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Combined incentive actions, focusing on primary care professionals, to improve cervical cancer screening in women living in socioeconomically disadvantaged geographical areas: a study protocol of a hybrid cluster randomised effectiveness and implementation trial- RESISTE

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ABSTRACT

Introduction Cervical cancer (CC) causes thousands of deaths each year. Nearly 100% of cases are caused by oncogenic strains of human papillomavirus (HPV). In most industrialised countries, CC screening (CCS) is based on the detection of HPV infections. For many reasons including lower adherence to CCS, underserved women are more likely to develop CC, and die from it. We aim to demonstrate that the use of incentives could improve screening rates among this population.

Methods and analysis Our cluster randomised, controlled trial will include 10 000 women aged 30–65 years eligible for CCS, living in deprived areas in four French departments, two mainlands and two overseas, and who did not perform physician-based HPV testing within the framework of the nationally organised screening programme. HPV self-sampling kit (HPVss) will be mailed to them. Two interventions are combined in a factorial analysis design ending in four arms: the possibility to receive or not a financial incentive of €20 and to send back the self-sampling by mail or to give it to a health professional, family doctor, gynaecologist, midwife or pharmacist. The main outcome is the proportion of women returning the HPVss, or doing a physician-based HPV or pap-smear test the year after receiving the HPVss. 12-month follow-up data will be collected through the French National Health Insurance database. We expect to increase the return rate of HPV self-samples by at least 10% (from 20% to 30%) compared with the postal return without economic incentive.

Ethics and dissemination Ethics approval was first obtained on 2 April 2020, then on July 29 2022. The ethics committee classified the study as interventional with low risk, thus no formal consent is required for inclusion. The use of health insurance data was approved by the Commission Nationale Informatique et Libertés on 14 September 2021 (ref No 920276). An independent data security and monitoring committee was established. The main trial results will be submitted for publication in a peer-reviewed journal.

Trial registration number NCT04312178.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A large cluster randomised clinical trial is currently running in four French departments, two mainlands and two overseas.
⇒ A total of 10 000 women living in deprived areas will be included in the study.
⇒ The study will evaluate two motivational actions, the possibility of returning self-testing for human papillomavirus at a health professional and an economic incentive, and test their possible synergy.
⇒ As the definition of the low socioeconomic group relies on the place of residency, no individual assessment will be conducted.
⇒ We will not be able to reach women with invalid addresses, or who are homeless, which leaves a fraction of women, perhaps the most vulnerable, outside of screening

INTRODUCTION

Cervical cancer (CC) is considered one of the most lethal cancers worldwide. In 2020, we estimate 604 127 the number of new cases, causing 341 831 deaths around the world.[1] With these statistics CC ranks fourth both as

the most frequently diagnosed cancer and the main cause of cancer death in women.[2]

Prior infection with high-risk human papillomavirus (HPV) is the major cause of developing CC.[3] That is why many countries adopted HPV test for their national screening strategy.

According to a WHO report, approximately 85% of the worldwide deaths caused by CC. occur in low-income and middle-income countries.[4] The correlation between social deprivation and CC incidence is also verified in high-income countries. A study carried out in France by Bryere *et al*[5] assessed the relationship between socio-economic environment and CC incidence. The results showed a statistically significant increase in the incidence of many cancers in the most disadvantaged populations, which was particularly notable for CC (21.1%).

This study concluded that, in total, nearly 15 000 cases of cancer could be avoided in France each year by improving the living conditions and promoting the health of the most disadvantaged populations.[5] Same findings were recently described in the USA where New York's lowest-SES (Socio-economic Status) neighbourhoods, populated predominantly by black and Hispanic residents, had CC. incidence rates 73% higher than the mostly White populations of the city's highest-SES neighbourhoods.[6]

Suboptimal adherence to recommended screening programme has been strongly correlated with the development of CC., and in several high-income countries more than half of CC.s, and 70% of death, occur in women who are inadequately screened.[7 8] A recent US study has shown that the proportion of women without up-to-date screening increased significantly from 2005 to 2019 (from 14.4% to 23.0%; p<0.001), with significantly higher rates in those living in rural vs urban areas (26.2% vs 22.6%; p=0.04) and those without versus with private insurance (41.7%vs 18.1%; p<0.001).[9]

Many strategies have been tested to improve screening uptake. These interventions were based on reminders to women using written letters,[10–15] text messages,[16] targeted media (videos, brochures or fact sheets),[17–19] on television,[20] and face-to-face educational programmes.[17 21] A study recently conducted in the USA has shown that health navigators triple the likelihood that women seeking assistance will make contact with Pap-smear test services, but most of them still fail to schedule Pap-smear testing despite assistance from navigators, illustrating that interventions beyond health navigators are needed to reduce CC disparities.[22]

Sending HPV self-sampling (SS) kits is suggested for women who do not attend physician-based CC screening (CCS), and this approach has demonstrated positive results. A French questionnaire study was conducted in two departments with a low participation rate in the screening programme.[23] Among 349 women participating in the study, 81% accepted the use of SS, preferably at home. The study showed also that knowledge about CC screening programme is significantly influenced by educational level.[23] Many studies performed in low-income countries also showed significant acceptability of SS.[24–26] A systematic review, with 18 studies including 22 118 women with low participation uptake, compared SS versus physician sampling, and showed that the two sampling methods are quite similar regarding the HPV detection rate.[27] Also SS showed a significant increase in acceptability and preference compared with physician sampling.[27]

Although most studies agree on the benefit of sending an SS kit, one of the limitations to its use is that the return rate is only about 20%, regardless of the country concerned,[28–33] meaning that 80% of these high-risk women are left out.

The main objective of our study is to overcome this barrier to screening, as this is where most of the failure occurs.

This research is the first to assess simultaneously two interventions targeting the return step of SS kits: financial incentive and the possibility to meet a healthcare professional when returning the HPV kit.

METHODS: PARTICIPANTS, INTERVENTIONS AND OUTCOMES

Patient and public involvement

It was not possible to involve the public concerned by the study in the steps of design and conduct of the trial. However, we intend to state recommendations based on women's opinions about our intervention through our qualitative study.

Study setting

This study is coordinated by the Dijon Bourgogne University Hospital. It is including women living in disadvantaged areas in four French departments, two in metropolitan France, Alsace and Bouches-du-Rhône and two in overseas France, Reunion Island and Martinique.

This study was authorised by the Ministry of Solidarity and Health to derogate from the organised national CCS programme.[34]

Study design, participant, randomisation, intervention and study calendar

Study design. The RESISTE study is a pragmatic multicentric, open-label cluster randomised trial using a factorial plan 2*2. The clusters are the IRIS (Ilots Regroupés pour une Information Statistique/grouped Unit for statistical information), which are the smallest administrative divisions of the French territory, designed to contain about 2000 inhabitants. IRIS are classified into five quintiles of deprivation, according to the European Deprivation Index,[35] quintiles 4 and 5 corresponding to the most deprived. However, this score is not adopted in Martinique, that is why we designed a model based on the 60% poverty line using INSEE (Institut National de la Statistique et des études Economiques/ National Institute of Statistics and Economic Studies) data.[36]

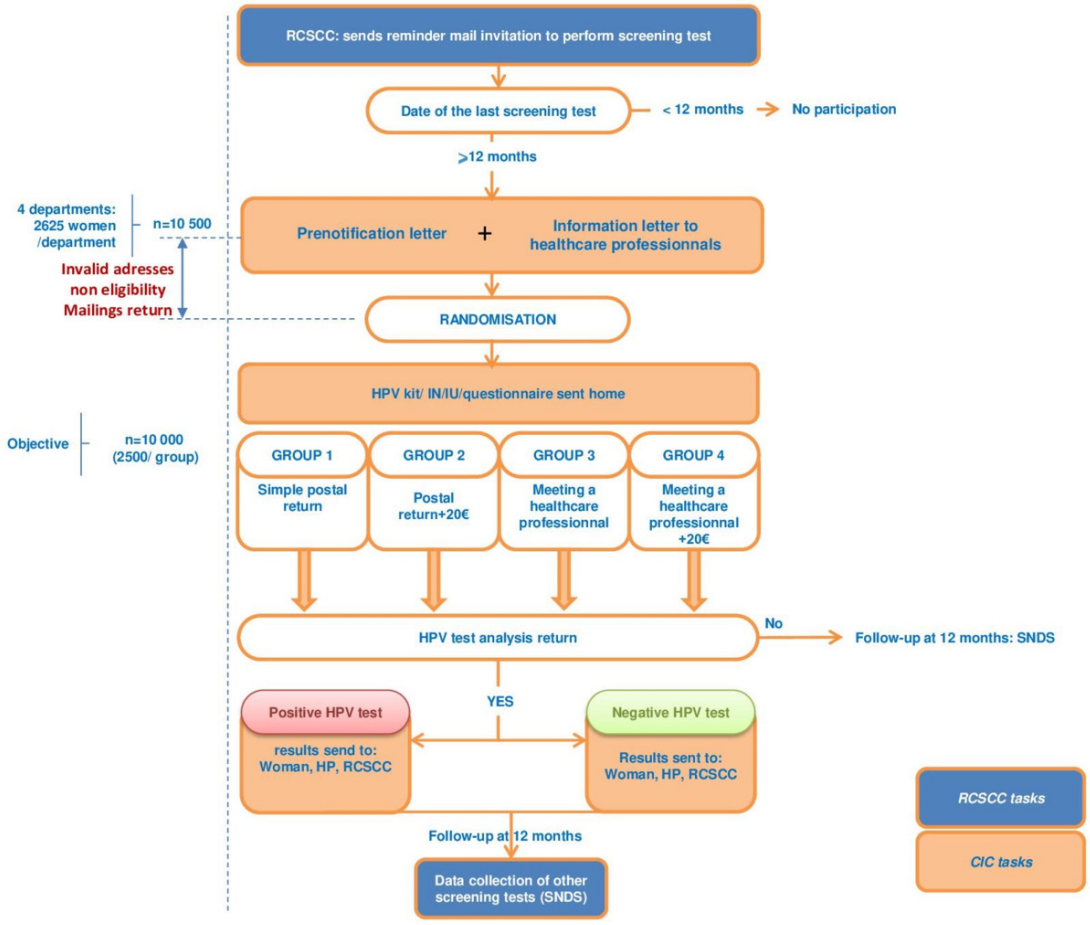


Figure 1 Study design and overall management of women according to their allocation group. CIC, clinical investigational centre; HP, health professional; IN, information note; IU: instruction for use; RCSCC, regional cancer screening coordination centre.

Participants. Women aged 30–65 years, covered by health insurance or SMA (State medical Assistance), living in IRIS 4 and 5 and followed by the Regional cancer screening coordination centres (RCSCC) in the four departments where the study is being conducted, eligible for CCS, and not having responded within 1 year to their last invitation for HPV-based CCS will be considered for inclusion. Women not eligible for CCS, as well as those whose addresses are declared wrong by the post office services, will not be considered for inclusion. Assuming a 5% rate of inaccurate addresses or ineligibility, a total of 10 500 women will be selected at random, 2625 in each of the 4 departments, to have at least 10 000 of them receiving the HPV SS kit.

Randomisation (figure 1). RCSCC (Regional Cancer Screening Coordiation Centres) in the four study departments, send us the addresses, of women to be recalled within the organised screening programme. These addresses are geolocated to identify, among the women to be recalled, those living in IRIS 4 and 5. Among these, a prenotification letter is sent to 2625 women, selected at random, in each of the 4 departments, to consider about 5% of women for whom the address is inaccurate or who are not eligible for screening (eg, women who have had a hysterectomy or having done a screening test during the last 3 years). Once the list of eligible women is established, the IRIS is randomised into four arms, stratified according to the level of deprivation (four or five of the EDI/Poverty line index). Randomisation will also consider the number of women included in each IRIS, in order to minimise the difference in average IRIS size in each arm, and therefore minimise the difference in arms size. Women not selected for participation in our study are being managed by their RCSCC according to the national screening programme.

Intervention. Women selected will receive an HPV-self sampling kit, containing information on how to perform the vaginal swab, information about the study, a small questionnaire to collect personal information and a prepaid envelope to send the sample back. According to the arm in which their IRIS of residency has been randomised women will be offered to put the swab in a mailbox using the prepaid envelope or to give it to the health professional of their choice, family doctor, gynaecologist, midwife, or pharmacist, and for each of these two modalities, women will be offered, or not, to receive a €20 voucher once their sample has arrived at the lab for HPV testing. The combination of these two interventions

Table 1 Factorial plan of the intervention

	Control B	Action B (delivered to a health professional)
Control A	**Group 1**: return by post without Financial incentive. Control A+control B)	**Group 3**: deliver to a health Professional without financial Incentive. (Action B+control A)
Action A (Financial Incentive)	**Group 2:** return by post with Financial incentive. (Action A+control B)	**Group 4:** deliver to a health Professional with financial Incentive. (Action A+action B)

will be analysed according to a multifactorial plan, ending up with 4 arms of 650 women in each of the 4 departments (2500 in each arm in total, see table 1).

This is a pragmatic trial so, apart from the intervention being tested, no other changes are made to the organised CCS programme. Women who will be tested HPV positive will be invited, by the screening centre to which they are affiliated, to have a cytological examination and further exams were ever needed, as per the last recommendations of the French High Authority for Health (Haute Autorité de Santé) (figure 2).

Implementation study

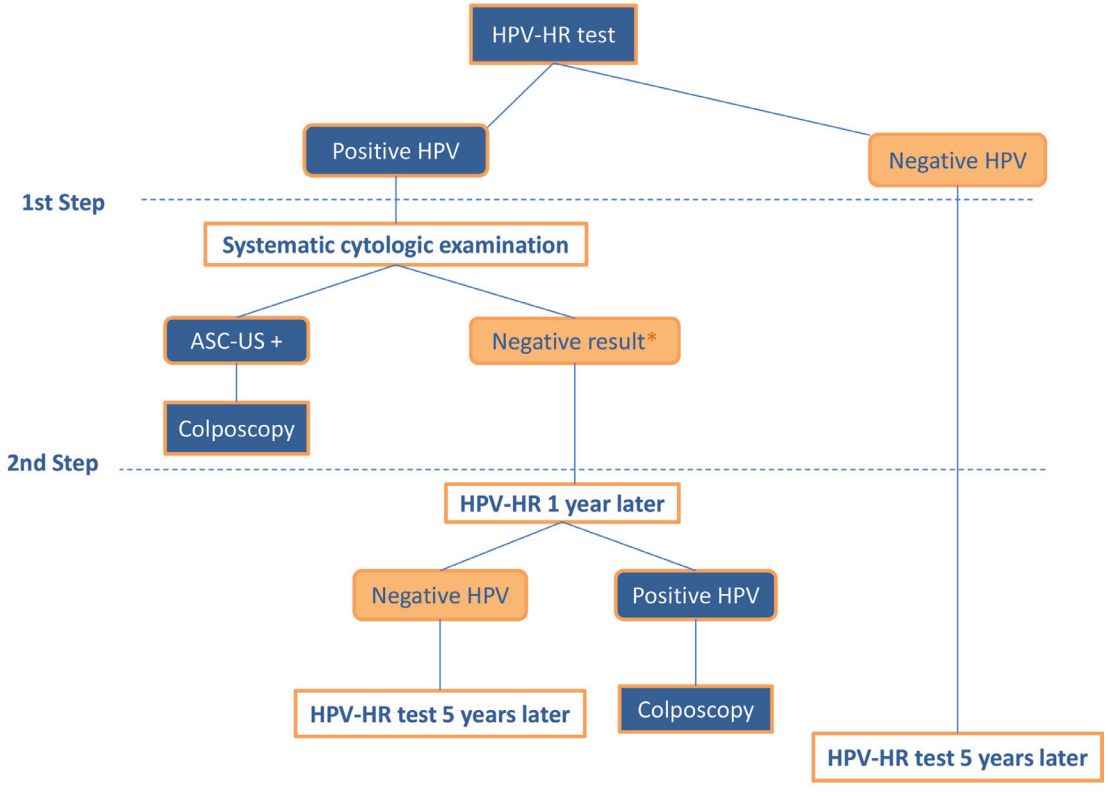
The efficacy assessment will be completed by an implementation study in Réunion Island and Alsace. A qualitative socioanthropological approach will be used in order to understand the mechanisms of production of the desired effects (and in particular the role of incentives), to identify the barriers and facilitating levers to its implementation, and to know if the results are transferable to other contexts. In addition, the qualitative study will explore the ethical aspects of incentive actions and research ethics from the point of view of the various actors.

Health technology assessment

The aim here is to assess the two incentives (incentive to meet a professional or financial incentive), from cost-effectiveness and budgetary impact point of view, and then to provide more general elements of analysis on the place of financial incentives in prevention, in particular for certain populations, as well as their acceptability.

Study calendar

The start of the study has been delayed because of the switch from pap smear to HPV test for CCS in France which has been decided in France in 2020. Nevertheless, the women have been selected and IRIS randomised in the two overseas departments. Prenotification letters have been sent to 2625 women in each of the 2 overseas departments, Reunion Island and Martinique, in November 2021 and December 2021, respectively, and we started



*negative result for intraepithelial or malignant lesion

Figure 2 French health authority (Haute Autorité de Santé) guideline for cervical cancer screening.

sending HPVss on the first week of January 2022. Inclusions have started in February 2022 in the Bouches du Rhône department, and will only be starting in January 2023 in Alsace, because of the delay in implementing HPV-based CCS in all age groups. The final results of the study are, therefore, expected in the second half of 2024.

Objectives

Primary objective

The primary objective is to assess the main effects of two incentives: financial incentive (intervention A) and/or meeting a healthcare professional (intervention B) after sending a HPVss kit at home.

Secondary objectives

To assess: (1) the frequency of detection of pre-cancerous lesions and early CC, (2) adherence of health professionals to the recommendations for downstream management in the two situations following a positive HPV test: abnormal or normal pap-smear test, (3) the elements of the implementation of the intervention, that is,the acceptability of women and health professionals, as well as the elements of context, geographical, sociocultural territory, density and nature of the healthcare offer that contributes to its effectiveness or ineffectiveness, (4) unexpected effects of the intervention, such as the generation of anxiety among women, or the overtreatment of cervical lesions, (5) the economic assessment of the two incentives compared with returning the SS-kit by mail or simply handing it to the healthcare provider, both in terms of cost-effectiveness analysis and budgetary impact.

Outcomes

Primary outcomes

The primary outcome is to assess, at 12 months after sending HPV kit, the proportion of women returning the HPV kit, or visiting a health professional, after receiving the kit, to perform a pap-smear or HPV test.

Secondary outcomes

For the secondary outcomes, assessment measures will include, 12 months after sending the kits:

1. Efficacy of early diagnosis: proportion of women with histological anomaly CIN2, CIN3, or early stage cancer (FIGO1a) among all women included in the study then among those who performed HPV test.
2. The efficacy of participation in screening: proportion of women:
   a. Having a full screening sequence: negative HPV test, pap smear (instead of HPV test), or positive HPV test followed by pap smear or colposcopy.
   b. Performing pap smear straight away (no HPV test).
   c. Returning the HPV test without performing any other screening tests.
3. The efficacy of medical care: the proportion of women receiving adequate management after:
   a. Identification of high-risk lesions (CIN2, CIN3 or early-stage cancer) based on pap smear results.
   b. Positive HPV test and normal pap smear.
4. Qualitative assessment of barriers to adequate CCS and the perception of the intervention by some of the participating women and health professionals.
5. Differential cost-effectiveness ratios associated with financial incentives vs no compensation and expressed in terms of cost per complication avoided.

Sample size calculation

According to the results of the Dutch modelling study showing that SS would have health benefits if the participation rates increases by at least 6%, we planned this study in order to have sufficient power to conclude on the effectiveness of the incentives assuming a 10% increase in the proportion of women performing HPV test or a pap-smear compared with the control group. The sample size calculation was also based on the following assumptions: 20% return rates of simple postal return group, no interaction between incentives, participants spreading over 100 IRIS, and intracluster correlation coefficient at 0.02. Analysis will be carried out independently in each department, with an alpha risk of 1%. The inclusion of 2500 women in each department will allow us to conclude on the effectiveness of the incentives with a power of 95% under the prespecified assumptions, that is, 625 in each arm and 1250 in each compared group according to the factorial plan. Calculation has been performed using R, clusterPower package, cpa.binary function.[37]

Recruitment

Information sheets and all other documents sent in the pre-notification postal mail and with HPV kit are available only in French.

In Réunion, Martinique and Bouches-du-Rhône, more than 2000 women are monthly reminded using mail invitation. In Alsace, the number of reminders is about 50 000 on yearly basis. That's why there is a high inclusion potential in all selected departments.

METHODS: ASSIGNMENT OF INTERVENTION

Allocation

Women meeting the inclusion criteria will be selected or randomly chosen if the number of eligible women exceeds the objective of inclusions. The arms are randomly allocated at the IRIS level by a structure independent of the investigator and the project manager, based on the EDI score (4 or 5) and the number of women included in each IRIS.

All study reporting and regulatory authorisations will be available on the study website under construction (www.etuderesiste.fr).

Blinding

By the nature of the study, blinding of the intervention is not possible. However, Zelen method[38] was adopted, meaning that women are allocated to one of the four arms of the protocol because of the randomisation of their place of residency (IRIS), and not on an individual

basis. So, women are only informed about their group allocation (HPV kit terms of return).

This is a very relevant method to avoid deception bias (women not receiving their preferred treatment) leading to recruitment difficulties. Moreover, the use of cluster randomised design allows to minimise the risk of contamination into different arms. Finally, all analyses will be conducted by a statistician blinded to allocation to the control or intervention groups.

METHODS: DATA COLLECTION MANAGEMENT AND ANALYSIS

Data collection methods

Clinical data will be collected through an e-CRF (electronic Case Report Form) on Cleanweb platform. Eligibility criteria, test results, and follow-up data will be collected from mailing returns, virology lab, RCSCC and SNDS (Système National des Données de Santé/National Health Data System) respectively. Surveys will also be entered into the e-CRF.

Administrative data related to sending a pre-notification letter, HPV kit and test results dates will be collected using an Access database.

For the cost-effectiveness study, data will be extracted from the national health insurance databases SNDS: for a period of 2 years before and 1 year after sending HPV kit. Analysis of these data will be performed by Hospinnomics, (Paris School of Economics- Assistance publique Hôpitaux de Paris).

Data management

All data management will be carried out at Dijon University Hospital. A data manager will check the consistency of data collected on the e-CRF. Queries will be generated if missing or inconsistent information are found. All coherence criteria are detailed in the data management plan.

Data collected from SNDS will be managed by a specialised team in health data analysis, then, will be chained to e-CRF data for statistical analysis.

Statistical method

Descriptive analysis

Women's characteristics (age, type of health insurance, referent doctor existence, HPV vaccination status, inclusion period) and IRIS characteristics (department, geographical contest, population density, deprivation index) will be described for each arm and groups being compared (arms 1+2 vs arms 3+4 groups, ie, women having to return the sample by mail vs to a health professional, and arms 1+3 vs arms 2+4, ie, women not benefiting from a voucher vs those who do). Qualitative variables will be expressed with their 95% CI and compared using the χ^2 test. For the quantitative variables, mean (±SD) or median (IQR) values will be calculated.

Comparison will be performed using variance analysis or a non-parametric test according to data distribution.

Primary outcome analysis

The primary criterion is the proportion of women performing a CCS test (HPV kit return, pap smear after HPV kit reception). It will be described in each arm of each department.

The main effects of the two actions will be simultaneously estimated by the mean of a generalised estimating equations (GEE) using a Logit link function in order to consider the intracluster correlation. Their respective effect will be estimated through the OR and its 99% CI using GEE approach and tested with bilateral test of Wald (α=0.01) for each department.

OR will also be adjusted for individual variables (age, inclusion period) and contextual variables (IRIS, deprivation index) that could have an a priori prognostic value on the response rate and that will be listed before analyses.

The synergistic or antagonistic effect will also be investigated by introducing an interaction term between the two actions. In case of significant interaction between action A and action B, marginal effects would not be appropriate.[39] Then, in addition to the model with the interaction term, three different estimations would be reported: (1) group 1 vs group 2 (efficacy of action A) (2) group 1 vs group 3 (efficacy of action B) (3) group 1 versus group 4 (efficacy of action A+B).

Analysis of HPV kit return rates will be carried out in each department. In case of consistency of the effects between the four departments, the global effect of actions A and B will be estimated.

Secondary analysis

Secondary analysis of the primary outcome

Secondary analyses will test whether the effect of each action depends on: health insurance coverage, deprivation score of IRIS, and the age of women. These analyses will be carried out on an exploratory basis to generate a hypothesis.

Secondary outcome analysis

Analysis of secondary outcomes will be carried out using the same approach described above.

The efficiency of the intervention will be determined by a cost-effectiveness ratio representing the cost per complication avoided.

Significance threshold

The main analyses, supposing no interaction between the incentives, would be performed in each department at 1% alpha risk.

The study sample size allows performing subgroup analyses, especially in the case of qualitative interaction. This would lead to three comparisons, 2 to 2 arms, although this is not the main assumption for the sample size calculation. Then a threshold would be defined at 0.017 (0.05/3) controlling the alpha risk at 5% in each department. Of note, the power of these analyses would be >80% assuming a 10% increase in the proportion of women performing HPV tests or a pap smear compared with the control group.

Statistical software

Analysis will be performed using R or SAS software, using the latest version. Statisticians will be blinded to the study groups.

Analysis of qualitative survey

To guide data interpretation and transferability of results, we will use ASTAIRE tool (AnalySis of Transferability and support for Adapting InteRventions to health promotion). Different grids are available, for our study RESISTE, we will choose 'assistance grid' for the design and description of an intervention to make it potentially transferable.

Analysis of cost-effectiveness

A differential cost-effectiveness ratio associated with each arm of the intervention will be calculated by comparing the difference in average costs with the difference in average efficiencies. According to the French National Health Agency's guidelines, the analysis will be carried out from a societal perspective (all payers: mandatory health insurance, complementary health insurance, patients).

In order to test the robustness of the conclusions, probabilistic and deterministic sensitivity analysis will be carried out on the parameters likely to influence the results.

METHODS: MONITORING

Data monitoring

As the study was deemed interventional with low risk by the ethics committee, legally, no formal monitoring is requested. Nonetheless, the study will be monitored for quality and regulatory compliance. The sponsor (Dijon Bourgogne University Hospital) will supervise monitoring sessions. The frequency will depend on inclusion rates, questions and pending issues from earlier audits.

Harms: steering data and safety monitoring committees

The coordinating centreat University Hospital Dijon-Bourgogne, Clinical Investigation Centre (CIC INSERM 1432), is assigned the responsibility of all study aspects: ethical, regulatory, study coordination, data management and publication strategy.

Steering committee composition: one representative of each study screening centre, a methodologist, a sponsor representative, the study investigator and the project manager.

This committee will meet regularly to assess study progress and try to solve pending issues.

Once a year, a face-to-face meeting will be organised.

On the other hand, we intend to set up a scientific committee composed of a methodologist, an ethics specialist, a gynaecologist, two general practitioners, a pharmacist, a midwife and a representative of a patient's association.

The main task of this committee is to ensure that the study is progressing according to the protocol, suggests, if applicable, modification or study stop (after discussion and justification).

The study could be stopped in case of poor inclusion rate, bad data quality, low implementation study rates in the considered departments, control group contamination or any other reason making the study unnecessary or non-ethical.

Auditing

The study has been deemed interventional with low risk by the ethics committee, so, by law, no formal auditing will be necessary.

ETHICS AND DISSEMINATION

Research ethics approval

Ethics approval was given by the South-West Overseas Ethics Committee on 2 April 2020. The protocol was amended thereafter.

The study obtained funding from the French Ministry of health in 2019 (PREPS-19-0008) and the National Cancer Institute (INCa DePrev…). The study is promoted by Dijon Bourgogne University Hospital (France).

Authorisation for holding the computerised databases was granted on 14 September 2021 by the national data monitoring committee (Commission Nationale Informatique et Libertés, CNIL). This long delay was due to the long processing deadlines of CNIL after sending questions about data flow to maintain data privacy for enrolled subjects.

The study was registered in clinicalTrials.gov with the identifier NCT04312178 on 18 March 2020, at the French Research Agency with identifier 2020-A0022-37, and at CNIL with a request for authorisation number 920 276.

Protocol amendment

The study is currently running according to the fourth version, of 10 June 2022, approved by the ethics committee on 29 July 2022.

Consent or assent

The study is classified as interventional research with low risk according to the first-approved version of the protocol and is considered part of the organised screening programme. No formal consent is thus required for recruitment. However, women have the right of objection to collecting follow-up health data.

Confidentiality

Before inclusion in the study, no identifying data will be sent to us, only ID numbers will be used for geolocation. Personal data will only be available for the coordinating centre after women's selection. During the trial and after, personal information of enrolled women will be saved on CHU Dijon Bourgogne local servers. These servers are highly secured.

Access to data

The final trial dataset will only be accessible to the investigational team at CIC (clinical investigational centre) CHU (University Hopsital Centre) Dijon Bourgogne.

Ancillary and post-trial care

As the study does not affect the usual care, no post-trial care has been scheduled. No ancillary studies have been planned so far.

Dissemination policy

A manuscript with the primary study results of the intervention study will be published in a peer-reviewed journal. Separate manuscripts will be written on each of the secondary aims, and will also be submitted for publication in peer-reviewed journals.

The first part of the qualitative survey has been published early in 2022,[40] and briefly presented at Eurogin 2022 meeting in Dusseldorf.

The results will be presented at scientific meetings, and specific communication will be organised to target health professionals, policy decision-makers, regulatory bodies and women.

Recruitment is ongoing; the first women's group was recruited on 6 January 2022 on Reunion island.

DISCUSSION

This will be the first study to provide rigorous evidence regarding the effectiveness of two incentive actions using a factorial plan. Furthermore, the inclusion of departments with very different cultural, geographical and socioeconomic backgrounds is a strong point, as it allows territorial specificities to be considered. This approach could facilitate the generalisation of the strategy or at least analyse the contextual elements that contribute to the success or failure of the proposed interventions. The French Health Agency emphasised the need for such a study, especially for under-screened women, or those living in remote areas.[41] Many studies focused on the efficacy evaluation of SS versus standard clinician-sampling or the acceptability of the intervention.[42–47] But to our best knowledge, our study is the first to assess the combination of two complementary incentive approaches, one focusing on removing motivation barriers to screening for women, and the other aiming to assess the role of interaction with a health professional in improving women's adherence to the screening cascade following a positive HPV test.

Qualitative research prior to our trial was carried out on Reunion island with 35 women and 20 healthcare providers.[40] The purpose of this study was to understand screening barriers and assess the anticipated acceptability of our intervention. Results were interesting, in fact, among all women who could be eligible for the Resiste trial, 90% expressed their wish to perform SS. The study also outlined the lack of awareness regarding disease origins and prevention for the majority of women interviewed. That's why the role of health professionals could be very important to overcome this barrier. However, the same study found that 74% of women who had prior visits mentioned the lack of information shared by physicians when conducting screening tests, and 17% felt embarrassed to ask for further details.[40] Offering the possibility to meet healthcare providers seems to be effective when conditioned with appropriate information time. Moreover, 74% of women had concerns about performing SS, mostly related to the ability to understand instructions (54%), quality of self-collected sample and storage conditions (22%).[40] Professionals focused on the need to reassure women about their worries, by providing remote or on-site support with the help of health professionals and territorial health actors.[40] That's why the involvement of health actors is one of the areas we would like to explore in our study.

However, this screening strategy may have several limits; for example, homeless women or those whose addresses are not updated in the SC databases cannot be reached by our intervention. That is why other solutions should be considered for these populations.

Finally, if the results of our study prove to be significant, the adoption of the proposed strategy will have to overcome certain obstacles, such as the definition of a standard deprivation score applicable at the national level, the implementation of geolocation tools for screening centres in order to carry out interventions adapted to the place of residency, or the study of specific solutions for women living in remote areas and for whom postal items are difficult to distribute. On the other hand, the use of financial incentives raises ethical and acceptability issues for health authorities, health professionals and the end users, even for interventions that have demonstrated a health benefit.[40] Many of these topics will be assessed by our study.

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