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Implementation of the HepC*link* test-and-treat community strategy targeting Pakistani migrants with hepatitis C living in Catalonia (Spain) compared with the current practice of the Catalan health system: budget impact analysis

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ABSTRACT

Objectives To perform a budget impact analysis of the HepC*link* test-and-treat strategy in which community health agents offer hepatitis C virus (HCV) testing, diagnosis and treatment to the Pakistani population living in Catalonia compared with the current practice of the Catalan health system (without targeted screening programmes).

Methods We estimated the population of adult Pakistani migrants registered at the primary care centres in Catalonia by means of the Information System for the Development of Research in Primary Care (n=37 972 in 2019, Barcelona health area). This cohort was followed for a time period of 10 years after HCV diagnosis (2019–2028). The statistical significance of the differences observed in the anti-HCV positivity rate between screened and non-screened was confirmed (α=0.05). The budget impact was calculated from the perspective of the Catalan Department of Health. Sensitivity analyses included different levels of participation in HepC*link*: pessimistic, optimistic and maximum.

Results The HepC*link* scenario screened a higher percentage of individuals (69.8%) compared with the current scenario of HCV care (39.7%). Viraemia was lower in the HepC*link* scenario compared with the current scenario (1.7% vs 2.5%, respectively). The budget impact of the HepC*link* scenario was €884 244.42 in 10 years.

Conclusions Scaling up the HepC*link* strategy to the whole Catalan territory infers a high budget impact for the Department of Health and allows increasing the detection of viraemia (+17.8%) among Pakistani migrants ≥18 years. To achieve a sustainable elimination of HCV by improving screening and treatment rates, there is room for improvement at two levels. First, taking advantage of the fact that 68.08% of the Pakistani population had visited their primary care physicians to reinforce targeted screening in primary care. Second, to use HepC*link* at the community level to reach individuals with reluctance to use healthcare services.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The long time scope (2019–2028) permits a realistic assessment of the budget impact.
⇒ We used a biologically plausible model which is fitted with local data on disease epidemiology and the effectiveness of directly acting antiviral agents in Catalonia, Spain.
⇒ Cost of treatment was drawn from the Catalan Health System Cost Database and published literature from Spain for patient cost; however, indirect costs were not included.
⇒ The possibility of reinfection once treated was not considered in our model.

INTRODUCTION

Chronic hepatitis C remains an important public health problem in the European Union (EU)/European Economic Area (EEA) and the UK, with an estimated 3.9 million persons having active hepatitis C virus (HCV) infection[1] in the region. The landscape of HCV treatment has changed rapidly since 2013, especially when pan-genotypical direct-acting antiviral (DAA) HCV treatment that cures about 95% of HCV infections became available, making HCV elimination possible.[2] Identifying and treating all HCV-infected people including at-risk groups will be essential to address the health and economic burden due to HCV in the region and to meet the WHO elimination goals by 2030.[3]

Migrants from high and intermediate HCV-prevalent countries (anti-HCV ≥5% and ≥2%, respectively) are an important and overlooked group with increased HCV infection

risk in the EU/EEA and often do not have additional HCV risk factors.[4–6] Approximately 11% of the EU/EEA adult population is foreign born, 79% of which were born in HCV-endemic (anti-HCV prevalence ≥1%) countries.[5] Anti-HCV prevalence among migrants from endemic countries residing in the EU/EEA is estimated at 1.6–2.3% corresponding to ~580 000 HCV infections or 14% of the chronic hepatitis C burden in the EU/EEA.[5] Migrants from Romania and Russia (50–60 000 cases each) contribute massively to the high burden and so do migrants from Italy, Morocco, Pakistan, Poland and Ukraine (25–35 000 cases each).[5] In Spain, the estimated HCV antibody prevalence among the whole migrant population is 1.6%.[7]

A study that assessed positive anti-HCV test rate in Catalonia using data from the Information System for the Development of Research in Primary Care (SIDIAP (acronym in Catalan); the SIDIAP contains anonymised, longitudinal health data of over 5.6 million people (80% and 10.2% of the Catalan and Spanish population, respectively))[8] revealed that, between 2011 and 2016, the positive anti-HCV test rate was higher among migrants of Asian origin (9.78 of 103 (95% CI 9.21 to 10.35)) and European and Northern American origin (5.64 of 103 (95% CI 5.33 to 5.96)), compared with the Spanish-born population (3.68 of 103 (95% CI 3.61 to 3.75)).[9] A previous study in Catalonia in 2008 reported that the Pakistani migrant community had the highest anti-HCV seroprevalence at 14.9%.[10]

Given that primary care physicians (PCPs) are likely not to prioritise migrants for viral hepatitis testing,[9] developing innovative and sustainable strategies to facilitate screening, treatment initiation and completion will improve health outcomes and must be evaluated. HepC*link*[11] was a pilot study designed to determine whether a community intervention that brings together HCV education, screening and simplified access to treatment in Pakistani migrants living in Catalonia was feasible and targeted a sample of Pakistani migrants in the Barcelona health area, where 85.89% of this population reside.[12]

In this study, we assess the budget impact of scaling up the HepC*link*[13] test-and-treat community strategy to Pakistanis living in the entire Catalonia region, compared with the current practice of the Catalan health system, in order to help policymakers to further consider this model as an HCV micro-elimination strategy.

METHODS

Study design

In this budget impact analysis, two approaches of diagnosis and treatment of Pakistanis living in Catalonia (Spain) were compared by using the Consolidated Health Economic Evaluation Reporting Standards 2022 Checklist.[14] The first approach was the current and usual scenario where no specific HCV screening programme targeting a particular population is in place. In this approach, only people who attend primary care centres could potentially be tested for HCV and referred to a specialist for treatment. The second one was the scenario which includes the implementation of HepC*link* strategy. In brief, HepC*link* was a community-based education and test-and-treat project in which community health agents used an educational module to raise awareness and promote behavioural changes, offer HCV testing and diagnosis, and facilitate treatment to the Pakistani population. The analysis has been raised from the perspective of the Catalan Department of Health (payer).

Temporal horizon

A cohort of Pakistanis aged 18 years or over and residing in Catalonia is being followed for a time period of 10 years after HCV diagnosis (2019–2028). The long time scope permits a realistic assessment of the economic impact of patients who require indefinite annual follow-up visits after cure.

Setting and participants

Catalonia is an autonomous community in northeast Spain, with over 7.5 million inhabitants. The Catalan Health Institute provides universal health access and is funded predominantly by public taxes. We included adult Pakistani migrants in Catalonia registered at the primary care centres (CAP (acronym in Catalan)) in the cohort.

Estimated population

We estimated the population of Pakistani migrants registered at the CAPs in Catalonia by the means of SIDIAP sample of 46 066 individuals for the year 2019 (Barcelona health area). For the purpose of this analysis, we selected the people aged 18 years or over, so the final sample was 37 972 individuals (online supplemental appendix A) and scaled up the results to the whole Catalonia region.[12]

Current scenario

Patients with HCV symptoms access the public healthcare system through the CAPs (figure 1A) 86% of the time through visits to the PCPs, and 14% through the emergency units. The first test performed is a serological test, which determines the presence of HCV antibodies (anti-HCV). Then, a reflex HCV RNA test is performed which means that in the case of a positive anti-HCV result, an HCV RNA test is run immediately on the same sample. If the subsequent HCV RNA test is negative, HCV infection is effectively ruled out. If the reflex HCV RNA test is positive, a diagnosis of active HCV infection is confirmed, and the individual might be referred to the specialist for further laboratory analysis and treatment.[15] Once laboratory results are obtained, a primary care nurse contacts the patient to schedule a visit to the CAP. The PCP then requests further blood tests that allow for the calculation of the Fibrosis-4 (FIB-4) score,[16] performs HCV genotyping and refers the patient to a hepatologist. Additionally, hepatologists request elastography and a complete abdominal ultrasound if the degree of fibrosis is F3 or greater. At the end of antiviral treatment (EOT), an HCV

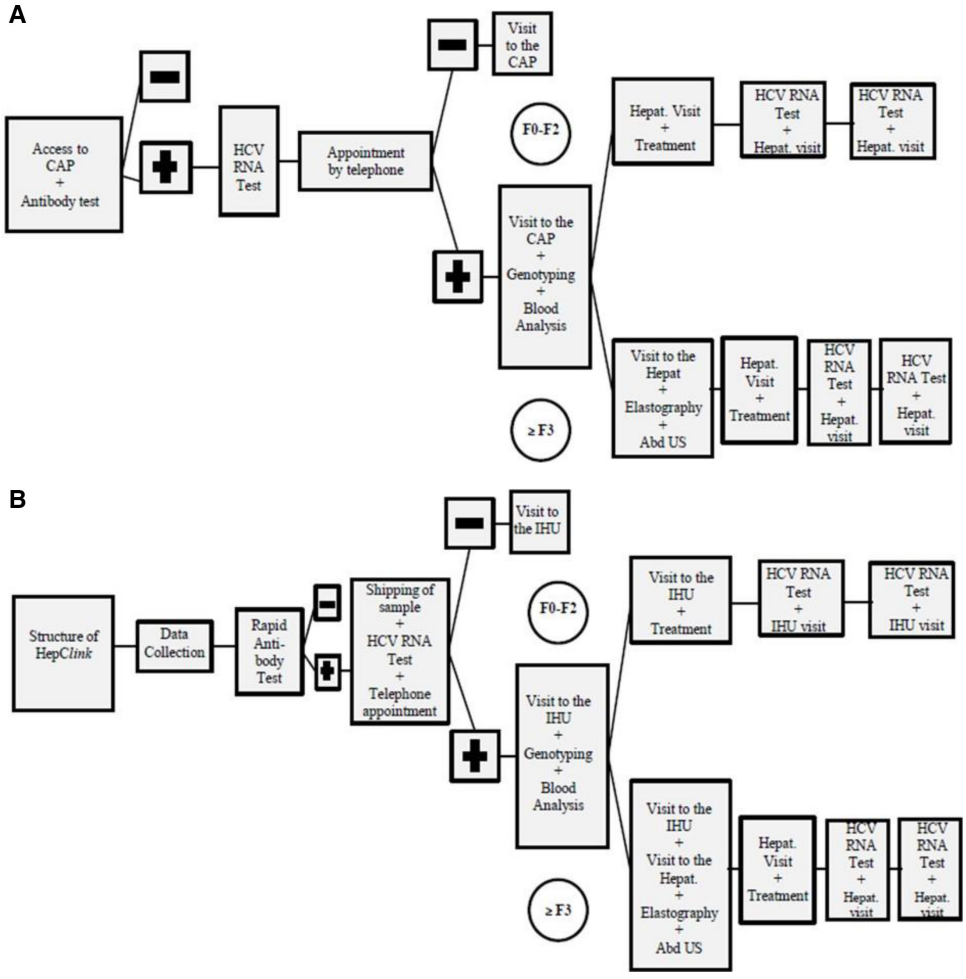

Figure 1 Itineraries without community screening (A) and with screening (B). Based on the usual practice in the Catalan health system and the HepC*link* pilot test, the differences in care in the approach to hepatitis C without and with community screening are reflected. Abd US, abdominal ultrasound; CAP, primary care centre (acronym in Catalan); F0–F2, fibrosis grade F0–F2; ≥F3, fibrosis grade equal to or higher than F3; HCV, hepatitis C virus; Hepat, hepatologist; IHU, International Health Unit.

RNA test is requested to determine viral load. Three months after the EOT, another HCV RNA test is requested to evaluate sustained virological response (SVR). HCV-diagnosed patients with F2 or greater continue to be monitored annually indefinitely. We assumed that there is no further transmission among Pakistani individuals. We did not model treatment uptake because it is high in Spain due to unrestricted access to DAA since 2017.[17] The consumption of resources in this scenario is shown in table 1.

The HepC*link* scenario

In the second scenario, 50% of the target population[18] agree to participate in the HepC*link* preventive screening and follow the care itinerary illustrated in figure 1B. The HepC*link* care itinerary begins with the assembling of necessary resources to start the programme. Seeking proximity to the Pakistani community, we estimated that 28 community health agents would be necessary to visit the 313 municipalities[12] where the population is located within 1 year allocating adequate time to each participant. These agents usually work 36 hours per week (43 effective weeks per year). Accordingly, we resolved not to visit more than four people per hour or visit more than one municipality in a week. The daily activity of each agent was divided into 4 hours of fieldwork and 4 hours of travel or preparation (4 days per week). On the last working day of the week, agents are engaged in planning tasks for 4 hours. Once the programme is implemented, the agents offer education on viral hepatitis with an interactive tool implemented on a tablet (Heparjoc[19]), followed by rapid HCV antibody testing for participants. If the result is positive, confirmatory testing is offered through the collection of a dried blood spot (DBS) sample for HCV RNA testing in a central laboratory. We assumed that people who reject this confirmatory test would not go to the CAP either, because we considered that they remained asymptomatic in the short term and had no incentive to change their behaviour. The nurses contact the participants to arrange visits to the International Health Unit of each of the health areas of Catalonia and deliver the results. If the HCV RNA test result is negative, participants are counselled on how to prevent the disease. In HCV RNA

Table 1 Consumption of resources in the care itinerary without screening through the Catalan healthcare system

Concept	No of units	Assigned criteria
Access to the health system		
Visit to the primary care physician	1	Access route for 86% of patients
Visit to the emergency of the CAP	1	Access route for 14% of patients
Diagnosis and monitoring of HCV infection and liver disease		
Antibody test	1	If suspected HCV infection
HCV RNA test	1	To all patients with HCV antibodies
HCV RNA test at EOT	1	At the end of treatment
HCV RNA test at SVR	1	3 months after completing treatment
Appointments by telephone	1	To programme a visit to the primary care physician
Visit to the primary care physician	1	To deliver HCV RNA test results
1st visit to the hepatologist	1	To all HCV RNA-positive patients
2nd visit to the hepatologist	1	To all HCV RNA-positive patients
3rd visit to the hepatologist	1	To all HCV RNA-positive patients
4th visit to the hepatologist	1	In patients with fibrosis ≥F3
HCV genotyping test	1	To all HCV RNA-positive patients
Elastography	1	Patients from F3 (FIB-4 criterion)
Blood tests	1	To all HCV RNA-positive patients
Abdominal ultrasound	1	Patients from F3 (FIB-4 criterion)
Treatment and follow-up		
Treatment F0–F1	1	Patients with degree of fibrosis F0–F1
Treatment F2	1	Patients with degree of fibrosis F2
Treatment F3	1	Patients with degree of fibrosis F3
Treatment F3 HCC	1	F3 patients with HCC
Treatment F4	1	Patients with degree of fibrosis F4
Treatment F4 DC	1	F4 patients with DC
Treatment F4 HCC	1	F4 patients with HCC
Follow-up with SVR F2	1	F2 patients with SVR
Follow-up with SVR F3	1	F3 patients with SVR
Follow-up with SVR F4	1	F4 patients with SVR

CAP, primary care centre (acronym in Catalan); DC, decompensated cirrhosis; EOT, end of antiviral treatment; FIB-4, Fibrosis-4; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; SVR, sustained virological response.

positive cases, a blood sample was obtained for HCV genotyping and FIB-4[16] score during the visit. In a subsequent visit, patients with up to F2 fibrosis commence treatment. At this point, the healthcare itinerary is the same as in the current scenario for patients with fibrosis stage F3 or greater, as explained above. The remaining 50% of the population who do not participate in the screening behave the same as in the first scenario (figure 1A). The consumption of resources in this scenario is shown in table 2.

Liver disease stage classification

Patients with viraemic HCV were classified into four fibrosis degrees: F0–F1, F2, F3 and F4.[17] The distribution was weighted according to the predominant genotypes in Pakistan[20] and the fibrosis observed in individuals with viraemic HCV receiving treatment in the Catalan Public Health System (online supplemental appendix B). There were three additional aggravated categories: F3 patients with hepatocellular carcinoma (HCC), F4 patients with decompensated cirrhosis and F4 patients with HCC (table 3).

Transitions

The clinical course develops with annual transitions and we assumed that patients with F3 and F4 degrees have been in this stage for more than 12 months. F0–F1, F2, F3 and F4 patients who do not reach an SVR after DAA treatment may progress to a higher degree of fibrosis depending on their age.[17] Patients with F3 and F4 degrees can progress to their aggravated subcategories where

Table 2 Consumption of resources in the care itinerary with screening*

Concept	No of units	Assigned criteria
Programme structure		
Training of health agents	5.00	Training sessions[13]
Tablets	28.00	1 for each agent[13]
Coordinating nurses	7.00	1 for each health region[13]
Health agents in Barcelona	20.00	Expenses by health region[13]
Health agent in Tarragona	1.00	Expenses by health region[13]
Health agent in Terres de l'Ebre	0.80	Expenses by region according to time dedicated[13]
Health agents in Girona	1.20	Expenses by region according to time dedicated[13]
Health agent in Lleida	0.70	Expenses by region according to time dedicated[13]
Health agent in Alt Pirineu i Aran	0.20	Expenses by region according to time dedicated[13]
Health agents in Catalunya Central	1.30	Expenses by region according to time dedicated[13]
Travels in Barcelona	6944.00	2 travels per agent per day[30]
Other travels	1805.44	2 travels per agent per day[31]
Data entry	1.00	Time dedicated at deployment[13]
Heparjoc educational tool	1.00	Transfer of rights (educational interactive support)[19]
Data collection		
Epidemiological questionnaires	1.00	Filled out by all participants[13]
Informed consent forms	1.00	Filled out by all participants[13]
Personal data forms	1.00	Filled out by all participants[13]
Follow-up data forms	1.00	Filled out by the patients with viraemia[13]
Screening		
Rapid antibody test	1.00	Provided to all participants[13]
DBS collection materials	1.00	Antibody-positive participants who agree[13]
Gloves	2.00	For all participants[13]
Alcohol	28.00	Provided to all agents[13]
Gauze	2.00	For all participants[13]
Plasters	2.00	For all participants[13]
Antiseptics	28.00	Provided to all agents[13]
Pencils	140.00	5 units provided per agent[13]
Felt pens/markers	140.00	5 units provided per agent[13]
Diagnosis and monitoring of HCV infection and liver disease		
Appointments by telephone	1.00	To deliver HCV RNA test results[13]
1st visit to the IHU	1.00	To deliver HCV RNA test results[13]
2nd visit to the IHU	1.00	HCV genotyping and assessment of analyses[13]
3rd visit to the IHU	1.00	Delivery of HCV RNA test results at EOT for patients with fibrosis ≤F2[13]
4th visit to the IHU	1.00	Delivery of HCV RNA test results at SVR for patients with fibrosis ≤F2[13]
1st visit to the hepatologist	1.00	Elastography and abdominal ultrasound request for patients with fibrosis ≥F3[13]
2nd visit to the hepatologist	1.00	Elastography and abdominal ultrasound assessment[13]
3rd visit to the hepatologist	1.00	Delivery of HCV RNA test results at EOT for patients with fibrosis ≥F3[13]
4th visit to the hepatologist	1.00	Delivery of HCV RNA test results at SVR for patients with fibrosis ≥F3[13]

Continued

Table 2 Continued

Concept	No of units	Assigned criteria
DBS processing for blood elution	1.00	To all DBS samples[13]
HCV RNA test from DBS	1.00	To all DBS samples[13]
HCV RNA test at EOT	1.00	At the end of treatment[13]
HCV RNA test at SVR	1.00	3 months after completing treatment[13]
HCV genotyping test	1.00	To all HCV RNA-positive patients[13]
Elastography	1.00	In patients with fibrosis ≥F3 (FIB-4)[13]
Blood tests	1.00	To all HCV RNA-positive patients[13]
Abdominal ultrasound	1.00	In patients with fibrosis ≥F3 (FIB-4)[13]
Mailings by post	0.02	To all DBS samples[13]
Envelopes	1.00	To all DBS samples[13]
Sample submission forms	1.00	To all DBS samples[13]
Treatment and follow-up		
Treatment F0–F1	1.00	Patients with fibrosis degree F0–F1[17]
Treatment F2	1.00	Patients with fibrosis degree F2[17]
Treatment F3	1.00	Patients with fibrosis degree F3[17]
Treatment F3 HCC	1.00	F3 patients with HCC[17]
Treatment F4	1.00	Patients with fibrosis degree F4[17]
Treatment F4 DC	1.00	F4 patients with DC[17]
Treatment F4 HCC	1.00	F4 patients with HCC[17]
Follow-up with SVR F2	1.00	F2 patients with SVR[17]
Follow-up with SVR F3	1.00	F3 patients with SVR[17]
Follow-up with SVR F4	1.00	F4 patients with SVR[17]

*The consumption of resources in this table is the adaptation of the HepC*link* pilot study to the whole Catalan territory proposed by the authors and based on their clinical, laboratory and community health experience.
DBS, dried blood spot; DC, decompensated cirrhosis; EOT, end of antiviral treatment; FIB-4, Fibrosis-4; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; IHU, International Health Unit; SVR, sustained virological response.

their death is assumed. Ninety-three per cent of patients achieved SVR after receiving treatment (table 3).

Treatments

We assumed that all diagnosed patients receive DAAs, which consist of the prescription and dispensation of sofosbuvir plus velpatasvir or glecaprevir plus pibrentasvir for 12 weeks. Given that aggravated states are infrequent and in order not to underestimate the resources required to treat them all, those patients with more severe diseases were charged with the therapies corresponding to the worst possible prognosis. Specifically, patients with HCC received in addition to the basic treatment: chemotherapy, transplantation, post-transplant care and palliative care. We added dispensing expenses for HCC according to the specific disease stage for patients with decompensated cirrhosis.

Costs

Adopting the context of the Department of Health (payer), only the direct costs necessary to diagnose, treat and follow-up patients diagnosed with HCV infection in Catalonia during 2019 were included. We calculated prices from official sources taking 2020 as the base year. Prices were deflated by the consumer price index (CPI)[21] values for Catalonia until June, which is when the public health rates are published. Data from 2019, the period in which the CPI decreased, are not updated. The details of all the costs together with their sources are shown in table 4.

Models

For the population calculations, we created a model for each scenario using the parameters shown in table 3. In the case of costs, we integrated the population results arising from the resources and prices according to each scenario. We included a comparative diagnostic impact between the two scenarios which involves the differences in relative value for the number of people tested and the number of viraemic cases diagnosed; these parameters allowed us to determine the number of avoided liver cancer and death cases in a decade by using the annual transitions in table 3 and liver-related mortality taken from the literature (HCC: 43% annual probability, decompensated cirrhosis: 13.3% annual probability).[17]

Table 3 Parameters used in the population estimates

Parameter	Value	CI/source
Target population (online supplemental appendix A)		
% Pakistanis over 18 years	82.43	95% CI: 82.08 to 82.78 N=46 066
Liver disease stage classification		
% F0–F1	55.14	17 20 Online supplemental appendix B
% F2	16.86	
% F3	11.79	
% F3 HCC	0.13	
% F4	15.197	
% F4 DC	0.643	
% F4 HCC	0.24	
Annual transitions		
SVR with treatment	93%	17
F0–F1 to F2	9.95%	
F2–F3	12.67%	
F3–F3 HCC	1.10%	
F3–F4	12.09%	
F4–F4 DC	4%	
F4–F4 HCC	1.5%	
Itinerary without screening (online supplemental appendix C)		
% tested at the CAP (HCV antibody test)	39.7	95% CI: 39.2 to 40.19 N=37 972
% seroprevalence among tested (positive antibody test)	7.5	95% CI: 7.07 to 7.91 N=15 073
% Viraemic infections among anti-HCV positive (HCV RNA positive)	33.6	95% CI: 30.73 to 36.23 N=1129
Itinerary with HepC*link* community screening (online supplemental appendix D)		
% tested in the community (HCV antibody test)	50	18
% seroprevalence among tested (positive HCV antibody test)	4.37	95% CI: 2.28 to 6.47 N=366
% seropositive patients who accept DBS sample collection	93.79	95% CI: 81.89 to 100 N=16
% viraemic infections among DBS tested (HCV RNA positive)	33.33	95% CI: 9.48 to 57.19 N=15

CAP, primary care centre (acronym in Catalan); DBS, dried blood spot; DC, decompensated cirrhosis; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; SVR, sustained virological response.

To measure the budget impact, the difference in costs between the two scenarios is accumulated for each year, until the total effect is generated at the end of the period analysed (2019–2028). The software used in all cases was Microsoft Excel.

Contrast differences in proportions

When analysing the implementation of a preventive programme, the diagnostic capacity is a key element and, therefore, the difference in the proportion of test positivity in both approaches was tested at a significance level of α=0.05. Regarding the anti-HCV positivity rate (2.25>1.96), the statistical significance of the differences observed between screened and non-screened was confirmed, rejecting the null hypothesis that they were the same.

Sensitivity analysis

The degree of public acceptance of the HepC*link* screening proposal is the variable that generates the greatest uncertainty. To control it, a univariate sensitivity analysis was performed with three additional levels of participation: pessimistic (25%), optimistic (75%) and maximum value (100%). As treatment with DAAs is effective against

Table 4 Unit prices used in the cost estimation based on 2020

Concept	Prices (based on 2020)	Source
Medical visits		
Visit to the primary care physician	€50	32
Visit to the emergency at the CAP	€75	
1st visit to the hepatologist	€171	
Rest of hepatology visits	€80	
Diagnostic tests		
Antibody test	€5.43	32
HCV RNA test	€53.11	
HCV genotyping test	€105	
Elastography	€87	
Blood tests	€2.69	
Abdominal ultrasound	€72	
Treatments		
Treatment F0–F1	€6734	17 32 33
Treatment F2	€6734	
Treatment F3	€6734	
Treatment F3 HCC	€162 557.88	
Treatment F4	€6734	
Treatment F4 DC	€164 924.86	
Treatment F4 HCC	€162 557.88	
Follow-up		
Follow-up with SVR F2	€116.725	17
Follow-up with SVR F3	€116.725	
Follow-up with SVR F4	€168.49	
HepC*link* programme structure		
Training of health agents	€300	13 34
Tablet	€120	
Gross salary of programme coordinator nurse	€12 970.56	
Gross salary of Barcelona health agent	€17 010.12	
Gross salary of Camp de Tarragona health agent	€17 010.12	
Gross salary of Terres de l'Ebre health agent	€17 010.12	
Gross salary of Girona health agent	€17 010.12	
Gross salary of Lleida health agent	€17 010.12	
Gross salary of Alt Pirineu i Aran health agent	€17 010.12	
Gross salary of Catalunya Central health agent	€17 010.12	
Travels in Barcelona	€3.92	30
Other travels	€7	31
Gross salary of data entry personnel	€13 302.72	34
Heparjoc (transfer of rights)	€200	13
HepC*link* data collection		

Continued

Table 4 Continued

Concept	Prices (based on 2020)	Source
Epidemiological questionnaires (printing)	€0.01	13
Informed consent forms (printing)	€0.01	
Personal data forms (printing)	€0.01	
Follow-up data forms (printing)	€0.01	
Screening and visits for HepC*link*		
Rapid antibody test	€1.16	13 32
DBS collection materials	€4.50	
Gloves	€0.03	
Alcohol	€2.77	
Gauze	€0.01	
Plasters	€0.03	
Antiseptic	€10.70	
Pencils	€0.27	
Felt pens/markers	€1	
Visit to the IHU	€50	
HepC*link* DBS transportation and testing		
DBS processing for blood elution	€2.50	13 32
HCV RNA test in DBS	€53.11	
Mailings by post	€5.86	
Envelopes	€0.10	
Sample submission forms	€0.01	

CAP, primary care centre (acronym in Catalan); DBS, dried blood spot; DC, decompensated cirrhosis; HCC, hepatocellular carcinoma; HCV, hepatitis C virus; Heparjoc, educational interactive support; IHU, International Health Unit; SVR, sustained virological response.

all genotypes, in the HepC*link* screening itinerary, we assessed to exclude the genotyping test. Finally, we evaluated how the intervention would affect costs if it incorporated a single step to access the HCV RNA test and FIB-4 score test in addition to the exclusion of genotyping test. This implies that the laboratory establishes the diagnosis of viraemic cases and liver disease stage using the same sample as currently performed in certain tertiary care hospitals. This avoids an extra medical visit and we simulated this scenario for all the patients.

Alternative scenario

Given that most of the Pakistani population (93.66%)[12] is concentrated in three health areas (Barcelona (85.89%), Camp de Tarragona (4.3%) and Terres de l'Ebre (3.47%)), we evaluated the diagnosis impact and the budget impact limiting the HepC*link* screening to this scope (174 municipalities).[12]

Patient and public involvement

There was no public or patient involvement during design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

The adult population of Pakistani migrants in Catalonia registered at the CAPs in 2019 was 44 214 individuals (online supplemental appendix E).

The current scenario

In the current scenario, 17 554 (39.7%) people were tested, of which 444 (2.5%) were HCV RNA positive. The liver fibrosis staging of the viraemia cases were: F0–F2 (72%), F3–F4 (27.6%) and patients with HCC (0.4%). During the 2019–2028 period, the cost of carrying out this approach was €5 649 432.79. In 2019, the total expenditure was €5 141 322.70. In 2020, costs decreased to €277 994.02. This reduction increased in the 2021–2026 period, with total costs going from €43 992.38 to €26 399.98. In 2027, the expenditure stabilised at €26 399.96 (online supplemental appendix E).

The HepC*link* scenario (with screening in the community)

In the HepC*link* scenario, 30 883 (69.8%) people were tested, of which 523 (1.7%) were HCV RNA positive. The liver fibrosis staging of the viraemia cases were: F0–F2 (72%), F3–F4 (27.6%) and patients with HCC (0.4%). During the period 2019–2028, costs with the

implementation of HepC*link* were €6 533 677.21. In 2019, the total expenditure was €5 935 160.30. In 2020, costs decreased to €327 456.92. This reduction increased in the 2021–2026 period, going from €51 819.86 to €31 097.28. In 2027, the expenditure stabilised at €31 097.25 (online supplemental appendix E).

Impact on HCV diagnosis

By implementing the HepC*link* programme, an additional 13 329 people (+75.93%) were tested for HCV, and 79 (+17.79%) new viraemic infections were diagnosed, avoiding 7 deaths and 6 liver cancer cases.

Budget impact

The budget impact of implementing HepC*link* in the 2019–2028 period was €884 244.42, as shown in online supplemental appendix E. Its distribution by items was as follows: €577 670.22 for setting up the structure of the HepC*link* programme; €658 209.45 for the initial administration of DAAs; €90 406.82 for following up the participants throughout the period; €33 535.65 for HepC*link* screening; and €666.23 for data collection support. The two items that reduce the budget gap are the costs of accessing primary care (–€469 625) and the diagnostic costs (–€6618.97).

Sensitivity analysis

The sensitivity analysis on the degree of participation showed that at the pessimistic level of 25%, the budget impact was €715 828. At an optimistic level of 75%, it increases to €1 052 556.40, and at the maximum of 100% achieves €1 210 756.72. Avoiding the genotyping test in the HepC*link* programme would reduce the budget impact down to €852 534.42 (–3.59%). If all the medical centres implemented integrated testing for HCV RNA and FIB-4 in a single step and excluded the genotyping, the budget impact would be reduced to €871 999.42 (–1.38%).

Alternative scenario

By implementing the HepC*link* programme in the three health areas with the highest numbers of Pakistani migrants, an additional 12 485 people (+71.12%) were tested for HCV, and 74 (+16.67%) new viraemic infections were diagnosed, avoiding 6 deaths and 5 liver cancer cases.

The budget impact of implementing HepC*link* in these three areas in the 2019–2028 period was €745 730.14, as shown in online supplemental appendix E.

DISCUSSION

In this study, we evaluated the budget impact of the implementation of an HCV test-and-treat community strategy targeting people from Pakistan living in Catalonia, Spain. The analysis has been raised from the perspective of the Catalan Department of Health (payer). Results revealed that the HepC*link* would allow increasing testing (+75.93%) and diagnostic rates (+17.8%), compared with the current standard practice of HCV care. However, the budget impact of implementing this community-based strategy in the whole Catalan territory is high (€884 244 in 10 years), mainly driven by the implementation costs during the first year. This budget impact could be reduced by €138 514 by focusing efforts on the three areas in Catalonia where Pakistani migrants reside predominantly which would slightly lower testing rates (+71.12% vs +75.93%) while providing similar diagnostic rates (+16.67% vs +17.8%).

Even though the community screening led to an increased diagnostic rate, the HCV RNA positivity found was lower than in the current standard of care (1.7% vs 2.5%). This might be explained by the fact that patients who visit the primary care are likely symptomatic and have a higher probability to be diagnosed with a viraemic infection. Comparable results were obtained in a similar study.[22] However, in the mentioned study, people from Pakistan were the most likely migrant group to be tested, which could reflect the enthusiasm of PCPs in sites with a high density of such patients. Unfortunately, this is not the case in the current standard of healthcare in Catalonia. Even if screening in primary care increases, the screening rates may not suffice to achieve elimination. Therefore, alternative strategies including community outreach will be needed to reach out to individuals who do not frequent the primary care, as reinforced by European Centre for Disease Prevention and Control (ECDC) guidelines.[1]

Identifying HCV-infected people in migrants originating from HCV-endemic countries without hurting sensibilities or commit inequities is a great challenge, but it is an achievable goal if this specific screening programmes are driven by the WHO recommendations of prioritising efforts in at-risk groups and combating stigma to ensure that all individuals have access to healthcare.[3] In this regard, previous work[23] suggested some considerations that can be very helpful for successful migrant screening: working with community-based organisations to overcome cultural or language barriers and guaranteeing voluntary and confidential participation not linked to immigration enforcement or employment opportunities. Also, the ECDC has developed a guidance in this sense, encouraging all EU/EEA member countries to offer screening to migrant populations from HCV-endemic countries and facilitating linkage to treatment and care. Reviewing the experiences from different countries, we can distinguish three approaches: (a) testing is offered to all migrants coming from HCV-endemic countries; (b) screening is recommended among all migrants from HCV-endemic countries and (c) testing is offered to those with risk factors, with no special targeting for immigrants from HCV-endemic countries.[24]

Evidence has indicated that screening migrants for viral hepatitis is likely to be clinically effective and cost-effective.[4 25–27] Such studies typically involve motivated clinicians and suggest that a large proportion of people will be tested and referred for therapy. However, a large-scale

trial that aimed to examine the frequency of screening in migrants by primary care practitioners who were encouraged to screen these migrants, either by providing these physicians with an educational programme (controls) or by incentivising the practitioners to screen for viral hepatitis by use of funding and support (intervention group), found that testing for viral hepatitis was less common than expected; few people were tested in control practices and incentivised general practitioners tested 19.5% of eligible patients, which was substantially lower than the testing projections used in previous models (which estimated that 40% of eligible patients would be tested).[22] On the other hand, bringing screening into the community improves the number of people who can be rapidly screened and linked to care.[28]

The cost dynamics observed throughout the 2019–2028 period are rational at all stages. In the first year, spending for HepC*link* is higher, because that is when the initial diagnosis and treatment of patients occur. In the subsequent years, cost decreases once patients respond to treatment and the majority are cured with some lost to death.

The budget impact of implementing HepC*link* in the whole territory during the 2019–2028 period is €884 244.42, which is well explained, as it implies putting in place a new structure that also increases costs to enable testing of larger populations and having more patients under costly treatments. The reduction in costs observed in primary care access makes sense and this is due to the fact that in the HepC*link* scenario, individuals who participate in the screening are approached in their communities.

The value that generates the greatest uncertainty is the assumption of 50% participation rate in the HepC*link* programme. The sensitivity analysis for different participation rates showed that at the pessimistic level of 25%, the budget impact is €715 828. At an optimistic level of 75%, it increases to €1 052 556.40, and at a maximum of 100%, it is €1 210 756.72. This trend reflects the increasing costs in the management of viraemic HCV infection. Participation is a key element to reaching efficiency in community programmes such as HepC*link* and, therefore, future studies should assess how to incentivise participation and explore if patients prefer primary care or community-based care as suggested in a previous study.[22]

The nature of the study has some limitations. First, in the context of the Department of Health (payer), we do not include indirect costs. Second, we have to take into consideration that there are individuals of this population in an irregular migration status who might not be covered by the healthcare database, but the use of SIDIAP as a source of information has the advantage of being more accurate than the official census of the foreign population. Third, there is the possibility that some participants in the HepC*link* programme who are seropositive will not agree for the DBS sample to be collected to confirm the diagnosis, and possibly attend the primary care throughout the year. However, that was the case of a very small proportion of participants (6.21%) and should not affect the conclusions of the study. Fourth, side-effects of DAA treatment have not been taken into account; while in practice, this could result in a higher cost of HCV treatment. Currently, side-effects are however infrequent and mild. Finally, the risk of reinfection and transmission is not covered in this study and the possibility of overlap between different HCV risk groups was disregarded. However, we expect that the probability of reinfection and transmission in this specific group is low. Individuals with hepatitis C in this group are assumed to have been infected mostly due to poor healthcare practices in their home country.[29] In general, HCV infection in this group is not caused by drug dependence or by sexual transmission among men who have sex with men.

The use of official data sources, having representative data from the majority of primary care centres, as well as the ability to validate the health itineraries with specialists well versed in daily practice, provide robustness in the analysis. The long time scope permits a realistic assessment of the economic impact of patients who require indefinite annual follow-up visits after cure.

Scaling up the HepC*link* strategy to the whole Catalan territory infers a high budget impact for the Department of Health and allows for increasing the diagnosis of viraemic cases (+17.8%) in the Pakistani population ≥18 years of age in Catalonia, avoiding seven deaths and six liver cancer cases. To achieve a sustainable elimination of HCV in this population by improving screening and treatment rates, there is room for improvement at two levels. First, reinforcing targeted screening in primary care, taking advantage of the fact that 68.08% of the Pakistani population had visited their PCPs (online supplemental appendix F). Second, at the community level, using the HepC*link* strategy to reach the individuals with reluctance to use the health system services. It would be imperative to explore the feasibility of this multilevel approach in future studies in Spain as a micro-elimination strategy.

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REFERENCES

1 ECDC. Prevention of hepatitis B and C in the EU/EEA and the UK. 2020. Available: https://ecdc.europa.eu/sites/default/files/documents/hepatitis-B-and-C-prevention_1.pdf [Accessed 06 Apr 2022].
2 Falade-Nwulia O, Suarez-Cuervo C, Nelson DR, *et al*. Oral direct-acting agent therapy for hepatitis C virus infection: a systematic review. *Ann Intern Med* 2017;166:637–48.
3 World Health Organization. *Global health sector strategy on viral hepatitis 2016-2021*. Global Hepatitis Programme Department of HIV/AIDS, 2016: 56.
4 Seedat F, Hargreaves S, Nellums LB, *et al*. How effective are approaches to migrant screening for infectious diseases in Europe? A systematic review. *Lancet Infect Dis* 2018;18:e259–71.
5 Falla AM, Ahmad AA, Duffell E, *et al*. Estimating the scale of chronic hepatitis C virus infection in the EU/EEA: a focus on migrants from anti-HCV endemic countries. *BMC Infect Dis* 2018;18:42.
6 Mason LM, Duffell E, Veldhuijzen IK, *et al*. Hepatitis B and C prevalence and incidence in key population groups with multiple risk factors in the EU/EEA: a systematic review. *Euro Surveill* 2019;24:1800614.
7 Lazarus JV, Bromberg DJ, del Amo J, *et al*. Hepatitis C prevalence among the migrant population in Spain: a systematic review and meta-analysis. *Enfermedades Infecciosas y Microbiología Clínica* 2019;37:222–30.
8 Bolíbar B, Fina Avilés F, Morros R, *et al*. SIDIAP database: electronic clinical records in primary care as a source of information for epidemiologic research. *Med Clin (Barc)* 2012;138:617–21.
9 Reyes-Urueña J, Celly A, Moreno S, *et al*. Hepatitis C virus: testing rate and attrition at linkage to specialized care, Catalonia, Spain 2011-2016. *J Viral Hepat* 2021;28:288–99.
10 Valerio L, Barro S, Pérez B, *et al*. Seroprevalencia de Marcadores de hepatitis Crónica Vírica en 791 Inmigrantes Recientes en Cataluña, España. *Recomendaciones de Cribado y de Vacunación Contra La Hepatitis B Revista Clínica Española* 2008;208:426–31.
11 Martró E, Ouaarab H, Saludes V, *et al*. Pilot hepatitis C micro-elimination strategy in Pakistani migrants in Catalonia through a community intervention. *Liver Int* 2022;42:1751–61.
12 IDESCAT. Població Pakistanesa per Municipis de Catalunya a 1 de Gener del 2019. Available: http://www.idescat.cat/poblacioestrangera/?nac=d426&b=6&t=2019 [Accessed 23 Jul 2020].
13 I Prat JG, Ouaarab H, Rafi T, *et al*. Hepatitis C micro-elimination pilot strategy in Pakistani migrants in catalonia through the implementation of a community intervention: interim results of the HEPC-link study. *J Hepatol* 2020;73:S340.
14 Husereau D, Drummond M, Augustovski F, *et al*. Consolidated health economic evaluation reporting standards (CHEERS) 2022 explanation and elaboration: a report of the ISPOR CHEERS II good practices task force. *Value Health* 2022;25:10–31.
15 Crespo J, Lázaro P, Blasco AJ, *et al*. Hepatitis C reflex testing in Spain in 2019: a story of success. *Enferm Infecc Microbiol Clin (Engl Ed)* 2021;39:119–26.
16 Hudson M, Sheron N, Rowe IA, *et al*. Should we screen for cirrhosis *BMJ* 2017;358:j3233.
17 Buti M, Domínguez-Hernández R, Casado MÁ, *et al*. Healthcare value of implementing hepatitis C screening in the adult general population in Spain. *PLoS ONE* 2018;13:e0208036.
18 Bil JP, Schrooders PAG, Prins M, *et al*. Screening and prevention of infectious diseases in newly arrived migrants. integrating hepatitis B, hepatitis C and HIV screening into tuberculosis entry screening for migrants in the Netherlands, 2013 to 2015. *Euro Surveill* 2018;23:17.
19 Ouaarab H. Cribratge de LES hepatitis Mitjançant El Joc HEPARJOC. Institut Català de la Salut; 2018.
20 Mahmud S, Al-Kanaani Z, Chemaitelly H, *et al*. Hepatitis C virus genotypes in the Middle East and North Africa: distribution, diversity, and patterns. *J Med Virol* 2018;90:131–41.
21 INE. Cálculo de Variaciones del Índice de Precios de Consumo. Instituto Nacional de Estadística; Available: https://www.ine.es/varipc/
22 Flanagan S, Kunkel J, Appleby V, *et al*. Case finding and therapy for chronic viral hepatitis in primary care (Hepfree): a cluster-randomised controlled trial. *Lancet Gastroenterol Hepatol* 2019;4:32–44.
23 Noori T, Hargreaves S, Greenaway C, *et al*. Strengthening screening for infectious diseases and vaccination among migrants in Europe: what is needed to close the implementation gaps? *Travel Med Infect Dis* 2021;39:101715.
24 ECDC. Public health guidance on screening and vaccination for infectious diseases in newly arrived migrants within the EU/EEA; 2018.
25 Suijkerbuijk AWM, van Hoek AJ, Koopsen J, *et al*. Cost-effectiveness of screening for chronic hepatitis B and C among migrant populations in a low endemic country. *PLOS ONE* 2018;13:e0207037.
26 Geue C, Wu O, Xin Y, *et al*. Cost-effectiveness of HBV and HCV screening strategies – A systematic review of existing modelling techniques. *PLOS ONE* 2015;10:e0145022.
27 Al Khayat M, Eijsink JFH, Postma MJ, *et al*. The cost-effectiveness of hepatitis C virus screening strategies among recently arrived migrants in the Netherlands. *Int J Environ Res Public Health* 2020;17:6091.
28 Rein DB, Lesesne SB, Smith BD, *et al*. Models of community-based hepatitis B surface antigen screening programs in the U.S. and their estimated outcomes and costs. *Public Health Rep* 2011;126:560–7.
29 Ayoub HH, Al Kanaani Z, Abu-Raddad LJ. Characterizing the temporal evolution of the hepatitis C virus epidemic in Pakistan. *J Viral Hepat* 2018;25:670–9.
30 TMB. Tarifes del Metro de Barcelona 2020. Transports Metropolitans de Barcelona. Available: https://www.tmb.cat/ca/tarifes-metro-bus-barcelona [Accessed 23 Jul 2020].
31 ViaMichelin. Rutas Y Mapas. 2020. Available: https://www.viamichelin.es/ [Accessed 23 Jul 2020].

32 ICS. Preus Públics dels Serveis Sanitaris de l'Institut Català de la Salut. DOGC núm. 8153, de 12.06.2020; 2020. 1–172.
33 OSSC. Central de Resultats Àmbit Sociosanitari. Observatori del Sistema de Salut de Catalunya. Departament de Salut. Generalitat de Catalunya; 2017.
34 ICS. Llibre de Retribucions del personal Estatutari [Institut Català de la Salut]. 2019. Available: http://ics.gencat.cat/web/.content/documents/transparencia/personal/2019-Taules-retributives-estatutaris-gener-juny.pdf