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研究課題名(和文) An innovative system to investigate HPV vaccine efficacy and increase cervical screening in young women

研究課題名(英文) An innovative system to investigate HPV vaccine efficacy and increase cervical screening in young women

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研究成果の概要(和文)：若い女性の子宮頸がんが増加しており、この多くの女性達は子宮頸癌検診を受けていない。本研究は、受診率向上へのHPV自己採取検査(SS)の有効性を検討した。検診受診者のSS道具の受入れや安全性に関する実現可能性の研究と、30歳未満の道具の受入れに関する質的研究を行った。職場健診で、医師による子宮頸癌検診とHPV検査の前に受けたSSは、痛みと恥ずかしさが有意に少なく、よりリラックスでき、指示も分かりやすいと回答した。安全性への懸念は報告されていない。しかし、道具が注射器や台所用品のようだと若い女性の感想があり、小さな道具が好まれる傾向があった為、これからより小さい道具を用いた研究を行う予定である。

研究成果の概要(英文)：Cervical cancer is increasing in Japanese women of reproductive age. Most women who develop cervical cancer are under-screened. This study investigated whether HPV self-sampling (SS) might be an effective means of increasing screening uptake in young Japanese women. It took place in two parts: a feasibility study to examine the acceptability and safety of the SS device in women already attending for screening and a qualitative study investigating the acceptability of the device in women <30yrs of age. Women attending their annual workplace check-up underwent SS followed by a physician-led Pap smear and HPV test. Women found SS significantly less painful, less embarrassing and could relax more ($p<0.001$). They also found the instructions easy to use. No safety issues were reported. However, in the second study, younger women thought the SS device 'looked like a syringe' or a 'kitchen utensil' and they preferred a smaller device. Further studies will take place with the smaller device.

研究分野：公衆衛生学・疫学

キーワード：子宮頸がん 検診 HPV 自己採取HPV検査 受診向上

1. 研究開始当初の背景

Cervical cancer incidence and mortality is increasing in Japan, especially in women of reproductive age¹. While HPV vaccination status will play an important role in a woman's lifetime-risk for cervical cancer, at present, most women who develop cervical cancer are either under-screened or never screened. Non-participation in screening undermines the efficiency of a cervical screening programme, which depends to a large extent on high population coverage. Organized cervical screening coverage in Japanese women is between 30%-40%¹.

Strategies that overcome barriers to screening are essential to improve uptake, particularly in hard-to-reach women. HPV self-sampling for high risk oncogenic HPV types (hereafter self-sampling) is a simple alternative to clinician-led speculum examination, which allows women to take their own sample using a brush, lavage or other collection device in the comfort and convenience of their own home.

Furthermore, one further advantage of HPV self-sampling it is gives us the opportunity to obtain vital epidemiological data on HPV prevalence in both vaccinated and unvaccinated cohorts.

One review of the clinical accuracy of HPV self-sampling versus physician-led screening found that self-sampling was "at least if not more" sensitive for cervical intraepithelial neoplasia grade 2 or more (CIN2+) than conventional cytology. It also indicated that self-sampling may improve compliance to screening participation in non-attendees since women report less embarrassment, less discomfort and higher levels of relation during the test compared to physician sampling². However, no study on the acceptability of HPV self-sampling has been undertaken in Japan.

2. 研究の目的

This study aimed to investigate whether HPV self-sampling could help engage young Japanese women who had never attended for cervical screening to participate in cervical screening and evaluate the prevalence in high risk HPV infection in vaccinated and non-vaccinated cohorts.

3. 研究の方法

(1) Feasibility study

To ascertain the usability, acceptability, and safety of the self-sampling device, we first of all carried out a pilot study in

women already attending for screening as part of their annual workplace health check-up. This study took place between November 2013 and March 2014 and involved 203 women aged between 20 and 42yrs (Figure 1).

Women underwent self-sampling, a physician led Pap smear and then filled out a questionnaire developed for a Japanese population and based on previous research on HPV self-sampling acceptability³. It assessed socio demographic characteristics, history of tampon use, comprehension of self-sampling instructions, attitudes towards the size of self-sampling device, attitudes towards the self-sampling and physician-led test, ease of use and intention to use self-sampling if it offered as a screening option in the future.

Attitudes towards both tests investigated embarrassment, pain (physical discomfort), unpleasantness (mental discomfort), confidence that the test had been conducted correctly, and degree of relaxation during both tests on a four-point scale ranging from 'not at all' to 'extremely'. Acceptance of self-sampling was assessed by stated willingness to use the test again in the future.

The HPV test was Hybrid Capture 2 (HC2) (Qiagen, Germany) and the HPV self-sampling device was the Evalyn brush (Rover, the Netherlands).

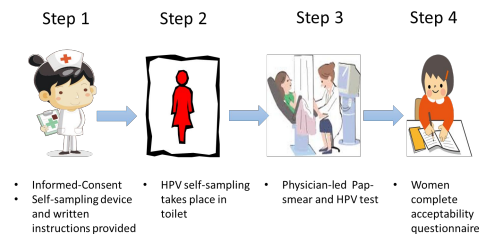


Figure 1. Study flow

(2) Qualitative study

We interviewed 20 young women under the age of 25 years to get their opinion on the Evalyn self-sampling brush and whether they might prefer a smaller, less brightly colored device that had been devised by an engineering student of Asian origin in Canada (Her Swab, Eve Medical, Canada).



4. 研究結果

(1) Feasibility Study

Usability

Over 90% of participants found the length and size of the device to be just right and the instructions 'easy' or 'very easy' to understand (Figures 2a, 2b and 2c)⁴.

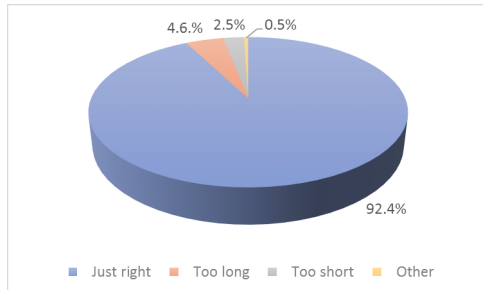


Figure 2a Impressions of length of the self-sampling device

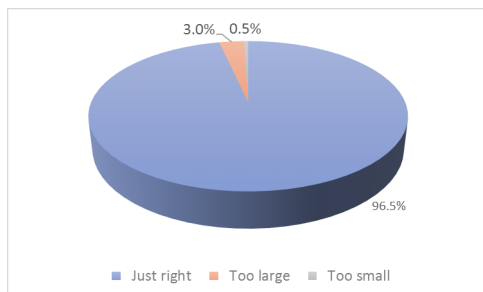


Figure 2b Impressions of size of the self-sampling device

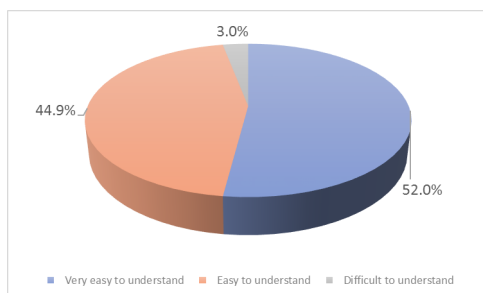


Figure 2c Comprehension of Instruction sheet

Acceptability

Compared to physician-led testing, women found self-sampling significantly less painful, less embarrassing and could relax more ($p < 0.001$). The results of the paired-sample t-test are shown in Table 1⁴. A p-value of < 0.05 was considered statistically significant.

Table 1 Differences in perceptions of both tests

| Feeling during the test | Physician Sampling | Self-Sampling | t-test for differences ^a | | |
|-------------------------|--------------------|---------------|-------------------------------------|-----------------|---------|
| | | | t | df ^b | p-value |
| Embarrassed | 1.74 | 1.14 | 9.19 | 146 | <0.0001 |
| Pain | 1.53 | 1.29 | 3.76 | 146 | <0.0001 |
| Unpleasantness | 1.14 | 1.18 | -0.93 | 146 | 0.36 |
| Degree of relaxation | 2.27 | 1.90 | 5.04 | 146 | <0.0001 |
| Confident done properly | 1.37 | 2.17 | -9.93 | 146 | <0.0001 |

df= degrees of freedom

Apart from confidence that the test had been performed correctly, participants had a better or similar experience with self-sampling compared to a physician led test (Figure 3).

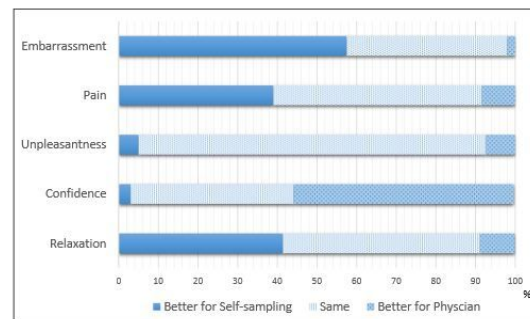


Figure 3. Comparison of experiences with both tests

Accuracy and safety.

No safety issues were reported. Concordance of both tests was good. While there were no cases of CIN2 or more, the Kappa agreement for LSIL was high at 0.82⁴.

(2) Qualitative study

Based on the results of quantitative studies carried out in the UK^{5,6}, where young Asian women found the Evalyn brush to be intimidating and 'looking like a utensil to clean the shower tiles', we interviewed 20 young Japanese women to get their opinions on the Evalyn brush compared to a newer option, Her Swab. Similar to the UK study, we found that Japanese women in their 20s regarded the Evalyn brush to be intimidating and compared it to a medical syringe. They also found the bright pink color to be 'too loud' and 'similar to a kitchen utensil'. All 20 women stated they would be more comfortable using the smaller, pastel-colored Her Swab. For this reason we chose to switch the device we would use in the study from the Evalyn Brush to Her Swab. Since Her Swab is not yet available for commercial use in Japan, it took over 18 months for us to be able to obtain the devices and the study investigating acceptability in women < 30 yrs, as well as high risk HPV prevalence will take place in 2017.

Conclusions

The result of this first study on HPV self-sampling acceptance in Japanese women are encouraging. They indicate that HPV self-sampling might be an acceptable alternative to conventional physician led cervical screening, if women can be

assured about the accuracy of the test results. Women had no issues with the size of the sampling device and found the instructions for use easy to follow in an unsupervised setting, regardless of SES. However, to assess whether self-sampling may be an effective tool to increase cervical screening rates in Japanese women >30yrs, further large-scale studies are needed.

References:

1. Cancer Registry and Statistics. Cancer Information Service, National Cancer Center, Japan, <http://ganjoho.jp/regstat/statistics/dl/index.html> in Japanese).

2. Schmeink CE, Bekkers RL, Massuger LF, Melchers WJ. The potential role of self-sampling for high-risk human papillomavirus detection in cervical cancer screening. *Rev Med Virol.* 2011; 21: 139-53.

3. Waller J, McCaffery K, Forrest S, Szarewski A, Cadman L, Austin J, et al. Acceptability of unsupervised HPV self-sampling using written instructions. *Journal of medical screening.* 2006;13(4):208-13.

4. Hanley SJ, Fujita H, Yokoyama S, Kunisawa S, Tamakoshi A, Dong P, et al. HPV self-sampling in Japanese women: A feasibility study in a population with limited experience of tampon use. *Journal of medical screening.* 2016;23(3):164-70

5. Cadman L, Ashdown-Barr L, Waller J, Szarewski A. Attitudes towards cytology and human papillomavirus self-sample collection for cervical screening among Hindu women in London, UK: a mixed methods study. *The journal of family planning and reproductive health care / Faculty of Family Planning & Reproductive Health Care, Royal College of Obstetricians & Gynaecologists.* 2015;41(1):38-47.

5 . 主な研究論文等

Publications (3)

1. ハンリーシャロン、子宮頸がん予防のための HPV ワクチンと自己採取 HPV 検査の普及が急務、Opinion、(2) 45, 2014 (査読なし)

2. Hanley SJ, Fujita H, Yokoyama, S, Kunisawa S, Tamakoshi A, Dong, P, Kobayashi N, Watari H, Kudo M, Sakuragi N, HPV self-sampling in Japanese women: A feasibility study in a population with limited experience of tampon use, *J Med Screen*, 23(3):164-70, 2016, DOI: 10.1177/0969141315625702 (Peer-reviewed)

3. Hanley SJ, Fujita H, Peixin D, Tamakoshi A, Sakuragi K, Challenges in breast and cervical cancer control in Japan, *Lancet Oncology*, 17(9), e372, 2014, DOI: 10.1016/S1470-2045(16)30411-9 (Peer-reviewed)

Presentations (11)

1. Sharon Hanley: A Comparative Study of Attitudes toward HPV Self-sampling and Physician-led cervical Screening in Japanese women, Asia-Oceania Research Organisation on Genital Infection and Neoplasia (AOGIN 2014) Peking, China, April 16th, 2014
2. Sharon Hanley: A Pilot Study Investigating Acceptability of HPV Self-Sampling in Japanese Women of Reproductive Age, 20th World Congress of Epidemiology, Anchorage, USA, 20th August 2014
3. Sharon Hanley: Acceptance in HPV self-sampling in Japanese women- Does History of Tampon use matter, 28th International Papilloma Virus Conference, Seattle, USA, August

22nd, 2014

4. シャロン・ハンリー：新たな子宮頸がん検診システムの構築：働く女性の自己採取 HPV 検査の受容の検討、第 29 回日本女性医学学会学術集会、都市センターホテル、東京都、2014 年 11 月 2 日
5. ハンリーシャロン、新たな子宮頸がん検診システムの構築：札幌市内の働く女性の自己採取 HPV 検査の受容の検討、第 66 回北海道公衆衛生学会、北海道大学 学術交流会館、北海道、札幌市、2014 年 12 月 2 日
6. ハンリーシャロン、HPV Self Sampling: A Novel Method to Increase Cervical Screening Uptake in Japanese Women, 第 25 回日本疫学会学術総会、愛知県、名古屋市、2015 年 1 月 24 日
7. ハンリーシャロン、The Role of HPV Self-Sampling to Increase Cervical Cancer Screening Uptake: A Study on Acceptance, Usability and Clinical Accuracy 第 67 回日本産科婦人科学会学術講演会、パシフィコ横浜、神奈川県、横浜市、2015 年 04 月 10 日
8. Sharon Hanley、Global Trends in Cervical Cancer Prevention: Screening and Vaccination, 1st International Conference on Preventing Cervical Cancer Through Education, Vaccination and Screening, Hokkaido University Frate Hall, Sapporo,

Hokkaido, March 15th, 2016,

9. ハンリーシャロン、子宮頸がん予防のグローバル戦略：一次予防と二次予防 -自己採取 HPV 検査を含めて、第一回国際シンポジウム、子宮頸がん予防の戦略：検診とワクチン、北海道大学学術交流会館、北海道、札幌市、2016 年 03 月 16 日
10. ハンリーシャロン、HPV 検査を応用した新しい検診システム導入への取り組み、第 64 回北日本産科婦人科学会総会・学術講演会、ロイトン札幌北海道、札幌市 2016 年 09 月 20 日
11. ハンリーシャロン、北海道における HPV 検査を応用した新しい検診システム導入への取り組み、東京慈恵医科大学、東京都港区、札幌市 2016 年 11 月 6 日

Organized International Symposium (1)

1. 1st International Conference on Preventing Cervical Cancer Through Education, Vaccination and Screening, Hokkaido University, Sapporo, Hokkaido, March 15th-16th 2016

6. 研究組織

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