An Age-adapted, Easy-to-implement Score For Integrated Bundled, Rapid HIV/HCV Testing

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BACKGROUND

- Undiagnosed or unlinked HIV-and/or HCV-infected populations still remain an issue worldwide.
- Integrated, bundled, rapid HCV/HIV testing has been proposed, but testing recommendations slightly differ between the two diseases: **HCV testing** is recommended for high-risk groups and all persons born between 1945 and 1965; **HIV testing** is recommended for everyone between the ages of 13 and 64.
- Our objective is to evaluate **which HCV self-reported risk factors are associated with higher rates of infection, considering age as differences may exist.**
- We also focus **on creating an easy-to-implement score**.

METHODS

- From November 2016 to September 2017, we conducted a sub-analysis of the DRIVE03 study (NCT03145753), which was carried out at four primary care centers, including non-HIV-infected people aged 18-70 years.
- After participants completed an HIV/HCV risk questionnaire (Table-1), an HCV screening was performed using rapid tests, (anti-VHC WB/S/P, TürkLab Laboratories , Izmir, Turkey), for those with any positive response, and in all those aged 50-70 years-old.
- Two multivariable models were created, one for participants younger than 50 and other for those older than 50. These models included the questions that exhibited the strongest association with a positive HCV result in the univariable analysis (p<0.10 were considered).

Table-1 HIV/HCV risk of exposure and indicator conditions (RE&IC) questionnaire

Date of test:	Gender:	Project code:
Date of birth :	Educational level:	Country of Origin :
HIV or HCV test result (*Positive/Negative/Invalid):*		

Risk of Exposure	Yes	No
1.Have you ever had sexual intercourse without condom protection, which could represent a risk for acquiring HIV / AIDS in the last 30 years, unless you are with a close partner or always use condoms?		
2.Have you ever had a partner with HIV or HCV infection?		
3.Have you ever had man-to-man sex?		
4.Had you ever received any blood or blood product transfusion before 1990?		
5.Have you ever used any illicit or recreational intravenous drugs?		
6.Do you think you could have acquired HIV or HCV infection for any reason?		
Indicator conditions: *Have you ever had any of the diseases below?*	Yes	No
7. Sexually transmitted infection (Syphilis, Gonorrhea, urethritis, genital herpes…)		
8. Lymphoma		
9. Cervical or anal cancer or dysplasia		
10. Herpes Zoster		
11. Hepatitis B or C or any other hepatic disorder		
12. Mononucleosis-like syndrome		
13. Thrombocytopenia/Unexplained leucopenia		
14. Seborrheic dermatitis		
15. Unknown origin/unexplained fever		
16. Repeated oral or vaginal candidiasis without antibiotic use		
17. Oral hairy leukoplakia		
18. Unexplained prolonged (>3 months) diarrhea		
19. Unexplained weight loss		
20. *Mycobacterium tuberculosis* Disease		
21. Pneumonia		

*All responses were considered as a risk for HIV infection. Questions in bold (2, 3, 4, 5, 6, 7, 8, 9, 11, 13, 20) indicate the performance of a rapid HCV test if answered affirmatively.

The results of this study with a large sample size indicate that it is possible to correctly classify more than 90% of the general population with respect to HCV infection using only five simple questions.

RESULTS

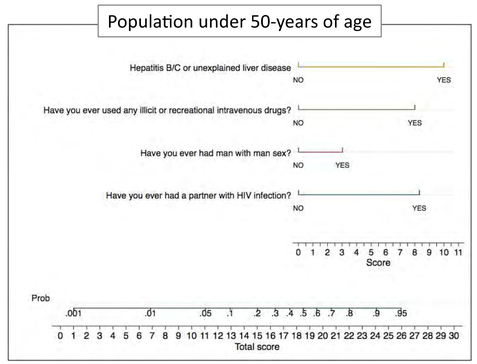
A total of **7991** participants were included in the study and filled out the RE&IC questionnaire; **65.9% were women**, the **median age was 43 years (IQR 33-53**). Most of participants **(40.6%) had secondary education**, followed by **33.3% with university studies** and 25.1% with primary education. The most frequent place of origin **was Spain (75.5%),** followed by **Latin America (15.4%).** Of the total of 7991 participants**, 2894 (36.2%) answered affirmatively to any of the HCV-related questions**. Moreover, **2557 patients were over 50 years old** and were consequently tested. Of them, only 867 (33.9%) presented a positive questionnaire. A total of **4717 HCV tests were performed**, and **52 (1.1%) were positive**.

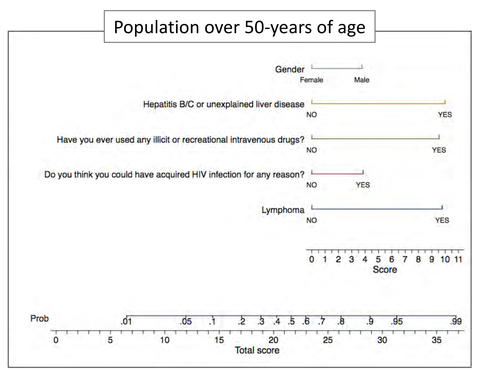
Table 2. Best predictors of HCV infection in the multivariate regression models

Questionnaire items answered as "yes"	Adjusted OR (95% CI)	p
< 50 years of age (n = 5,401); AUROC = 0.91		
Have you ever had an HIV or HCV-infected partner?	26.6 (7.6 – 92.9)	<0.001
Have you ever had man with man sex?	3.3 (0.8-13.5)	0.095
Have you ever used parenteral illicit or recreational drugs?	23.6 (4.2 - 131.8)	<0.001
Have you had hepatitis or unexplained liver disease?	51.0 (17.4 - 154.9)	<0.001
> 50 years of age (n = 2,535); AUROC = 0.89		
Male Gender	3.1 (1.4-7.2)	0.007
Have you ever used parenteral illicit or recreational drugs?	18.1 (4.2-77.8)	<0.001
Do you think you could have acquired HCV infection for any reason?	3.2 (1.4-7.5)	0.007
Have you ever had lymphoma?	19.4 (2.1-183.3)	0.010
Have you ever had hepatitis or unexplained liver disease?	20.8 (8.6 - 50.3)	<0.001

AUROC: area under the ROC curve**;** CI: confidence interval; HCV: hepatitis C virus; OR: odds ratio

Figure 1. Nomogram of best HCV infection predictors for both age groups





RESULTS

Table 3 shows the diagnostic values of short questionnaires for predicting HCV infection in comparison to the complete questionnaire, using a probability cutoff point equal to 0.5. Both models present a specificity of 99.9% and a negative predictive value higher than 99%.

	< 50 years (n = 5,401)	> 50 years (n = 2,535)
Sensitivity	5.0%	23.3%
Specificity	99.9%	99.9%
Positive predictive value	50.0%	77.8%
Negative predictive value	99.7%	99.1%
Correctly classified	99.6%	99.0%

CONCLUSIONS

- Two easy-to-implement, age-adapted models can predict the majority of HCV status in general population.
- This work contributes to the implementation of targeted HCV testing in routine clinical practice, as well as to the design of combined HCV/HIV testing programs.

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