

**Title:** Improving the detection of infectious diseases in at-risk migrants with an innovative integrated multi-infection screening digital decision support tool (IS-MiHealth) in Primary care: a pilot cluster-randomized controlled trial

**Running title:** Personalized migrants' screening increases the detection of infections

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The results of this study have been submitted and accepted as an oral communication to the ECCMID conference 2021.

**Funding:** PERIS 2017 SLT002/16/0045, Catalanian government

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## Abstract

**Background:** There are major shortfalls in the identification and screening of at-risk migrant groups. This study aims to evaluate the effectiveness of a new digital tool (IS-MiHealth) integrated into the electronic patient record system of primary care centres in detecting prevalent migrant infections. IS-MiHealth provides targeted recommendations to health professionals for screening multiple infections, including HIV, hepatitis B and C, active tuberculosis, Chagas disease, strongyloidiasis, and schistosomiasis, based on patient characteristics (including variables of country of origin, age, sex).

**Methods:** A pragmatic pilot cluster-randomised controlled trial was deployed from March to December 2018. Eight primary care centres in Catalonia, Spain, were randomly allocated 1:1 to use of the digital tool for screening, or to routine care. The primary outcome was the monthly diagnostic yield of all aggregated infections. Intervention and control sites were compared before and after implementation with respect to their monthly diagnostic yield using regression models. This study is registered on ISRCTN (ISRCTN14795012).

**Results:** 15,780 migrants registered across the 8 centres had at least one visit during the intervention period (March to December 2018), of which 14,598 (92.51%) fulfilled the criteria to be screened for at least one infection. There were 210 (2.57%) individuals from the intervention group with new diagnoses compared with 113 (1.49%) from the control group (OR:2.08 95%CI 1.63-2.64,  $p<0.001$ ). The intervention centres raised their overall monthly diagnosis rate to 5.80 (95%CI 1.23-10.38,  $p=0.013$ ) extra diagnoses compared to the control centres. This monthly increase in diagnosis in intervention centres was also observed if we consider all cases together of HIV, hepatitis B and C, and active TB cases

(2.72,[95% CI 0.43-5.00]; p=0.02) and was observed as well for the parasitic infections' group (Chagas disease, strongyloidiasis, and schistosomiasis) 2.58 (95% CI 1.60-3.57; p<0.001).

**Conclusions:** The IS-MiHealth increased screening rate and diagnostic yield for key infections in migrants in a population-based primary care setting. Further testing and development of this new tool is warranted in larger trials and in other countries.

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## INTRODUCTION

Migration is a complex and growing global phenomenon of critical importance to European countries, particularly in recent years with unprecedented rises in migration flows to and within the EU/EEA.<sup>1,2</sup> Migrants face an increased burden of certain infections<sup>3</sup> including HIV, viral hepatitis and tuberculosis(TB)<sup>4</sup> compared to host population. Similarly, certain parasitic diseases not endemic in Europe are highly prevalent in migrant populations,<sup>5,6</sup> Strongyloidiasis despite being considered endemic in Spain in the past<sup>7</sup> it is much more prevalent in tropical and subtropical areas, particularly in those areas with poor hygienic conditions,<sup>8</sup> with migrant population prevalence is estimated above 12%.<sup>9</sup> Chagas diseases is only endemic in migrant populations<sup>10</sup> although at risk of community transmission in non-endemic areas.<sup>11</sup>

In addition, despite limiting data on the impact of COVID-19 on morbidity and mortality among migrant population, particularly those living in refugee camps, detention or reception centres may be at particularly high risk for COVID-19 exposure.<sup>12</sup>

Screening on arrival is almost non-existent and many countries historically have only focused on TB screening.<sup>13</sup> One study in Sweden reported that a TB screening programme targeting refugees only contributed to 15% of the total cases, suggesting that with this approach other migrant groups are missed, and they could be potentially targeted in other settings such as Primary Care.<sup>14</sup> In addition, moving from routine HIV testing from sexual health and antenatal clinics to non-traditional settings (e.g., Primary Care) to reduce the pool of undiagnosed HIV infection in the population is cost-effective.<sup>15</sup>

Innovative integrated programmes, to deliver more cost-effective screening to high-risk migrants on arrival are a key step to meet global and regional elimination targets for key infections.<sup>13</sup> The health professionals' lack of expertise, particularly primary care providers, in assessing

individual differences (gender, age, origin) of migrant related conditions often means that these infections go undetected. This contributes to worse health outcomes, widening health inequities, and could sustain disease transmission with a high cost for health systems.<sup>16,17</sup> Adopting multi-disease screening approach, is now considered a good strategy although its cost-effectiveness needs to be demonstrated in larger studies.<sup>18</sup> The ECDC published new guidance in 2018<sup>19</sup> calling for innovative strategies to deliver multi-disease screening to migrants. Data on cost-effectiveness are scarce and limited to single disease screening, but they suggest moderate to high cost-effectiveness of migrant screening programs depending on migrant group and disease targeted.<sup>20-24</sup>

With the aim of improving patient care by strengthening medical decisions, there has been a development of clinical decision support systems(CDSS) in the last decade.<sup>25</sup> In such tools, the characteristics of an individual extracted from structured or unstructured data or both, are matched to a computerized algorithm with patient-specific assessments.<sup>25</sup> The recommendations to the clinical staff to make a decision can manifest as computerized reminders, or clinical workflow tools. The decrease in test duplication at primary care supports the cost-effectiveness of implementing CDSS in screening.<sup>26,27</sup> Evidence on infections remains low, with some studies suggesting an increased screening of hepatitis C by 5 fold.<sup>28</sup> So far, no evidence on CDSS supporting the screening on migrant populations have been developed.

We developed an innovative digital tool (IS-MiHealth) integrated into the electronic patient record(EPR) system of primary care that provides targeted recommendations through computer prompts to health professionals on screening migrant population for multiple infections . IS-MiHealth was integrated in the EPR used in most primary care centres in Catalonia(eCAP). This pilot study aimed to evaluate the effectiveness

of the IS-MiHealth tool including the increasing detection rate, the screening rate performed as well as the feasibility and acceptability of the tool.

## **METHODS:**

### *Study design and setting*

A pragmatic pilot randomised cluster-controlled trial was implemented to assess the effectiveness of the digital tool IS-MiHealth conducted in eight primary care centres (PCC) randomized 1:1 located in four areas of Catalonia, Spain: Barcelona, Manresa, Lleida, and Tortosa from March to December 2018. All areas have a high migrant density accounting for 20% or more of the total population.<sup>29</sup>

### *Population*

Eligible participants were migrants aged >16 years old, (excluding foreign-born population from Western Europe, North America, Australia, or New Zealand) who attended a visit at a PCC during the intervention period (March to December 2018) for any reason and who accepted to be screened according to the criteria of health professionals. No exclusion criteria was set concerning the year of arrival to provide the screening recommendation except for TB where a limit for five years since arrival to the host country was established. This criterion was established due to all infections (except for TB) being chronic and also to the fact that for some of them, particularly HIV, the infection risk remains after the migration.<sup>30</sup>

Health professionals offered eligible patients to be tested according to an individual risk assessment that included the country of origin, sex, and age, irrespective of the reason for consultation as part of good clinical practice. In this regard and as part of the routine care standard procedures,

oral consent was provided by the patients who agreed to be screened. As per the consent of minors aged 17, adults responsible of the minor should consent as well in the visit any screening test conducted. The blood tests and referrals to any specialist were performed according to the standard procedures of each centre.

#### *Screening recommendations based on individual risk assessment*

To develop the screening recommendations, including the selection of the infections to be screened and the screening criteria for each infection, European screening guidelines for migrants were comprehensively reviewed. Thereafter, a consensus workshop was conducted with Infectious diseases experts, primary care physicians, and Public Health officers to develop a final screening algorithm with screening criteria for each condition that considered country of origin prevalence and incidence data. The screening algorithm included seven infections– HIV, hepatitis B and C, active TB, Chagas disease, strongyloidiasis and schistosomiasis - and has been published elsewhere.<sup>31</sup>

Briefly, HIV serological test was offered following ECDC recommendations to individuals >16 years coming from countries with a prevalence >1%;<sup>32</sup> active TB was screened through a chest radiography in migrants from countries with an incidence >50/100,000, as agreed in a consensus workshop and inspired by the pre-arrival TB screening programme reflected in the NICE guidelines (United Kingdom) and introducing a time-frame of 5 years since the arrival to the host country;<sup>33</sup> HBV (HBs Antigen and HBV IgG) and HCV IgG serological tests were offered (also following ECDC guidelines) to those individuals >16 years coming from countries with >2% prevalence.<sup>19</sup> *Strongyloidiasis* and *Schistosoma* serological tests were offered to those individuals >16 years coming from endemic areas, also defined in the ECDC guidelines.<sup>34</sup> A Chagas disease test was offered to individuals coming from the 17 endemic countries at all ages based on a previous cost-effectiveness study.<sup>20</sup>

Countries of origin were aggregated into areas of origin adapting the international classification of the United Nations Statistics Division<sup>35</sup> (supplementary file 1).

#### *Health centres selection and randomisation*

First, a comparative analysis of the health centres in the study areas was performed to select the pairs of PCC in each area with more similar characteristics, including for each centre: number of health professionals, migration density, and mean socio-economic index of the population attended<sup>36</sup> (supplementary file 2). Therefore, for each study area, two of the PCCs with more similar characteristic were selected, and the PCC were contacted (through their director) and invited to participate in the study. They were randomly assigned 1:1 in blocks using a matched pairs design with a statistical software to be an intervention or a control centre within each study area.

#### *The intervention procedure*

In the intervention centres the multi-disease screening programme was implemented using the IS-MiHealth tool. IS-MiHealth, set a series of logical rules that provide real-time prompts to health professionals on infectious diseases screening for migrants<sup>37</sup>. For conducting the individual risk assessment, the tool displays reminders based on three variables -sex, age, and country of origin- that are directly collected by the administrative staff of the health centres, and that are routinely registered in the electronic patient record(EPR) system of PCC included in the study (*Estació-Clinica d'Atenció Primària-eCAP*); therefore, when a migrant comes to the health centre for any reason, the health professional receives a pending task assignment with recommendation on the diseases that should be considered for screening based on this person's background characteristics (supplementary file 3). IS-MiHealth is also able to identify if a person had already a diagnosis of any of the conditions included in the algorithm

(based on ICD-10 code diagnosis) or if a diagnostic test had been performed for any condition included in the program. This includes ICD-10 codes registered and tests performed in other centres in Catalonia that use the same EPR (eCAP). In such cases, the automated electronic prompt does not appear for that condition (see explicative video at: <https://vimeo.com/368313593>).

Health professionals from the intervention centres received automated electronic prompts with recommendations for screening if the individual meets screening criteria for each condition, alongside holding a standard training session. In the control centres, health professionals followed the routine care although they received a training session before the intervention started, where the screening algorithm was presented, and it was available to them for consultation. They were informed about the study and that they would be compared with other centres where the screening decision making tool would be implemented. In both cases, health professionals were responsible for ordering a blood test or a chest radiography and to refer to the specialist if required.

#### *Training session*

Training sessions were targeted to centres' staff including nurses, medical doctors, and other technicians. The session covered background information on each infection, including epidemiology, diagnostic tools, available treatments, specific clinical aspects, or risk factors that may be of importance for some infections (e.g., immunosuppressant condition for Chagas disease or strongyloidiasis), screening recommendations and also the importance of the whole care pathway ensuring the access to any specialised care. A manual with the screening recommendation for each infection was provided to each centre.

#### *Study procedures*

Serological tests and chest radiography in the case of TB were performed following the same procedures in all centres to screen each disease. The serological test for HIV and viral hepatitis were performed according to each centre referral laboratory. The *Strongyloides* serology was an ELISA test, (Kit based on IVD *Strongyloides stercoralis* crude antigen, SCIMEDX, Dover, NJ, USA) and *Schistosoma* tests was an indirect hemagglutination test -Schistosomiasis Fumouze). Laboratory diagnosis of *T. cruzi* infection was established by two serological ELISA tests, following international recommendations. One was a commercial ELISA with recombinant antigens (BioELISA Chagas, Biokit S.A., Barcelona, Spain), and the other was an in-house ELISA with whole *T. cruzi* epimastigotes antigen. Diagnosis of *T. cruzi* infection was defined by positivity in the two serological tests. All serological tests were available at PCC except the serology of strongyloidiasis and schistosomiasis that were not available in both intervention and control Tortosa centres. In case of a confirmed diagnosis, the individual was referred to the required specialist as appropriate for receiving specific treatment.

#### *Data*

Routine health data were extracted from the SIDIAP (*Sistema d'Informació per al Desenvolupament de la Investigació en Atenció-Primària*) database containing anonymized data. All data points in the control and intervention groups were obtained, with baseline data from the six years before the screening program implementation (January-2012) until the end of the intervention period (December-2018) of the migrant individuals attended in any of the eight centres including only structured variables routinely collected in the EPR. Data on diagnostics were extracted, including chest x-rays and serologies performed and test results performed for HIV, HBV, and HCV, Chagas disease, strongyloidiasis, schistosomiasis in 2018 and the diagnosis of each disease from 2012 to 2018 based on ICD-10 codes registered by health

professionals. The additional information extracted was socio-demographic characteristics including age, sex, country of origin, entry and exit date to the PCCs, whether the patient fulfilled or not the screened criteria, number, and dates of visits to each centre from 2012 to 2018. Additionally, other data were extracted such as any immunosuppressant treatment or any ICD-10 code on cancer or autoimmune disease in 2018.

### *Data analysis*

Summary statistics were presented as frequencies for categorical variables and as means (with standard deviations) for normally distributed continuous variables or medians (with IQR-Interquartile range) for non-normally distributed continuous variables. Associations were tested with Fisher-Exact tests for categorical variables and odds ratios were computed. Mixed-effects logistic regression models were used to identify associations between the screening rate performed and socio-demographic, and other health conditions, using area as a random intercept. The significance level was established at the 5% level. Sample size and statistical power was contingent on the budget to design and implement the pilot intervention. Assuming 2,000 subjects per cluster, with 4 sites in intervention and 4 control sites, 75 monthly periods before and 9 post intervention, and effect size of 1.5 standard deviations could be detected under a 5% significance level with 59% statistical power.

The primary outcome measure was the monthly diagnostic yield of all aggregated imported conditions included in the study and all aggregated low-endemic conditions. Secondary outcomes were the aggregated monthly diagnostic yield of TB, HIV, HCV, HVB, Chagas disease, strongyloidiasis and schistosomiasis, the screening proportion for each condition and to evaluate factors associated with having a higher screening rate, such as sex, age, immunosuppression status, being attended in an intervention centre, fulfilling the screening criteria, or coming from specific geographic areas. To analyse the intervention effect on the outcomes, a difference-in-differences approach was performed using a



generalized linear model. Intervention units were compared before and after implementation with respect to the average diagnostic rate of 2012-2018. Sandwich-robust standard errors were clustered at the intervention-level.

All data analyses were performed R-3.6.3 for the primary outcome. Packages described in the supplementary file 4. Stata 16 (Stata-Corp-LP,USA) was used for secondary outcomes. The study was reported by using the CONSORT –extension checklist for cluster trials(supplementary file 5).

### *Ethics and Registration*

This study was approved on 16/12/2016 by the Ethics committee of Hospital-Clínic, Barcelona(HCB/2016/0858) and IDIAPJGoL (IDIAP: 4R17/066) . The study protocol was registered in the ISRCTN platform, ISRCTN14795012.

## **RESULTS**

The eight PCCs in Catalonia had a reference population ranging from 16,122 to 30,831 people, of which 13,574 to 20,882 attended at least one visit during the intervention period. The total number of migrants with any record registered in the eight PCCs was 28,179, varying between centres from 2,070 to 6,188. A total of 15,780 (56.0%) individuals attended any of the eight centres in 2018 at least once (Figure 1). Lastly, the number of health professionals working in each PCCs ranged from 17 to 40. The main characteristics of the PCCs by study area are summarised in the supplementary file 6. The main characteristics of the migrant population by the PCC and by study area are summarised in Table 1.

A total 14,598 (92.5%) of the total migrant population of the eight PCCs fulfilled the criteria to be screened for at least one condition according to the country of origin, sex, and age. Table 1 shows the percentage of individuals that fulfilled the screening criteria for each condition according to epidemiological background by study area and in both intervention and control PCCs. There were no differences in the percentage of people with criteria to be screened for any infection in the intervention PCCs compared with the control sites in three of the study areas (Table1); and in one area (Barcelona), a higher percentage of people with screening criteria for any infection was found in the intervention centre (table 1). Concerning parasitic infections, no differences were observed in two areas, a higher percentage of people fulfilling the screening criteria were observed in the control centre, and the other study area a higher percentage of people with screening criteria was observed in the intervention area.

#### *Diagnostic yield*

During the intervention period, there were a total of 210(2.6%) diagnoses (3 HIV, 148 hepatitis B, 7 hepatitis C, 4 active TB, 55 strongyloidiasis, 2 schistosomiasis and 3 Chagas disease cases), in the intervention centres compared with 113 (1.5%) diagnoses in the control centres (9 HIV, 96 hepatitis B, 5 hepatitis C, 6 active TB, 2 strongyloidiasis, 1 schistosomiasis and 1 Chagas diseases cases), Resulting in a relative increased yield measured as odds ratio of 2.1 95%CI (1.6-2.6,p<0.001). The monthly diagnostic yields are presented in Figure 2. The figure presents the locally smoothed trends of the intervention and control centres in diagnoses during the post intervention period and up to 6 years prior to implementation. Before implementation, there were no significant differences in monthly diagnostic rate between intervention and control PCCs in the reference period(2012-2014) compared with the period 2014-2016 (p=0.493) and the period 2016-2018, (p=0.921). After implementation,

the intervention centres raised their overall monthly diagnostic rate to 5.8 (95%CI 1.2-10.4;  $p=0.013$ ) extra diagnoses compared to the control group. This monthly increase in diagnosis in intervention sites was also observed if we consider all cases together of HIV, hepatitis B and C, and active TB cases (2.7, [95%CI 0.4-5.0];  $p=0.02$ ) and was observed as well for the parasitic infections' group (Chagas diseases, strongyloidiasis, and schistosomiasis) 2.6 (95%CI 1.6-3.6;  $p<0.001$ ). Supplementary file 8 displays the estimates alongside their uncertainty intervals.

*Secondary outcome: screening performance.*

The total screening tests performed across centres for each disease and the screening performance among those fulfilling the screening criteria are summarised in Table 2. The proportion of screening number for all diseases was significantly higher in the intervention vs control centres for all conditions. Among those who fulfilled the screening criteria, 201/1,373(14.6%) were screened for HIV in the intervention centres compared with 84/948(8.9%) in the control centres (HIV OR 1.6 [95%CI 1.2-2.1];  $p=0.002$ ); for hepatitis B, 406/3,445(11.8%) were screened in the intervention centres vs 256/2,784 (9.2%)(HBV OR 1.3 [95%CI 1.1-1.5];  $p=0.005$ ); for HCV, 413/3,299 (12.5%) in the intervention centres vs 236/2,644 (8.9%) in the control centres (HCV OR 1.4 [95%CI 1.2-1.7];  $p<0.001$ ); for TB, 59/1168(5.1%) individuals were screened in the intervention centres vs 41/1,215(3.4%) (TB OR 1.6 [95%CI 1.1-2.4],  $p=0.027$ ). The screening performance among those who fulfilled screening criteria for Chagas disease was 95/1,454 (6.5%) in the intervention centre compared with 20/1,663 (1.2%) individuals in the control centres (OR 5.3 [95%CI 3.2-8.7];  $p<0.001$ ); for strongyloidiasis 373/5,878 (6.4%) individuals were screened in the intervention centres compared with 28/4,635 (0.6%) in the control centres, (OR 11.2, [95%CI 7.6-16.4];  $p<0.001$ ) and for schistosomiasis, 82/1,084 (7.6%) were screened in the

intervention centres compared with 1/685(0.2%) in the control centres (OR 59.6, [95%CI 8.3-431.4];  $p<0.001$ ). Further details of the screening performance by study area is provided in Supplementary file 7.

In the mixed effect adjusted logistic regression model for evaluating factors associated with the screening performed for any infectious diseases, patients that attended an intervention centre were 1.4 (95%CI 1.2-1.5;  $p<0.001$ ) times more likely to have a screening test performed than those who attended the control centres. Females (OR 1.2, [95%CI 1.1-1.3],  $p<0.001$ ), individuals with a known immunosuppressed status (1.5, [95%CI 1.3-1.7],  $p<0.001$ ), and individuals with an Asian origin (OR 1.2, [95%CI 1.0-1.5];  $p=0.035$ ) were more likely to be tested (table 3A).

When the screening performance of the parasitic infections (Chagas diseases, strongyloidiasis and schistosomiasis) was exclusively evaluated, an association was found with the intervention (OR 7.5, [95%CI 5.6-10.2];  $p<0.001$ ), with having fulfilled the screening criteria (OR 5.9, [95%CI 2.7-12.9];  $p<0.001$ ), with an immunosuppressed status (1.5, 1.2-1.9,  $p<0.001$ ) and with an American (OR 1.6, [95%CI 1.2-2.2];  $p=0.001$ ) and an Asian (OR 1.8 [95%CI 1.2-2.7];  $p=0.004$ ) origin.(table 3B)

## DISCUSSION

Our study suggests an increased screening, detection, and diagnostic yield for all infections in intervention centres where the IS-MiHealth tool was implemented. In particular, the detection rate was increased for the parasitic infections (Chagas diseases, strongyloidiasis, and schistosomiasis). The total detection yield was much higher in the intervention group particularly for strongyloidiasis and for hepatitis B and this may be attributed to a better screening performance together with a higher number of individuals with screening criteria in both intervention and control centres for these infections, being more than 10,000 for strongyloidiasis and more than 6,000 for hepatitis B. However, the detection

yield was higher in control group for HIV and TB. The low numbers from this pilot study prevented to have conclusive results about the detection yield differences for each infection. We also found a higher screening proportion for all the conditions, and for the parasitic infections the likelihood of being tested was more than seven times higher in the intervention centres using the tool compared with the control centres. Therefore, our data shows that the implementation of our digital tool appears to modify the clinician behaviour with regards to routinely screening for infections in migrant populations and that guidelines or education alone are insufficient to influence practice. Besides fulfilling the screening criteria, other factors such as a patient immunosuppression have been also independently associated with a higher testing rate, suggesting that health professionals modify their diagnostic workup among this high-risk population.

In recent years, there has been a call for clear guidance on screening and vaccination of migrant populations.<sup>19</sup> It has been acknowledged that innovative and tested interventions should be designed and implemented with multi-disease screening approaches, and that primary care may be the best approach to ensure high uptake to screening.<sup>38</sup> There have been multiple studies aimed to screen infections in the migrant populations.<sup>39,40</sup> However, these screening programs are not based on an individual risk assessment of the cut-off prevalence of the infection in the country of origin as our program has established,<sup>31</sup> only few of them are at primary care settings and they usually only include HIV, viral hepatitis, and TB.<sup>39</sup> Furthermore, formal screening of new-arriving migrants in special clinics may miss many migrant groups compared to primary care where screening can be routinely delivered.<sup>41</sup>

This study represents the first attempt to test an innovative CDSS that delivers and integrates a multi-infections screening program for migrants at PCC. The integration of the digital tool in the routine health information system and the individual risk-based assessment, provides the

clinician with targeted and tailored screening option, individualised to the patients' risk factors. All of this, alongside to the fact of including infections that have evidence-based report a clear benefit to be screened for,<sup>19,20</sup> and the fact of being a multi-disease approach, may reduce the cost impact on health system.<sup>42</sup> Although there exist other screening tools for migrant, they usually target other topics such as mental health and they are not integrated in the EPR.<sup>43</sup>

The IS-MiHealth tool is low cost to run (estimated around 10,000€ including its maintenance for 5 years in one EPR system) but further cost-effectiveness and cost-analysis are now warranted and will be a focus of the next stage of this research. Studies demonstrating the cost-effectiveness of targeting migrant population in screening programmes at primary care, have been performed for single diseases, including TB,<sup>24</sup> HIV,<sup>15</sup> viral hepatitis,<sup>44</sup> strongyloidiasis<sup>45</sup> and Chagas disease.<sup>20</sup> However, there is a lack of data on cost-effectiveness of multiple infections. Preliminary results of the qualitative assessment of IS-MiHealth show that the prompts helped the general practitioners to perform screening, especially in imported diseases that are unfamiliar to health professionals, highlighting the importance of continuous training in primary care. Further comprehensive and robust methodological feasibility studies should properly explore behavioural patterns in primary care doctors to improve the intervention's effectiveness. In addition, IS-MiHealth should be tested and assessed its feasibility in other European regions, what implies its integration in other EPR systems to assess the external validity of the results. Furthermore, other conditions that highly affects migrants, such as latent TB, vaccination uptake, female genital mutilation, or mental health among others, could also be included into the screening recommendations. Finally, the findings from this study could be used to advocate for the integration of the screening program into the national health systems of other countries that experience high migration influxes. Although we could not analyse data on treatments and

follow-up, since these objectives were beyond our study, we guaranteed the access to the whole care pathway to all individuals that were tested in our study; and this is an essential component that should be considered when implementing this kind of programmes.

### *Strengths and limitations*

The main strength of this study design lies with the randomization of the algorithm implementation, its integration in the EPR system based on key structured variables routinely collected; also, the data extraction from the EPR system avoided the use of questionnaires for data collection purposes. Moreover, our study design allows to visually inspect the trends in outcomes of the intervention and control centres up to 6 years before implementation, providing further suggestive evidence that the estimated increase was caused by the program introduction.

This study is not without limitations. First, the date of arrival to the country was not collected in the e-CAP system, thus not providing adequate information to fulfil the active TB screening criteria based on the IS-MiHealth recommendations (to screen migrants that arrived in the country within the last five years). Second, a technical limitation was regarding the missing values of key variables such as the country of origin for some migrant individuals although this percentage was estimated to be below 5%. In this regard, the registry of these variables among the administrative staff who collect the demographic data in the EPR system should be advocated and guaranteed. The retrospective data collection may have led to inaccuracies or measurement error even if these were independent of the random assignment. For example, we could not verify the reason for being tested in both intervention and control centres and some patients may have been tested for reasons beyond the screening purpose. Our results are underpowered and do not imply the validity of the tool outside of the Spanish setting. Finally, the screening algorithm

was developed considering the country prevalence for each infection, but it could be further improved in subsequent iterations by including migrant data-driven approaches

## **CONCLUSIONS**

This study provides suggestive evidence for the increased detection of infectious diseases in migrant populations, and in particular, for imported disease, following the implementation of a novel digital tool in primary care. Our results support integrated multi-disease screening programmes based on an individual risk assessment. Further studies should aim at validating the tool at a larger scale and assess its feasibility and efficiency as a previous step in the implementation of routine care.

## **CONTRIBUTIONS**

ARM and ES applied for funding acquisition, did the study design, literature search, coordinated the recruitment, data analysis, development of the software and drafted the manuscript; AnC supported the literature review, data analysis, did the tables and drafted the manuscript; XdL, CJA and AQG coordinated the training to the PCCs and the recruitment, supported the data analysis and were in charge of the project administration; MSB and AC, contributed to the study design, data analysis, did the figures and drafting the manuscript; LCV, MMG, ERM, NSB, SSD, RDL, CAM, coordinated the recruitment in their respective centres and supported the data interpretation and validation, SH contributed to the data analysis, data interpretation and drafting the manuscript. All authors contributed to the review, editing, final drafting and commenting on the manuscript.



## **CONFLICTS OF INTEREST**

All authors declare no competing interest.

## **FUNDING**

The work was supported by the Catalanian government [PERIS 2017 SLT002/16/0045]

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the manuscript.

## **ACKNOWLEDGEMENTS.**

We thank to Manuel Medina and Francesc Fina from SISAP (Sistema d'Informació dels Serveis d'Atenció Primària) and Eduardo Hermosilla from SIDIAP for collaboration in the development of the IS-MiHealth tool.

The ISGlobal team is partially supported by the Agència de Gestió d'Ajuts Universitaris i de Recerca (AGAUR) (2014SGR26) and by the Tropical Disease Cooperative Research Network (RICET) (RD12/0018/0010). SH is funded by the Academy of Medical Sciences (SBF005\1111) and the NIHR (NIHR Advanced Fellowship NIHR300072),

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## LIST OF TABLES AND FIGURES

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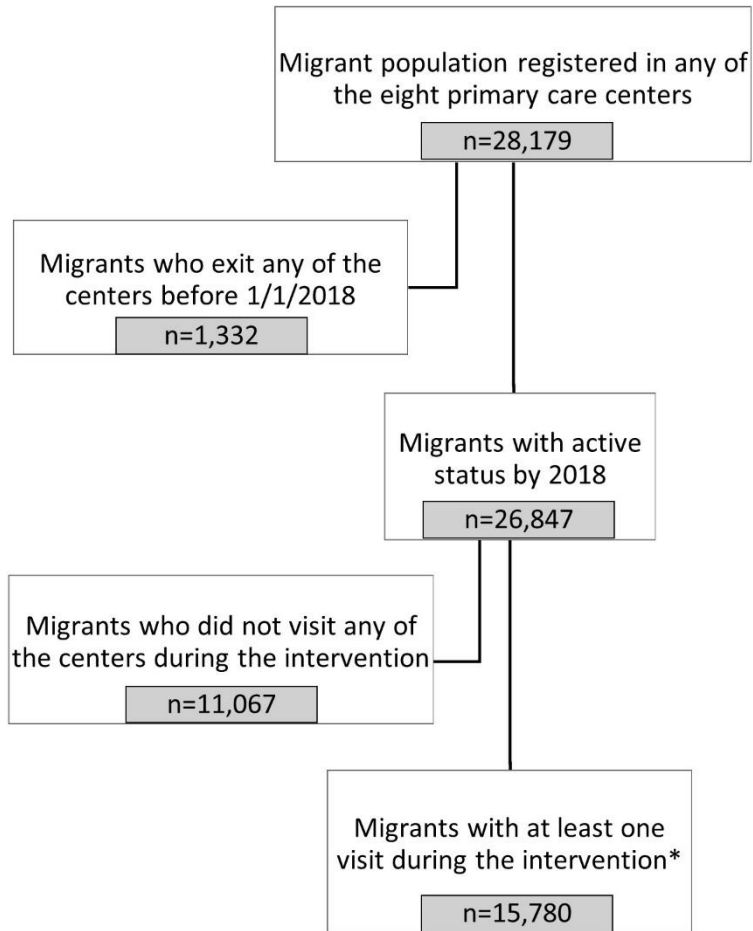


Figure 1. Flow chart of the study population.

Legend figure 1. \*=study population

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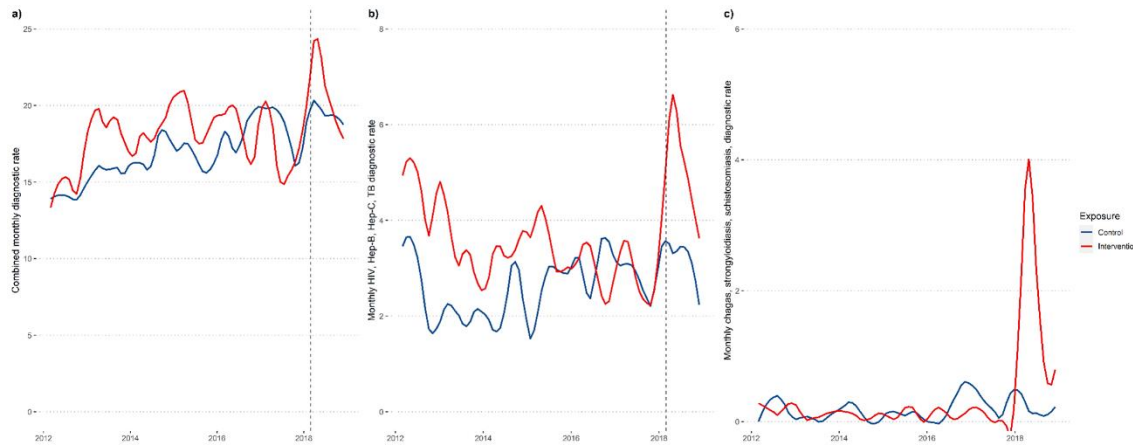


Figure 2. Monthly diagnostic rates of the intervention and control PCC, before and after implementation, March 2018.

Legend Figure 2: Monthly diagnostic rate local regression lines (LOESS) of outcomes intervention (red) and control (blue) centres.

Abbreviations: HIV: human immunodeficiency virus, Hep-B: hepatitis B virus, Hep-C: hepatitis C virus, TB: tuberculosis, 95%CI: 95% confidence interval

Table 1. Socio-demographic characteristic of the migrant population attended in the Primary Care Centres included in the study.

	Barcelona			Manresa			Lleida			Tortosa			Total		
	Control n (%)	Intervention n (%)	p- value	Control n (%)	Intervention n (%)	p- value	Control n (%)	Intervention n (%)	p- value	Control n (%)	Intervention n (%)	p- value	Control n (%)	Intervention n (%)	p- value
Total targeted population	2,343	1,161		1,423	1,864		1,929	3,410		1,914	1,736		7,609	8,171	
Immunosuppression status in 2018	256 (10.9)	117 (10.1)	0.443	251 (17.6)	300 (16.1)	0.240	295 (15.3)	578 (17.0)	0.116	393 (20.5)	280 (16.1)	0.001	1,195 (15.7)	1,275 (15.6)	0.861
<b>Region of origin</b>															
Southern Europe	535 (22.8)	203 (17.5)	<0.001	21 (1.5)	45 (2.4)	0.005	57 (3.0)	92 (2.7)	<0.001	24 (1.25)	32 (1.8)	<0.001	637 (8.4)	372 (4.6)	<0.001
Central and Eastern Europe	188 (8.0)	77 (6.6)		237 (16.7)	302 (16.2)		500 (25.9)	818 (24.0)		428 (22.4)	421 (24.3)		1,353 (17.8)	1,618 (19.8)	
Northern Europe		66 (5.7)			33 (1.8)			17 (0.5)			95 (5.5)				
Anglo-Saxon	262 (11.2)	9 (0.8)		24 (1.7)	0 (0)		15 (0.78)	0 (0)		80 (4.2)	0 (0)		381 (5.0)	211 (2.6)	
America		518 (44.6)		0 (0.00)	459 (24.6)		504 (14.8)	504 (14.8)		0 (0)	183 (10.5)		38 (0.5)	9 (0.1)	
Latin-America and the Caribbean	38 (1.6)			280 (19.7)	807 (43.3)		355 (18.4)	979 (28.7)		303 (15.8)	755 (43.5)		1,819 (23.9)	1,664 (20.4)	
Northern Africa	881 (37.6)	89 (7.7)			168 (9.0)			871 (25.5)			57 (3.3)				
Sub Saharan Africa		59 (5.1)		662 (46.5)	50 (2.7)			129 (3.8)		684 (35.7)	193 (11.1)		1,957 (25.7)	2,630 (32.2)	
Middle East (Asia)	60 (2.6)	128 (11.0)		146 (10.3)	0 (0)		551 (28.6)	0 (0)		115 (6.0)	0 (0)		681 (9.0)	1,108 (13.6)	
Eastern Asia	16 (0.7)	0 (0)			0 (0)		404 (20.9)			280 (14.6)			455 (6.0)	431 (5.3)	
Oceania	75 (3.2)			53 (3.7)			47 (2.4)			0 (0)			286 (3.8)	128 (1.6)	
	286 (12.2)			0 (0)			0 (0)			0 (0)			2 (0.03)	0 (0)	
	2 (0.1)			0 (0)			0 (0)			0 (0)			0 (0)		
Sex (female)	1,454 (62.1)	679 (58.48)	0.041	782 (55.0)	1,038 (55.7)	0.676	984 (51.0)	1,542 (45.2)	<0.001	959 (50.1)	827 (47.6)	0.137	4,179 (54.9)	4,086 (50.0)	<0.001
Age in years (mean, SD)	38.4 (13.0)	38.3 (12.4)	0.733	38.87 (13.3)	38.39 (12.9)	0.299	39.04 (12.2)	40.47 (12.1)	<0.001	39.89 (13.7)	39.89 (13.9)	0.990	39.03 (13.0)	39.56 (12.8)	0.010
<b>Screening criteria</b>															
Screening criteria – Chagas	813 (34.7)	475 (40.9)	<0.001	239 (16.8)	401 (21.5)	0.001	326 (16.9)	413 (12.1)	<0.001	285 (14.9)	165 (9.5)	<0.001	1,663 (21.9)	1,454 (17.8)	<0.001
Screening criteria - Strongyloidiasis	1,449 (61.8)	865 (74.5)	<0.001	1,346 (94.6)	1,752 (94.0)	0.466	1,840 (95.4)	3,261 (95.6)	0.678	1,764 (92.2)	1,562 (90.0)	0.020	6,399 (84.1)	7,440 (91.1)	<0.001
Screening criteria - Schistosomiasis	124 (5.3)	31 (2.7)	<0.001	146 (10.3)	170 (9.1)	0.272	415 (21.5)	883 (25.9)	<0.001	118 (6.2)	55 (3.2)	<0.001	803 (10.6)	1,139 (13.9)	<0.001
<b>Screening criteria of any imported disease</b>	1,457 (62.2)	869 (74.9)	<0.001	1,347 (94.7)	1,756 (94.2)	0.575	1,840 (95.4)	3,261 (95.6)	0.678	1,766 (92.3)	1,562 (90.0)	0.015	6,410 (84.2)	7,448 (91.2)	<0.001
Screening criteria - HIV	110 (4.7)	56 (4.8)	0.886	192 (13.5)	220 (11.8)	0.147	422 (21.9)	956 (28.0)	<0.001	224 (11.7)	141 (8.1)	0.001	948 (12.5)	1,373 (16.8)	<0.001

Screening criteria - HBV	628 (26.8)	351 (30.2)	0.033	405 (28.5)	549 (29.5)	0.535	956 (45.6)	1,879 (55.1)	<0.001	795 (41.5)	666 (38.4)	0.051	2,784 (36.6)	3,445 (42.2)	<0.001
Screening criteria - HCV	527 (22.5)	262 (22.6)	0.961	384 (27.0)	499 (26.8)	0.890	942 (48.8)	1,882 (55.2)	<0.001	791 (41.3)	656 (37.8)	0.029	2,644 (34.8)	3,299 (40.4)	<0.001
Screening criteria - TB*	687 (29.3)	443 (38.2)	<0.001	166 (11.7)	182 (9.8)	0.079	206 (10.7)	428 (12.6)	0.042	156 (8.2)	115 (6.6)	0.079	1,215 (16.0)	1,168 (14.3)	0.003
<b>Screening criteria of any infection</b>	1,814 (77.4)	1,021 (87.9)	<0.001	1,371 (96.4)	1,805 (96.8)	0.442	1,867 (96.8)	3,316 (97.2)	0.340	1,799 (94.0)	1,605 (92.4)	0.064	6,851 (90.0)	7,747 (94.8)	<0.001

I=intervention; C= control; m=mean; SD=standard deviation; TB: TB screening criteria included only those that were entered the system more than 5 years ago.

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**Table 2. Screening tests performed for infectious diseases included in the screening program among those who attended the PCC during the intervention.**

	Control	Intervention	OR (95% CI)	p-value <sup>2</sup>
Total population	7,609	8,171		
Number of <i>T. cruzi</i> disease screening tests	24 (0.3)	102 (1.3)	4.14 (2.63-6.52)	<0.001
Screening number among those with screening criteria	20/1663 (1.2)	95/1454 (6.5)	5.26 (3.20-8.65)	<0.001
Number of <i>Strongyloides</i> screening tests	32/5695 <sup>1</sup> (0.6)	375/6435 <sup>1</sup> (5.8)	10.92 <sup>1</sup> (7.58-15.74)	<0.001
Screening number among those with screening criteria	28/4635 <sup>1</sup> (0.6)	373/5878 <sup>1</sup> (6.4)	11.15 <sup>1</sup> (7.58-16.40)	<0.001
Number of <i>Schistosoma</i> screening tests	2/5695 <sup>1</sup> (0.04)	100/6435 <sup>1</sup> (1.6)	39.34 <sup>1</sup> (9.64-160.50)	<0.001
Screening number among those with screening criteria	1/685 <sup>1</sup> (0.2)	82/1084 <sup>1</sup> (7.6)	59.64 <sup>1</sup> (8.25-431.36)	<0.001
<b>Total screening number of any parasitic infection</b>	49/5695 <sup>1</sup> (0.9)	407/6435 <sup>1</sup> (6.3)	7.78 <sup>1</sup> (5.77-10.49)	<0.001
<b>Screening number among those with screening criteria</b>	44/4644 <sup>1</sup> (1.0)	405/5886 <sup>1</sup> (6.9)	7.73 <sup>1</sup> (5.65-10.57)	<0.001
Number of HIV screening tests	403 (5.3)	726 (8.9)	1.40 (1.23-1.60)	<0.001
Screening number among those with screening criteria	84/948 (8.9)	201/1373 (14.6)	1.56 (1.18-2.06)	0.002
Number of HBV screening tests	639 (8.4)	827 (10.1)	1.16 (1.04-1.30)	0.009
Screening number among those with screening criteria	256/2784 (9.2)	406/3445 (11.8)	1.27 (1.07-1.51)	0.005
Number of HCV screening tests	628 (8.3)	790 (9.7)	1.13 (1.01-1.26)	0.038
Screening number among those with screening criteria	236/2644 (8.9)	413/3299 (12.5)	1.39 (1.17-1.65)	<0.001
Number of active TB screening tests	221 (2.9)	376 (4.6)	1.56 (1.31-1.85)	<0.001
Screening number among those with screening criteria	41/1215 (3.4)	59/1168 (5.1)	1.60 (1.06-2.42)	0.027
<b>Number of screening tests for any condition</b>	984/7609 (12.9)	1411/8171 (17.3)	1.34 (1.22-1.46)	<0.001
<b>Screening number among those with screening criteria</b>	885/6851 (12.9)	1359/7747 (17.5)	1.36 (1.24-1.50)	<0.001

1. The Tortosa region is excluded. 2. Multilevel mixed-effect logistic regression

**Table 3. Factors associated with being screened for any infectious diseases (3A) and for parasitic infections (Chagas disease, strongyloidiasis, schistosomiasis (3B))**

3A

	Crude OR (95% CI)	p-value	Adjusted OR (95% CI) <sup>1</sup>	p-value
<b>Screening criteria</b>	1.16 (0.96-1.38)	0.120	1.07 (0.88-1.31)	0.494
<b>Group Intervention</b>	1.34 (1.22-1.46)	<0.001	<b>1.35 (1.23-1.48)</b>	<b>&lt;0.001</b>
<b>Age</b>	1.00 (0.99-1.00)	0.042	1.00 (0.99 -1.00)	0.007
<b>Sex (female)</b>	1.21 (1.10-1.32)	<0.001	<b>1.22 (1.11-1.33)</b>	<b>&lt;0.001</b>
<b>Continent<sup>2</sup> (origin)</b>				
Europe	Base		Base	
America	1.03 (0.91-1.17)	0.655	0.98 (0.86-1.13)	0.835
Africa	1.06 (0.95-1.18)	0.312	1.04 (0.93-1.18)	0.437
Asia	1.22 (1.03-1.46)	0.023	<b>1.22 (1.01-1.46)</b>	<b>0.035</b>
Oceania	6.24 (0.39-100.14)	0.196	5.76 (0.35-94.61)	0.219
<b>Immunosuppressed status in 2018</b>	1.46 (1.31-1.63)	<0.001	<b>1.47 (1.32-1.65)</b>	<b>&lt;0.001</b>

1.Mixed effect logistic regression model 2. European countries exclude Spain;

3B

	Crude OR (95% CI)	p-value	Adjusted OR (95% CI) <sup>1</sup>	p-value
<b>Screening criteria</b>	17.13 (4.24-69.12)	<0.001	<b>5.92 (2.72-12.88)</b>	<b>&lt;0.001</b>
<b>Group Intervention</b>	7.78 (5.77-10.49)	<0.001	<b>7.51 (5.56-10.15)</b>	<b>&lt;0.001</b>
<b>Age</b>	1.01(1.00-1.02)	0.005	1.01 (1.00-1.02)	0.012
<b>Sex (female)</b>	1.14 (0.94--1.38)	0.183	1.18 (0.97-1.44)	0.098
<b>Continent<sup>2</sup> (origin)</b>				
Europe	Base		Base	
America	2.50 (1.88-3.31)	<0.001	<b>1.61 (1.20-2.16)</b>	<b>0.001</b>
Africa	1.55 (1.18-2.04)	0.002	1.10 (0.83-1.46)	0.393
Asia	2.70 (1.80-4.02)	<0.001	<b>1.77 (1.18-2.66)</b>	<b>0.004</b>
Oceania	Empty	---	Empty	---
<b>Immunosuppressed status in 2018</b>	1.59 (1.26-2.00)	<0.001	<b>1.53 (1.22-1.94)</b>	<b>&lt;0.001</b>

The Tortosa area is excluded in this analysis. 1.Mixed effect logistic regression model 2. European countries exclude Spain;