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Prevalence of Hepatitis B Virus, Hepatitis C Virus, and HIV Infection Among Patients With Newly Diagnosed Cancer From Academic and Community Oncology Practices

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IMPORTANCE Universal screening of patients with newly diagnosed cancer for hepatitis B virus (HBV), hepatitis C virus (HCV), and HIV is not routine in oncology practice, and experts disagree about whether universal screening should be performed.

OBJECTIVE To estimate the prevalence of HBV, HCV, and HIV infection among persons with newly diagnosed cancer.

DESIGN, SETTING, AND PARTICIPANTS Multicenter prospective cohort study of patients with newly diagnosed cancer (ie, identified within 120 days of cancer diagnosis) at 9 academic and 9 community oncology institutions affiliated with SWOG (formerly the Southwest Oncology Group) Cancer Research Network, a member of the National Clinical Trials Network, with enrollment from August 29, 2013, through February 15, 2017. The data analysis was conducted using data available through August 17, 2017.

MAIN OUTCOMES AND MEASURES The accrual goal was 3000 patients and the primary end point was the presence of HBV infection (previous or chronic), HCV infection, or HIV infection at enrollment. Patients with previous knowledge of infection as well as patients with unknown viral viral status were evaluated.

RESULTS Of 3092 registered patients, 3051 were eligible and evaluable. Median (range) age was 60.6 (18.2-93.7) years, 1842 (60.4%) were female, 553 (18.1%) were black, and 558 (18.3%) were Hispanic ethnicity. Screened patients had similar clinical and demographic characteristics compared with those registered. The observed infection rate for previous HBV infection was 6.5% (95% CI, 5.6%-7.4%; n = 197 of 3050 patients); chronic HBV, 0.6% (95% CI, 0.4%-1.0%; n = 19 of 3050 patients); HCV, 2.4% (95% CI, 1.9%-3.0%; n = 71 of 2990 patients); and HIV, 1.1% (95% CI, 0.8%-1.6%; n = 34 of 3045). Among those with viral infections, 8 patients with chronic HBV (42.1%; 95% CI, 20.3%-66.5%), 22 patients with HCV (31.0%; 95% CI, 20.5%-43.1%), and 2 patients with HIV (5.9%; 95% CI, 0.7%-19.7%) were newly diagnosed through the study. Among patients with infections, 4 patients with chronic HBV (21.1%; 95% CI, 6.1%-45.6%), 23 patients with HCV (32.4%; 95% CI, 21.8%-44.5%), and 7 patients with HIV (20.6%; 95% CI, 8.7%-37.9%) had no identifiable risk factors.

CONCLUSIONS AND RELEVANCE Results of this study found that a substantial proportion of patients with newly diagnosed cancer and concurrent HBV or HCV are unaware of their viral infection at the time of cancer diagnosis, and many had no identifiable risk factors for infection. Screening patients with cancer to identify HBV and HCV infection before starting treatment may be warranted to prevent viral reactivation and adverse clinical outcomes. The low rate of undiagnosed HIV infection may not support universal screening of newly diagnosed cancer patients.

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Supplemental content

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Universal screening of patients with newly diagnosed cancer for hepatitis B virus (HBV), hepatitis C virus (HCV), and HIV is not routine in oncology practice, and experts disagree about whether screening should be recommended. Several arguments favor universal screening. Although the US population prevalence rate of previous HBV is estimated to be 4.7%, of chronic HBV to be 0.3%, of HCV to be 1.3%, and of HIV infections to be 0.3%,[1-5] population studies suggest that infections with these viruses are more prevalent among persons who are old enough to have higher rates of cancer.[3,6] Patients with undiagnosed chronic HBV, HCV, and HIV infections pose transmission risks to family members and health care workers.[7-9] In addition, with effective treatments available, not screening for these viruses misses an opportunity to reduce future morbidity associated with these infections and to avoid viral reactivation during treatment, with resulting morbidity and mortality.[10] This may be a particular issue as more patients with cancer are treated with therapies that alter the immune system.

Screening all 1.6 million patients with newly diagnosed cancer in the United States for HBV, HCV, and HIV each year will increase the cost of cancer care and may have low yield and negligible influence on patient outcomes. In populations with a very-low prevalence of infection, the likelihood of false-positive tests increases, leading to additional patient anxiety and possible delays in cancer treatment. Even among those with true-positive tests, potentially harmful delays in cancer treatment might occur, or clinicians might switch to "less toxic" cancer treatments with uncertain effectiveness to avoid potential adverse outcomes such as viral reactivation.[11] Because the true risk of severe adverse events associated with most cancer treatments in persons with latent infections is unknown, the putative benefits of delaying or modifying cancer treatment remain speculative, while the risk that these changes pose to outcomes for patients with newly diagnosed cancer are real.

A major limitation in the debate about universal screening is the fact that the prevalence of these viruses among patients with newly diagnosed cancer is unknown. In addition, in an era with increased emphasis on viral screening in primary care, we do not know the extent to which patients with newly diagnosed cancer are aware of their viral status.[12-14] To better inform these issues and to guide viral screening decisions in practice, we undertook a multicenter prospective cohort study to estimate the prevalence of HBV, HCV, and HIV infection among persons with newly diagnosed cancer. We also sought to characterize prevalence by whether viral infection was previously vs newly diagnosed at the time of testing, by the presenting types of cancer, and by self-reported risk factors for the viruses.

Key Points

Question What is the prevalence of hepatitis B virus, hepatitis C virus, and HIV infection among patients with newly diagnosed cancer?

Findings In this cohort study of 3051 patients with newly diagnosed cancer, infection rates were 6.5% for previous hepatitis B virus, 0.6% for chronic hepatitis B virus, 2.4% for hepatitis C virus, and 1.1% for HIV. Among patients with viral infections, 42.1% of patients with chronic hepatitis B virus, 31.0% of patients with hepatitis C virus, and 5.9% of patients with HIV were newly diagnosed through the study.

Meaning Screening patients with newly diagnosed cancer to identify hepatitis B virus and hepatitis C virus infection before starting treatment may be warranted to prevent viral reactivation and adverse clinical outcomes; universal screening for HIV infection may not be warranted.

Methods

Institutions and Patients

Recruitment occurred in 9 academic and 9 community oncology institutions (representing 41 cancer clinics) affiliated with SWOG (formerly the Southwest Oncology Group) Cancer Research Network, a National Cancer Institute–sponsored cancer clinical trials cooperative group and a member of the National Clinical Trials Network. Patients were required to sign informed consent forms, provided in English or Spanish, or translated into other languages as needed. Institutional review board approval was provided by the Protocol Review Committee of the Cancer Therapy Evaluation Program on August 5, 2013.

Patients were eligible if they were 18 years or older and if they presented for evaluation or treatment of a malignant neoplasm at the clinic within 120 days of initial diagnosis, as confirmed by medical record. Patients were required to be enrolled within 90 days following their first clinic visit. Those patients presenting for second opinions of confirmed new malignant neoplasms were eligible, including those who had started cancer treatment at other facilities. Individuals were not eligible if they were diagnosed with a new malignant neoplasm within the last 5 years, with the exception of basal cell or squamous cell skin cancer, in situ cervical cancer, or in situ breast cancer.

The study protocol (Supplement 1) stipulated that all patients presenting for evaluation or treatment of a new malignant neoplasm (including hematologic) should be invited to be screened for HBV, HCV, and HIV. Previous documentation of testing within 365 days before study registration, either via blood testing results or by providing acceptable viral status documentation, including viral test results or viral load documentation, was also acceptable. Universal screening was not the previous routine at most of the participating clinics.

A run-in phase involving 7 selected sites and 312 patients was conducted to examine the feasibility of study procedures and acceptability to patients. The results of the run-in phase were previously reported.[15] End point data for run-in participants are included in this report.

To determine the representativeness of the sample, we compared patients who were enrolled with all patients who were evaluated for participation in the study. Participating institutions submitted aggregate data about all patients with newly diagnosed cancer, aged 18 years and older, presenting to each registering cancer clinic during enrollment. Data collected included the number of patients who had viral testing and the number of patients who were positive for each virus and type of cancer. Demographic information (age, sex, race,

ethnicity, and type of cancer) were also collected in aggregate to assess generalizability of the registered cohort.

Determination of Viral Status

Patients were defined as positive or negative for previous HBV, chronic HBV, HCV, or HIV based on standard diagnostic criteria for each virus (eTable 1 in Supplement 2). Central review of participating clinics' viral status source documentation was conducted by 2 study investigators (J.P.H. and M.A.K.) for all site-reported positive cases and any cases where individual test results were inconsistent with the site-submitted viral status. A random sample of site-reported negative cases was also reviewed to assess the potential for false-negative reports. Based on this review, it was determined that a central review of all negative cases was not required.

Viral Risk Survey

Enrolled patients completed a survey that included demographic questions and questions pertaining to risk factors for viral hepatitis or HIV. The questions were drawn from the National Health Interview Survey[1] and the Centers for Disease Control and Prevention.[2]

Statistical Considerations

The primary study end point was the presence of previous HBV, chronic HBV, HCV, or HIV infection (positive vs negative result). Rates of each viral infection were calculated, and 95% CIs were generated using binomial estimation. To better reflect national prevalence rates in patients with cancer, we also calculated adjusted estimates for each type of viral infection using Surveillance, Epidemiology, and End Results Program cancer registry data to account for differences between distributions in type of cancer, age (<65 vs >65 years), and race (white vs nonwhite) in the study population vs those of the overall population of patients with cancer in the United States.[16] Viral infection rates were further examined according to whether the infection was previously diagnosed vs newly diagnosed as reported by patients and/or their physician before study testing, by presenting type of cancer, and by self-reported risk factors for each virus.

The prespecified target accrual was 3000 eligible patients, requiring 3061 enrollments to account for an ineligibility estimate of 2.0%. The study was designed to estimate prevalence rates; 3000 patients was sufficient to allow estimation of the upper bound of the CI for the prevalence of each virus to within 25.0% of the observed prevalence estimate (the relative accuracy or relative prevalence) if the true prevalence was 2.5% or higher. The relative accuracy was higher (worse) if the prevalence estimate was lower (42.5% for a prevalence of 1.0% and 64.7% for a prevalence of 0.5%).

Additional secondary objectives included the evaluation of known sociodemographic, clinical, and behavioral factors potentially associated with HBV, HCV, and/or HIV infection. Treatment outcomes at 6 months for viral-positive patients were also examined.

Odds ratios, 95% CIs, and *P* values were derived from Fisher exact test. Comparisons between groups were reported as statistically significant if $P < .05$ using 2-sided tests.

Results

Study Eligibility

Study S1204 (Viral Screening in Newly Diagnosed Cancer Patients) was activated on August 29, 2013, and completed accrual on February 15, 2017. In total, 3092 patients were registered (**Figure 1**), representing 20% of 15 666 patients with newly diagnosed cancer entering the participating clinics during the study period. In addition, registered patients were similar to patients evaluated for participation in the study with respect to demographic factors and type of cancer (eTable 2 in Supplement 2). Forty-one patients were not eligible for analysis (38 patients did not meet trial eligibility criteria, and 3 patients withdrew consent immediately after registration). Thus, 3051 patients had viral testing for at least 1 of the 3 viruses and were considered evaluable, achieving the prespecified accrual goal.

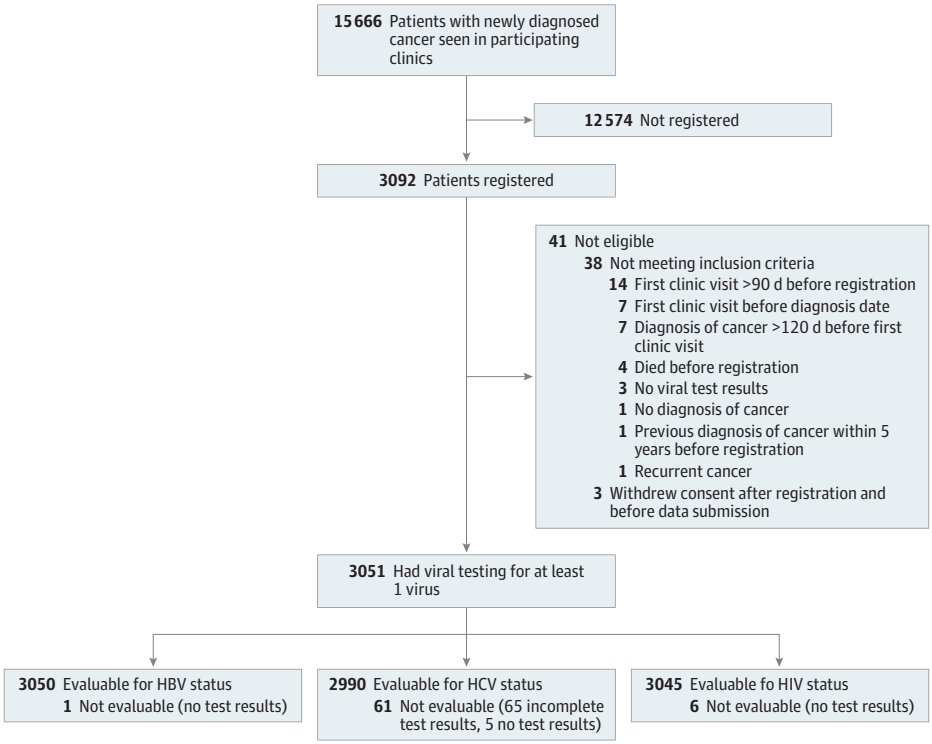
Patient Characteristics

The 3051 patients registered from 14 geographically diverse states included 1096 (35.9%) from the West or Midwest and 1955 (64.1%) from the South or Northeast (**Table**). Of these evaluable patients (median [range] age, 60.6 [18.2-93.7] years), 1842 (60.4%) were female, 553 (18.1%) were black, and 558 (18.3%) were Hispanic ethnicity. The predominant types of cancer were breast (1058 of 3051, [34.7%]), blood/marrow (369 [12.1%]), colorectal (362 [11.9%]), and lung (356 [11.7%]). Compared with a sample of patients with the same types of cancer based on Surveillance, Epidemiology, and End Results Program incidence data[16] (Table 2), the S1204 study sample was younger (≥65 years, 35.5% vs 56.2%), had a similar sex distribution (female, 60.4% vs 63.7%), but was more racially and ethnically diverse, including more black patients (18.1% vs 11.3%) and more Hispanic patients (18.3% vs 8.7%) than the US population of patients with cancer. Compared with the US population of patients with cancer, the study sample overrepresented patients with breast cancer (34.7% vs 14.8%) and underrepresented patients with prostate cancer (3.3% vs 11.1%) and other cancers (12.8% vs 34.5%) (Table and eTable 3 in Supplement 2).

HBV Prevalence

One patient was not evaluable for the HBV analysis because no HBV testing results were available. Among the 3050 patients with evaluable HBV viral status, 197 patients had previous HBV. The observed rate of previous HBV infection was 6.5% (197 of 3050 patients; 95% CI, 5.6%-7.4%), including 25 patients (0.8%) who were previously diagnosed and 172 (5.7%) who were newly diagnosed (**Figure 2** and eTable 4 in Supplement 2). Therefore, 87.3% (95% CI, 81.8%-91.6%) of previous HBV cases were unknown (ie, newly diagnosed) at the time of study registration. The adjusted estimate of previous HBV infection—assuming the same distribution of cancers, age, and race as in the US cancer population—was 5.3%. Previous HBV infection was most common in patients with prostate cancer (12.0%; 95% CI, 6.4%-20.0%) and gastrointestinal cancers other than liver or colorectal (9.4%; 95% CI, 6.0%-13.8%) (**Figure 3** and eTable 4 in Supplement 2).

Figure 1. Flow Diagram for Primary Analysis



Nineteen of 3050 patients (0.6%; 95% CI, 0.4%-1.0%) had chronic HBV, including 11 patients (0.4%; 95% CI, 0.2%-0.6%) who were previously diagnosed and 8 (0.3%; 0.1%-0.5%) who were newly diagnosed (Figure 2 and eTable 4 in Supplement 2). Therefore, 42.1% (95% CI, 20.3%-66.5%) of chronic HBV cases were unknown at the time of study registration. After adjustment for cancer, age, and race, the estimate of chronic HBV infection was 0.4%. Chronic HBV infection was most common in patients with liver cancer (4 of 62, 6.5%; 95% CI, 1.8%-15.7%) (Figure 3 and eTable 4 in Supplement 2).

A sensitivity analysis excluding patients with liver cancer showed similar observed rates of previous HBV (6.4% vs 6.5%) and chronic HBV (0.5% vs 0.6%). More patients with chronic HBV received biologic therapy compared with patients with previous HBV (4 of 19 [21.1%] vs 8 of 197 [4.1%]; $P = .01$) and compared with HBV-negative patients (4 of 19 [21.1%] vs 154 of 2834 [5.4%]; $P = .01$) (eTable 5 in Supplement 2).

HCV Prevalence

Five patients were not evaluable for the HCV analysis owing to absent HCV testing results. An additional 56 patients lacked RNA confirmation of a positive HCV screening test; these patients were categorized as unknown HCV (eTable 1 in Supplement 2). Among the 2990 patients with evaluable HCV viral status, 71 patients had HCV, and the observed HCV infection rate was 2.4% (95% CI, 1.9%-3.0%), including 49 patients (1.6%; 95% CI, 1.2%-2.2%) previously diagnosed and 22 (0.7%; 95% CI, 0.5%-1.1%) newly diagnosed (Figure 2 and eTable 4 in Supplement 2). Therefore, 31.0% (95% CI, 20.5%-43.1%) of HCV cases were unknown at the time of study registration. The adjusted estimate of HCV infection accounting for type of cancer, age, and race was 1.9%; HCV was most common in patients with liver cancer (9 of 52 [17.3%]; 95% CI, 8.2%-30.3%) (Figure 3 and eTable 4 in Supplement 2). In sensitivity analysis, excluding patients with liver cancer modestly reduced the observed rate of HCV (2.1% vs 2.4%).

HIV Prevalence

Six patients were not evaluable for the HIV analysis owing to absent HIV testing results. Among the 3045 patients evaluable for HIV status, 34 patients had HIV, and the observed infection rate was 1.1% (95% CI, 0.8%-1.6%), including 32 patients (1.1%; 95% CI, 0.7%-1.5%) previously diagnosed and 2 (0.1%; 95% CI, 0%-0.2%) newly diagnosed (Figure 2 and eTable 4 in Supplement 2). Therefore, 5.9% (95% CI, 0.7%-19.7%) of HIV cases were unknown at the time of study registration. After adjustment for cancer type, age, and race, the estimate of HIV was 1.0%. HIV was most common in patients with gastrointestinal tract cancers other than liver or colorectal (5 of 235 [2.1%]; 95% CI, 0.7%-4.9%) and in patients with blood or marrow cancers (7 of 369 [1.9%]; 95% CI, 0.8%-3.9%). HIV was also more common among patients with other cancers (9 of 390 [2.3%]; 95% CI, 1.1%-4.3%) (Figure 3 and eTable 4 in Supplement 2).

Risk Factors Associated With Viral Infections

Several demographic, clinical, and behavioral factors were associated with viral infection (**Figure 4**). Previous HBV infection risk was highest in those who had sexual contact with HIV-positive persons (35.9% vs 6.1%; odds ratio, 8.66; 95% CI, 4.08-17.66; $P < .001$), had self-reported infection with HCV or HIV (23.3% vs

Table. Characteristics and Geographic Distribution of 3051 Evaluable Enrolled Patients

Characteristic	Study Sample (N = 3051), No. (%)[a]	United States, %[b]
Age		
Median (range), y	60.6 (18.2-93.7)	NA
>65 y	1084 (35.5)	56.2
Female sex	1842 (60.4)	63.7
Race		
White	2281 (74.8)	84.2
Black	553 (18.1)	11.3
Asian	102 (3.3)	4.0
Other	115 (3.7)	0.6
Ethnicity		
Hispanic	558 (18.3)	8.7
Non-Hispanic	2478 (81.2)	91.3
Not reported	15 (0.5)	NA
Cancer type		
Blood or marrow	369 (12.1)	7.8
Breast	1058 (34.7)	14.8
Gastrointestinal tract, colorectal	362 (11.9)	8.0
Gastrointestinal, liver	62 (2.0)	1.6
Gastrointestinal, other	235 (7.7)	7.1
Head and neck	112 (3.7)	3.4
Lung	356 (11.7)	11.8
Prostate	100 (3.3)	11.1
Other[c]	392 (12.8)	34.5
Missing	5 (0.2)	NA
Region[d]		
West and Midwest	1096 (35.9)	43.3
South and Northeast	1955 (64.1)	56.7

Abbreviation: NA, not applicable.

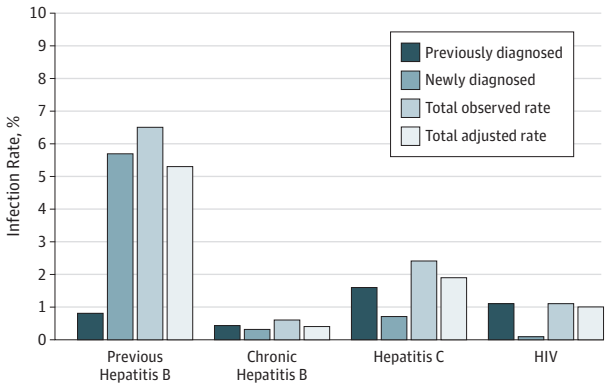
[a] Because of rounding, percentages may not total 100.

[b] US Cancer population rates were derived from Surveillance, Epidemiology, and End Results Program incidence data and represent the proportion in the US cancer population with the same cancer distribution as observed in S1204 (Viral Screening in Newly Diagnosed Cancer Patients).

[c] Other cancer type is described in eTable 3 in Supplement 2.

[d] Number of registrations from each state with participating institutions: West and Midwest region (California [n = 714], Colorado [n = 54], Hawaii [n = 86], Idaho [n = 6], Illinois [n = 74], Kansas [n = 3], Missouri [n = 102], Montana [n = 33], and Oregon [n = 24]); and South and Northeast region (Massachusetts [n = 100], Louisiana [n = 419], New York [n = 256], South Carolina [n = 541], and Texas [n = 639]).

Figure 2. Viral Infection Rates by Type of Virus



Total observed rate is the sum of rates for patients with previously and newly diagnosed viral infection. Total adjusted rates were calculated to reflect the anticipated rate in the US cancer population with similar cancer type, age, race, and ethnicity distribution using Surveillance, Epidemiology, and End Results Program (SEER) incidence data.

5.4%; odds ratio, 5.32; 95% CI, 3.52-7.93; $P < .001$), or were born in high HBV prevalence regions (20.6% vs 4.8%; odds ratio, 5.11; 95% CI, 3.61-7.18; $P < .001$); previous HBV infection risk was lower among those who completed the HBV vaccine series (3.3% vs 6.8%; odds ratio, 0.47; 95% CI, 0.20-0.96; $P = .04$). Chronic HBV infection was highest among those born in a high HBV prevalence region (2.6% vs 0.4%; odds ratio, 7.04; 95% CI, 2.39-19.97; $P < .001$). HCV infection risk was highest in those who injected drugs (23.9% vs 1.7%; odds ratio, 17.87; 95% CI, 9.61-32.42; $P < .001$), or were tested because they had blood exposure or injection drug use or transfusion before 1992 (16.7% vs 2.1%; odds ratio, 9.20; 95% CI, 3.78-20.21; $P < .001$), or because of symptoms (13.2% vs 2.2%; odds ratio, 6.78; 95% CI, 2.48-15.95; $P < .001$). Infection risk with HIV was highest in those who had sexual contact with other HIV-positive persons (41.0% vs 0.6%; odds ratio, 109.42; 95% CI, 46.31-262.72; $P < .001$), had unprotected sex with men who have sex with men, multiple, or anonymous partners (13.7% vs 0.6%; odds ratio, 24.53; 95% CI, 11.34-52.64; $P < .001$), or were diagnosed or treated for a sexually transmitted disease (6.5% vs 0.5%; odds ratio, 12.93; 95% CI, 6.14-28.01; $P < .001$).

Many patients with infection had no known risk factors, including 54 patients with previous HBV (27.4%; 95% CI, 21.3%-34.2%), 4 with chronic HBV (21.1%; 95% CI, 6.1%-45.6%) 23 with HCV (32.4%; 95% CI, 21.8%-44.5%), and 7 with HIV (20.6%; 95% CI, 8.7%-37.9%).

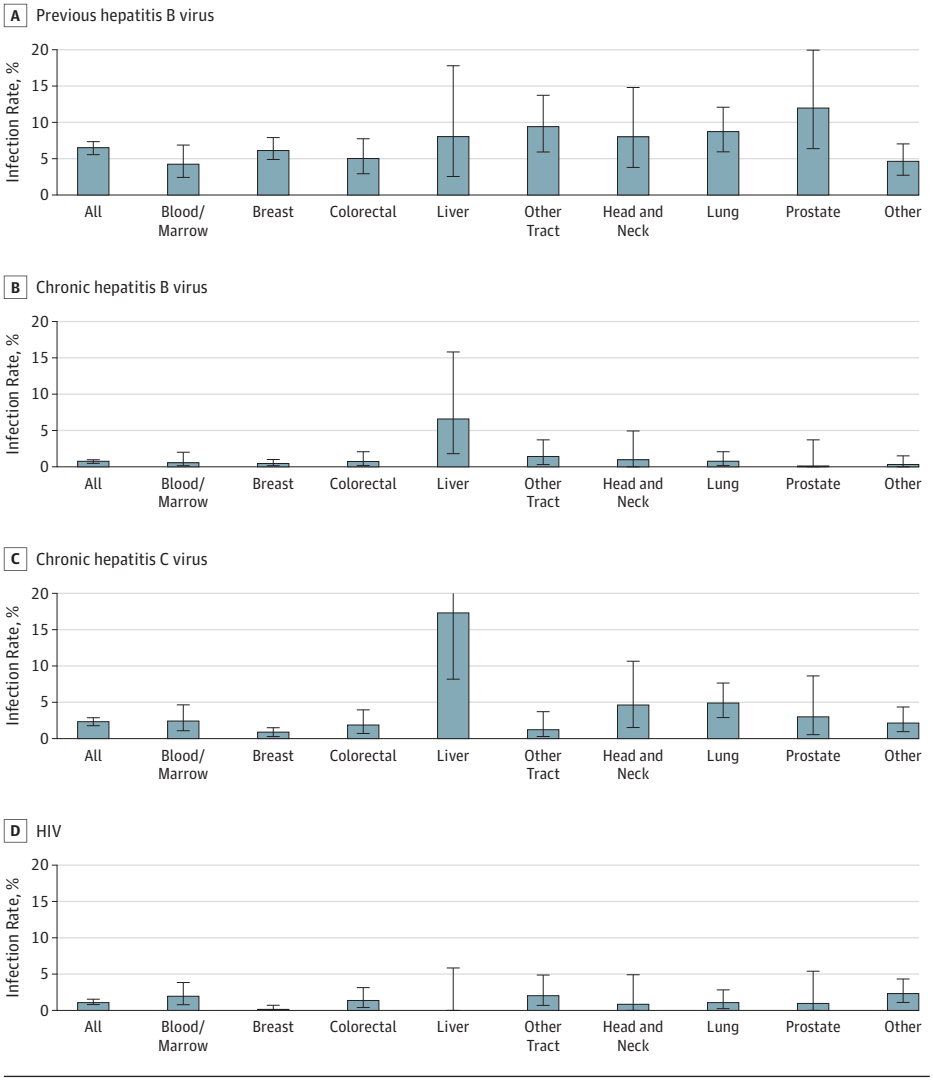
Treatment Outcomes

Within 6 months following registration, 18 of 152 patients with previous HBV infection (11.8%) and 4 of 49 with HCV infection (8.2%) received antiviral or antiretroviral drugs. Most patients with chronic HBV (11 of 15 [73.3%]) and HIV infection (20 of 30 [66.7%]) received antiviral or antiretroviral drugs (eTable 6 in Supplement 2); 131 of 224 patients (58.5%) with any type of viral infection experienced a change in cancer treatment by 6 months. A minority of patients (18 of 224 [8.0%] among patients with any infection) experienced a change in cancer treatment attributable to viral-positive status; fewer (14 of 224 [6.3%]) changed cancer treatment and added antiviral or antiretroviral therapy. Among patients with any viral infection, patients newly diagnosed with viral infection were less likely than patients previously diagnosed with viral infection to have any antiviral or antiretroviral drug use by 6 months (19.6%; 9.5% vs 32.7%; $P < .001$) and more likely to have change in cancer treatment (58.5%; 65.1% vs 50.0%; $P = .03$).

Discussion

In a prospective study of patients with newly diagnosed cancer from a nationwide multicenter sample, we observed that

Figure 3. Observed Infection Rates by Type of Virus and Cancer



The whiskers indicate the 95% CIs for the prevalence estimate for each cancer type. GI indicates gastrointestinal.

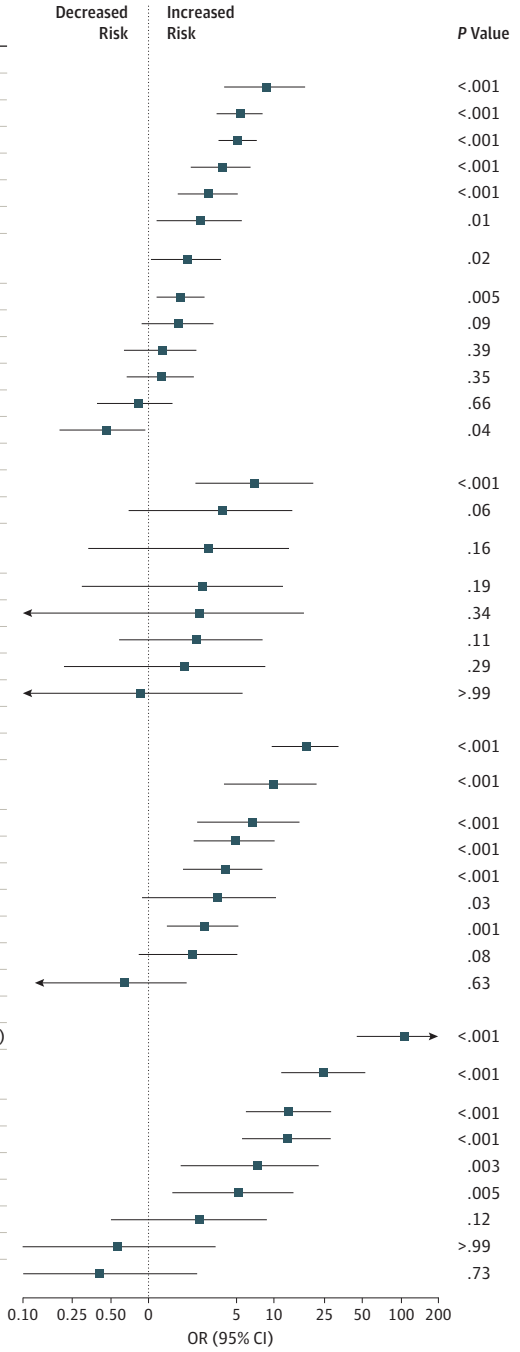
6.5% had previous HBV infection, 0.6% had chronic HBV infection, 2.4% had HCV infection, and 1.1% had HIV infection. Importantly, 87.3% of previous patients with HBV, 42.1% of patients with chronic HBV, 31.0% of patients with HCV, and 5.9% of patients with HIV did not know their viral status at the time of study registration. Cancers that had the highest prevalence of infection included liver, gastrointestinal tract other than liver or colorectal, head and neck, lung, and prostate; however, within-cancer frequencies differed substantially by type of viral infection. Only 8.0% of patients with any viral infection changed cancer treatments because of viral-positive status.

Oncology practice guidelines vary regarding their recommendations for viral screening. The American Society of Clinical Oncology and National Comprehensive Cancer Network guidelines[17,18] recommend screening for HBV infection before starting anti-CD20 therapy or hematopoietic cell transplantation. The National Comprehensive Cancer Network[17,19] recommends that patients with risk factors for HBV infection should also be screened, although universal screening should be considered for centers where risk-based screening cannot be effectively performed. Others have called for universal HBV screening. Opinions vary regarding the clinical management of HCV infection during cancer therapy. Some studies have noted increases in the HCV RNA during chemotherapy and increases in liver function tests, but the clinical significance of these findings and implications for treatment remains uncertain.[20,21] The Centers for Disease Control and Prevention recommends universal one-time screening for HIV among persons from ages 13 to 64, and one-time screening for HCV among persons born between 1945 and 1965.[9,22] The American Society of Clinical Oncology and The National Comprehensive Cancer Network do not have recommendations for universal HCV and HIV screening, but The National Comprehensive Cancer Network recommends HIV screening for persons with newly diagnosed lymphomas. Despite these recommendations, viral status is unknown for many individuals.

Our results suggest that the overall prevalence of HBV and HCV infection in patients with cancer is similar to that of

Figure 4. Association of Important Predictive Factors and Incidence of Viral Infection

Question	Present Rates, %	Absent Rates, %	Odds Ratio (95% CI)	P Value
Previous HBV				
Sexual contact with HIV-positive person	35.9	6.1	8.66 (4.08-17.66)	<.001
Self-reported infection with HCV or HIV	23.3	5.4	5.32 (3.52-7.93)	<.001
Born in high HBV prevalence region	20.6	4.8	5.11 (3.61-7.18)	<.001
Injected drug use	19.6	6.0	3.85 (2.21-6.44)	<.001
Unprotected sex with high-risk person	16.2	6.0	3.01 (1.75-4.98)	<.001
Sexual contact with hepatitis-positive person	15.2	6.3	2.67 (1.19-5.40)	.01
Unprotected set with MSM, multiple, or anonymous partners	12.0	6.2	2.04 (1.06-3.68)	.02
Diagnosis or treatment for STD	10.4	6.0	1.81 (1.18-2.73)	.005
Blood transfusion between 1978-1985	10.6	6.3	1.76 (0.89-3.22)	.09
Needle-stick exposure	8.1	6.4	1.30 (0.64-2.40)	.39
Household contact with hepatitis-positive person	8.1	6.4	1.29 (0.69-2.25)	.35
High-risk occupation	5.5	6.5	0.83 (0.40-1.55)	.66
Completed HBV vaccine (3 or more doses)	3.3	6.8	0.47 (0.20-0.96)	.04
Chronic HBV				
Born in high HBV prevalence region	2.6	0.4	7.04 (2.39-19.97)	<.001
Needle-stick exposure	2.0	0.5	3.83 (0.70-13.75)	.06
Unprotected set with MSM, multiple, or anonymous partners	1.7	0.6	3.05 (0.34-13.21)	.16
Unprotected sex with high-risk person	1.5	0.6	2.73 (0.30-11.80)	.19
Sexual contact with hepatitis-positive person	1.5	0.6	2.58 (0.06-16.99)	.34
Diagnosis or treatment for STD	1.3	0.5	2.46 (0.59-7.90)	.11
Self-reported infection with HCV or HIV	1.1	0.6	1.97 (0.22-8.50)	.29
Household contact with hepatitis-positive person	0.5	0.6	0.87 (0.02-5.62)	>.99
HCV				
Injected drug use	23.9	1.7	17.87 (9.61-32.42)	<.001
Tested because of blood exposure, injected drug use, or transfusion before 1992	16.7	2.1	9.20 (3.78-20.21)	<.001
Tested because of symptoms	13.2	2.2	6.78 (2.48-15.95)	<.001
Blood transfusion between 1978-1985	9.6	2.1	4.94 (2.27-9.85)	<.001
Tested because born between 1945-1965	8.0	2.1	4.04 (1.87-8.02)	<.001
Self-reported infection with HIV	7.7	2.3	3.54 (0.90-10.11)	.03
Snorted cocaine	5.6	2.1	2.80 (1.44-5.12)	.001
Needle-stick exposure	5.0	2.3	2.26 (0.85-5.06)	.08
High-risk occupation	1.5	2.5	0.61 (0.12-1.89)	.63
HIV				
Sexual contact with hepatitis-positive person	41.0	0.6	109.42 (46.31-262.72)	<.001
Unprotected set with MSM, multiple, or anonymous partners	13.7	0.6	24.53 (11.34-52.64)	<.001
Diagnosis or treatment for STD	6.5	0.5	12.93 (6.14-28.01)	<.001
Unprotected sex with high-risk person	9.2	0.8	12.83 (5.64-27.86)	<.001
Self-reported infection with HBV	7.3	1.0	7.44 (1.84-22.24)	.003
Diagnosis or treatment for tuberculosis	5.2	1.0	5.26 (1.55-14.17)	.005
Injected drug use	2.8	1.1	2.60 (0.50-8.55)	.12
Needle-stick exposure	0.7	1.2	0.57 (0.01-3.44)	>.99
High-risk occupation	0.5	1.2	0.41 (0.01-2.48)	.73



Associations are shown within each virus type in descending order of the odds ratio. Selected questions had results that were poorly defined and they were excluded from the figure including, for chronic hepatitis B virus: injected drugs (0% for present vs 0.6% for absent; odds ratio [OR], 0; 95% CI, 0-6.12; $P > .99$); high-risk occupation (0% vs 0.7%; OR, 0; 95% CI, 0-3.13; $P = .63$); sexual contact with HIV-positive person (0% vs 0.6%; OR, 0; 95% CI, 0-17.64; $P > .99$); blood transfusion between 1978 and 1985 (0% vs 0.6%; OR, 0; 95% CI, 0-5.28; $P > .99$); and completed the hepatitis B virus vaccine (≥3 doses) (0% vs 0.7%; OR, 0; 95% CI, 0-2.53; $P = .39$). For HIV, the following observations are not shown: blood transfusion between 1978 and 1985 (0% vs 1.2%; OR, 0; 95% CI, 0-2.65; $P = .40$) and exchanged sex for drugs or money (0% vs 1.2%; OR, 0; 95% CI, 0-8.80; $P > .99$). HBV indicates hepatitis B virus; HCV, hepatitis C virus; MSM, men who have sex with men; STD, sexually transmitted disease.

the general population. In the United States, the prevalence of previous HBV infection is approximately 5% and chronic HBV infection is approximately 0.3%; the prevalence of chronic HCV is 1.3% overall.[4,5,22,23] The corresponding rates in our study, after adjustment to account for differences in cancer type, age, race, and ethnicity between the study cohort and the general cancer population rates, were 5.3% for previous HBV, 0.4% for chronic HBV, and 1.9% for HCV. Im-

portantly, a substantial proportion of persons with previous (87.3%) and chronic (42.1%) HBV infections as well as a large proportion of persons with HCV infections (31.0%) were undiagnosed before protocol screening, indicating that there is a large reservoir of patients with cancer and undiagnosed hepatitis virus infections.

Strengths and Limitations

The study had several strengths including a large sample size and an ethnically, racially, and geographically diverse population. We noted several limitations. First, the study was designed to estimate prevalence using testing procedures that were currently being employed in clinical practice. As a pragmatic-design screening study, there was wide variability in testing practices across participating clinics, particularly for HBV. Variability in screening approaches influenced detection rates, and thus our results, compared with a standardized (nonpragmatic) design. The unavailability of RNA samples for confirmation of HCV for a subset of patients suggested that the HCV estimate may be biased low. Further, although the registered sample was very similar to the screened sample with respect to known factors that could influence viral prevalence rates, only 20% of patients with cancer at the sites were registered, raising a concern about selection bias, especially with respect to unmeasured factors that could influence the prevalence rates. We noted that standardization had a modest influence on the estimates, suggesting that our study sample was reasonably representative of the general US cancer population, at least with respect to the variables used for standardization. Finally, we acknowledged that false-positive identification of previous HBV does exist, although it is rare.[24]

Conclusions

Previous studies suggested that overall awareness of HBV[25-27] and HCV[28] status was low among infected persons. Our results were consistent with these studies, suggesting that substantial portions of HBV and HCV infections prevalent at the time of cancer diagnosis were unknown to patients. Many patients had no known risk factors for infection, suggesting that current risk-based models for screening may be insufficient. Thus, we believe our results warrant consideration of universal testing of patients with newly diagnosed cancer for HBV and HCV infection, particularly if such an approach is shown to be cost-effective. The yield from viral screening could be enhanced by examining risk factors before testing, although the feasibility of risk factor screening in oncology practice is, to our knowledge, untested.[29] Given that most HIV-infected patients in our study knew their viral status, the yield of universal HIV testing among patients with newly diagnosed cancer may likely be low. Although age-directed screening is recommended for HIV and HCV, uptake rates in primary care are variable and low overall.[30-33] Studies evaluating the role of antiviral therapies for infected patients during cancer treatment are ongoing.

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Acquisition, analysis, or interpretation of data: Ramsey, Unger, Loomba, Hwang, Konerman, Arnold, Menter, Thomas, Michels, Jorgensen, Burton, Bhadkamkar, Hershman.
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Input on Conduct of the Study Related to Hepatitis B Virus and Hepatitis C Virus Infection Status: Loomba, Hwang, Konerman.

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