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Cervical cancer vaccination for my daughter, no thanks:

A research synthesis on parental explained barriers to delayed or non-acceptance of HPV vaccination in high-income (OECD) nations. Parental expressed reasons on why they delay or rejected HPV vaccination for their daughters aged 9-17 within OECD nations between 2008 and 2016.

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ABSTRACT

Background: The organization for economic co-operation and development (OECD) member states have a high income and developed infrastructure including good preventive healthcare systems. The World Health Organization recommends that Human Papillomavirus (HPV) vaccination should be given to young girls as they believe it's the best available method to reduce cervical cancer morbidity and mortality. They have formulated HPV vaccination policies targeting to increase coverage for young girls before sexual debut. Parents are key contact persons in achieving higher vaccination rates as they have to make the decision to consent before their under-age daughters is vaccinated. Through responses, we may understand the main reasons to why parents delayed or declined to accept their daughters to be vaccinated. The responses from parents of non-vaccinated girls will give public health and promotion programs the needed information. These finding may help optimize HPV vaccination coverage while offering protection to the population.

Objective: To determine and identify themes, factors and barriers explaining why parents decide to delay or refuse to accept HPV vaccination for their daughter's aged 9-17, through systematic review of qualitative and quantitative primary studies. Due to current trends in information source in media and internet, the researcher wanted to ascertain whether social media and religion plays a central role in parental decline or delay a decision on HPV vaccination.

Methods: comprehensive search from several selected databases ranging from 2008 to 2016 were done and primary sources identified followed by critical appraisal. A desire for combination of qualitative and quantitative articles led to the utilization of a Qualitative Meta-summary. The method consisted of extraction, separation of findings, editing of findings, grouping of similar findings, abstraction and Size effect calculation.

Results: Twenty-three studies consisting of ten quantitative and 13 qualitative were synthesized. A total of 15458 parents had reported HPV vaccination. There were 246 reasons identified (both similar and different) with a total of 31740 responses (parents had more than one response). The responses were categorised into twenty groups which were further abstracted into seven broad categories. They consisted of vaccine related, parental concerns and perceptions, girl child factors, general factors, provider health factors, pharmaceutical or government-related factors, social media and religious reasons.

Conclusion: Vaccine related responses including drug safety, unknown future adverse effect and doubts on the vaccine was a major reason for non-vaccination. Parental concerns, girl child related reasons and lack of information played a role in parental decision. The health provider, pharmaceutical and government related reasons adding to social media though were of less effect, they were part of reasons for refusal to accept HPV vaccination. Both qualitative and quantitative combination with Qualitative metasummary synthesis gave the review large response and size effect. However the similar grouped findings had both quantitative and qualitative articles enabling the synthesis to determine the ‘what’ and ‘why’ using both questionnaires and interview responses. These parental explained reasons if addressed through collective measures by primary public health services could contribute to decrease refusal hopefully increasing HPV vaccination coverage. Future research in length of protection, induced and natural HPV immunogenicity difference, drug efficacy comparison of Pap smear with the vaccine will reduce doubts and enhance future acceptance.

ABBREVIATIONS.

CDC.....	Center for Disease Control
EU.....	European Union
ECDC.....	European Centre for Disease Control
GP.....	General Practitioner
HIV.....	Human Immune deficiency Virus
HPV.....	Human Papillomavirus
OECD.....	Organisation for Economic Co-operation and Development.
QARI.....	Qualitative Analysis Review Instrument
SAS.....	Statistical Analysis Software
SPSS.....	Statistical Package for the Social Sciences
UIT.....	Universitetet i Tromsø
WHO.....	World Health Organization
USA.....	The United States of America

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CHAPTER 1

BACKGROUND.

High-income countries are grouped together under an Umbrella organization established in 1961. The Organisation for Economic Co-operation and Development (OECD) member countries consists of 34 nations. They are characterised by high income, bigger economies, better healthcare, well-developed infrastructure, less population growth and good transport systems. The countries include Canada, Mexico and USA (North America), Chile (South America), Australia and New Zealand (Oceania), Japan, Israel and S. Korea (Asia) and Turkey. The bulk of the nation's fall under the European Union and partners consisting of Austria, Belgium, Denmark and France. Others including Germany, Greece, Iceland, Ireland, Italy, Luxembourg and Netherlands. Included also are Norway, Portugal, Slovenia, Spain, Sweden, Czech Republic, Estonia, Finland and Hungary. Poland, Slovak Republic, Switzerland and United Kingdom(1, 2)

Cervical cancer is a disease affecting the lower end of the uterus. It occurs when cervical cells begin to divide uncontrollably producing abnormal cells which can invade surrounding tissues. Metastasis occurs when cells break from the primary tumour and spreads to other sites. Infection with Human Papillomavirus (HPV) is strongly correlated with cervical cancer, and the virus is transmitted sexually (3). Cervical cancer is the outcome of persistent infection with HPV, which accounts for approximately 95% of incidences (4). There are over 100 known different types of HPV that exist (5). Among them, two types of HPV (16& 18) causes more than three-quarters of cervical cancers. About 75% of all females have had infections at particular time in their life without knowing it (6). There are no seen signs and symptoms of infection as it's resolved spontaneously. Persistent infection with different types of HPV 16 and 18 leads to pre-cancerous lesions which if untreated proceeds to progress into cervical cancer which is a slow process that takes many years before detection. The known risk factors are early age sexual initiation and multiple partners with the lack of timely screening as an important element in developing cervical cancer (7). A regular Pap smear screening in older women is used for early detection of the virus though there is no known drug for treatment and immune system clears the virus in most cases (3). According to WHO, Vaccination of young girls with HPV vaccine before sexual debut combined with screening are key in achieving cervical cancer and prevention (8). Currently, there exist two vaccines which protect against HPV 16 and 18 that accounts for 70% of all cervical cancers. Gardasil is used for both girls and boys while Cervarix is for girls only. Gardasil protects further from HPV 6 and 11 which causes anogenital warts. (9)

CHAPTER 2

2.0 GLOBAL PERSPECTIVE

Vaccination policies against cervical cancer (HPV vaccines) have different implementation strategies from ages of 10-14 with some countries extending to 17 years based on age of sexual debut. In most European nations it is administered as part of primary healthcare and Parents are highly involved due to the age of uptake with consent required in most programs (10).

According to European centre for disease control, Gardasil and Cervarix protects against HPV 16 and 18 which causes 73% of cervical cancer. This means the remaining causes of approximately 30% is beyond the two vaccines (11). Cervical cancer is believed to develop over many years within an estimated period of 10-30 years. HPV vaccine against cervical cancer takes a longer time before antibodies effects can be identified. The HPV vaccine (Gardasil) shows a five to six-year protection after vaccination. The current HPV vaccination schedule includes two injections within a six month period as opposed to previous three injections for girls aged 10-14 (12). The exact duration of HPV vaccine protection is still not yet known though is carefully monitored by the medical authorities. (12).

2.1 CURRENT VACCINATION DETAILS.

Based on world health organization (WHO) 2014 publication data, over 270,000 women died in 2012 due to cervical cancer and 528,000 new cases were detected during the year (8).

Within the European Union, (EU) nations consisting of 29 countries (inclusive of Norway and Iceland though all are not OECD members) cervical cancer was the second most common cancer after breast cancer affecting women of ages 15–44. The current estimate indicates that every year there are around 33 000 cases of cervical cancer in the EU and 15 000 deaths. The primary cause of cervical cancer is related to persistent infection of the genital tract by a high-risk human Papillomavirus type (12, 13). By 2010, Denmark, France, Ireland, Italy, Latvia, Luxembourg, the Netherlands, Norway, Portugal, Romania, Slovenia, Sweden and the United Kingdom had a national HPV vaccination coverage systems in place (12).

The European Union members consisting majorly of OECD had variant coverage ranging from 17% to 84% for the reporting countries. Portugal (84%), the United Kingdom (80%) and Denmark (79%) were at the top of that range.(12). In Poland where vaccination is not tax funded, 3513 cases were reported with 1856 deaths in 2012 and Vaccination is at less than 10% (14). HPV centre information for Germany indicates 4995 cervical cancer cases with 1566 death in 2012. In Norway based on SYSVAK 2014 national HPV vaccination data

vaccination coverage is estimated to be 76% (15). The Norwegian cancer registry reported 1542 cases of cervical cancer in 2012 with 330 death during the year (16). Most OECD members in Pacific, Asia, Americas and Europe reported cases ranging from 203 (Israel) to 13960 (Mexico). There were reported death from cervical cancer ranging from 50 (New Zealand) to 4769 (Mexico). Vaccination rates ranged from less than 10% in Poland to 84% in Portugal. (14, 17-27).

2.2 STUDY RATIONALE.

Cervical cancer causes death ranging from tens to thousands of women in OECD countries. It's one of the cancers with known causes associated with HPV. Preventive mechanisms involve cervical smear check for women above 29 years and HPV vaccination for pre-adolescent girls (13). the vaccinations is believed to protect the girls and young women from age nine until 29 years when they are eligible for Pap smear. Most of the countries that have introduced HPV vaccination are from the WHO regions Americas, Europe and West Pacific regions which are in OECD (13, 27). The current rates of vaccination are different between countries. There has been a reported decline in cervical cancer within high-income countries as indicated by Centre for Disease control (CDC) and European Centre for Disease control (ECDC). The ECDC countries reported higher vaccination coverage on HPV vaccine launch in Europe followed by reduced uptake in different parts during the years after initial launch. There was great enthusiasm during the launch of HPV vaccination but by 2012 until now there has been a declining uptake (12). According to WHO, HPV vaccinations as part of national immunisation programmes for girls aged 9-13 years from countries with the prevention of cervical cancer should be a public health priority (8). The initiative is feasible and financially sustainable, as cost-effectiveness has been evaluated. In nations with vaccination policy and high income, HPV vaccination is administered with parental consent for minors. This research intended to answer the question on reasons as to why some parents are declining to accept HPV vaccination for their children. Based on their experiences, are there common factors that will answer 'why' some have decided not to vaccinate? Some parents obtained their information on vaccination through media. Based on research done in the USA on conflict of print media on HPV vaccination, it was found that there were both pro-vaccine and anti-vaccination coverage (28). Furthermore, there was a reported decline of HPV vaccination based on negative media reporting in Japan (29). Whether this affected parental decision is not confirmed through research.

2.3 STUDY BENEFITS AND JUSTIFICATION

Singular qualitative and quantitative studies provide insights into the reasons and responses as to why national HPV vaccination is lower than expected in some countries. Different studies have indicated parental concerns leading to refusal of their daughters receiving HPV vaccine within the OECD countries. Through synthesizing the data from several primary qualitative and quantitative studies, the researcher intended to obtain a final abstracted responses from parents whose daughters are not vaccinated. These collective parental responses could provide a more comprehensive list of barriers and explanations answering ‘why’ they delayed or refused to vaccinate their daughters against HPV. By understanding these common barriers policymakers and health care providers may be able to address low HPV vaccination rates. This systematic review aims to add knowledge to existing literature on the topic while enhancing chances of future research on HPV vaccination in different parts of OECD. A previous qualitative review study was done on barriers and facilitators of HPV vaccination but did not consider developed nations with HPV vaccination policies (30). Based on current databases there is no documented combined synthesis for both qualitative and quantitative data in answering the ‘why’ and ‘what’ reasons for decline. Furthermore previous reviews did not consider girl’s age range of 10-14. The parental role in HPV acceptance or refusal needs to be reviewed in finding their experiences to refusal which may assist in future decision making by public health implementers (31)

2.4 RESEARCH QUESTION

Why are parents making a decision to delay or refuse their daughters aged 9-17 to be vaccinated against HPV within high-income OECD countries?

2.5 STUDY OBJECTIVES.

This study review had two objectives which were:

- i. To determine and identify themes, factors and barriers explaining why parents decide to delay or refuse to accept HPV vaccination for their daughters aged 9-17 through a systematic review of quantitative and qualitative primary studies.
- ii. Based on reported media reports in both USA and Japan, this research had an objective to determine the role played by social media and religion in parental decline or delay the decision on HPV vaccination.

CHAPTER 3

METHODS AND DESIGN

3.0 RESEARCH PROTOCOL.

The protocol for this systematic review study was registered and accepted by PROSPERO number CRD42016033820 (32). The systematic review method by Joanna Briggs Institute with research quick reference guide was used (33, 34). The next step was the identification of all qualitative and quantitative required articles on the topic of interest with needed data for this research. The articles answering research question were classified based on search strategies and inclusion-exclusion criteria.

3.1 LITERATURE SEARCH STRATEGIES.

The initial search from MEDLINE using Papillomavirus Vaccines"[Mesh] AND ("Parents"[Mesh]) AND ("Refusal to Participate"[Mesh] OR "Refusal to Treat"[Mesh] OR "Treatment Refusal"[Mesh] OR "Withholding Treatment"[Mesh] OR "Medication Adherence"[Mesh] OR "Proxy"[Mesh] OR "Patient Participation"[Mesh] OR "Patient Compliance"[Mesh] OR "Denial (Psychology)"[Mesh] yielded few hits.

The researcher then conducted a broad, in-depth search that was comprehensive to capture all detailed and relevant articles for this review. The population, place, people, problem and participants criterion, was set. The intervention method used was HPV vaccination acceptance or rejection with research interest on those who have rejected. The outcomes of interest were determined before commencing the search as parents who have not vaccinated their girls/daughters against HPV by either delaying or refusing to accept HPV vaccination. It was noted that some quantitative research articles had a comparison of HPV and other childhood vaccines uptake. Anti-vaccination campaign sites and blogs were searched to find if there was any published work on their activism as part of pre-research data gathering. These databases that were applied included: PUBMED-MEDLINE, SCOPUS, CINAHL, Global health library, UiT (University of Tromsø) Library, Web of Science, HighWire, Google Scholar, science.gov, Grey Literature Library and individual country HPV vaccination sites.

Additional university sites were searched for theses that were not yet published as part of grey literature. The reference sites abstracts were saved using EndNote ×7.4 software. Some abstracts were copied and pasted in a particular file of abstracts in word format. The terms used were;

Parents OR guardians OR girls OR daughters AND HPV vaccination OR human papillomavirusvaccination OR HPV immunization OR cervical cancer vaccination AND HPVvaccination barriers OR HPV vaccination challenges OR human papillomavirus

vaccination refusal OR HPV vaccination delay OR HPV vaccination hesitation. Mesh terms were used during the search and limits were applied for years with all languages allowed. Hand searching was done on reference lists to identify papers that could not be found through the internet search.

3.2 INCLUSION AND EXCLUSION CRITERIA.

Articles with data from non-vaccinated girls aged from 9 to 17 were included. Articles with parental response to girls aged 18 were included based on the age of consent which is done by the parent or if the decision not to vaccinate was done before age 18. Those above 18 years were excluded as well as all boys. Only primary data articles that were researched within OECD countries which numbers to 34 were considered (35). Data from nations with HPV vaccination policy and program were considered while countries in OECD without HPV vaccination program were not included. Countries with the recently introduced national program were excluded from the review. The excluded countries were Turkey, Hungary, Poland, Estonia and Slovakia (36-40) having proposed programs after 2014 or did not have a vaccination programme. Publications from January 2009 to January 2016 were included in the search. Only articles with data gathered involving parents or guardians or girls in allocated age were included. Research articles with data from health practitioners and other HPV vaccination groups were included in this review. Review articles and randomized control studies were excluded. The language of publication was not limited and it included articles in English, French, Italian, Spanish, Korean and any other language spoken in the OECD countries. The researchers included Grey articles and unpublished but valuable sources based on content and relevance to the topic of review. Both qualitative and quantitative research articles were included. Articles with girls or daughters contribution without parental involvement were excluded unless parental consent was given before data collection. Primary articles with responses from Human Immuno-deficiency Virus (HIV) infected girls were excluded. Articles with girls as study subjects were not considered as the researcher's interest were on parental responses. Articles which had both parents and daughters views were included with only parental responses considered. This review population of interest was parents who have declined HPV vaccination. To enable extraction based on the method chosen, only qualitative studies with stated quantifiable numbers of interviewees were included. Quantitative primary sources with reported findings as odds ratios (with no actual population of non-vaccinated girls) were not included (41).

Table 1: General data overview (characteristics and bias outcome).

Table 1								
Study	study designs/ language	place and country	participants facility	study participants	data collection method/tool	data collection period	year of publication	bias assessment result/ tool used
Amanda F. Dempsey et al.	Qualitative interview/ English	Michigan USA	outpatient family medicine or paediatric clinics	Mothers of 11-17-year-old females	open-ended telephone interview	January-march 2007	2009	Medium CASP
Sami L. Gottlieb et al.	Qualitative/q quantitative/ English	North Carolina USA	5 counties	parents/guardians of girls aged 10-18	Telephone interview	July-October 2008	2009	Low CASP
Nava Yeganeh et al	quantitative cohort/ Spanish English	Los Angeles the USA	Children's Hospital	parents/guardians to 11-17 girls	verbal Questionnaire	May-June 2008	2010	Medium CASP
Paul L. Reiter et al	quantitative cross-sectional study/ English	North Carolina the USA	State wide	parents of daughters 13-17 old	verbal Questionnaire (Computer-assisted telephone interview)	2008	2010	Low/ Stanford University
Hee Sun Kang, Linda Moneyham	quantitative cross-sectional descriptive/ Korean	Seven regions S. Korea	9 High schools	parents and Daughters 10th and 11th grade	Questionnaires	December 2008 to April 2009	2010	Medium Stanford university
Gina Ogilvie et al.	Quantitative cross-sectional/ english	British Columbia Canada	14 HSDAs	parents of girls 11-12 years	Questionnaire	September 2008-June 2009	2010	Medium Stanford university
Christina G. Dorell, Tammy A. Santibanez et al.	Quantitative cross-sectional/ English	country wide USA	COUNTRY WIDE	Parents/guardians of 13-17	Questionnaire	Jan-Feb. 2008/9,10	2011	Low/ Stanford university
Charlene A. Wong et al.	Quantitative cross-sectional/ English spanish	USA	Nationwide survey	Parents of 9-17 girls	Questionnaire	January-December 2010	2011	Medium Stanford university

Cayce C. Hughes et al.	Qualitative interview/ English	Philadelphia USA	Children's Hospital	Mother, girl, clinician of 11-18 aged girls	Semi-structured interview	March -June 2010	2011	Low/ CASP
Daniel Gordon et al.	Qualitative interview/ English	London UK	School setting	Mothers of 11-17-year-old daughters	Interviews	June-September 2010	2011	Medium CASP
Laura M. Kester et al.	Quantitative cross-sectional/ Spanish english	Countrywide USA	47 states Online countrywide	Mother/daughter pair ages 14-17	Questionnaire	2010	2012	Medium Stanford university
Tabassum H. Laz, et al.	Quantitative cross-sectional/ English	USA	Nationwide survey	Parents of 11-17aged daughters	Questionnaire	Jan.-December 2010	2012	Low Stanford university
Alice Ma et al.	Quantitative cross-sectional english	Wellington New Zealand	School setting 16	parents/guardians of 10-14	Questionnaire/database	2011	2012	Low/ Stanford university
Julie Haesebaert et al.	Quantitative/ Qualitative interview French	Rhône-Alpes France	General practitioner	Parents of daughters aged 14-18	questionnaire/semi-structured interview	June-July 2008	2012	Low CASP
Paul L. Reiter et al.	Quantitative cross-sectional English	Ohio USA	5subgroups of Appalachia region	parents of female aged 13-17	Questionnaire/database	2008-2011	2013	Medium/ Stanford university
Maria Grandahl et al.	Qualitative interview/ Swedish	Uppsala Sweden	School Health Service 11 municipalities	parents of daughters aged 11-17	Interviews	March 2012-April 2013	2013	Medium CASP
Jessica L. Vercruyse	Qualitative interview/ English	Massachusetts USA	Children's Hospital	Parents of daughters aged 13-17	Interviews	Sep-12	2013	High/ CASP
Christina Dorell et al.	Quantitative cross-sectiona/ Italian	USA	Nationwide survey	parents of daughters aged 13-17	Questionnaire/database	2010-2011	2014	Low Stanford university
Paul L. Reiter.,Kunal Gupta et al.	Quantitative cross-sectional	USA	Nationwide survey	parents of daughters aged 10-15	Questionnaire/database	2010-2011	2014	Medium

Cristina Giambi et al.	Quantitative cross-sectional/ English	country wide Italy	56 local health units	Parents /guardians to girls aged 11-17	Questionnaire	November 2012- July 2012	2014	Low/ Stanford university
Rebecca B. Perkins, et al.	Qualitative interview/ English Spanish Haitian creole	Massachusetts USA	public/private clinic	parents and daughters aged 12 and 18	Interview	Sep.2012 and August 2013	2014	Medium/ CASP
Rie Wakimizu et al.	Qualitative interview/ Japanese	Tokyo Japan	Three paediatric clinics	parents of daughters aged 12	interview semi structured	July 2011- april 2012	2014	Medium CASP
Jihan Salad et al.	Qualitative interview/ Dutch Somali	Amsterdam Netherlands	Community health service	parents of daughters aged 12	interview semi structured	Jul-13	2015	Medium CASP

3.3 SYSTEMATIC REVIEW STUDY SELECTION.

The researcher assessed the primary articles abstracts from the exhaustive literature search independently and made a decision based on the headline, topic and the abstract content. Articles that were fit to be included in the synthesis were selected for further checks. A few database sites were searched independently by an externally requested researcher (Femi) for credibility and reduction of bias which yielded close results regarding article numbers. This review had the external reviewer and the researcher disagreeing on the inclusion of some articles, a third tie-breaker (Stanislav) were contacted for articles with disagreements and a consensus was reached. The two lists made with the articles were compared, and a consensus was attained on those to be included based on set criteria. The researcher did further hand searching from reference lists and other systematic reviews related to the topic of interest to increase the number of primary studies.

3.4 QUALITY ASSESMENT OF PRIMARY DATA.

Cohort and qualitative research articles were appraised using the Critical Appraisal Skills Programme tool (CASP) for (42). The Assessment of methodological selection, response and observation of methodological bias was done and the usefulness of reports determined (43). The researcher utilised Stanford University critical appraisal tool for cross-sectional studies in cross sectional studies (44). An additional tool was added for assessment of selection, performance, attrition, detection and reporting biases for quantitative studies (45). The researcher and external reviewer agreed on all 32 articles appraisal list using the fore

mentioned tools. All included primary studies were based on critical appraisal results. One thesis was included in this review despite low quality and bias, the researcher consulted the independent reviewer and a consensus was reached (46). One article was removed despite qualifying during appraisal based on consent by the subjects who were considered minors. Although our target age was girls below 17 years, one article had aggregated age of 16-18 which still required parental consent (47). The researcher contacted primary authors by emails and phones to obtain clarifications and additional information on primary data of interest before decisions were made.

3.5 METHOD FOR DATA SYNTHESIS.

Qualitative Meta-summary process.

The data synthesis was done according to the method developed by Sandelowski (Handbook for Synthesizing Qualitative Research page 151-196). The method included several techniques in data synthesis that consisted of extraction, separation of findings, editing of findings, grouping of similar findings, abstraction and Size effect calculation (41, 48).

Extraction of findings

The process involved classifications, setting of criteria and identifications of themes, observations, responses and generated data from questionnaires. The target population for extraction were set and only responses from parents in quantitative articles were considered. The subject's responses by parents with non-vaccinated daughters were considered for this synthesis. Non-specific responses grouped as 'other' 'no reasons' and 'non-stated reasons' were excluded while 'most' 'almost' and 'some' were translated to percentages as recommended by primary authors consideration. Responses with less than 1% and having sample size of less than twenty were not extracted. Articles with results reported as standard deviations were calculated using total numbers to give them a quantifiable estimated figure for this review (49-52). The researcher considered themes from qualitative research while all primary authors were excluded (48).

Separating of findings.

The researcher separated the discussions, quotations, stories, and cases that had been used in generating the final results. Attention was paid to all comparison from previous studies, analytical procedures and coding's from the primary sources with intention of clearly separating them. each findings were treated as a unit and linked to the sources with participants thoughts, feelings, responses, opinions and behaviours considered collectively for this synthesis (48).

Editing the findings

The researcher maintained closeness to primary author's findings while maintaining the original meanings and findings while avoiding any distortions. All findings had responses indicated for additional purposes as the numerical strength was an important part of extraction.

Grouping of similar findings.

The findings were judged based on the content and re-reading. Those with similarities from each primary research were grouped together to form several groups (48). Their size effects were noted through percentages where all responses were added to a total number representing 100%. The finding result total number of responses from the parents were added together and a percentage calculated using the overall total responses.

Abstracting of findings.

The extracted, separated, edited and grouped findings underwent further abstraction process. This involved further reduction of many statements of extracted, edited and grouped findings into more parsimonious groups (48). Abstraction involved back and forth editing between statements which were topically similar from extracted findings. This led to development of statements that led to final set that captured the content of all findings while preserving the context (48). Files were created to suit new category of groups which depended on parental factors, girl child related factors, health provider, pharmaceutical companies, government and media factors (41, 48).

Size effect calculation.

This involved calculating manifest frequency and intensity effect with magnitude of size noted. All the similar grouped findings had percentages which were added after abstraction. The total effect was noted with all responses from abstracted data totalling to 100%.

Justification of Qualitative Meta-summary method

Research synthesis methods are variant as noted by several researchers. According to several authors (30, 41, 53) both qualitative and quantitative primary articles have been integrated using mixed methods. This has been done independently with qualitative and quantitative findings assembled separately. The major challenge previously encountered by researchers has been merging together of qualitative and quantitative findings to give systematic reviews the statistical strength while preserving the content. This synthesis had primary data either quantitative or qualitative based on interviews or questionnaires addressing the 'what' and 'why' parents took the decision not to accept HPV vaccination. The presumed differences

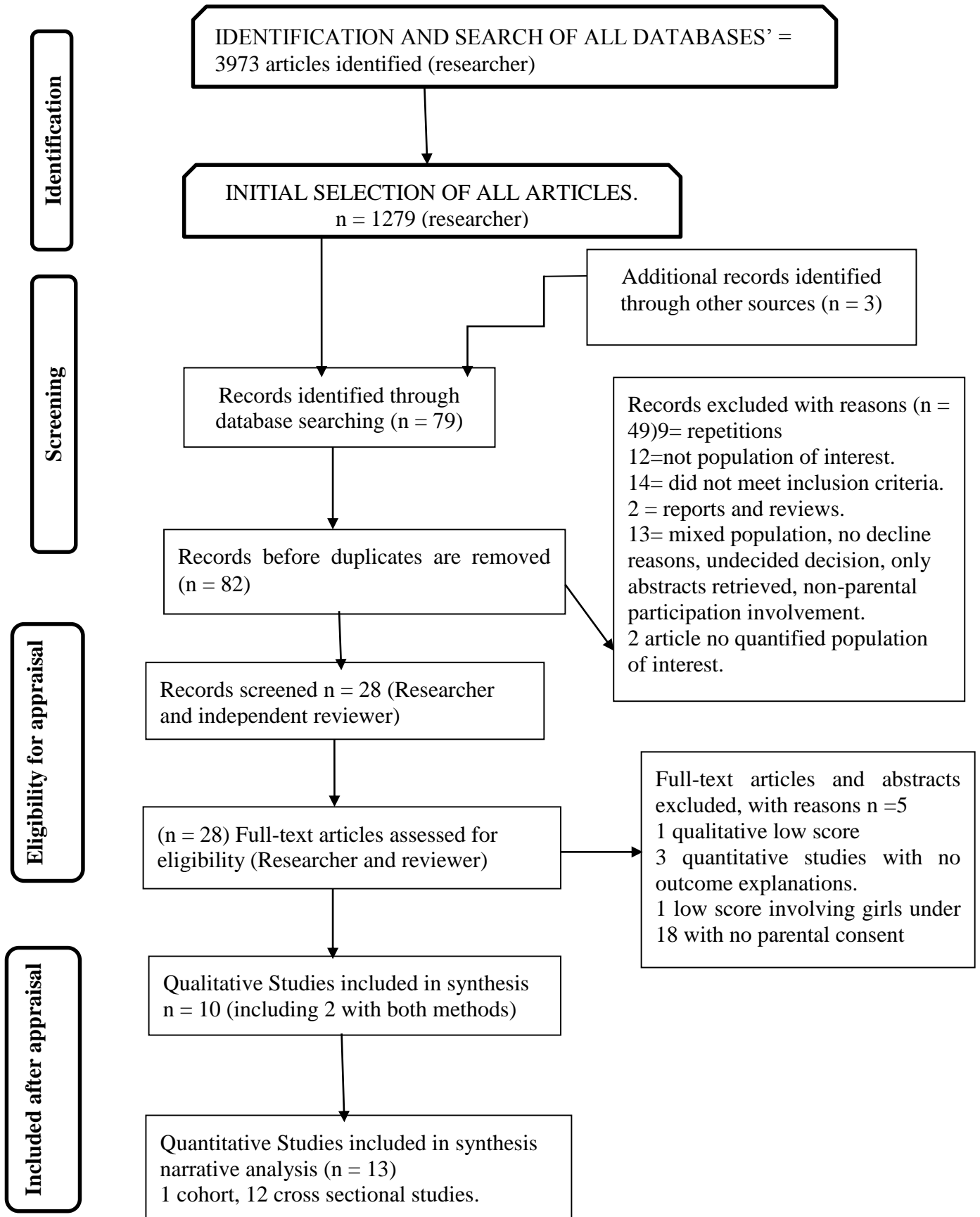
between quantitative and qualitative data could only be bridged using Qualitative Meta-summary method (41, 48).

Previous studies in the USA utilised meta-analysis and thematic synthesis separately with different reviews (30, 54). The reasons based on responses from questionnaires in quantitative primary data had variant findings which addressed 'What' part. The second review addressed 'Why' components using qualitative data. There was a reported previous major challenge of how to integrate and combine the two methods while answering this research question. This review addressed this by extraction, separation of findings, editing of findings, grouping of similar findings, abstraction and Size effect calculation (41). The Qualitative Meta-summary method as applied by the researcher could address the could address the 'why' and 'what' of the research question (55).

3.6 GENERAL EXTRACTION OF QUALITATIVE AND QUANTITATIVE DATA.

Although the researcher's intention was to combine the articles using Qualitative Metasummary synthesis, comparison between qualitative and quantitative articles could give further details. Before synthesis was done, different primary articles were extracted to give a general view of the included data. The qualitative data for this research were extracted using QARI tool which was captured the details of interest according to this systematic review (34). Quantitative data was entered into Excel spread sheet with created titles including authors, year of research and publication, the location of the study and type of settings. The QARI extraction tool included methods, settings, geographical context and participants. This similarities and differences were noted and highlighted in discussion of this review. Quantitative primary research extraction tool was developed in Microsoft Excel to suit this review. The details were finally combined and included in general extraction table. The details included: study authors, place/subjects of interest location, participants and population in the study, outcome measures (acceptance and decline) and the explanations for the decline.

Fig 1 PRISMA FLOW DIAGRAM(56)



CHAPTER 4

4.0 STUDY RESULTS - DATA CHARACTERISTICS.

Several data bases were searched, and all the results were combined yielding 3173 articles related to HPV vaccination. Further refining by the researcher based on inclusion-exclusion criteria was done, and 1279 articles identified. All the abstracts for 1279 articles underwent quick preview with filters applied for the year of research and publication, human subjects, abstracts availability with a focus on identifying articles of interest. A total of seventy nine articles had been identified with three added from hand searching. Twenty eight articles were selected for appraisal by the systematic synthesis reviewer and external reviewer by consensus. They both appraised the articles independently, and ten qualitative and thirteen quantitative were agreed for final inclusion (figure 1). There were twelve articles categorised as cross-sectional studies and one cohort study. There were ten qualitative studies which included two with both quantitative and qualitative methodologies with qualitative part meeting the set criteria for this study.

4.1 RESEARCH RESULT- PARTICIPANT CHARACTERISTICS.

The majority of studies (n=14) representing 60% of the data were undertaken in the USA. The remaining (n=9) were one each from South Korea, Canada, United Kingdom, New Zealand, France, Sweden, Italy, Japan and Netherlands (Table 1). The population involved was parents, guardians or caretakers of daughters or female children aged between 9-18 years. The parental reported mean age ranged from 41-45.1 years across all the study groups. Most studies and data collection was undertaken from 2007-2013 with the majority of studies done from 2008 until 2013. The intervention involved offers to vaccinate girls aged 9-18 by General practitioner (GP), paediatrics units, children's hospitals, school-based nurse, Gynaecologist and other vaccination centres in different countries. Health facilities including Outpatient, paediatrics units and children's hospital formed majority of participants location (n=9). Other areas included nationwide based surveys (n=5), school-based programs (n=4) and county, state or regional based study locations (n=5). The majority of primary studies included in this review (n=13) collected their data using questionnaires, interviews (n=8) and both methodologies (n=2). One study had a comparison of HPV vaccination to Pap smear check-up which is only applicable to older women and not under 18 years girls (57). The outcome of interest included parental reluctance to accept, refusal, and delay or deferral of HPV vaccination for their daughters (Table 1).

Most of the primary data collection had been done in English (n=13), English and Spanish combination (n=3) English Spanish and Haitian Creole combination (n=1). Those originally

collected in Italian, Korean, Japanese, French, Dutch-Somali combination and Swedish had one initial article each (n=6). All articles were published or translated to English even though the first language was non-English. A total of 38577 parents participated in both quantitative and qualitative primary research. Bias assessment was done using CASP and Stanford University tool for bias assessment with majority of the data having low to medium bias (n=22). One article was included based on consensus despite having a high bias. The researcher and external reviewer evaluated the article independently, and there was no agreement until a third independent tie-breaker had to conclude. The article was included based on the understanding that low sample size might have caused it. Different data articles had differing conclusions by the authors ranging from parental responsibility with the public health and promotion roles.

4.2 META SUMMARY RESULTS-EXTRACTED OUTCOMES.

A total of twenty three articles from the primary research were considered consisting of 15458 parents as participants. The 23 primary data had a total of 246 reasons given by 15458 parents on why they delayed, refused, rejected or both to HPV vaccination to their daughters aged 9-17 years. These reasons were either similar or different from each primary article (table 2). These were based on interviews and questionnaires obtained from the results, with discussions and primary researcher's views excluded. The qualitative articles had 62 reasons, and quantitative contributed to 184 total reasons from parents. The article with the highest number of reasons given had 23 while the lowest had two reasons (51, 58). The 246 reasons had 31740 responses from 15458 parents indicating an average of 129 responses for every reason given by parents for parents giving more than one response for different reasons (table 2).

4.3 SEPARATED AND EDITED FINDINGS.

Among the 246 reasons given, several of them were similar with different authors enabling grouping together. Similar reasons from both qualitative of quantitative studies were identified, scrutinized and compared by researcher before pooling together. The merged similar reasons produced 20 grouped finding (Table 2 Categories column).

Table 2: extracted, separated and edited findings.

study	Total participants	rejected or delayed/Refused HPV Vaccination	Reasons for decline of HPV vaccination	grouping based on Similar reasons	Number of responses
Amanda F. Dempsey et al.	53	19	Vaccine safety (not enough data on safety, vaccines are linked to autism, many vaccines are declared safe but later become unsafe)	1	n=8
			low perceived risk of infection(no family cancer history, cervical cancer is not deadly, daughter taught the right thing to do, HPV not contagious)	9	n=7
			Age-related (too young, wish to wait until older age, it can harm an adolescent.)	2	n=7
			Knowledge related (need more personal information, medical establishment need to know more on HPV vaccine)	12	n=6
			Financial issue/cost (lack of insurance coverage).	10	n=3
			Physician's recommendations to wait on the vaccine.	13	n=2
			Deep beliefs about vaccines (problematic to get several vaccines at one time, don't generally like vaccines)	15	n=2
			Control over health-related decision (daughter will make her decision, daughter did not want the vaccine)	4	n=2
			Religious values playing a role in decision	17	n=1
Sami L. Gottlieb et al.	886	780	Need more information about the vaccine.	12	n=169
			Daughter too young	2	n=128
			Never heard of the vaccine or not aware daughter could get it	6	n=118
			Haven't been to the doctor gotten around to it yet	13	n=99
			Daughter isn't having sex yet.	3	n=98
			Doctor did not recommend vaccine or recommended against it	13	n=57
			The vaccine is too new.	6	n=52
			The vaccine is not necessary or daughter not at risk.	8	n=35
			The vaccine is unsafe.	1	n=30
			Vaccine not available yet.	19	n=27
			Still deciding.	6	n=13
			Vaccine costs too much.	10	n=12
			Health insurance doesn't cover the vaccine.	10	n=12
			Daughter has a fear of shots.	15	n=6
The parent did not ask the provider about the vaccine.	13	n=6			
The vaccine might make daughter have sex.	14	n=4			
Nava Yeganeh et al	73	38	Parental attitudes (needs more information).	12	n=22
			Missed opportunity MD did not offer the vaccine.	13	n=8
			Parents have concerns about safety.	1	n=7
			Lack of access Not had time to go to the doctor.	19	n=6

			Other:distrust of “government “biased approach, and daughter does not need it.	18	n=6
			Vaccine too expensive/not covered by insurance.	10	n=3
			The parent does not know where to get it.	19	N=3
			Parents worried that vaccine will encourage daughter to have sex	14	n=3
			Religious beliefs oppose it.	17	n=3
			The clinic did not have it available.	19	n=3
Paul L. Reiter, Kunal Gupta et al	2786	560	Vaccine safety concern/side effects.	1	n=156
			Vaccination not needed or not necessary.	8	n=99
			Daughter not sexually active.	3	n=96
			Lack of knowledge.	12	n=89
			Did not receive provider recommendation.	13	n=54
			Daughter not appropriate age.	2	n=38
			Family/parent decision.	17	n=20
			Need more information/new vaccine.	12	n =19
			Costs.	10	n=15
			The daughter should make a decision.	4	n=11
			Don’t believe in vaccinations.	7	n=7
			Handicapped/special needs/illness.	16	n=5
			Not a school requirement.	8	n=4
			Daughter fearful.	15	n=4
			No doctor or doctor’s visit not scheduled.	13	n=2
Religion/orthodox.	17	n=2			
Effectiveness concern.	11	n=2			
Hee Sun Kang, Linda Moneyham	667	657	The HPV vaccine is not popular.	6	n=557
			Not many people I know had been vaccinated.	6	n=556
			Nobody had recommended.	13	n=543
			High cost.	10	n=540
			Unfamiliar.	6	n=532
			Don’t know where to go.	19	n=505
			Doubt on effectiveness.	11	n=449
			Fear of injection.	15	n=427
			Mistrust.	7	n=420
			Long distance.	19	n=405
			Low risk.	9	n=403
Lack of time.	19	n=374			
Gina Ogilvie et al.	2025	697	Safety of the vaccine.	1	n=209
			Prefer to wait until daughter is older.	2	n=110
			No enough information to make an informed decision.	12	n=87
			The vaccine is too new.	6	n=50
			Daughter not at risk of cervical cancer.	9	n=37
			I do not believe in vaccines, HPV no different.	7	n=18
			My physician advised me not to have Daughter receive	13	n=17
			Daughter is too young.	2	n=14
More research needed.	11	n=13			

			Daughter is not sexually active.	3	n=13
			Vaccine is a ploy by pharmaceutical company.	18	n=12
			Consent will encourage sexual activity.	14	n=11
			Will educate daughter on abstinence & safe sex.	5	n=10
			Too many needles.	15	n=10
Charlene A. Wong et al.	2205	1105	Does not need vaccine.	8	n=238
			Does not know enough about vaccine.	12	n=196
			Not sexually active.	3	n=162
			Worried about safety of vaccine.	1	n=160
			Too young for vaccine.	2	n=109
			Doctor did not recommend it.	13	n=61
			Too expensive.	10	n=18
Cayce C. Hughes et al.	20	11	Children not at risk (not the right time, Too young maybe at later age)	2	n=5
			Safety and efficacy (more information needed).	1	n=3
Daniel Gordon et al.	20	10	Low risk, not sexually active.	3	n=10
			Cultural and religious norms protection against sex.	17	n=10
			Safety concerns(new, untested, from nowhere)	1	n=9
			No herd immunity(sexually transmitted) no need	8	n=1
			Too young (should wait for suitable age)	2	n=8
			Media reports on the vaccine.	20	n=2
			Luck of parental information on the vaccine.	12	n=1
Laura M. Kester et al.	501	256	Concern for vaccine side effect.	1	n=90
			Concern for danger to daughter.	1	n=90
			Provider non-recommendation.	13	n=86
			Doubt of vaccine efficacy.	11	n=33
			Long lapse in doctor's visit.	19	n=29
			Lack of insurance or finance.	10	n=28
			Concern for increased ease for daughter to have sex	14	n=19
Tabassum H. Laz, et al.	2171	910	Does not need the vaccine.	8	n=233
			Worried about vaccine safety.	1	n=176
			Do not know enough about the vaccine.	12	n=151
			Not sexually active.	3	n=102
			Too young for the vaccine.	2	n=59
			Doctor did not recommend.	13	n=50
			Too expensive.	10	n=11
Alice Ma et al.	86	35	This vaccine is too new, and more research needed	6	n=26
			I am concerned about the safety of this vaccine.	1	n=21
			My daughter is too young.	2	n=15
			My daughter is not sexually active.	3	n=14
			I will educate my daughter about abstinence and safe sex instead	5	n=9
			My daughter is not at risk of cervical cancer	9	n=8
			I don't think I received enough information to make an Informed choice.	12	n=7
			I felt rushed/pressured to make a decision.	18	n=6
			I don't trust pharmaceutical companies.	18	n=5

			The information I read on the internet about it.	20	n=5
			Medical reasons (e.g. prior allergic reaction to vaccine)	16	n=2
			I don't want to expose my daughter to too many needles	15	n=2
			I don't trust the public healthcare system.	18	n=2
			It might encourage dangerous and inappropriate sexual behaviour	14	n=2
			A doctor advised me that my daughter shouldn't get it	13	n=1
Julie Haesebaert et al.	210	80	More information New drug, Low experience feared side effects.	1	n=41
			Wait for physician's decision and opinion.	13	n=22
			Daughters will make their decision.	4	n=15
			Too early to discuss the sexual matters, this will encourage early sexual activity.	14	n=5
			Preference to pap smear than HPV.	5	n=4
			GP is against vaccination.	13	n=1
Paul L. Reiter, Mira L. Katz et al.	1951	587	Vaccination not needed or not necessary.	8	n=116
			Daughter not sexually active.	3	n=106
			Lack of knowledge.	12	n=99
			Vaccine safety concern/side effects.	1	n=73
			Did not receive provider recommendation.	13	n=61
			Daughter not appropriate age.	2	n=45
			Need more information/new vaccine.	12	n=30
			Costs.	10	n=21
			Family/parents' decision.	17	n=19
			Child fearful.	15	n=12
			Handicapped/special needs/illness.	16	n=9
			No doctor or doctor's visit not scheduled.	13	n=6
			The child should make a decision.	4	n=6
			Don't believe in vaccinations.	7	n=5
			Not a school requirement.	8	n=4
			No obstetrician/gynaecologist.	13	n=3
			Increased sexual activity concern.	14	n=2
			Effectiveness concern.	11	n=2
			Daughter already sexually active.	3	n=1
			Religion/orthodox.	17	n=1
Maria Grandahl et al.	25	25	Inadequate information given.	12	n=16
			It will encourage sex easily.	14	n=14
			Too young.	2	n=13
			New vaccine scepticism.	6	n=13
			She will decide on her own.	4	n=12
			Other preventive methods should be offered instead.	5	n=11
			She is scared of needles.	15	n=10
			Other existing conditions (diabetes, asthma).	16	n=8
			Advised by professionals not to allow.	13	n=7
			The school nurse was not supportive, knew less.	12	n=6
			Religious and faith do not allow.	17	n=4

			Vaccine not needed-don't need to vaccinate everything	8	n=4
			No trust in government, too pushing.	18	n=4
			Previous vaccination mistakes (H1N1) memories.	18	n=3
			Individual freedom, more thinking and reflection	19	n=2
Jessica L. Vercruysse	62	25	Side effects.	1	n=9
			Peer and media influence.	20	n=9
			Lack of knowledge on HPV vaccine.	12	n=15
			The newness of the vaccine.	6	n=10
			Religious beliefs (vaccine un-necessary).	17	n=8
			Needle phobia and Number of doses.	15	n=12
			Not offered by a physician (missed opportunity).	13	n=7
Christina Dorell et al.	4103	1377	Concerns about lasting health problems.	1	n=847
			Wonder about the effectiveness of the vaccine.	11	n=739
			The teen is not sexually active.	3	n=727
			The belief that the vaccine is not needed.	8	n=681
			Heard, read bad things about the vaccine in the news TV, the radio, in the newspaper, or on the Internet.	20	n=567
			Lack knowledge about the vaccine.	12	n=480
			Feel that there are too many shots.	15	n=368
			The vaccine was not recommended by. Health care provider.	13	n=279
			Have concerns about short-term problems, like fever or discomfort	1	n=262
			Getting the vaccine was not convenient.	8	n=142
			The teenager was ill at the time.	16	n=130
			Have concerns about cost.	10	n=96
			Missed or couldn't get an appointment.	13	n=47
			Unable to find a health care provider who had the vaccine available	19	n=41
Paul L. Reiter Joan R. Cates et al.	617	419	Less information more needed.	12	n=87
			Too young for vaccination.	2	n=86
			Safety and side effects.	1	n=56
			The drug is too new.	6	n=53
			No healthcare provider recommendation.	13	n=53
			Daughter not sexually active.	3	n=21
			The vaccine might promote sexual activity.	14	n=3
Cristina Giambi et al.	1738	1331	Fear of adverse events.	1	n=1064
			No confidence in a new vaccine.	7	n=1012
			Discordant information on HPV vaccination.	12	n=865
			Scarce information on HPV vaccination.	12	n=719
			Regular pap-test can prevent cervical cancer.	5	n=665
			Our daughter is young and not sexually active.	2	n=599
			HPV vaccination not useful.	8	n=545
			HPV vaccination not compulsory.	8	n=505
			No confidence in vaccinations.	7	n=452
			Other health care workers' advice Against vaccination.	13	n=373
			The family doctor's advice against HPV vaccination.	13	n=319

			Familiars/friends' advice against HPV vaccination.	13	n=319
			Scarce promotion of HPV vaccination.	12	n=292
			HPV vaccination promotes sexual risk behaviours.	14	n=213
			Fear of injection.	15	n=186
			HPV infection is not severe.	9	n=186
			Contraindications to vaccination.	16	n=106
			Alternative medical approach, excluding vaccinations	5	n=106
			We were not able to respect the date.	19	n=53
			We did not know that HPV vaccine was free-of-charge	12	n=53
			Getting a date for vaccination is difficult.	19	n=26
			Vaccination service is difficult to reach.	19	n=13
			Religious concerns.	17	n=3
Rebecca B. Perkins, et al.	124	53	The vaccine was never offered.	13	n=23
			Luck of information.	12	n=11
			Too young for the vaccine.	2	n=7
			Safety concerns.	1	n=6
			Not necessary, she is abstaining.	3	n=3
			Vaccination could promote unsafe sex.	14	n=2
			Negative adverse effects found on the internet.	1	n=1
Rie Wakimizu et al.	20	4	Distrust in HPV vaccine safety and side effects.	1	n=4
			Not sexually active, no boyfriend.	3	n=3
			Respect adolescent's opinion.	4	n=2
			Embarrassed explaining sexual intercourse details.	19	n=2
			The cost, it's expensive.	10	n=2
			Bad publicity regarding HPV vaccination.	20	n=2
Jihan Salad et al.	6	2	Unknown and negative side effects.	1	n=2
			Objects of research.	11	n=2
			The government is encouraging sex.	14	n=2
			Too young for HPV vaccination.	2	n=2
			Luck of information and language barrier.	12	n=1
Christina G. Dorell, Tammy A. Santibanez, et al.	18228	6477	Vaccination not needed or not necessary.	8	n=1189
			Daughter not sexually active.	3	n=1171
			Lack of knowledge.	12	n=1089
			Did not receive provider recommendation.	13	n=742
			Safety concerns/adverse effects.	1	n=478
			Daughter not appropriate age.	2	n=473
			More information/new vaccine.	12	n=321
			Family/parents' decision.	17	n=238
			Costs.	10	n=162
			Child should make decision.	4	n=92
			Handicapped/special needs/illness.	16	n=68
			Child fearful.	15	n=59
			No doctor or doctor's visit not scheduled.	13	n=48
23	38582	15458	246	20	31740

4.4 GROUPED SIMILAR FINDINGS.

The findings in 20 groups were calculated from the total responses to obtain the effect of size. Less information and knowledge contributed the highest percentage of 15.22% of the total responses with 25/246 reasons representing 10.2% of overall findings. Lack of trust in government and pharmaceuticals represented the lowest percentage of responses with 0.12%. Advice from a general practitioner and other healthcare providers had the highest number of reasons given (29/246) from 19 articles. Safety and side effects were the greatest most reason given by authors represented 91% (21/23) of primary data with nine qualitative articles and 12 quantitative (Table 3).

Table 3: grouped similar findings with size effect (31740 responses representing the total)

Table 3.					
No	Finding results	authors	Primary data n/23%	Total findings F/246 %	Total 31740 responses By %
1	<u>Safety and side effects</u> Unsafe, untested, distrust in vaccine due to side effects, unknown adverse effects, the concern of lasting health problem, not enough data, fear for adverse events.	Amanda F. Dempsey et al., Sami L. Gottlieb et al., Nava Yeganeh et al., Paul L. Reiter, Kunal Gupta et al and Gina Ogilvie et al. Charlene A. Wong et al., Cayce C. Hughes et al., Daniel Gordon et al, and Laura M. Kester et al. Tabassum H. Laz, et al. Alice Ma et al. ,Julie Haesebaert et al. Paul L. Reiter, Mira L. Katz et al.and Jessica L. Vercruyssen. Christina Dorell et al. Paul L. Reiter, Joan R. Cates et al. Cristina Giambi et al. Rebecca B. Perkins, et al. Rie Wakimizu et al. Jihan Salad et al. Christina G. Dorell, Tammy A. Santibanez, et al. Nine quantitative and twelve qualitative articles.	21 91%	24 9.8%	3802 11.98 %
2	<u>Daughter/ girl/child age</u> Too young, not appropriate age, wait until an older age, prefer to wait, not the right time.	Amanda F. Dempsey et al., Sami L. Gottlieb et al., Paul L. Reiter, Kunal Gupta et al., Gina Ogilvie et al., Charlene A. Wong et al., Cayce C. Hughes et al., Daniel Gordon et al., Tabassum H. Laz, et al. Alice Ma et al., Paul L. Reiter, Mira L. Katz et al., Maria Grandahl et al., Paul L. Reiter Joan R. Cates et al., Cristina Giambi et al., Rebecca B. Perkins, et al., Jihan Salad et al., Christina G. Dorell, Tammy A. Santibanez, et al. Nine quantitative, seven qualitative	16 69.6%	17 6.9%	1718 5.41%

3	<u>Daughter sexually active/non-active</u> Not yet having sex, already having a boyfriend, no boyfriend yet, she is abstaining,	Sami L. Gottlieb et al., Paul L. Reiter, Kunal Gupta et al., Gina Ogilvie et al., Charlene A. Wong et al., Daniel Gordon et al., Tabassum H. Laz, et al., Alice Ma et al., Paul L. Reiter, Mira L. Katz et al., Christina Dorell et al., Paul L. Reiter Joan R. Cates et al., Rebecca B. Perkins, et al., RieWakimizu et al., Christina G. Dorell, Tammy A. Santibanez, et al.	13 56.5%	14 5.7%	2527 7.96%
		Four qualitative and nine quantitative			
4	<u>Daughter decide</u> She will make her decision; she will decide on her own; I respect adolescent opinion,	Amanda F. Dempsey et al., Paul L. Reiter, Kunal Gupta et al., Julie Haesebaert et al., Paul L. Reiter, Mira L. Katz et al., Maria Grandahl et al., RieWakimizu et al., Christina G. Dorell, Tammy A. Santibanez, et al.	7 30.4%	7 2.8%	140 0.44%
		Four qualitative, three quantitative			
5	<u>Other methods</u> She is abstaining, other methods will do, regular pap smear, safe sex preferred, an alternative medical approach not vaccines.	Gina Ogilvie et al., Alice Ma et al., Julie Haesebaert et al., Maria Grandahl et al., Cristina Giambi et al.,	5 21.7%	6 2.4%	805 2.54%
		Two qualitative and three quantitative			
6	<u>Doubts on HPV vaccine</u> The new vaccine, never heard of it, not popular, not so many are vaccinated, still deciding.	Sami L. Gottlieb et al., Hee Sun Kang, Linda Moneyham., Gina Ogilvie et al., Alice Ma et al., Maria Grandahl et al., Jessica L. Vercruysse., Paul L. Reiter Joan R. Cates et al.,	7 30.4%	11 4.5%	1980 6.23%
		Three qualitative, four quantitative			
7	<u>No trust in drug</u> Don't believe in the drug/ vaccination, no confidence, mistrust in drug	Paul L. Reiter, Kunal Gupta et al., Hee Sun Kang, Linda Moneyham., Gina Ogilvie et al., Paul L. Reiter, Mira L. Katz et al., Cristina Giambi et al.,	5 21.7%	6 2.4%	1914 6.03%
		Five quantitative articles.			
8	<u>Vaccine not necessary</u> Not needed, inconvenient, not compulsory.	Sami L. Gottlieb et al., Paul L. Reiter, Kunal Gupta et al., Charlene A. Wong et al., Daniel Gordon et al., Tabassum H. Laz, et al., Paul L. Reiter, Mira L. Katz et al., Maria Grandahl et al., Christina Dorell et al., Cristina Giambi et al., Christina G. Dorell, Tammy A. Santibanez, et al.	10 43.5%	14 5.7%	3796 11.96%
		three qualitative and seven quantitative			
9	<u>Low risk to cervical cancer</u> Low perceived risk, infection not common,	Amanda F. Dempsey et al., Hee Sun Kang, Linda Moneyham., Gina Ogilvie et al., Alice Ma et al., Cristina Giambi et al.,	5 21.7%	5 2.0%	641 2.02%
		one qualitative and four quantitative			

10	Cost related. No insurance, too expensive, not covered by insurance.	Amanda F. Dempsey et al., Sami L. Gottlieb et al., Nava Yeganeh et al., Paul L. Reiter, Kunal Gupta et al., Hee Sun Kang, Linda Moneyham., Charlene A. Wong et al., Laura M. Kester et al., Tabassum H. Laz, et al., Paul L. Reiter, Mira L. Katz et al. Christina Dorell et al., Rie Wakimizu et al., Christina G. Dorell, Tammy A. Santibanez, et al.	12	13	923
		Three qualitative and ten quantitative.	52.1%	5.3%	2.91%
11	<u>Doubt on effectiveness</u> Objects of research, more research needed	Paul L. Reiter, Kunal Gupta et al., Hee Sun Kang, Linda Moneyham., Gina Ogilvie et al., Laura M. Kester et al., Paul L. Reiter, Mira L. Katz et al., Christina Dorell et al., Jihan Salad et el.	7	7	1240
		one qualitative and six quantitative	30.4%	2.8%	3.91%
12	<u>Less information and knowledge</u> Need more information, lack knowledge, inadequate, scarce and discordant information, scarce promotion details.	Amanda F. Dempsey et al., Sami L. Gottlieb et al., Nava Yeganeh et al., Paul L. Reiter, Kunal Gupta et al., Gina Ogilvie et al. Charlene A. Wong et al., Daniel Gordon et al., Tabassum H. Laz, et al., Alice Ma et al., Paul L. Reiter, Mira L. Katz et al., Maria Grandahl et al., Jessica L. Vercruysse., Christina Dorell et al. Paul L. Reiter Joan R. Cates et al., Cristina Giambi et al., Rebecca B. Perkins, et al. Jihan Salad et al., Christina G. Dorell, Tammy A. Santibanez, et al	18	25	4831
		Seven qualitative and eleven quantitative	78.2%	10.2%	15.22 %
13	<u>Advised against, no visit or no recommendation.</u> Told to wait, no vaccine, missed opportunity from General Practitioner (GP) Nurse, paediatrician, gynaecologist, family member, friends and health facility.	Amanda F. Dempsey et al., Sami L. Gottlieb et al., Nava Yeganeh et al., Paul L. Reiter, Kunal Gupta et al., Hee Sun Kang, Linda Moneyham., Gina Ogilvie et al., Charlene A. Wong et al., Laura M. Kester et al., Tabassum H. Laz, et al., Alice Ma et al., Julie Haesebaert et al., Paul L. Reiter, Mira L. Katz et al., Maria Grandahl et al., Jessica L. Vercruysse., Christina Dorell et al., Cristina Giambi et al., Rebecca B. Perkins, et al., Christina G. Dorell, Tammy A. Santibanez, et al.	19	29	3298
		Six qualitative and thirteen quantitative	82.6%	11.8%	10.38 %
14	<u>HPV vaccine will encourage/ increase sex.</u> Concern over inappropriate sexual behaviour & unsafe sex.	Sami L. Gottlieb et al., Nava Yeganeh et al., Gina Ogilvie et al., Laura M. Kester et al., Alice Ma et al., Julie Haesebaert et al., Paul L. Reiter, Mira L. Katz et al., Maria Grandahl et al., Paul L. Reiter Joan R. Cates et al., Cristina Giambi et al., Rebecca B. Perkins, et al., Jihan Salad et al.	12	12	280
		Five qualitative and seven quantitative	52.2%	4.9%	0.88%

15	<u>Fear of Injections.</u> Too many injections or needles, needle phobia, scaring.	Amanda F. Dempsey et al., Sami L. Gottlieb et al., Paul L. Reiter, Kunal Gupta et al., Hee Sun Kang, Linda Moneyham., Gina Ogilvie et al., Alice Ma et al., Paul L. Reiter, Mira L. Katz et al., Maria Grandahl et al., Jessica L. Vercruysse., Christina Dorell et al., Cristina Giambi et al., Christina G. Dorell, Tammy A. Santibanez, et al.	12	12	1098
		Four qualitative eight quantitative	52.2%	4.9%	3.46%
16	<u>Other medical conditions</u> Contra-indicated, special needs handicapped, medical reasons and sickness.	Paul L. Reiter, Kunal Gupta et al., Alice Ma et al., Paul L. Reiter, Mira L. Katz et al., Maria Grandahl et al., Christina Dorell et al., Cristina Giambi et al., Christina G. Dorell, Tammy A. Santibanez, et al.	7	7	328
		one qualitative and six quantitative	30.4%	2.8%	1.03%
17	Religion and family decision roles in deciding. Religion/orthodox opposes, against family beliefs, cultural and religious values.	Amanda F. Dempsey et al., Nava Yeganeh et al., Paul L. Reiter, Kunal Gupta et al., Daniel Gordon et al., Paul L. Reiter, Mira L. Katz et al., Maria Grandahl et al., Jessica L. Vercruysse., Cristina Giambi et al., Christina G. Dorell, Tammy A. Santibanez, et al.	9	11	309
		four qualitative and five quantitative	39.1%	4.5%	0.97%
18	Lack of trust in Government, pharmaceutical companies. Don't trust public health, rushed& pressured decision, previous vaccine mistrust.	Nava Yeganeh et al., Gina Ogilvie et al., Alice Ma et al., Maria Grandahl et al.,	4	7	38
		one qualitative three quantitative	17.4%	2.8%	0.12%
19	<u>Difficulty in obtaining services.</u> Vaccine not available, no access, any time, no provider, could not make it on time, individual freedom threat, long queue, distance.	Sami L. Gottlieb et al., Nava Yeganeh et al., Hee Sun Kang, Linda Moneyham., Laura M. Kester et al., Maria Grandahl et al., Christina Dorell et al., Cristina Giambi et al., RieWakimizu et al.	8	14	1489
		3 qualitative and 4 quantitative	34.8%	5.7%	4.69%
20	<u>Media and internet influence</u> Information read online, peer and media influence, bad publicity, media reports.	Daniel Gordon et al., Alice Ma et al., Jessica L. Vercruysse., Christina Dorell et al., Rie Wakimizu et al.	5	5	585
		4 qualitative and 1 quantitative	21.7%	2.0%	1.84%
			23	246	31740

4.5 ABSTRACTED RESULTS WITH CALCULATED SIZE EFFECT

This research identified 20 different reasons directed towards vaccine, parents, girl child, general provider and pharmaceutical. The twenty major findings were further abstracted to form seven groups with the size effect noted based on collective responses. After extraction separation, editing, grouping of similar responses and abstraction of findings, several grouped results were carefully formulated. The seven abstracted results included (a) vaccine related (b) parental concerns and perceptions (c) girl child factors (d) general factors (e) health provider factors (f) pharmaceutical and government-related factors and (g) social media and religious concerns. Primary data had safety and side effects with 91% content as the highest with the lack of trust having 17.4% as the lowest. On total reasons, less information and knowledge accounted for 10.2% of reasons by parents with media and internet having 2% (table 4).

Table 4: abstracted results (7 grouped reasons and size effect).

combination	content	Percentage size effect
1 Vaccine related response	<p><u>1. Safety and side effects:</u> Unsafe, untested, distrust in vaccine due to side effects, unknown adverse effects, the concern of lasting health problem, not enough data, fear for adverse events.</p> <p><u>6. Doubts on HPV vaccine:</u> The new vaccine, never heard of it, not popular, not so many are vaccinated, still deciding.</p> <p><u>7. No trust in drug:</u> Don't believe in the drug/ vaccination, no confidence, mistrust in drug.</p> <p><u>11. Doubt on effectiveness:</u> Objects of research, more research needed</p>	28.15%
2 Parental factors, concerns & perceptions.	<p><u>5. Other methods:</u> She is abstaining, other methods will do, regular pap smear, safe sex preferred, an alternative medical approach not vaccines.</p> <p><u>8. Vaccine not necessary:</u> Not needed, inconvenient, not compulsory.</p> <p><u>14. HPV vaccine will encourage/ increase sex:</u> Concern over inappropriate sexual behaviour & unsafe sex.</p> <p><u>19. Difficulty in obtaining services:</u> Vaccine not available, no access, any time, no provider, could not make it on time, individual freedom threat, long queue, distance.</p>	22.05%
3 Girl child Related reasons	<p><u>2. Daughter/ girl/child age:</u> Too young, not appropriate age, wait until an older age, prefer to wait until an older age, not the right time.</p> <p><u>3. Daughter sexually active/non-active:</u> Not yet having sex, already having a boyfriend, no boyfriend yet, she is abstaining,</p> <p><u>4. Daughter decide:</u> She will make her decision; she will decide on her own; I respect adolescent opinion,</p> <p><u>15. Fear of Injections:</u> Too many injections or needles, needle phobia, scaring.</p>	17.67%
4 General factors	<p><u>12. Less information and knowledge:</u> Need more information, lack knowledge, inadequate, scarce and discordant information, scarce promotion details.</p>	15.22%

5	Health provider factors.	<u>13. Advised against, no visit or no recommendation.</u> Told to wait, no vaccine, missed opportunity from General Practitioner (GP) Nurse, pediatrician, gynecologist, family member, friends and health facility. <u>16. Other medical conditions:</u> Contra-indicated, special needs handicapped, medical reasons and sickness.	11.21%
6	Pharmaceutical, government related reasons	<u>10. Cost related:</u> No insurance, too expensive, not covered by insurance. <u>18. Lack of trust in:</u> Government, pharmaceutical companies. Don't trust public health, rushed & pressured decision, previous vaccine mistrust.	3.3%
7	Social media and religious reasons	<u>17. Religion and family decision roles in deciding:</u> Religion/orthodox opposes, against family beliefs, cultural and religious values. <u>20. Media and internet influence:</u> Information read online, peer and media influence, bad publicity, media reports.	2.81%

Vaccine-related responses.

Quoted responses in Safety and side effects concerns included: Unsafe, untested, distrust in vaccine based on side effects and unknown adverse effects. There was reported concern of unknown lasting future health problem, not enough data and fear of adverse events in future. Safety and side effects accounted for 11.98% of parental responses. Doubts on HPV vaccine, no trust in the drug and doubt on the effectiveness of the drug represented 6.23%, 6.03% and 3.91% of responses. Parents claimed that they did not vaccinate their daughters because the vaccine was new, never heard of it, not popular, not so many are vaccinated, and some were still deciding. Some reported that they don't believe in the drug or vaccination, any confidence, mistrust in drug, objects of research, and they felt more research was needed on HPV vaccine. Vaccine-related responses accounted for a total of 28.15% of the responses after a combination of responses.

Parental factors, concerns and perception.

In the data, 11.96% of responses indicated that the vaccine was not necessary, inconvenient and not compulsory for schooling system. Difficulty in obtaining services, Vaccine not available, no access, no time, no provider, parents could not make it on time, individual freedom threat, long queue and distance had 4.69% response. Other methods, low risk and parental concern over the outcome of vaccination had 2.5%, 2.02% and 0.88% responses. The reasons given included; she is abstaining, other methods will are better, regular Pap smear, safe sex preferred and alternative medical approach, not vaccine. Parents considered daughter to be of low perception risk, infection not common, HPV vaccine will encourage inappropriate sexual behavior and promote unsafe sex. This gave a total of 22.05% of responses.

Girl child-related reasons.

Data indicated that 7.96% of responses from the parents gave reasons related to their daughter's active or no active sexual activity. The reasons were: Not yet having sex, already having a boyfriend, no boyfriend yet and she is abstaining. Girl child age concern reasons were; too young, not appropriate age, need to wait until an older age and not the right time signifying 5.41% of responses. Fear of injections, too many injections or needles, needle phobia and its scaring had 3.46% of the total responses. Less than 0.44% of total responses indicated that parents felt that she will make her decision, she will decide on her own, and I respect the adolescent opinion. Combined responses had a perfect representation of 17.67%.

General factors.

The highest single response reported as less information and lack of knowledge on HPV vaccination. This accounted for 15.22% of the responses as to why parents did not vaccinate their daughters against HPV. The information they had was discordant, inadequate and scarce with the reported lack of health promotion details. This was 10.2% of total reasons for 78.2% of primary data sources and parents wanted more information.

Health provider factors.

The General Practitioner (GP), nurse, pediatrician, gynecologist, family member, friends and health facility contributed to a parental decision as expressed through reasons given. The reasons from the data include advice not to vaccinate, told to wait, no vaccine, missed opportunity from first encounter and no recommendation given by the health providers in 10.38% of responses. Medical conditions, special needs children, sickness and vaccine contraindications had 1.03% responses. The combined factors added to 11.21% of responses.

Pharmaceutical and government related reasons.

Overall 2.91% of responses were attributed to cost. The reasons given as cost related included no insurance, too expensive and not covered by insurance. Data indicated that 0.12% of all responses were due to lack of trust, combination of 3.3% of responses. There was reported lack of trust in government; pharmaceutical companies, public health, previous vaccine mistrust and feeling from parents of pressured to make the decision.

Social media and religious reasons.

A total of 1.84% responses indicated media and internet influence in a decision against vaccination. The quoted reasons were Information read online, peer and media influence, bad publicity and media reports. Approximately 0.97% of responses had religion and family decision roles considered in deciding not to vaccinate their daughters against HPV. Data

reasons were named as religion orthodox opposes, against family beliefs, cultural and religious values influencing the decision. This combination of factors contributed to 2.81% of all responses from parents.

CHAPTER 5

5.0 DISCUSSION

Qualitative and Quantitative Data Results.

According to Qualitative Met-analysis's based on Sandelowski, both qualitative and quantitative primary data was combined to give the study its size effect (59). However the two methods used in primary articles were compared to identify similarities and differences. One of the major reasons expressed by parents in qualitative research articles was safety and side effects concern which was quoted in 90% (9/10) primary articles. In quantitative data sources, more articles quoted advise against vaccination by health personnel, friends and lack of visit as a major reason (13/13) representing 100% against HPV vaccination. The least expressed reason for the decline according to qualitative research articles was a low risk of cervical cancer and doubt on effectiveness which both had only one article representing 10%. Other medical conditions, lack of trust in government and pharmaceuticals had one qualitative article with reasons for the decline.

Media concern and internet reasons were least expressed in quantitative articles (1/13). According to this review all findings that did not express trust in the drug were qualitative. None of quantitative primary source expressed lack of trust in the drug. Safety and side effects had the highest number of articles of 21 (qualitative 9, 12 quantitative). Less information and knowledge had total of 18 primary sources (7 qualitative, 11 quantitative). Advice against HPV vaccination had total of 19 articles (6 qualitative, 13 quantitative sources). This research clearly indicates that both qualitative and quantitative articles had more similarities than differences on parental responses. The results suggest both methodologies had similar outcomes despite their different approach. The notable difference was the quantity of respondents with quantitative research having a higher sample size compared to qualitative methods. The researcher noted that most (19/20) of the quantitative 'what' question was supported by qualitative 'why' responses as all the initial twenty similar findings consisted of both quantitative and qualitative results. It was further noted that only qualitative articles gave the reasons to why parents delayed vaccination based on no trust in the drug which was not mentioned in all quantitative articles. Twenty one research articles out of twenty three indicated safety concern as a major reason why parents declined, this included both quantitative and qualitative articles.

5.1 DISCUSSION-QUALITATIVE METASUMMARY RESULTS

High-income nations grouped as OECD have several challenges to low HPV vaccination since it was licensed.

Vaccine-related responses

This systematic review categorized parental decisions into seven major findings as main explanations supporting the data on low HPV vaccination in OECD nations. Homogenized pooled results indicated 28.15% of responses were vaccine-related factors as primary reasons for not vaccinating their girl child with HPV vaccine.

It was represented by 28.15% of all responses explaining why they took the decision not to vaccinate. Their shared experiences were based on safety, Unsafe and untested HPV vaccine and distrust in vaccine based on side effects. They believed that the vaccine had unknown adverse effects and associated long lasting future problem. Their decision was based on belief and experience that HPV vaccine does not have enough data and due to this, there is fear of future adverse events. HPV vaccine as reported by the parents of non-vaccinated daughters is mistrusted with some parents who do not believe in the vaccine. The low confidence in the HPV vaccination was based on belief that their daughters are objects of research and they felt that more research needed on this vaccine. Other published articles expressed more doubts on claim of safety with vaccine adverse event reporting system higher than recommended (60). At the moment there is less systematic metasummary review highlighting this finding. According to Neural Dynamics Research Group publication, a list of severe adverse reactions to HPV vaccination with reported unknown vaccine benefits were reported (60).

Parental factors attributed to non-vaccination.

Globally it's claimed the HPV vaccine risks remain unknown with its benefits still doubtful to the vaccinated population as protection is believed to be 70% for those immunized and the remaining 30% non-protection unsure (60). According to European center for disease control (ECDC), there has been doubting on period protection span according to randomized control studies were done with suggestions of a booster vaccine needed after nine years. Developed nations had 35 000 death in 2012 out from total death of 266 000 from cervical cancer. (8). The current data indicates that developed countries have few cervical cancer-related death believed to be due to early screening success and not vaccination. This review result indicates parents thought the vaccine is not necessary, and it was inconveniencing them (11). The claim by parents that the vaccine was not available, they did not have time, the queue was long, there was no provider, and they were busy indicates their priorities.

They believed that the vaccine was not a necessity, not compulsory for school and it's an inconvenience to them. It's still unknown if more effort by parents could have changed parental decision leading to more acceptance to HPV vaccination. This research finding of parental feeling that HPV vaccine will encourage inappropriate and unsafe sex has similar results with a systematic review done in the USA among adolescents (61). Abstinence, safe sex and male circumcision among the religious group were some of the reasons given by parents for making HPV and cervical cancer at lower risk. This preference collaborates with other findings which preferred screening as the best preventive method than HPV vaccination (62)

Girl child-related reasons.

Mothers were protective in responses towards their daughters with genuine concerns that need to be addressed. The age factor and the number of injections totaling to 3 recommended at 0, 1, and six-month schedule at ages 9-12 was a limitation to some parents (63). The feeling of their daughter being too young and fragile, no boyfriend yet, not the right time, too many and fearful injections made parents feel that the girl child will make her decision at a later age (61). This barrier was expressed in the previous systematic review and the review found out older girls are likely to be vaccinated than younger age and this review suggests an increased flexible age can increase coverage.

General factors

HPV vaccination results were characterized by lack of information and knowledge by the parents. This review identified inconsistent, inadequate, scarce and non-available information on HPV vaccine as a primary single most factor as to why parents did not vaccinate their daughters. It was indicated by 15.22% of the responses who gave the reason for their decision. The service provider's knowledge about vaccination was not shared with the parents at satisfaction level to enable them to make a decision. These study findings agree with the previous review which stated that health care provider messages are often not delivered in a way that is clearly and easily understood by young women. It could have been central in explaining experiences on the lack of information on HPV vaccine (64). The most convenient method of administering HPV vaccine is through school-based systems, pediatrics clinic, and health facility or at GP clinic as indicated by the primary data. The information relayed from providers is given directly or through children to parents before decisions made. Health Providers and parents do not have enough time to share all information on HPV vaccination as communication using pamphlets and printouts do not convince the parents to make a decision. The different, inadequate or scarce details with

reported lack of health promotion details contribute to delay or decline of HPV vaccination. Research in the USA suggested ways of reducing the barriers brought by information gap with a triage communication. A parent, health provider and institutions triangle will be essential in providing information and knowledge leading to more acceptances (65).

Health provider factors.

Health providers play a significant role in HPV vaccine delivery to children, and their decision is central to enabling parents to accept or reject the vaccine. Healthcare system depends centrally on providers recommendations on service uptake. A recommendation not to vaccinate, wait for some time, child's current condition does not allow vaccination made parents delay or refuse their daughters to be vaccinated. Previous systematic reviews reported missed opportunity to be one of the barrier to HPV vaccination (61). Healthcare providers did not recommend HPV vaccination to parents during their routine visit leading parents to opt out. A change in message delivery system and communication mechanism between the parents and health providers could improve the acceptance while limiting missed an opportunity (61). Expert views on HPV vaccination barriers indicate that Health care provider communication is vital, and the results are encouraging. Where early and well-orchestrated communication is achieved, more parents seemed to accept the vaccine for their daughters (66). Primary prevention mechanism will be better if the parents can be empowered so that they can request for the service in places where health provider does not initiate. Public health promotion can be vital in giving information to the parents in advance. More detailed information compared to the shorter period communication between the health provider and the parent will empower the parent to initiate the process.

Pharmaceutical and government related reasons.

This review had more primary data from the USA than the rest of OECD nations. The health system funding has variations, and most developed countries have either tax paid healthcare system or government insurance. Tax paid to finance involves service provision to the populations with all costs incurred through citizen's tax payment. The USA has a mixed system of private funding and health insurance accounting for a larger coverage. Medicare, which is government financed has been improving slowly, and more Americans are getting a medical cover (67). A systematic review in the USA indicated that HPV vaccination cost and lack of insurance coverage are noted. The estimated cost per dose is \$350; the vaccine is expensive, and some parents do not have insurance. It will be better for subsidies or full government funding to enable the non-insured population to have access (64, 68).

According to published articles marketing strategy for the vaccine, Gardasil had Merck (manufacturer) funded educational programmes. The professional medical associations (PMAs) was used as a marketing strategy to promote the use of their vaccine(69). Whether parents considered this as a factor in being pushed to accept the vaccine is unknown. The linkage between manufacturers, lobbying and government interest remains unexplained in understanding parental decisions. Independent educators with no vested interest should be giving the information on the significance of HPV vaccination. Providers agree that HPV alone will not prevent cervical cancer and screening is needed too.

Social media and religious reasons.

Current social media and traffic online combined with religious beliefs influences parental decision making. Media reports in the USA and Japan were reported to have affected HPV vaccination. This review had an objective to ascertain whether the decision to reject or delay HPV vaccination by the parent depended majorly on social media and religion dependent reasons. Anti-vaccine websites and the media have been considered a smaller contributing factor in the parental decline to HPV vaccination. In Japan, the suspension of the official recommendation for the vaccine was due to reported side effects. A study done after negative media news indicated discontinuation among those on the vaccine (29). The effects of the information vacuum filled in by media speculations and non-verified sources might have an impact on responses accounting for 2.81% which was the least of all factors. The media news from Japan had more impact on nation's vaccination. Research done by obstetrics and gynecologists indicated that none of their daughters were vaccinated after the news on reported side effects. If health providers are not willing to accept their daughters to be vaccinated after reported negative news, the general public has no reason to take the vaccine (70). A more consultative decision with all stakeholders and concerned parties with evidence-based reasons are needed to face negative media coverage while encouraging HPV vaccination. Religious beliefs was a less contributing factor to the rejection of HPV vaccination as noted with results.

5.2 STRENGTH AND WEAKNESSES OF THIS STUDY.

This study was heterogeneous as combined both quantitative and qualitative primary data sources as opposed to other systematic reviews. This review had a large number of findings with 31740 responses given to 246 reasons which was good for broad synthesis. Most grouped similar findings had quantitative and qualitative articles which responded to 'what' and 'why' component as the questionnaires had responses in interviews. The size effect through abstraction was met after grouping of findings. This Qualitative meta-summary

enabled the reviewer to assess the impact of individual primary reports and findings on synthesis results. High-income OECD members covering over 34 countries gave an extensive coverage facilitating further research inferences reaching a wider audience. The cost of HPV vaccine is known to be high, and affordability is a major factor in developing nations. This study concentrated on high-income countries looking at factors beyond cost as reported by tax and insurance-based funding of HPV vaccine. The review contacted external individuals to give credibility while limiting bias. The publication period from January 2009 to January 2016 was after licensure of Gardasil, which occurred in 2006. This review concentrated only on parents who girls had aged 9-18 who had not been vaccinated as required by voluntary vaccination programs. By including the grey literature and thesis articles during the review, the research work avoided publication bias. The author utilized references from other systematic reviews in broadening the data sources. Primary articles with raised questions were re-evaluated, and Telephone and email contacted the authors. There were written clarifications strengthened the study.

Primary data sources were considered based on a parental decision on vaccination, delay or refusal of HPV vaccine. Most of the collected data did not verify or validate whether the parental choice of declining was true or false. It was based on trust as expressed by respondents. The majority of data source was done in the USA representing 60% of the articles representing abias towards one source. This research was centered on parents of daughters aged 10-18 as the population of interest. The parental responses were impartial as pharmaceutical companies, government and health provider's responses were not considered. Some articles from OECD nations were not considered based on lack of HPV vaccination policy creating more bias. The author noted that although different countries were presented through primary article, this research could not verify all the 34 countries health systems as they are diverse with some having no clear policy on HPV vaccination.

Qualitative Meta-summary synthesis is reflection of judgement made by the reviewer. There is no criteria set for what a finding should be and what to abstract and how similar findings determined. The synthesis method is relatively new with less documented research based on qualitative metasummary. Developed nations have different systems of health structures and funding mechanisms, this variance explains why parental decline in Scandinavian nations is less compared to the USA. Tax based funding, government insurance, private insurance and out of pocket payments are some of the funding mechanisms in different nations.

More research is needed on individual country factors that are making nations like Norway with public funded programs with lower than 78% (15). It's estimated that almost 9 out of

every 10 of cervical cancer death are from developing nations, yet the HPV vaccine is available, affordable and accessible to high-income countries. More research is needed on developing country's factors other than cost-related barriers.

CHAPTER 6

6.0 CONCLUSION.

Low HPV vaccination coverage is attributed to many reasons as given by different implementers of vaccination programs within OECD nations. The parent determines the decision to vaccinate at targeted age as required by regulation for the benefit of girl Child's future. This systematic review focused on decisions made based on several factors of which if addressed, the parents might change their decision and accept HPV vaccine to be administered. These shared and expressed responses are directed at different levels. The majority of these responses include vaccine-related reasons, parental factors, girl child related and general factors. Health provider related factors, pharmaceuticals or government, social and religious related factors contributed less to the parental decision to decline. Public health activities on cervical cancer prevention are centrally attached to parents. Providing adequate evidence-based, transparent, and accessible information to parents about HPV infection, vaccine safety, adverse effects, and the appropriate age for vaccination may make health care professionals able to reduce concerns and misconceptions about the vaccine. The researcher believes a well organized health promotion strategy directed at each group with suitable monitoring mechanisms will provide the best solution in developed countries. The researcher of this review concludes that these parental explained reasons if addressed through collective measures by primary public or private health prevention players will decrease refusal and increase HPV vaccination coverage. Further research is required in assessing immunity of vaccinated and non-vaccinated groups to ascertain the protection difference by measuring antibodies from naturally acquired and vaccine-induced protection.

7.0 APPENDIXES

Appendix 1. Data and findings Extraction Template for Qualitative Evidence

Method	
Methodology	
Interventions	
Setting	
Geographical	
Cultural	
Participants	
Data analysis	
Author's conclusions	
Reviewer's Conclusion	
Finding	
Illustrations from publication (including page number)	
Evidence	Unequivocal
	Plausible
	Unsupported
Category	

Appendix 2: STANFORD UNIVERSITY APPRAISAL TOOL.
APPRAISAL TOOL FOR CROSS-SECTIONAL RESEARCH.

Cross-sectional Study Section P: Brief Summary of Paper:
Descriptive information (short sentences)

Exposure factors:

Outcomes ascertained:

Main source of subjects:

Inclusion criteria:

Exclusion criteria:

Primary source of data:

Follow-up subsequent to cross-sectional study: Yes No
 Number considered for enrolment:

Enrolled Number enrolled:

Number included in analysis:

Statistical methods:

Other relevant information:

Sections P-R: Cross-sectional Study

Section Q: Specific methodological issues

(Y= Yes, S= substandard, NC= Not Clear, NR= Not Reported, N=NO,NA= Not Applicable, NQ= Not Qualified to Assess); cite apage number for key comments.

<u>CRITERIA</u>	Y	S	N	NC	NR	NA	NQ	comments
Similar sampling procedures for all subjects								
Similar ascertainment of exposure for all subjects								
Similar referral and diagnostic procedures for all subjects								
Diagnostic criteria for diseased clear, precise, and valid								
Characteristics of subjects at enrolment.								
All aspects of exposure measured (level, dose, duration)								
Co-exposure measured								
Recall bias controlled								
Data collection valid and reliable								
Effect of duration of disease discussed								

Section R: Author's key results.

Section S Conclusions and assessment of the article

- i. Strengths of the paper
- ii. Weaknesses of the paper
- iii. Reviewer's conclusions (if different from authors)
- iv. Clinical relevance.
 - Highly relevant
 - Relevant
 - Questionable relevance
 - Irrelevant
 - Not qualified to evaluate
- v. Scientific merit
 - Very good
 - Good
 - Scientifically admissible
 - Scientifically inadmissible

Section S: Conclusions assessment of the article

- vi. The Type of study:
 - Randomized controlled trial conducted & interpreted correctly
 - Controlled trial with evidence of comparability of groups
 - Well-designed cohort or case-control study
 - Case series or cohort study without controls
 - Opinions of competent authorities based on clinical experience, descriptive studies, research, or studies not classified in the preceding categories
 - Other, including substandard of the above
- vii. Recommendations concerning possible additional specialized reviewer
- viii. Should any article referenced be added to the list of papers to be criticized? If yes, which?

Appendix 3 risk of bias assessment tool for quantitative research.

Table 2 Design-specific criteria to assess for risk of bias for benefits (45)

RISK OF BIAS	CRITERION	CCTs OR COHORT	CROSS-SECTIONAL
Selection bias	Were participants analysed within the groups they were originally assigned to?	x	
	Did the study apply inclusion/exclusion criteria uniformly to all comparison groups?	X	x
	Did strategy for recruiting participants into the study differ across study groups?	x	
	Does the design or analysis control account for important confounding and modifying variables through matching, stratification, multivariable analysis, or other approaches?	X	x
The bias In performance	the researchers rule out impact from intervention or unintended exposure which can give biased outcome?	X	x
	Has study maintain fidelity to the intervention protocol?	x	
Attrition bias	If attrition (overall or differential non-response, dropout, loss , or exclusion of participants) was a concern, were missing data handled appropriately (e.g., intention-to-treat analysis and imputation)?	X	x
Bias in detection	In prospective studies, was the length of follow-up different between the groups, or in case-control studies, was the time period between the intervention/exposure and outcome the same for cases and controls?	x	
	Were the outcome assessors blinded to the intervention or exposure status of participants?	x	x
	Were interventions/exposures assessed/defined using valid and reliable measures, implemented consistently across all study participants?	x	x
	Were outcomes assessed/defined using valid and reliable measures, implemented consistently across all study participants?	x	x
	Were confounding variables assessed using valid and reliable measures, implemented consistently across all study participants?	x	x
Reporting bias	Were the potential outcomes pre-specified by the researchers? Are all pre-specified outcomes reported?	x	x

QUANTITAVE RESEARCH BIAS ASSESMENT.

STUDY	Selection bias	Performance bias	Attrition bias	Detection bias	Reporting bias	comments

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