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Assessing testing rates for viral hepatitis B and C by general practitioners in Flanders, Belgium: a registry-based study

Rob Bielen,[1,2] Özgür M Koc,[1,2,3] Dana Busschots,[1,2] Geert Robaeys,[1,2,4] Bert Aertgeerts,[5,6] Bert Vaes,[5] Pavlos Mamouris,[5] Catharina Mathei,[5] Geert Goderis,[5] Frederik Nevens[4]

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For numbered affiliations see end of article.

Correspondence to
Dr Rob Bielen;
rob.bielen@uhasselt.be

ABSTRACT

Objectives Chronic infections with hepatitis B virus (HBV) and hepatitis C virus (HCV) have a major impact on mortality worldwide. Although effective treatments are available for both HBV and HCV infection, <50% of the patients are even diagnosed in Belgium. This study assessed the real-life testing—and diagnosis rate by general practitioners (GPs) in Flanders, Belgium.

Setting We assessed the testing rate for HBV and HCV in 48 primary care practices with electronic medical records linked into one central registry in Flanders, Belgium.

Participants The registry contains data of 440 140 patients over 20 years, which corresponds to 2.2% of the total Flemish population yearly. The primary care practices are distributed across Flanders and the patient population is representative for the distribution of age, gender and socioeconomic status at the community level.

Results Of 440 140 patients included in the registry, 7892 (1.8%) patients were screened for hepatitis B surface antigen (HBsAg) and 7206 (1.6%) for hepatitis C antibody (HCV Ab) of whom 369 (4.7%) and 163 (2.3%) tested positive, respectively. Of 14 059 patients with chronic liver enzyme elevation, 1112 (7.9%) and 1395 (9.9%) were tested for HBsAg and HCV Ab, respectively. There was no improvement in testing rates over time.

Conclusions This study demonstrates that real-life testing uptake for viral hepatitis B and C is suboptimal in the general practices in Flanders, even in patients with chronically elevated liver enzymes. As GPs play a crucial role in prevention, diagnosis and linkage to care, efforts and strategies to increase the testing uptake for HBV and HCV are urgently needed.

Strengths and limitations of this study

- This is the first study to assess testing for both hepatitis B surface antigen and hepatitis C antibody in real-life by general practitioners.
- The patient population is representative for age, gender and socioeconomic status for the whole region of Flanders, making it possible to provide an audit of testing practices in Flanders.
- Due to the study design, ethnicity and sexual preference could not be reported, and the testing rate could be an underreported if patients were tested elsewhere, but this is minimalised by using the encoded diagnoses.

INTRODUCTION

Chronic viral hepatitis, mainly due to infections with hepatitis B virus (HBV) and hepatitis C virus (HCV), is a major global health problem. Worldwide, ~257 million people live with chronic HBV infection and 70–85 million people live with chronic HCV infection.[1 2] The viral hepatitis pandemic is responsible for up to 1.4 million deaths annually, making it the seventh leading cause of mortality globally.[3]

Treatment for chronic viral hepatitis has substantially improved over the last decades. Long-term suppression of HBV DNA levels can be achieved in all chronic HBV patients leading to an improvement in survival by preventing disease progression, and consequently liver cancer development.[4 5] Direct-acting antivirals (DAAs) have revolutionised HCV treatment and can cure >90% of people with chronic HCV infection.[6–10] Furthermore, with the availability of safe and effective vaccines to prevent HBV infection, the WHO developed a strategy towards eliminating viral hepatitis as a public health threat by 2030.[11] Nevertheless, despite the progressive nature of the disease and the highly effective treatment, only a small proportion of patients with chronic viral hepatitis are diagnosed and are being treated.[12 13]

In Flanders, Belgium, universal HBV vaccination strategy was already implemented in 1999, both for adolescents and newborns.[14] Since 2008, the immunisation coverage for HBV is >95%.[15] Nevertheless, due to migration, the mandatory notification rate of acute HBV infections remained stable from 2009 to

2015 (range 43–70 acute HBV cases).[16] This was slightly lower in 2016 and 2017 (36 and 33 acute HBV cases, respectively). Prevalence studies of hepatitis B surface antigen (HBsAg) are outdated, but the prevalence of chronic HBV infection is estimated around 0.7%.[17 18] Of an estimated 64 000 patients chronic HBV patients (95% CI 54 000 to 77 000), only 46% have been diagnosed.[19] With recent advancements in treatment of chronic HBV infection, secondary prevention is possible.[20 21] There is, however, no national plan to reduce the burden of HBV infection.[22] Voluntary blood donors have been screened for HBV since 1972. HBV testing is also recommended during the first trimester of pregnancy.[23] Healthcare workers are being tested and vaccinated, but no other testing strategies are recommended.[24] Thus, improving testing uptake, diagnosis rate and linkage to care is necessary.

Concerning HCV infection, in 2015, there were an estimated 66 200 (95% CI 24 200 to 77 600) viremic HCV infections in Belgium, of which ~43% were diagnosed.[17 25] To reach the 2030 targets of the WHO, diagnosis rates should have been increased by 10% each year beginning in 2016, to achieve a total of 3030 patients diagnosed annually by 2018. These targets have not been reached and are not being monitored. Government funded DAA therapy has been available since 2015 for patients with severe fibrosis or cirrhosis (≥F3 Metavir stage).[26 27] Additionally, treatment became available to ≥F2 patients in 2017 and has become available for all patients in 2019.[28 29] Since 2014, there is a national hepatitis C plan, but none of the objectives concerning screening (including better informing general practitioners [GPs]) have been implemented.[22] Given the significant clinical and economic burden of HCV, increasing detection rates is a priority.[30]

Several studies have shown a lack of screening for HCV in primary care in the USA but reports about HBsAg testing by GP's in real-life are absent.[31–33] In Germany, in one prospective screening study, 85% of HBsAg and 65% of hepatitis C antibody (HCV Ab)-positive patients were previously undiagnosed in the primary care setting.[34] Thus, monitoring of real-life testing and diagnosis rates is a gap in the current policy internationally. The goal of this observational study was to investigate the real-life testing and diagnosis rate of HBV and HCV in primary care in Flanders.

MATERIALS AND METHODS

Study design

This is an analysis of testing and diagnosis rate of HBV and HCV infection in around 50 primary care practices all linked in the INTEGO project.[35] INTEGO is a registration network, which collects data from >100 GPs since 1994.[35] These practices are distributed across Flanders, Belgium and the INTEGO patient population is representative for the Flemish population for age distribution, gender distribution and socioeconomic status at the community level.[35] Every patient visiting these practices is eligible for inclusion within the registry. Data are collected yearly, and in 2015, 48 practices and 111 physicians cooperated for this project, which led to data collection of 123 261 patients, or ~2% of the Flemish population.[35] In total, the INTEGO registry contains data of 440 140 patients over 20 years. Patient characteristics and diagnoses are encoded in the INTEGO registry using the International Classification of Primary Care (ICPC-2) codes by the participating GPs.[36] Furthermore, all laboratory tests performed by GP's are included in the database. As such, the INTEGO registry contained 4 478 275 diagnoses and 44 747 161 laboratory results up to 2015.[35] Data collection is regulated by an opting-out procedure, which is approved by the privacy commission in Belgium.

All patients registered in these practices between 1996 and 2015 were eligible for inclusion in this study. The laboratory test results concerning HBsAg and HCV Ab of all patients were collected using the INTEGO registry. After removal of duplicates, data were collected of all individuals ever tested for HBsAg and/or HCV Ab. Only two tests were being used across the different laboratories in Belgium, that is, Cobas Roche and Architect Abbott. A positive value for HBsAg and HCV Ab is defined by a cut-off value of 1.0, a negative value as <0.9 and borderline results between 0.9 and 1.0. For the purpose of this study, all tests ≥0.9 were withheld as possibly positive for both HBsAg and HCV Ab tests. The following baseline data were collected: year of birth, gender, HBsAg tests and dates of tests, HCV Ab tests and dates of tests, and all results of aspartate transaminase (AST)/alanine aminotransferase (ALT) tests. Based on ICPC-2 codes registered by the GPs, data were collected on chronic alcohol abuse, diabetes, overweight and pregnancy. The dates of these registrations were also collected to collect information on time of these events versus HBV/HCV testing. HIV status was only collected of patients tested for HCV or HBV infection. Age at time of first testing of HBV or HCV infection was calculated. As HCV or HBV testing could also be performed in hospital settings, on referral of the GP, there could be an underestimation of these testing rates. Therefore, ICPC-2 codes on viral hepatitis were also added to minimise this risk.

For our second research question, we extracted all patients with chronically elevated liver enzymes, as defined by at least two AST or ALT elevations (>40 IU/L), 6 months apart. Patient characteristics were collected using the ICPC-2 codes with the same methodology.

Objectives

The primary endpoint of this study was to investigate the overall testing and diagnosis rate of HBV and HCV infection by primary care providers. As secondary endpoint, we analysed the testing and diagnosis rate of HBV and HCV in patients with elevated liver enzymes.

Statistical analysis

All analyses were performed using IBM SPSS V.24. Descriptive statistics of patient characteristics are presented: for continuous variables, means and SD, for categorical

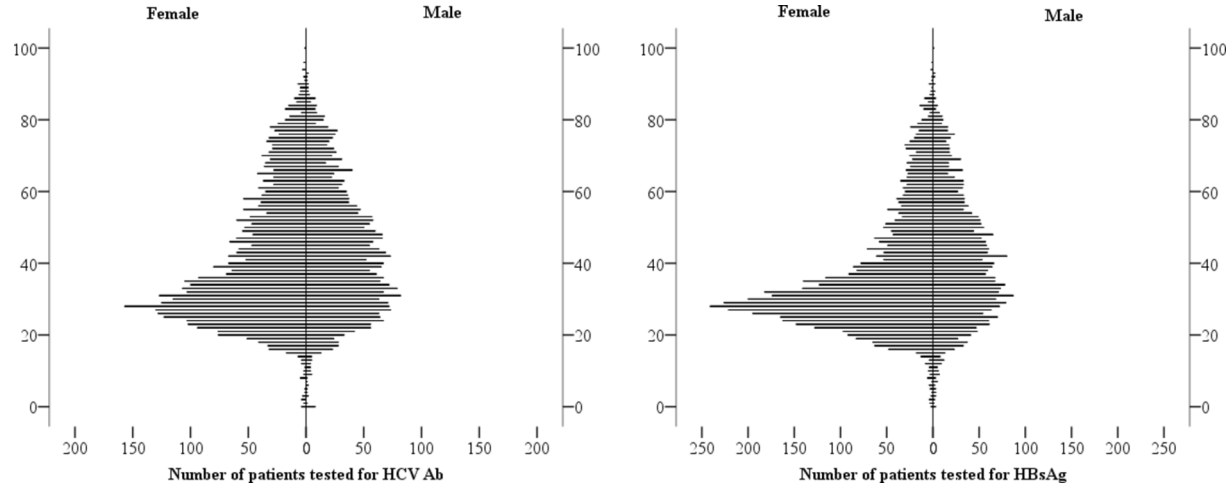

Figure 1 Number of patients (x-axis) tested for HBsAg (left) and HCV Ab (right), distributed by age (y-axis) and gender. HBsAg, hepatitis B surface antigen; HCV Ab, hepatitis C antibody.

variables proportions and percentages. Independent t-tests were used for the comparison of two continuous variables. When violating the assumptions for parametric tests (eg, normal distribution, homogeneity of variance), the Mann-Whitney U test was used instead. Categorical data were analysed with the χ^2 test or Fisher's exact test. Using the significant values (p<0.10), a multiple logistic regression model was executed. Model selection was done in a stepwise backward manner based on significance (p<0.05). Results were considered significant at the 0.05 level.

RESULTS

Overall testing for HBsAg and HCV Ab

In total, 10 684 patients were screened for HBsAg or HCV Ab between 1996 and 2015. The majority of patients tested were female: n=6500 (60.8%). Mean age at the time of the first test was 40±17 years. More specifically, 7892 were screened for HBsAg and 7206 for HCV Ab. Thus, out of the total of 440 140 patients in INTEGO registry, 1.8% and 1.6% of the patients were screened for HBV and HCV infection, respectively. In figure 1, the distribution of tested patients by age and gender is provided. Both for HBV and HCV infection, there is a clear overrepresentation of women in the reproductive age.

Characteristics of patients with positive HBsAg or HCV Ab

In tables 1 and 2, the association of patient characteristics on HBsAg and HCV Ab positivity in patients tested for these diseases is illustrated. Of the patients tested for HBsAg and HCV Ab, 4.7% and 2.3% tested positive, respectively. Only 42.3% of the HBsAg-positive individuals had at least one AST/ALT elevation. In multivariate regression analysis, HBsAg positivity was associated with chronically elevated liver enzymes (OR 1.60; 95% CI 1.23 to 2.07). Of the HBsAg-tested patients, 55.9% (4414/7892) were also screened for HCV, and 54.1% (4267/7892) for HIV infection. Moreover, HBsAg-positive patients were significantly less tested for HCV and HIV compared with HBsAg-negative patients.

Patients with elevated liver enzymes, older patients (mean age at time of testing 49 vs 42 years), people who use drugs and HIV-infected patients all had a higher chance of being HCV Ab positive in multivariate analysis. A total of 111 (68.1%) HCV-positive patients had at least one AST/ALT elevation. Again, only 61.3% (4414/7206) of the HCV-tested patients were also tested for HBsAg and only 54.1% (3902/7206) for HIV, and significantly less HCV Ab-positive patients were tested.

Testing for HBsAg and HCV Ab in patients with chronic liver enzymes elevation

There were 14 059 patients who had an elevation of AST or ALT ≥40 IU/L, at least twice, and 6 months apart. These patients were considered to have chronic liver enzymes elevation. The majority of these patients were male: n=9481 (67.4%). Mean age at the time of the first measurement of elevated liver enzymes was 55±16 years. Of these patients, only 1112 (7.9%) were tested for HBsAg and 1395 (9.9%) were tested for HCV Ab.

In figure 2, the evolution of testing is provided per time block of 5 years. There was no improvement in testing rates between these subgroups over time.

Of the patients who had at least once a chronic elevation of liver enzymes, 5.6% (305/5429) were tested for HBsAg and 7.6% (412/5429) for HCV Ab. In patients with chronic elevation and in addition two to four repeated AST/ALT elevations, 8.0% (493/6128) were screened for HBsAg and 9.8% (598/6128) for HCV Ab. Finally, in patients with more than five repeated AST/ALT elevations, 12.6% (314/2501) and 15.6% (385/2501) were screened for HBsAg and HCV Ab.

Patient characteristics associated with testing uptake for HBsAg and HCV Ab are demonstrated in tables 3 and 4. Patients with more than five repeated elevated liver tests were more likely to be screened for HBsAg, patients with HCV Ab positivity less likely. The same findings apply for

Table 1 Relation of baseline characteristics to HBsAg-positive and HBsAg-negative patients

Variable	Univariate analysis (χ^2 and Student's t-test) HbsAg+ n=369	HbsAg– n=7523	P value	Multivariate analysis (backward regression) P value	OR	95% CI
Elevated liver enzymes						
AST/ALT elevated at least once	156 (42.3%)	2678 (35.6%)	**0.010**	n.s.		
AST/ALT elevated at least twice	127 (34.4%)	2022 (26.9%)	**0.002**	n.s.		
AST/ALT elevated at least twice, >6 months	75 (20.3%)	1037 (13.8%)	**0.001**	<0.001	**1.60**	1.23 to 2.07
Age first HCV Ab or HbsAg test (y) (mean±SD)	38±16	39±17	0.360			
Gender (male)	160 (43.4%)	2826 (37.6%)	**0.028**	n.s.		
Chronic alcohol abuse	11 (3.0%)	200 (2.7%)	0.739			
Drug abuse	2 (0.5%)	110 (1.5%)	0.177			
Diabetes	43 (11.7%)	915 (12.2%)	0.807			
Overweight	–	15 (0.2%)	0.641			
Viral hepatitis test within pregnancy	37 (10.0%)	761 (10.1%)	0.956			
Coinfection						
HIV positive	–	9 (0.2%)	0.999			
HCV Ab positive	1 (0.7%)	66 (1.5%)	0.525			
Test HIV Ab (yes)	98 (26.6%)	4169 (55.4%)	<0.001			
Test HCV (yes)	144 (39.0%)	4270 (56.8%)	<0.001			

ALT, alanine transaminase; AST, aspartate transaminase; HBsAg, hepatitis B surface antigen; HCV Ab, hepatitis C antibody; y, year.
Significant values that were used in the regression model are highlighted in bold.

testing for HCV Ab: patients with more than five repeated elevated liver tests were more likely to be screened, and patients with HBsAg positivity less likely. Patients were also more likely to be screened for HCV Ab when the patient was younger at the time of elevated liver enzymes. If these patients were screened for one of these infections, they were far more likely to be tested for other blood-borne viral infections as well.

DISCUSSION

In this study, we evaluate the real-life testing and diagnosis rate of HBV and HCV infection by GPs in Flanders, Belgium using the INTEGO registry. These data are representative for age and gender distribution and socioeconomic status in the Flemish community. Only 1.8% of the total INTEGO registry population were tested for HBsAg, and only 1.6% for HCV Ab between 1996 and 2015. Testing rates did not improve over time despite the development of very effective antiviral drugs. When testing was performed, it was most often done in women of reproductive age. HBsAg testing has been recommended in pregnant women for several years[37]; however, HCV Ab testing has only been recommended for pregnant women with an increased risk of HCV infection.[38] These higher testing rates in young women reflects the lack of an effective screening policy in Belgium, as the male gender is associated with a higher prevalence of viral hepatitis.[39 40]

To our knowledge, this is the first study internationally to assess the testing rate in routine practice for HBsAg by GPs. The low testing rate for HCV Ab in our study is in contrast with the findings of the recent hepatitis C report of the Belgian Institute of Health (WIV-ISP).[39] Based on the number of serology requests to the National Institute for Health and Disability Insurance (RIZIV/INAMI) and extrapolated data of the permanent sample, an instrument designed by the InterMutualistisch Agentschap-Agence InterMutualiste (IMA-AIM),[41] there was a yearly testing uptake of 2.5% for HCV and 33.4% of the Belgian population would have been tested during the last 9 years.[39] At least our findings indicate that these high testing rates are not performed by GPs. Internationally, several studies assessed screening uptake for HCV in the general practice setting, and screening rates ranged from 4.3% to 15.8%.[31–33] Even though these studies were conducted in large integrated healthcare systems or managed care organisations, many patients remained unscreened. This could be explained by the lack of knowledge about screening guidelines, the complexity of risk-based screening guidelines and reluctance to discuss socially undesirable behaviours.[42 43] In another study in Australia,

Table 2 Relation of baseline characteristics to HCV Ab-positive and HCV Ab-negative patients

Variable	Univariate analysis (χ^2 and Student's t-test) HCV Ab+ n=163	HCV Ab– n=7043	P value	Multivariate analysis (backward regression) P value	OR	95% CI
Elevated liver enzymes						
AST/ALT elevated at least once	111 (68.1%)	2931 (41.6%)	<0.001	**0.016**	**2.28**	1.16 to 4.46
AST/ALT elevated at least twice	92 (56.4%)	2223 (31.6%)	<0.001	n.s.		
AST/ALT elevated at least twice, >6 months	66 (40.5%)	1206 (17.1%)	<0.001	**0.020**	**2.18**	1.13 to 4.21
Age first HCV Ab or HbsAg test (y) (mean±SD)	49±18	42±18	<0.001	**0.023**	**1.02**	1.00 to 1.04
Gender (male)	78 (49.9%)	3032 (43.0%)	0.231			
Chronic alcohol abuse	5 (3.1%)	212 (3.0%)	0.999			
Drug abuse	20 (12.3%)	98 (1.4%)	<0.001	<0.001	**11.86**	5.17 to 27.19
Diabetes	28 (17.2%)	916 (13.0%)	0.126			
Overweight	–	5 (0.1%)	0.999			
Viral hepatitis test within pregnancy	6 (3.7%)	440 (6.2%)	0.179			
Coinfection						
HIV Ab positive	2 (3.4%)	14 (0.4%)	**0.023**	**0.008**	**8.76**	1.78 to 43.16
HBsAg positive	1 (1.5%)	143 (3.3%)	0.525			
Test HIV (yes)	58 (35.6%)	3844 (54.6%)	<0.001			
Test HBV (yes)	67 (41.1%)	4347 (61.7%)	<0.001			

ALT, alanine transaminase; AST, aspartate transaminase; HBsAg, hepatitis B surface antigen; HCV Ab, hepatitis C antibody; y, year.
Significant values that were used in the regression model are highlighted in bold.

gaps in knowledge of GPs on viral hepatitis ranged from natural history to diagnosis and treatment availability.[44] Furthermore, GPs indicated in a national survey in New Zealand that insufficient training was a major barrier to treat HCV, and confidence rose significantly when being trained. Interestingly, GPs consistently underestimated the prevalence of HCV in their practice.[45]

In patients with chronic liver enzyme elevation, testing uptake for HBV (7.9%) and HCV (9.9%) were low. Factors that could potentially induce AST/ALT elevation, such as alcohol abuse or diabetes (as a surrogate marker for non-alcoholic steatohepatitis) did increase the odds of being tested for viral hepatitis. Having multiple repeated elevated AST/ALT values increased the testing uptake. Nevertheless, in patients with more than five repeated elevated tests (>40 IU/L), still 85% were not tested. This gap should be closed as the HCV Ab prevalence was 10-fold higher in patients with elevated liver enzymes in primary care.[46]

As testing was only performed on indication and not in all individuals, there was a high rate of HBsAg (4.7%) and HCV Ab (2.3%) positivity, far higher than the

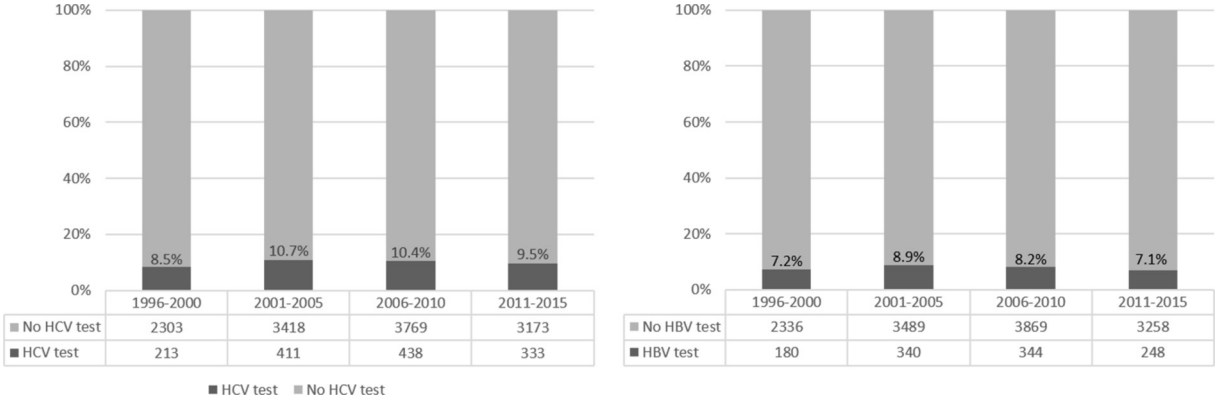

Figure 2 Evolution of testing rates over time for HBsAg (left) and HCV Ab (right). HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HCV Ab, hepatitis C antibody.

Table 3 Relation of baseline characteristics to uptake for HBsAg testing in patients with chronically elevated liver enzymes

	Univariate analysis (χ^2 and Student's t-test)			Multivariate analysis (backward regression)		
Variable	Test HBV n=1112	No test HBV n=12946	P value	P value	OR	95% CI
Age first elevation AST/ALT levels (y) (mean±SD)	52±15	55±16	**<0.001**	n.s.		
Number of tests with chronic elevation						
1	305 (27.4%)	5124 (39.6%)	**<0.001**	0.005		
2–4	493 (44.3%)	5635 (43.5%)	**<0.001**	0.137	1.22	0.94 to 1.59
≥5	314 (28.2%)	2187 (16.9%)	**<0.001**	0.001	**1.66**	1.23 to 2.26
Gender (male)	691 (62.1%)	8790 (67.9%)	**<0.001**	n.s.		
Chronic alcohol abuse	88 (7.9%)	701 (5.4%)	**0.001**	n.s.		
Drug abuse	7 (0.6%)	59 (0.5%)	0.488			
Diabetes	310 (27.9%)	3035 (23.4%)	**0.001**	n.s.		
Overweight	1 (0.1%)	20 (0.2%)	0.725			
Viral hepatitis test within pregnancy	20 (1.8%)	113 (0.9%)	**0.002**	n.s.		
Coinfection						
HIV Ab positive	–	–	–			
HCV Ab positive	45 (4.8%)	34 (7.6%)	**0.032**	0.015	**0.56**	0.35 to 0.90
Test HCV (yes)	947 (85.2%)	448 (3.5%)	<0.001			
Test HIV (yes)	410 (36.9%)	377 (2.9%)	<0.001			

ALT, alanine transaminase; AST, aspartate transaminase; HBsAg, hepatitis B surface antigen; HCV Ab, hepatitis C antibody; y, year. Significant values that were used in the regression model are highlighted in bold.

expected prevalence of HBV (0.7%) and HCV (0.87%) from previous seroepidemiological studies in the general Belgian population.[17] In regard to HCV-positive patients, the presence of drug use or HIV positivity significantly increased the odds of HCV positivity. However, only a small proportion of the study population demonstrated these risk factors.

This study has several limitations. Although this registration network is representative for socioeconomic status at the community level, high-risk behaviour could still be underreported, as it is challenging to discuss sensitive personal behaviour, especially when this is not relevant to the medical care visit.[43 47 48] Furthermore, the capacity to opt-out of the INTEGO registry potentially reduces the involvement of people at risk of hepatitis C participating in the system. The asymptomatic nature of viral hepatitis infection reduces the likelihood of people with the infection to request testing.[49 50]

Due to the design of the study, no data on ethnicity and sexual preference were available. This is a concern as migration from countries with a high endemic prevalence of HBV infection is an important factor for HBV prevalence in developed countries.[51] Also, only screening results of laboratory tests conducted by the GP are available, thus, there could be an underestimation of the number of tested patients if they were screened elsewhere. By using ICPC-2 codes for viral hepatitis, the risk of underreporting HBV-infected and HCV-infected patients was lowered.

This study clearly indicates the lack of an effective screening strategy for HBV and HCV in Belgium. Several studies have shown a lack of screening for HCV in primary care in the USA.[31–33] In Germany, 85% of HBsAg and 65% of HCV Ab-positive patients were previously undiagnosed in the primary care setting.[34] Simple interventions using electronic health record reminders and education can increase HCV screening both for risk-based screening guidelines and birth cohort screening.[52 53] Importantly, in ~50% of the patients, screening was not performed for other blood-borne viruses, and this was even more explicit in patients who were positive for HBsAg or HCV Ab. This could be an underestimation if these patients were referred to hospitals for further workup, but since the transmission routes of these viruses are mostly the same, combined testing should be offered. In France, current screening guidelines have been simplified to address this issue, and combined testing should be offered to every adult at least once in a lifetime.[54] Simplifying screening guidelines in Belgium and educating or reminding GPs to screen for viral hepatitis will be crucial to increase the diagnosis rate.

CONCLUSION

This study demonstrates that real-life testing uptake for viral hepatitis B and C is low in the general practices in

Table 4 Relation of baseline characteristics to uptake for HCV Ab testing in patients with chronically elevated liver enzymes

	Univariate analysis (χ^2 and Student's t-test)			Multivariate analysis (backward regression)		
Variable	Test HCV n=1395	No test HCV n=12663	P value	P value	OR	95% CI
Age first elevation AST/ALT levels (y) (mean±SD)	54±16	55±16	**0.001**	**0.034**	**1.01**	1.00 to 1.02
Number of tests with chronic elevation						
1	412 (29.5%)	5017 (39.6%)	**<0.001**	**0.006**		
2–4	598 (42.9%)	5530 (43.7%)	**<0.001**	0.146	0.74	0.50 to 1.11
≥5	385 (27.6%)	2116 (16.7%)	**<0.001**	0.106	1.51	0.92 to 2.47
Gender (male)	838 (60.1%)	8643 (68.3%)	**<0.001**	n.s.		
Chronic alcohol abuse	107 (7.7%)	682 (5.4%)	**0.001**	n.s.		
Drug abuse	13 (0.9%)	53 (0.4%)	**0.013**	n.s.		
Diabetes	401 (28.7%)	2944 (23.2%)	**<0.001**	n.s.		
Overweight	1 (0.1%)	20 (0.2%)	0.518			
Viral hepatitis test within pregnancy	15 (1.1%)	116 (0.9%)	0.557			
Coinfection						
HIV Ab positive	–	–	–			
HbsAg positive	50 (5.3%)	25 (15.2%)	**<0.001**	<0.001	**0.32**	0.19 to 0.54
Test HIV (yes)	506 (36.3%)	281 (2.2%)	<0.001			
Test HBV (yes)	947 (67.9%)	165 (1.3%)	<0.001			

ALT, alanine transaminase; AST, aspartate transaminase; HBsAg, hepatitis B surface antigen; HCV Ab, hepatitis C antibody; y, year.
Significant values that were used in the regression model are highlighed in bold.

Flanders, even in patients with chronically elevated liver enzymes. As GPs play a crucial role in prevention, diagnosis and linkage to care, efforts to increase uptake for testing for HBV and HCV should target GPs.

Patient and public involvement

No patients were involved in setting the research question or the outcome measures, nor were they involved in developing plans for design or implementation of the study. Encoded data were provided directly from the INTEGO registry. There are no plans to disseminate the results of the research to study participants or the relevant patient community.

Author affiliations
[1]Faculty of Medicine and Life Sciences, Universiteit Hasselt, Hasselt, Belgium
[2]Department of Gastroenterology, Ziekenhuis Oost-Limburg, Genk, Belgium
[3]Medical Microbiology, School of NUTRIM, Maastricht University Medical Centre, Maastricht, Belgium
[4]Department of Gastroenterology and Hepatology, University Hospitals KULeuven, Leuven, Belgium
[5]Department of Public Health and Primary Care, KU Leuven, Leuven, Belgium
[6]CEBAM, Belgian Centre for Evidence Based Medicine, Leuven, Belgium

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Contributors RB, OMK, BA, BV, GG and FN: conceived and designed the study. FN: obtained funding for the work. RB, PM and BV: acquired the data. Analysis was conducted by RB, and all authors assisted with interpretation of the data. RB, OMK and FN: drafted the manuscript. RB, OMK, DB, GR, BA, BV, PM, CM, GG and FN: reviewed the manuscript and provided feedback. RB: had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All authors read and approved the final version before submission.

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Competing interests RB has received travel grants from Abbvie, MSD and Gilead to attend scientific congresses. OMK has received travel grants from Gilead to attend scientific congresses. DB has received a travel grant from Abbvie. FN has received research grants, consultancy agreements and travel grants from UCB, Ipsen, Roche, Astellas, Ferring, Novartis, Janssen-Cilag, Abbvie, Gilead, CAF, Intercept, Gore, BMS, MSD, Promethera Biosciences, Ono Pharma and Durect. GR has received research grants from MSD, AbbVie, Janssen Pharmaceuticals, and has acted as a consultant/advisor and for Gilead Sciences, Abbvie, MSD and BMS. BA, BV, PM, CM and GG report no conflict of interest.

Patient consent for publication Not required.

Ethics approval Ethical committee approval of KU Leuven and Hasselt University was obtained for this study (S60363).

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Data sharing statement Data may be obtained from a third party and are not publicly available. Data may be obtained from the Intego registry. Contact details: Academisch Centrum voor Huisartsengeneeskunde, KU Leuven, Address: Kapucijnenvoer 33, blok J, bus 7001, 3000 Leuven, E-mail: intego@kuleuven.be.

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