PEER REVIEW HISTORY

ARTICLE DETAILS

Title (Provisional)

Delivering an innovative multi-infection and female genital mutilation screening to high-risk migrant populations (ISMiHealth): study protocol of a cluster randomised controlled trial with embedded process evaluation

Authors

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VERSION 1 - AUTHOR RESPONSE

Reviewers' comments:

Reviewer 1: Dr. Christian Morberg Wejse, Aarhus Universitet

The protocol is well written, the trial is registered, and the relevant SPIRIT checklist is completed.

Response: Thanks to the reviewer for his positive feedback on our work.

It would perhaps be worthwhile to mention that when the trial is reported, that CONSORT guidelines will be followed.

Response: We have included that the CONSORT reporting guidelines will be followed.

- Page 8 (paragraph 2): 'When reporting the trial results, the Consolidated Standards of Reporting Trials (CONSORT) guidelines for randomised trials will be followed.'

No particular considerations are made in the statistical analysis plan on the fact that this is a cluster randomized trial, which requires increased sample size because of the so-called 'design effect' which increases with cluster size. https://www.bmj.com/content/358/bmj.j3064

Response: Thanks to the reviewer for the comment and for the reference that the reviewer shared with us and that we have carefully read.

For the ISMiHealth project, we previously conducted a pilot cluster randomized trial (CRT) in Catalonia in 2018 (doi: 10.1093/jtm/taab100). In such study, since it was a pilot trial, we did not estimate a sample size; however, we carried out an evaluation of different parameters of the clusters to compare pairs of homogeneous clusters in the same area(https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9635062/bin/supplementary_tables_28062021_arm_taab100.docx).

In the current study, we have estimated the sample size using the results of the pilot study. We used the results of the difference in difference analysis of the pilot cluster study comparing the difference in diagnostic yields between the intervention and control centres before and after the intervention. With an intervention effect of 2 (from the pilot study analysis), and assuming an effect standard deviation of 2, a correlation coefficient between measurements of 0.5 and the typical values for significance (alpha = 0.05) and power (1-beta = 0.80) we estimated a sample size of 32 PCCs. Hence, we took into account the intra cluster correlation (the correlation coefficient between measurements = 0.5) and, therefore, the design effect for the estimation of the sample size (doi: 10.1186/1471-2288-9-39).

The use of clusters would perhaps require a trial design which takes this into consideration, such as using the stepped-wedge design instead of a pilot trial.

Response: We believe that a parallel CRT design with a baseline period fits better with our study objectives than a stepped-wedge design (doi: 10.1136/bmj.h391) in which all clusters

will be exposed to the intervention at one point (i.e., all centres will have the ISMiHealth software integrated in the health information system). We are interested in comparing the performance of both types of clusters before and after the intervention, where both groups received training materials and training sessions provided by our research group, but only the intervention clusters had the integration of the ISMiHealth tool in their health information systems.

Also, it is recommended to follow the parallel CRT design when the clusters are homogeneous and small (doi: 10.1136/bmj.h391), as they are in our study. Our clusters share similar characteristics (i.e., a high percentage of migrant populations, similar number of health professionals), and, in addition, they were paired considering the most similar characteristics and randomised. The clusters are small given that the health professionals of the primary care centres (the users of the tool) can reach an approximate maximum of 42 individuals per centre. Therefore, we believe that a parallel CRT would be more effective to achieve our objectives taking into account the characteristics of our clusters.

Reviewer 2: Dr. Ingvil Sorbye, Oslo Universitetssykehus

This protocol paper describes a cluster randomised controlled trial with embedded process evaluation assessing the effectiveness, health impact, feasibility and acceptability of a systematic multidisease screening tool aimed at migrants 15 years and above contacting primary health care structures for any complaint.

The aim of the paper is original and describes an innovative approach that may have an impact on health outcomes of migrants, known to be poorer compared to non-migrants.

The aim and the specific objectives of the study are clearly defined. The Methods section is sound. The paper is generally well written and follows the guidelines for protocol papers.

However, there are some points that need better clarification for the reader:

Response: Thanks to the reviewer for appreciating the work done by our research group. We have considered the suggestions in order to improve the manuscript.

1. The study targets women 15 years or above. Regarding FGM it is unclear why it is relevant that health staff has little knowledge of how to identify women at risk.

(Introduction, page 6, lines 3-4).

This wording is confusing, as surely the objective is to identify women living with FGM to screen for complaints that may be treated, rather than prevention given that the median age of the procedure is <10 years in most countries where the practice is occurring. Please rephrase these sentences.

Response: Thanks to the reviewer for her comment. We have rephrased this sentence to stress the importance of identifying women living with FGM and treating their sequelae, as is the objective of our screening programme. The prevention of FGM has already been implemented in Catalonia and Andalusia (Spain) through specific protocols targeting <15 years old girls. However, our ISMiHealth tool targets general practitioners who attend ≥15 years old population to identify women who previously suffered FGM and who could benefit from the identification and treatment of FMG's potential sequelae. Paediatric care has not been included in the intervention so far.

- Pages 5-6 (paragraph 3): 'A Spanish study reported a profound lack of knowledge of health professionals about FGM, which suggests an underdiagnosis of cases and their sequelae, insufficient implementation of protocols of action, and scarce referral of women who suffered FGM to the appropriate specialized services and professionals to attend their health needs (12).'

2. In the Introduction, page 6, lines 22-24 it states: ".. the public health system provides universal coverage and free access to health care to everybody, irrespective of the migration status of an individual". Does that include also irregular migrants?

How does this align with the description in Methods, page 7, lines 46-47: "In Catalonia, the registration in the municipal residents´register grants access to the health system, and accordingly to primary care".

Please clarify if this study will enable the inclusion of irregular migrants or not, and if not irregular migrants can be included in this study, this is a limitation which should be described under Methods.

Response: Thanks to the reviewer for requesting clarification. Indeed, the public health system in Spain provides universal health coverage, including for migrants with irregular status. Each autonomous community has the competence to establish the procedures for accessing health care in each situation. In the case of Catalonia, the registration to the municipal census, which can be done irrespective of the migration status, grants access to the public healthcare system and entitles the users to access primary care if a registry in any municipality of Catalonia for more than three months is accredited. Also, under special circumstances, if the previous criterion is not fulfilled (https://catsalut.gencat.cat/ca/coneix-catsalut/acces-sistema-salut/nivells-cobertura/que-son-i-com-sassignen/). We have included the following sentence in the Methods section to clarify the inclusion of undocumented migrants in the study.

- Page 8 (paragraph 1): ‘In Catalonia, the registration in the municipal residents’ register grants access to the health system and, accordingly, to primary care irrespective of their legal status as long as the registry in any municipality of Catalonia for more than three months is accredited and also under special circumstances if this criterion is not fulfilled (25).’

3. Methods:

The intervention is clearly described. I miss a better description of the "non-tool based arm", i.e. standard care in this context, given that all health workers in intervention and non-intervention sites will receive similar training. Please add a paragraph after "Intervention" to describe the standard care/non-tool based arm.

Response: We have added a paragraph describing the standard of care of the control arm after the 'Intervention' subsection.

- Pages 10-11 (paragraph 4): '***Standard care***

  Control centres (non-tool based arm) will follow the current clinical practice, including the serological tests and the referral pathway of positive cases. When a migrant patient attends the PCC for any reason, health professionals will decide which diseases/conditions should be screened for, according to the existing national/regional guidelines and supported by the aforementioned training programme on the epidemiological background of the conditions.'

4. Statistical analyses:

The SAP is attached and explains well the planned statistical analyses.

Under "Sample size", page 11, line 56: Please update the actual/planned start date.

Response: Thanks to the reviewer for the comment. The ISMiHealth technical pilot test started in October 2023 while the intervention started in January 2024. The methodology was written in future tense since the manuscript was written before the intervention started. Thus, the manuscript modifications were also written in future tense.

- Page 12 (paragraph 4): ‘The technical pilot test will be conducted from October to December 2023, and the intervention will start in January 2024.’

In addition, we have made minor modifications to the SAP presented in the annex file (Annex 2) to match what is published in the trial registry (SAP v2.0 September 16, 2024).

5. Trial status: Please update the planned or actual starting date and the expected end date of the study.

Response: We have updated the actual starting date and the expected end date of the study in the manuscript and in the trial registry.

- Page 20 (paragraph 2): ‘Protocol version 7.0, December 18 2023. The start date of the trial is January 1, 2024 and the expected completion date is December 31, 2024.’

Thank you for your time and consideration of the manuscript.

Sincerely,

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