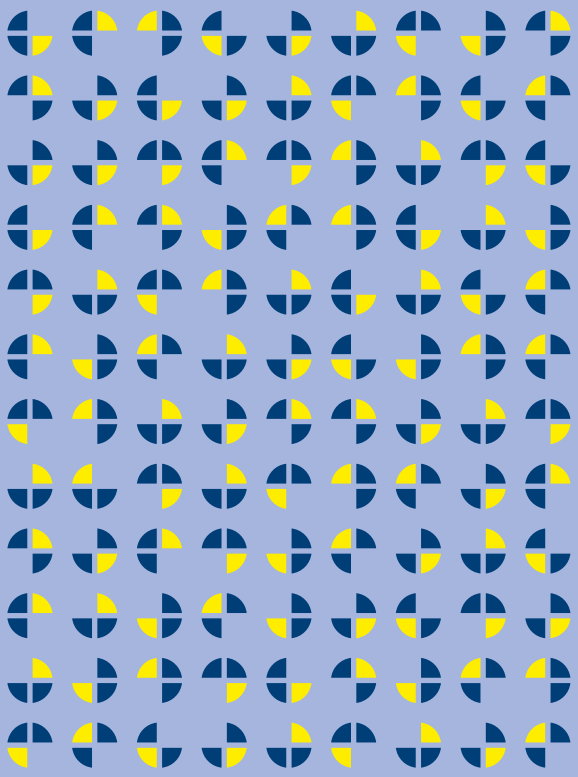
ACCESS TO CERVICAL CANCER SCREENING AMONG UNDERPRIVILEGED WOMEN

Interventional study evaluating cervical cancer screening strategies for underprivileged women encountered through Doctors of the World programmes in France



EXECUTIVE SUMMARY

MÉDECINS DU MONDE

FUNDING
Médecins du Monde and Institut national du cancer (INCA).

PRINCIPAL INVESTIGATOR
Médecins du Monde

PRINCIPAL WRTITERS OF THE REPORT
Laura Reques (MdM), Camille Rolland (MdM)

EDITORIAL BORAD
Najat Lahmidi (MdM), Sophie Laurence (MdM), Ezequiel Aranda-Fernandez (MdM), Antonio Lazzarino (EPISTATA), Camille Gutton (MdM), Niklas Luhmann (MdM)

CONTACT
laura.reques-sastre@medecinsdumonde.net

Date of publication of the report: September 2019
Graphic design: Christophe le Drean

The opinions expressed in this report apply only to the investigators who conducted the study and do not necessarily reflect the opinion of its funders.

INTRODUCTION

The genital human papillomavirus (HPV) infection is the most frequent sexually transmitted viral infection in the general population. The persistence of certain genotypes of HPV can result in precancerous lesions that can turn into cervical cancer after 5 to 20 years.[1,2] Cervical cancer is the fourth most common and the most deadly type of cancer among women. However, its distribution is very heterogeneous. 80% of new cases of cervical cancer occur in developing countries.[3]

In France, cervical cancer affects nearly 3,000 women and causes around 1,100 deaths every year.[4] Currently, the primary screening test used to detect precancerous lesions and early-stage cancer is the pap smear. Nevertheless, the rate of screening coverage, which is estimated at 55-60%, is thought to be insufficient.[5] Screening coverage is especially low among women with limited access to the healthcare system and women of low socio-economic status. In addition, a large proportion of underprivileged women come from countries with a high incidence of cervical cancer.[6,7]

HPV screening tests are cost effective and associated with a higher compliance rate among women.[8] The self-sampling technique has been described as easier, less painful, and faster than a pap smear (PS).[9] In response to the low coverage rate and barriers to screening, several countries in the Western world have chosen to incorporate HPV testing into their screening strategies. In France, the latest recommendations from the French National Authority for Health (HAS) already include HPV testing.[10]

The women who take part in Doctors of the World (MdM) programmes represent vulnerable groups, particularly exposed to HPV and at risk of developing cervical cancer. In addition, they are widely under-screened due to their more limited access to preventive programs and healthcare.[11] Screening strategies using self-sampling could eliminate certain barriers to screening in this population.

OBJECTIVE

The study's main objective was to compare the proportion of participants who had completed a screening test and the proportion of detected cytological abnormalities (·ASC-US) with two strategies that included a dedicated prevention consultation followed by:

- A referral to a partner centre for a pap smea (PS)r;
- An HPV test using a self-collected sample (SCS), and a referral to a partner centre for a pap smear if the HPV test was positive.

The secondary objectives were to describe the characteristics of the participants, evaluate their level of knowledge, practises and attitudes before and after the consultation, identify factors associated with access to screening programmes, and formalise partner networks to provide cervical cancer screening (CCS) to underprivileged women.

METHODOLOGY

Interventional, multi-centric, comparative, and randomised research in four types of programmes: reception, healthcare, and orientation centres (CASO); reception, orientation, and support centres (CAOA); Squat/Shantytown programmes; and Sex Worker programmes (SWP) in four cities (Lyon, Bordeaux, Rouen, and Paris). The study took place from March 2017 to December 2018.

All women aged 25 to 65 whose last pap smear was done more three years ago, whose first pap smear was done more than one year ago, or who had never had a pap smear in their life were included. Exclusion criteria included a complete hysterectomy and the absence of sexual intercourses.

The teams conducted an adapted, individual consultation using counselling techniques to inform the women and raise awareness about HPV infections, cervical cancer, and screening strategies.

At the end of the prevention consultation, the women were separated into two study groups: 1. The control group "pap smear" (PS), in which study

participants were directed oriented towards partner associations and institutions for a pap smear; 2) The experimental group "HPV self-collected sample" (SCS-HPV), in which a self-collected sample was tested for HPV, followed by a referral to partner associations for a pap smear if the results were positive. The study was randomised by one-month periods.

The test selected for the analysis was a real-time PCR ABBOTT. This test was used to detect 14 genotypes of HPV (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 66, and 68). The PS were performed by partner structures in accordance with their standard procedures. Personal, medical and social data were entered into an electronic patient record tool (DPI). The partner centres forwarded the results of the pap smears to MdM by confidential mail.

A descriptive analysis was conducted using the demographic, socio-economic, and clinical variables for each programme type and the variables regarding participants' knowledge and attitudes with respect to cervical cancer. The comparability of the groups was evaluated using the Chi-2 and ANOVA tests for the categorical variables and the t-Student test for the continuous variables. The comparison of the screening completion rate was calculated using Cox regression. The rate of cervical abnormalities detection was calculated using logistic regression. All analyses were repeated with the sample restricted to CASO/CAOA programs.

RESULTS

Cervical cancer and sexual and reproductive health prevention consultation

An initial sample of 799 women attended a sexual and reproductive health prevention consultation. The mean age of the women was 41.0 years (standard deviation [SD] = 10.1). The participants in the CASO/CAOA programmes were primarily African (85.0%) and recent immigrants to France (41.5% had been in the country for less than 3 months). The participants in the "Squat" programmes were mostly European (75.0%) and had a lower level of education (65.4% had completed up to primary school or less). Participants from SWP were older (mean: 48.4 years, SD = 6.8) and came exclusively from East Asia.

With respect to socio-economic variables, only 19.3% of participants had a permanent home and 28.1% had a reported profession. Among the study participants, 67.6% did not have health coverage, and 73.9% had an irregular administrative status.

Regarding gynaecological consultation variables, most participants had limited access to sexual and reproductive health resources: 22.4% had never had a gynaecological consultation, 53.5% did not use contraception, 54.8% did not have friends or family with whom they could discuss topics related to sexual and reproductive health, 45.5% had never had a mammography, and 53.4% had never had a PS.

The five questions related to the participant's knowledge and attitudes towards cervical cancer improved after the consultation, with p values of <0.001. This increase is particularly marked for the following indicators: "knowledge of screening frequency", which increased from 11.9% to 56.7%; "knowledge of centres that perform PS", which increased from 15.3% to 55.7%; and "knowledge of cervical cancer causes", which increased from 18.6% to 61.3%.

Interventional study

Out of the 799 study participants attending the sexual and reproductive health prevention consultation, 112 (14%) were excluded (67 were up to date with their screening schedule, 13 had never had sexual intercourses, and eight had a complete hysterectomy). The final analytical sample included 687 women, from which 304 were assigned to the control group (PS) and 383 to the experimental group (SCS-HPV).

In the control group, 19 women declined the PS (6.3%), 165 were lost to follow-up (54.2%), and 120 (39.5%) had the PS done. 11 cytological abnormalities were detected: 8 ASC-US (three of which were associated to HPV), 2 LSIL and 1 HSIL.

In the experimental group, out of the 383 randomised women, 365 (95.3%) took a self-collected sample to test for HPV, 0.8% decline the test,

and 3.9% did not carry out the test despite their initial agreement and were considered to be lost to follow-up. Out of the HPV tests done, 226 were negative, 127 were positive, and 9 could not be interpreted. In total, 34.4% of tests were positive.

Out of the total number of women who tested negative, 65.9% collected their results and 62.5% of women who tested positive collected their results. Among women with HPV positive test, 47 PS (34.6%) were conducted, and 9 cytological abnormalities were detected (1 ASC-US, 3 cases of LSIL, and 5 cases of HSIL).

With respect to the rate of test completion, the participants in the experimental group were approximately twice as likely to be tested compared to women in the control group (39.5% compared to 71.3%), with a p value of less than 0.001 (risk ratio 1.80: CI 95% [1.55-2.10]; p <0.001). The control group took an average of 18.6 days (SD = 34.5) to complete the screening tests, and the experimental group took an average of 9.5 days (SD = 23.8, p<0.001). The hazard ratio (HR) for the screening completion rate for the experimental group compared to the control group was 2.48 (CI 95% [1.99-3.08]; p <0.001).

2.0% of women presented with cytological abnormalities associated with an HPV infection in the control group and 2.3% in the experimental group. The odds ratio (OR) was 1.20 (CI 95% [0.42-3.40]; p = 0.7). One of the study's hypotheses was that the proportion of detected cytological abnormalities would be higher in the experimental group. It is likely that the absence of statistically significant differences was due to the insufficient sample size.

In the control group, 184 women were lost to follow-up (60.5%). In the experimental group, 18 women were lost to follow-up before the self-collected sample was taken (4.7%), and 86 were lost to follow-up before a PS could be performed (63.2% of women who tested positive for HPV).

The results for the sample restricted to CASO/CAOA programmes were the same as the primary analysis. The difference between the completion rate of each group was even greater (HR 2.98; CI 95% [2.32-3.82]; p <0.001).

CONCLUSION AND RECOMMENDATIONS

The women in the study are in a precarious condition with respect to their socio-economic status (lack of permanent housing or employment) and healthcare access (lack of medical coverage, lack of knowledge about their rights, language and socio-cultural barriers). These circumstances mean that over half of the participants had never been tested for cervical cancer.

Additionally, a prevention consultation adapted to their needs improved their knowledge and interest about CCS. Testing for HPV using a vaginal self-collected sample was well accepted.

Providing a vaginal self-collected sample kit for HPV testing is an innovative and effective method that boosts participation in CCS. Nevertheless, regardless of the strategy used, a number of women were lost to follow-up after being referred to partner centres for a PS, even when their HPV test was positive.

This points to the complexity of treating women in vulnerable situations and undermines the benefit of increasing primary HPV screening coverage through self-sampling.

For this reason, it is crucial to develop and assess appropriate follow-up and support methods for these women and explore more accessible triage scenarios.

It is also important that decision-makers consider the socio-economic status of women and offer CCS options designed to reduce discrimination and unequal access. In order to reach this objectives, we recommend:

For our projects:

- ➔ Incorporate sexual and reproductive health activities that include prevention consultations, counselling, and the opportunities to receive CCS for women between the ages of 25 and 65 years old;
- ➔ Facilitate access to screening and services specialized in the sexual and reproductive health of vulnerable women through reception and support;

- Offer follow-up system for women in vulnerable situations in healthcare facilities to promote and improve screening completion, the result-collection process, and additional treatments based on the nature of the lesions;
- Improve and/or develop tools (adapted messaging and training in sexual and reproductive health counselling) to boost healthcare access and especially access to CCS;
- Evaluate new screening access strategies for our audiences with respect to "outreach «oriented actions by consulting partners and other stakeholders operating in the field;
- Promote advocacy and training with respect to interpreting services, healthcare mediation, and peer liaisons within healthcare facilities to overcome socio-cultural barriers;
- Monitor the implementation of the French National Organised CCS Plan and, if needed, develop an advocacy strategy to promote the access of under-tested populations.

For healthcare facilities and partner organisations:

- Improve sexual and reproductive health prevention activities for women in vulnerable situations by further developing the available tools and with counselling training;
- Facilitate access to screening services and services specialised in sexual and reproductive health for women in vulnerable situations;
- Implement outreach systems to promote healthcare, primary prevention, and CCS;
- Include interpreting services, health mediation services, and peer liaisons to overcome socio-cultural and language barriers;
- Simplify the treatment pathway by opting for consultations based on time slots that don't require appointments and longer office hours;
- Incorporate and evaluate adapted support and follow-up systems to limit loss to follow-up.

For political decision-makers:

- Incorporate primary screening strategies based on HPV self-sampling into dedicated, adapted, and appropriate consultations to facilitate the access of vulnerable women to CCS provided in local healthcare centres (PMI, CPEF, Cegid, CMS, and PASS) and partner associations;
- Promote primary HPV screening in outreach actions, such as social housing, squats, shantytowns and areas frequented by sex workers. In the event of a positive test, direct patients to the closest healthcare centre for a further exam;
- Further examine the topic or opt for more accessible triage scenarios, such as:
- Implementing a "point of test care" in local healthcare centres where patients can have an HPV test and receive the results in under an hour and have a PS if the results are positive;
- Implementing reflex triage systems based on cervical samples in local healthcare centres that include a primary exam, HPV test, and a cytological exam in the event of a positive result using the same sample.

For researchers:

- Conduct socio-anthropological studies to better characterise the barriers to access and the main reasons why vulnerable women in France do not complete the CCS process;
- Continue to study self-sampling as a method that could lead to increased acceptance of CCS and carry out satisfaction and acceptability studies;
- Continue to conduct prospective studies focused on vulnerable women with the following outcome variables: completion of the screening process, histopathological characterisation of precancerous lesions, and completion of the treatment cascade.
- Develop and study the effectiveness of triage test which can be performed using vaginal samples and self-collected samples, to avoid having to schedule women for a second appointment for a PS and cytological exam.
- Conduct a comprehensive evaluation of the performance and impact of screening that includes epidemiological, economic, and public health concerns. Special attention should be paid to assessing the system's ability to reduce regional and social inequalities.

REFERENCES

1. Centre National de Référence des Papillomavirus Humains (CNR HPV), Institut Pasteur. Référence des Papillomavirus Humains (CNR HPV), Institut Pasteur. In 2018. Disponible sur: www.pasteur.fr/fr/centre-medical/fiches-maladies/cancer-du-coluterus-papillomavirus
2. Garnier A, Brindel P. Prévention et dépistage du cancer du col de l'utérus. Boulogne [Internet]. Billancourt: Institut National du Cancer; 2013. Disponible sur: www.ecancer.fr/publications/75-prevention/735-prevention-et-depistage-du-cancer-ducolde-luterus.
3. GLOBOCAN [Internet]. Disponible sur: https://onlinelibrary.wiley.com/doi/full/10.3322/caac.21492)
4. Estimations nationales de l'incidence et de la mortalité par cancer en France métropolitaine entre 1990 et 2018 / 2019 / Maladies chroniques et traumatismes / Rapports et synthèses / Publications et outils / Accueil [Internet]. [cité 31 mai 2019]. Disponible sur: http://invs.santepubliquefrance.fr/Publications-et-outils/Rapports-et-syntheses/Maladies-chroniques-et-traumatismes/2019/Estimations-nationales-de-l-incidence-et-de-la-mortalite-par-cancer-en-France-metropolitaine-entre-1990-et-2018
5. Haute Autorité de Santé. Etat des lieux et recommandations pour le dépistage du cancer du col de l'utérus en France en 2010. 2011.
6. Barré S, Massetti M, Leleu H, Catajar N, de Bels F. Caractérisation des femmes ne réalisant pas de dépistage du cancer du col de l'utérus par frottis cervico-utérin en France. Centre HPV; 2016.
7. Dalmont, C. et al. Cancer du col et précarité, accès aux soins. Bulletin du Cancer. Bulletin du Cancer; 2009.
8. Leinonen, M. et al. Age-Specific Evaluation of Primary Human papillomavirus screening versus conventional cytology in randomized setting. Journal of the National Cancer Institute; 2009.
9. Arbyn M, Verdoodt F, Snijders PJF, Verhoef VMJ, Suonio E, Dillner L, et al. Accuracy of human papillomavirus testing on self-collected versus clinician-collected samples: a meta-analysis. Lancet Oncol. févr 2014;15(2):172-83.
10. Haute Autorité de Santé. Évaluation de la recherche des papillomavirus humains (HPV) en dépistage primaire des lésions précancéreuses et cancéreuses du col de l'utérus et de la place du double immunomarquage p16/Ki67 Synthèse et recommandations. 2019.
11. Médecins du Monde. Rapport de l'Observatoire de l'accès aux droits et aux soins dans les programmes de Médecins du Monde en France en 2018. In 2019. p. 185.