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Development of a risk prediction score for screening for HBV, HCV and HIV among migrants in France (STRADA study)

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Development of a risk prediction score for screening for HBV, HCV and HIV among migrants in France (STRADA study)

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1 **Abstract (297 words)**

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3 **Background:** Migrants from high HIV, HBV or HCV endemicity regions, have a great burden of
4 these infections and related diseases in the host countries. This study aimed to assess the predictive
5 capacity of the TROD (*Test Rapide d'Orientation Diagnostique*) Screen questionnaire for HIV,
6 HBV and HCV infections among migrants arriving in France.
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11 **Methods:** An observational and multicenter study was conducted between January 2017 and
12 March 2020 among migrants in centers of the French Office for Immigration and Integration
13 (OFII). A self-questionnaire on demographic characteristics, personal medical history and sexual
14 behaviors was completed. Participants were tested for HIV, HBV and HCV with rapid tests. For
15 each infection, the test performance was assessed using receiver operating characteristics curves,
16 using area under the curve (AUC) as a measure of accuracy.
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21 **Results:** Among 21133 regular migrants seen in OFII centers, 15343 (72.6%) were included in
22 the study. The mean age of the participants was 35.6 years (SD±11.1). The prevalence [95%CI] of
23 HBV, HCV and HIV was 2.0% [1.8–2.2], 0.3% [0.2–0.4], and 0.3% [0.2–0.4] respectively. Based
24 on the sensitivity–specificity curve analysis, the cut-offs point [95%CI] chosen for the risk score
25 were: for HBV infection in men, 2.5 [95%CI: 2.5-7.5]; for HBV infection in women, 6.5 [95%CI:
26 0.5-6.5]; for HCV infection, 9.5 [95%CI: 9.5-12.5]; and for HIV infection, 10.5 [95%CI: 10.0-
27 18.5]. Test performance was highest for HIV (AUC=82.15%, 95%CI 74.54%-87.99%), followed
28 by that for HBV in men (AUC=79.22%, 95%CI 76.18%-82.26%), for HBV in women
29 (AUC=78.83, 95%CI 74.54%; 82.10%) and that for HCV (AUC=75.95%, 95%CI 68.58%-
30 83.32%).
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34 **Conclusion:** The TROD screen questionnaire showed good overall performance for predicting
35 HIV, HBV and HCV infections among migrants in OFII centers. It could be used to optimize
36 screening for these infections and to propose rapid screening test to those who are at high risk.
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40 **Keywords:** Risk score; HBV; HCV; HIV; migrants
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Strengths and limitations of this study

- This study was that it included a large number of migrants from several different countries. This study may capture estimates from different profiles of migrants in several centers.
- The migrants participating in the study are regular migrants receiving permit to stay, that might have higher socio-economic status than other categories such as asylum seekers and it should be tested in this population.
- Not all migrants having their medical consultation at OFII centers were proposed to participate to the study, due to shortage of time staff or language barrier.
- There may be a bias of underreporting information, as some participants, being at the OFII center, may feel uncomfortable to disclose some sexual behaviors.
- Using these tools, a considerable number of infections could be missed, which could cause an ethical issue.

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Background

Viral hepatitis (including hepatitis B and hepatitis C) as well as HIV infection are among the most common chronic infectious diseases worldwide and a major public health problem [1,2]. In 2015, HIV infection was involved in 1.06 million deaths, while viral hepatitis led to 1.34 million deaths, due to chronic or long-term complications, such as cirrhosis, liver failure and hepatocellular carcinoma [2]. These infections disproportionately affect regions of the world, with high prevalence in low-income countries [2,3]. In low endemicity regions, the mobile population or migrants have a great burden of these infections and related diseases [4,5]. A meta-analysis on hepatitis B virus (HBV) prevalence among immigrants found an overall pooled seroprevalence of infection of 7.2% (95% CI: 6.3%–8.2%). In addition, a subgroup analysis showed that HBV prevalence reflected that in the region of origin, particularly for those from intermediate or high prevalence regions including Middle East, East Asia and sub-Saharan Africa [6]. Another meta-analysis found an overall anti-HCV antibody prevalence among migrants of 1.9% (95% CI, 1.4–2.7%), with higher prevalence among migrants from Sub-Saharan Africa, Asia, and Eastern Europe [7].

France is a country of low endemicity for these infections, the estimated prevalence of HIV infection was 0.41%, of chronic HBV infection 0.93% and of chronic hepatitis C virus (HCV) infection 0.60% in 2020 in the general adult population [8]. People born abroad and mobile populations such as immigrants and travelers from countries with a relatively high HIV, HBV or HCV endemicity are vulnerable groups for these infections [9,10]. In a cross-sectional survey (AfroBaromètre 2016) conducted among Afro-Caribbeans living in the Paris area in 2016, the prevalence of HIV and HBsAg was 1.4% and 1.7% respectively among participants born in France, both 2.6% among those born in Haïti, and 1.7% and 7.0% respectively for those born in sub-Saharan Africa [10]. Almost 20% of them have never been screened for HIV or HBV. In addition, 40% of HIV-positive participants and 77% of those living with HBV were unaware of their seropositive status.

In recent years, with the development of rapid screening tests, HIV, HBV and HCV screening rate has highly increased in France [11]. However, many people remain undiagnosed and unaware of their infection status, including people from sub-Saharan Africa or Asia who were less likely to receive HIV, HBV or HCV screening, fearing mostly of discrimination, but also because of the fact that most of them did not have a regular residence permit. It was also known that migrant populations have a lack of knowledge about these infections and are less likely to be screened for [10,12]. Given the high prevalence of these infections in migrant populations, they might be at an increased risk of transmission or acquisition.

1 In many European countries, it is common for migrants from countries with high HBV endemicity
2 to be systematically offered screening for HIV, HBV and HCV. Morbidity and mortality from
3 these infections can be reduced by early diagnosis through screening at risk people for these
4 infections and offering appropriate medical management [6,13], which should also contribute to
5 secondary prevention of HIV, HBV and HCV infections. Besides, for at risk patients, the
6 vaccination against HBV should be proposed.
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11 STRADA study, which was designed to evaluate a new strategy for screening for infectious
12 diseases among the migrants admitted in the French Office for Immigration and Integration (OFII)
13 departments and to validate a self-screening questionnaire for tuberculosis (TB Screen) as well as
14 HIV, HBV and HCV ("TROD Screen" questionnaire), showed a high acceptability of the
15 participants for HIV and hepatitis screening [14].
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20 The objective of this study is to assess the predictive capacity of the TROD Screen risk factor self-
21 reported questionnaire for HIV, HBV and HCV infection among migrants during their medical
22 visit in the OFII.
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Methods

Study design and participants

This was a prospective multicenter and observational study, carried out between January 2017 and March 2020 among migrants in 21 centers of the French Office for Immigration and Integration (OFII) including: 3 centers in Ile-de-France (Cergy, Melun, Montrouge), 16 centers outside Ile-de-France (Bordeaux, Dijon, Grenoble, Lille, Limoges, Lyon, Marseille, Montpellier, Nantes, Nice, Orléans, Rennes, Reims, Rouen, Strasbourg, Toulouse) and 2 overseas centers (Cayenne, Pointe-à-Pitre). Individuals were included during the compulsory medical visit at time of the delivery of their first residence permit. Eligible participants were migrants aged 18 years or more and who consented to participate to this study.

Study intervention and data collection

Participants completed online the anonymous TROD Screen questionnaire. This self-administrated questionnaire was translated into 10 languages (English, Arabic, Chinese, Bengali, Russian, Lingala, Portuguese, Spanish, Turkish, Haitian Creole) and included data related to sociodemographic, personal medical history and sexual behaviors. A few data were retrieved from medical records (year of birth, gender, height, weight and nationality). Then, a rapid screening test for HBV, HCV or HIV infections was proposed to the participants who could refuse or choose between tests. The participants who reported prior testing, but forgot the result of the test were encouraged to be tested again. However, those who were aware of their status (for example for HIV or HBV) or those who documented a vaccination against HBV were not tested.

A nurse performed the rapid screening test or TROD (*Test Rapide d'Orientation Diagnostique*), using TOYO HCV Test (for HCV) [15], TOYO HBsAb Test (for HBV) [16], and INSTI HIV1/HIV2 Test (for HIV) [17]. Then the doctor or nurse announced the results. In case of a positive result, participant was offered to be referred to a specialized hospital consultation to confirm the diagnosis and initiate adapted treatments.

Variables definition

The outcome was a positive rapid screening test for HBV, HCV or HIV infections. It was used as the gold standard for calculating the sensitivity and specificity of various combination of participants' characteristics for predicting HBV, HCV or HIV infection.

A number of independent predictor factors were used for the prediction of HBV, HCV or HIV infection. (1) Sociodemographic characteristics: age, (years), gender (male or female), weight status (Underweight (BMI<18); Normal weight (BMI 18 and 25) or Overweight/Obesity

(BMI>25)), endemic area for each infection knowledge of HIV, HBV and HCV. (2) Personal history: HIV, HBV or HCV screening, vaccination against HBV, dental treatment, surgery, abortion, caesarean section or difficult childbirth, history of liver disease, tattoos or piercings, prison, blood transfusion, living with a person infected with viral hepatitis, psychoactive substance use (injection or snorting). (3) Sexual behaviors: geographical origin of sexual partner, number of sexual partners during the last 12 months and sexual practices and orientation.

Statistical analysis

Statistical analyses were performed using R software version R 3.6.3. The participants' characteristics were described using absolute frequencies, proportions for categorical variables, or means and standard deviation (SD) for continuous variables.

A cross-analysis between explanatory factors and each infection (HBV, HCV and HIV) was performed using a Student's t test or Wilcoxon for the means and a Chi-square or Fisher test for the proportions.

Binary logistic regression models were fitted to identify factors associated with HBV, HCV or HIV infection. In the univariate analysis, independent variables with p-value less than 0.25 were included in multivariable logistic regression analysis in order to control potential confounders. The final multivariable model was performed using a stepwise selection procedure, which was based on the likelihood ratio test (p-value<0.05). The Akaike information criterion (AIC) was used to select the final model. Results were reported as adjusted odds ratios (aOR) with 95% confidence intervals (CI).

The discriminating capacity of the TROD Screen questionnaire for HBV, HCV and HIV was evaluated by using the predictive value of the questionnaire, its sensitivity, its specificity as well as the 95% confidence intervals. A ROC curve was used to determine the cutoff score of the questionnaire for each infection.

By assuming, that the HBV prevalence is higher in men than in women, we carried out the analysis on HBV infection by stratifying by sex, in order to obtain risk scores specific to the men and women included in this study.

Patient and public involvement statement

None.

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Results

Characteristics of study participants

A total of 21133 participants realized a rapid test during their medical visit. Among them 15343 participants who had the rapid screening test and completed the TROD screen questionnaire, were included in this analysis. Their socio-demographic characteristics are described in Table 1. The mean age of the participants was 35 years (SD±11), and 62.8% were female. More than one-third (36.5%) of them were overweight or obese. Among the participants, 23.9%, 16.3%, and 2.7% came from a high endemicity area of HCV, HBV and HIV respectively. History of dental care (72.0%), surgery (32.7%), piercing and tattoo (31.0%), blood transfusion (3.7%), psychoactive substance consumption (3.1%) and liver problem (2.2%) were reported. A little more than one-fifth of the female participants reported history of abortion or cesarean section or difficult childbirth (21.4%), and 3.9% of them declared being pregnant at the moment of the survey.

Regarding the sexual behaviors, 10.3% of the migrants seen reported two sexual partners or more during last 12 previous months, while 38.6% reported a sexual partner born in Asia Middle East or Africa. About 10% (1211) of participants reported anal intercourses.

Almost one-third of the participants (32.0%) reported a history of screening for Hepatitis B, 26.4% for Hepatitis C and 47.5% for HIV. In addition 4291 migrants reported a vaccination against HBV. The overall seroprevalence [95%CI] of HBV, HCV and HIV was 2.0% [1.8 – 2.2], 0.3% [0.2 – 0.4], and 0.3% [0.2 – 0.4] respectively.

Development of the risk score of HBV, HCV and HIV infection

Univariable logistic regression analyses were used to select explanatory variables for adjusted models. Multivariable logistic regression models were fitted to determine factors associated with each infection. The coefficient values (and adjusted odds-ratio (aOR)) of each variable were obtained. Only significant variables in the parsimonious models were selected to be used in the development of the risk score in each infection, which were as follows (Table 2):

- For HBV infection in men: *endemic area of HBV, history of dental care, history liver problems and vaccination against Hepatitis B;*
- For HBV infection in women: *endemic area of HBV, history liver problems, living with someone who has had viral hepatitis and vaccination against Hepatitis B;*
- For HCV infection: *endemic area of HCV, history of blood transfusion and abortion or cesarean section or difficult childbirth;*
- For HIV infection: *endemic area of HIV, history of blood transfusion and sexual identity.*

Determination of cut-off points

To determine the score for each level of the variables, weighted points were assigned to each of the final associated factors. The β -coefficients of each variable were multiplied by a constant (we have chosen 5), and rounded to the nearest integer (Table 3).

Based on the sensitivity–specificity curve analysis (Figure 1), the cut-offs point was chosen for the risk score for HBV (both in men, and women), HCV and for HIV infections, with maximum sensitivity and specificity. The sensitivity, specificity, and AUC values and their 95%CI corresponding to each cut-off are detailed in Table 4. These cut-offs points were used to differentiate participants with a high risk of each infection (i.e. HBV, HCV and HIV infection) and those with a low risk. Indeed, participants whose score was lesser than the cut-off were supposed to have low risk.

Furthermore, 5509 men realized a rapid test for HBV and completed the TROD screen questionnaire. The optimal threshold for HBV was 2.5 [95%CI: 2.5; 7.5] (Table 4). At this cut-off, we would have performed 2346 tests, detected 144 HBV infections, and we would have avoided 3163 tests but missed 19 HBV infections (Table 4).

Regarding women, 9341 individuals realized a rapid test for HBV and completed the TROD screen questionnaire during their visits. The optimal threshold for HBV was 6.5 [95%CI: 0.5; 6.5] (Table 4). At this cut-off, we would have performed 1982 tests, detected 83 HBV infections, and we would have avoided 7359 tests but missed 47 HBV infections (Table 4).

For HCV, 15216 migrants realized a rapid test during their visits and completed the TROD screen questionnaire. The optimal threshold for HCV was 9.5 [95%CI: 9.5; 12.5] (Table 4). At this cut-off, we would have performed 4950 tests, detected 31 HCV infections, and we would have avoided 10266 tests but missed 10 HCV infections (Table 4).

For HIV infection, 15100 migrants realized a rapid test during their visits and completed the TROD screen questionnaire. The optimal threshold for HBV was 10.5 [95%CI: 10.0; 18.5] (Table 4). At this cut-off, we would have performed 3483 tests, detected 39 HIV infections, and we would have avoided 11617 tests but missed 9 HIV infections (Table 4).

Discussion

This large French nationwide study was carried out among migrants in order to evaluate the capacity of the TROD Screen questionnaire to predict HBV, HCV or HIV infection, which may assist health practitioners and policymakers in optimal screening of these infections in migrants. Therefore, we developed a risk score for these infections using a combination of participants' characteristics, including sociodemographic, personal health related history and behaviors, mainly sexual behaviors. With the determination of a cut-off point, this score allowed us to classify participants into subgroups at low and high risk for these infections.

In view of the AUC, the specificity and the sensitivity, our scoring models, showed good discrimination and calibration, particularly for HBV infection in men and HIV infection. For a predictive questionnaire, it has expected a sensitivity greater than 80% with lower specificity compared to the rapid test. For HBV infection in women and HCV infection, even though the specificity and the sensitivity were not good enough, their discriminatory capacity remained acceptable (AUC >70%). Globally, as demonstrated by our results, the use of these tools could avoid realize a considerable number of rapid tests, with a reduction in the workload of health professionals.

The endemic area of origin of the participants remains the important characteristic in the construction of these scores. Indeed, the endemic area is predictive of the risk of HBV, HCV and HIV infection among migrants in France. Participants from medium and/or high endemicity areas were the most likely to have a positive rapid test. In medium or high endemicity areas, which are generally included countries with limited resources, strategies for the prevention and diagnosis of these infections remain poorly available or accessible [18]. Therefore, there is a low rate of screening test for viral hepatitis as well as availability verified blood products. Migrants from these areas have a high probability of having been in contact or being a chronic carrier of one of these viruses before their migration process [19].

For HBV infection, either in men or women, vaccination against HBV and history of liver problems were predictive of the risk of HBV. Vaccination against HBV was associated with low probability to have HBV-positive test in both men and women. In low-income countries, availability and access to HBV vaccines remains a challenge [20]. In these regions, contact with this virus occurred for the most part in the perinatal period and during early childhood, most often leading to an evolution to chronicity [20–22]. Even though, vaccination against HBV (with complete or incomplete schedule) predicted low risk for HBV infection, participants who reported history of liver pathology were more likely to have positive test for HBV. Even if only 2 to 10% of HBV infections are symptomatic or evolve to chronic form [23], it is important to make further investigations in migrants who have reported a history of liver problems, as suggested in our study.

1 In addition, history of blood transfusion is also predictive of HCV and HIV infection. Till the last
2 decade, in low-income countries, the risk of transfusion transmitted infections remained high due
3 to unsafe transfusion practices. HIV or HCV are the main transfusion transmitted infections
4 reported and must be at the center of prevention strategies [24,25]. These unsafe transfusion
5 practices in those regions are more often correlated to other unsafe practices especially in invasive
6 procedures like abortion or cesarean section. Thus, in our predictive analysis, in migrant women,
7 history of abortion or cesarean section or difficult childbirth and living with someone who had
8 viral hepatitis have predicted respectively HCV and HBV infection.
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11 Reporting being homosexual or bisexual has been found to be highly predictive of HIV infection
12 among migrants. This is in line with several studies, which highlighted that men who have sex
13 with men were at higher risk of Sexually Transmitted Infections, including HIV infection,
14 especially when having multiple sexual partners and unprotected anal intercourse [26,27].
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1 **Conclusion**

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3 The TROD screen questionnaire showed acceptable overall performance for predicting HIV, HBV
4 and HCV infections in migrants seen in OFII centers. That should provide the OFII’s medical staff
5 and other health care workers receiving migrants, optimal diagnosis tools based on the risk
6 assessment, leading to the proposal of a rapid screening test for these infections. It could be also
7 helpful for orienting those with high risk for the biological confirmation.
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Availability of data and materials

The datasets used during the current study are not publicly available but could be available from the corresponding author on reasonable request.

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Author Contributions Statement

MD, FT conceived and designed the study. LY-K, PB, and IY performed the statistical analysis. MD, FT and OC acquired funding for the project. IY wrote the first draft of the manuscript. All the authors revised the manuscript and approved the final manuscript.

Ethics declarations

Ethics approval and consent to participate

All procedures of this study were in accordance with the ethical approval granted by an Independent Ethics Committees (CPP Ile de France IV, N° IRB 3835, Ref. 2016/43NI) and by the French data protection authority (CNIL) (n°2008669). All methods were carried out in accordance with relevant guidelines and regulations. The study was also registered in ClinicalTrial.gov (NCT02959684). Informed consent was obtained in writing from all individual participants included in the study.

Consent for publication

Not applicable.

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Competing interests

The authors declare that they have no competing interests.

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Table 1: Participants' characteristics

Participants' characteristics	Total = 15343		HBV-positive n=293	HCV-positive n=42	HIV-positive n=47
	N	n (%) or mean (±SD)	n (prevalence)	n (prevalence)	n (prevalence)
<u>Sociodemographic characteristics</u>					
Age, years	15343	35 (±11)	37.3 (±9.5)*	44.5 (±15.0)***	37.6 (±9.4)
Gender	15343		***	°	°
Male		5707 (37.2)	164 (3.0)	17 (0.3)	20 (0.4)
Female		9636 (62.8)	129 (1.4)	25 (0.3)	27 (0.3)
BMI (kg/m ²)			°	°	°
Underweight	15343	907 (5.9)	12 (1.8)	2 (0.2)	2 (0.2)
Normal weight		8830 (57.6)	167 (2.0)	23 (0.3)	24 (0.3)
Overweight/ Obesity		5606 (36.5)	114 (2.1)	12 (0.3)	21 (0.4)
Endemic area of HCV	15327		***	***	***
Low		2393 (15.6)	8 (0.3)	1 (4.10 ⁻⁴)	1 (4.10 ⁻⁴)
Medium		9278 (60.5)	114 (1.3)	16 (0.2)	14 (0.2)
High		3656 (23.9)	171 (4.9)	25 (0.7)	31 (0.9)
Endemic area HBV	13884		***	***	***
Low		7686 (55.3)	39 (0.5)	10 (0.1)	4 (5.10 ⁻⁴)
Medium		3938 (28.4)	117 (3.1)	22 (0.6)	24 (0.6)
High		2260 (16.3)	122 (5.6)	7 (0.3)	17 (0.8)
Endemic area HIV	11390		***	**	***
Low		8317 (73.0)	102 (1.3)	17 (0.2)	11 (0.1)
Medium		2763 (24.3)	142 (5.4)	18 (0.7)	29 (1.1)
High		310 (2.7)	25 (8.1)	0 (0.0)	1 (0.3)
Knowledge of Hepatitis B infection	15343	10852 (70.7)	200 (1.9)°	32 (0.3)°	30 (0.3)°
Knowledge of Hepatitis C infection	15343	10335 (67.5)	175 (1.8)**	29 (0.3)°	26 (0.3)°
Knowledge of HIV infection	15343	13168 (85.8)	246 (1.9)°	36 (0.3)°	43 (0.3)°
<u>Personal history</u>					
Screened for Hepatitis B infection	12631	4044 (32.0)	101 (2.6)***	11 (0.3)°	13 (0.3)°
Screened for Hepatitis C infection	12286	3239 (26.4)	50 (1.6)°	13 (0.4)°	8 (0.2)°
Screened for HIV infection	14176	6733 (47.5)	169 (2.6)***	27 (0.4)*	28 (0.4)*
Vaccination against HBV	9446	4291 (45.4)	45 (1.1)***	8 (0.2)°	9 (0.2)*
History of dental care	14990	10797 (72.0)	161 (1.5)***	32 (0.3)°	26 (0.2)*
History of surgery	15061	4930 (32.7)	78 (1.6)°	17 (0.3)°	17 (0.4)°
History of piercing or tattoo	15343	4751 (31.0)	65 (1.4)***	15 (0.3)°	22 (0.5)*
History of blood transfusion	15343	572 (3.7)	15 (2.7)°	8 (1.4)***	7 (1.2)***
History liver problems	15343	333 (2.2)	22 (7.0)***	3 (0.9)°	0 (0.0)°
Abortion or cesarean section or difficult childbirth ^Φ	9635		*	***	***
		2057 (21.4)	39 (2.0)	14 (0.7)	16 (0.8)
Pregnant ^Φ	9443	2057 (3.9)	5 (1.4)°	1 (0.3)°	0 (0.0)°
Living with someone who has had viral hepatitis [§]	15343		***	°	°
		369 (2.4)	26 (7.3)	2 (0.6)	0 (0.0)
Healthcare worker or barber	15343	1066 (6.9)	15 (1.5)°	4 (0.4)°	4 (0.4)°
Being in jail	15048	80 (0.5)	4 (5.0)°	0 (0.0)°	0 (0.0)°
<u>Behaviors</u>					
Inject or snort psychoactive substance	14987		°	°	°
		462 (3.1)	9 (2.0)	2 (0.4)	0 (0.0)

1	Number of sexual partners in last 12	13037			
2	previous months				
3	0	990 (7.6)	19 (2.0)	2 (0.2)	2 (0.2)
4	1	10700 (82.1)	194 (1.9)	24 (0.2)	36 (0.3)
5	2 and more	1347 (10.3)	23 (1.8)	5 (0.4)	5 (0.4)
6	Sexual partner born in Asia Middle	13889	***	°	*
7	East or Africa	5360 (38.6)	137 (2.6)	19 (0.4)	25 (0.5)
8	Sexual identity	14768	***	°	***
9	No sex	2011 (13.6)	26 (1.3)	7 (0.4)	1 (0.1)
10	Heterosexual women	7777 (52.7)	109 (1.5)	18 (0.2)	27 (0.4)
11	Heterosexual men	4632 (31.4)	139 (3.1)	11 (0.2)	13 (0.3)
12	Homosexual & Bisexual	348 (2.4)	4 (1.2)	2 (0.6)	6 (1.7)
13	Having anal sex, Yes	12469	1211 (9.7)	16 (1.4)°	4 (0.3)°
14					8 (0.7)*
15	Outcomes				
17	HBV – positive	14849	293 (2.0)		2 (0.7)°
18	HCV – positive	15214	42 (0.3)	2 (5.3)°	3 (1.1)*
19	HIV – positive	15099	47 (0.3)	3 (7.1)*	3 (7.1)***
20				3 (6.8)***	

p-value (Khi2 or Fischer tests) : ° NS, * <0.05, ** <0.01, *** <0.001
§ : Mother, Sexual partner, household member
Φ : only in female participants

Table 2 : Associated factors with HBV, HCV and HIV among migrants in France

Participants' characteristics s	HBV infection Men (n=5707)	HBV infection Women (n=9636)	HCV infection (n= 15343)	HIV infection (n= 15343)
	aOR [95%CI]	aOR [95%CI]	aOR [95%CI]	aOR [95%CI]
Endemic area of HBV (low: aOR = 1)				
Medium	7.62 [4.51 – 13.67]***	4.65 [2.86 – 7.79]***		
High	15.83 [9.40 – 28.35]***	6.68 [4.06 – 11.29]***		
Endemic area of HCV (low: aOR = 1)				
Medium			4.09 [0.83 – 73.85]°	
High			13.97 [2.94 – 250.21]**	
Endemic area of HIV (low: aOR = 1)				
Medium				8.31 [4.25 – 17.50]**
High				2.23 [0.12 – 11.57]°
History of dental care (No: aOR = 1)	0.65 [0.47 – 0.89]**			
History of blood transfusion (No: aOR = 1)			4.67 [1.96 – 9.90]***	3.65 [1.47 – 7.79]***
History liver problems (No: aOR = 1)	3.13 [1.46 – 6.07]***	3.40 [1.72 – 6.19]***		
Abortion or cesarean section or difficult childbirth ^Φ (No: aOR = 1)			2.40 [1.20 – 4.60]*	
Living with someone who has had viral hepatitis § (No: aOR = 1)		6.03 [3.43 – 10.08]***		
Sexual identity (No sex: aOR = 1)				
Heterosexual women				5.88 [1.24 – 105.03]°
Heterosexual men				4.75 [0.95 – 86.29]°
Homosexual & Bisexual				44.60 [7.45 – 849.71]**
Vaccination against HBV (No: aOR = 1)	0.63 [0.41 – 0.96]*	0.21 [0.11 – 0.36]***		

p-value : ° NS, * <0.05, ** <0.01, *** <0.001
§ : Mother, Sexual partner, household member
Φ : only in female participants

Table 3 : Score assignment

	β -Coefficient	β -Coefficient multiplied by 5	Score mark
HBV infection (men)			
Endemic area of HBV (Low = 0)			
Medium	2.03	10.15	10
High	2.76	13.80	14
History of dental care (No = 0)	-0.44	-2.20	-2
History liver problems (No = 0)	1.14	5.70	6
Vaccination for Hepatitis B (No = 0)	-0.46	-2.30	-2
Risk score [Endemic area of HBV : Low = 0; Medium = 10; High = 14] - 2 * [History of dental care] + 6 * [History liver problems] - 2 * [Vaccination for Hepatitis B]			
HBV Female (women)			
Endemic area of HBV (Low = 0)			
Medium	1.54	7.70	8
High	1.90	9.50	10
History liver problems (No = 0)	1.22	6.10	6
Living with someone who has had viral hepatitis (No = 0)	1.80	9.00	9
Vaccination for Hepatitis B (No = 0)	-1.58	-7.90	-8
Risk score (female) : [Endemic area of HBV : Low = 0; Medium = 8; High = 10] + 6 * [History liver problems] + 9 * [Living with someone who has had viral hepatitis] - 8 * [Vaccination for Hepatitis B]			
HCV infection			
Endemic area of HCV (Low = 0)			
Medium	1.41	7.05	7
High	2.64	13.20	13
History of blood transfusion (No = 0)	1.54	7.70	8
Abortion or cesarean section or difficult childbirth^Φ (No = 0)	0.87	4.35	4
Risk score : [Endemic area of HCV : Low = 0; Medium = 7; High = 13] + 8 * [History of blood transfusion] + 4 * [Abortion or cesarean section or difficult childbirth]			
HIV infection			
Endemic area of HIV (Low = 0)			
Medium	2.12	10.60	11
High	0.80	4.0	4
History of blood transfusion (No = 0)	1.29	6.45	6
Sexual identity (No sex = 0)			
Heterosexual women	1.77	8.85	9
Heterosexual men	1.56	7.80	8
Homosexual & Bisexual	3.80	19.0	19
Risk score : [Endemic area of HIV : Low = 0; Medium = 11; High = 4] + 6 * [History of blood transfusion] + [Sexual identity: No sex = 0; Heterosexual women = 9; Heterosexual men = 8; Homosexual & Bisexual = 19]			

Table 4 : Performance parameters

	Optimal threshold [95% CI]	Sensitivity [95% CI]	Specificity [95% CI]	AUC [95% CI]	Score >=Optimal threshold	Negative rapid test	Positive rapid test	Total
HBV infection (men)	2.5 [2.5 ; 7.5]	88.34 [73.62 ; 92.64]	58.81 [57.76 ; 71.49]	79.22 [76.18 ; 82.26]	No	44 (TN)	19 (FN)	3163
					Yes	102 (FP)	144 (TP)	2346
					Total	146	163	5509
HBV infection (women)	6.5 [0.5 ; 6.5]	63.85 [60.00 ; 86.15]	79.38 [60.95 ; 80.10]	78.83 [74.54 ; 82.10]	No	12 (TN)	47 (FN)	7359
					Yes	199 (FP)	83 (TP)	1982
					Total	211	130	9341
HCV infection	9.5 [9.5 ; 12.5]	75.61 [58.54 ; 87.80]	67.58 [66.90 ; 74.83]	75.95 [68.58 ; 83.32]	No	256 (TN)	10 (FN)	10266
					Yes	119 (FP)	31 (TP)	4950
					Total	375	41	15216
HIV infection	10.5 [10.0 ; 18.5]	81.25 [68.75 ; 91.67]	77.12 [76.59 ; 82.85]	82.15 [74.54 ; 87.99]	No	608 (TN)	9 (FN)	11617
					Yes	144 (FP)	39 (TP)	3483
					Total	752	48	15100

TN= true negative; FN= false negative; FP= false positive; TP= true positive

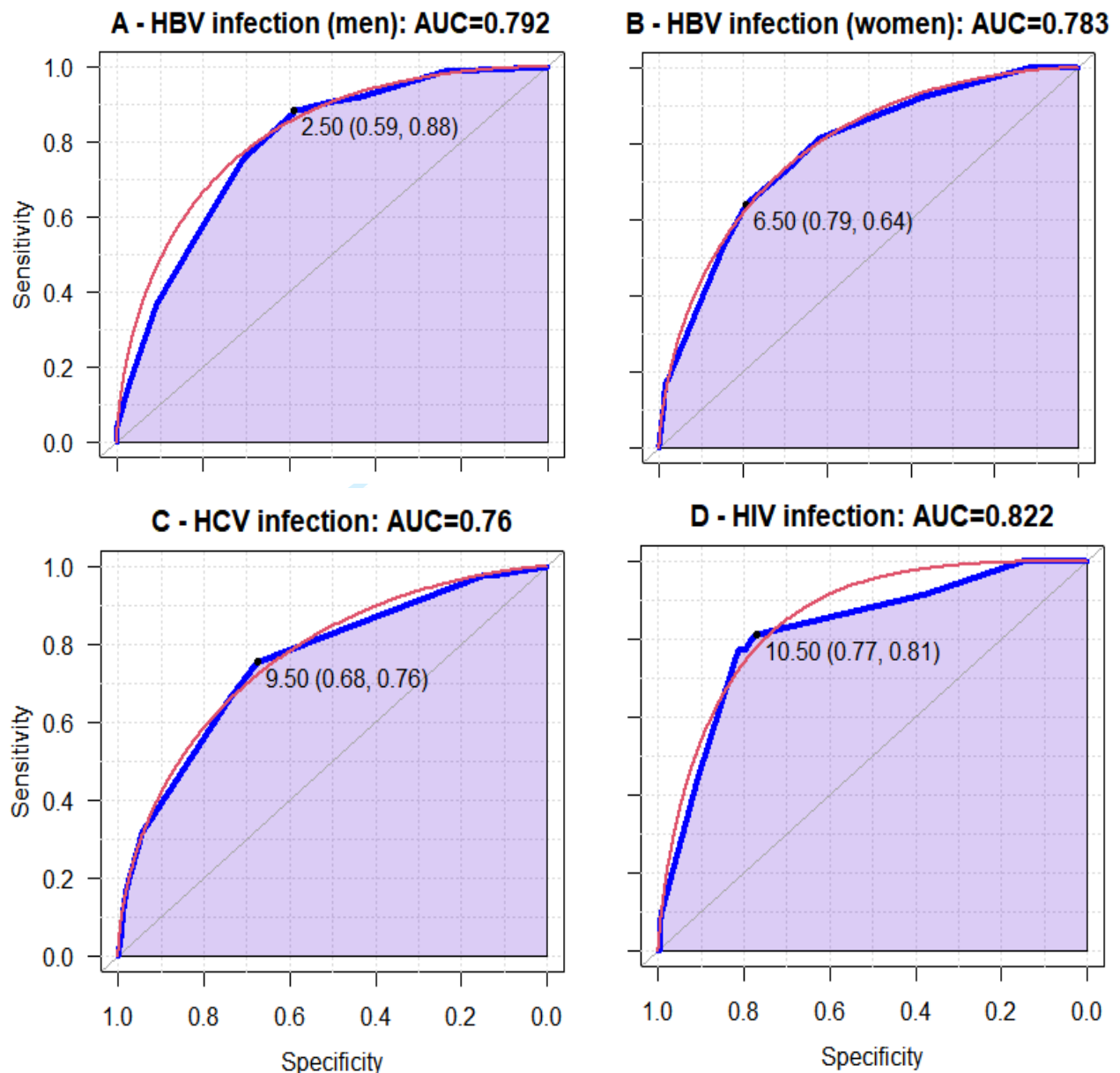


Figure 1. Receiver operating characteristics (ROC) curve for multivariable logistic regression models, with the area under the curve (AUC) and cut-offs of HBV in men (A), HBV in women (B), HCV (C) and HIV infection (D) screening

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Development of a risk prediction score for screening for HBV, HCV, and HIV among migrants in France: results from a multicentre observational study (STRADA study)

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Development of a risk prediction score for screening for HBV, HCV, and HIV among migrants in France: results from a multicentre observational study (STRADA study)

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Abstract (297 words)

Objectives: Migrants from high HIV, HBV, or HCV endemicity regions have a great burden of these infections and related diseases in the host countries. This study aimed to assess the predictive capacity of the TROD Screen questionnaire for HIV, HBV, and HCV infections among migrants arriving in France.

Design: An observational and multicenter study was conducted among migrants. A self-questionnaire on demographic characteristics, personal medical history, and sexual behaviors was completed.

Setting: The study was conducted in the centers of the French Office for Immigration and Integration (OFII).

Participants: Convenience sampling was used to select and recruit adult migrants between January 2017 and March 2020.

Outcome measures: Participants were tested for HIV, HBV, and HCV with rapid tests. For each infection, the test performance was assessed using receiver operating characteristics curves, using area under the curve (AUC) as a measure of accuracy.

Results: Among 21,133 regular migrants seen in OFII centers, 15,343 were included in the study. The participants' mean age was 35.6 years (SD±11.1). The prevalence [95%CI] of HBV, HCV, and HIV was 2.0% [1.8–2.2%], 0.3% [0.2–0.4%], and 0.3% [0.2–0.4%], respectively. Based on the sensitivity–specificity curve analysis, the cut-off points [95%CI] chosen for the risk score were: for HBV infection in men, 2.5 [2.5–7.5]; for HBV infection in women, 6.5 [0.5–6.5]; for HCV infection, 9.5 [9.5–12.5]; and for HIV infection, 10.5 [10.0–18.5]. Test performance was highest for HIV (AUC=82.15%, [74.54–87.99%]), followed by that for HBV in men (AUC=79.22%, [76.18–82.26%]), for HBV in women (AUC=78.83, [74.54–82.10%]), and that for HCV (AUC=75.95%, [68.58–83.32%]).

Conclusion: The TROD screen questionnaire showed good overall performance for predicting HIV, HBV, and HCV infections among migrants in OFII centers. It could be used to optimize screening for these infections and to propose rapid screening tests to those who are at high-risk.

Keywords: Risk score; HBV; HCV; HIV; migrants.

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Strengths and limitations of this study

- This study was that it included a large number of migrants from several different countries. This study may capture estimates from different profiles of migrants in several centers.
- The migrants participating in the study are regular migrants receiving permits to stay; they might have a higher socio-economic status than other categories, such as asylum seekers, and it should be tested in this population.
- Not all migrants having their medical consultation at OFII centers were proposed to participate in the study due to a shortage of time, staff, or language barriers.
- There may be a bias toward underreporting information, as some participants, being at the OFII center, may feel uncomfortable disclosing some sexual behaviors.
- Using these tools, a considerable number of infections could be missed, which could cause an ethical issue.

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Background

Viral hepatitis (including hepatitis B and hepatitis C) as well as HIV infection are among the most common chronic infectious diseases worldwide and a major public health problem [1,2]. In 2015, HIV infection was involved in 1.06 million deaths, while viral hepatitis led to 1.34 million deaths due to chronic or long-term complications such as cirrhosis, liver failure, and hepatocellular carcinoma [2]. These infections disproportionately affect regions of the world, with a high prevalence in low-income countries [2,3]. In low-endemicity regions, the mobile population or migrants have a great burden of these infections and related diseases [4,5]. A meta-analysis on hepatitis B virus (HBV) prevalence among immigrants found an overall pooled seroprevalence of infection of 7.2% (95% CI: 6.3%–8.2%). In addition, a subgroup analysis showed that HBV prevalence reflected that in the region of origin, particularly for those from intermediate or high-prevalence regions including the Middle East, East Asia, and sub-Saharan Africa [6]. Another meta-analysis found an overall anti-HCV antibody prevalence among migrants of 1.9% (95% CI, 1.4–2.7%), with a higher prevalence among migrants from Sub-Saharan Africa, Asia, and Eastern Europe [7].

France is a country with low endemicity for these infections; the estimated prevalence of HIV infection was 0.41%, of chronic HBV infection was 0.93%, and of chronic hepatitis C virus (HCV) infection was 0.60% in 2020 in the general adult population [8]. People born abroad and mobile populations such as immigrants and travelers from countries with a relatively high HIV, HBV, or HCV endemicity are vulnerable groups for these infections [9,10]. In a cross-sectional survey (AfroBaromètre 2016) conducted among Afro-Caribbeans living in the Paris area in 2016, the prevalence of HIV and HBsAg was 1.4% and 1.7%, respectively, among participants born in France, both 2.6% among those born in Haiti, and 1.7% and 7.0%, respectively, for those born in sub-Saharan Africa [10]. Almost 20% of them have never been screened for HIV or HBV. In addition, 40% of HIV-positive participants and 77% of those living with HBV were unaware of their seropositive status.

In recent years, with the development of rapid screening tests, HIV, HBV, and HCV screening rates have highly increased in France [11]. However, many people remain undiagnosed and unaware of their infection status, including people from sub-Saharan Africa or Asia who were less likely to receive HIV, HBV, or HCV screening, fearing mostly discrimination but also because most of them did not have a regular residence permit. It was also known that migrant populations have a lack of knowledge about these infections and are less likely to be screened for them [10,12]. Given the high prevalence of these infections in migrant populations, they might be at increased risk of transmission or acquisition.

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In many European countries, it is common for migrants from countries with high HBV endemicity to be systematically offered screening for HIV, HBV, and HCV. Morbidity and mortality from these infections can be reduced by early diagnosis through screening at-risk people for these infections and offering appropriate medical management [6,13], which should also contribute to the secondary prevention of HIV, HBV, and HCV infections. Besides, for at-risk patients, a vaccination against HBV should be proposed.

The STRADA study, which was designed to evaluate a new strategy for screening for infectious diseases among the migrants admitted in the French Office for Immigration and Integration (OFII) departments and to validate a self-screening questionnaire for tuberculosis (TB Screen) as well as HIV, HBV, and HCV (“TROP Screen”), showed a high acceptability of the participants for HIV and viral hepatitis screening [14].

The objective of this study is to assess the predictive capacity of the TROP Screen risk factor self-reported questionnaire for HIV, HBV, and HCV infection among migrants during their medical visit in the OFII.

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Methods

Study design and participants

This was a prospective multicenter and observational study carried out between January 2017 and March 2020 among migrants in the French Office for Immigration and Integration (OFII) centers. There are 32 OFII centers, including 28 in mainland France and 4 overseas. During our study, all OFII centers were invited to participate, but only 21 OFII centers have accepted, including 3 centers in Ile-de-France (Cergy, Melun, Montrouge), 16 centers outside Ile-de-France (Bordeaux, Dijon, Grenoble, Lille, Limoges, Lyon, Marseille, Montpellier, Nantes, Nice, Orléans, Rennes, Reims, Rouen, Strasbourg, Toulouse), and 2 overseas centers (Cayenne, Pointe-à-Pitre). Individuals were included during the compulsory medical visit at the time of the delivery of their first residence permit. Eligible participants were migrants aged 18 years or more who consented to participate in this study.

Study intervention and data collection

Participants completed the anonymous TROD Screen questionnaire online. This self-administrated questionnaire was translated into 10 languages (English, Arabic, Chinese, Bengali, Russian, Lingala, Portuguese, Spanish, Turkish, and Haitian Creole) and included data related to sociodemographic, personal medical history, and sexual behaviors. A few pieces of data were retrieved from medical records (year of birth, gender, height, weight, and nationality). Then, a rapid screening test for HBV, HCV, or HIV infections was proposed to the participants, who could refuse or choose between tests. The participants who reported prior testing but forgot the result of the test were encouraged to be tested again. However, those who were aware of their status (for example, HIV or HBV) or those who documented a vaccination against HBV were not tested.

A nurse performed the rapid screening test using the TOYO HCV Test (for HCV) [15], the TOYO HBsAb Test (for HBV) [16], and the INSTI HIV1/HIV2 Test (for HIV) [17]. Then the doctor or nurse announced the results. In the event of a positive result, the participant was offered to be referred to a specialized hospital consultation to confirm the diagnosis and initiate adapted treatments.

Variables definition

The outcome was a positive rapid screening test for HBV, HCV, or HIV infections. It was used as the gold standard for calculating the sensitivity and specificity of various combinations of participants' characteristics for predicting HBV, HCV, or HIV infection.

A number of independent predictor factors were used for the prediction of HBV, HCV, or HIV infection. (1) Sociodemographic characteristics: age (years), gender (male or female), weight status (Underweight (BMI<18); Normal weight (BMI 18 and 25), or Overweight/Obesity (BMI>25)), endemic area for each infection, knowledge of HIV, HBV, and HCV. (2) Personal history: HIV, HBV or HCV screening, vaccination against HBV, dental treatment, surgery, abortion, caesarean section or difficult childbirth, history of liver disease, tattoos or piercings, prison, blood transfusion, living with a person infected with viral hepatitis, psychoactive substance use (injection or snorting). (3) Sexual behaviors: geographical origin of sexual partner, number of sexual partners during the last 12 months, and sexual practices and orientation.

Statistical analysis

Statistical analyses were performed using R software version R 3.6.3. The participants' characteristics were described using absolute frequencies, proportions for categorical variables, or means and standard deviation (SD) for continuous variables.

A cross-analysis between explanatory factors and each infection (HBV, HCV, and HIV) was performed using a Student's t test or Wilcoxon for the means and a Chi-square or Fisher test for the proportions.

Binary logistic regression models were fitted to identify factors associated with HBV, HCV, or HIV infection. In the univariate analysis, independent variables with a p-value less than 0.25 were included in the multivariable logistic regression analysis in order to control potential confounders. The final multivariable model was performed using a stepwise selection procedure, which was based on the likelihood ratio test (p-value<0.05). The Akaike information criterion (AIC) was to select the final model. Results were reported as unadjusted odds ratios (OR), and adjusted odds ratios (aOR) with 95% confidence intervals (CI). There was no missing data in all predictor variables and outcomes, and we carried out a complete-case analysis for the outcomes.

Model performance was evaluated in terms of discrimination. The discriminating capacity of the TROD Screen questionnaire for HBV, HCV, and HIV was evaluated using the predictive value of the questionnaire, its sensitivity and specificity, as well as the 95% confidence intervals. A ROC curve was used to quantify discrimination and determine the cutoff score of the questionnaire for each infection. That also assesses whether those with higher predicted risks are more likely to have an HBV, HCV, or HIV infection.

To make the models easier to use in clinical practice, we created a risk score for evaluating the likelihood of HBV, HCV, or HIV infection based on multivariable regression coefficients, which were rescaled and rounded to the nearest whole number. To determine the score for each level of

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the variables, weighted points were assigned to each of the final associated factors. The β -coefficients of each variable were multiplied by a constant (we have chosen 5), and rounded to the nearest integer [18,19]. Based on the sensitivity–specificity curve analysis (Figure 1), the cut-offs point was chosen for the risk score for HBV (both in men, and women), HCV and for HIV infections, with maximum sensitivity and specificity.

By assuming that the HBV prevalence is higher in men than in women, we carried out the analysis on HBV infection by stratifying by sex in order to obtain risk scores specific to the men and women included in this study.

Patient and public involvement statement

None.

Results

Characteristics of study participants

A total of 21,133 participants realized a rapid test during their medical visit. Among them, 15,343 participants who had the rapid screening test and completed the TROD screen questionnaire were included in this analysis. Their socio-demographic characteristics are described in Table 1. The mean age of the participants was 35 years (SD±11), and 62.8% were female. More than one-third (36.5%) of them were overweight or obese. Among the participants, 23.9%, 16.3%, and 2.7% came from a high endemicity area of HCV, HBV, and HIV, respectively. History of dental care (72.0%), surgery (32.7%), piercing and tattooing (31.0%), blood transfusion (3.7%), psychoactive substance consumption (3.1%), and liver problems (2.2%) were reported. A little more than one-fifth of the female participants reported a history of abortion, cesarean section, or difficult childbirth (21.4%), and 3.9% of them declared being pregnant at the moment of the survey.

Regarding sexual behaviors, 10.3% of the migrants seen reported two sexual partners or more during the last 12 months, while 38.6% reported a sexual partner born in Asia, the Middle East, or Africa. About 10% (1211) of participants reported anal intercourses.

Almost one-third of the participants (32.0%) reported a history of screening for hepatitis B, 26.4% for hepatitis C, and 47.5% for HIV. In addition, 4291 migrants reported a vaccination against HBV. The overall seroprevalence [95%CI] of HBV, HCV, and HIV was 2.0% [1.8 – 2.2], 0.3% [0.2 – 0.4], and 0.3% [0.2 – 0.4], respectively.

Development of the risk score for HBV, HCV, and HIV infection

Univariable logistic regression analyses were used to select explanatory variables for adjusted models. Multivariable logistic regression models were fitted to determine factors associated with each infection. The coefficient values (and adjusted odds-ratio (aOR)) of each variable were obtained. Only significant variables in the parsimonious models were selected to be used in the development of the risk score in each infection, which were as follows (Table 2):

- For HBV infection in men: *endemic area of HBV, history of dental care, history of liver problems, and vaccination against hepatitis B;*
- For HBV infection in women: *endemic area of HBV, history of liver problems, living with someone who has had viral hepatitis, and vaccination against hepatitis B;*
- For HCV infection: *endemic area of HCV, history of blood transfusion, and abortion, or cesarean section, or difficult childbirth;*
- For HIV infection: *endemic area of HIV, history of blood transfusion, and sexual identity.*

Determination of cut-off points

The sensitivity, specificity, and AUC values and their 95%CI corresponding to each cut-off are detailed in Table 4. These cut-off points were used to differentiate participants with a high risk of each infection (i.e. HBV, HCV, and HIV infection) from those with a low risk. Indeed, participants whose score was less than the cut-off were supposed to have low risk.

Furthermore, 5,509 men realized a rapid test for HBV and completed the TROD screen questionnaire. The optimal threshold for HBV was 2.5 [95%CI: 2.5; 7.5] (Table 4). At this cut-off, we would have performed 2,346 tests, detected 144 HBV infections, avoided 3,163 tests, and missed 19 HBV infections (Table 4).

Regarding women, 9,341 individuals realized a rapid test for HBV and completed the TROD screen questionnaire during their visits. The optimal threshold for HBV was 6.5 [95%CI: 0.5; 6.5] (Table 4). At this cut-off, we would have performed 1,982 tests, detected 83 HBV infections, and avoided 7,359 tests but missed 47 HBV infections (Table 4).

For HCV, 15,216 migrants realized a rapid test during their visits and completed the TROD screen questionnaire. The optimal threshold for HCV was 9.5 [95%CI: 9.5; 12.5] (Table 4). At this cut-off, we would have performed 4,950 tests, detected 31 HCV infections, and avoided 10,266 tests but missed 10 HCV infections (Table 4).

For HIV infection, 15,100 migrants realized a rapid test during their visits and completed the TROD screen questionnaire. The optimal threshold for HBV was 10.5 [95%CI: 10.0; 18.5] (Table 4). At this cut-off, we would have performed 3,483 tests, detected 39 HIV infections, avoided 11,617 tests, and missed 9 HIV infections (Table 4).

Discussion

This large French nationwide study was carried out among migrants in order to evaluate the capacity of the TROD Screen questionnaire to predict HBV, HCV, or HIV infection, which may assist health practitioners and policymakers in optimal screening of these infections in migrants. Therefore, we developed a risk score for these infections using a combination of participants' characteristics, including sociodemographic, personal health-related history, and behaviors, mainly sexual behaviors. With the determination of a cut-off point, this score allowed us to classify participants into subgroups at low and high risk for these infections.

In view of the AUC, the specificity, and the sensitivity, our scoring models showed good discrimination and calibration, particularly for HBV infection in men and HIV infection. For a predictive questionnaire, it is expected to have a sensitivity greater than 80% with lower specificity compared to the rapid test. For HBV infection in women and HCV infection, even though the specificity and the sensitivity were not good enough, their discriminatory capacity remained acceptable (AUC >70%). Globally, as demonstrated by our results, the use of these tools could avoid a considerable number of rapid tests, resulting in a reduction in the workload of health professionals.

The endemic area of origin of the participants remains an important characteristic in the construction of these scores. Indeed, the endemic area is predictive of the risk of HBV, HCV, and HIV infection among migrants in France. Participants from medium and/or high endemicity areas were the most likely to have a positive rapid test. In medium- or high-endemicity areas, which are generally countries with limited resources, strategies for the prevention and diagnosis of these infections remain poorly available or accessible [20]. Therefore, there is a low rate of screening tests for viral hepatitis as well as the availability of verified blood products. Migrants from these areas have a high probability of having been in contact with or being chronic carriers of one of these viruses before their migration process [21].

For HBV infection, either in men or women, vaccination against HBV and a history of liver problems were predictive of the risk of HBV. Vaccination against HBV was associated with a low probability of having an HBV-positive test in both men and women. In low-income countries, availability and access to HBV vaccines remain a challenge [22]. In these regions, contact with this virus occurred for the most part in the perinatal period and during early childhood, most often leading to an evolution to chronicity [22–24]. Even though vaccination against HBV (with a complete or incomplete schedule) predicted a low risk for HBV infection, participants who reported a history of liver pathology were more likely to have a positive test for HBV. Even if only 2-10% of HBV infections are symptomatic or evolve to chronic form [25], it is important to make

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1 further investigations in migrants who have reported a history of liver problems, as suggested in
2 our study.
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5 In addition, the history of blood transfusions is also predictive of HCV and HIV infection. Till the
6 last decade, in low-income countries, the risk of transfusion-transmitted infections remained high
7 due to unsafe transfusion practices. HIV or HCV are the main transfusion-transmitted infections
8 reported and must be at the center of prevention strategies [26,27]. These unsafe transfusion
9 practices in those regions are more often correlated to other unsafe practices, especially in invasive
10 procedures like abortion or cesarean section. Thus, in our predictive analysis, in migrant women,
11 history of abortion, cesarean section, or difficult childbirth and living with someone who had viral
12 hepatitis have predicted, respectively, HCV and HBV infection.
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15 Reporting being homosexual or bisexual has been found to be highly predictive of HIV infection
16 among migrants. This is in line with several studies, which highlighted that men who have sex
17 with men are at higher risk of Sexually Transmitted Infections, including HIV infection, especially
18 when having multiple sexual partners and unprotected anal intercourse [28,29].
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20 Despite our study providing useful risk score for predicting HIV, HBV, and HCV infections,
21 several limitations need to be addressed. It is possible that answers to questions may be subject to
22 sub-declarations. Even though it is a nationwide study, participant may not be representative of all
23 migrants in France, and this tool needs external validation before using it in another context.
24 Furthermore, variables such as sexually transmitted infections and alcohol have not been included
25 in the questionnaire, since they may be the predictors of HIV, HBV or HCV infection.
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Conclusion

The TROD screen questionnaire showed acceptable overall performance for predicting HIV, HBV, and HCV infections in migrants seen in OFII centers. That should provide the OFII’s medical staff and other health care workers receiving migrants, optimal diagnosis tools based on the risk assessment, leading to the proposal of a rapid screening test for these infections. It could also be helpful for orienting those at high risk for biological confirmation.

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Availability of data and materials

The datasets used during the current study are not publicly available but could be available from the corresponding author on reasonable request.

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Author Contributions Statement

MD, FT conceived and designed the study. LY-K, PB, and IY performed the statistical analysis. MD, FT and OC acquired funding for the project. IY wrote the first draft of the manuscript. All the authors revised the manuscript and approved the final manuscript.

Ethics declarations

Ethics approval and consent to participate

All procedures of this study were in accordance with the ethical approval granted by an Independent Ethics Committees (CPP Ile de France IV, N° IRB 3835, Ref. 2016/43NI) and by the French data protection authority (CNIL) (n°2008669). All methods were carried out in accordance with relevant guidelines and regulations. The study was also registered in ClinicalTrial.gov (NCT02959684). Informed consent was obtained in writing from all individual participants included in the study.

Consent for publication

Not applicable.

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Competing interests

The authors declare that they have no competing interests.

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Table 1: Participants' characteristics

Participants' characteristics	Total = 15343		HBV-positive n=293	HCV-positive n=42	HIV-positive n=47
	N	n (%) or mean (±SD)	n (prevalence)	n (prevalence)	n (prevalence)
<u>Sociodemographic characteristics</u>					
Age, years	15343	35 (±11)	37.3 (±9.5)*	44.5 (±15.0)***	37.6 (±9.4)
Gender	15343		***	°	°
Male		5707 (37.2)	164 (3.0)	17 (0.3)	20 (0.4)
Female		9636 (62.8)	129 (1.4)	25 (0.3)	27 (0.3)
BMI (kg/m ²)			°	°	°
Underweight	15343	907 (5.9)	12 (1.8)	2 (0.2)	2 (0.2)
Normal weight		8830 (57.6)	167 (2.0)	23 (0.3)	24 (0.3)
Overweight/ Obesity		5606 (36.5)	114 (2.1)	12 (0.3)	21 (0.4)
Endemic area of HCV	15327		***	***	***
Low		2393 (15.6)	8 (0.3)	1 (4.10 ⁻⁴)	1 (4.10 ⁻⁴)
Medium		9278 (60.5)	114 (1.3)	16 (0.2)	14 (0.2)
High		3656 (23.9)	171 (4.9)	25 (0.7)	31 (0.9)
Endemic area HBV	13884		***	***	***
Low		7686 (55.3)	39 (0.5)	10 (0.1)	4 (5.10 ⁻⁴)
Medium		3938 (28.4)	117 (3.1)	22 (0.6)	24 (0.6)
High		2260 (16.3)	122 (5.6)	7 (0.3)	17 (0.8)
Endemic area HIV	11390		***	**	***
Low		8317 (73.0)	102 (1.3)	17 (0.2)	11 (0.1)
Medium		2763 (24.3)	142 (5.4)	18 (0.7)	29 (1.1)
High		310 (2.7)	25 (8.1)	0 (0.0)	1 (0.3)
Knowledge of Hepatitis B infection	15343	10852 (70.7)	200 (1.9)°	32 (0.3)°	30 (0.3)°
Knowledge of Hepatitis C infection	15343	10335 (67.5)	175 (1.8)**	29 (0.3)°	26 (0.3)°
Knowledge of HIV infection	15343	13168 (85.8)	246 (1.9)°	36 (0.3)°	43 (0.3)°
<u>Personal history</u>					
Screened for Hepatitis B infection	12631	4044 (32.0)	101 (2.6)***	11 (0.3)°	13 (0.3)°
Screened for Hepatitis C infection	12286	3239 (26.4)	50 (1.6)°	13 (0.4)°	8 (0.2)°
Screened for HIV infection	14176	6733 (47.5)	169 (2.6)***	27 (0.4)*	28 (0.4)*
Vaccination against HBV	9446	4291 (45.4)	45 (1.1)***	8 (0.2)°	9 (0.2)*
History of dental care	14990	10797 (72.0)	161 (1.5)***	32 (0.3)°	26 (0.2)*
History of surgery	15061	4930 (32.7)	78 (1.6)°	17 (0.3)°	17 (0.4)°
History of piercing or tattoo	15343	4751 (31.0)	65 (1.4)***	15 (0.3)°	22 (0.5)*
History of blood transfusion	15343	572 (3.7)	15 (2.7)°	8 (1.4)***	7 (1.2)***
History liver problems	15343	333 (2.2)	22 (7.0)***	3 (0.9)°	0 (0.0)°
Abortion or cesarean section or difficult childbirth ^Φ	9635		*	***	***
		2057 (21.4)	39 (2.0)	14 (0.7)	16 (0.8)
Pregnant ^Φ	9443	2057 (3.9)	5 (1.4)°	1 (0.3)°	0 (0.0)°
Living with someone who has had viral hepatitis [§]	15343		***	°	°
		369 (2.4)	26 (7.3)	2 (0.6)	0 (0.0)
Healthcare worker or barber	15343	1066 (6.9)	15 (1.5)°	4 (0.4)°	4 (0.4)°
Being in jail	15048	80 (0.5)	4 (5.0)°	0 (0.0)°	0 (0.0)°
<u>Behaviors</u>					
Inject or snort psychoactive substance	14987		°	°	°
		462 (3.1)	9 (2.0)	2 (0.4)	0 (0.0)

1	Number of sexual partners in last 12	13037			
2	previous months				
3	0	990 (7.6)	19 (2.0)	2 (0.2)	2 (0.2)
4	1	10700 (82.1)	194 (1.9)	24 (0.2)	36 (0.3)
5	2 and more	1347 (10.3)	23 (1.8)	5 (0.4)	5 (0.4)
6	Sexual partner born in Asia Middle	13889	***	°	*
7	East or Africa	5360 (38.6)	137 (2.6)	19 (0.4)	25 (0.5)
8	Sexual identity	14768	***	°	***
9	No sex	2011 (13.6)	26 (1.3)	7 (0.4)	1 (0.1)
10	Heterosexual women	7777 (52.7)	109 (1.5)	18 (0.2)	27 (0.4)
11	Heterosexual men	4632 (31.4)	139 (3.1)	11 (0.2)	13 (0.3)
12	Homosexual & Bisexual	348 (2.4)	4 (1.2)	2 (0.6)	6 (1.7)
13	Having anal sex, Yes	12469	1211 (9.7)	16 (1.4)°	4 (0.3)°
14					8 (0.7)*
15	Outcomes				
17	HBV – positive	14849	293 (2.0)		2 (0.7)°
18	HCV – positive	15214	42 (0.3)	2 (5.3)°	3 (1.1)*
19	HIV – positive	15099	47 (0.3)	3 (7.1)*	3 (7.1)***
20				3 (6.8)***	

22 p-value (Khi2 or Fischer tests) : ° NS, * <0.05, ** <0.01, *** <0.001
23 § : Mother, Sexual partner, household member
24 Φ : only in female participants

28 **Table 2 : Associated factors with HBV, HCV and HIV among migrants in France**

30	Participants' characteristics s	HBV infection	HBV infection	HCV infection	HIV infection
31		Men (n=5707)	Women (n=9636)	(n= 15343)	(n= 15343)
32		aOR [95%CI]	aOR [95%CI]	aOR [95%CI]	aOR [95%CI]
33	Endemic area of HBV (low: aOR = 1)				
34	Medium	7.62 [4.51 – 13.67]***	4.65 [2.86 – 7.79]***		
35	High	15.83 [9.40 – 28.35]***	6.68 [4.06 – 11.29]***		
36	Endemic area of HCV (low: aOR = 1)				
37	Medium			4.09 [0.83 – 73.85]°	
38	High			13.97 [2.94 – 250.21]**	
39	Endemic area of HIV (low: aOR = 1)				
40	Medium				8.31 [4.25 – 17.50]**
41	High				2.23 [0.12 – 11.57]°
42	History of dental care (No: aOR = 1)	0.65 [0.47 – 0.89]**			
43	History of blood transfusion (No: aOR = 1)			4.67 [1.96 – 9.90]***	3.65 [1.47 – 7.79]***
44	History liver problems (No: aOR = 1)	3.13 [1.46 – 6.07]***	3.40 [1.72 – 6.19]***		
45	Abortion or cesarean section or difficult				
46	childbirth ^Φ (No: aOR = 1)			2.40 [1.20 – 4.60]*	
47	Living with someone who has had viral				
48	hepatitis § (No: aOR = 1)		6.03 [3.43 – 10.08]***		
49	Sexual identity (No sex: aOR = 1)				
50	Heterosexual women				5.88 [1.24 – 105.03]°
51	Heterosexual men				4.75 [0.95 – 86.29]°
52	Homosexual & Bisexual				44.60 [7.45 – 849.71]**
53	Vaccination against HBV (No: aOR = 1)	0.63 [0.41 – 0.96]*	0.21 [0.11 – 0.36]***		

56 p-value : ° NS, * <0.05, ** <0.01, *** <0.001
57 § : Mother, Sexual partner, household member
58 Φ : only in female participants

Table 3 : Score assignment

	β -Coefficient	β -Coefficient multiplied by 5	Score mark
HBV infection (men)			
Endemic area of HBV (Low = 0)			
Medium	2.03	10.15	10
High	2.76	13.80	14
History of dental care (No = 0)	-0.44	-2.20	-2
History liver problems (No = 0)	1.14	5.70	6
Vaccination for Hepatitis B (No = 0)	-0.46	-2.30	-2
Risk score [Endemic area of HBV : Low = 0; Medium = 10; High = 14] - 2 * [History of dental care] + 6 * [History liver problems] - 2 * [Vaccination for Hepatitis B]			
HBV Female (women)			
Endemic area of HBV (Low = 0)			
Medium	1.54	7.70	8
High	1.90	9.50	10
History liver problems (No = 0)	1.22	6.10	6
Living with someone who has had viral hepatitis (No = 0)	1.80	9.00	9
Vaccination for Hepatitis B (No = 0)	-1.58	-7.90	-8
Risk score (female) : [Endemic area of HBV : Low = 0; Medium = 8; High = 10] + 6 * [History liver problems] + 9 * [Living with someone who has had viral hepatitis] - 8 * [Vaccination for Hepatitis B]			
HCV infection			
Endemic area of HCV (Low = 0)			
Medium	1.41	7.05	7
High	2.64	13.20	13
History of blood transfusion (No = 0)	1.54	7.70	8
Abortion or cesarean section or difficult childbirth[†] (No = 0)	0.87	4.35	4
Risk score : [Endemic area of HCV : Low = 0; Medium = 7; High = 13] + 8 * [History of blood transfusion] + 4 * [Abortion or cesarean section or difficult childbirth]			
HIV infection			
Endemic area of HIV (Low = 0)			
Medium	2.12	10.60	11
High	0.80	4.0	4
History of blood transfusion (No = 0)	1.29	6.45	6
Sexual identity (No sex = 0)			
Heterosexual women	1.77	8.85	9
Heterosexual men	1.56	7.80	8
Homosexual & Bisexual	3.80	19.0	19
Risk score : [Endemic area of HIV : Low = 0; Medium = 11; High = 4] + 6 * [History of blood transfusion] + [Sexual identity: No sex = 0; Heterosexual women = 9; Heterosexual men = 8; Homosexual & Bisexual = 19]			

Table 4 : Performance parameters

	Optimal threshold [95% CI]	Sensitivity [95% CI]	Specificity [95% CI]	AUC [95% CI]	Score >=Optimal threshold	Negative rapid test	Positive rapid test	Total
HBV infection (men)	2.5 [2.5 ; 7.5]	88.34 [73.62 ; 92.64]	58.81 [57.76 ; 71.49]	79.22 [76.18 ; 82.26]	No	44 (TN)	19 (FN)	3163
					Yes	102 (FP)	144 (TP)	2346
					Total	146	163	5509
HBV infection (women)	6.5 [0.5 ; 6.5]	63.85 [60.00 ; 86.15]	79.38 [60.95 ; 80.10]	78.83 [74.54 ; 82.10]	No	12 (TN)	47 (FN)	7359
					Yes	99 (FP)	83 (TP)	1982
					Total	111	130	9341
HCV infection	9.5 [9.5 ; 12.5]	75.61 [58.54 ; 87.80]	67.58 [66.90 ; 74.83]	75.95 [68.58 ; 83.32]	No	256 (TN)	10 (FN)	10266
					Yes	19 (FP)	31 (TP)	4950
					Total	175	41	15216
HIV infection	10.5 [10.0 ; 18.5]	81.25 [68.75 ; 91.67]	77.12 [76.59 ; 82.85]	82.15 [74.54 ; 87.99]	No	608 (TN)	9 (FN)	11617
					Yes	44 (FP)	39 (TP)	3483
					Total	652	48	15100

TN= true negative; FN= false negative; FP= false positive; TP= true positive

Figure 1. Mean Receiver operating characteristics (ROC) curve for multivariable logistic regression models. Each blue line indicates the ROC curve. (A) Depicted the area under the curve (AUC) for the HBV infection in men, the AUC for this model was 0.792, indicating a good fit. The threshold was 2.50, specificity = 0.88 and sensitivity = 0.59. (B) Showed the AUC for HBV in women, which was 0.788. The threshold was 6.50, specificity = 0.79 and sensitivity = 0.64. (C) The curve for HCV has an AUC of 0.760, indicating a fair fit for the score. The threshold was 9.50, specificity = 0.76 and sensitivity = 0.68. (D) Depicted the AUC for the HIV infection. The AUC for this model is 0.822, indicating a good fit. The threshold was 10.50, specificity = 0.81 and sensitivity = 0.77.

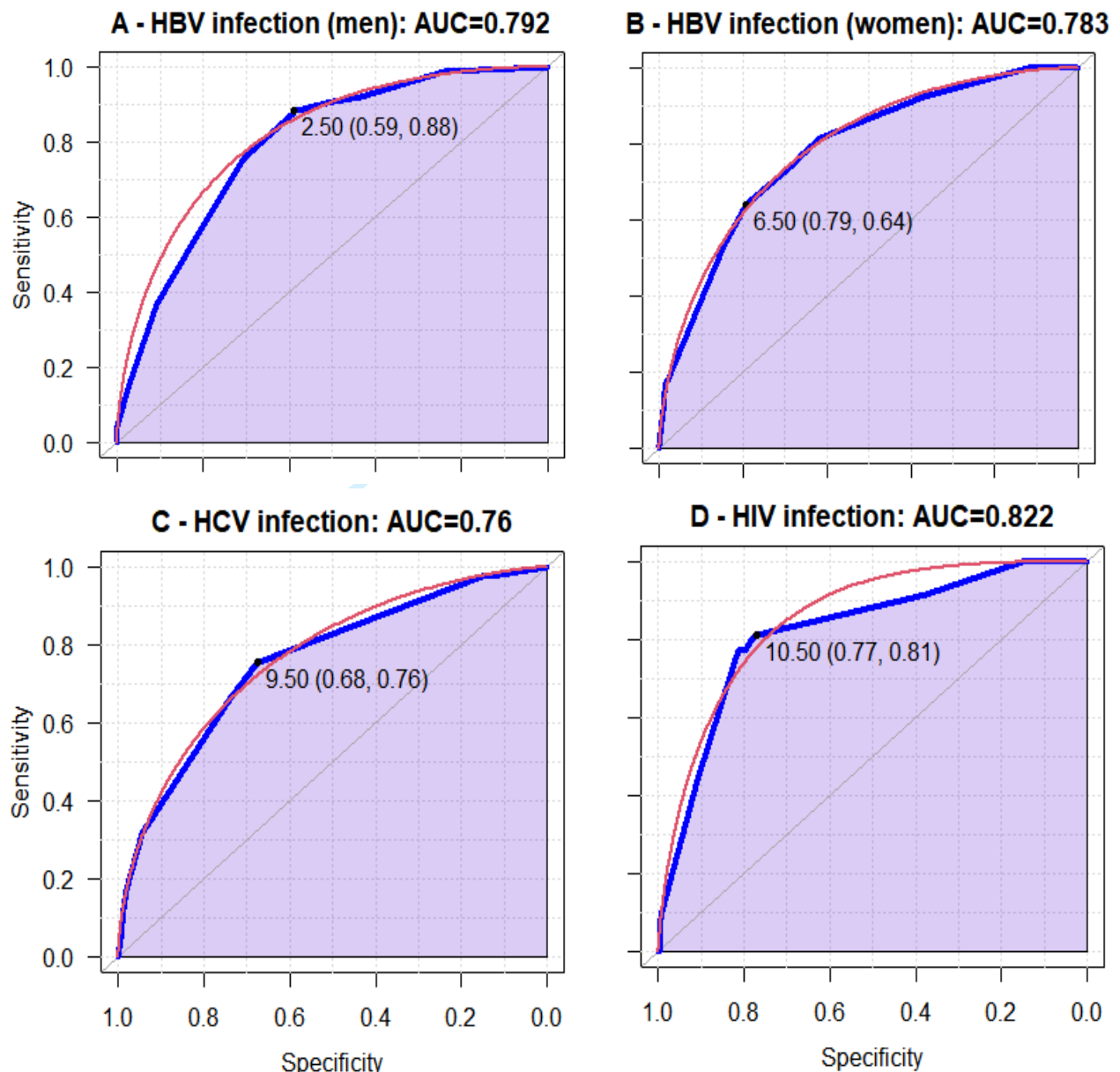


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TRIPOD Checklist: Prediction Model Development

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	4
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	6
	5b	Describe eligibility criteria for participants.	6
	5c	Give details of treatments received, if relevant.	NA
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	6
	6b	Report any actions to blind assessment of the outcome to be predicted.	6
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	6-7
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	Explain how the study size was arrived at.	NA
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	NA
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	7
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	7
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	NA
Risk groups	11	Provide details on how risk groups were created, if done.	NA
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	8
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	8
Model development	14a	Specify the number of participants and outcome events in each analysis.	8-9
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	9
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	9
	15b	Explain how to use the prediction model.	9
Model performance	16	Report performance measures (with CIs) for the prediction model.	9
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	11
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	10-11
Implications	20	Discuss the potential clinical use of the model and implications for future research.	10-11
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	13
Funding	22	Give the source of funding and the role of the funders for the present study.	13

We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.

BMJ Open

Development of a risk prediction score for screening for HBV, HCV, and HIV among migrants in France: results from a multicentre observational study (STRADA study)

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Development of a risk prediction score for screening for HBV, HCV, and HIV among migrants in France: results from a multicentre observational study (STRADA study)

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Abstract (297 words)

Objectives: Migrants from high HIV, HBV, or HCV endemicity regions have a great burden of these infections and related diseases in the host countries. This study aimed to assess the predictive capacity of the TROD Screen questionnaire for HIV, HBV, and HCV infections among migrants arriving in France.

Design: An observational and multicenter study was conducted among migrants. A self-questionnaire on demographic characteristics, personal medical history, and sexual behaviors was completed.

Setting: The study was conducted in the centers of the French Office for Immigration and Integration (OFII).

Participants: Convenience sampling was used to select and recruit adult migrants between January 2017 and March 2020.

Outcome measures: Participants were tested for HIV, HBV, and HCV with rapid tests. For each infection, the test performance was assessed using receiver operating characteristics curves, using area under the curve (AUC) as a measure of accuracy.

Results: Among 21,133 regular migrants seen in OFII centers, 15,343 were included in the study. The participants' mean age was 35.6 years (SD±11.1). The prevalence [95%CI] of HBV, HCV, and HIV was 2.0% [1.8–2.2%], 0.3% [0.2–0.4%], and 0.3% [0.2–0.4%], respectively. Based on the sensitivity–specificity curve analysis, the cut-off points [95%CI] chosen for the risk score were: 2.5 [2.5–7.5] for HBV infection in men; 6.5 [0.5–6.5] for HBV infection in women; 9.5 [9.5–12.5] for HCV infection; and 10.5 [10.0–18.5] for HIV infection. Test performance was highest for HIV (AUC=82.15%, [74.54–87.99%]), followed by that for HBV in men (AUC=79.22%, [76.18–82.26%]), for HBV in women (AUC=78.83, [74.54–82.10%]), and that for HCV (AUC=75.95%, [68.58–83.32%]).

Conclusion: The TROD screen questionnaire showed good overall performance for predicting HIV, HBV, and HCV infections among migrants in OFII centers. It could be used to optimize screening for these infections and to propose rapid screening tests to those who are at high-risk.

Keywords: Risk score; HBV; HCV; HIV; migrants.

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Strengths and limitations of this study

- This study included a large number of migrants from several different countries, which may capture estimates from different profiles of migrants in several centers.
- The migrants participating in the study are regular migrants receiving permits to stay; they might have a higher socio-economic status than other categories, such as asylum seekers, and these risk scores should be tested in this population.
- Not all migrants having their medical consultation at OFII centers were proposed to participate in the study due to a shortage of time, staff, or language barriers.
- There may be a bias related to underreporting information, as some participants, being at the OFII center, may feel uncomfortable disclosing some sexual behaviors.
- Using these tools, a considerable number of infections could be missed, which could cause an ethical issue.

Background

Viral hepatitis (including hepatitis B and hepatitis C) as well as HIV infection are among the most common chronic infectious diseases worldwide and a major public health problem [1,2]. In 2015, HIV infection was involved in 1.06 million deaths, while viral hepatitis led to 1.34 million deaths due to chronic or long-term complications such as cirrhosis, liver failure, and hepatocellular carcinoma [2]. These infections disproportionately affect regions of the world, with a high prevalence in low-income countries [2,3]. In low-endemicity regions, the mobile population or migrants have a great burden of these infections and related diseases [4,5]. A meta-analysis on hepatitis B virus (HBV) prevalence among immigrants found an overall pooled seroprevalence of infection of 7.2% (95% CI: 6.3%–8.2%). In addition, a subgroup analysis showed that HBV prevalence reflected that in the region of origin, particularly for those from intermediate or high-prevalence regions including the Middle East, East Asia, and sub-Saharan Africa [6]. Another meta-analysis found an overall anti-HCV antibody prevalence among migrants of 1.9% (95% CI, 1.4–2.7%), with a higher prevalence among migrants from Sub-Saharan Africa, Asia, and Eastern Europe [7].

France is a country with low endemicity for these infections; the estimated prevalence of HIV infection was 0.41%, of chronic HBV infection was 0.93%, and of chronic hepatitis C virus (HCV) infection was 0.60% in 2020 in the general adult population [8]. People born abroad and mobile populations such as immigrants and travelers from countries with a relatively high HIV, HBV, or HCV endemicity are vulnerable groups for these infections [9,10]. In a cross-sectional survey (AfroBaromètre 2016) conducted among Afro-Caribbeans living in the Paris area in 2016, the prevalence of HIV and HBsAg was 1.4% and 1.7%, respectively, among participants born in France, both 2.6% among those born in Haiti, and 1.7% and 7.0%, respectively, for those born in sub-Saharan Africa [10]. Almost 20% of them have never been screened for HIV or HBV. In addition, 40% of HIV-positive participants and 77% of those living with HBV were unaware of their seropositive status.

In recent years, with the development of rapid screening tests, HIV, HBV, and HCV screening rates have highly increased in France [11]. However, many people remain undiagnosed and unaware of their infection status, including people from sub-Saharan Africa or Asia who were less likely to receive HIV, HBV, or HCV screening, fearing mostly discrimination but also because most of them did not have a regular residence permit. It was also known that migrant populations have a lack of knowledge about these infections and are less likely to be screened for them [10,12]. Given the high prevalence of these infections in migrant populations, they might be at increased risk of transmission or acquisition.

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In many European countries, it is common for migrants from countries with high HBV endemicity to be systematically offered screening for HIV, HBV, and HCV. Morbidity and mortality from these infections can be reduced by early diagnosis through screening at-risk people for these infections and offering appropriate medical management [6,13], which should also contribute to the secondary prevention of HIV, HBV, and HCV infections. Besides, for at-risk patients, a vaccination against HBV should be proposed.

The STRADA study, which was designed to evaluate a new strategy for screening for infectious diseases among the migrants admitted in the French Office for Immigration and Integration (OFII) departments and to validate a self-screening questionnaire for tuberculosis (TB Screen) as well as HIV, HBV, and HCV (“TROP Screen”), showed a high acceptability of the participants for HIV and viral hepatitis screening [14].

The objective of this study is to assess the predictive capacity of the TROP Screen risk factor self-reported questionnaire for HIV, HBV, and HCV infection among migrants during their medical visit in the OFII.

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Methods

Study design and participants

This was a prospective multicenter and observational study carried out between January 2017 and March 2020 among migrants in the French Office for Immigration and Integration (OFII) centers. There are 32 OFII centers, including 28 in mainland France and 4 overseas. During our study, all OFII centers were invited to participate, but only 21 OFII centers have accepted, including 3 centers in Ile-de-France (Cergy, Melun, Montrouge), 16 centers outside Ile-de-France (Bordeaux, Dijon, Grenoble, Lille, Limoges, Lyon, Marseille, Montpellier, Nantes, Nice, Orléans, Rennes, Reims, Rouen, Strasbourg, Toulouse), and 2 overseas centers (Cayenne, Pointe-à-Pitre). Individuals were included during the compulsory medical visit at the time of the delivery of their first residence permit. Eligible participants were migrants aged 18 years or more who consented to participate in this study.

Study intervention and data collection

Participants completed the anonymous TROD Screen questionnaire online. This self-administrated questionnaire was translated into 10 languages (English, Arabic, Chinese, Bengali, Russian, Lingala, Portuguese, Spanish, Turkish, and Haitian Creole) and included data related to sociodemographic, personal medical history, and sexual behaviors. A few pieces of data were retrieved from medical records (year of birth, gender, height, weight, and nationality). Then, a rapid screening test for HBV, HCV, or HIV infections was proposed to the participants, who could refuse or choose between tests. The participants who reported prior testing but forgot the result of the test were encouraged to be tested again. However, those who were aware of their status (for example, HIV or HBV) or those who documented a vaccination against HBV were not tested.

A nurse performed the rapid screening test using the TOYO HCV Test (for HCV) [15], the TOYO HBsAb Test (for HBV) [16], and the INSTI HIV1/HIV2 Test (for HIV) [17]. Then the doctor or nurse announced the results. In the event of a positive result, the participant was referred to a specialized hospital consultation to confirm the diagnosis and initiate adapted treatments.

Variables definition

The outcome was a positive rapid screening test for HBV, HCV, or HIV infections. It was used as the gold standard for calculating the sensitivity and specificity of various combinations of participants' characteristics for predicting HBV, HCV, or HIV infection.

A number of independent predictor factors were used for the prediction of HBV, HCV, or HIV infection. (1) Sociodemographic characteristics: age (years), gender (male or female), weight

status (Underweight (BMI<18); Normal weight (BMI 18 and 25), or Overweight/Obesity (BMI>25)), endemic area for each infection, knowledge of HIV, HBV, and HCV. (2) Personal history: HIV, HBV or HCV screening, vaccination against HBV, dental treatment, surgery, abortion, caesarean section or difficult childbirth, history of liver disease, tattoos or piercings, prison, blood transfusion, living with a person infected with viral hepatitis, psychoactive substance use (injection or snorting). (3) Sexual behaviors: geographical origin of sexual partner, number of sexual partners during the last 12 months, and sexual practices and orientation.

Statistical analysis

Statistical analyses were performed using R software version R 3.6.3. The participants' characteristics were described using absolute frequencies, proportions for categorical variables, or means and standard deviation (SD) for continuous variables.

A cross-analysis between explanatory factors and each infection (HBV, HCV, and HIV) was performed using a Student's t test or Wilcoxon for the means and a Chi-square or Fisher test for the proportions.

Binary logistic regression models were fitted to identify factors associated with HBV, HCV, or HIV infection. In the univariate analysis, independent variables with a p-value less than 0.25 were included in the multivariable logistic regression analysis in order to control potential confounders. The final multivariable model was performed using a stepwise selection procedure, which was based on the likelihood ratio test (p-value<0.05). The Akaike information criterion (AIC) was to select the final model. Results were reported as unadjusted odds ratios (OR), and adjusted odds ratios (aOR) with 95% confidence intervals (CI). There was no missing data in all predictor variables and outcomes, and we carried out a complete-case analysis for the outcomes.

Model performance was evaluated in terms of discrimination. The discriminating capacity of the TROD Screen questionnaire for HBV, HCV, and HIV was evaluated using the predictive value of the questionnaire, its sensitivity and specificity, as well as the 95% confidence intervals. A ROC curve was used to quantify discrimination and determine the cutoff score of the questionnaire for each infection. That also assesses whether those with higher predicted risks are more likely to have an HBV, HCV, or HIV infection.

To make the models easier to use in clinical practice, we created a risk score for evaluating the likelihood of HBV, HCV, or HIV infection based on multivariable regression coefficients, which were rescaled and rounded to the nearest whole number. To determine the score for each level of the variables, weighted points were assigned to each of the final associated factors. The β -coefficients of each variable were multiplied by a constant (we have chosen 5), and rounded to the

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nearest integer [18,19]. Based on the sensitivity–specificity curve analysis (Figure 1), the cut-offs point was chosen for the risk score for HBV (both in men, and women), HCV and for HIV infections, with maximum sensitivity and specificity.

By assuming that the HBV prevalence is higher in men than in women, we carried out the analysis on HBV infection by stratifying by sex in order to obtain risk scores specific to the men and women included in this study.

Patient and public involvement statement

None.

Results

Characteristics of study participants

A total of 21,133 participants realized a rapid test during their medical visit. Among them, 15,343 participants who had the rapid screening test and completed the TROD screen questionnaire were included in this analysis. Their socio-demographic characteristics are described in Table 1. The mean age of the participants was 35 years (SD±11), and 62.8% were female. More than one-third (36.5%) of them were overweight or obese. Among the participants, 23.9%, 16.3%, and 2.7% came from a high endemicity area of HCV, HBV, and HIV, respectively. History of dental care (72.0%), surgery (32.7%), piercing and tattooing (31.0%), blood transfusion (3.7%), psychoactive substance consumption (3.1%), and liver problems (2.2%) were reported. A little more than one-fifth of the female participants reported a history of abortion, cesarean section, or difficult childbirth (21.4%), and 3.9% of them declared being pregnant at the moment of the survey.

Regarding sexual behaviors, 10.3% of the migrants seen reported two sexual partners or more during the last 12 months, while 38.6% reported a sexual partner born in Asia, the Middle East, or Africa. About 10% (1211) of participants reported anal intercourses.

Almost one-third of the participants (32.0%) reported a history of screening for hepatitis B, 26.4% for hepatitis C, and 47.5% for HIV. In addition, 4291 migrants reported a vaccination against HBV. The overall seroprevalence [95%CI] of HBV, HCV, and HIV was 2.0% [1.8 – 2.2], 0.3% [0.2 – 0.4], and 0.3% [0.2 – 0.4], respectively.

Development of the risk score for HBV, HCV, and HIV infection

Univariable logistic regression analyses were used to select explanatory variables for adjusted models. Multivariable logistic regression models were fitted to determine factors associated with each infection. The coefficient values (and adjusted odds-ratio (aOR)) of each variable were obtained (Table 2). Only significant variables in the parsimonious models were selected to be used in the development of the risk score in each infection, which were as follows (Table 3):

- For HBV infection in men: *endemic area of HBV, history of dental care, history of liver problems, and vaccination against hepatitis B;*
- For HBV infection in women: *endemic area of HBV, history of liver problems, living with someone who has had viral hepatitis, and vaccination against hepatitis B;*
- For HCV infection: *endemic area of HCV, history of blood transfusion, and abortion, or cesarean section, or difficult childbirth;*
- For HIV infection: *endemic area of HIV, history of blood transfusion, and sexual identity.*

Determination of cut-off points

The sensitivity, specificity, and AUC values and their 95%CI corresponding to each cut-off are detailed in Table 4. These cut-off points were used to differentiate participants with a high risk of each infection (i.e. HBV, HCV, and HIV infection) from those with a low risk. Indeed, participants whose score was less than the cut-off were supposed to have low risk.

Furthermore, 5,509 men realized a rapid test for HBV and completed the TROD screen questionnaire. The optimal threshold for HBV was 2.5 [95%CI: 2.5; 7.5] (Table 4). At this cut-off, we would have performed 2,346 tests, detected 144 HBV infections, avoided 3,163 tests, and missed 19 HBV infections (Table 4).

Regarding women, 9,341 individuals realized a rapid test for HBV and completed the TROD screen questionnaire during their visits. The optimal threshold for HBV was 6.5 [95%CI: 0.5; 6.5] (Table 4). At this cut-off, we would have performed 1,982 tests, detected 83 HBV infections, and avoided 7,359 tests but missed 47 HBV infections (Table 4).

For HCV, 15,216 migrants realized a rapid test during their visits and completed the TROD screen questionnaire. The optimal threshold for HCV was 9.5 [95%CI: 9.5; 12.5] (Table 4). At this cut-off, we would have performed 4,950 tests, detected 31 HCV infections, and avoided 10,266 tests but missed 10 HCV infections (Table 4).

For HIV infection, 15,100 migrants realized a rapid test during their visits and completed the TROD screen questionnaire. The optimal threshold for HBV was 10.5 [95%CI: 10.0; 18.5] (Table 4). At this cut-off, we would have performed 3,483 tests, detected 39 HIV infections, avoided 11,617 tests, and missed 9 HIV infections (Table 4).

Discussion

This large French nationwide study was carried out among migrants in order to evaluate the capacity of the TROD Screen questionnaire to predict HBV, HCV, or HIV infection, which may assist health practitioners and policymakers in optimal screening of these infections in migrants. Therefore, we developed a risk score for these infections using a combination of participants' characteristics, including sociodemographic, personal health-related history, and behaviors, mainly sexual behaviors. With the determination of a cut-off point, this score allowed us to classify participants into subgroups at low and high risk for these infections.

In view of the AUC, the specificity, and the sensitivity, our scoring models showed good discrimination and calibration, particularly for HBV infection in men and HIV infection. For a predictive questionnaire, it is expected to have a sensitivity greater than 80% with lower specificity compared to the rapid test. For HBV infection in women and HCV infection, even though the specificity and the sensitivity were not good enough, their discriminatory capacity remained acceptable (AUC >70%). Globally, as demonstrated by our results, the use of these tools could avoid a considerable number of rapid tests, resulting in a reduction in the workload of health professionals.

The endemic area of origin of the participants remains an important characteristic in the construction of these scores. Indeed, the endemic area is predictive of the risk of HBV, HCV, and HIV infection among migrants in France. Participants from medium and/or high endemicity areas were the most likely to have a positive rapid test. In medium- or high-endemicity areas, which are generally countries with limited resources, strategies for the prevention and diagnosis of these infections remain poorly available or accessible [20]. Therefore, there is a low rate of screening tests for viral hepatitis as well as the availability of verified blood products. Migrants from these areas have a high probability of having been in contact with or being chronic carriers of one of these viruses before their migration process [21].

For HBV infection, either in men or women, vaccination against HBV and a history of liver problems were predictive of the risk of HBV. Vaccination against HBV was associated with a low probability of having an HBV-positive test in both men and women. In low-income countries, availability and access to HBV vaccines remain a challenge [22]. In these regions, contact with this virus occurred for the most part in the perinatal period and during early childhood, most often leading to an evolution to chronicity [22–24]. Even though vaccination against HBV (with a complete or incomplete schedule) predicted a low risk for HBV infection, participants who reported a history of liver pathology were more likely to have a positive test for HBV. Even if only 2-10% of HBV infections are symptomatic or evolve to chronic form [25], it is important to make

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1 further investigations in migrants who have reported a history of liver problems, as suggested in
2 our study.
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5 In addition, the history of blood transfusions is also predictive of HCV and HIV infection. Till the
6 last decade, in low-income countries, the risk of transfusion-transmitted infections remained high
7 due to unsafe transfusion practices. HIV or HCV are the main transfusion-transmitted infections
8 reported and must be at the center of prevention strategies [26,27]. These unsafe transfusion
9 practices in those regions are more often correlated to other unsafe practices, especially in invasive
10 procedures like abortion or cesarean section. Thus, in our predictive analysis, in migrant women,
11 history of abortion, cesarean section, or difficult childbirth and living with someone who had viral
12 hepatitis have predicted, respectively, HCV and HBV infection.
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16 Reporting being homosexual or bisexual has been found to be highly predictive of HIV infection
17 among migrants. This is in line with several studies, which highlighted that men who have sex
18 with men are at higher risk of Sexually Transmitted Infections, including HIV infection, especially
19 when having multiple sexual partners and unprotected anal intercourse [28,29].
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23 Despite our study providing useful risk score for predicting HIV, HBV, and HCV infections,
24 several limitations need to be addressed. It is possible that answers to questions may be subject to
25 sub-declarations. Even though it is a nationwide study, participant may not be representative of all
26 migrants in France, and this tool needs external validation before using it in another context.
27 Furthermore, variables such as sexually transmitted infections and alcohol have not been included
28 in the questionnaire, since they may be the predictors of HIV, HBV or HCV infection.
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Conclusion

The TROD screen questionnaire showed acceptable overall performance for predicting HIV, HBV, and HCV infections in migrants seen in OFII centers. That should provide the OFII’s medical staff and other health care workers receiving migrants, optimal diagnosis tools based on the risk assessment, leading to the proposal of a rapid screening test for these infections. It could also be helpful for orienting those at high risk for biological confirmation.

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Availability of data and materials

The datasets used during the current study are not publicly available but could be available from the corresponding author on reasonable request.

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Author Contributions Statement

MD: conceptualisation, methodology, validation, writing-review and editing, project administration and is responsible for the overall content as guarantor. IY: formal analysis, data curation, writing-original draft preparation. LY-K: data collection, formal analysis, data curation, writing-review and editing. PB: data collection, formal analysis, data curation, writing-review and editing. FT: conceptualisation, methodology, validation, writing-review and editing, project administration. OR-T: writing-review and editing, project administration. FR-T: writing-review and editing. FL: writing-review and editing. DZ: writing-review and editing. OC: conceptualisation, methodology, validation, writing—review and editing. All authors approved the final version of the manuscript for publication.

Ethics declarations

Ethics approval and consent to participate

All procedures of this study were in accordance with the ethical approval granted by an Independent Ethics Committees (CPP Ile de France IV, N° IRB 3835, Ref. 2016/43NI) and by the French data protection authority (CNIL) (n°2008669). All methods were carried out in accordance with relevant guidelines and regulations. The study was also registered in ClinicalTrial.gov (NCT02959684). Informed consent was obtained in writing from all individual participants included in the study.

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Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Table 1: Participants' characteristics

Participants' characteristics	Total = 15343		HBV-positive n=293	HCV-positive n=42	HIV-positive n=47
	N	n (%) or mean (±SD)	n (prevalence)	n (prevalence)	n (prevalence)
<u>Sociodemographic characteristics</u>					
Age, years	15343	35 (±11)	37.3 (±9.5)*	44.5 (±15.0)***	37.6 (±9.4)
Gender	15343		***	°	°
Male		5707 (37.2)	164 (3.0)	17 (0.3)	20 (0.4)
Female		9636 (62.8)	129 (1.4)	25 (0.3)	27 (0.3)
BMI (kg/m ²)			°	°	°
Underweight	15343	907 (5.9)	12 (1.8)	2 (0.2)	2 (0.2)
Normal weight		8830 (57.6)	167 (2.0)	23 (0.3)	24 (0.3)
Overweight/ Obesity		5606 (36.5)	114 (2.1)	12 (0.3)	21 (0.4)
Endemic area of HCV	15327		***	***	***
Low		2393 (15.6)	8 (0.3)	1 (4.10 ⁻⁴)	1 (4.10 ⁻⁴)
Medium		9278 (60.5)	114 (1.3)	16 (0.2)	14 (0.2)
High		3656 (23.9)	171 (4.9)	25 (0.7)	31 (0.9)
Endemic area HBV	13884		***	***	***
Low		7686 (55.3)	39 (0.5)	10 (0.1)	4 (5.10 ⁻⁴)
Medium		3938 (28.4)	117 (3.1)	22 (0.6)	24 (0.6)
High		2260 (16.3)	122 (5.6)	7 (0.3)	17 (0.8)
Endemic area HIV	11390		***	**	***
Low		8317 (73.0)	102 (1.3)	17 (0.2)	11 (0.1)
Medium		2763 (24.3)	142 (5.4)	18 (0.7)	29 (1.1)
High		310 (2.7)	25 (8.1)	0 (0.0)	1 (0.3)
Knowledge of Hepatitis B infection	15343	10852 (70.7)	200 (1.9)°	32 (0.3)°	30 (0.3)°
Knowledge of Hepatitis C infection	15343	10335 (67.5)	175 (1.8)**	29 (0.3)°	26 (0.3)°
Knowledge of HIV infection	15343	13168 (85.8)	246 (1.9)°	36 (0.3)°	43 (0.3)°
<u>Personal history</u>					
Screened for Hepatitis B infection	12631	4044 (32.0)	101 (2.6)***	11 (0.3)°	13 (0.3)°
Screened for Hepatitis C infection	12286	3239 (26.4)	50 (1.6)°	13 (0.4)°	8 (0.2)°
Screened for HIV infection	14176	6733 (47.5)	169 (2.6)***	27 (0.4)*	28 (0.4)*
Vaccination against HBV	9446	4291 (45.4)	45 (1.1)***	8 (0.2)°	9 (0.2)*
History of dental care	14990	10797 (72.0)	161 (1.5)***	32 (0.3)°	26 (0.2)*
History of surgery	15061	4930 (32.7)	78 (1.6)°	17 (0.3)°	17 (0.4)°
History of piercing or tattoo	15343	4751 (31.0)	65 (1.4)***	15 (0.3)°	22 (0.5)*
History of blood transfusion	15343	572 (3.7)	15 (2.7)°	8 (1.4)***	7 (1.2)***
History liver problems	15343	333 (2.2)	22 (7.0)***	3 (0.9)°	0 (0.0)°
Abortion or cesarean section or difficult childbirth ^Φ	9635		*	***	***
		2057 (21.4)	39 (2.0)	14 (0.7)	16 (0.8)
Pregnant ^Φ	9443	2057 (3.9)	5 (1.4)°	1 (0.3)°	0 (0.0)°
Living with someone who has had viral hepatitis [§]	15343		***	°	°
		369 (2.4)	26 (7.3)	2 (0.6)	0 (0.0)
Healthcare worker or barber	15343	1066 (6.9)	15 (1.5)°	4 (0.4)°	4 (0.4)°
Being in jail	15048	80 (0.5)	4 (5.0)°	0 (0.0)°	0 (0.0)°
<u>Behaviors</u>					
Inject or snort psychoactive substance	14987		°	°	°
		462 (3.1)	9 (2.0)	2 (0.4)	0 (0.0)

1	Number of sexual partners in last 12	13037			
2	previous months				
3	0	990 (7.6)	19 (2.0)	2 (0.2)	2 (0.2)
4	1	10700 (82.1)	194 (1.9)	24 (0.2)	36 (0.3)
5	2 and more	1347 (10.3)	23 (1.8)	5 (0.4)	5 (0.4)
6	Sexual partner born in Asia Middle	13889	***	°	*
7	East or Africa	5360 (38.6)	137 (2.6)	19 (0.4)	25 (0.5)
8	Sexual identity	14768	***	°	***
9	No sex	2011 (13.6)	26 (1.3)	7 (0.4)	1 (0.1)
10	Heterosexual women	7777 (52.7)	109 (1.5)	18 (0.2)	27 (0.4)
11	Heterosexual men	4632 (31.4)	139 (3.1)	11 (0.2)	13 (0.3)
12	Homosexual & Bisexual	348 (2.4)	4 (1.2)	2 (0.6)	6 (1.7)
13	Having anal sex, Yes	12469	1211 (9.7)	16 (1.4)°	4 (0.3)°
14					8 (0.7)*
15	Outcomes				
17	HBV – positive	14849	293 (2.0)		2 (0.7)°
18	HCV – positive	15214	42 (0.3)	2 (5.3)°	3 (1.1)*
19	HIV – positive	15099	47 (0.3)	3 (7.1)*	3 (7.1)***
20				3 (6.8)***	

22 p-value (Khi2 or Fischer tests) : ° NS, * <0.05, ** <0.01, *** <0.001
23 § : Mother, Sexual partner, household member
24 Φ : only in female participants

28 **Table 2 : Associated factors with HBV, HCV and HIV among migrants in France**

30 Participants' characteristics s	HBV infection Men (n=5707)	HBV infection Women (n=9636)	HCV infection (n= 15343)	HIV infection (n= 15343)
31	aOR [95%CI]	aOR [95%CI]	aOR [95%CI]	aOR [95%CI]
33 Endemic area of HBV (low: aOR = 1)				
34 Medium	7.62 [4.51 – 13.67]***	4.65 [2.86 – 7.79]***		
35 High	15.83 [9.40 – 28.35]***	6.68 [4.06 – 11.29]***		
36 Endemic area of HCV (low: aOR = 1)				
37 Medium			4.09 [0.83 – 73.85]°	
38 High			13.97 [2.94 – 250.21]**	
39 Endemic area of HIV (low: aOR = 1)				
40 Medium				8.31 [4.25 – 17.50]**
41 High				2.23 [0.12 – 11.57]°
42 History of dental care (No: aOR = 1)	0.65 [0.47 – 0.89]**			
43 History of blood transfusion (No: aOR = 1)			4.67 [1.96 – 9.90]***	3.65 [1.47 – 7.79]***
44 History liver problems (No: aOR = 1)	3.13 [1.46 – 6.07]***	3.40 [1.72 – 6.19]***		
45 Abortion or cesarean section or difficult 46 childbirth ^Φ (No: aOR = 1)			2.40 [1.20 – 4.60]*	
47 Living with someone who has had viral 48 hepatitis § (No: aOR = 1)		6.03 [3.43 – 10.08]***		
49 Sexual identity (No sex: aOR = 1)				
50 Heterosexual women				5.88 [1.24 – 105.03]°
51 Heterosexual men				4.75 [0.95 – 86.29]°
52 Homosexual & Bisexual				44.60 [7.45 – 849.71]**
53 Vaccination against HBV (No: aOR = 1)	0.63 [0.41 – 0.96]*	0.21 [0.11 – 0.36]***		

56 p-value : ° NS, * <0.05, ** <0.01, *** <0.001
57 § : Mother, Sexual partner, household member
58 Φ : only in female participants

Table 3 : Score assignment

	β -Coefficient	β -Coefficient multiplied by 5	Score mark
HBV infection (men)			
Endemic area of HBV (Low = 0)			
Medium	2.03	10.15	10
High	2.76	13.80	14
History of dental care (No = 0)	-0.44	-2.20	-2
History liver problems (No = 0)	1.14	5.70	6
Vaccination for Hepatitis B (No = 0)	-0.46	-2.30	-2
Risk score [Endemic area of HBV : Low = 0; Medium = 10; High = 14] - 2 * [History of dental care] + 6 * [History liver problems] - 2 * [Vaccination for Hepatitis B]			
HBV Female (women)			
Endemic area of HBV (Low = 0)			
Medium	1.54	7.70	8
High	1.90	9.50	10
History liver problems (No = 0)	1.22	6.10	6
Living with someone who has had viral hepatitis (No = 0)	1.80	9.00	9
Vaccination for Hepatitis B (No = 0)	-1.58	-7.90	-8
Risk score (female) : [Endemic area of HBV : Low = 0; Medium = 8; High = 10] + 6 * [History liver problems] + 9 * [Living with someone who has had viral hepatitis] - 8 * [Vaccination for Hepatitis B]			
HCV infection			
Endemic area of HCV (Low = 0)			
Medium	1.41	7.05	7
High	2.64	13.20	13
History of blood transfusion (No = 0)	1.54	7.70	8
Abortion or cesarean section or difficult childbirth[†] (No = 0)	0.87	4.35	4
Risk score : [Endemic area of HCV : Low = 0; Medium = 7; High = 13] + 8 * [History of blood transfusion] + 4 * [Abortion or cesarean section or difficult childbirth]			
HIV infection			
Endemic area of HIV (Low = 0)			
Medium	2.12	10.60	11
High	0.80	4.0	4
History of blood transfusion (No = 0)	1.29	6.45	6
Sexual identity (No sex = 0)			
Heterosexual women	1.77	8.85	9
Heterosexual men	1.56	7.80	8
Homosexual & Bisexual	3.80	19.0	19
Risk score : [Endemic area of HIV : Low = 0; Medium = 11; High = 4] + 6 * [History of blood transfusion] + [Sexual identity: No sex = 0; Heterosexual women = 9; Heterosexual men = 8; Homosexual & Bisexual = 19]			

Table 4 : Performance parameters

	Optimal threshold [95% CI]	Sensitivity [95% CI]	Specificity [95% CI]	AUC [95% CI]	Score >=Optimal threshold	Negative rapid test	Positive rapid test	Total
HBV infection (men)	2.5 [2.5 ; 7.5]	88.34 [73.62 ; 92.64]	58.81 [57.76 ; 71.49]	79.22 [76.18 ; 82.26]	No	44 (TN)	19 (FN)	3163
					Yes	102 (FP)	144 (TP)	2346
					Total	146	163	5509
HBV infection (women)	6.5 [0.5 ; 6.5]	63.85 [60.00 ; 86.15]	79.38 [60.95 ; 80.10]	78.83 [74.54 ; 82.10]	No	12 (TN)	47 (FN)	7359
					Yes	99 (FP)	83 (TP)	1982
					Total	111	130	9341
HCV infection	9.5 [9.5 ; 12.5]	75.61 [58.54 ; 87.80]	67.58 [66.90 ; 74.83]	75.95 [68.58 ; 83.32]	No	256 (TN)	10 (FN)	10266
					Yes	19 (FP)	31 (TP)	4950
					Total	175	41	15216
HIV infection	10.5 [10.0 ; 18.5]	81.25 [68.75 ; 91.67]	77.12 [76.59 ; 82.85]	82.15 [74.54 ; 87.99]	No	608 (TN)	9 (FN)	11617
					Yes	44 (FP)	39 (TP)	3483
					Total	652	48	15100

TN= true negative; FN= false negative; FP= false positive; TP= true positive

Figure 1. Mean Receiver operating characteristics (ROC) curve for multivariable logistic regression models. Each blue line indicates the ROC curve. **(A)** Depicted the area under the curve (AUC) for the HBV infection in men, the AUC for this model was 0.792, indicating a good fit. The threshold was 2.50, specificity = 0.88 and sensitivity = 0.59. **(B)** Showed the AUC for HBV in women, which was 0.788. The threshold was 6.50, specificity = 0.79 and sensitivity = 0.64. **(C)** The curve for HCV has an AUC of 0.760, indicating a fair fit for the score. The threshold was 9.50, specificity = 0.76 and sensitivity = 0.68. **(D)** Depicted the AUC for the HIV infection. The AUC for this model is 0.822, indicating a good fit. The threshold was 10.50, specificity = 0.81 and sensitivity = 0.77.

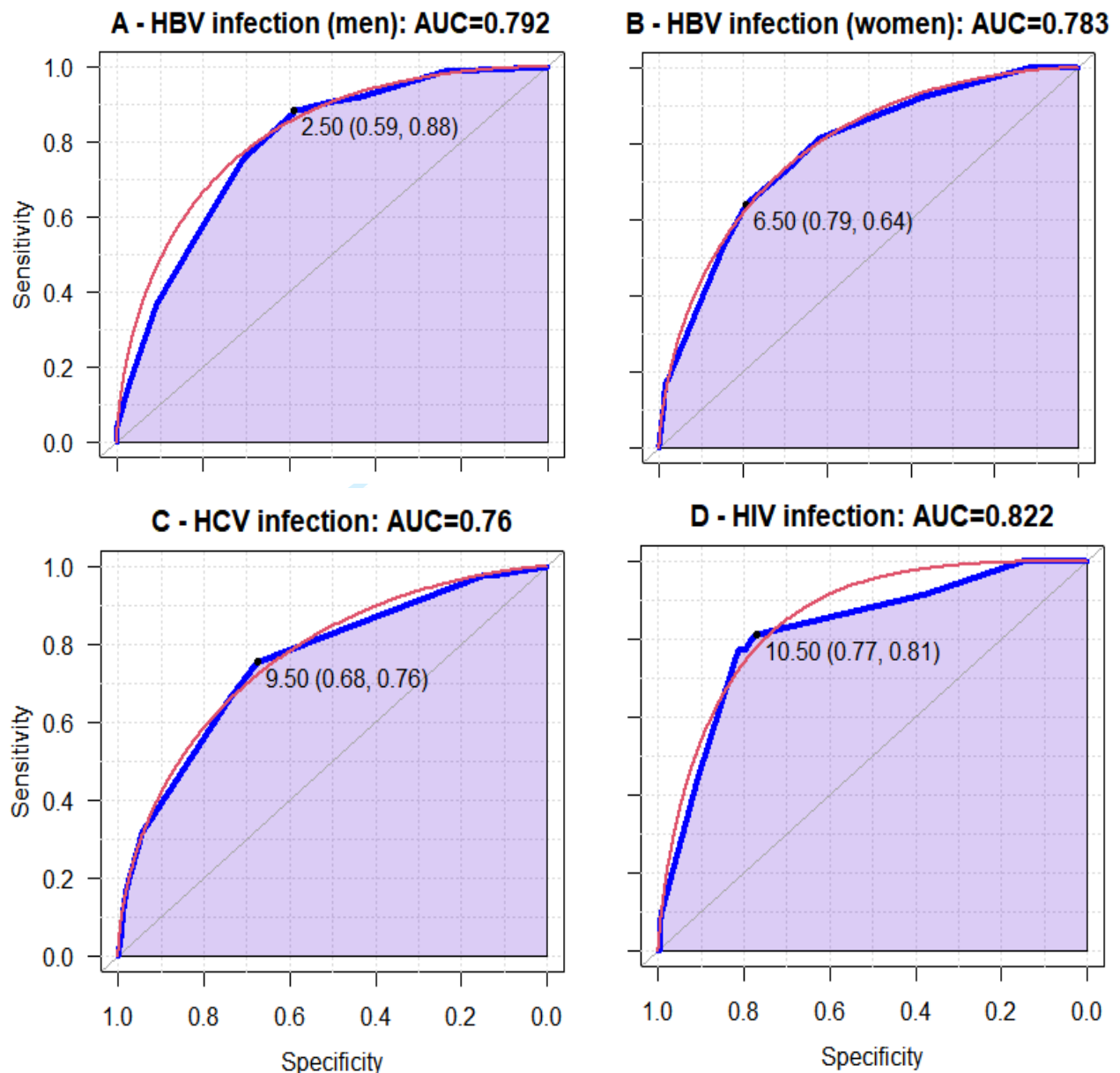


Figure 1. Mean Receiver operating characteristics (ROC) curve for multivariable logistic regression models. Each blue line indicates the ROC curve. (A) Depicted the area under the curve (AUC) for the HBV infection in men, the AUC for this model is 0.792, indicating a good fit. The threshold was 2.50, specificity = 0.88 and sensitivity = 0.59. (B) Showed the AUC for HBV in women, which was 0.783. The threshold was 6.50, specificity = 0.79 and sensitivity = 0.64. (C) The curve for HCV has an AUC of 0.760, indicating a fair fit for the score. The threshold was 9.50, specificity = 0.76 and sensitivity = 0.68. (D) Depicted the AUC for the HIV infection. The AUC for this model is 0.822, indicating a good fit. The threshold was 10.50, specificity = 0.81 and sensitivity = 0.77.

TRIPOD Checklist: Prediction Model Development

Section/Topic	Item	Checklist Item	Page
Title and abstract			
Title	1	Identify the study as developing and/or validating a multivariable prediction model, the target population, and the outcome to be predicted.	1
Abstract	2	Provide a summary of objectives, study design, setting, participants, sample size, predictors, outcome, statistical analysis, results, and conclusions.	2
Introduction			
Background and objectives	3a	Explain the medical context (including whether diagnostic or prognostic) and rationale for developing or validating the multivariable prediction model, including references to existing models.	4
	3b	Specify the objectives, including whether the study describes the development or validation of the model or both.	5
Methods			
Source of data	4a	Describe the study design or source of data (e.g., randomized trial, cohort, or registry data), separately for the development and validation data sets, if applicable.	6
	4b	Specify the key study dates, including start of accrual; end of accrual; and, if applicable, end of follow-up.	6
Participants	5a	Specify key elements of the study setting (e.g., primary care, secondary care, general population) including number and location of centres.	6
	5b	Describe eligibility criteria for participants.	6
	5c	Give details of treatments received, if relevant.	NA
Outcome	6a	Clearly define the outcome that is predicted by the prediction model, including how and when assessed.	6
	6b	Report any actions to blind assessment of the outcome to be predicted.	6
Predictors	7a	Clearly define all predictors used in developing or validating the multivariable prediction model, including how and when they were measured.	6-7
	7b	Report any actions to blind assessment of predictors for the outcome and other predictors.	NA
Sample size	8	Explain how the study size was arrived at.	NA
Missing data	9	Describe how missing data were handled (e.g., complete-case analysis, single imputation, multiple imputation) with details of any imputation method.	NA
Statistical analysis methods	10a	Describe how predictors were handled in the analyses.	7
	10b	Specify type of model, all model-building procedures (including any predictor selection), and method for internal validation.	7
	10d	Specify all measures used to assess model performance and, if relevant, to compare multiple models.	NA
Risk groups	11	Provide details on how risk groups were created, if done.	NA
Results			
Participants	13a	Describe the flow of participants through the study, including the number of participants with and without the outcome and, if applicable, a summary of the follow-up time. A diagram may be helpful.	8
	13b	Describe the characteristics of the participants (basic demographics, clinical features, available predictors), including the number of participants with missing data for predictors and outcome.	8
Model development	14a	Specify the number of participants and outcome events in each analysis.	8-9
	14b	If done, report the unadjusted association between each candidate predictor and outcome.	9
Model specification	15a	Present the full prediction model to allow predictions for individuals (i.e., all regression coefficients, and model intercept or baseline survival at a given time point).	9
	15b	Explain how to use the prediction model.	9
Model performance	16	Report performance measures (with CIs) for the prediction model.	9
Discussion			
Limitations	18	Discuss any limitations of the study (such as nonrepresentative sample, few events per predictor, missing data).	11
Interpretation	19b	Give an overall interpretation of the results, considering objectives, limitations, and results from similar studies, and other relevant evidence.	10-11
Implications	20	Discuss the potential clinical use of the model and implications for future research.	10-11
Other information			
Supplementary information	21	Provide information about the availability of supplementary resources, such as study protocol, Web calculator, and data sets.	13
Funding	22	Give the source of funding and the role of the funders for the present study.	13

We recommend using the TRIPOD Checklist in conjunction with the TRIPOD Explanation and Elaboration document.