ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΕΣΣΑΛΙΑΣ

ΤΜΗΜΑ ΙΑΤΡΙΚΗΣ

"Assess the reporting quality of randomized-controlled trials of Human Papilloma Virus (HPV) vaccines in cervical cancer prevention, based on CONSORT statement"

Πρόγραμμα Μεταπτυχιακών Σπουδών (ΠΜΣ) «Μεθοδολογία Βιοϊατρικής Έρευνας, Βιοστατιστική και Κλινική Βιοπληροφορική»

ΜΠΑΣΔΕΚΗ ΑΝΤΩΝΙΑ

ΜΕΤΑΠΤΥΧΙΑΚΗ ΦΟΙΤΗΤΡΙΑ

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Abstract

Background:

Physicians are based on the results of RCTs. It is important the reporting of these results to be completed and accurated. Uptoday the quality of RCTs in this disease have never been evaluated.

Methods: We searched PubMed Database for assess in the reporting quality of randomized-controlled trials of Human Papilloma Virus (HPV) vaccines in cervical cancer prevention , based on CONSORT statement. Quality of reporting was assessed using a 24-item questionnaire based on the revised CONSORT checklist. Given that all selected Randomized Controlled Trials (n=136) were published after 2006, the reporting quality was evaluated overall, and for pre -CONSORT version 2010 (2006-2009) - and post-CONSORT version 2010 (2010-1015) periods.

Results:

136 eligible trials were identified through literature research strategy. The comparison of pre -CONSORT version 2010 (2006-2009) - and post-CONSORT version 2010 (2010-1015) periods revealed a significant improvement ($p < 0.05$). These items were endpoints, sample size, statistical methods, participant flow, patient recruitment periods, intention-to-treat analysis, estimation of effects, ancillary analyses, adverse events and overall evidence.

Conclusion: Reporting quality of Randomized- controlled trials of Human Papillomavirus (HPV) vaccines in cervical cancer prevention it was improved across all items after issuing of CONSORT version 2010 statement implementation. Endorsement of the CONSORT statement may optimize the reporting quality and enhance the validity of research.

Background

Cervical cancer is the third most common cancer in women and the fourth most common cause of death worldwide. Infection with certain types of human papillomavirus (HPV) is necessary to develop cervical cancer. This has led to an increase in effectiveness of screening for cervical cancer using Pap smears and the development of primary prevention through the use of prophylactic vaccines against HPV.

The prophylactic vaccine stimulates the development of the humoral immune response, which occurs after contact with the “virus-like particles” (VLPs), which are non-infectious structures and simulate a natural HPV infection. The two oncogenic types included in both vaccines are HPV 16 and 18, responsible for at least 70% of the cases of cervical cancer worldwide. In the case of the quadrivalent vaccine, it also

included two non-oncogenic types of HPV, responsible for approximately 90% of cases of anogenital condylomata acuminata.

Safety and tolerability of both vaccines have been evaluated extensively with similar profiles in the vaccinated and control groups, irrespective of age or ethnicity. Studies about safety assessment indicated that local and systemic injection-related symptoms were generally mild. Serious adverse effects (AE) that are considered to be vaccine related are rare and similar to other vaccine types. Studies indicate that the most common AE is injection-related local reaction, such as pain, swelling and erythema with a rate of 95% of light to moderate intensity. Regarding systemic symptoms, fever, nausea, vomiting, dizziness, myalgia and diarrhea were reported.Severe AE, such as severe headache with hypertension, gastroenteritis and bronchospasm, were described in 0.5%.15 There are more data available of AE associated with the quadrivalent vaccine than the bivalent vaccine; however, the major AE for the latter vaccine is also in the injection-related local pain (78%).

Both HPV vaccines are classified as Pregnancy Category B by the FDA. Therefore, the vaccine is not recommended for pregnant women, because there are not enough data to ensure safety to the fetus. Studies have also demonstrated efficacy and safety of the vaccine in heterosexual and homosexual men. This is important as HPV also causes disease in men.

A clinical trial is a prospective biomedical or health related research study of human subjects designed to test new methods of screening, prevention, diagnosis, or treatment of a disease. These studies are conducted by physicians and other health professionals in a controlled environment to help determine the safety and efficacy of biological products, devices, drugs, medical treatments, procedures, or therapies to improve health. Clinical trials are conducted in phases that help answer different scientific questions.

Phase I trials

Test a new drug or treatment for the first time to evaluate safety and identify side effects in a small group of people.

Phase II trials

Study an experimental drug or treatment to determine its effectiveness and further evaluate safety in a large group of people.

Phase III trials

Confirm the drug or treatment effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the drug or treatment to be used safely in larger groups of people.

Phase IV trials

Are done after the drug or treatment has been marketed to gather information on the drug's effect in various populations and any side effects associated with long term use.

Late 90s, an international group of scientists, trialists, methodologists and journal editors developed and published a checklist of essential items that they proposed to be included in reports, accompanied by a diagram for documenting the flow of participants through a trial, known as the Consolidated Standards of Reporting Trials (CONSORT) statement. The statement has been translated into several languages and is accessible via internet (http://www.consort-statement.org) in order to enhance the public awareness. Its use is recommended by the International Committee of Medical Journal Editors, the Council of Editors, and the World Association of Medical Editors; to date, more than 300 biomedical journals, have adopted. Since the initial issuing, the original CONSORT statement was revised twice and updated to a 25 items checklist and a four-stage flow diagram, in order to facilitate critical appraisal and interpretation by providing guidance to authors about how to improve the reporting of their trials. In addition, extensions of the CONSORT Statement have been developed for other types of study designs, interventions and data.

The clinical study is very important because the doctors are based in these studies and help us improve the biomedical research.

Also it is reliable, while promoting medical Science.

Methods

Study identification & selection

Studies meeting the following criteria were included: several trials were blind, double-blind randomized clinical trials evaluating safety and adverse effects of human papillomavirus (HPV) vaccines studied subjects were older than nine years old, study participants with high risk of contracting, such as female sex workers and women who were sexual partners of HIV-infected men, and pregnant women.

Search and selection of literature

The studies were identified by only one database (PubMed Database 136 Papers) following medical subject heading terms and/or text words: (vaccines OR vaccination) AND (randomized controlled trial) OR (controlled clinical trial) OR (randomized controlled trials) OR (random location) OR (double blind method) OR (single blind method) OR (clinical trial) AND (Human papillomavirus) OR (HPV)

OR (papillomavirus) OR (papillomavirus*). Reference lists of the identified publications for additional pertinent studies were reviewed. Language English were imposed.

Consort statement

The CONSORT began in 1993, 30 experts comprised of medical journal editors, clinical trialists, epidemiologists, and methodologists met in Ottawa, Canada with the aim of developing a new scale to assess the quality of randomized controlled trial (RCT) reports. However, during preliminary discussions, participants felt that many of the suggested scale items were irrelevant because they were not regularly reported by authors. In fact, there was accumulating evidence that the quality of reports of RCTs was less than optimal. Therefore, unanimous agreement steered the remainder of the workshop to focus on ways to improve the reporting of RCTs.

Participants nominated items to be included in the checklist for which there was evidence, whenever possible, that not adequately reporting this information could lead to biased estimates of the benefits of the intervention under investigation. One outcome of the meeting was the Standardized Reporting of Trials (SORT) statement. This statement consisted of a 32-item checklist and flow diagram in which investigators were encouraged to report on the various aspects of how RCTs were conducted. Concurrently, and independently, another group of experts, the Asilomar Working Group on Recommendations for Reporting of Clinical Trials in the Biomedical Literature, convened in Asilomar (California), USA, were working on a similar mandate. This group also published a proposal which included a checklist of recommended items for authors to consider when reporting RCTs.

At the suggestion of Drummond Rennie, Deputy Editor of JAMA, representatives from both groups met in 1996, in Chicago, USA. The remit of this group was to merge the best of the SORT and Asilomar proposals into a single, coherent evidence-based recommendation. It was felt that a single recommendation would have a better likelihood of appealing to journals and thus improve dissemination. The meeting resulted in the Consolidated Standards of Reporting Trials (CONSORT) Statement, which was first published in 1996.Further meetings of the Group in 1999 and 2000 led to the publication of the revised CONSORT statement 2001. Following a meeting in January 2007, a further revision was developed and the CONSORT 2010 statement was published on March 24, 2010. Since the revision in 2001, the evidence base to inform CONSORT has grown considerably; empirical data had highlighted new concerns regarding the reporting of randomized controlled trials, such as selective outcome reporting.

Therefore, a CONSORT Group meeting was convened. Thirty-one members of the CONSORT group met in Montebello, Canada in January 2007 to update the 2001 CONSORT Statement. In addition to the accumulating evidence relating to existing checklist items, several new issues had come to prominence since 2001. Some participants were given primary responsibility for aggregating and synthesizing the relevant evidence on a particular checklist item of interest. Based on that evidence,

the group deliberated the value of each item. As in prior CONSORT versions, only those items deemed fundamental to reporting an RCT were kept. Moreover, an item may be fundamental to a trial but not included, such as approval by an institutional ethical review board, because funding bodies strictly enforce ethical review and medical journals usually address reporting ethical review in their instructions for authors. Other items may seem desirable, such as on-site monitoring, but a lack of empirical evidence or any consensus on their value cautions against inclusion at this point. The checklist thus addresses the minimum criteria.

After the meeting, the CONSORT Executive convened teleconferences and in-person meetings to revise the checklist. After seven major iterations, a revised checklist was distributed to the larger group for feedback. With that feedback, the Executive met twice in person to consider all the comments and to produce a penultimate version. That served as the basis for writing the first draft of this paper, which was then distributed to the group for feedback. After consideration of their comments, the Executive finalized the statement. (The CONSORT Executive then drafted an updated explanation and elaboration (E&E) manuscript, with assistance from other members of the larger group. The substance of the 2007 CONSORT meeting provided the material for the update. The updated E&E was distributed to the entire group for additions, deletions, and changes. That final iterative process converged to the CONSORT 2010 E&E. On March 24, 2010, eight journals simultaneously published the CONSORT 2010 Statement, and two journals published the CONSORT 2010 E&E.A summary of the specific changes to the CONSORT checklist was included in the CONSORT Statement.)The modified questionnaire separates the reporting of the recruitment from the follow up as well as the reporting of outcomes from the reporting of precision of their estimated effect. All items were investigated in terms of whether they were reported or not. In case of inadequate reporting or complete failure to report an item, those CONSORT checklist items were considered as negative responses.

Data abstraction

Given that all Randomized Controlled Trials qualified for this analysis were reported after 2006, the CONSORT version 2010 was used to define two reporting periods give .The selected manuscripts were grouped in two publication periods; The pre - CONSORT version 2010 (2006-2009) - and post-CONSORT version 2010 (2010-2015).The compliance to the CONSORT statement was assessed with reference to complete response and objective response rate.

The two publication periods pre -CONSORT version 2010 (2006-2009) - and post-CONSORT version 2010 (2010-2015) were compared by estimating the odds ratio (OR), with the respective 95% confidence interval, of reporting an item at one period relative to the other. Association between reporting of an item from CONSORT checklist and publication period was tested using the Fisher' exact test. Statistical significance was considered at the two-sided 0.05 level.

Results

Eligible studies

Detailed results of the literature research are presented in Figure 1.

The research strategy identified 5720 potentially eligible studies by searching Medline (through PubMed, n = 136). Thereafter, these articles were retrieved and screened for eligibility. Overall, a total of 136 unique articles remained for analysis having complete full-text evaluation. The inter-rater agreement level between the reviewers in article evaluation for eligibility and in extracting the data was both relatively high.

Study characteristics

The 136 eligible articles were published during the period 2006-2015. Thirty manuscripts were published during the pre CONSORT version 2010 period (2006-2009) while one hundred six were published in the post CONSORT version 2010 period (2010-2015).

Main results

Items were reported in almost all studies were the eligibility criteria for participants (100%), precise details of the interventions in each group (100%).

Overall, the reporting was improved across all items after CONSORT statement's implementation (Figure 2). In addition, the reporting of allocation concealment and implementation of randomization was poor in the majority of the reports.

The comparison of the two periods pre -CONSORT version 2010 (2006-2009) - and post-CONSORT version 2010 (2010-2015) revealed a significant improvement ($p < 0.05$) because the 106 papers at post -CONSORT version 2010 (2010-2015) had better results and more reliable from the 30 papers of pre -CONSORT version 2010 (2006-2009). This is being because the new version is much more valid the results as seen in Figure 2 the two graphs of explains the difference of the method which I used. These items were endpoints, sample size, statistical methods, participant flow, patient recruitment periods, intention-to-treat analysis, estimation of effects, ancillary analyses, adverse events and overall evidence, which are much more likely to be reported in the pre -CONSORT version 2010 (2006-2009) - and post-CONSORT version 2010 (2010-2015),(Table 2). The median CONSHORT checklist score was (10,7)in 136 Papers. The score was higher in post-CONSORT reporting period version 2010 (2010-2015) in 106 papers10,86) than 30 papers in pre -CONSORT version 2010 (2006-2009) (10,70).

Overall, the reporting was improved across all items after CONSORT statement's implementation (Figure 2).

Discussion

This study is very important because it was the first time that I used this method pre - CONSORT version 2010 (2006-2009) - and post-CONSORT version 2010 (2010-2015) periods. This was a difficult method and the Research was not sufficient. The studies were identified by only one database (PubMed Database 136 Papers) following medical subject heading terms and/or text words. Studies meeting the following criteria were included: several trials were blind, double-blind randomized clinical trials evaluating safety and adverse effects of human papillomavirus (HPV) vaccines studied subjects were older than nine years old, study participants with high risk of contracting, such as female sex workers and women who were sexual partners of HIV-infected men, and pregnant women. The comparison of the two periods pre - CONSORT version 2010 (2006-2009) - and post-CONSORT version 2010 (2010-2015) revealed a significant improvement ($p < 0.05$) because the 106 papers at post - CONSORT version 2010 (2010-2015) had better results and more reliable from the 30 papers of pre -CONSORT version 2010 (2006-2009).Physicians are based on the results of RCTs. It is important the reporting of these results to be completed and accurated. Uptoday the quality of RCTs in this disease have never been evaluated.

Conclusion

The present study investigated the quality and transparency of reporting of randomized controlled trials of Human Papilloma Virus (HPV) vaccines in cervical cancer prevention. The differences between pre -CONSORT version 2010 (2006-2009) - and post-CONSORT version 2010 (2010-2015) periods reporting periods as well as between high and low quality studies were explored.

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Figure 1: Flow diagram of citations through the retrieval and the screening process

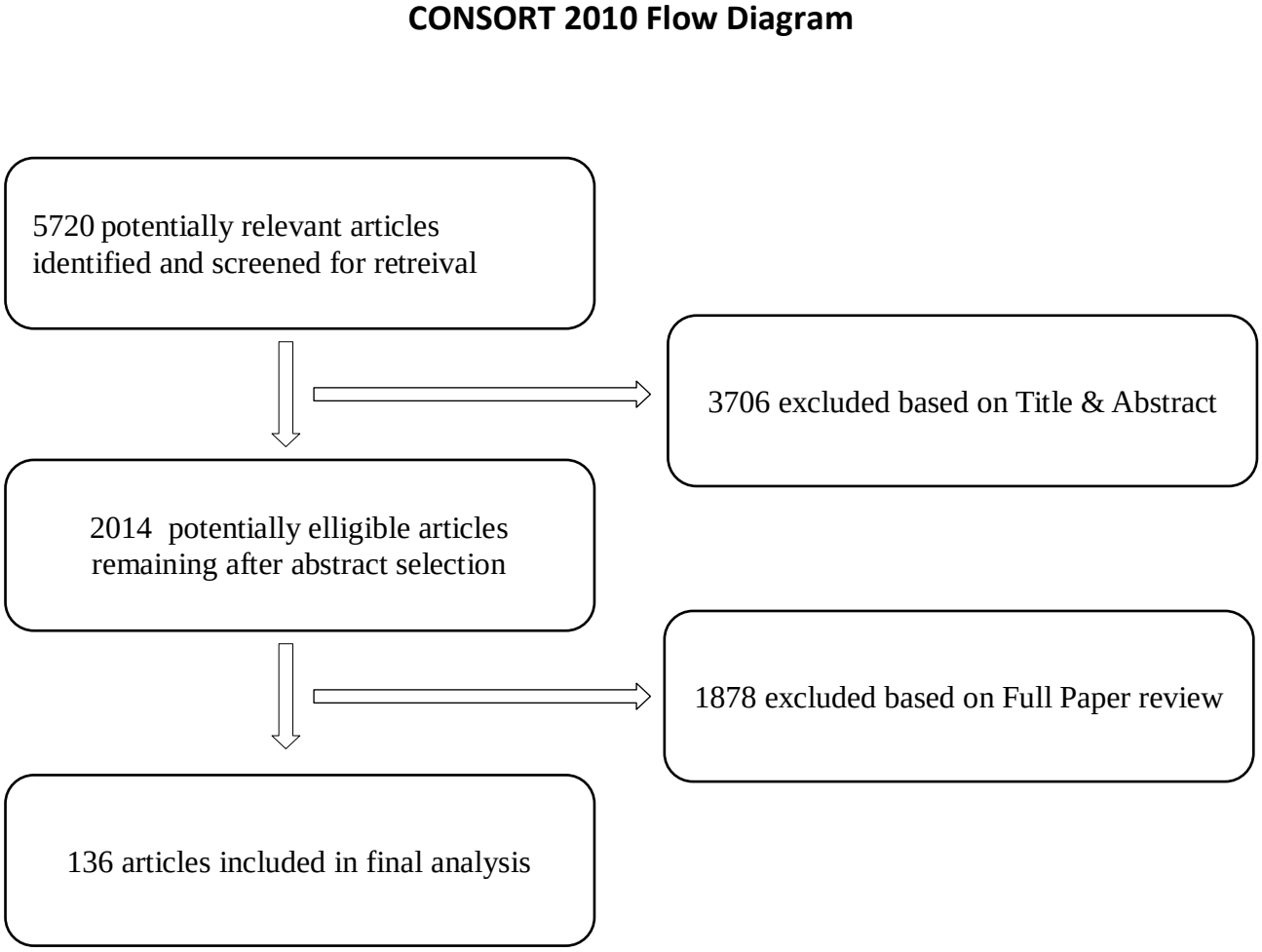


Table 1: Distribution of papers by journals

Journal	Papers (%*)	Consort endorser†
Acad Pediatr.	1(0,73%)	No
Acta Obstet Gynecol Scand.	1(0,73%)	yes
Ann Behav Med.	1(0,73%)	yes
Asian Pac J Cancer Prev.	1(0,73%)	No
BMC Health Serv Res.	1(0,73%)	yes
BMC Public Health.	1(0,73%)	yes
BMJ.	2(1,47%)	yes
Br J Cancer.	1(0,73%)	No
Cancer Discov.	1(0,73%)	No
Cancer Epidemiol Biomarkers Prev.	4(2,94%)	No
Cancer Epidemiol.	1(0,73%)	No
Cancer Immunol Immunother.	1(0,73%)	No
Cancer Prev Res (Phila).	1(0,73%)	No
Cancer Sci.	2(1,47%)	No
Clin Vaccine Immunol.	4(2,94%)	No
Curr Med Res Opin.	1(0,73%)	No
Eur J Obstet Gynecol Reprod Biol	1(0,73%)	yes
Health Technol Assess.	1(0,73%)	yes
Hong Kong Med J.	1(0,73%)	No
Hum Vaccin Immunother.	8(5,88%)	No
Hum Vaccin.	6(4,41%)	No
Int J Cancer.	8(5,88%)	No
Int J Gynaecol Obstet.	1(0,73%)	yes
Int J Gynecol Cancer.	3(2,20%)	No
Int Q Community Health Educ	1(0,73%)	No
Ir J Med Sci.	1(0,73%)	No

J Acquir Immune Defic Syndr.	3(2,20%)	yes
J Adolesc Health.	6(4,41%)	yes
J Am Coll Health.	1(0,73%)	No
J Clin Virol.	1(0,73%)	No
J Community Health	1(0,73%)	No
J Health Commun.	1(0,73%)	No
J Health Psychol.	1(0,73%)	yes
J Immunol.	1(0,73%)	No
J Infect Dis.	6(4,41%)	yes
J Korean Med Sci.	1(0,73%)	yes
J Natl Cancer Inst.	3(2,20%)	No
J Obstet Gynaecol Res.	1(0,73%)	yes
J Sex Med.	1(0,73%)	No
J Womens Health (Larchmt).	1(0,73%)	No
JAMA.	3(2,20%)	No
Jpn J Clin Oncol.	1(0,73%)	No
Lancet Oncol.	3(2,20%)	yes
Lancet.	4(2,94%)	yes
N Engl J Med	4(2,94%)	yes
Patient Educ Couns.	1(0,73%)	No
Pediatr Infect Dis J.	6(4,41%)	No
Pediatrics.	5(3,67%)	yes
PLoS One.	3(2,20%)	yes
Prev Sci.	1(0,73%)	No
Sex Transm Dis.	3(2,20%)	yes
Vaccine.	17(12,5%)	yes
Value Health.	1(0,73%)	No
Wien Klin Wochenschr.	1(0,73%)	No

*The percentage of articles published in the journal

†According to the list "CONSORT Endorsers - Journals" provided in *http://www.consort-statement.org*. *(http://www.consort-statement.org/about-consort/consort-endorsement/consort-endorsers---journals/#journalst)*

Table 2: Proportion of reporting of 30 data items in a total of 136 randomized clinical trials in small cell lung cancer by publication period (pre -CONSORT version 2010 (2006-2009) - and post-CONSORT version 2010 (2010-2015) and combined)*

Dataitems	Combined 2006-20015 (n = 136)†	pre - CONSORT version 2010 (2006-2009 (n = 30)	post-CONSORT version 2010 (2010-2015) (n = 106)	ΔPost-CONSORT – Post-CONSORT	OR, 95% CI ¥	P-value‡ FET Two-tailed
TITLE/ABSTRACT						
1. Randomizedintitle/abstract	0,61 (83)	4,60 (15)	6,81 (78)	7,69 (63)	1,4717(0.7416 to 2.9204)	P = 0.2691
INTRODUCTION						
2. Scientific background in introduction	0,79(108)	8,28 (27)	7,04 (81)	6,59 (54)	0.8491(0.4683 to 1.5393)	P = 0.5899
METHODS						
3. Eligibility criteria for participants	0,70(96)	6,74 (22)	6,46 (74)	6,34 (52)	0.9520(0.5095 to 1.7788)	P = 0.8774
4. Precise details of the interventions in each arm	0,67(92)	6,13 (20)	6,28 (72)	6,34(52)	1.0189(0.5372 to 1.9325)	P = 0.9544
5. Objectives	0,19(27)	3,0(10)	1,48(17)	0,85 (7)	0.4811(0.1996 to 1.1600)	P = 0.1032
6. End-points	0,044(6)	0,61(2)	0,34(4)	0,24 (2)	0.5660(0.0988 to 3.2415)	P = 0.5227
7. Sample size	0,044(6)	0,30 (1)	0,43(5)	0,48 (4)	1.4151(0.1592 to 12.5811)	P = 0.7555
8. Method of randomization (sequence generation)	0,71(97)	6,13(20)	6,72 (77)	6,95(57)	1.0896(0.5761 to 2.0611)	P = 0.7918
9. Allocationconcealment	0,007(1)	0 (0)	0,08 (1)	0,12 (1)	0.8592(0.0341 to 21.6298)	P = 0.9265
10. Implementation of randomization	0,70(96)	6,13 (20)	6,63(76)	6,83(56)	1.0755(0.5683 to 2.0353)	P = 0.8231
11. Blinding (masking)	0,30(42)	3,98(13)	2,53(29)	1,95(16)	0.6313(0.2924 to 1.3630)	P = 0.2415
12. Statisticalmethods	0,44(60)	0,30(1)	5,15(59)	7,08(58)	16.6981(2.2203 to 125.5833)	P = 0.0062
RESULTS						
13. Participant flow	0,80(110)	7,66(25)	7,42 (85)	7,32 (60)	0.9623(0.5267 to 1.7580)	P = 0.9004
14. Periods: a. Recruitment	0,044(6)	0,61 (2)	0,34(4)	0,24 (2)	0.5660(0.0988	P = 0.5227

					to 3.2415)	
b. Follow-up	0,015(2)	0 (0)	0,17 (2)	0,24 (2)	1.4319(0.0669 to 30.6307)	P = 0.8183
15. Baseline data	0,98(134)	9,2 (30)	9,08(104)	9,03(74)	0.9811(0.5527 to 1.7416)	P = 0.9481
16. "Intention-to-treat" analysis	0,88(120)	8,28 (27)	8,12(93)	8,05(66)	0.9748(0.5405 to 1.7583)	P = 0.9325
17. a. Outcomes and	0,66(90)	6,44 (21)	6,02(69)	5,86 (48)	0.9299(0.4929 to 1.7543)	P = 0.8225
b. Estimation of effects	0,71(97)	7,36 (24)	6,37(73)	5,98(49)	0.8608(0.4659 to 1.5907)	P = 0.6324
18. Ancillary analyses	0,12 (17)	2,4 (8)	0,78(9)	0,12 (1)	0.3184(0.1131 to 0.8964)	P = 0.0302
19. Adverseevents	0,05(7)	0,30(1)	0,52 (6)	0,61(5)	1.6981(0.1967 to 14.6584)	P = 0.6302
DISCUSSION						
20. Interpretation of the results	0,044(6)	0,61 (2)	0,34 (4)	0,24 (2)	0.5660(0.0988 to 3.2415)	P = 0.5227
21. Generalizability	0,86(118)	7,36 (24)	8,20 (94)	8,54(70)	1.1085(0.6057 to 2.0286)	P = 0.7383
22. Overallevidence	0,29(40)	3,37(11)	2,53(29)	2,19 (18)	0.7461(0.3340 to 1.6668)	P = 0.4752

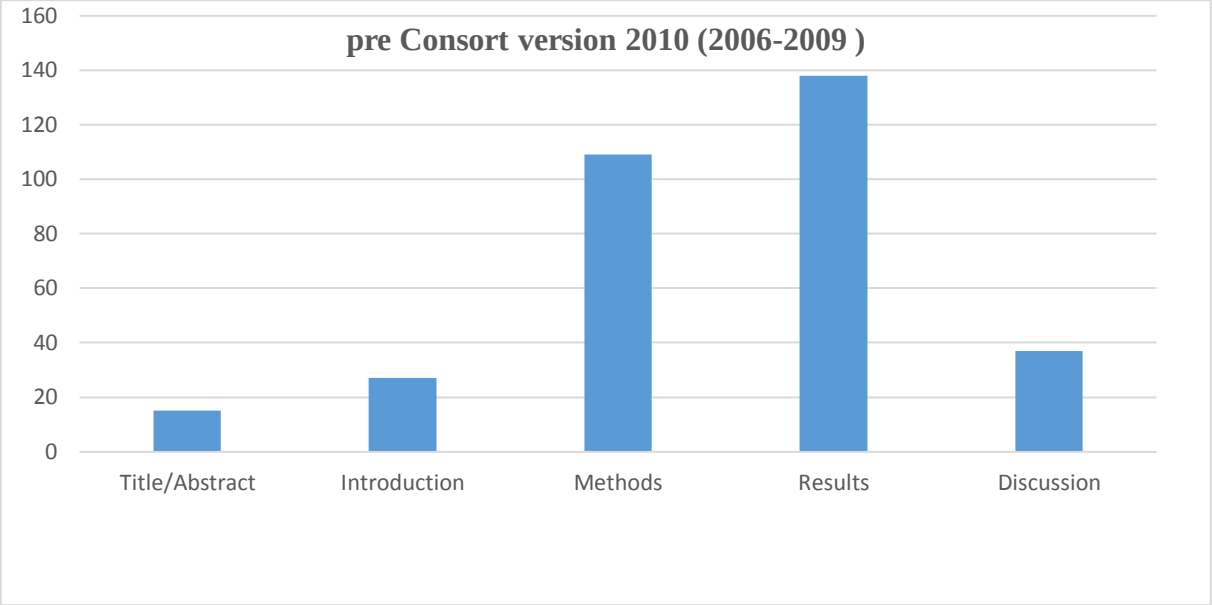
*CONSORT= Consolidated Standards of Reporting Trials

† The percentage of articles reporting the CONSORT item

¥ Odds ratio of reporting an item at pre -CONSORT version 2010 (2006-2009) - and post-CONSORT version 2010 (2010-1015) periods.

‡ P-Values from Fisher's exact test for testing the association between reporting an item and publication period.

Figure 2: Comparison between pre Consort version 2010 (2006-2009) and post Consort version 2010 (2010-2015) periods.



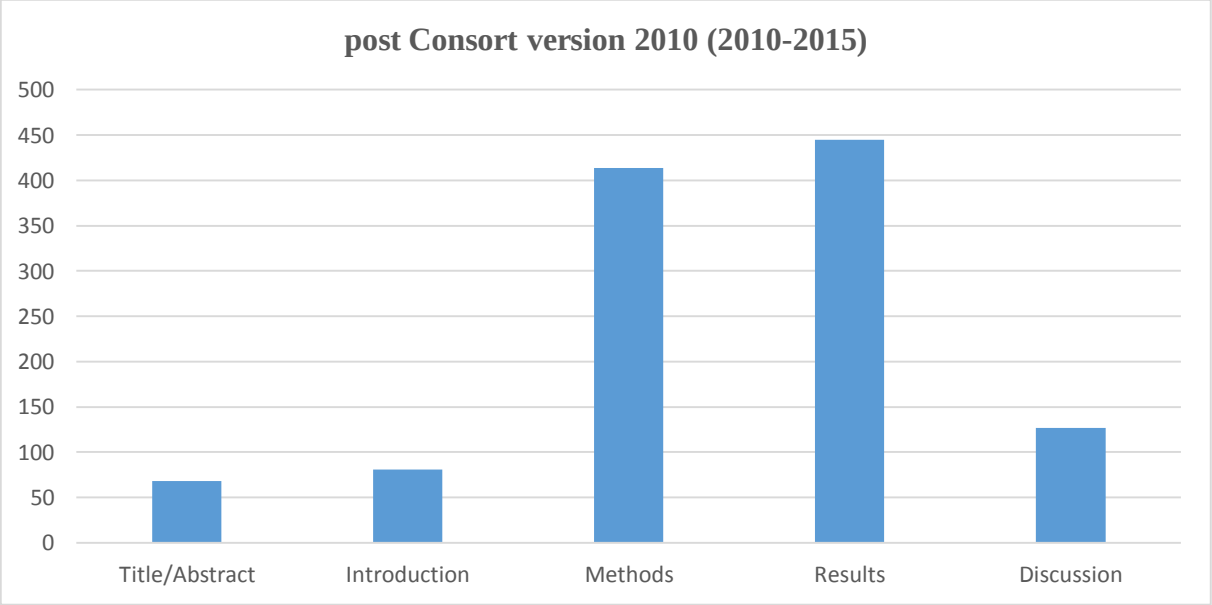
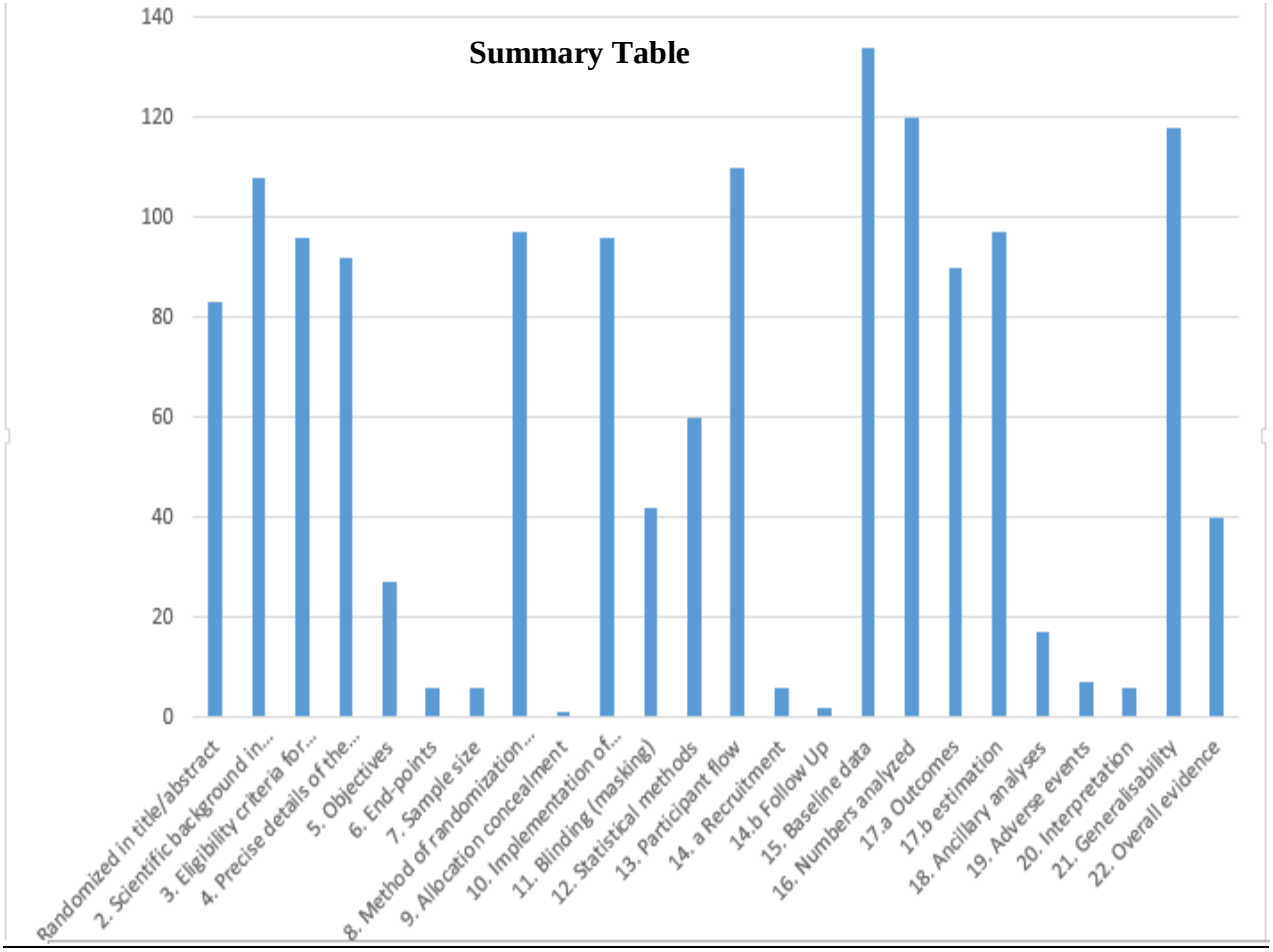


Figure 3: Summary Table of all the results.



Annex: Results of the research.

			Title/Abstract	Introduction	Methods										Results
REF ID	JOURNAL	YEAR	1. Randomized in title/abstract	2. Scientific background in introduction	3. Eligibility criteria for participants	4. Precise details of the interventions in each arm	5. Objectives	6. End-points	7. Sample size	8. Method of randomization (sequence generation)	9. Allocation concealment	10. Implementation of randomization	11. Blinding (masking)	12. Statistical methods	13. Participar flow
Villa LL, 2006	Br J Cancer.	2006	1	1	1	1	0	0	0	1	0	1	0	0	1
Insinga RP, 2007	Cancer Epidemiol Biomarkers Prev.	2007	0	1	1	1	1	0	0	0	0	0	0	0	1
García-Piñeres A, 2007	Clin Vaccine Immunol.	2007	0	1	0	0	0	0	0	0	0	0	0	0	0
Garland SM, 2007	Clin Vaccine Immunol.	2007	0	1	1	0	0	0	0	0	0	0	0	0	0
Kaufmann AM, 2007	Int J Cancer.	2007	1	0	0	0	0	0	0	1	0	1	1	0	0
Pedersen C, 2007	J Adolesc Health.	2007	0	1	1	1	0	0	0	0	0	0	0	0	1
FUTURE II Study Group., 2007	J Infect Dis.	2007	0	1	1	1	0	0	0	1	0	1	0	0	1
Hildesheim A, 2007	JAMA.	2007	1	1	1	1	1	0	0	1	0	1	0	0	1
Paavonen J, 2007	Lancet.	2007	1	1	1	1	0	0	0	1	0	1	1	0	1
Garland SM, 2007	N Engl J Med.	2007	0	1	1	1	0	1	0	1	0	1	1	0	1
FUTURE II Study Group., 2007	N Engl J Med.	2007	0	1	1	1	0	0	0	1	0	1	1	0	1

Reisinger KS, 2007	Pediatr Infect Dis J.	2007	1	1	1	1	1	0	0	1	0	1	1	0	1
Gerend MA, 2008	Ann Behav Med.	2008	0	1	0	0	1	0	0	1	0	1	0	0	1
Paavonen J, 2008	Curr Med Res Opin.	2008	0	1	1	1	1	0	0	1	0	1	0	0	1
Tay EH, 2008	Int J Gynaecol Obstet.	2008	0	1	0	0	1	0	0	0	0	0	0	0	1
Kang S, 2008	Int J Gynecol Cancer.	2008	1	1	1	1	0	0	0	1	0	1	1	0	1
Wheeler CM, 2008	Vaccine.	2008	0	1	0	0	0	0	0	0	0	0	0	0	1
Insinga RP, 2008	Value Health.	2008	1	1	1	1	1	0	0	1	0	1	0	0	1
Six L, 2008	Wien Klin Wochenschr.	2008	1	1	1	1	0	0	0	1	0	1	1	0	1
Sigurdsson K, 2009	Acta Obstet Gynecol Scand.	2009	0	1	0	1	1	0	1	0	0	0	0	0	1
Garland SM, 2009	Cancer Epidemiol Biomarkers Prev.	2009	1	1	0	0	0	0	0	1	0	1	1	0	1
Trottier H, 2009	Cancer Epidemiol Biomarkers Prev.	2009	0	1	1	1	0	0	0	0	0	0	0	0	1
Olsson SE, 2009	Hum Vaccin.	2009	0	0	1	1	1	1	0	0	0	0	0	0	1
Einstein MH, 2009	Hum Vaccin.	2009	1	1	1	0	0	0	0	1	0	1	1	0	1
Konno R, 2009	Int J Gynecol Cancer.	2009	1	1	1	0	0	0	0	1	0	1	1	0	0
Anderson JS, 2009	J Acquir Immune Defic Syndr.	2009	1	1	1	1	1	0	0	1	0	1	1	0	1
Petäjä T, 2009	J Adolesc Health.	2009	1	1	1	1	0	0	0	1	0	1	0	0	1

García-Piñeres AJ, 2009	J Immunol.	2009	0	1	0	0	0	0	0	0	0	0	0	0	0
GlaxoSmithKline Vaccine HPV-007 Study Group, 2009	Lancet.	2009	1	1	1	1	0	0	0	1	0	1	1	1	1
Muñoz N, 2009	Lancet.	2009	1	0	1	1	0	0	0	1	0	1	1	0	1
Wacholder S, 2010	BMJ.	2010	1	0	1	1	0	0	0	1	0	1	0	0	1
Ngan HY, 2010	Hong Kong Med J.	2010	1	1	1	1	1	0	0	1	0	1	1	0	1
Konno R, 2010	Int J Gynecol Cancer.	2010	1	1	1	1	0	0	0	1	0	1	1	0	1
Fahy A, 2010	Ir J Med Sci.	2010	1	0	1	0	0	0	0	1	0	1	0	0	1
Levin MJ, 2010	J Acquir Immune Defic Syndr.	2010	0	1	0	0	0	0	0	0	0	0	1	0	1
Medina DM, 2010	J Adolesc Health.	2010	1	1	1	1	0	0	0	1	0	1	1	0	1
Garcia-Sicilia J, 2010	J Adolesc Health.	2010	0	1	1	1	0	0	0	1	0	1	0	0	1
Kim YJ, 2010	J Korean Med Sci.	2010	1	1	1	1	0	0	0	1	0	1	1	0	1
Muñoz N, 2010	J Natl Cancer Inst.	2010	1	1	1	1	0	0	0	1	0	1	0	0	1
Bhatla N	J Obstet Gynaecol Res.	2010	1	1	1	1	0	0	0	1	0	1	1	0	1
Zimmerman RK, 2010	J Womens Health (Larchmt).	2010	1	1	1	1	0	0	0	1	0	1	0	0	1
Bigman CA, 2010	Patient Educ Couns.	2010	0	1	0	0	1	0	0	0	0	0	0	1	1
Vesikari T, 2010	Pediatr Infect Dis J.	2010	0	1	1	1	0	0	0	1	0	1	0	0	1

Block SL, 2010	Pediatr Infect Dis J.	2010	0	1	1	1	0	0	0	0	0	0	0	0	1
Reisinger KS, 2010	Pediatrics.	2010	1	0	1	1	1	0	0	1	0	1	0	0	1
Coseo S, 2010	Sex Transm Dis.	2010	0	1	1	1	0	0	0	0	0	0	0	0	1
Dauner JG, 2010	Vaccine.	2010	0	1	0	0	0	0	0	0	0	0	0	0	0
Arguedas A, 2010	Vaccine.	2010	1	1	0	0	0	0	0	1	0	1	0	0	1
Arguedas A, 2010	Vaccine.	2010	0	1	0	0	0	0	0	1	0	1	0	0	1
de Vos van Steenwijk PJ, 2011	Cancer Discov.	2011	1	1	1	1	0	0	0	1	0	1	0	1	1
Insinga RP, 2011	Cancer Epidemiol Biomarkers Prev.	2011	0	0	1	1	0	0	0	0	0	0	0	0	0
Konno R, 2011	Cancer Sci.	2011	1	1	1	1	0	0	1	1	0	1	1	0	1
Leroux-Roels G, 2011	Clin Vaccine Immunol.	2011	1	1	0	0	0	0	0	1	0	1	0	0	0
Einstein MH, 2011	Hum Vaccin.	2011	1	1	0	0	0	0	0	1	0	1	1	0	0
Einstein MH, 2011	Hum Vaccin.	2011	0	0	0	0	0	0	0	0	0	0	0	0	0
Romanowski B, 2011	Hum Vaccin.	2011	1	1	1	1	0	0	0	1	0	1	1	0	1
Moreira ED Jr, 2011	Hum Vaccin.	2011	1	1	1	1	0	0	0	1	1	1	1	0	0
Haupt RM, 2011	Int J Cancer.	2011	1	1	1	0	0	0	0	1	0	1	0	0	0
Petäjä T, 2011	Int J Cancer.	2011	0	1	0	1	0	0	0	0	0	0	0	0	0

Ault KA, 2011	Int J Cancer.	2011	0	1	1	1	0	0	0	1	0	1	0	0	1
Stoler MH, 2011	Int J Cancer.	2011	0	1	0	0	0	0	0	0	0	0	0	0	1
Kepka D, 2011	J Community Health.	2011	1	0	1	0	0	0	0	1	0	1	0	1	0
Kreimer AR, 2011	J Natl Cancer Inst.	2011	0	1	0	0	0	0	0	0	0	0	0	0	1
Neuzil KM , 2011	JAMA.	2011	1	1	0	0	1	0	1	1	0	1	0	0	1
Kreimer AR, 2011	Lancet Oncol.	2011	1	1	1	0	0	0	0	1	0	1	1	1	1
Giuliano AR, 2011	N Engl J Med.	2011	1	1	1	1	0	0	1	1	0	1	1	0	1
Wheeler CM	Pediatr Infect Dis J.	2011	1	1	1	0	0	0	0	1	0	1	0	0	1
Esposito S, 2011	Pediatr Infect Dis J.	2011	1	1	1	1	0	0	0	1	0	1	0	0	1
Dempsey AF, 2011	Sex Transm Dis.	2011	0	1	1	1	0	0	1	0	0	0	0	0	1
Schmeink CE, 2011	Vaccine.	2011	1	1	1	1	0	0	0	1	0	1	0	0	1
Al-Naggar RA, 2012	Asian Pac J Cancer Prev.	2012	0	0	0	0	1	0	0	0	0	0	0	1	1
Mantzari E, 2012	BMC Health Serv Res.	2012	1	1	1	1	0	0	0	1	0	1	0	1	1
Joura EA, 2012	BMJ.	2012	1	1	1	1	1	0	0	1	0	1	1	1	1
Wiley DJ, 2012	Cancer Epidemiol.	2012	0	0	1	1	0	0	0	0	0	0	0	1	1
de Vos van Steenwijk PJ, 2012	Cancer Immunol Immunother.	2012	1	1	0	0	0	0	0	1	0	1	0	0	1

Matys K, 2012	Clin Vaccine Immunol.	2012	1	1	1	0	0	0	0	1	0	1	1	0	1
Jardine D, 2012	Hum Vaccin Immunother.	2012	1	1	1	1	0	0	0	1	0	1	1	1	0
Roteli-Martins CM, 2012	Hum Vaccin Immunother.	2012	0	1	1	1	0	0	0	0	0	0	0	1	1
Palmroth J, 2012	Int J Cancer.	2012	1	1	1	1	0	0	0	1	0	1	0	1	1
Szarewski A, 2012	Int J Cancer.	2012	0	0	1	0	0	0	0	0	0	0	0	1	0
Pedersen C, 2012	J Adolesc Health.	2012	1	1	0	1	0	0	0	1	0	1	0	1	0
Krawczyk A, 2012	J Am Coll Health.	2012	0	0	0	0	1	0	0	1	0	1	0	0	1
Rowhani-Rahbar A, 2012	J Clin Virol.	2012	0	1	0	0	1	0	0	0	0	0	0	1	1
Gainforth HL, 2012	J Health Psychol.	2012	0	1	1	0	0	0	0	0	0	0	0	0	1
Weinberg A, 2012	J Infect Dis.	2012	0	0	0	1	1	0	0	0	0	0	0	1	0
Watson-Jones D, 2012	J Infect Dis.	2012	1	0	1	1	0	0	0	1	0	1	0	1	1
Khatun S, 2012	Jpn J Clin Oncol.	2012	1	1	1	1	0	0	0	1	0	1	0	1	1
Lehtinen M, 2012	Lancet Oncol.	2012	1	1	1	1	0	0	0	1	0	1	1	1	1
Wheeler CM, 2012	Lancet Oncol.	2012	1	1	1	1	0	0	0	1	0	1	1	1	1
Suh CA, 2012	Pediatrics.	2012	0	1	1	1	1	0	0	1	0	1	0	1	1
Kempe A, 2012	Pediatrics.	2012	0	1	0	1	0	0	0	1	0	1	0	1	1

Watson-Jones D, 2012	PLoS One.	2012	1	1	1	1	0	0	0	1	0	1	0	1	1
Hopfer S, 2012	Prev Sci.	2012	1	1	0	1	0	0	0	1	0	1	0	0	1
Li R, 2012	Vaccine.	2012	1	0	0	0	0	0	0	1	0	1	1	1	1
Brown B, 2012	Vaccine.	2012	1	0	0	0	0	1	0	1	0	1	0	1	0
Szilagyi PG, 2013	Acad Pediatr.	2013	1	1	1	1	0	0	0	1	0	1	0	1	1
Hofman R, 2013	BMC Public Health.	2013	0	1	1	1	0	0	1	0	0	0	0	1	1
Safaeian M,2013	Cancer Prev Res (Phila).	2013	1	0	1	1	0	0	0	1	0	0	0	1	1
Yoshikawa H, 2013	Cancer Sci.	2013	1	1	1	1	0	0	0	1	0	1	1	1	1
Bertaut A, 2013	Eur J Obstet Gynecol Reprod Biol.	2013	0	0	1	1	1	0	0	0	0	0	0	1	0
Levi M, 2013	Hum Vaccin Immunother.	2013	0	1	1	1	0	0	0	0	0	0	0	1	1
Safaeian M, 2013	Hum Vaccin Immunother.	2013	1	1	1	1	0	0	0	0	0	0	0	1	0
Mehta P, 2013-2014	Int Q Community Health Educ.	2013	1	1	0	0	0	0	0	1	0	1	0	1	1
Clark LR, 2013	J Adolesc Health.	2013	0	1	1	1	0	0	0	0	0	0	0	1	1
Sow PS, 2013	J Infect Dis.	2013	1	1	1	1	0	0	0	1	0	1	1	1	1
Dobson SR, 2013	JAMA.	2013	1	1	0	1	1	0	0	1	0	1	0	1	1
Fiks AG, 2013	Pediatrics.	2013	0	1	1	1	1	0	0	1	0	1	0	1	0

Luna J,2013	PLoS One.	2013	1	1	1	1	0	0	0	1	0	1	0	0	1
Herrero R ,2013	PLoS One.	2013	1	0	1	1	0	0	0	1	0	1	1	1	1
Gerend MA, 2013	Sex Transm Dis.	2013	1	0	1	1	0	0	0	1	0	1	1	1	1
Denny L ,2013	Vaccine.	2013	1	0	1	1	0	0	0	1	0	1	1	1	1
Goldstone SE, 2013	Vaccine.	2013	0	1	0	0	0	0	0	0	0	0	0	0	0
Nelson EA, 2013	Vaccine.	2013	1	1	0	0	0	0	0	1	0	1	0	1	1
Petousis-Harris H, 2013	Vaccine.	2013	1	1	0	1	1	0	0	1	0	1	0	1	1
C Kitchener H,2014	Health Technol Assess.	2014	1	1	1	1	1	0	0	1	0	1	0	1	1
Gilca V, 2014	Hum Vaccin Immunother.	2014	0	1	1	1	1	1	0	0	0	0	0	1	1
Zhu F, 2014	Hum Vaccin Immunother.	2014	1	0	1	1	0	0	0	1	0	1	0	1	1
Romanowski B,2014	Hum Vaccin Immunother.	2014	1	0	1	0	0	0	0	1	0	1	1	0	0
Toft L, 2014	Hum Vaccin Immunother.	2014	1	1	0	0	0	0	0	1	0	1	0	0	1
Zhu FC,2014	Int J Cancer.	2014	1	1	1	1	0	0	0	1	0	1	1	1	1
Bell RA, 2014	J Health Commun.	2014	1	0	1	0	0	0	0	1	0	1	0	0	1
Lang Kuhs KA	J Infect Dis.	2014	0	1	1	1	0	0	0	0	0	0	0	1	1
Toft L, 2014	J Infect Dis.	2014	1	1	1	1	0	0	0	1	0	1	1	1	1

Porras C, 2014	J Natl Cancer Inst.	2014	0	0	0	0	0	1	0	1	0	1	0	1	1
Coskuner ER,2014	J Sex Med.	2014	1	1	0	1	0	0	0	1	0	1	0	1	1
Skinner SR, 2014	Lancet.	2014	1	1	1	1	0	0	0	1	0	1	1	1	1
Schwarz TF,2014	Pediatr Infect Dis J.	2014	1	1	1	1	0	0	0	1	0	1	1	1	1
Ferris D,2014	Pediatrics.	2014	0	1	1	1	0	0	0	0	0	0	0	1	1
Hildesheim A, 2014	Vaccine.	2014	1	1	1	1	0	0	0	1	0	1	0	1	1
Van Damme P,2014	Vaccine.	2014	1	1	1	1	0	0	0	1	0	1	0	0	0
Patel A, 2014	Vaccine.	2014	1	0	0	0	1	0	0	1	0	1	0	1	1
Lin CJ, 2014	Vaccine.	2014	1	0	1	1	0	0	0	1	0	1	0	1	1
Brown J, 2014	Vaccine.	2014	0	1	1	1	0	0	0	0	0	0	0	1	1
Krajden M, 2014	Vaccine.	2014	0	1	0	0	0	0	0	0	0	0	0	1	1
Giuliano AR, 2015	J Acquir Immune Defic Syndr.	2015	0	1	1	1	0	0	0	1	0	1	0	1	1
Joura EA, 2015	N Engl J Med	2015	1	1	1	1	0	1	0	1	0	1	1	1	0