Effect of a Brief Web-Based Educational Intervention on Willingness to Receive the Human Papillomavirus Vaccine in Japan: A Randomized, Controlled Trial

INTRODUCTION

1a-i) Key features/functionalities/components of the intervention and comparator in the METHODS section of the ABSTRACT

A brief educational intervention using scientific information presented in an easy-to-read format.

1a-ii) Level of human involvement in the METHODS section of the ABSTRACT

We recruited 1,660 participants aged 20 years and older in March 2018 via a webpage and provided them "fully automated" with a 10-item questionnaire related to the following aspects: awareness regarding HPV infection and vaccine, willingness for immunization, and actions for prevention.

1a-iii) Primary condition or target group in the title

The target was not specific disease.

1b-i) Identify the mode of delivery in the title

Effect of a Brief "Web-Based" Educational Intervention on Willingness to Receive the Human Papillomavirus Vaccine in Japan: A Randomized, Controlled Trial

1b-ii) Non-web-based components or important co-interventions in title

The study aimed to assess the effects of these behavioral insights utilizing fundamental scientific information on vaccine benefits, along with statistics on cervical cancer.

ABSTRACT

This study aimed to assess the effects of these behavioral insights utilizing fundamental scientific information on vaccine benefits, along with statistics on cervical cancer. We recruited 1,660 participants aged 20 years and older in March 2018 via a webpage and provided them fully automated with a 10-item questionnaire related to the following aspects: awareness regarding HPV infection and vaccine, willingness for immunization, and actions for prevention. This study aimed to assess the effects of these behavioral insights utilizing fundamental scientific information on vaccine benefits, along with statistics on cervical cancer.

METHODS

Participants were randomly allocated (1:1) to each group. Intervention was performed using an automatic web-based allocation system stratified with sex (female/women, male/men) and age (20s, 30s, 40s, 50s, and 60s) of the participants. Randomization was performed by Macromill, Inc web-research system.

1b-iii) Open vs. closed, web-based (self-assessment) vs. face-to-face assessments in the METHODS section of the ABSTRACT

No change.

1b-iv) RESULTS section in abstract must contain use data

We recruited 1,660 participants aged 20 years and older in March 2018 via a webpage and provided them fully automated

1b-v) CONCLUSIONS/DISCUSSION in abstract for negative trials

CONCLUSION

We recruited 1,660 participants aged 20 years and older in March 2018 via a specially designed webpage for this study. These were registered members of the research panel owned by Macromill, Inc. (Tokyo, Japan).

Participants were randomly allocated (1:1) to each group. Intervention was performed using an automatic web-based allocation system stratified with sex (female/women, male/men) and age (20s, 30s, 40s, 50s, and 60s) of the participants. Randomization was performed by Macromill, Inc web-research system.

3b) CONSORT: Important changes to methods after trial commencement (such as eligibility criteria), with reasons

No change.

4a) CONSORT: Eligibility criteria for participants

These were registered members of the research panel owned by Macromill, Inc. (Tokyo, Japan). The participants were 20 years old or above as on March 12th-13th, 2018.

4a-i) Computer / Internet literacy

We randomly assigned each participant to respond to an identical questionnaire after (Intervention group) or prior to (Control group) providing behavioral insights material (BI-material) using fundamental scientific information presented in an easy-to-read format (as displayed in Figures 1 and 2).

4b) CONSORT: Description of trial design (such as parallel, factorial) including allocation ratio

Participants were randomly allocated (1:1) to each group. Intervention was performed using an automatic web-based allocation system stratified with sex (female/women, male/men) and age (20s, 30s, 40s, 50s, and 60s) of the participants. Randomization was performed by Macromill, Inc web-research system.

5) CONSORT: Describe the interventions for each group with sufficient details to allow replication, including how and when they were actually administered

4b-i) Bug fixes, Downtimes, Content Changes

Our study is performed as web-based trial.

4b-ii) Report how institutional affiliations are displayed

No change.

5-i) Mention names, credential, affiliations of the developers, sponsors, and owners

These were registered members of the research panel owned by Macromill, Inc. (Tokyo, Japan).

5-ii) Describe the history/development process

I described the process in the discussion session about behavioral insights. Information materials are designed primarily to increase effectiveness; they are based on a specific purpose rather than a template.

5-iii) Revisions and updating

This intervention material is the first edition.

5-iv) Quality assurance methods

Our intervention material is designed primarily to increase effectiveness; they are based on a specific purpose rather than a template.

5-iv) Quality assurance methods

The intervention material (BI-material) was designed by us, resulting in a moderate cost; therefore, this intervention is more reliable and cost-effective than those used in previous studies. The first author of this article (YS) is a core member of the behavioral design team in Yokohama, which was established as the first non-governmental nudge unit in Japan. Thus, this BI-material is reliable in view of the BI methodology.

5-v) Ensure replicability by publishing the source code, and/or providing screenshots/screen-capture video, and/or providing flowcharts of the algorithms used

We displayed the source and flowchart in the manuscript.

5-vi) Digital preservation

This material is freely used as a material for the education in our department. However we have not provided yet in free access website.

5-vii) Access

Participants were registered members of the research panel owned by Macromill, Inc. (Tokyo, Japan).

5-viii) Mode of delivery, features/functionality/components of the intervention and comparator, and the theoretical framework

Participants were registered members of the research panel owned by Macromill, Inc. (Tokyo, Japan).
Participants were registered members of the research panel owned by Macromill, Inc. (Tokyo, Japan). If this manuscript would be published, we will provide this material through our department website and through SNS.

5a) Describe use parameters
Not applicable for our study.

5a) Clarify the level of human involvement
This material was provided through web-site. There were no human involvement.

5a) Report any prompts/reminders used
Not applicable for our study.

5a-ii) Describe any co-interventions (incl. training/support)
Not applicable for our study.

5b) CONSORT: Any changes to trial outcomes after the trial commenced, with reasons
We recruited a total of 1,660 participants in March 2018 via a specially designed webpage for this study. These were registered members of the research panel owned by Macromill, Inc. (Tokyo, Japan).

7a) CONSORT: How sample size was determined
The sample size was calculated as powered 80% to detect a 10% effect in the intervention group (increased from 40% in the control to 50% in the intervention group) with a two-sided p value of 0.05. P values less than 0.05 were regarded as significant. The hypothetical baseline willingness rate in the control group was determined based on our previous study. The sample size was calculated as 776 when the effect of intervention estimated a 10% increase. The number of participants recruited was double of the calculated sample size because of the difficulty of estimating the baseline willingness and the intervention effect.

7b) CONSORT: When applicable, explanation of any interim analyses and stopping guidelines
The primary outcome is the rate of willingness on the HPV vaccine for their daughters. The secondary outcome is the sub-analysis of sexes.

8a) CONSORT: Method used to generate the random allocation sequence
Participants were randomly allocated (1:1) to each group after providing their consent. Intervention was performed using an automatic web-based allocation system stratified with sex (female/women, male/men) and age (20s, 30s, 40s, 50s, and 60s) of the participants. Randomization was performed by Macromill, Inc web-research system. Participants and investigators were blinded to the distribution (double-blinded). Once the upper limit of each stratum was reached, new participants could not be added to the web system. This ensured uniform distribution of the stratification factors. In the intervention group, we provided the BI-material prior to answering questions related to preventive awareness, following consent for the online study. The control group was provided with the same material as that provided to the intervention group after all responses were completed.

8b) CONSORT: Type of randomisation; details of any restriction (such as blocking and block size)
Participants were randomly allocated (1:1) to each group after providing their consent. Intervention was performed using an automatic web-based allocation system stratified with sex (female/women, male/men) and age (20s, 30s, 40s, 50s, and 60s) of the participants. Randomization was performed by Macromill, Inc web-research system. Participants and investigators were blinded to the distribution (double-blinded). Once the upper limit of each stratum was reached, new participants could not be added to the web system. This ensured uniform distribution of the stratification factors. In the intervention group, we provided the BI-material prior to answering questions related to preventive awareness, following consent for the online study. The control group was provided with the same material as that provided to the intervention group after all responses were completed.

9) CONSORT: Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned
Not applicable for our study.

10) CONSORT: Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions
Randomization was performed by Macromill, Inc web-research system.

11a) CONSORT: Blinding - If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how
Participants and investigators were blinded to the distribution (double-blinded).

11a-ii) Describe e.g., whether participants knew which intervention was the “intervention of interest” and which one was the “comparator”
Not applicable for our study.

11b) CONSORT: If relevant, description of the similarity of interventions
Not applicable for our study.

12a) CONSORT: Statistical methods used to compare groups for primary and secondary outcomes
Statistical evaluation comprised the student’s t-test, the chi-square (2) test, and multiple regression analyses.

12a-i) Imputation techniques to deal with attrition / missing values
Not applicable for our study. There were no missing values.

12b) CONSORT: Methods for additional analyses, such as subgroup analyses and adjusted analyses
Same as the primary outcome analysis.

RESULTS

13a) CONSORT: For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome
Not applicable for our study. All participants receive intended treatment.

13b) CONSORT: For each group, losses and exclusions after randomisation, together with reasons
Not applicable for our study.

13b-ii) Attrition diagram
Not applicable for our study.

14a) CONSORT: Dates defining the periods of recruitment and follow-up
From March 12th to 13th 2018, 1,660 participants were recruited.

We have no follow-up period.

14a-ii) Indicate if critical “secular events” fell into the study period
Not applicable for our study.

14b) CONSORT: Why the trial ended or was stopped (early)
Not applicable for our study.

15) CONSORT: A table showing baseline demographic and clinical characteristics for each group
The following variables displayed no significant differences between the two groups: marital status (P= 0.86), children (P= 0.84), household income (P= 0.58), sex (P= 0.26), education (P= 0.58), and tobacco use (P= 0.30) (Table 1).

15i) Report demographics associated with digital divide issues
Not applicable for our study.

16a) CONSORT: For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups
Not applicable for our study. All participants answered questionnaire and received intervention as allocated.

16i) Report multiple “denominators” and provide definitions
Not applicable for our study.

17a) CONSORT: For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)
Only 21.2% of the respondents displayed a favorable attitude toward HPV immunization for their daughters (Q6). However, an additional 40 (4.8%) participants responded affirmatively in the intervention group (aOR=1.32, 95% CI=1.04-1.69) compared to those in the control group (Table 2). For Q7, there were additional 33 (3.9%) satisfied respondents willing for their sons’ vaccination in the intervention group (aOR=1.38, 95% CI=1.05-1.80) compared to those in the control group (Table 2).

17a-i) Presentation of process outcomes such as metrics of use and intensity of use
Not applicable for our study.

17b) CONSORT: For binary outcomes, presentation of both absolute and relative effect sizes is recommended
Only 21.2% of the respondents displayed a favorable attitude toward HPV immunization for their daughters (Q6). However, an additional 40 (4.8%) participants responded affirmatively in the intervention group (aOR=1.32, 95% CI=1.04-1.69) compared to those in the control group (Table 2). For Q7, there were additional 33 (3.9%) satisfied respondents willing for their sons’ vaccination in the intervention group (aOR=1.38, 95% CI=1.05-1.80) compared to those in the control group (Table 2).

18) CONSORT: Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory
Differences were identified in Q6 (Men; aOR=1.46, 95% CI=1.05-2.02 vs Women; aOR=1.20, 95% CI=0.83-1.73) and Q7 (Men; aOR=1.53, 95% CI=1.08-2.18 vs Women; aOR=1.21, 95% CI=0.80-1.83). The awareness in men showed a significant positive change (by 8.2%, P=0.02, Supplement 1) upon intervention by fundamental scientific information; however, this was not observed in women (P=0.22, Table 3, Supplement 2).

There were no additional analysis other than planned analysis.

18-i) Subgroup analysis of comparing only users
Not applicable for our study.

19) CONSORT: All important harms or unintended effects in each group
Not applicable for our study.

19-i) Include privacy breaches, technical problems
Not applicable for our study.

19-ii) Include qualitative feedback from participants or observations from staff/researchers
Not applicable for our study.

DISCUSSION
20) CONSORT: Trial limitations, addressing sources of potential bias, imprecision, multiplicity of analyses
20-i) Typical limitations in ehealth trials
Third, selection bias existed as the respondents were Japanese enrolled by an internet survey company.

21) CONSORT: Generalisability (external validity, applicability) of the trial findings
21-i) Generalizability to other populations
Our study reveals a positive outlook towards the HPV vaccination following brief, web-based educational intervention, especially among male participants. Such an approach is extremely effective to overcome challenges related to communication and information overload.

21-ii) Discuss if there were elements in the RCT that would be different in a routine application setting
Not applicable for our study.

22) CONSORT: Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence
22-i) Restate study questions and summarize the answers suggested by the data, starting with primary outcomes and process outcomes (use)
We conducted a web-based randomized controlled trial (RCT) to assess the benefits of BI-material employing fundamental scientific information and motivate individuals to take the HPV vaccine. Our results showed that providing brief scientific information could increase the positive awareness of HPV vaccination. This effect was observed typically among male participants. Similar minor interventions may potentially modify mindsets favorably. However, such brief digital information failed to affect the mindset in women. In terms of the coronavirus disease (COVID-19) pandemic, a difference in awareness of prevention strategies was observed between the sexes; therefore, it is essential to build a method appropriate for sex subgroups to transform general behavior via the internet and social networking service (SNS).

22-ii) Highlight unanswered new questions, suggest future research
We recognize several limitations in this study. First, the sustainability of effective change was not evaluated. Typically, with respect to health issues, taking action requires time. Therefore, a study should assess not only a change in mindset but also the appropriate course of action. We have already performed a RCT (UMIN000039273) assessing the sustainability of general acceptance and concrete behavior for HPV vaccination. This effect was observed typically among male participants. Similar minor interventions may potentially modify mindsets favorably. However, such brief digital information failed to affect the mindset in women. In terms of the coronavirus disease (COVID-19) pandemic, a difference in awareness of prevention strategies was observed between the sexes; therefore, it is essential to build a method appropriate for sex subgroups to transform general behavior via the internet and social networking service (SNS).

Other information
23) CONSORT: Registration number and name of trial registry
UMIN000049745
URL: https://www.umin.ac.jp/english/

24) CONSORT: Where the full trial protocol can be accessed, if available
Not applicable for our study.

25) CONSORT: Sources of funding and other support (such as supply of drugs), role of funders
We received research funding from the Japan Agency for Medical Research and Development (grant no. 15ck0106103h0102).

X26-i) Comment on ethics committee approval
The study protocol was approved by the Institutional Research Ethics Committee of Yokohama City University School of Medicine (A180200004). The trial registration number is UMIN000049745.

X26-ii) Outline informed consent procedures
In the intervention group, we provided the BI-material prior to answering questions related to preventive awareness, following consent for the online study. The control group was provided with the same material as that provided to the intervention group after all responses were completed.

X26-iii) Safety and security procedures
Not applicable for our study.

X27-i) State the relation of the study team towards the system being evaluated
We have no COI between study team and the survey company.