Research protocol title: Delivering an Innovative Multi-disease Screening and Vaccination Tool to High-risk Migrant Populations (IS-MiHealth)

Promoter: Barcelona Institute for Global Health (ISGlobal)

Principal investigator: Ana Requena Méndez

Address: Carrer Roselló 132, 4 08035, Barcelona

Co-Investigators: Angeline Cruz
Stella Evangelidou
Ethel Sequeira
Alessandra Queiroga
Ermengol Coma
Carina Aguilar
Laura Medina
Angela Martinez
Elisabet Ferrer
Joaquín Salas
José Vázquez
Nicolás Piqueras
María Pilar Luzón
María del Pilar Requena
Silvia Vallejo
Marta Vázquez
Constanza Jacques Avino

Setting: Primary care centres in Catalonia and Andalusia

Version: 2.0

Date: June 7, 2022

RESEARCH PROTOCOL

1. JUSTIFICATION

Migration is a significant, **complex, and growing global phenomenon** of critical importance to European countries[1]. Having good health is key for a smooth and prompt integration process into the host community[2]. However, heterogeneous socio-economic, cultural, and legal factors across European countries affect migrants' physical and psychological health and determine the availability, accessibility, acceptability, and quality of services in the new host environment[3]. **Unprecedented rises in migration** to and within the European Union (EU) in recent years have resulted in **numerous challenges for health services**[4]; also, in Spain where the foreign population represented in July 2020 11.2% of the total Spanish population[5]. The need for integrated programmes to deliver **effective and cost-effective services** to high-risk migrants is now a key step for the medical services within the EU[6].

Migrants may have particular health needs; they are **disproportionately affected by key infections**, including tuberculosis (**TB**), human immunodeficiency virus (**HIV**), hepatitis B virus (**HBV**) and hepatitis C virus (**HCV**) in Europe; and this has been associated with the incidence in the country of origin, socio-economic risk factors and other comorbidities on arrival to the host Europe[7]. A decline in TB incidence in most European countries in recent decades has slowed due to the re-emergence of TB in vulnerable populations, including migrants[7]. Overall, approximately 33% of TB cases in the EU were foreign-born in 2016 but there is considerable variation between countries[8]. In 2018, almost half of the new HIV cases (42%) within the EU occurred in the migrant population[9] and hepatitis B and C prevalence in migrants in Europe is estimated to be 6 and 2 times higher, respectively, than the general population[10]. In addition, a homogeneous strategy in European countries including Spain on **vaccines and preventable diseases** in migrant adult populations is still lacking[11]. And this will be particularly crucial for the COVID-19 vaccine strategy to elucidate if the national strategy will also explicitly include asylum seekers, refugees and undocumented migrants who should not be left behind in the fight against the COVID-19[12], but also to evaluate how the vaccination records will be registered and traced in the migrant mobile population. Similarly, certain **imported diseases**, only prevalent in migrant populations[13-16], are at risk of transmission in non-endemic areas under special circumstances (through transplants, blood-transfusion or congenitally)[15] and are potentially severe, particularly if there is a diagnosis delay, in immunosuppressed patients[16]. Finally, **female genital mutilation** is a neglected condition, with estimates about 38000 migrant women in some European countries[17]. In Spain, a study reported a profound lack of knowledge around the concept, typology, countries with a high prevalence of female genital mutilation and protocols of action for health professionals, who are then unable to identify and detect risk factors[18].

Health systems need to be prepared to respond to both immediate and long-term health needs of migrants with an **inter and multidisciplinary approach**, considering the migrants' backgrounds and the impacts of poverty and gender on health. The need for integrated programmes to **deliver more effective and cost-effective services to high-risk migrants is now a key step** for the medical services within European countries[6].

Accordingly, health systems are responsible for providing an efficient, economic, and affordable solution to be implemented at primary care and hospital level. However, primary care is usually the first contact point of the migrant population with the health system and therefore, these health facilities are key to guarantee the early detection of migrant health needs. It should be added post-migration transmission and complications of communicable diseases and other conditions prevalent in migrants could be prevented or reduced by enhanced screening and vaccination strategies focused on migrant populations[19].

Screening and vaccination policies may improve the communicable diseases and the female genital mutilation prevention, diagnosis, and treatment if the legal and policy environment is conductive. Screening all of these conditions may be beneficial either because there is a transmission risk through community exposure, transplants, blood transfusion or congenitally or because severe complications and sequel may be prevented if the diseases are early identified[6].

Data on cost-effectiveness are scarce but suggest **moderate to high cost-effectiveness of migrant screening programmes depending on the migrant group and disease targeted**. Cost-effectiveness studies evaluating **screening for TB in** migrant populations have shown a clear benefit of screening among high prevalence groups, close contacts of those with known TB,

and migrants at entry if they originate from intermediate- or high-TB-incidence countries defined as >60/100000 and >120/100000, respectively[11]. These studies demonstrated that increased cost-effectiveness was associated with higher TB incidence in the country of origin, suggesting that programmes will be more cost-effective when targeting migrants from countries of origin with a high incidence TB. However, most TB screening programmes in Europe target asylum seekers and refugees and, therefore, miss other circulating migrant groups[11] that could be potentially targeted in other settings such as primary care. In addition, the average cost per patient of TB in Spain has been estimated to be 10,262€, with an estimation of the total cost in Spain during 2016 of around 40 million€[20]. This cost increases significantly when associated with patient admission and could be potentially everted if proper measures are established to improve the early detection of the disease.

Approaches such as **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 infections in the population have been recommended[21]. A recent health economics analysis has demonstrated that HIV screening in primary care in high HIV prevalence areas is cost-effective[22] and pilot studies have demonstrated the feasibility and acceptability of implementing routine HIV and other communicable diseases screening tests among patients and healthcare professionals in primary care. **Implementation of targeted HBV and HCV screening programmes to increase early diagnosis and treatment is important to reduce the burden of chronic hepatitis B and C** among migrants[23], which has **also been demonstrated for Chagas disease**[24].

The **new guidelines from the European Centre for Disease Control and Prevention**[11] on infectious diseases screening and vaccination in new-arriving migrant populations and alongside country-specific guidelines, promote screening implementation at the primary care level[25]. In particular. ECDC guidelines **call for innovative approaches to multi-disease testing and vaccination** in high-risk migrants[11]. Nevertheless, how best to implement these new guidelines is not clear and there is an urgent need to explore country-specific implementation to assess effectiveness and cost-effectiveness[6].

Current migrant screening programmes across Europe are too narrow in focus, focusing mainly on active TB and mainly on asylum seekers and refugees[6]. Also, recommendations are often expert-opinion driven and rarely evidence-informed. In general, comparison of these strategies across countries or regions has been performed for single diseases, such as TB or hepatitis, but not comprehensively across all relevant conditions. In addition, the implementation of screening programmes requires coordination between health care providers, social services and policymakers and should include insights from diverse disciplines (Economics, Epidemiology, Clinical Practice, Psychology or Social science)[6]. In this regard, the **need for integrated programs of migrant health care, including screening and vaccination programmes**, has introduced a challenge to medical services within the EU[19].

The current value of a systematic screening at primary care level has not been properly evaluated and the practical implementation of screening programmes remains a challenge at primary care level[6], particularly when including imported diseases. In this regard, one of the main determinants of barriers that delay and decrease the detection rate of communicable diseases, generate health inequalities, increase morbidity and DALYs associated, and also increase the risk of transmission of disease within migrant communities is the **lack of expertise of health professionals in assessing the risk of communicable diseases** and other conditions in migrants including the epidemiological risk considering their individual differences (sex,

age, epidemiological origin)[18]. This may combine to affect health outcomes of migrants, generating health inequities and sustaining disease transmission, and consequently increasing the cost for health systems. Although migrant screening guidelines are becoming increasingly available, most of the screening strategies designed require the health professionals´ active commitment to navigate much deeper into the guidance until finding the epidemiological information on the country of origin that is needed for the individual-based risk assessment to take the appropriate screening decision. In many cases, **guidelines do not provide specific information by country of origin and a general recommendation is provided considering all migrants as a homogeneous group**. Therefore, in many settings, the screening programme is overestimating the population at risk, thereby wasting the scarce health resources of the health system - for example, low prevalence of HBV and HCV in most Latin American countries would not justify screening of these infections to migrants coming from these countries.

With the aim of improving patient care by strengthening medical decisions, there has been an outstanding development of clinical decision support systems in the last decade[26]. In such tools, the characteristics of an individual patient are matched to a computerized clinical staff knowledge base in patient-specific assessments and recommendations are then presented in electronic patient record system (EPR) to the clinical staff for decision. The decrease in consultation time, wrong diagnosis, and test duplication at primary care settings support the cost-effectiveness of implementing CDSS in screening[27].

Our research group has already developed an **innovative prototype digital software (CRIBMI)**[28]. This user-friendly and simple software was designed by the Barcelona Institute for Global Health (ISGlobal) in collaboration with the Jordi Gol Institute for Primary Care Research (IDIAP Jordi Gol) and the Fundació Clinic Recerca Biomédica (FCRB) and was tested in four PCCs in Catalonia. In addition, this software was already **integrated into the electronic patient record (EPR) system** in Catalonia at primary care level (**eCAP**). The software uses routinely structured health data (country of origin, sex, and age) collected by the administrative staff of the health centre and registered in the EPR system, and **through simple algorithms, generates an automated screening decision support system** able to inform clinicians about screening on targeted conditions in migrants based on an individual risk- assessment. It currently includes eight conditions: 7 communicable diseases (HIV, HBV, HCV, TB, Chagas diseases, strongyloidiasis and schistosomiasis) and one key health condition (female genital mutilation)[29]. Data shows the digital tool is feasible to implement, acceptable to healthcare professionals and migrants, and well adapted to the primary care context[30], with data suggesting that the digital tool is improving the diagnosis of imported conditions but also other common communicable diseases in migrants when comparing it with a standard training programme[30].

The **aim** of this study is to implement and test **a digital tool that will use routine health data to perform an individualized risk assessment** (using a set of parameters: age, sex, country of origin) and it will provide recommendations for primary care health professionals in several health aspects: communicable diseases, vaccinations, and female genital mutilation. This can better utilize scarce health care resources and at the same time, improve the knowledge of health professionals on migrant health conditions.

BIBLIOGRAPHY

1. Willekens F, et al. International migration under the microscope. Science (80-). 2016;352(6288):897 -9.
2. OECD. Working Together for Local Integration of Migrants and Refugees. Working Together for Local Integration of Migrants and Refugees. 2018.
3. Bradby H, et al. Public health aspects of migrant health: a review of the evidence on health status for refugees and asylum seekers in the European Region. Copenhagen: WHO Regional Office for Europe, Health Evidence Network synthesis report. 2015.
4. MINISTERO DELL´INTERNO. Study Group on the reception system. Report on the reception of migrants and refugees in Italy. Aspects, procedures, problems. Rome; 2015.
5. Instituto Nacional de Estadística. Cifra de población. Provisionales a 1 de Julio 2020.
6. Seedat F, et al How effective are approaches to migrant screening for infectious diseases in Europe? A systematic review. Lancet Infect Dis [Internet]. 2018;18(9):e259 -71.
7. European Centre for Disease Prevention and Control (ECDC). Assessing the burden of key infectious diseases affecting migrant populations in the EU/EEA. Stockholm. 2014. doi:10.2900/28792. 2014.
8. Lönnroth K, et al. Tuberculosis in migrants in low-incidence countries: Epidemiology and intervention entry points. Int J Tuberc Lung Dis. 2017;21(6):624 -36.
9. European Centre for Disease Prevention and Control (ECDC), World Health Organization (WHO). HIV/AIDS surveillance in Europe 2019 - data 2018. 2019.
10. Hahné SJM, et al. Infection with hepatitis B and C virus in Europe: A systematic review of prevalence and cost-effectiveness of screening. BMC Infect Dis. 2013;13(1).
11. European Centre for Disease Prevention and Control (ECDC). Public health guidance on screening and vaccination for infectious diseases in newly arrived migrants within the EU/EEA. 2018.
12. Mukumbang F. Are asylum seekers, refugees and foreign migrants considered in the COVID-19 vaccine discourse?. BMJ Glob Health. 2020; 5(11): e004085.
13. Asundi A, et al. Prevalence of strongyloidiasis and schistosomiasis among migrants: a systematic review and meta-analysis. Lancet Glob Heal 2019;7(2):e236 -48.
14. Requena-Méndez A, et al. Prevalence of Chagas Disease in Latin-American Migrants Living in Europe: A Systematic Review and Meta-analysis. PLoS Negl Trop Dis. 2015;9(2):1 -15.
15. Requena-Méndez A, et al. Health Policies to Control Chagas disease transmission in European Countries. PLoS Negl Trop Dis. 2014;8(10).
16. Requena-Méndez A, et al. Evidence-based guidelines for screening and management of strongyloidiasis in non-endemic countries. Am J Trop Med Hyg. 2017;97(3):645 -52.
17. Jordal M, et al. Challenges in providing quality care for women with female genital cutting in Sweden - A literature review. Sex Reprod Healthc [Internet]. 2018;17(September 2017):91 -6. Available from: https://doi.org/10.1016/j.srhc.2018.07.002
18. González-Timoneda A, et al. Knowledge, attitudes and practices of primary healthcare professionals to female genital mutilation in Valencia, Spain: Are we ready for this

challenge? BMC Health Serv Res. 2018;18(1):1 -13.

19. Gushulak B, et al. Migrants and emerging public health issues in a globalized world: threats, risks and challenges, an evidence-based framework. Emerg Health Threats J. 2010;2:e10.
20. Gullón JA, et al. Tuberculosis Costs in Spain and Related Factors. Arch Bronconeumol 2016;52(12):583 -9.
21. Leber W, et al. Effectiveness and cost-effectiveness of implementing HIV testing in primary care in East London: Protocol for an interrupted time series analysis. BMJ Open. 2017;7(12):1 -8.
22. Baggaley RF et al. Cost-effectiveness of screening for HIV in primary care: a health economics modelling analysis. Lancet HIV. 2017;4:e465 -74.
23. Suijkerbuijk AWM, et al. Cost-effectiveness of screening for chronic hepatitis B and C among migrant populations in a low endemic country. PLoS One. 2018;13(11):1 -16.
24. Requena-Méndez A, et al. Cost-effectiveness of Chagas disease screening in Latin American migrants at primary health-care centres in Europe: a Markov model analysis. Lancet Glob Heal. 2017;5(4):e439 -47.
25. Public Health England. Migrant health guide. Available from: www.gov.uk/government/organisations/public-health-england
26. Van Dort BA, et al. Optimizing clinical decision support alerts in electronic medical records: a systematic review of reported strategies adopted by hospitals. J Am Med Informatics Assoc 2020. 2021 Jan 15;28(1):177-183.
27. Sutton RT, et al. An overview of clinical decision support systems: benefits, risks, and strategies for success. npj Digit. Med. 2020;6;3(1):17.
28. Requena-Méndez A. Migrant Health Conference -ISTM. In: CRIBMI: Improving screening strategies for migrants in Primary Care (PC). 2018.
29. Sequeira-Aymar E, et al. Recommendations for the screening for infectious diseases, mental health, and female genital mutilation in immigrant patients seen in Primary Care. Aten Prim 2020;52(3):193 -205.
30. Sequeira-Aymar E, Cruz A, Serra-Burriel M, di Lollo X, Gonçalves AQ, Camps-Vilà L, et al. 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. J Travel Med. 2021;1–11.

2. HYPOTHESIS

Screening programmes for migrant-related diseases differ widely, and detailed descriptions of their effectiveness are currently lacking. Comprehensive data on the design and performance of screening programmes for both communicable diseases and female genital mutilation and recommendations for vaccination in migrant groups in Spain would enable opportunities for cross-regional sharing of information and homogenizing best practice.

Our hypothesis is that migrants´ overall health status may be improved by increasing the detection of certain infectious diseases and other conditions for which effective care is available. This can be achieved through a systematic screening of these conditions that can facilitated by using innovative and digital solutions implemented in the routine health care.

3. OBJECTIVES

General objective: To develop an integrated and primary care based, communicable diseases and female genital mutilation screening and vaccination programme for migrant populations in Spain in order to promote better health and integration.

Specific objectives:

Aim 1: To develop a Spanish consensus guidance on migrant screening and vaccination recommendations based on existing European examination/screening programmes and on a consensus of a country-expert transdisciplinary national collaborative network.

Aim 2: To scale-up and validate a simple and user-friendly innovative digital tool that will be integrated into the local electronic patient record system of primary care in two different settings (Catalonia and Andalusia) and that aims to facilitate targeted screening and vaccination coverage to recently arrived migrants presenting for a routine appointment. This digital tool will support health professionals to follow best-practice recommendations; while considering patients' individual characteristics (country of origin, age,sex) and therefore specific risk factors.

4. STUDY DESIGN

This study will be developed into two sub-studies in order to accomplish the specific objectives.

4.1.1 Study 1 related to aim 1. Spanish consensus guidance on migrant screening and vaccination recommendations

a. **A comparative review and analysis of existing screening programmes** will be performed across Catalonia and Andalusia. We will comprehensively review screening policies and vaccination policies for migrants and the access to these programmes in Spain, including: health care settings, type of migrants (asylum seekers/refugees/undocumented), diseases included, gender perspective (specific programmes for women), target higher-risk subgroups (e.g., immunosuppressed), access to treatment and follow-up (particularly for female genital mutilation) and inter-disciplinarity of the programmes.

b. **A survey on migrant health screening strategies and vaccinations policies for migrants** will be conducted targeting national experts to (i) assess what screening strategies for migrant on infectious diseases, vaccination uptake and female genital mutilation are being implemented; (ii) to provide the contact details from their National Ministry of Health experts, responsible of asylum seekers programmes, blood banks, national transplant organizations, and antenatal care units of Spain.

c. **A report with the review results** that will be presented in a consensus workshop will be developed.

d. **A consensus workshop with national experts** aimed will be carried out to establish which diseases will be included in the final screening algorithm and what will be

defined as the screening criteria for each condition. The tentative elements to include are HIV, HBV, HCV, TB, selected parasitic infections, vaccination uptake and female genital mutilation. For most of the communicable diseases and for vaccination uptake, the screening criteria will be fully aligned with the current ECDC screening guidelines and recommendations. The screening criteria used in the previous project (CRIBMI) will be reviewed and updated. In the previous project, HIV test was offered following ECDC recommendations to those individuals coming from countries with a prevalence >1%. HBV and HCV tests were offered (also following ECDC guidelines) to those individuals coming from countries with >2% prevalence. Strongyloidiasis and schistosomiasis tests were offered to those individuals coming from endemic areas, also defined in the ECDC guidelines. Chagas disease test was offered to those individuals coming from the 17 Chagas endemic countries. Nevertheless, active TB was screened in migrants from countries with an incidence >50/100000. Furthermore, exploring the risk of female genital mutilation was considered in all women between 15 and 50 age years-old that come from countries where this practice is frequent. Vaccination records will be requested from all individuals.

4.1.2 Study 2 related to aim 2. Operational implementation of a pilot screening programme using the IS-MiHealth software and evaluation of its feasibility, impact, equity, and cost. The study will be registered in clinical.trials.gov

a. Study design and subjects.

A pragmatic cluster controlled randomised trial will be conducted in 60 primary care centres (PCCs) of Catalonia and Andalusia to explore and assess the effectiveness of the digital tool IS-MiHealth. In Catalonia, 32 PCCs will compose the sample size (see sample calculation below) and in Andalusia 6 centres will be selected to conduct the pilot study. Eligible participants will be Health professionals working at the corresponding PCCs. Indirect participants will be migrant populations aged >16 years, excluding foreign-born population from Western countries (Western Europe, North America, Australia, or New Zealand), that arrived at Spain in the last five years and are attending the PCCs for any reason. No exclusion criteria will be set concerning the year of arrival to provide the screening recommendation except for active TB where a limit of five years since the arrival to the host country will be established. These criteria will be established since all the infections, except for active tuberculosis, are chronic infections and because a higher risk of such infections has also been seen in long term migrants.

b. Health centres selection, randomisation and masking.

Regarding the selection of the participating PCCs in Catalonia, the IDIAJGol research team will find other areas where there are referents with an interest in participating in the study. The list of PCCs belonging to these areas, where the referral to the reference laboratory is more feasible, will be provided. With this final list, we will proceed with the randomization stratified by area and by density of migrant population in the area (low vs. high). For the selection of the PCCs in Andalusia, an IT committee of the Andalusian Health Service (SAS) will provide a list of the possible centres that could participate in the study and the randomization will be carried using the same stratification method mentioned previously. The randomization will be performed through a statistical software for each pair of selected health centres stratified by study area. Therefore, for each pair of PCCs, one PCC will be randomly selected to implement the screening programme through the IS-MiHealth software, and it will be compared with the other PCC of the same area where the PCCs do follow

the current practices in the routine care. In both cases, health professionals will receive a training session on migrant health; the training contents will include for each condition, epidemiological aspects, diagnosis, treatment and the screening recommendation.

c. Implementation strategy.

The implementation strategy designed will be carried out in three phases and using mixed methodology. For the study of the implementation process, three PCCs, per study setting (3 in Catalonia and 3 in Almeria) will be selected by convenience from the intervention branch. In the pre-implementation phase, the local needs, resources, barriers, and facilitators will be assessed through the conduction of focus group (FG) discussions for professionals and the migrant population, with the aim of adapting the intervention to the contexts of each setting. FGs for professionals and migrants will be carried out separately. In the implementation phase, real-time monitoring of the strategy will be performed (by a data manager and a study coordinator from each PCC) in order to identify opportunities for improvement and optimization of the process. The technical monitoring will help identify errors in the implementation of the alerts in the EPR system, to be mitigated in real-time. In the post-implementation phase, participants´ opinions will be assessed through FG discussions of professionals and the migrant population with the aim of improving different aspects of the intervention. FGs will be carried out independently for each group. Therefore, 2 FGs will be carried out for each group, health professionals and migrant patients, one pre-intervention and the other post-intervention at each PCC. These FG discussions will be carried out in the corresponding PCC and will last approximately 90 minutes. Quantitative indicators will also be taken to evaluate the outcomes of the implementation. Additionally, an ad-hoc survey of the programme acceptance, targeting health professionals and a sample of migrants will be performed.

5. INTERVENTION

The implementation of the screening programme will be facilitated using a simple and user-friendly tool that helps health professionals to follow best-practice recommendations while taking into account patients' individual characteristics: country of origin, age,sex. IS-MiHealth set a series of rules that provide real-time prompts to health professionals on screening of infectious diseases and female genital mutilation for migrants.

In Catalonia, the digital tool has already been integrated to the EPR system (e-CAP), program shared by all PCCs that are part of the Catalan Institute of Health, as part of a pilot study. The 3 demographic variables (country of origin, age and sex) are routinely collected by the PCC´s administrative staff and documented in electronic medical records. Once the administrator collects these variables in the computer system, the tool will generate an alert that will be reflected once the patient’s medical history is reopened. Therefore, when the migrant patient goes to the consultation with the health professional, the alert will appear containing the recommendations for screening and vaccination of the different diseases/conditions. The data of the patients is not registered nor collected by the digital tool, it is only used to produce the alert.

In Andalusia, the digital tool will be integrated for the first time into the primary care EPR system (DIRAYA). Similar to what is described above for Catalonia, the alert will be generated from demographic data but, in this case, the information is centralized in the Database of Users (BDU) of the SAS. Each user in such BDU is uniquely identified by their Andalusian Health History Number (NUHSA). The tool will be linked to specific user data (NUHSA) to be able to

apply the screening algorithm. Therefore, in this scenario the tool does not collect any personal data but use it to generate the alert.

Once the health professional accesses the digital tool, he/she will have to mark in a check-list produced by the tool, the diseases that the patient has already been screened and/or vaccinated. This information (the check-list) will be registered and will be protected on a server under a secured environment ensuring data protection policy. In addition, access to the primary care environment (DIRAYA) requires a prior identification by the healthcare professional on a private and secured connection.

Training sessions

Health professionals from both intervention and control centres will receive a training session targeting staff of the centres including nurses, medical doctors, and other technicians. The session will cover background information on each infection, including epidemiology, diagnostic tools, treatment available, particular aspects in high-risk groups such as immunosuppressed patients, data on cost-effectiveness, and screening and vaccination recommendations for migrants.

Participants´ selection

Therefore, when an individual comes to the PCC for any reason, the health professional will receive a message, in the electronic patient record, inserted as a pending task assignment with a recommendation on the diseases that should be considered for screening, based on this person's background characteristics. The tool 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 International Classification Diagnosis codes) or if a diagnostic test had been performed for any condition included in the program. In such cases, the automated electronic prompt does not appear for that condition. A pilot test will be conducted with 3 health professionals to assure the correct functioning of the tool. In the control centres, we will hold just a training session with the same screening recommendations as for the intervention centres but will not initiate the tool/prompts onto the EPR system. When the patient comes to the PCC, health professionals will decide what diseases/conditions should be screened and/or vaccinated for according to the information received either through the digital software (intervention centres) or based on their knowledge on the epidemiological background of the diseases (control centres), which was included in the training programme. In any case, health professionals will be responsible for requesting a blood test or a chest radiography, the vaccination and/or the derivation to a specialist.

Participant´s selection for the feasibility and acceptability evaluation (focus group discussions and survey)

General practitioners (GP) and nurses from the selected PCCs will be invited by an electronic mail sent by a member of their PCC leadership team. Among those that express interest to participate, the research team will perform a selection based on personal characteristics (professional category, sex, age and time of contract with the Catalan Institute of Health) in order to obtain discourse variability in the FG.

Migrant population will be selected by one GP in each PCC. The GP will select his/her own patients based on the following characteristics: sex, age and geographical area of origin. Each GP will call his/her patients to explain the study and invite them to participate. Oral consent will be obtained in that phase and registered in patient clinical history followed by the written consent on the day of the FG discussion. All FGs will be conducted in the PCCs, with 8-10 participants in each group.

For the survey of the programme acceptance, a list of possible candidates (sex and gender-balanced) will be made for both groups, health professionals and migrant patients. The same member of the PCC leadership team that sent the invite to the GP and nurses for the FGs of the 6 participating PCCs will send an anonymous questionnaire via email or WhatsApp, using the secured LimeSurvey platform, to the chosen health professionals and migrant patients. Candidates will receive the invitation email with a link to the anonymous survey and their access to it will represent their consent to participate.

6. STUDY PROCEDURES, TREATMENT AND CALENDAR OF THE STUDY.

In line with the existing national guidelines, active TB will be screened with chest radiography. If radiographic findings are compatible with TB, or if TB symptoms are present, the person should be immediately referred to a specialist for full diagnostic workup. For HIV testing, a standard HIV ELISA test will be performed. For HBV, the Australian antigen (HBsAg) and the IgG Core (IgG anti-HBc) serological test will be performed. For HCV, an IgG-HCV test will be performed. For Chagas disease, strongyloidiasis and schistosomiasis, a serological test will be also performed. All of them they will be processed in the reference laboratory facility of the PCC, being all of them based on the commercial tests available in each hospital of reference.

Primary or boost vaccinations will be offered according to the guidelines of each centre in line with the National recommendations. Finally, for female genital mutilation, a gynaecological physical examination will be performed and/or referral to a gynaecologist will be carried out if required. A preventive protocol will be applied for girls at risk of this practice.

In the case of a positive test result or diagnosis, the individuals will be referred to receive specialized care as appropriate.

7. DATA ANALYSIS

a. Sample size. For estimating the number of PCCs that will compose the sample in Catalonia, we have considered that the mean migration rate in all settings is higher than 10%, then the achieved confidence level will exceed 95% when 32 centres are participating. A comparative analysis of the PCCs will be first performed to select 16 pairs of PCCs with more similar characteristics (e.g., number of health professionals of the PCC, migration density in the municipality or setting) to assure the validity of the results.

b. Feasibility and acceptability analysis. FGs will be conducted in the PCCs, with 8-10 participants in each group. Data will be collected through digital audio and video recording of the FG discussion in each PCC. All FGs will be manually transcribed by one interviewer and field notes will be made during or after the FG discussion. A thematic content analysis will be performed to evaluate the data from each FG. It will consist of six-phases: become familiar with the data, generate initial codes, search for themes, review themes, define final themes and write-up. In order to validate the data, the coding and final categories will be triangulated by the research team. To complement this analysis, the analysis of the survey of the programme acceptance will be carried out.

c. Analysis impact of the tool. The effectiveness of the tool will be evaluated and compared in each pair of PCCs, in the intervention compared with the control group.

d. The **primary outcome** measure will be the increased detection rate of all aggregated conditions included in the study in the intervention-PCCs compared with the control-PCCs. Conditions: 1. Chagas diseases, strongyloidiasis, schistosomiasis, HIV, viral hepatitis B, viral hepatitis C, active tuberculosis, female genital mutilation, vaccination status of the migrant population (including COVID-19).
Secondary outcomes will be the proportion of **screening tests performed for each condition and other 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**. All cases will be classified using pre-defined case definitions, including the number of diagnoses codified through the ICD-10 code, number of positive laboratory tests, and referrals to specialists. To analyse the effect of the intervention on the outcomes, a difference in differences approach will be performed using a generalized linear model. Intervention units will be compared before and after implementation with respect to the monthly diagnostic rate. Significant deviations between intervention and control centres before implementation will be suggestive of the main underlying assumption, parallel trends prior to implementation. Sandwich-robust standard errors will be clustered at the intervention-level. For secondary outcomes, mixed effects logistic regression models will be used to identify associations between the screening rate performed and socio-demographic, and, other health conditions, using area as a random intercept.

Study variables:

1. Sociodemographic characteristics of the professionals (general practitioners-GP): age, sex, primary care team (PCT)
2. Socio demographic characteristics of migrants: age, sex, country of origin, assigned PCT, assigned doctor
3. Characteristics of the PCT: intervention or control centre, number of professionals (GP and nurses), urban/rural centre, index of socioeconomic depravation (MEDEA), Standard Quality of Healthcare migration density, number of migrants with active status in the year of the implementation of the tool; number of migrants who did not visit any of the centres during the intervention; number of migrants with at least one visit during the intervention period
4. Variables related to the use of alerts: number of migrants with screening criteria for each condition, number of screening tests performed for each conditions, date of entry/exit into the system, date of visits, referral to specialists
5. Laboratory or clinical variables: X-rays, serological or microbiology tests for the conditions studied (HIV, HBV, HDC, Chagas disease, strongyloidiasis, and schistosomiasis). In addition, other laboratory parameters will be included (hemogram, including haemoglobin, platelets, leucocytes, neutrophils, lymphocytes, and eosinophils, IgE, liver and renal function - creatinine, urea, AST, ALT, GGT, bilirubin, coagulation…)
6. Diagnostic variables: Diagnoses of each disease/condition (HIV, HBV, HCV, Chagas disease, strongyloidiasis, schistosomiasis, female genital mutilation and vaccination) based in ICD-10 codes registered by health professionals in the last 10 years including the intervention period.
7. Drug related to the diseases included in the study (e.g., ivermectine for strongyloidiasis) prescribed during the intervention period.
8. Co-morbidities: Other diseases diagnoses based on ICD-10 codes registered by health professionals into the system in the last 10 years including the intervention period. The aim is to study the possible association of other diseases (diseases associated with immunosuppression, mental health conditions, cardiovascular and other diseases, other infectious diseases...) with the studied diseases/conditions. In addition, to carry out the

cost-effectiveness study (an economic analysis that will be essential to achieve the second objective of the study) all parameters must be considered to adjust the model, including the comorbidities of the diseases.

9. Immunosuppression status: Here it will include the prescription and billing of immunosuppressive drugs in the last 10 years including the intervention period as well as ICD-codes on transplant, haematological diseases, cancer and related diagnoses, and autoimmune diseases in the last 10 years for determination of immunosuppression status.
10. Minimum basic data set (CMBD) variables: hospitalization dates, primary diagnoses during hospitalizations, laboratory parameters during hospitalizations, drugs prescribed during hospitalization or outpatient units, cost associated or attributed to hospitalization, number of visits in outpatient units

e. Cost of the screening programme and the tool. For each pair of PCCs, the cost of the software tool will be evaluated and compared with the standard care (non-tool based), considering: 1. Costs associated with screening and subsequent treatment of diseases and their sequelae; 2. Cost-saving resources allocated to the screening programme in primary care will be estimated. Besides the prevalence estimates for each condition, the number of cases will be compared with the previous notification rates of the notifiable diseases and with other prevalence studies or registries, if any, for the rest of diseases. Finally, the software tool will be compared with other innovative ways of improving the operationalization of the screening programmes implemented in other countries, such as United Kingdom or Sweden.

f. Gender perspective. Results will also report gender inequalities concerning the access to screening programmes or differences in health professionals´ decision to screen specific female-related-conditions (e.g., female genital mutilation compared with TB or other communicable diseases).

g. Study limitations. The retrospective data collection can lead to inaccuracy or insufficient information of some variables. Also, underestimation of female genital mutilation cases might result due to less referral of potential affected patients to specialists. Recommendations are up to the healthcare worker to inform and the patient to accept it, therefore results may vary significantly by PCC. On the other hand, since the data of date of arrival to the country is not routinely collected at PCCs, it might not provide the adequate information to fulfil the active TB screening criteria proposed in the recommendations.

h. Other aspects. A business plan model will be developed including the integration of the software in an application programming interface (API) to facilitate and simplify the implementation and maintenance of the software and the registry of the evidence of modifications of the software in the Property Management System Block Changes.

8. ETHICS

The study will be performed according to Ethical Principals of Medical Research (WMA Declaration of Helsinki, Fortaleza Brazil, October 2013) and following the International Ethical Guidelines for Biomedical Research. It will be carried out in accordance with the protocol and with the pertinent legal requirements: -Law 14/2007 of July 3rd on Biomedical Research, since this is a research project that does not involve medicines.

The study protocol will be submitted to the ethical committee of the Hospital Clinic, IDIAP Jordi Gol in Barcelona and Hospital Poniente in Almeria. The application will consider in both cases all ethical considerations, including those reflected in the Charter of Fundamental Rights of the European Union and the European Convention on Human Rights and its Supplementary Protocols. No research will start until ethical approval of the new study protocol has been gained and the REA has received a scanned copy of all documents proving compliance with existing EU/national legislation on ethics.

The screening programme will only provide advice or recommendations to health professionals for screening and early detection of infectious diseases, vaccination, and female genital mutilation in migrant patients according to the current guideline recommendations that should be considered during the routine practice and that will be agreed during the workshop with experts and will be summarised in a consensus document. Therefore, it will be the health professional, the direct beneficiary, who will finally decide what tests should be offered to each individual as part of the clinical practice. Accordingly, an explicit written consent form from the migrant individual will not be necessary.

However, all individuals will be properly informed in compliance with relevant national and local regulations about the procedures and tests that are indicated in each case. As part of the routine health care, all patients being attended at those selected centres will be informed by the health professional about the diseases that should be screened according to their epidemiological background. Therefore, the person will be fully aware of the implications of different screening test results, including that some of the diseases are notifiable, while others are not. It will also be stressed that screening decision is voluntary and that not accepting the screening will in no way influence the care they will receive, or the assessment of the asylum rights or other resident permit criteria. Careful information, using translators as required, will be provided to all study subjects that cannot speak Spanish. As part of the standard health care, they will be informed that if there is a positive test or a diagnosis of any of the diseases, they will be treated or referred to a specialist as appropriate.

On the other hand, for the execution of the FG discussions the preselection of candidates, health professionals and migrants, will be performed by a member of the PCC leadership team and by a GP, respectively. After expressing interest and accepting to participate in the study, by e-mail for the group of professionals and giving their oral consent by phone for the migrant group, they will be summoned for the date of the FG. In each of the FG discussions, signatures in the individual informed consents will be collected after explaining the study and the participant information sheet.

Objection by participants/patients

To avoid any suspicion of coercion, this study follows the code of conduct in case of objection/resistance of (1) health professionals to follow the recommendations that the tool is providing, or (2) of the individuals to be tested for any of the conditions following the current guidelines recommendations. This code of conduct describes both verbal objection/resistance, and non-verbal or behavioural expressions of objection/ resistance. Behaviour needs to be interpreted as objection if it is different from, or more intense than, usual behaviour in routine care.

Potential impact of the research

This research project is not expected to have any possibly harmful impact on the individuals involved. If an individual is diagnosed with one of the diseases screened, he/she will be referred and treated as appropriate according to the routine care standard procedures of each centre.

9. DATA MANAGEMENT AND DATA PROTECTION

-The project involves handling personal data that are routinely collected in healthcare services. The Primary Care Information System (SISAP) will supervise the technical monitoring of the tool in the implementation phase of the study.

Data extraction. The data extraction process will be performed according to the principles established by the healthcare services, including the data protection policies in this regard. All processing of patients' personal data collected within the study will be conducted according to conventional confidentiality.

In the Catalan Institute of Health, data will be extracted from the electronic patient record system eCAP and pseudo anonymized by IT staff of the System for the Development of Research in Primary Care (SIDIAP) Institute. The study variables will be pseudo-anonymized, with technical and functional separation, by a SIDIAP data manager. SIDIAP will be responsible for the data processing in Catalonia. Regarding SIDIAP source data, the strict SIDIAP security standards will be followed. Aggregated data will also be obtained via SIDIAP during the process of implementation of the tool in the Catalan Institute of Health with the sole objective of technical monitoring to identify alert errors and provide subsequent remediation

In Andalusia, the data will be extracted by a specialized IT committee of the SAS Institution of the area involved in this project. The information will be extracted retrospectively and will include: 1) the check-list from the tool and 2) the demographic and clinical variables from the BDU. Then, the IT committee will link this information with the laboratory data of the reference hospital (Hospital de Poniente in Almeria) and will pseudo-anonymize the data. Thereafter, the biostatistician responsible for the data analysis will only have access to pseudo-anonymized data without personal or sensible information. Thus, the privacy of individuals will be protected. In this regard, details on the health of migrants may have the consideration of sensitive data, as described in article 8 of Directive 95/46/EC (data revealing racial or ethnic origin, political opinions, religious or philosophical beliefs, trade-union membership, data concerning health and sex life) and therefore such data will be aggregated when applicable (region will be provided instead of country of origin) to avoid the identification of the individuals. When applicable, specific authorization by the national data protection authority will be obtained.

Data processing and management. A data processing agreement will be undertaken with the Catalan Institute of Health/IDIAPJGoL and with Distrito Poniente (Almeria), for the ownership and use of research data. Also, a plan for the ongoing custodial responsibilities for the research data at the conclusion of the project will be carried out, including recommendations for the disposal and destruction of the research data.

Concerning the data-management, the treatment, communication, and transfer of personal data of all participants will be adjusted in compliance with EU Regulation 2016/679 of the European Parliament and the Council of April 2, 2016 related to the people physical protection

with regards to the processing of personal data and the free circulation of data, being binding as of May 25, 2018. All data analysis will be conducted on pseudo-anonymized data and no personal data or data that could potentially identify an individual will be included in the final report.

For the qualitative study in Catalonia, the manager of each PCT participating in the project will send an email to the professionals (GPs and nurses) and those who declare interest in participating will be selected to be part of the focus groups. The migrants who will participate in the focus groups of the study will be invited in a visit or by telephone by their own doctor and will sing the consent form on the day of the focus groups. The qualitative study data wull be obtained through the informed consents of the participants, in accordance with the provisions of articles 6.1 a) and 9.2 a) of the RGPD. Digital audios and video recordings will be stored and secured in the local server of ISGlobal (VPN) where only participating investigators will have access to it. These will be erased after five years of completion of the study. No international data transfer will take place of the recordings made in the FG discussions. For the survey of the programme acceptance, the secured LimeSurvey platform will be used as previously explained.

Pseudo-anonymized data will also be stored in ISGlobal's VPN and only participating investigators will have access to the data-base and integrity and security of data will be maintained. In addition, a password will be requested to all researchers for accessing the data registering any access. Also, a regular backup will be generated to avoid loss of information. An adequate documentation of data (metadata) -i.e., adding semantic descriptions, annotations, etc. to the data will facilitate identification and support effective reuse of research data. Only encrypted data will be transferred to third parties and other countries, which in no case will contain information that can directly identify the participant (such as name, initials, address, social security number, etc.). In the event of such a transfer, it would be for the same purpose of the study described and would guarantee confidentiality.

If a transfer of encrypted data takes place outside the EU, either in entities related to the hospital where the patient is involved, to service providers or researchers working with us, the data of the participants will be protected by safeguards such as contracts or other mechanisms established by the data protection authorities.

In addition to the rights already provided for in the previous legislation (access, modification, opposition and cancellation of data, deletion in the new Regulation) participants can also limit the processing of data collected for the project that are incorrect, request a copy or be transferred to a third party (portability). In order to exercise these rights, the participants must contact the principal investigator of the study or the Data Protection Officer of ISGlobal via lopd@isglobal.org. Also, the participants have the right to contact the Data Protection Agency if they remain unsatisfied.

This project does not prevent advanced data usage. In accordance with the provisions of article 35 of the RGPD, the project does not meet the necessary characteristics that require the performance of an impact assessment.

Reutilization of data First, a standardized communications protocol to retrieve (meta) data by their identifier, free and universally implementable, will be generated, including a clear and accessible data usage license. After 10 years, all data will be eliminated and destroyed.

Data will be anonymously uploaded in the repository, and those records that may lead to the individual identification of the participants will be removed or grouped with the aim of keeping their identity hidden at all times. Likewise, the possibility of withdrawing all the individual information of a patient will be guaranteed when so expressed. The data will be stored in a repository created specifically for this purpose in the ISGlobal data centre in the Campus Mar (Carrer del Dr. Aiguader, 88), which requires prior appointment with IT staff and therefore only those responsible for computer security and researchers linked to the project will have access to them. A series of protocols are in place to test and maintain network security, and to provide access management policies for network drives, databases and remote access. The system is protected from power interruptions, with controlled access to authorized users only.

The study does not involve biological samples.

10. FUNDING

The IS-MiHealth project received funding (87.120,00€) from the Health Research Fund Call 2021 of The Ministry of Science and Innovation to support this study economically. Study investigators will not receive any personal compensation or extra salary for participating in this study.

11. RESULTS COMMUNICATION

The promoter and investigators commit to publish the results of the study in journal articles, other scientific publications and communications to congresses. Authorship in case of publication will be decided according to quantitative and qualitative input to the study. The principal investigator will be the first or last author of the articles.