**Project Protocol**

**Topic**

Evaluating the effectiveness of different invitational strategies for increasing participation of cervical cancer screening

**Scientific title**

Evaluating the effectiveness of different invitational strategies for cervical cancer screening using stratified randomized controlled trial

**Study hypothesis**

The telphone-call reminding only and telphone-call scheduled appointment can increase the participating rate of cervical cancer screening compared with ordinary invitation by postcards or letters.

no specific invitation.

**Background and study aims**

In Taiwan, Pap smear test for cervical cancer screening has been implemented since 1995, previous study has shown that Pap smear test can substantially decrease the cervical cancer incidence and mortality rates. However, the regulated triennial participate rate, a policy key performance index, has never reached 70% in Taiwan, indicates the methods of inviting people to attend the Pap smear test still have room to improve. Because of the universal coverage of health insurance in Taiwan, the utilization of health care is high. Outpatient visits provide a good opportunity to deliver screening services.

Therefore, 6 hospitals (see Figure 1 and Table 1) in Changhua County were invited to join this evaluating program for different invitation strategies.

The aim of this study was to assess the effectiveness of increasing the participation rate of cervical cancer screening by different invitational strategies, especially for telphone-call reminding only (TCRO) and telphone-call scheduled appointment (TCSA).

**Study design**

Stratified randomized controlled trial (see Figure 2)

After the linking of National Cervical Cancer Registry and 6 hospitals administration database, we stratified those women into 3 groups: clinical visits of 1-3 time, >=4 times, and no record at all, according to yearly frequency of outpatient visits in each hospital between 2006/1/1 and 2006/12/31. Then, the randomized procedure might conduct the computer and generate the random number within each group for random assignment into no-invitation, postcard, telephone-call reminding only, and telephone-call scheduled appointment.

**Participants**

Those women live in Changhua County and aged 30-69 without Pap smear test more than 3 years were eligible subjects for this study.

**Intervention**

We conducted the stratified randomized controlled trial to evaluate the different intervention of invitation on cervical cancer screening. First, we linked the Pap smear registry data with 6 hospitals administration database then stratified subjects by times of hospital visit between 2006/1/1 and 2006/12/31, including 1-3 time, >=4 times, and no record. It because the times of hospital visit can represent the residents’ affiliation or royalty on different hospitals. Therefore, this factor has been treated by stratification. We had four interventions as different invitation strategies:

1. No-invitation:

Generally speaking, there is common propaganda by mass media for cervical cancer screening in Taiwan, such as TV, website, radio, etc. In this study, we did not propose any specific invitation for this group. But, women might take Pap smear by their own intention and schedule or be “caught up” by the reminder during their outpatient medical visits.

2. Postcard reminding:

The address information could be ascertained and collected from Changhua County Population Registry and also National Cervical Cancer Registry System. We conducted the general postcard to remind those women that they should take the Pap smear to protect your health and you can go to any clinic/hospital to ask this service.

3. Telephone-call reminding only (TCRO)

For those eligible women who had clinic visit(s) in either one of these 6 hospitals, their contact information would be update by hospital registry system. The specific nurse assistants would have telephone call for each woman in this arm. They would remind that they did not have Pap smear longer than 3 years, so please they go to clinic/hospital to take Pap service as soon as possible. We designed three times telephone call and one call in each month continuously.

4. Telephone-call scheduled appointment (TCSA)

For those eligible women who had clinic visit(s) in either one of these 6 hospitals, their contact information would be update by hospital registry system. The specific nurse assistants would have telephone call with scheduled appointment for each woman in this arm. The scheduled appointment was provided for each woman according to their available date and time and clinic scheduled service during the phone call invitation and conversation.

**Quality Control for Invitation**

To assure the quality of reminding and invitation for eligible cervical cancer screening following the standard procedure, first, we invited the local hospitals to join this program and held serval consensus meeting with those who were responsible for the task of cervical cancer screening in each hospital. The one-day training course was provided for those call/recall nurse assistants before intervention starting. The training course included eligible lists of this study by different arms, including postcard, telephone-call reminding only (TCRO), and telephone-call scheduled appointment (TCSA). The lists in EXCEL file for TCRO and TCSA were embedded the variables of dates of three times telephone invitation, results after call, and notes after contacts. For the lists in EXCEL file of postcard, we provided the full address by each subjects for postcard preparation, and the sending dates were also recorded.

To standardize the invitation procedure, the contents of TCRO and TCSA were standardized before implementation. A course of training is needed for the nurses at the OPD to acquire the skill of invitation and adopt a positive toward the invitation process. For the TRCO, the specific assistants would remind that they did not have Pap smear longer than 3 years, so please they go to clinic/hospital to take Pap service, do not forget. For the arm of TCSA, the specific assistants would let the women know she did not take Pap smear more than 3 years and scheduled appointment was provided for each woman according to their available date and time to meet clinic scheduled service during the phone call invitation and conversation.

**Confidentiality for the data management**

1. Linking for the Population Household Registry, National Cervical Cancer Registry, and 6 hospitals administration database

In our study, the big data management for the first stage was centralized, executed and assigned one specialist and expertise on statistical software who is government official employee, including data linking, randomization, generating invitation lists by each arm and hospital.

1. Study implementation

For each hospital, the specific assistants has been trained by training course before invitation implementation and signed the confidential agreement during this project. The telephone call and all records were collected by these assistants in person and keep those data by password. They also used the password in separate mail for result files sending.

**Primary outcome measures**

We defined the primary endpoint was whether those women participated Pap smear or not within 4 months follow-up duration since first invitation. All the Pap smear dates were ascertained from Taiwanese National Cervical Cancer Registry System. All the telephone-call invitation was collected by specific data sheet, including date and results. The below figure illustrate the follow-up definition. Three times invitation were carried out one-call in one month and allow one month for study observational follow-up. Therefore, total is 4 months length for study implementation. For example, the subject A would be recorded as completed screening case and calculated the follow-up duration between first date of invitation and the date of taking Pap smear. The subject B was the censored subject as incomplete case and count the follow-up time as months.



**Secondary outcome measures**

None.

**Data Collection**

1. Data collection on invitation implementation

The 4 types’ invitational strategies for TCRO and TCSA were collected three dates of telephone calls, reaching study subjects or family relatives, and notes after contacts.

2. Data collection for primary outcome

We ascertained the primary outcome by linking the database of National Cervical Cancer Screening database. The date of taking Pap smear can be retrieved after the invitation initiated. For the completed screening subjects, the observational duration was calculated by first date of invitation and date of Pap smear test.

**Statistical plan and sample size, power calculation**

**Statistical analysis**

We conducted univariate and multivariable logistic regression models to analyze the effectiveness in different hospital visits and different strategies compared with no-invitation arm, also used Poisson regression taking hesitating period for participating the Pap smear test into account.

**Sample size determination**

For the sample size determination, assumed the statistical power of 90% and two-tailed α-level of 5%, the minimal sample size requirement is 102 subjects based on the increasing 10% participation rate based on 15% and 10% participation rate within 4 months for telephone-call scheduled appointment and no-invitation groups, respectively. Therefore, in both arms of clinical visits 1-3 and >=4 times, we decided randomly allocated 200, 200, 150, and 150 for no-invitation, postcard, telephone-call reminding only (TCRO), and telephone-call scheduled appointment (TCSA). In no-record stratification, we decided to generate 300 and 300 subjects for no-invitation and postcard, respectively.

Based on the minimal sample size with 150 for each hospital, the power would be expected to reach 97.6%, assumed 10% increasing participation. In this study, combing 6 hospitals samples, the power would be reached more than 99%. Each sample size was demonstrated in Figure 2.

**Possible benefits and risks of participating**

This program were expected to increasing the participation rate of cervical cancer screening. There are no risks of taking part in the study.

**Grant support**

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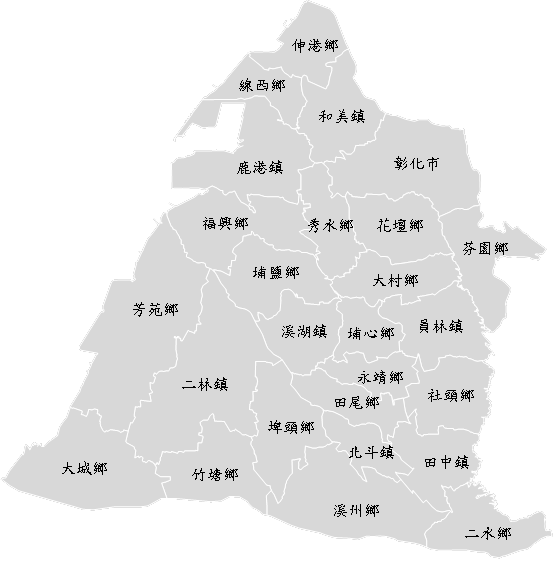
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**Ethics approval**

The project for the implementation was approved and authorized by Health Promotion Administration, Ministry of Health and Welfare (DOH97-HP-1505). The data analysis and evaluation was reviewed and approved by Ethics Committee of Chang Gung Memorial Hospital, 15/2/2016, ref: 104-9946B. The English certificate of IRB approval has been demonstrated in Appendix.

**ISRCTN registry**

Figure 1. The 6 hospitals in Changhua County, Taiwan



**彰化基督教醫院**

**秀傳紀念醫院**



**彰濱秀傳紀念醫院**



**彰化基督教醫院鹿基分院**



**彰化基督教醫院二林分院**



**員林何醫院**



Figure 2. The flowchart diagram of stratified randomized controlled trial for cervical cancer screening invitation strategies

Table 1. The Background of 6 hospitals in Changhua

|  |  |  |  |
| --- | --- | --- | --- |
| Hospital | Level | Address | Beds |
| 彰化基督教醫院  Changhua Christian Hospital | Medical Center | 500彰化市南校街135號  135 Nanxiao St., Changhua City, Changhua, 500, Taiwan | 1672 |
| 彰濱秀傳醫院  Chang Bing Show Chwan Memorial Hospital | Regional Hospital | 505彰化縣鹿港鎮鹿工路6號  6 Lugong Rd., Lukang Zhen, Changhua, 505, Taiwan | 1126 |
| 秀傳紀念醫院  Show-Chwan Memorial Hospital | Regional Hospital | 500彰化市中山路一段542號  542, Sec. 1 Chung-Shan Rd., Changhua, 500 Taiwan | 747 |
| 彰化基督教醫院鹿基分院  Changhua Christian Lukang Branch Hospital | Local Hospital | 505彰化縣鹿港鎮中正路480號  480, Jhongjheng Rd., Lukang Township, Changhua, 505, Taiwan | 273 |
| 彰化基督教醫院二林分院  Changhua Christian Erlin Branch Hospital | Local Hospital | 526彰化縣二林鎮大成路一段558號  558, Sec. 1, Dacheng Rd., Erlin Township, Changhua, 526, Taiwan | 294 |
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