 3629 who received HBsAg testing. Abbreviations: HCV: hepatitis C virus, Chronic HCV infected patients: patients with a detectable HCV RNA and/or HCV genotype result available, HBsAg: hepatitis B surface antigen; anti-HBc: hepatitis B core antibody; anti-HBs: hepatitis B surface antibody).

receiving hepatitis B-directed care laboratory tests (HBV DNA or HBeAg). Half (50%) of HBV-susceptible persons did not have documentation of hepatitis B vaccination.

HCV and HBV share common modes of transmission, and persons with HBV/HCV coinfection are at increased risk of liver-related complications [15]. While our results showed that 86% of HCV-infected patients were tested for HBsAg, only 55% received complete hepatitis B seromarker testing. Persons with HCV infection should be screened for hepatitis B with all three seromarkers: HBsAg, anti-HBs, and anti-HBc [8,10] to best identify persons who would benefit from hepatitis B vaccination. Other studies have identified a gap in complete HBV seromarker testing. In an analysis between 2014 through 2016 of a cohort of 14,099 hepatitis C-diagnosed patients in the United States, 75% were HBsAg tested and 1.1% were HBsAg-positive; however, only 38% and 43% received anti-HBc and anti-HBs testing, respectively, which may have missed persons who could have benefited from hepatitis B vaccination [6].

All patients with chronic HBV infection (HBsAg-positive for >6 months) require regular monitoring of liver aminotransferase and HBV DNA levels [16,18] to identify the approximately 20%–40% that will require treatment [16,17]. The AASLD recommends that those with elevated HBV DNA (>20,000 IU/mL) should be treated [18], especially those who are co-infected with HCV. This is because patients co-infected with HBV/HCV are at higher risk of progressing to liver cirrhosis and/or hepatocellular carcinoma [15]. Further, cases of HBV reactivation have been reported among patients receiving direct-acting antivirals for HCV infection although it is a rare outcome [19,20]. Reactivation can result in hepatocellular injury, fulminant hepatitis, liver failure, and death [21]. Thus, persons who test HBsAg-positive, and possibly those who test anti-HBc-positive, should receive HBeAg and HBV DNA testing to monitor for reactivation and need for HBV antiviral therapy [8,18]. Our results identified a gap in care as a minority of HBsAg-positive patients with HCV coinfection received HBV DNA and/or HBeAg testing.

Testing for hepatitis B with all three serologic markers is necessary to identify persons susceptible to HBV-infection that could benefit from hepatitis B vaccination [8]. CDC recommends that all patients with chronic liver disease, including HCV-infection, receive hepatitis B vaccine [22]. Hepatitis B vaccine is the most effective measure to prevent HBV infection and its complications [11]. The vaccine confers protection in>90% of adults who receive the complete vaccine series [23], and immunity lasts at least 3 decades [24]. Patients with chronic liver disease (including HCV-infection) should be vaccinated to reduce morbidity and mortality associated with viral hepatitis [22]. Hepatitis B testing should not be a barrier to vaccination, and thus, can be done at the same time that a dose of hepatitis B vaccine is given [22]. Our results showed that only 25% of HBV susceptible patients received a complete hepatitis B vaccine series. This is consistent with prior studies. Data from the National Health Interview Survey showed only 25% of all adults aged $\geq$ 19 years and 29% of adults with chronic liver disease received the complete three-dose hepatitis B vaccine series [7,25]. Strategies are needed to overcome this gap.

There are a few potential causes of gaps identified in hepatitis B testing, linkage to care and vaccination in this health system. First, our data indicated that 45% of patients did not receive complete HBV seromarker testing. This could be due to lack of provider awareness of testing recommendations, forgetting to order all 3

Table 1
Demographic and comorbidities by HBV state among chronic HCV infected patients attending Grady Health System.

	All HCV-Infected patients	HBsAg-positive	Anti-HBc-positive	Anti-HBc/Anti-HBs-Positive	Anti-HBs positive	HBV Susceptible
n	4224 (%)	43 (%)	789 (%)	678 (%)	190 (%)	642 (%)
Sex						
Male	2840 (67)	38 (88)*	593 (75)*	463 (68)*	113 (59)	371(58)
Female	1383 (33)	5 (12)*	196 (25)*	215 (32)*	77 (41)	271 (42)
Missing	1 (<1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Age						
18–30 years	49 (1)	1(2)	1 (<1)	0 (0)	15 (8)*	5(<1)
31–49 years	422 (10)	12 (28)	48 (6)*	67 (10)	39 (21)*	79 (12)
50–74 years	3651 (86)	30 (70)	727 (92)*	597 (88)	132 (69)*	541 (84)
>74 years	100 (2)	0 (0)	13 (1)	14 (2)	4 (2)	17 (3)
Missing	2 (<1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Race						
White	616 (15)	8 (19)	74 (9)*	89(13)	35 (18)	105 (16)
Black	3293 (78)	32 (74)	684 (87)*	562 (83)	147 (77)	520 (81)
Other (Asian, API/AI, Hispanic)	64 (2)	3(7)	12(2)	20(3)	7(4)	10(2)
Missing	251 (6)	0(0)	19(2)	7(1)	1(<1)	7(1)
Insurance						
Uninsured	606 (14)	1 (2)*	87 (11)*	95 (14)*	34 (18)	136 (21)
Public (Medicaid, Medicare)	2364 (56)	30 (70)*	496(63)*	405 (60)*	103 (54)	320 (50)
Private	321 (8)	4 (9)	60 (8)	43 (6)	15 (8)	54 (8)
Unknown	933 (22)	8 (19)	146 (18)	135 (20)	38 (20)	132 (21)
Co-morbidities						
HIV-infected	284 (7)	7 (16)*	52 (7)	77 (11)*	24 (13)*	38 (6)
Diabetes	1038 (25)	5 (12)	186 (24)	153 (23)	35(18)*	168 (26)
Obesity (BMI $\geq$ 30)	858 (20)	4 (9)	152 (19)*	126 (19)*	40 (21)	165 (26)
Depression	1189 (28)	13 (30)	200 (25)	202 (30)	72 (38)*	172 (27)
Chronic kidney disease	796 (19)	9 (18)	156 (20)	156 (23)	38 (20)	116 (18)
Alcohol abuse	774 (18)	4 (9)	172 (22)	130 (19)	38 (20)	117(18)
Tobacco use	2062 (49)	16 (37)*	422 (53)*	359(53)*	116 (61)	387 (60)

HCV: hepatitis C virus.
Chronic HCV infected patients: patients with a detectable HCV RNA and/or HCV genotype result available.
HBsAg: hepatitis B surface antigen; anti-HBc: hepatitis B core antibody; anti-HBs: hepatitis B surface antibody; HBV susceptible: tested negative to all 3 HBV seromarkers (HBsAg, anti-HBc, anti-HBs).
BMI: body mass index.
98% of patients with diabetes were determined with HgA1c values, 19 patients received a diabetes designation through diabetes listed on the encounter list or problem list.
* P-Value < 0.05 compared to susceptible HBV status.

Table 2
Hepatitis B directed care by each HBV status among chronic HCV infected patients in Grady Health System.

	HBsAg-positive	Anti-HBc-positive only
n	43 (%)	789(%)
HBeAg Performed	17 (40)	64 (8)
HBV DNA Performed*	9 (21)	148 (19)

HCV: hepatitis C virus.
Chronic HCV infected patients: patients with a detectable HCV RNA and/or HCV genotype result available.
HBsAg: hepatitis B surface antigen; anti-HBc: hepatitis B core antibody; HBeAg: Hepatitis B e Antigen.
* Routine testing for HBV DNA among isolated anti-HBc positive patients started in 2015 after reports of HBV reactivation among patients with HCV treated with DAA were published in the literature.

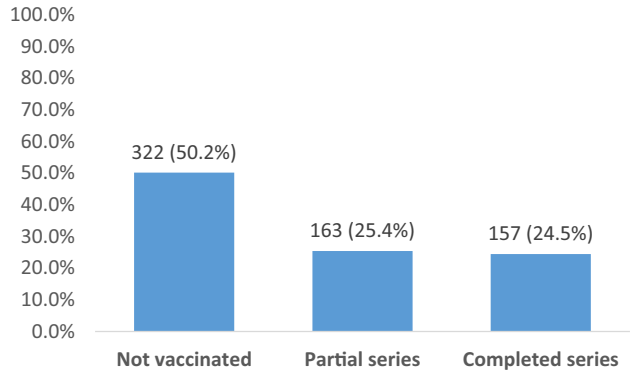

Fig. 2. Hepatitis B vaccine receipt among 642 chronic HCV infected patients HBV susceptible* to hepatitis B virus infection in Grady Health System, 2004–2016. (Footnote: *Of persons with negative HBV serologic markers (HBsAg-negative, anti-HBs-negative, and anti-HBc-negative)).

HBV seromarkers, or due to missing data as some of the testing may have been conducted at an outside facility. Fortunately, our data did not identify racial disparities or lack of insurance or having public insurance as a barrier to receipt of complete HBV testing. Further, patients with HIV, chronic kidney disease, alcohol abuse, or tobacco use had higher rates of receiving complete HBV testing which signals more complete care in these populations. Second, primary care and specialty services may operate in silos in this health system; as a result, positive tests do not always result in liver directed care when indicated. For instance, the gastroenterology department has been caring for patients with chronic HBV infection, whereas the liver clinic cares for patients with chronic HCV infection, and other health matters are managed by a separate primary care provider. Third, hepatitis B vaccination required 3-doses over 6 months which may have led to missed orders in subsequent visits.

To overcome barriers to hepatitis B testing and vaccination, in 2015 the primary-care based liver clinic at Grady implemented an EHR template note with a section for the clinician to complete during the patient encounter regarding hepatitis B diagnosis and vaccination status. In addition, the clinical pharmacists have taken a role in updating vaccination status in the EHR immunization sec-

tion during follow up visits. However, if a patient received a hepatitis B vaccination outside of Grady, and the provider noted this in the EHR note, information may not have been abstracted from the EHR, thus underestimating vaccine coverage in the registry. Other interventions that can be used to overcome gaps include EHR prompts for testing and vaccination, EHR standing orders for all 3 HBV seromarkers, provider education and feedback, and colocation of testing services for at risk populations [26].

This analysis was subject to limitations. The HCV registry had missing and incomplete data related to demographics, laboratory results, comorbidities, and vaccination status. There may have been misclassification of comorbidities as they were ascertained from encounter or problem lists in the EHR. In addition, data pre-2010 may be less complete since it was from a legacy EHR system with incomplete information, however an analysis of HCV-related laboratory data dates showed that more than 70% of the data came from the post 2010 time period. Further, it was not possible to ascertain a specific date for which a patient entered the health system, thus limiting our analysis of various interventions. In addition, 45% of HCV infected patients did not have complete HBV seromarker testing data, thus, limiting the completeness of our results, including our assessment of appropriate hepatitis B vaccination rates in HBV susceptible patients. However, despite this limitation, we still had a sizable sample to analyze. Finally, the analysis applies to a single health system and may not be generalizable to other health systems.

5. Conclusions

Using an EHR registry of HCV-infected patients, we identified gaps in hepatitis B testing and prevention in that population. Only 55% of HCV infected patients received complete HBV seromarker testing, less than 40% of patients co-infected with HBV/HCV had laboratory evidence of receiving hepatitis B directed care, and only 50% of HBV susceptible patients received at least one dose of the three-dose hepatitis B vaccine series. Strategies are needed to increase hepatitis B testing, linkage to hepatitis B-directed care of HBV/HCV co-infected patients, and to increase uptake in hepatitis B vaccination for HCV-infected patients within the Grady Health System.

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Conflict of interest statement

Aaron M. Harris: No conflicts to report.
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Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

References

[1] Hofmeister MG, Rosenthal EM, Barker LK, Rosenberg ES, Barranco MA, Hall EW, et al. Estimating prevalence of hepatitis C virus infection in the United States, 2013–2016. Hepatology 2018.
[2] Roberts H, Kruszon-Moran D, Ly KN, Hughes E, Iqbal K, Jiles RB, et al. Prevalence of chronic hepatitis B virus (HBV) infection in US households: national health and nutrition examination survey (NHANES), 1988–2012. Hepatology 2015.
[3] Allison RD, Tong X, Moorman AC, Ly KN, Rupp L, Xu F, et al. Increased incidence of cancer and cancer-related mortality among persons with chronic hepatitis C infection, 2006–2010. J Hepatol 2015;63:822–8.
[4] Ly KN, Hughes EM, Jiles RB, Holmberg SD. Rising mortality associated with hepatitis C virus in the United States, 2003–2013. Clin Infect Dis 2016;62:1287–8.
[5] Tyson GL, Kramer JR, Duan Z, Davila JA, Richardson PA, El-Serag HB. Prevalence and predictors of hepatitis B virus coinfection in a United States cohort of hepatitis C virus-infected patients. Hepatology 2013;58:538–45.
[6] Moorman AC, Xing J, Rupp LB, Gordon SC, Spradling PR, Boscarino JA, et al. Hepatitis B virus infection and hepatitis C virus treatment in a large cohort of hepatitis C-infected patients in the United States. Gastroenterology 2018;154:754–8.
[7] Yue X, Black CL, O'Halloran A, Lu PJ, Williams WW, Nelson NP. Hepatitis A and hepatitis B vaccination coverage among adults with chronic liver disease. Vaccine 2018;36:1183–9.
[8] Abara WE, Qaseem A, Schillie S, McMahon BJ, Harris AM. Hepatitis B vaccination, screening, and linkage to care: Best practice advice from the American College of Physicians and the Centers for Disease Control and Prevention. Ann Intern Med 2017;167:794–804. https://www.ncbi.nlm.nih.gov/pubmed/29159414.
[9] Ponde RA, Cardoso DD, Ferro MO. The underlying mechanisms for the 'anti-HBc alone' serological profile. Arch Virol 2010;155:149–58.
[10] AASLD-IDSA. Recommendations for testing, managing, and treating hepatitis C. https://www.hcvguidelines.org/.
[11] Schillie S, Vellozzi C, Reingold A, Harris A, Haber P, Ward JW, Nelson NP. Prevention of hepatitis B virus infection in the United States: Recommendations of the advisory committee on immunization practices. MMWR Recomm Rep 2018;67:1–31. https://www.ncbi.nlm.nih.gov/pubmed/29939980.
[12] Hachem CY, Kramer JR, Kanwal F, El-Serag HB. Hepatitis vaccination in patients with hepatitis C: practice and validation of codes at a large veterans administration medical centre. Aliment Pharmacol Ther 2008;28:1078–87.
[13] Jacobs RJ, Meyerhoff AS, Saab S. Immunization needs of chronic liver disease patients seen in primary care versus specialist settings. Dig Dis Sci 2005;50:1525–31.
[14] Miller L. Utilization of an Electronic Medical Record to Evaluate the Hepatitis C Care Cascade in a Large, Urban Health System, 2004-2016. Hepatology; 66: 537A; 2017.
[15] Kruse RL, Kramer JR, Tyson GL, Duan Z, Chen L, El-Serag HB, et al. Clinical outcomes of hepatitis B virus coinfection in a United States cohort of hepatitis C virus-infected patients. Hepatology 2014;60:1871–8.
[16] Cohen C, Holmberg S, McMahon B, Block J, Brosgart C, Gish R, et al. Is chronic hepatitis B being undertreated in the United States? J Viral Hepatitis 2011;18:377–83.
[17] Lok AS, McMahon BJ. Chronic hepatitis B. Hepatology 2007;45:507–39.
[18] Terrault NA, Lok ASF, McMahon BJ, Chang KM, Hwang JP, Jonas MM, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. Hepatology 2018;67:1560–99.
[19] Bersoff-Matcha SJ, Cao K, Jason M, Ajao A, Jones SC, Meyer T, et al. Virus Reactivation associated with direct-acting antiviral therapy for chronic hepatitis C virus: a review of cases reported to the U.S. food and drug administration adverse event reporting system. Ann Intern Med. 2017;166:792–8.
[20] Wang C, Ji D, Chen J, Shao Q, Li B, Liu J, et al. Hepatitis due to reactivation of hepatitis B virus in endemic areas among patients with hepatitis C treated with direct-acting antiviral agents. Clin Gastroenterol Hepatol 2017;15:132–6.

[21] Lok AS, Ward JW, Perrillo RP, McMahon BJ, Liang TJ. Reactivation of hepatitis B during immunosuppressive therapy: potentially fatal yet preventable. Ann Intern Med 2012;156:743–5.
[22] Jackson S, Lentino J, Kopp J, Murray L, Ellison W, Rhee M, et al. Immunogenicity of a two-dose investigational hepatitis B vaccine, HBsAg-1018, using a toll-like receptor 9 agonist adjuvant compared with a licensed hepatitis B vaccine in adults. Vaccine 2018;36:668–74.
[23] Bruce MG, Bruden D, Hurlburt D, Zanis C, Thompson G, Rea L, et al. Antibody levels and protection after hepatitis B vaccine: results of a 30-year follow-up study and response to a booster dose. J Infect Dis 2016;214:16–22.
[24] Williams WW, Lu PJ, O'Halloran A, Kim DK, Grohskopf LA, Pilishvili T, et al. Surveillance of vaccination coverage among adult populations - United States, 2015. MMWR Surveill Summ 2017;66:1–28.
[25] Hsu L, Bowlus CL, Stewart SL, Nguyen TT, Dang J, Chan B, et al. Electronic messages increase hepatitis B screening in at-risk Asian American patients: a randomized, controlled trial. Dig Dis Sci 2013;58:807–14.