Improving knowledge, attitudes, and uptake of cervical cancer prevention among female students: A systematic review and meta-analysis of school-based health education

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Abstract

Objective

Schools are an ideal environment for promoting cervical cancer prevention among young women. This systematic review and meta-analysis aimed to examine: 1) the effectiveness of school-based education for improving i) knowledge and perceptions of cervical cancer, HPV infection and vaccination, and cervical cancer screening; ii) attitudes and intentions toward, and uptake of HPV vaccination and cervical cancer screening among female students; and 2) the methodological quality of studies testing school-based cervical cancer education.

Methods

Medline, EMBASE, CENTRAL, PsycINFO, CINAHL, Web of Science, and ERIC literature databases were searched from inception to November 2020. English language publications describing RCTs of any form of cervical cancer education delivered to female students in a school setting were eligible for inclusion. Included studies were assessed for methodological quality using the revised Cochrane risk of bias tool for randomized trials and the GRADE approach. Standardized Mean Differences and Odds Ratios were calculated and meta-analytically pooled using random-effects models. Subgroup analysis explored heterogeneity.

Results

Of the 13 included studies, only one study was judged overall as having a low risk of bias. School-based education improved knowledge about cervical cancer and HPV infection. It also improved knowledge of and intentions toward HPV vaccination. Although education was ineffective in improving cervical cancer and HPV infection risk perceptions, and attitudes about HPV vaccination, a subgroup analysis found printed education materials focused on HPV-related content may have significant positive effects on risk perceptions. School-based education did not significantly increase HPV vaccination uptake; however, a face-to-face active approach seemed beneficial in a subgroup analysis. Heterogeneity (I^2) ranged between 0% to 93%, and the quality of evidence was rated from low to moderate.

Conclusions

High-quality evidence from methodologically rigorous studies is needed to provide stronger guidance regarding the benefits of school-based education in improving knowledge and behaviours toward cervical cancer prevention.

1. Introduction

Globally, the incidence of cervical cancer has increased from approximately 530,000 cases per year to 570,000 cases per year between 2012 and 2018.[1] In 2018, about 311,000 women died from cervical cancer worldwide. In the next 50 years, more than 44 million women, with a large proportion of these in Low-and-Middle income countries (LMICs), will be diagnosed with cervical cancer if effective preventive measures are not implemented.[3]

Prophylactic Human Papillomavirus (HPV) vaccination offers some protection against all types of HPV infection associated with cervical cancer. [2] Since 2009, the World Health Organization (WHO) has recommended HPV vaccination for girls aged 9 to 26 years [3] before becoming sexually active. However, because HPV infection does not account for the development of all cases of cervical cancer, and the HPV vaccine does not offer complete protection, regular cervical cancer screening is still recommended. The greatest benefit of screening is gained when women are screened early at an age-eligible period. [4] A single lifetime screening test significantly decreases the risk of cervical cancer mortality. [5] Routine screening on a more frequent basis increases these benefits. [6]

There is inadequate knowledge about cervical cancer, and a high prevalence of negative attitudes and perceptions about HPV vaccination and cervical screening among age-eligible female adolescents and young people. [7] This is associated with low levels of intention toward uptake and completion of HPV vaccination. [8] Global estimates have shown that less than 35% of age-eligible adolescents (between ages 10-20) in high-income countries, and less than 3% of age-eligible adolescents in LMICs, have received the full HPV vaccine dose. [9]

In recent years, a decline in HPV vaccine uptake has been reported. This decline follows media coverage about HPV vaccine safety concerns in many parts of the world including Denmark, Japan, Ireland, Netherlands and France. [10-12] In 2013, Japan achieved an HPV vaccination initiation and completion rate of over 70%. However, after unconfirmed reports about adverse reactions by the media, the rate decreased to 0.6% in 2014.[13] A review of 28 studies reported moderate intentions (19%-44%) toward HPV vaccination among female adolescents in Germany, Hong Kong and America. [14] Cervical cancer screening uptake among age-eligible young women varies internationally. [15] In the UK, almost two-thirds of age-eligible young

women between 25 and 29 years have undergone cervical cancer screening.[16] In contrast, screening rates of between less than 1% to 27.5% have been recorded in LMICs. [17]

Adolescence and young adulthood are critical periods in the life course, with health-related attitudes and behaviours developed during this time tracking into adulthood. [18] Promoting health during adolescence and in young adulthood builds their capacity to engage in good health and wellbeing, and provides a key to preventing diseases in later life. [19] Schools are an important setting for health promotion because they reach a large proportion of adolescents and young adults who spend a significant proportion of their lives at school. [20] Schools also foster learning; therefore, it is feasible to include education and learning about health as part of the curriculum. [19] Educating children in schools can influence transfer of knowledge, attitudes and behaviours to parents [21] because parental decision is paramount in students' health-seeking behaviours.

High prevalence of HPV infection,[22] early sexual initiation (before 18 years),[23] multiple sexual partners,[24] and increasing use of oral contraceptives[23] have been reported among female adolescents and young women across countries, including the United States of America, Europe and sub-Saharan Africa. Therefore, providing cervical cancer information is essential to improving health decision-making and performing preventive health behaviours.[25-30] However, evidence regarding the effectiveness of school-based education in improving cervical cancer prevention among female adolescents and young women remains unclear.[31] Previous reviews suggest school-based education appears promising in improving HPV vaccination uptake;[32-34] however, the findings are limited by the inclusion of methodologically weak and non-randomized studies. This review aimed to examine:

a. The effectiveness of school-based cervical cancer education for improving i) knowledge and perceptions of cervical cancer, HPV infection and vaccination, and cervical cancer screening; and ii) attitudes and intentions toward, and uptake of HPV vaccination and cervical cancer screening among female students.
b. The methodological quality of school-based cervical cancer education according to the revised Cochrane risk of bias tool for randomized trials (ROB 2).

2. Methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were used to report the methodology of this review (**PROSPERO registration: CRD42021230788**).[35] (see supplementary file (S) S1 for complete checklist).

2.1 Data sources

A computer-based literature search was conducted using seven databases *(Medline, EMBASE, CENTRAL, PsycINFO, CINAHL, Web of Science, ERIC)* from the date of inception to November 2020. A search of the grey literature and the reference list of included studies was also performed. The search strategy was developed and executed in consultation with a medical librarian (see S2-S3 for details).

2.2 Inclusion/exclusion criteria

Types of study: Studies eligible for inclusion were randomized control trials (RCTs) because they are the gold standard for measuring the effectiveness of interventions. [36] No limits were placed on the year of publication. However, due to the prohibitive cost of translation, only studies reported in English were included. Studies were excluded if they were non-randomized trials and controlled before-after studies, abstracts, editorials, letters, dissertations, protocol papers, conference proceedings, surveys or questionnaires and qualitative studies or mixed methods without an intervention component.

Types of population/participants: Studies were included if they involved: (a) females or girls (of all ages) receiving cervical cancer education (including HPV vaccination and cervical cancer screening) or cervical cancer prevention services in primary, high schools, colleges or universities; (b) clear stratification of results for girls in a mixed-gender population. Primary, high and tertiary school students were included in this review because their age profile is consistent with the eligible age for HPV vaccination which ranges from 9 to 26 years. [2] Studies were excluded if they involved only boys (of all ages) receiving cervical cancer education and cervical cancer prevention services in school as cervical cancer does not directly affect them.

Types of interventions: Any form of cervical cancer education delivered in a school environment was included. Cervical cancer education was defined as information, behavioural instruction and advice related to cervical cancer prevention to improve understanding, skills, and attitudes toward HPV vaccination and cervical cancer screening. The education could be delivered via face-to-face, online, printed materials, computer-assisted, and health information websites. Studies were excluded if they were: (a) using interventions to assist in cervical cancer diagnosis, treatment, and management; and (b) interventions delivered outside school settings (i.e., not delivered in primary or high schools or universities or colleges).

Comparator: The comparator was a control condition with either usual care or no education. Usual care was defined as providing: participants with information unrelated to cervical cancer; general health information; and routine general cervical cancer information.

Types of outcomes: Cervical cancer and HPV-related knowledge, attitudes and perceptions, and intentions and uptake of HPV vaccination and cervical cancer screening. Knowledge was defined as students' understanding about any or a combination of the following: cervical cancer progression and diagnosis; HPV vaccination; cervical cancer screening; treatment and complications of cervical cancer; and appropriate facilities for vaccination, screening, and seeking for treatment of cervical cancer. Attitudes were defined as beliefs, feelings, and behaviours toward HPV vaccination and screening. On the other hand, perceptions were defined as the risk perceptions (perceived susceptibility or seriousness) of cervical cancer and HPV infection. Intentions were defined as participants' willingness to get HPV vaccination or cervical cancer screening.

2.3 Identification of studies

All titles and abstracts were downloaded into endnote, exported into COVIDENCE and de-duplicated. The titles and abstracts of each article were independently screened for relevance by two reviewers (AGA and PGK). Two reviewers (AGA and PGK) also independently examined retrieved full-text references. The Kappa coefficient, which examines the inter-rater reliability of coding, was 0.94 for the title and abstract screening and 0.91 for full-text screening. The two reviewers discussed any disagreements over inclusion or exclusion; if no consensus was reached, a third reviewer (LM) was consulted.

Selection of included studies*:* At the full-text review stage, all eligible RCTs were selected for data extraction.

2.4 Data extraction:

An a priori review-specific data extraction form was designed, tested with five randomly selected studies and refined. Information extracted from the selected studies included author, year, study design, sample (age, number of participants and type of participants), intervention (education type, method of delivery, and theoretical framework), control condition, description of the intervention (content, source of information, presentation mode and duration), outcome measures (primary and secondary outcomes), follow-up time points and findings.

Dealing with missing data: In a case of missing data, publication author(s) were contacted three times (at 4-week intervals) to provide further information. Some authors provided the needed data (n=3), others explained that data was lost given the elapsed time (n=2), and some did not respond (n=3).

2.5 Meta-analysis

Measurement of effects: Data were analyzed using Review Manager (RevMan) software 5.3.[37] Both continuous and dichotomous data were extracted from each study for meta-analysis. Equal sample sizes were assumed for the intervention and control groups if studies did not report this information or there was no response from authors. Means and standard deviations for multiarmed trials or trials with more than one population subgroup comparing two or more active interventions against a control were combined using RevMan.[38]

Standardized mean difference (SMD), Hedges' (adjusted g) and its standard error were calculated for all studies reporting means, standard deviations/standard errors, samples sizes, mean differences, and test statistics (F-test or t-test) using Cochrane recommended formulae,[38] Campbell collaboration formulae and effect size calculator,[39] and RevMan.[37] Odds ratio (OR) was also calculated for studies reporting numbers. Data was transformed, and OR was converted to SMD and vice versa depending on the dominant unit of measure for a particular outcome.[40, 41] Sensitivity analysis was conducted, and no variation of effect sizes among included studies was found.

Analysis methods: The generic inverse-variance method was used to analyse continuous data. For dichotomous data (uptake of HPV vaccination), due to low events and small study sizes, the Mantel-Haenszel method was used. Due to the different populations, settings and intervention characteristics, the data were pooled for outcomes using the random effect model.[42] This model assumes that the studies are not all estimating the same intervention effect but estimate intervention effects that follow a distribution across studies.[42] Forest plots were created for each outcome. Pooled effect sizes were considered small, medium, and large for values of 0.2, 0.5 and 0.8 respectively.[43]

2.6 Unit of analysis

Cluster randomized studies: We included one cluster RCT; however, individual randomization of students in schools was performed. Therefore, the design effect was not calculated to adjust for effect estimates.

Choice of measurement points: For trials reporting outcomes at multiple time points, such as at immediate follow-up with longer follow-up, we extracted all data and combined in meta-analyses with the longest follow-up points.

2.7 Assessment of heterogeneity

Statistical heterogeneity of effect sizes was examined using the Q test and I^2 statistics. Values between 0% to 40% indicated no or low heterogeneity, 30% to 60% represented moderate heterogeneity, 50% to 90% represented substantial heterogeneity, and 75% to 100% indicated considerable heterogeneity. Clinical heterogeneity was examined by observing variation in population, intervention characteristics and outcomes. Sources of variation between studies were explored through subgroup analysis.

2.8 Subgroup analysis

Pre-specified subgroup analyses were conducted to investigate heterogeneity based on intervention characteristics and study features including: *i) method of education delivery* - online delivery vs. face-to-face delivery (didactic or non-didactic format) vs. printed education materials,[44] *ii) presentation mode (*single-mode learning; verbal or non-verbal vs. multimodal learning; verbal and non-verbal),[45] *iii) source of information* - involving a peer-delivered component vs. not involving peer-delivered component including researchers, facilitators and teachers,[46] *iv) content of information*-HPV-related content vs. cervical cancer-related content vs. HPV and cervical cancer related, *v) intensity of education, vi) length of follow-up* - immediate vs. one week to 6 months follow-up, *vii) pedagogical approach* - constructive vs. instructive. Constructivist approach was defined as any learner-centered education which actively involves students in planning, ideas creation, and problem-solving activities. Instructive/transmissive approach was defined as any teacher-centered education in which the teacher designs lessons in a predetermined order and students passively acquire specified knowledge and skills.[47] These characteristics form the basic principles of teaching and learning and are likely to modify the intervention, leading to different outcome effects. The intensity of education was not considered as planned due to an insufficient number of studies.

2.9 Risk of bias and certainty of evidence assessment

The ROB 2 was used to determine the methodological quality of included studies. The quality of the studies was assessed independently by two reviewers (AGA and PGK) according to five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome and

selection of the reported results.[48] Bias was categorised as: Low risk of bias, some concerns, and high risk of bias.[48] For each outcome, the overall quality of evidence was assessed by the GRADEpro GDT software.[49] Based on the level of risk of bias, inconsistency, indirectness, and imprecision, the quality of evidence was graded as not serious, serious, and very serious.[49] Publication bias was not assessed due to an insufficient number of studies.[38] The inter-rater reliability of risk of bias was computed as Kappa coefficient of 0.93, and disagreements were resolved through discussion.

3. Results

3.1 Search results

A total of 3353 citations were identified. Of the 49 citations that underwent full-text review, 36 were excluded because they did not meet the inclusion criteria. The remaining 13 RCTs were included in the review. See S4 for the study selection process.

3.2 Characteristics of included studies

3.2.1 Study population and intervention characteristics

Thirteen trials met the inclusion criteria for this review, and their characteristics are reported in Table 1. Most trials (n=8, 62%) were conducted in the United States of America (USA) and were two-armed RCTs (n=7, 88%). Sample sizes ranged from 62 to 661 (total n=2,012). Less than half of the trials (31% and 46%) involved college and undergraduate students. Participants' mean age ranged between 16 and 22 years.

All trials used brief or one-off education intervention to provide information to students. In all trials, procedures were implemented to promote recall. About half of the trials (n=6, 46%) used verbal presentation, including written and spoken words. Others included non-verbal presentation (i.e., video only or illustrations-roleplays or photo) and multimodal presentation (a combination of verbal and non-verbal). A majority of the interventions described in the included trials (n=9, 69%) adopted an instructive approach (i.e., printed education materials or face-to-face or online delivery modalities). The online delivery (n=6, 46%) was mostly used; others included face-to-face delivery only, printed education materials delivery only, and mixed delivery modality (face-to-face and printed education materials). Online delivery included participants receiving information via websites, smartphone applications, and emails accessible by devices such as computers, smartphones and iPads.

More than half of the trials (n=9, 69%) were non-peer delivered using schoolteachers, researchers and facilitators for information sources. Almost all the trials (n=12, 92%) focused on HPV information, including risk factors, transmission and vaccination. Trials rarely reported the duration of intervention sessions. However, a few (n=4, 31%) reported sessions ranging between 1.25 and 90 mins. More than half of the trials (n=8, 62%) did not report the theoretical framework of the intervention used. The remaining studies (n=5, 38%) used the following theories to design their interventions: Health Belief Model; Exemplification theory and Culture-centric narrative theory; Situation-specific theoretical framework and storytelling/Narrative Communication theory; Bandura's Social Cognitive Theory, Erikson's Development Theory and Jessor's Risk Reduction Model; and Information-motivation-behavioural skills.

3.2.2 Outcomes

The study outcomes were; a) Knowledge and perceptions of cervical cancer, HPV infection and vaccination, and cervical cancer screening b) attitudes and intentions toward, and uptake of HPV vaccination and cervical cancer screening. All included trials measured at least one outcome using self-completed online or paper-based surveys. Nine trials assessed knowledge about cervical cancer, HPV infection and HPV vaccination, and of these, six trials were HPV-related. Four studies assessed risk perceptions of cervical cancer and HPV infection. For attitudes, four trials measured attitudes toward HPV vaccination. None of the included studies assessed knowledge and perceptions regarding cervical cancer screening. Most trials (n=12, 92%) calculated mean scores for knowledge, attitudes and perceptions. Other approaches included percentages, mean differences, F-test values and odds ratios.

Five trials assessed intentions toward HPV vaccination. No trial measured intentions toward cervical cancer screening. The uptake of HPV vaccination was assessed by three trials using participant self-report. None of the included studies assessed cervical cancer screening uptake. Mean scores were calculated for intentions for almost all included studies. The percentage of student participants getting HPV vaccination after implementation of the intervention was also calculated. The longest follow-up of study participants was six months, while the shortest was immediate post-intervention.

Table 1: Characteristics of studies

No	Study Country Design	Sample	Intervention	Control	Intervention description	Outcome measures and follow-up time-point/s
1.	Study: Baxter and Barata 2011 Country: Canada Design: 3-arm RCT	N= 193 IG1 n= 66 IG2 n=67 CG n= 60 Age (mean, SD): IG: 18.43 (0.93) CG: 18.43 (0.93) Type of participants: Undergraduate students	Education type: -IG 1 – Usual care + printed detailed information -IG 2 – Usual care + printed tailored information Method of delivery: Printed materials Theoretical framework: Not reported	Usual care: Written information on HPV and the vaccine but did not describe HPV as an STI	Content: IG1- Detailed information provided in-depth information about the sexual transmission of HPV. IG2- Tailored information mirrored detailed information, but there was an added emphasis on the greater benefit for sexually inexperienced females. Source of information: Researcher Presentation mode: Verbal (written words) Duration: Not reported	Primary: -HPV Knowledge (13 items) -HPV vaccination intent (one item) Secondary: Data points: Baseline; 6 months follow-up
2.	Study: Bennett, Patel et al. 2015[27] Country: USA Design: 2-arm RCT	N= 661 IG n= 330 CG n= 331 Age (mean, SD): IG :21 (0.13) CG: 21 (0.13) Type of participants: Undergraduate students	Education type: -Electronic; MeFirst website tailored education Method of delivery: online Theoretical framework: Not reported	Usual care: Webpage of text from the CDC Vaccine Information Statement on the quadrivalent HPV vaccine	Content: MeFirst intervention website was a unique, tailored and automatically configured for the individual participant based on their baseline survey responses. -It consisted of seven topic pages; -factual information on HPV and the HPV vaccine, -statistics on the incidence of HPV infection and cervical cancer -risks associated with HPV infection -costs of vaccination -safety and efficacy of the HPV vaccine -suggestions for how to talk to a doctor about the vaccine. Source of information: Researcher Presentation mode: Verbal (written words) Duration: Not reported	Primary: -HPV vaccination intent (one item) Secondary: -HPV knowledge (10-items) -Vaccine uptake (one – item) -HPV risk perception Data points: Baseline; 3 months follow-up
3.	Study: Christensen 2014[50]	N= 74 IG n= 37 CG n= 37 Age (mean, SD):	Education type: -Electronic; downloadable health	Usual care: American Cancer Society pamphlet on cervical cancer and HPV	Content: Not reported Source of information: Researcher	Primary: -Cervical cancer and HPV Knowledge (10 items on existing knowledge about Pap test

No	Study Country Design	Sample	Intervention	Control	Intervention description	Outcome measures and follow-up time-point/s
	Country: USA Design: 2-arm RCT	IG: 20.81 CG: 20.41 Type of participants: Undergraduate students	education app (MyPapp app) Method of delivery: Online Theoretical framework: Not reported		Presentation mode: Verbal (written words) Duration: Not reported	- Knowledge around misconceptions about Pap test (14 items) Secondary: Data points: Baseline; immediate follow-up
4.	Study:Doherty and Low 2008[51] Country: USA Design: 2 arm RCT	N= 68 IG n= 36 CG n= 32 Age (mean, SD): IG: 17.04 (1.41) CG: 17.04 (1.41) Type of participants: Undergraduate students	Education type: -Electronic; website Method of delivery: online Theoretical framework: Not reported	No education	Content: The website in the form of an HPV information FAQ sheet was divided into three sections: 1) Question and answer section 2) Personal story (video) 3) Self-quiz. -Personal story of a college-age female who was diagnosed with HPV at the college health center. - Implications of the HPV diagnosis (e.g., potential for infecting others, long-term health risks) and recommendations for how she should monitor the infection. Source of information: Peers and researcher Presentation mode: Multimode; verbal (written words) and non-verbal (video) Duration: Not reported	Primary: -HPV knowledge (15-items) -Attitudes toward HPV vaccination (7-items) Secondary: Data points: Baseline; immediate follow-up
5.	Study: Grandahl, Rosenblad et al. 2016[28] Country: Sweden Design: CRCT	N= 385 IG n= 239 CG n= 146 Age (mean, SD): IG: 16.15 (0.77) CG: 16.06 (0.73) Type of participants: high school	Education type: -Verbal; Face-to-face health interview, -Printed; flipcharts and 12-page leaflet Method of delivery: Face-to-face Theoretical framework: Health Belief Model	Usual care: General information, including those on sexual health and the standard health interviews.	Content: -General facts about the virus -Viral transmission -Causes, risk factors of HPV -Prevention of HPV -condom use and HPV vaccination -availability of vaccines and cost -Facts about the HPV vaccine -Importance for girls to attend future cervical cancer screening controls Source of information: School nurse	Primary: HPV vaccination uptake (one item) Data points: Baseline; 3 months follow-up

No	Study Country Design	Sample	Intervention	Control	Intervention description	Outcome measures and follow-up time-point/s
					Presentation mode: Multimode; verbal (spoken words and written words) and non-verbal (photos) Duration: 30 mins	
6.	Study: Hopfer and Hopfer 2012[29] Country: USA Design: 4-arm RCT	N=404 IG1, n= 101 IG2, n= 50 IG 3, n= 101 CG n= 152 Age (mean, SD): IG: 21 CG: 21 Type of participants: College women	Education type: -Electronic; Narrative Video IG1- a video of vaccine decision narratives delivered by peers IG2- a video of narratives delivered by medical experts IG3- a video of narratives delivered by a combination of peers and experts. Method of delivery: Online Theoretical framework: Exemplification theory and Culture-centric narrative theory	Non-narrative video (1) an informational video without narratives, (2) the campus website providing information about HPV and the vaccine, (3) no message	Content: Format of the narratives included: -Direct testimonials (e.g., college woman telling a story that motivated her to vaccinate) -Re-enactments (a re-created scenario of college women talking in a dorm room about what prompted them to vaccinate - Re-created scenario of women talking at the campus health waiting room discussing scheduling and insurance for the vaccine). Source of information: Peers Presentation mode: Non-verbal (video) Duration: 1.25 mins- 4.15 mins	Primary: -HPV vaccination intent (2-items) -HPV vaccine self-efficacy (2-items) -HPV vaccine uptake (one – item) Secondary: Data points: Baseline; 2 months follow-up
7.	Study: Kim, Lee et al.[52] 2020 Country: USA Design: 2-arm RCT	N= 104 IG1, n= 54 CG n= 50 Age (mean, SD): IG: 21.5 CG: 22 Type of participants: College women	Education type: Electronic; Storytelling video Method of delivery: Online Theoretical framework: Situation-specific theoretical framework and storytelling/Narrative Communication (SNC) theory	Usual care: Written information about HPV and HPV vaccine and CDC website	Content: -Three peer-paired cross-cultural and cross-generational (1st, 1.5- and 2nd) stories of Korean American college women's HPV vaccination experiences and their attitudes toward getting the HPV vaccination. -Scientific information— by a physician to correct common misconception about HPV vaccination Source of information: Peers and physician Presentation mode: Non-verbal (video) Duration: 17 mins	Primary: -HPV vaccination uptake (1-item) Secondary: -Knowledge about HPV (32-items) -Attitudes toward HPV vaccine (19-items) -Intent to vaccinate (1-item) Data points: Baseline; immediate follow-up; 2-months follow-up

No	Study Country Design	Sample	Intervention	Control	Intervention description	Outcome measures and follow-up time-point/s
8.	Study: McKeever et al. 2013[53] Country: USA Design: 2-arm RCT	N= 73 IG1, n= 41 CG n= 32 Age (mean, SD): IG: 19.92 CG: 19.87 Type of participants: College women	Education type: Verbal Electronic: video Participatory: Drama/roleplaying Method of delivery: Face-to-face Theoretical framework: Bandura's Social Cognitive Theory, Erikson's Development Theory, and Jessor's Risk Reduction Model	No intervention	Content: -Factual information about cervical cancer, HPV, HPV vaccination and the sexual risks that women face during young adulthood -Role-playing to enact vignettes about risky behaviours that predispose women to HPV. -Skill training set for self-confidence, empowerment, and personal motivation in a gaming format titled, "The Power to Change" for participants in groups Source of information: Peer educators Presentation mode: Multimode; verbal (spoken words) and non-verbal (illustration and video) Duration: 60 mins	Primary: -Cervical cancer and HPV knowledge (23 items) -Perceived susceptibility to and seriousness of cervical cancer and HPV (15 items) -Intent to seek HPV vaccination (1-item) Secondary: Data points: Baseline; one-month follow-up
9.	Study: Merzouk et al. 2011[26] Country: USA Design: 2-arm RCT	N= 626 IG1, n= 372 CG n= 254 Age (mean, SD): IG: Not reported CG: Not reported Type of participants: high school students	Education type: Usual care + Electronic: audio-visual presentation (DVD) Method of delivery: Face-to-face using DVD Theoretical framework: Not reported	Usual care: health class	Content: The HPV DVD presentation contained 3 major topics: -What is HPV? -How do I know I have HPV? -I have HPV. What do I do now? Source of information: School Teacher Presentation mode: Multimode; verbal (spoken words) and non-verbal (video) Duration: 15 mins	Primary: HPV-related knowledge (11-items) Secondary: Data points: Baseline; immediate follow-up
10.	Study: Nadarzynski et al. 2012[30] Country: UK Design: 4-arm RCT	N= 606 IG1, n= 164 IG2, n= 124 IG 3, n= 162 CG n= 156 Age (mean, SD): 21 (1.8) IG: Not reported CG: Not reported	Education type: Electronic: Website IG1: Usual care + HPV, IG2: Usual care + cervical cancer risk factors IG3: Usual care + HPV + cervical cancer risk factors	Usual care: basic description of cervical cancer	Content: IG1: Usual care + HPV, which included the same basic information plus a description of the causal role of HPV in cervical cancer IG2: Usual care + risk factor, which included the basic information plus information about cervical cancer risk factors IG3: Usual care + HPV + risk factor, which included all pieces of information	Primary: Risk perception cervical cancer (1-item) Secondary: Data points: Baseline; immediately follow-up; 1-week follow-up

No	Study Country Design	Sample	Intervention	Control	Intervention description	Outcome measures and follow-up time-point/s
		Type of participants: Undergraduate students	Method of delivery: Online Theoretical framework: Not reported		Source of information: Researcher Presentation mode: Verbal (written words) Duration: Not reported	
11.	Study: Perez et. al 2016[54] Country: USA Design: 2-arm RCT	N= 62 IG1 n= 31 CG n= 31 Age (mean, SD): 19 IG: Not reported CG: Not reported Type of participants: College students	Education type: usual care + verbal: face-to-face Method of delivery: Face-to-face Theoretical framework: Information-motivation-behavioural skills	Usual care: Vaccination information statement: brief overview of HPV, HPV-related cancers, and the HPV vaccine available online and student health centers Plus participants watched a set of short video clips that covered broad topics related to women's health, including what happens during a sexual health check, ways to improve access to health services, and methods of contraception	Content: -Educational content related to HPV and the HPV vaccine that addressed specific knowledge gaps identified among young adult women delivered in small groups -Motivational content delivered using motivational interviewing (MI) techniques, to help women identify the benefits and barriers to vaccination. -Skills-building content, which included a review of, a) ways to access the HPV vaccine (e.g., vaccine locations); b) methods for paying for the vaccine, including information related to insurance coverage and costs; c) reminder tools to ensure completion of the three-dose series; and d) approaches to communicating vaccine interest and concerns with parents and providers. -Problem-solving activities, group discussions, question and answer sessions Source of information: Facilitator Presentation mode: Multimode; verbal (spoken words and written words) and non-verbal (video) Duration: Not reported	Primary: -Knowledge of HPV and the HPV vaccine and cervical cancer (24-items) -HPV vaccination intention (7-items) -Attitudes toward vaccination (7-items) - Perceived susceptibility to and seriousness HPV and cervical cancer (9-items) HPV vaccination uptake (6-items) Secondary: Data points: Baseline; immediately follow-up; 4-weeks follow-up
12.	Study: Steckelberg et al. 2013[55] Country: Germany Design: 2-arm RCT	N= 105 IG1 n= 52 CG n= 53 Age (mean, SD): IG: 16.6(1.3) CG: 17.0 (1.5)	Education type: Usual care + printed information: numerical information Method of delivery: Printed materials	Usual care: standard leaflet on HPV vaccination	Content: -Numerical information on cancer risk and benefit of the HPV vaccination in terms of cervical cancer prevention Source of information: Researcher	Primary: HPV risk knowledge (6 items) attitude toward HPV vaccination (1-item) Secondary:

No	Study Country Design	Sample	Intervention	Control	Intervention description	Outcome measures and follow-up time-point/s
		Type of participants: Vocational school students	Theoretical framework: Not reported		Presentation mode: Verbal (written words) Duration: 90 mins	Data points: Baseline; immediate follow-up
13.	Study: Stock[56] et al. 2013 Country: USA Design: 2-arm RCT	N= 131 IG1, n= 70 CG n= 61 Age (mean, SD): 19.73 IG: Not reported CG: Not reported Type of participants: Undergraduates	Education type: Printed: HPV information sheet Method of delivery: Printed materials Theoretical framework: Not reported	No education	Content: -Basic information about HPV, including prevalence, transmission routes (emphasizing unprotected oral sex), diagnosis, and prevention. -HPV vaccine, Source of information: Researcher Presentation mode: Verbal (written words) Duration: Not reported	Primary: -HPV knowledge (7-items) -Vaccine uptake (1 – item) -HPV risk perception (1-item Secondary: Data points: Baseline; immediate follow-up

USA; United States of America, UK; United Kingdom, RCT; Randomized control trials, IG: intervention group, CG; control group

3.3 Risk of bias assessment

The methodological quality of the 13 included trials is presented in Table 2. Overall, only one trial met all the ROB 2 criteria and was judged as low risk for all five domains. The remainder were judged as having some concerns as there were issues with the randomization process and deviation from the intended intervention. Nine trials failed to provide information on the process of random allocation sequence generation and concealment. Twelve trials did not provide details on blinding of participants and interventionists. Due to the nature of some of the interventions (i.e., face-to-face education), blinding of interventionists was not possible. Trials that reported such situations were judged as deviations arising from trial context and were unlikely to affect outcomes.[48] Such trials were judged as low risk of bias according to the ROB 2 algorithm.

3.4 Effectiveness of school-based cervical cancer education on:

3.4.1 Knowledge about cervical cancer, HPV infection and HPV vaccination

As presented in Fig. 1, the pooled effect of nine RCTs indicated that school-based cervical cancer education compared to the control group improves knowledge about cervical cancer, HPV infection and HPV vaccination (Random effect: SMD=1.15, 95%CI: 0.67-1.63; participants=1436, 9RCTs). All studies showed consistency in the direction of the intervention effect. However, there was considerable heterogeneity (I^2=93%) between effect sizes, and this was explored further with subgroup analysis.

Subgroup analysis: The test for intervention characteristics subgroup differences suggests no significant subgroup effect (See S5, S6-S11). However, the pooled estimates for each subgroup were significant in favour of school-based education. Large effects were found for studies using: constructivist approach (Random effect: SMD=1.82, 95%CI: 0.35-3.29; participants=203, 3RCTs); both cervical cancer and HPV contents (Random effect: SMD=1.57, 95%CI: 0.22-2.92; participants=1227, 6RCTs) and longer follow-up periods (Random effect: SMD=1.55, 95%CI: 0.36, 2.74; participants=328, 2RCTs). However, there was substantial unexplained heterogeneity between trials with each group.

3.4.2 Risk perceptions of cervical cancer and HPV infection

Four trials contributed to the meta-analysis of school-based cervical cancer education effects on improving risk perceptions of cervical cancer and HPV infection versus the control group (see Fig. 1). There was uncertainty about whether it can improve risk perception of cervical cancer and HPV infection (Random effect: SMD=0.21, 95%CI: -0.15-0.57; participants=872, 4RCTs). The effect sizes of 3 studies favoured the intervention, of which two showed the greater impact of the education on improving the risk perceptions of

cervical cancer and HPV infection. However, these studies showed substantial heterogeneity between effect size estimates with I^2 of 76%.

Subgroup analysis: A significant subgroup effect was found for the delivery method (P=0.002) and informational content (p=0.0006), suggesting that these characteristics modify the impact of school-based cervical cancer education in comparison with no education or usual care (See S5, S14-S15). However, interventions using printed education materials and those focusing on HPV-related content had a moderately significant effect (Random effect: SMD=0.67, 95%CI: 0.32-1.03; participants=131, 1RCT).

3.4.3 Attitudes toward HPV vaccination

Fig. 2 presents the meta-analysis of four trials that examined attitudes of students toward HPV vaccination. Evidence showed that school-based cervical cancer education was ineffective in improving attitudes toward HPV vaccination (Random effect: SMD= -0.02, 95%CI: -0.17-0.14; participants=675, 4RCTs). There were inconsistencies in the direction of effect, with three trials showing no slight or significant impact of the intervention on risk perceptions of HPV and cervical cancer. There was no evidence of statistical heterogeneity (I^2=0%).

3.4.4 Intentions toward HPV vaccination

We conducted a meta-analysis of five RCTs assessing the intentions of female students toward HPV vaccination (see Figure 3). Compared to the control group, school-based cervical cancer education resulted in significant improvements in HPV vaccination intentions (Random effect: SMD=0.20, 95%CI: 0.05-0.36; participants=967, 5 RCTs). There was a small, pooled effect with low certainty of evidence given the wide confidence interval. Almost all the trials favoured the intervention, with two trials showing a greater impact of school-based health education. There was minimal statistical heterogeneity (I^2=22%) between effect sizes. However, given that clinical heterogeneity was present, subgroup analysis was performed to explore the differences in effect sizes.

Subgroup analysis: Although no significant subgroup effect was detected across all intervention characteristics, a significant small effect was observed for studies using single-mode presentation (Random effect: SMD=0.26, 95%CI: 0.06-0.46), participants=790, 4 RCTs), an instructive approach and HPV-related content (Random effect: SMD=0.24, 95%CI: 0.03-0.44; participants=832, 4 RCTs) (See S5, S18-S19). We are uncertain about this finding given the wide confidence intervals.

Table 2. Risk of Bias assessment

Study	Randomisation process	Deviations from intended interventions (*effect of assignment to intervention*)	Missing outcome data	Measurement of the outcome	Selection of the reported results	Overall
Baxter and Barata 2011	🟨	🟨	🟢	🟢	🟢	🟨
Bennett, Patel et al. 2015	🟢	🟨	🟢	🟢	🟢	🟨
Christensen 2014	🟨	🟨	🟢	🟢	🟢	🟨
Doherty and Low 2008	🟨	🟨	🟢	🟢	🟢	🟨
Grandahl, Rosenblad et al. 2016	🟨	🟨	🟢	🟢	🟢	🟨
Hopfer and Hopfer 2012	🟨	🟨	🟢	🟢	🟢	🟨
Kim, Lee et al. 2020	🟨	🟨	🟢	🟢	🟢	🟨
McKeever 2013	🟢	🟨	🟢	🟢	🟢	🟨
Merzouk 2011	🟨	🟨	🟢	🟢	🟢	🟨
Nadarzynski et al. 2012	🟨	🟨	🟢	🟢	🟢	🟨
Perez et al. 2016	🟢	🟨	🟢	🟢	🟢	🟨
Steckelberg et al. 2013	🟢	🟢	🟢	🟢	🟢	🟢
Stock et. al. 2013	🟨	🟨	🟢	🟢	🟢	🟨

Legend: ***Low risk*** 🟢 ***Some concerns*** 🟨 ***High risk*** 🔺

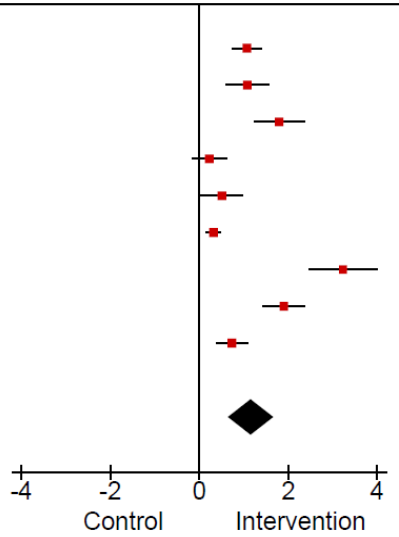
Figure 1: Effect of intervention (school-based cervical cancer education) compared to control (usual care/no education) on knowledge about and risk perceptions of cervical cancer and HPV infection

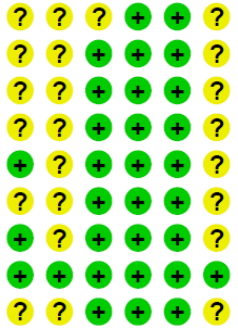
Outcome 1: Forest plot of knowledge about cervical cancer, HPV infection and HPV vaccination, n=1436

Study or Subgroup	SMD	SE	Intervention Total	Control Total	Weight	Std. mean difference IV, Random, 95% CI
Baxter 2011	1.0697	0.165	133	60	11.7%	1.07 [0.75 , 1.39]
Christensen 2014	1.0795	0.2497	37	37	11.0%	1.08 [0.59 , 1.57]
Doherty 2008	1.7923	0.29	36	32	10.5%	1.79 [1.22 , 2.36]
Kim 2020	0.2229	0.1969	54	50	11.5%	0.22 [-0.16 , 0.61]
Mckeever 2013	0.5076	0.2398	41	32	11.1%	0.51 [0.04 , 0.98]
Merzouk 2011	0.3184	0.0819	372	254	12.2%	0.32 [0.16 , 0.48]
Perez 2016 follow-up	3.2298	0.3929	31	31	9.4%	3.23 [2.46 , 4.00]
Steckelberg 2013	1.8989	0.2365	53	52	11.1%	1.90 [1.44 , 2.36]
Stock 2013	0.7353	0.1811	70	61	11.6%	0.74 [0.38 , 1.09]
Total (95% CI)			**827**	**609**	**100.0%**	**1.15 [0.67 , 1.63]**

Heterogeneity: Tau² = 0.48; Chi² = 116.93, df = 8 (P < 0.00001); I² = 93%

Test for overall effect: Z = 4.73 (P < 0.00001)



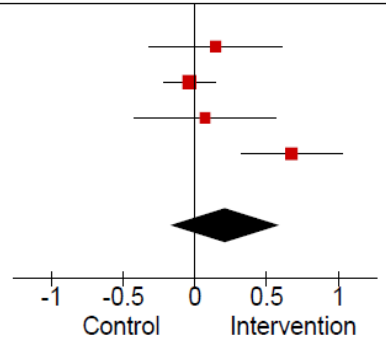


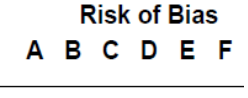
Outcome 2: Forest plot of risk perception of cervical cancer and HPV infection, n=872

Study or Subgroup	SMD	SE	Intervention Total	Control Total	Weight	Std. mean difference IV, Random, 95% CI
Mckeever 2013	0.1446	0.2362	41	32	21.9%	0.14 [-0.32 , 0.61]
Nadarzynski 2012 follow-up	-0.0388	0.0929	450	156	31.6%	-0.04 [-0.22 , 0.14]
Perez 2016 follow-up	0.0709	0.2541	31	31	20.7%	0.07 [-0.43 , 0.57]
Stock 2013	0.6745	0.1802	70	61	25.8%	0.67 [0.32 , 1.03]
Total (95% CI)			**592**	**280**	**100.0%**	**0.21 [-0.15 , 0.57]**

Heterogeneity: Tau² = 0.10; Chi² = 12.42, df = 3 (P = 0.006); I² = 76%

Test for overall effect: Z = 1.14 (P = 0.25)





Risk of bias legend
(A) Randomisation process
(B) Deviation from intended intervention
(C) Missing outcome data
(D) Measurement of the outcome
(E) Selection of the reported results
(F) Overall risk of bias

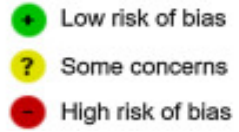


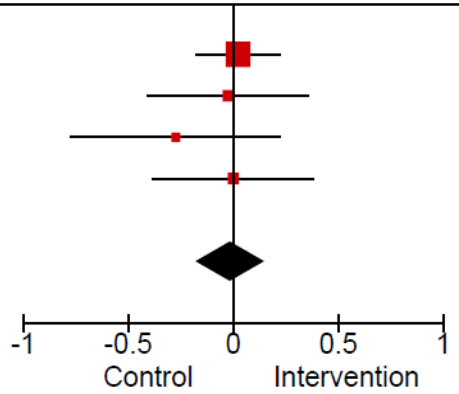
Figure 2: Effects of intervention (school-based cervical cancer education) compared to control (usual care/no education) on attitudes toward HPV vaccination

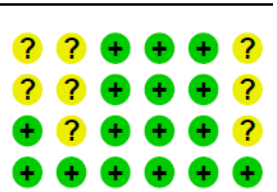
Outcome: Forest plot of attitudes toward HPV vaccination, n=675

Study or Subgroup	SMD	SE	Intervention Total	Control Total	Weight	Std. mean difference IV, Random, 95% CI
Hopfer 2012	0.0228	0.1027	252	152	58.4%	0.02 [-0.18 , 0.22]
Kim 2020	-0.0243	0.1963	54	50	16.0%	-0.02 [-0.41 , 0.36]
Perez 2016 follow-up	-0.2737	0.2553	31	31	9.5%	-0.27 [-0.77 , 0.23]
Steckelberg 2013	0	0.1952	53	52	16.2%	0.00 [-0.38 , 0.38]
Total (95% CI)			**390**	**285**	**100.0%**	**-0.02 [-0.17 , 0.14]**

Heterogeneity: Tau² = 0.00; Chi² = 1.17, df = 3 (P = 0.76); I² = 0%

Test for overall effect: Z = 0.21 (P = 0.83)





Risk of bias legend
(A) Randomisation process
(B) Deviation from intended intervention
(C) Missing outcome data
(D) Measurement of the outcome
(E) Selection of the reported results
(F) Overall risk of bias

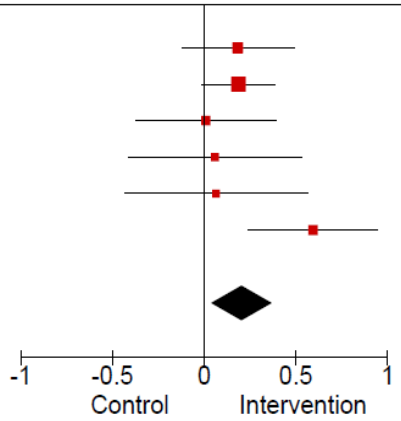
Figure 3: Effects of intervention (school-based cervical cancer education) compared to control (usual care/no education) on intentions toward and uptake of HPV vaccination

Outcome 1: Forest plot of intention toward HPV vaccination, n=967

Study or Subgroup	SMD	SE	Intervention Total	Control Total	Weight	Std. mean difference IV, Random, 95% CI
Baxter 2011	0.1835	0.1558	133	60	19.4%	0.18 [-0.12 , 0.49]
Hopfer 2012	0.1865	0.1029	252	152	33.3%	0.19 [-0.02 , 0.39]
Kim 2020	0.0098	0.1963	54	50	13.5%	0.01 [-0.37 , 0.39]
Mckeever 2013	0.0592	0.24	41	32	9.6%	0.06 [-0.41 , 0.53]
Perez 2016 follow-up	0.0646	0.2541	31	31	8.7%	0.06 [-0.43 , 0.56]
Stock 2013	0.5934	0.1791	70	61	15.6%	0.59 [0.24 , 0.94]
Total (95% CI)			**581**	**386**	**100.0%**	**0.20 [0.05 , 0.36]**

Heterogeneity: Tau² = 0.01; Chi² = 6.42, df = 5 (P = 0.27); I² = 22%

Test for overall effect: Z = 2.55 (P = 0.01)

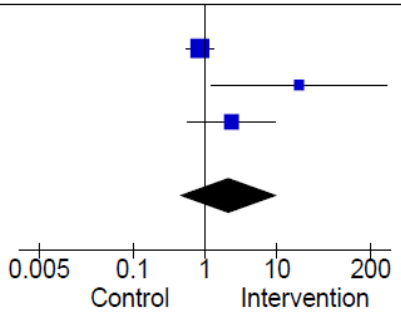


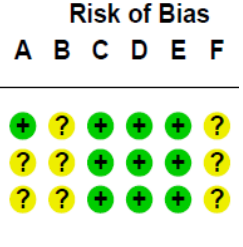
Outcome 2: Forest plot of HPV vaccination uptake, n=1150

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds ratio M-H, Random, 95% CI
Bennett 2015	39	330	45	331	47.9%	0.85 [0.54 , 1.35]
Grandhal 2016	15	239	0	146	17.7%	20.23 [1.20 , 340.69]
Kim 2020 follow-up	7	54	3	50	34.4%	2.33 [0.57 , 9.57]
Total (95% CI)		**623**		**527**	**100.0%**	**2.11 [0.48 , 9.20]**
Total events:	61		48			

Heterogeneity: Tau² = 1.12; Chi² = 6.89, df = 2 (P = 0.03); I² = 71%

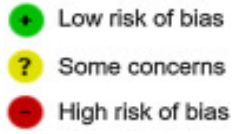
Test for overall effect: Z = 0.99 (P = 0.32)





Risk of bias legend

(A) Randomisation process
(B) Deviation from intended intervention
(C) Missing outcome data
(D) Measurement of the outcome
(E) Selection of the reported results
(F) Overall risk of bias



3.4.5 Uptake of HPV vaccination

Of the 13 trials, three RCTs were included in the meta-analysis assessing the uptake of HPV vaccination among female students (see Figure 3). The pooled estimate showed no impact of school-based education in increasing HPV uptake (Random effect: OR=2.11, 95%CI: 0.48-9.20, participants=1150, 3RCTs). However, two studies favoured the intervention, with one study showing a very large effect size (Random effect: OR=20.23, 95%CI: 1.20-340.69; participants=385, 2RCTs). There was substantial statistical heterogeneity (I^2=71%) between effect sizes. As a result, we proceeded to conduct a subgroup analysis.

Subgroup analysis: For this outcome, significant subgroup effects were found for the pedagogical approach and delivery method used by trials (See S5, S25-S26). A trial using a combination of the constructive approach and a face-to-face delivery method had a large positive impact on increasing uptake of HPV vaccination (Random effect: OR=20.23, 95%CI: 1.20-340.69; participants=385, 1RCT) compared to those using a combination of the instructive approach, online and printed materials. However, given the very wide confidence interval, the effect was uncertain.

3.5 Summary of findings and assessment of the quality of evidence

The assessment of the quality of evidence is summarised in Table 3; S30. Quality of evidence was deemed; low for three outcomes (knowledge about cervical cancer and HPV infection; Risk perceptions of cervical cancer and HPV infection, and HPV vaccination uptake); and moderate for two outcomes (attitudes and intentions toward HPV vaccination). The main drivers for downgrading the evidence were imprecision and unexplained heterogeneity.

Table 3: Summary of evidence for outcomes: Effect of school-based cervical cancer education compared to control (usual care/no education) among female students.

Outcomes	№ of participants (studies)	Relative effect (95% CI)	Absolute effect (95% CI)	Certainty of the evidence (GRADE)
Knowledge about cervical cancer and HPV infection	1436 (9 RCTs)	-	SMD **1.15 higher*** (0.67 higher to 1.63 higher)	⊕⊕◯◯ LOW [a,d]
Risk perception of cervical cancer and HPV infection	872 (4 RCTs)	-	SMD **0.21 higher** (0.15 lower to 0.57 higher)	⊕⊕◯◯ LOW [b,d]
Attitudes toward HPV vaccination	675 (4 RCTs)	-	SMD **0.02 lower** (0.17 lower to 0.14 higher)	⊕⊕⊕◯ MODERATE [d]
HPV vaccination intention	967 (5 RCTs)	-	SMD **0.2 higher*** (0.05 higher to 0.36 higher)	⊕⊕⊕◯ MODERATE [d]
HPV vaccination uptake	1150 (3 RCTs)	**OR 2.11** (0.48 to 9.20)	**83 more per 1,000** (45 fewer to 389 more)	⊕⊕◯◯ LOW [c,d]

GRADE Working Group grades of evidence
High certainty: *We are very confident that the true effect lies close to that of the estimate of the effect*
Moderate certainty: *We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different*
Low certainty: *Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect*
Very low certainty: *We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect*

CI: Confidence interval; SMD: Standardized mean difference; OR: Odds ratio
** Significant at p<0.05*

Explanations

a. Downgraded by 1 level for serious inconsistency: There is high degree of inconsistency evident, as measured by heterogeneity statistics in the meta-analysis (I^2=93%) indicating considerable heterogeneity, which was partially explained by subgroup analyses. A large degree of variation was also evident in measurement of the outcome with non-overlapping confidence intervals.
b. Downgraded by 1 level for serious inconsistency: There is high degree of inconsistency evident, as measured by heterogeneity statistics in the meta-analysis (I^2=76%) indication substantial heterogeneity, which was explained by subgroup analyses. A large degree of variation was also evident in measurement of the outcome with non-overlapping confidence intervals.
c. Downgraded by 1 level for serious inconsistency: There is high degree of inconsistency evident, as measured by heterogeneity statistics in the meta-analysis (I^2=71%) indication substantial heterogeneity, which was explained by subgroup analyses. A large degree of variation was also evident in measurement of the outcome with non-overlapping confidence intervals.
d. Downgraded by 1 level for serious imprecision: the 95% CI is wide and includes both important effects and negligible or no effect.

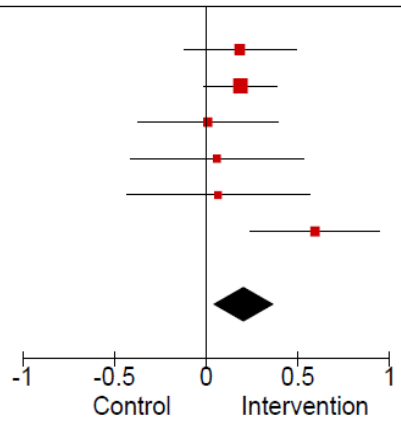
Figure 3: Effects of intervention (school-based cervical cancer education) compared to control (usual care/no education) on intentions toward and uptake of HPV vaccination

Outcome 1: Forest plot of intention toward HPV vaccination, n=967

Study or Subgroup	SMD	SE	Intervention Total	Control Total	Weight	Std. mean difference IV, Random, 95% CI	Risk of Bias A B C D E F
Baxter 2011	0.1835	0.1558	133	60	19.4%	0.18 [-0.12 , 0.49]	? ? ? + + ?
Hopfer 2012	0.1865	0.1029	252	152	33.3%	0.19 [-0.02 , 0.39]	? ? + + + ?
Kim 2020	0.0098	0.1963	54	50	13.5%	0.01 [-0.37 , 0.39]	? ? + + + ?
Mckeever 2013	0.0592	0.24	41	32	9.6%	0.06 [-0.41 , 0.53]	+ ? + + + ?
Perez 2016 follow-up	0.0646	0.2541	31	31	8.7%	0.06 [-0.43 , 0.56]	+ ? + + + ?
Stock 2013	0.5934	0.1791	70	61	15.6%	0.59 [0.24 , 0.94]	? ? + + + ?
Total (95% CI)			**581**	**386**	**100.0%**	**0.20 [0.05 , 0.36]**	

Heterogeneity: Tau² = 0.01; Chi² = 6.42, df = 5 (P = 0.27); I² = 22%

Test for overall effect: Z = 2.55 (P = 0.01)

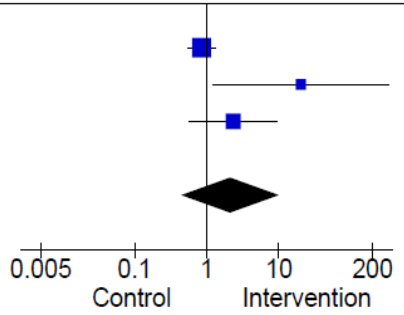


Outcome 2: Forest plot of HPV vaccination uptake, n=1150

Study or Subgroup	Intervention Events	Intervention Total	Control Events	Control Total	Weight	Odds ratio M-H, Random, 95% CI	Risk of Bias A B C D E F
Bennett 2015	39	330	45	331	47.9%	0.85 [0.54 , 1.35]	+ ? + + + ?
Grandhal 2016	15	239	0	146	17.7%	20.23 [1.20 , 340.69]	? ? + + + ?
Kim 2020 follow-up	7	54	3	50	34.4%	2.33 [0.57 , 9.57]	? ? + + + ?
Total (95% CI)		**623**		**527**	**100.0%**	**2.11 [0.48 , 9.20]**	
Total events:	61		48				

Heterogeneity: Tau² = 1.12; Chi² = 6.89, df = 2 (P = 0.03); I² = 71%

Test for overall effect: Z = 0.99 (P = 0.32)



Risk of bias legend
(A) Randomisation process
(B) Deviation from intended intervention
(C) Missing outcome data
(D) Measurement of the outcome
(E) Selection of the reported results
(F) Overall risk of bias

+ Low risk of bias
? Some concerns
− High risk of bias

4. Discussion

This review comprehensively examined the evidence for using school-based education to improve knowledge and perceptions about cervical cancer and HPV infection, as well as attitudes and intentions toward, and uptake of HPV vaccination and cervical cancer screening among female students.

Our study suggests that school-based cervical cancer education may increase knowledge about cervical cancer, HPV infection and HPV vaccination but not risk perceptions among female students. Although all the intervention characteristics did not appear to modify education in subgroup analysis, an active learning approach and combining cervical cancer and HPV-related contents may achieve greater effects. An active learning approach creates interest in students, develops independent learning, and allows students to apply knowledge.[57] This is likely to contribute to the longer information retention period observed in the present review.

To improve cervical cancer and HPV infection risk perceptions, printed education materials on HPV-related information may be useful, as observed in subgroup analysis**.** Printed education materials are potentially effective and consistent in changing knowledge and attitudes during public health education.[58] The fact that printed education materials are visually appealing to students and normalise students' usual learning approach compared with online and face-to-face delivery explains this finding. Additionally, printed education materials are often left with students and could be used as a point of reference at any given time. This finding suggests that adopting educational strategies similar to those used in a typical classroom environment appears to effectively change risk perceptions and improve understanding about cervical cancer and HPV infection.

Our findings showed that school-based cervical cancer education is likely to be ineffective in improving attitudes toward HPV vaccination. The use of a brief, one-time school-based cervical cancer education with no reinforcement of learning by the included studies could explain this finding. Brief education is time-limited education that focuses on improving understanding and changing behaviours about health diseases.[59] While available evidence supports its effectiveness in improving attitudes and behaviours, particularly in the short term,[59] there is insufficient evidence to support long term impacts.[60]

Although school-based education can positively impact knowledge acquisition and be retained over a more extended period, it alone may be insufficient to influence attitudes. The education should be part of a comprehensive approach, including: enabling school environment, inclusion of parents and comprehensive curriculum content, multicomponent strategies and adequate delivery, and implementation (i.e., equipping the skills of teachers and active learning methods).[61] These strategies have been considered best practices for enhancing school-based sexual/reproductive health education and proven effective in promoting condom use; hence, they could be adopted to promote attitudes about HPV vaccination. However, this resource-intensive approach may be challenging to implement in some countries and regions. Therefore, strengthening one-time education using reinforcement techniques may be helpful for health educators. These techniques include: having an action plan after education, sending summaries of key concepts, suggesting where skills can be applied, and organizing quizzes of various formats about cervical cancer.[62, 63] While school-based cervical cancer education may probably yield small benefits for improving HPV vaccination intentions among female students, it may generally not be helpful if aimed at increasing vaccination uptake rates**.** Intending to go for HPV vaccination could be significantly achieved by a single modality and a passive approach. However, vaccination uptake may increase if cervical cancer education is delivered via a face-to-face active learning approach by problem-solving techniques. Nevertheless, adding other behavioural approaches (i.e., reminders) may be beneficial.

Few included RCTs explored the effect of school-based cervical cancer education on improving HPV vaccination uptake among female adolescents and young women. In addition, none of the included RCTs focused on knowledge, attitudes, perceptions, and uptake of cervical cancer screening among female students. This finding could be explained by the fact that participants were mostly younger than 21 years and therefore not yet eligible for cervical cancer screening. According to the WHO cervical cancer screening guidelines and national policies of the studies reviewed, the recommended age for cervical cancer screening is between 21 and 30.[64] More robust studies among eligible young women are still needed to investigate the effect of school-based education on long-term HPV vaccination and cervical cancer screening uptake.

No relevant RCTs were identified which focused on populations in LMICs. Given most LMICs have either newly implemented HPV vaccination and cervical cancer screening programs or have none could explain this finding.[65] Fortunately, the Global Alliance for Vaccines and Immunization (GAVI) is making efforts to supply subsidised vaccines to some LMICs to commence HPV vaccination programmes.[66, 67] However, due

to a lack of political commitment,[68] and stretched health budgets,[60] most LMICs have not implemented these programmes. Therefore, school-based cervical cancer education campaigns in LMIC settings could increase student knowledge and grassroots advocacy for governments and global partners to introduce and sustain these programmes. In light of this, investments into high-quality cervical cancer education intervention research should be prioritised given the increasing burden of cervical cancer in these settings.

More than half of the included studies did not report using theoretical frameworks for designing their interventions. Theoretical models provide a blueprint for designing health interventions aimed at knowledge acquisition and behaviour change. School-based education underpinned by evidence-based behaviour change and health-promoting models may be beneficial. Thus, an integrated approach, which leverages key structural and content components of social-emotional and behavioural health prevention models is crucial. The World Health Organization's Health Promoting Schools (HPS) framework [69] and the integrated behaviour model (IBM)[70] could be considered. While the IBM draws on aspects of many of the frameworks used by the 38% of intervention studies included in this review,[70] the HPS framework is a whole-school approach to promoting health and educational attainment, and has been shown to improve behaviours such as tobacco and drug use.[69]

Although no published meta-analytic review has focussed solely on female students, we compared our results with systematic reviews in mixed populations. In line with Flood et al. (2020),[33] school-based education effectively improved HPV infection knowledge and vaccination intentions; however, there was contrasting evidence because they reported that school-based education improved attitudes and uptake of HPV vaccination. A possible explanation for these differences is that Flood et al. focussed on adolescent students between 15 and 17 years and other HPV-related diseases, including oral cancer. They also included both RCTs and non-RCTs.

Our findings should be interpreted with caution given that methodological shortcomings were identified for all but one of the included studies. These inadequacies were mainly related to concerns about the randomization process and inadequate information about the intervention assignment. Allocation concealment and blinding are essential in RCTs because they are used in controlling for confounding.[71] However, blinding is often poorly reported,[72] which raises concerns about the quality of many RCTs. To increase the quality of evidence for using school-based cervical cancer education, further RCTs are required

that are both designed and reported according to recommended guidelines such as the Consolidated Standards of Reporting Trials (CONSORT).

Limitations of this review

The present review had some limitations. First, this review was limited to English papers and potential for publication bias. Given non-English articles were not included in this review, relevant articles may have been missed. Second, due to the inadequate number of included trials, publication bias for all outcomes was not assessed as initially intended. We minimized the risk of missing quality papers published in other languages and publication bias by conducting searches in different databases and undertaking manual searches. Third, the presence of statistical and clinical heterogeneity affected the quality of evidence. This was due to the different population types, intervention characteristics and outcome measures. Fourth, the analysis and treatment of heterogeneity for this review may be potentially underpowered because of too few studies and student participants in some outcomes. As a result, when subgroup analysis was performed for some outcomes, the covariate for distribution was concerning and may not detect subgroup differences.[73] Finally, there were potential measurement errors. We noted variation in how outcomes were measured, for example, knowledge about cervical cancer and HPV infection. Although no standardized tool is available for measuring knowledge, a lack of consistency in measurement approaches across studies may reduce the validity of findings. Therefore, a standardized unit was used in meta-analysis to minimize errors in this review.

4.1 Practice implications

While robust evidence-based recommendations cannot be made based on this review, it appears that school-based cervical cancer education can improve student knowledge and increase intentions toward HPV vaccination to a limited extent. Information could be presented as either active interactions with students or passive, non-didactic approaches, and in the form of written text/images. Whereas active face-to-face engagement of female students may increase HPV vaccination uptake rates, less costly methods (i.e., written words/images) on health information websites can improve cervical cancer and HPV infection risk perceptions. An even cheaper strategy may involve using active face-to-face webinars for delivering cervical cancer information to increase vaccination rates.

In an era of pandemics leading to lockdowns and minimal face-to-face in-person interactions, these approaches could be useful in disseminating cervical cancer education. Reinforcement techniques should also be included in one-time health education lesson plans to promote recall. An objective to improve; risk perceptions of cervical cancer and HPV infection, attitudes and uptake of HPV vaccination may need other comprehensive approaches (including long-term follow-up) in addition to education.

5. Conclusion

This review identified methodological deficiencies in the included studies, indicating that more robust RCTs are needed, with LMICs as a priority setting. The moderate to low certainty evidence suggests that, generally, school-based education may effectively increase knowledge about cervical cancer, HPV infection and HPV vaccination. The education could probably improve HPV vaccination intentions but not attitudes, risk perceptions, and uptake among female students. Single modalities (i.e., spoken or written words or images or videos) and non-didactic ways (i.e., printed materials) may probably impact risk perceptions and intentions. Uptake of HPV vaccination may require a more active approach. We recommend that innovative teaching methods (i.e., game-based learning) be explored as they have been found useful in improving sexual health behaviours.[74] Given the rising health challenges worldwide, including COVID-19 vaccination knowledge and hesitancy; updated and innovative traditional education strategies with long-term follow-up could improve intentions and uptake of COVID-19 vaccination.

Future studies should utilize rigorous methodological study processes to explore the effect of current best practices for health education on improving knowledge and risk perception of HPV and cervical cancer, attitudes and intentions toward, and uptake of HPV vaccination and cervical cancer screening. This will allow uniformity in school-based health education strategies to build quality evidence to support its effectiveness among female adolescents and young women.

References

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: A Cancer Journal for Clinicians* 2018; 68: 394-424. DOI: 10.3322/caac.21492.

2. Drolet M, Benard E, Perez N, et al. Population-level impact and herd effects following the introduction of human papillomavirus vaccination programmes: updated systematic review and meta-analysis. *Lancet* 2019; 394: 497-509. 2019/07/01. DOI: 10.1016/s0140-6736(19)30298-3.

3. WORLD HEALTH ORGANIZATION. *Weekly epidemiological record*. October 2014 2014.

4. Hung M-C, Liu M-T, Cheng Y-M, et al. Estimation of savings of life-years and cost from early detection of cervical cancer: a follow-up study using nationwide databases for the period 2002–2009. *BMC Cancer* 2014; 14: 505. DOI: 10.1186/1471-2407-14-505.

5. Sankaranarayanan R, Nene BM, Shastri SS, et al. HPV screening for cervical cancer in rural India. *New England Journal of Medicine* 2009; 360: 1385-1394.

6. Peirson L, Fitzpatrick-Lewis D, Ciliska D, et al. Screening for cervical cancer: a systematic review and meta-analysis. *Systematic Reviews* 2013; 2: 35. DOI: 10.1186/2046-4053-2-35.

7. Kirubarajan A, Leung S, Li X, et al. Barriers and facilitators for cervical cancer screening among adolescents and young people: a systematic review. *BMC women's health* 2021; 21: 122. 2021/03/25. DOI: 10.1186/s12905-021-01264-x.

8. Amboree TL and Darkoh C. Barriers to Human Papillomavirus Vaccine Uptake Among Racial/Ethnic Minorities: a Systematic Review. *Journal of racial and ethnic health disparities* 2020 2020/10/08. DOI: 10.1007/s40615-020-00877-6.

9. Bruni L, Diaz M, Barrionuevo-Rosas L, et al. Global estimates of human papillomavirus vaccination coverage by region and income level: a pooled analysis. *The Lancet Global health* 2016; 4: e453-463. 2016/06/25. DOI: 10.1016/s2214-109x(16)30099-7.

10. Thamsborg LH, Andersen B, Larsen LG, et al. Danish method study on cervical screening in women offered HPV vaccination as girls (Trial23): a study protocol. *BMJ open* 2018; 8: e020294.

11. Canfell K. Towards the global elimination of cervical cancer. *Papillomavirus Research* 2019; 8: 100170. DOI: https://doi.org/10.1016/j.pvr.2019.100170.

12. Organisation WH. Vaccines and immunization, https://www.euro.who.int/en/health-topics/disease-prevention/vaccines-and-immunization/news/news/2017/07/collaboration-among-immunization-programmes-aims-to-bring-europe-closer-to-stopping-hpv (2017, accessed 08 July 2021).

13. Hanley SJB, Yoshioka E, Ito Y, et al. HPV vaccination crisis in Japan. *The Lancet* 2015; 385: 2571. DOI: https://doi.org/10.1016/S0140-6736(15)61152-7.

14. Loke AY, Kwan ML, Wong YT, et al. The Uptake of Human Papillomavirus Vaccination and Its Associated Factors Among Adolescents: A Systematic Review. *Journal of primary care & community health* 2017; 8: 349-362. 2017/11/23. DOI: 10.1177/2150131917742299.

15. Lancucki L, Fender M, Koukari A, et al. A fall-off in cervical screening coverage of younger women in developed countries. *Journal of medical screening* 2010; 17: 91-96. 2010/07/28. DOI: 10.1258/jms.2010.010017.

16. Health and Centre SCI. Cervical Screening Programme: England, statistics for 2014-15. Health and Social Care Information Centre Leeds, 2015.

17. Pengpid S and Peltzer K. Attitudes and practice of cervical cancer screening among female university students from 25 low, middle income and emerging economy countries. *Asian Pacific Journal of Cancer Prevention* 2014; 15: 7235-7239.

18. World Health Organization. *Health for the world's adolescents: a second chance in the second decade: summary*. 2014. World Health Organization.

19. Langford R, Bonell C, Komro K, et al. The Health Promoting Schools Framework: Known Unknowns and an Agenda for Future Research. *Health Educ Behav* 2016; 44: 463-475. DOI: 10.1177/1090198116673800.

20. Masini A, Marini S, Gori D, et al. Evaluation of school-based interventions of active breaks in primary schools: A systematic review and meta-analysis. *Journal of science and medicine in sport* 2020; 23: 377-384.

21. Monroe MC. Children teach their parents. *Nature Climate Change* 2019; 9: 435-436.

22. Lewis RM, Laprise J-F, Gargano JW, et al. Estimated prevalence and incidence of disease-associated human papillomavirus types among 15-to 59-year-olds in the United States. *Sexually transmitted diseases* 2021; 48: 273-277.

23. Scott RH, Wellings K and Lindberg L. Adolescent Sexual Activity, Contraceptive Use, and Pregnancy in Britain and the U.S.: A Multidecade Comparison. *Journal of Adolescent Health* 2020; 66: 582-588. DOI: https://doi.org/10.1016/j.jadohealth.2019.11.310.

24. Liu G, Hariri S, Bradley H, et al. Trends and patterns of sexual behaviors among adolescents and adults aged 14 to 59 years, United States. *Sexually transmitted diseases* 2015; 42: 20-26. 2014/12/17. DOI: 10.1097/olq.0000000000000231.

25. Christensen S. Evaluation of a nurse-designed mobile health education application to enhance knowledge of Pap testing. *Creat Nurs* 2014; 20: 137-143. DOI: http://dx.doi.org/10.1891/1078-4535.20.2.137.

26. Merzouk MD, Courtney P, Garrett-Albaugh S, et al. Knowledge of HPV in West Virginia High School Health Students and the Effects of an Educational Tool. *Journal of Pediatric and Adolescent Gynecology* 2011; 24: 278-281. DOI: 10.1016/j.jpag.2011.03.010.

27. Bennett AT, Patel DA, Carlos RC, et al. Human Papillomavirus Vaccine Uptake After a Tailored, Online Educational Intervention for Female University Students: A Randomized Controlled Trial. *Journal of Womens Health* 2015; 24: 950-957. DOI: 10.1089/jwh.2015.5251.

28. Grandahl M, Rosenblad A, Stenhammar C, et al. School-based intervention for the prevention of HPV among adolescents: a cluster randomised controlled study. *BMJ Open* 2016; 6. DOI: 10.1136/bmjopen-2015-009875.

29. Hopfer S and Hopfer S. Effects of a narrative HPV vaccination intervention aimed at reaching college women: a randomized controlled trial. *Prevention Science* 2012; 13: 173-182. DOI: 10.1007/s11121-011-0254-1.

30. Nadarzynski T, Waller J, Robb KA, et al. Perceived risk of cervical cancer among pre-screening age women (18-24 years): the impact of information about cervical cancer risk factors and the causal role of HPV. *Sexually Transmitted Infections* 2012; 88: 400-406. Randomized Controlled Trial

Research Support, Non-U.S. Gov't.

31. Fu LY, Bonhomme LA, Cooper SC, et al. Educational interventions to increase HPV vaccination acceptance: a systematic review. *Vaccine* 2014; 32: 1901-1920. 2014/02/18. DOI: 10.1016/j.vaccine.2014.01.091.

32. Walling EB, Benzoni N, Dornfeld J, et al. Interventions to Improve HPV Vaccine Uptake: A Systematic Review. *Pediatrics* 2016; 138 2016/06/15. DOI: 10.1542/peds.2015-3863.

33. Flood T, Wilson IM, Prue G, et al. Impact of school-based educational interventions in middle adolescent populations (15-17yrs) on human papillomavirus (HPV) vaccination uptake and perceptions/knowledge of HPV and its associated cancers: A systematic review. *Preventive medicine* 2020; 139: 106168. 2020/07/01. DOI: 10.1016/j.ypmed.2020.106168.

34. Barnard M, Cole AC, Ward L, et al. Interventions to increase uptake of the human papillomavirus vaccine in unvaccinated college students: A systematic literature review. *Preventive medicine reports* 2019; 14: 100884. 2019/06/14. DOI: 10.1016/j.pmedr.2019.100884.

35. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021; 372: n71. DOI: 10.1136/bmj.n71.

36. Hariton E and Locascio JJ. Randomised controlled trials—the gold standard for effectiveness research. *BJOG: an international journal of obstetrics and gynaecology* 2018; 125: 1716.

37. The Cochrane Collaboration. *Review Manager (RevMan) Version 5.3* The Nordic Cochrane Centre, Copenhagen 2014.

38. Higgins JP, Thomas J, Chandler J, et al. *Cochrane handbook for systematic reviews of interventions*. John Wiley & Sons, 2019.

39. Wilson D. Practical meta-analysis effect size calculator. The Campbell Collaboration, (2018, 08 April 2021).

40. Chinn S. A simple method for converting an odds ratio to effect size for use in meta-analysis. *Statistics in medicine* 2000; 19: 3127-3131.

41. Borenstein M, Hedges LV, Higgins JP, et al. *Introduction to meta-analysis*. John Wiley & Sons, 2021.

42. DerSimonian R and Laird N. Meta-analysis in clinical trials. *Controlled clinical trials* 1986; 7: 177-188.

43. Cohen J. Statistical power analysis for the social sciences. 1988.

44. Northcote M, Marshall L and Lenoy M. Theory, practice and reflection: The value of integrated learning systems from four different perspectives. In: *Teaching and Learning Forum* 2002.

45. Moreno R and Mayer R. Interactive Multimodal Learning Environments. *Educational Psychology Review* 2007; 19: 309-326. DOI: 10.1007/s10648-007-9047-2.

46. Vally Z and Abrahams L. The effectiveness of peer-delivered services in the management of mental health conditions: a meta-analysis of studies from low-and middle-income countries. *International Journal for the Advancement of Counselling* 2016; 38: 330-344.

47. Xie C, Wang M and Hu H. Effects of constructivist and transmission instructional models on mathematics achievement in Mainland China: A meta-analysis. *Frontiers in psychology* 2018; 9: 1923.

48. Sterne JA, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *bmj* 2019; 366.

49. GRADEpro GDT. GRADEpro Guideline Development Tool [Software]. McMaster University, 2020 (developed by Evidence Prime, Inc.), Available from gradepro.org (2020).

50. Christensen S. Evaluation of a nurse-designed mobile health education application to enhance knowledge of Pap testing. *Creat Nurs* 2014; 20: 137-143. Randomized Controlled Trial

Research Support, Non-U.S. Gov't.

51. Doherty K and Low KG. The Effects of a Web-Based Intervention on College Students' Knowledge of Human Papillomavirus and Attitudes toward Vaccination. *International Journal of Sexual Health* 2008; 20: 223-232. DOI: 10.1080/19317610802411177.

52. Kim M, Lee H, Kiang P, et al. A Storytelling Intervention in a Mobile, Web-Based Platform: A Pilot Randomized Controlled Trial to Evaluate the Preliminary Effectiveness to Promote Human Papillomavirus Vaccination in Korean American College Women. *Health Education & Behavior* 2020; 47: 258-263. DOI: 10.1177/1090198119894589.

53. McKeever AE. Human Papillomavirus Vaccine Education in Young Adult Women: Using Risk Reduction Models to Improve Vaccine Initiation and Completion Rates. *Journal of Gynecologic Oncology Nursing* 2013; 23: 12-23.

54. Perez GK, Cruess DG and Strauss NM. A brief information-motivation-behavioral skills intervention to promote human papillomavirus vaccination among college-aged women. *Psychology Research and Behavior Management* 2016; 9: 285-296. DOI: 10.2147/prbm.S112504.

55. Steckelberg A, Albrecht M, Kezle A, et al. Impact of numerical information on risk knowledge regarding human papillomavirus (HPV) vaccination among schoolgirls: a randomised controlled trial. *German medical science : GMS e-journal* 2013; 11.

56. Stock ML, Peterson LM, Houlihan AE, et al. Influence of Oral Sex and Oral Cancer Information on Young Adults' Oral Sexual-Risk Cognitions and Likelihood of HPV Vaccination. *Journal of Sex Research* 2013; 50: 95-102. DOI: 10.1080/00224499.2011.642904.

57. Sivan A, Leung RW, Woon C-c, et al. An implementation of active learning and its effect on the quality of student learning. *Innovations in education and training international* 2000; 37: 381-389.

58. Redman S and Paul C. *A review of the effectiveness of print material in changing health- related knowledge, attitudes and behaviour*. Copyright Agency, 1997, p.9.

59. Lamming L, Pears S, Mason D, et al. What do we know about brief interventions for physical activity that could be delivered in primary care consultations? A systematic review of reviews. *Preventive Medicine* 2017; 99: 152-163. DOI: https://doi.org/10.1016/j.ypmed.2017.02.017.

60. Young MM, Stevens A, Galipeau J, et al. Effectiveness of brief interventions as part of the Screening, Brief Intervention and Referral to Treatment (SBIRT) model for reducing the nonmedical use of psychoactive substances: a systematic review. *Systematic Reviews* 2014; 3: 50. DOI: 10.1186/2046-4053-3-50.

61. Vanwesenbeeck I. Comprehensive sexuality education. *Oxford Research Encyclopedia of Global Public Health*. 2020.

62. Bell DS, Harless CE, Higa JK, et al. Knowledge retention after an online tutorial: a randomized educational experiment among resident physicians. *Journal of general internal medicine* 2008; 23: 1164-1171.

63. Papaioannou EZ. After A Web Conference: How To Reinforce Learning (2021, accessed 27 July 2021).

64. World Health Organization. WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention, second edition. In: Organization. WH, (ed.). Geneva World Health Organization, 2021, p. 24-38.

65. Olson B, Gribble B, Dias J, et al. Cervical cancer screening programs and guidelines in low-and middle-income countries. *International Journal of Gynecology & Obstetrics* 2016; 134: 239-246.

66. Global Alliance for Vaccines and Immunization (GAVI). Human papillomavirus vaccine support, https://www.gavi.org/types-support/vaccine-support/human-papillomavirus (2021, accessed 01/12/2021).

67. Shinkafi-Bagudu Z. Global Partnerships for HPV Vaccine Must Look Beyond National Income. *JCO Global Oncology* 2020: 1746-1748. DOI: 10.1200/go.20.00504.

68. Duncan J, Harris M, Skyers N, et al. A Call for Low- and Middle-Income Countries to Commit to the Elimination of Cervical Cancer. *The Lancet Regional Health - Americas* 2021; 2: 100036. DOI: https://doi.org/10.1016/j.lana.2021.100036.

69. Langford R, Bonell C, Jones H, et al. The World Health Organization's Health Promoting Schools framework: a Cochrane systematic review and meta-analysis. *BMC Public Health* 2015; 15: 130. DOI: 10.1186/s12889-015-1360-y.

70. Yzer M. The integrative model of behavioral prediction as a tool for designing health messages. *Health communication message design: Theory and practice* 2012; 21.

71. Renjith V. Blinding in randomized controlled trials: what researchers need to know? *Manipal Journal of Nursing and Health Sciences (MJNHS)* 2017; 3: 45-50.

72. Hróbjartsson A, Pildal J, Chan A-W, et al. Reporting on blinding in trial protocols and corresponding publications was often inadequate but rarely contradictory. *Journal of clinical epidemiology* 2009; 62: 967-973.

73. Richardson M, Garner P and Donegan S. Interpretation of subgroup analyses in systematic reviews: a tutorial. *Clinical Epidemiology and Global Health* 2019; 7: 192-198.

74. Haruna H, Hu X and Chu SKW. Adolescent school-based sexual health education and training: a literature review on teaching and learning strategies. *Global Journal of Health Sciences,* 2018; 10: 172.