

Evaluation of Primary Versus Secondary Prevention of Cervical Cancer: an evidence
based literature review

Submitted by

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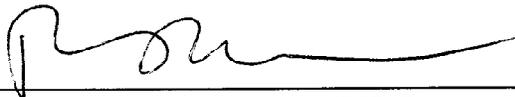
A project presented to the Department of
Physician Assistant of Wichita State University
in partial fulfillment of the
requirements for the degree
of Master of Physician Assistant

May, 2006

Wichita State University
College of Health Professions
Department of Physician Assistant

We hereby recommend that the research project prepared under our supervision by Jennifer L. Vestle entitled Evaluation of Primary Versus Secondary Prevention of Cervical Cancer: an evidence based literature review be accepted as partial fulfillment for the degree of Master of Physician Assistant.

Approved:



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5/8/06
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Abstract

Introduction: The Pap smear improves the probability of detecting cervical abnormalities, caused by Human Papillomavirus (HPV) at an early stage where HPV is more easily treated. Thus, the Pap smear is a valuable tool in the secondary prevention of cervical cancer. Cervical cancer is most commonly found in women who are middle-aged or elderly, low socio-economic status, and minorities. These women are less likely to attend Pap smear screening. Therefore, it is important to determine whether primary (i.e. condom use and awareness) or secondary prevention is more appropriate in reducing the morbidity and mortality of cervical cancer. Methodology: A systematic literature review was performed to assess the efficacy of primary and secondary prevention of cervical cancer. The articles reviewed included women of various age groups, their knowledge of cervical cancer, their attendance at Pap smear screening, risk factors for cervical cancer, and the value of Pap smears. Results: Pap smear screening was found to be an effective tool in decreasing the incidence of cervical cancer; however, to target women most at risk it is not as effective as primary prevention. In fact, several studies showed a majority of these high-risk women do not obtain Pap smears and are not aware of the link between HPV and cervical cancer. Furthermore, several studies also showed that condom use significantly reduces the contraction of sexually transmitted HPV, thus reducing the precursor to cervical cancer. Conclusion: In addition to promoting Pap smear screening, more consideration should be given toward education and condom use in the prevention of cervical cancer. Together these two prevention strategies can help reduce the morbidity and mortality of cervical cancer in women of all groups.

Table of Contents

LIST OF FIGURES.....	iv
ACKNOWLEDGEMENTS.....	v
CHAPTER	
I. INTRODUCTION.....	1
II. LITERATURE REVIEW.....	2
III. METHODOLOGY.....	5
IV. RESULTS.....	5
V. DISCUSSION	
Evidence in the literature.....	7
Weaknesses in the literature.....	12
Gaps in the literature.....	12
Validity of review.....	13
Weaknesses in the review.....	13
CONCLUSIONS.....	14
REFERENCES.....	18
APPENDICES	
A. Raw Data.....	20
B. Discarded articles.....	24
VITA.....	25

Figures

Figure

1.....6

Literature Review Flow Sheet

Figure

2.....7

Results

Acknowledgements

I would like to thank my family and friends for all of their support during my educational experience. Without their encouragement I could not have been where I am today. I would like to also thank Wichita State University PA Department and Dr. John Carter for all of their help throughout PA school and on my research project. Finally, I would like to dedicate this paper to my grandmother Edna Mercedes Jones as she is truly one of the most remarkable women I have ever or will ever meet.

Introduction

Despite the availability of screening tests and treatment, cervical cancer remains the third most common gynecological cancer in the United States¹. Nearly half of the 15,700 women who will be diagnosed with cervical cancer this year are diagnosed at a late stage, resulting in locally or regionally advanced disease that is more difficult to treat¹. However, with patient education, better screening procedures, and more advanced treatment options, the death rates from cervical cancer have been reduced dramatically since the early 1970s¹. The techniques listed above are important in detecting the disease in its earliest stages, but not all are implemented equally.

Cervical cancer begins as slightly abnormal squamous cellular changes, or dysplasia. If left untreated, these cells may progress to severe dysplasia, also known as high-grade squamous intraepithelial lesions, and then onto invasive carcinoma. Detecting cervical cancer while it is early invasive or pre-invasive significantly improves the probability of curing the disease. Once the cancer has spread to the lymphatic system or parametrial tissues adjacent to the cervix, successful treatment is less likely¹. The majority of these cervical cancers are squamous cell carcinomas, but the relative and absolute incidence of adenocarcinomas has recently been on the rise and now currently accounts for approximately 20 percent of invasive cervical cancers². The etiology of both histological types of cervical cancer is sexual exposure to the human papillomavirus (HPV)³.

HPV infection is widely known to be the most prevalent sexually transmitted disease in the United States, infecting approximately 5.5 million people annually⁴. The lifetime cumulative risk of contracting this virus is 80 percent⁵. Infection with high-risk

types of HPV are responsible for cervical cell changes and cancer. There are over 100 types of HPV that have been studied; however, the sexually transmitted types (HPV 16 and 18) are responsible for the majority of cervical cell infection by infecting the basal cells of the cervical epithelium⁴. The virus then can continue to replicate, if not removed by the immune system, and disrupt normal cellular function to cause dysplasia and later cervical cancer⁴.

The possibility of acquiring susceptibility factors can be decreased or even prevented, thus reducing or eliminating the risk of HPV infection. Decreasing these risk factors by condom use and awareness of the virus increases primary prevention of acquiring HPV, thereby reducing the morbidity and mortality of cervical cancer. However, primary prevention is not emphasized as a means of preventing cervical cancer. Obtaining the knowledge to protect oneself is difficult and the time and expertise of the health care provider may not be readily available. In addition, many women are not motivated to implement protection strategies. Primary prevention may be extremely beneficial when examining the United States female population in various subgroups such as socio-economic status, ethnicity, and age. These subgroups show higher morbidity and mortality associated with cervical cancer, mostly due to inequalities in the availability of Pap smears⁴.

Literature Review

Pap smears provide secondary prevention in the development of cervical cancer because they can detect cellular changes that lead to cervical abnormalities, while they are still easily treatable. These tests are associated with a reduction in morbidity and mortality from invasive cervical cancer and are 30-87% sensitive for dysplasia⁵. Another

test is also currently available that in addition to the Pap smear increases the probability of detecting abnormal cells before they progress into cancer⁷. This test checks for the presence of HPV DNA in the sample of cervical cells obtained. The Pap smear traditionally has been the preferred prevention strategy for cervical cancer by periodically screening women to identify abnormal cells and destroy them before they progress into invasive cancer⁸.

Several studies offer evidence to support Pap smear screening and reveal similar statistics that conclude screening provides a high degree of early detection and increased survival rates. Most clinicians rely solely on this type of prevention due to its effectiveness when able to be implemented yearly in women. Currently the American Cancer Society screening guidelines for cervical cancer suggest women begin to have annual Pap tests approximately three years after becoming sexually active or at age twenty-one¹. Screening should then be done annually thereafter until age 30 when a woman can be screened every two to three years if she has had three normal Pap smears, unless she has other risk factors such as immunosuppression or a previous history of cervical cancer¹. Older women and women that have had total hysterectomies with no history of cervical dysplasia may only require Pap smear screening every couple of years¹.

Cervical cancer is the only neoplastic disease capable of truly early detection. However, as mentioned above, several groups of women in the United States are repeatedly identified as not receiving routine or even any Pap smears. These specific identified groups remain grossly underscreened and consistently affected with the disease. These women, along with the rest of the United States population, are also

mostly unaware of the existence of HPV, how it is acquired, and its relationship to cervical cancer.

Several studies link HPV to cervical cancer and find common risk factors for acquiring HPV, which include acquired and genetic factors. The known susceptibility factors include age at first coitus, having multiple sexual partners, disregard for condom use, cigarette smoking, infection with other sexually transmitted diseases, and inheritance of mutations of chemical metabolizing genes and DNA repair⁶. The initiation and physiological processes involved in the development of cervical cancer are attributed to the interaction between acquired and genetic risk factors.

The Pap smear improves the probability of detecting cervical abnormalities while they are easily treatable and it is a valuable tool in the secondary prevention of cervical cancer. However, cervical cancer is most commonly found in middle-aged or elderly women, women of low socio-economic status, and ethnic women. These women are more likely to not attend Pap smear screening. Therefore, there is some discrepancy in whether primary (i.e. condom use and awareness) or secondary prevention is more appropriate in reducing the morbidity and mortality of cervical cancer. It is important to determine which method or technique is better in preventing the 4,900 avoidable deaths from cervical cancer in the United States each year⁶.

Purpose of the Study

The purpose of this study was to gather evidence regarding the prevention of cervical cancer. Investigation of evidence-based literature allows more insight towards a more effective prevention strategy for cervical cancer. The research question was stated

as: Is primary or secondary prevention better in decreasing the morbidity and mortality of cervical cancer in women of all groups in the United States?

Methodology

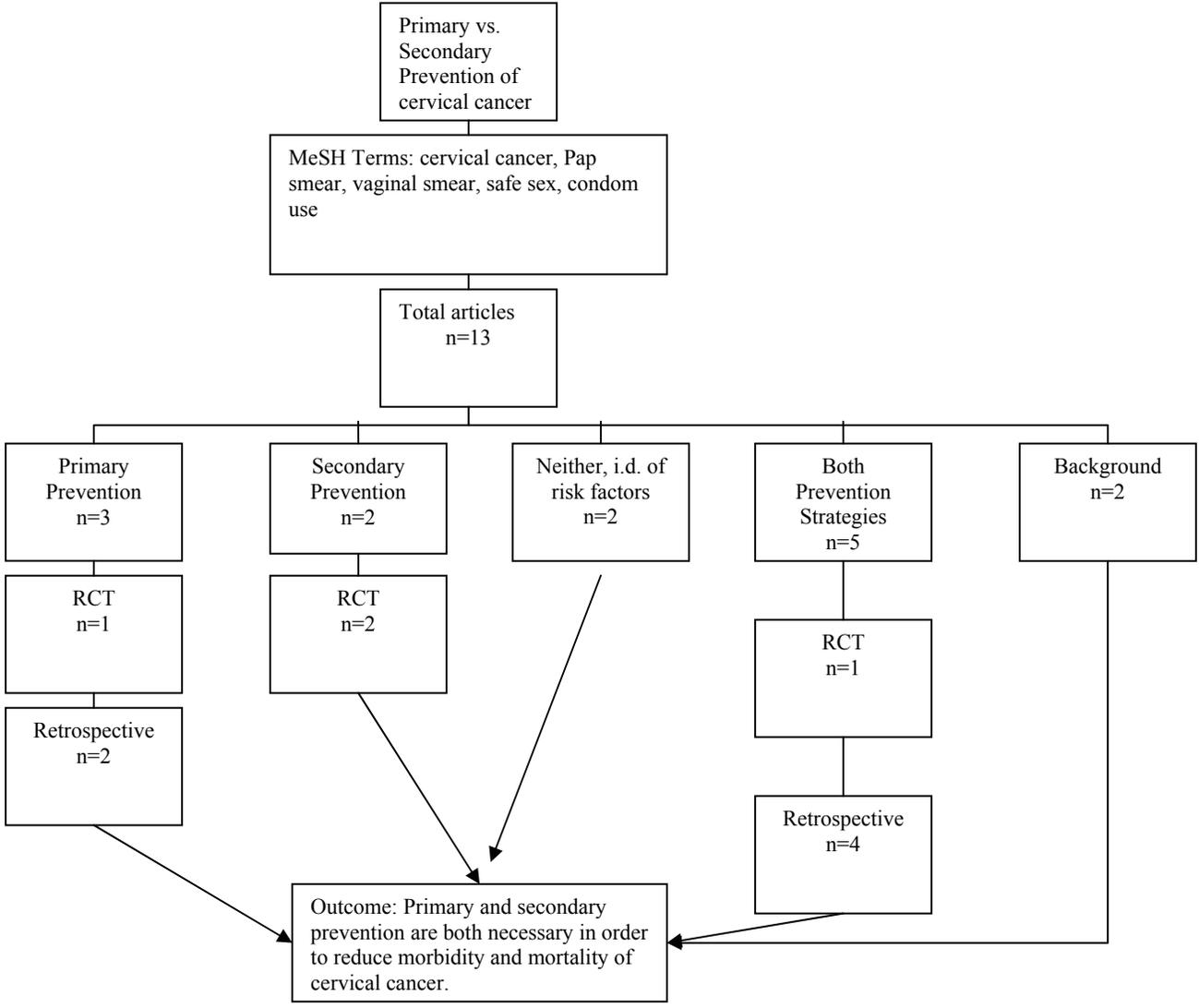
To assess the efficacy between primary and secondary prevention of cervical cancer, an evidence-based literature review was performed by using the Medline database from 1996 to the present date. The search was conducted using the key terms cervical cancer, Pap smear, vaginal smear, safe sex, condom use, and human papillomavirus. Articles were selected based on various criteria including articles that were peer-reviewed in reputable journals and articles with sufficient evidence to support the conclusion. Selected studies were randomized control studies and meta-analyses.

Results

From 1996 through 2005, thirteen articles met the inclusion criteria (Figure 1). Some of the articles addressed more than one outcome; therefore, there was some coinciding of information in the results section. Two of the articles contained background information regarding cervical cancer, such as information regarding the epidemiology, detection, risk factors, staging, guidelines, prevention, and recommendations^{1,7}.

Three studies addressed primary prevention of cervical cancer and found primary prevention to be more efficacious than secondary prevention in decreasing morbidity and mortality of cervical cancer^{7-8,12}. Two other articles touched on primary prevention; however, only identified risk factors for contracting HPV and did not conclude whether primary or secondary prevention is more efficacious.^{3,6}

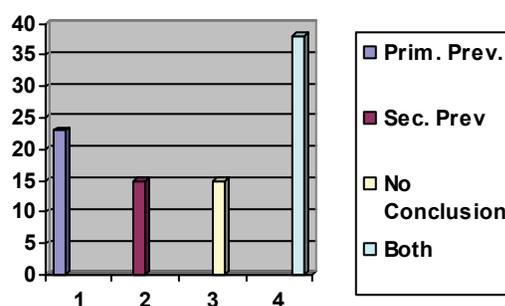
Figure 1: Literature Review Flow Sheet



Two articles were found that demonstrate Pap smears or secondary prevention as a more acceptable means to decrease the incidence of cervical cancer^{5,12}. Furthermore, five studies concluded that primary and secondary prevention are both necessary prevention strategies to target all women in order to decrease the precursors to the disease and later catch the disease at an early stage if the disease is contracted^{2,4,9-11}.

Overall, 23% of the articles found primary prevention to be better and 15% found secondary prevention to be better. Thirty-eight percent showed both prevention strategies to be better in decreasing the morbidity and mortality from cervical cancer. Fifteen percent of the articles were inconclusive (Figure 2).

Figure 2: Results (Percent)



Discussion

Evidence in the Literature

In the United States cervical cancer screening is provided to approximately 79% of the population, which has resulted in a very significant reduction in morbidity and mortality from invasive squamous cell carcinoma⁴⁻⁵. It has decreased death rates from cervical cancer significantly in the last 40 years⁹. With a sensitivity range of 30 to 87 percent for dysplasia and good specificity, the Pap smear can detect the disease process at an early stage when effective treatment options are still available⁵. Women diagnosed with cervical carcinoma in situ are 25 times less likely to die in the next four years than women diagnosed with invasive cervical cancer⁹. Pap smear screening is also very easily performed and relatively inexpensive.

It is predicted that 600,000 women in the United States are diagnosed with some type of cervical changes each year¹⁰. The National Breast and Cervical Cancer Early Detection Program identified 15,119 cervical intraepithelial neoplasias in 472,188 Pap tests, with an occurrence of 3.2 percent in the United States; age varied inversely with the rate of atypical Pap results¹⁰. Data is comparable in other countries that have implemented similar cervical cancer screening programs.

Studies in the Netherlands showed the number of women ages 35-54 diagnosed with invasive cervical cancer decreased from 18.6 per 100,000 women to 3.3 per 100,000 over a period of six years¹⁰. Also over a period of six years there was a 15 percent reduction in deaths from cervical cancer in England and Wales¹⁰. In British Columbia, data from 1955 to 1988 showed morbidity rates decreased from 28.4 to 4.2 per 100,000 and mortality rates from 11.4 to 2.3 per 100,000¹⁰. These data represent a reduction of 85 percent and 80 percent respectively¹⁰. Data are comparable in Iceland, Finland, and Sweden with reduction in mortality rates of 80 percent, 50 percent, and 34 percent respectively¹⁰. Over a twenty-year span between 1950 and 1970, the National Cancer Institute reported that morbidity and mortality of invasive cervical cancer had fallen by more than 70 percent and has continued to decline slowly since the early 1980s¹⁰.

One study which investigated the various roles of cervical cancer screening in women with cervical intraepithelial neoplasia 3 (CIN 3), among women previously diagnosed with mild to moderate dyskaryosis at six months, showed a calculated sensitivity and specificity of 97 percent and 65 percent respectively¹¹. The positive and negative predictive values were 4 percent and 99 percent respectively¹¹.

Another study revealed that 47% of invasive carcinoma from 1984-1987 and 1996 were not screened with Pap smears¹². Abnormal Pap tests were reported in 84% of these women, indicating that the prognosis of cervical cancer is encouraging when a patient has had the benefit of a Pap smear¹².

The addition of HPV screening to the Pap smear has further improved cervical cytology screening. Numerous epidemiological studies have recognized an established relationship between the presence of high risk HPV and cervical cancer¹¹. High risk HPV (types 16 and 18) are strongly associated with squamous cell carcinomas and adenocarcinomas respectively³. In one study of over 1000 cervical cancer specimens that screened for HPV DNA, researchers found that the prevalence of HPV DNA in cancers of the cervix was higher than 95%². For women that are greater than or equal to 30 years of age, HPV testing can decipher whether higher stages of CIN will be diagnosed in the next two years in women who had negative Pap smears⁵. The results of screening 11,085 women for CIN 2 showed HPV testing to have a higher sensitivity (97.1%) compared to (76.6%) for cytology and slightly less specificity (93.3%) than cytology (95.8%)⁵. As well as being more sensitive than just cytology alone, HPV testing can be reproduced exhibiting a 97% exact agreement⁵. The addition of HPV DNA testing, therefore, has medical significance for predicting the presence and the development of CIN 2/3+⁵.

Despite the availability of Pap smears and the dramatically reduced number of women developing cervical cancer, the death rate from cervical cancer in the United States is far higher than it should be. Over 90% of cervical cancer cases can be detected though Pap smear screening; however, Pap smears are not performed on one-third of women¹⁰. This fact accounts for cervical cancer remaining the second most common

female cancer and 15% of cancers worldwide¹⁰. Approximately 50% of women who are diagnosed with advanced cervical cancer have never had a Pap smear, and approximately 10% of these women have not had one in the previous five years before their diagnosis¹. Simply not attending Pap smear screening is a risk factor for developing invasive cervical cancer and increases a woman's risk by 3 to 10 times¹⁰.

There is a disproportional difference between ethnic, sub-economic groups, and age as a result of variable access to Pap smear screening and follow-up of pre-cancerous lesions⁸. Data from the United States show that 85 percent of women with greater than 13 years of education attained Pap smear screening in the last 3 years in comparison to the 69 percent of women with less than 12 years of education⁴. Another study indicates that never having had a Pap smear decreases with 47.5 percent of women with less than primary education to 14.4 percent of women with a college education⁴. Waller et. al also showed that women in older age groups that are already at an increased risk of cervical cancer did not attend screening as often as they should⁴. Suris et. al data further reveals that 12.5 percent of women ages 30 to 39 have never had a Pap smear compared to 63.6 percent of women ages 70 years and older¹⁰. Furthermore, Waller et. al showed a significant difference in cervical cancer screening among ethnic groups in the United States with 80 percent attendance in white and black groups and only 67% in Asian and Pacific Islander groups⁴.

Determining who is at risk for cervical cancer is just as important as determining what information women know regarding cervical cancer, including causes and prevention strategies. Several United States based studies looked at the public's awareness regarding HPV and its association with cervical cancer. One study identified

by Waller et. al demonstrated that 13% of sexually active college females were aware of HPV and less than 8% knew of an association between HPV and cervical cancer⁴. In addition, Williams et. al research questionnaire revealed approximately 47 percent of the female participants used a condom during their last intercourse experience and that concern regarding pregnancy was much higher than concern about HIV or STDs ($p < .02$)¹³. Seventy-five percent of the sample being studied reported that they were not concerned about contracting HIV/AIDS or other STDs together¹³. Throughout the study participants revealed a lack of condom use regardless of partner ($p = .28$) and concern regarding HIV/AIDS and other STDs ($p > .60$)¹³.

Further studies including Price et. al also demonstrate a similar lack of knowledge regarding risk factors for cervical cancer⁹. When 330 adult females were surveyed regarding their practices and perceptions on cervical cancer, the risk factors to be correctly identified by the women included early age at first intercourse, several male sexual partners, HPV infection, smoking, and having intercourse with men⁹. Only six percent of the women surveyed were able to correctly recognize all five risk factors⁹. Compared to other women their same age, only 10 percent thought themselves to be at increased risk for developing cervical cancer⁹. Even more disturbing was that only 52% of the women could identify one cervical cancer risk factor (multiple male sexual partners) and 20% could not even recognize one risk factor⁹. Price et. al concluded that this study may indicate that women believe that cervical cancer is a natural biological process of women and not one of any personal control⁹. Regardless of women's beliefs on the source of cervical cancer, most of them were able to identify that Pap smears are important and that the major obstacles to obtaining a Pap smear was the lack of health

insurance and being uncomfortable⁹. Seventeen percent of the women who did not receive regular Pap smear screening said that if their doctor informed them that they needed to be screened they would⁹.

Weaknesses in the Literature

One area of weakness in the literature is the type of population consistently chosen to study. In most studies, particularly the surveys to identify women's ignorance about the correlation between HPV and cervical cancer and the associated risk factors with contracting the virus, the population is mostly Caucasian college students. These women are at risk of contracting the disease; however, these are the majority of women receiving Pap smears. The women actually dying of the disease are older, non-Caucasian, and not attending college. More studies should be done to accurately reflect the knowledge of these women on HPV.

Another area of weakness in the literature is involving primary prevention strategies. Several studies identified a need to educate women regarding their sexual behaviors, the use of condoms, and the existence of HPV; however, none of the studies thoroughly explain how this should best be achieved. The studies fall short of actually demonstrating effective methods and schematic plans to accurately carry out a successful primary prevention campaign.

Gaps in the Literature

There are interesting areas of research involving primary prevention that are very limited. For example, there are very few studies that actually demonstrate primary prevention strategies and their effectiveness. It is assumed that condom use being a barrier form of contraception decreases HPV transmission and subsequently cervical

cancer because condom use has been shown to decrease transmission of other sexually transmitted diseases. However, there are no direct studies to verify this claim. Other areas that are lacking regarding primary prevention include a need for prospective studies to demonstrate that decreasing these risk factors truly does decrease HPV infection, instead of relying on retrospective studies which can be limited due to a person's inability to recall particular events many years ago.

Another area that deserves more research is causes for cervical cancer. Most research identifies the causal relationship between HPV and cervical cancer; however, there are very few cervical cancers that arise by a different carcinogenic route. More investigation needs to be conducted to identify the pathophysiology behind these types of cervical cancers.

Validity of the Review

Original articles for review were collected via Medline using the above mentioned key terms and were then selected through an organized method. Once articles were chosen they were checked carefully to certify that they met the inclusion criteria identified above in the methodology section. The data was then divided into appropriate categories and placed into Figure 1, which was then reviewed and assessed by the research advisor. There were seven discarded articles found during the article search; however, these did not meet inclusion criteria. Refer to appendix B for a complete listing of unused articles.

Weaknesses in the Review

All research involves some type of weaknesses, and this literature review was not an exception. Certain processes could have been done to make the results more valid.

For example, in this project the authors, journals, and funding institutions of the articles was all information available to the author and research advisor so that these types of information could potentially be seen as biased. Another example of weakness in the review is that the reader is presented the information concluded by the studies without knowing much else information regarding the study. They are unaware of the type of study and how the study was conducted.

Conclusions

Pap smear screening has proven to be an effective means of reducing the morbidity and mortality of cervical cancer. Due to its ability to identify precancerous lesions that need further treatment to prevent continued abnormal changes, the Pap smear can prevent practically all deaths from cervical cancer. As reported above, the implementation of nationwide screening programs has shown a significant reduction in cervical cancer development and death rates. With such an effective means of preventing cervical cancer, every woman should have regular Pap smears. According to the American Cancer Society, Pap smears should be performed every one to three years in women ages 18-40 and every year for women ages 40 and older¹⁰. Adolescents should begin screening when they become sexually active¹⁰.

The Pap smear can reduce morbidity and mortality from cervical cancer, although only if implemented continually and regularly. Screening women is a valuable tool in secondary prevention strategies; however, it is useless to women who do not have access to healthcare or are not aware of its importance. This results in many unfortunate missed opportunities to treat the disease in its earliest stages due to the women that are most at risk of not receiving the appropriate interventions.

To eliminate this disparity between women of various racial, class, and age groups, health care providers as well as other officials in society need to use alternative methods to ensure that women stop dying from this preventable disease. Primary prevention strategies need to be implemented more effectively to protect all women, regardless of who they are or where they live. These prevention strategies include education regarding the cause of cervical cancer of HPV. The majority of women in the United States are unaware of the association between HPV and cervical cancer. The women that are most aware of this association are most often white, educated, and in a higher socio-economic class. These women are also several times more likely to be attending regular Pap smear screening. With a better understanding of the link between cervical cancer and a sexually transmitted disease, these women may be more inclined to protect themselves during intercourse.

Other primary prevention strategies include focusing on other proven risk factors for cervical cancer. These include having intercourse at an early age as well as having multiple sexual partners throughout life. Educating adolescents on HPV before the onset of sexual activity may prevent some young females from engaging in risky behavior. Once adolescents have the necessary information to make educated decisions regarding their choices in sexual activity, they may choose abstinence or decrease the number of partners they have. However, focusing on knowledge as a prevention strategy proves difficult as many young women are already aware of risks of other STD's and pregnancy and choose to still engage in unprotected sex. Regardless of this dilemma, women of all ages should have information available so they can be careful when deciding who their sexual partners will be, who their sexual partners have had intercourse with, and how

many sexual partners they will have over life. Also, hopefully if any woman is uncertain about a particular sexual partner she will use a barrier method of contraception.

Primary prevention combined with secondary prevention can help decrease the number of women diagnosed with cervical cancer each year. Each method is important in order to target every woman in the United States and not just women that have access to health care or who receive Pap smears on a regular basis. Health care providers need to encourage their patients as well as relatives, friends, and colleagues to participate in regular Pap smears and to seek treatment upon receiving abnormal results. Also important is using local and state officials to develop better screening programs and public education programs to remind women, along with adolescents, about HPV and the risk factors associated with contracting the virus. Furthermore, these education programs can promote the use of a condom to prevent contracting the virus as well as demonstrate to them that cervical cancer can be treatable when cervical changes are discovered early.

The identification of the link between HPV and cervical cancer has resulted in more prevention strategies. The Pap smear allows for early recognition of abnormal cells for treatment and the use of HPV typing differentiates various abnormal cervical results from those that demand treatment to prevent progression to cervical cancer. Public education teaches that cervical cancer is initiated by a sexually transmitted disease and gives women an opportunity to make knowledgeable decisions concerning certain sexual activity choices. Knowledge of these primary and secondary prevention strategies can help protect all women from what is considered a preventable disease. Secondary prevention has proven to be an effective means of preventing cervical cancer and with increasing emphasis on primary prevention, whether through individual healthcare

providers or public awareness campaigns, women of certain subgroups that once experienced healthcare discrimination can increase their probability of protecting themselves against cervical cancer. Together these two prevention strategies can help reduce the morbidity and mortality of cervical cancer in women of all groups.

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Appendix A
Raw Data

Study year	Research Addresses 1.Prim. Prev 2.Sec. Prev 3.Both 4.Background	Level of Evidence 1.Random control 2.Retrospective 3.Background	Demographics Main Data	Findings	Supportive of Research 1.Yes, prim. prev. better 2.No, sec. prev. better 3.No conclusion, i.d. of risk factors 4.Both 5.Background
Williams, Bedor 2003	1.	2.	51, 18-31yo in psych courses @Northeast. St. Univ. ?'airres re: sex. Behavior and contraception	*<1/2 stud. using condoms *concern about STDs low, especially < pregnancy	1.
Bren 2004	4.	3.	N/A	Background: intro, risk factors, options, f/u recommendations	1., 5.
Suris 1999	3.	2.	N/A	Risk factors, prevention, detection, pap efficiency	4.
Shinn 2004	4.	3.	N/A	Background: epidemiology, detection, risk factors, staging, guidelines, prevention, recommendations	5.
Cothran, White 2001	1.	3.	N/A	Adolescents and STD exposure, knowledge regarding HPV, health care	1.

				providers and education regarding HPV	
Au 2004	1.	1.	83 cervical cancer pts. And 38 matched normal controls in Venezuela, 75pts and 76 matched normal controls in US	*Acquired and genetic susceptibility factors critical component for development of cervical cancer and different in 2 countries. *Precise susceptibility info on CC is useful for the development of efficient but different disease prevention programs	3.
Franco 1999	3.	2.	100,000 women infected with HPV and association with cervical cancer	*HPV is the primary cause of cervical cancer *Variability in HPV testing resulting in some false negative testing *Increase in risk factors associated with HPV led to increased risk of CC	4.
Altekruse, et.al 2002	1.	2.	124 women between the ages of 18 and 69 who had cervical carcinoma	*SCC and AC share HPV and sexual behavior as risk factors *SCC and AC however have different reproductive risk factors	3.
Waller, et. al 2004	3.	2.	N/A	*CC is associated with identifiable risk factors *Pap smears decrease the risk for CC *Most women diagnosed with CC not receiving paps *More education needed	4.

				towards id'd groups of women not receiving paps	
Nobbenhuis, et. al 1999	3.	1.	353 women with mild to moderate dyskaryosis. Cytology, colposcopy, and testing for HPV were monitored	*Persistent infection with high-risk HPV is necessary for development and maintenance of CIN 3 *Rigorous pap smear and HPV testing is necessary in order to diagnose dysplasia to treat in order to prevent CC *Women not receiving pap smear screening are at increased risk of cervical cancer if infected with HPV	4.
Price, et. al 1996	3.	2.	330 adult females perceptions and practices regarding cervical cancer	*94% of respondents were unable to correctly id all 5 risk factors associated with CC *20% were not able to id any of the 5 risk factors *pap smears cheap, effective, with reliable sensitivity and specificity	4.
ACOG 2005	1.	1.	11085 women, detection of CIN 2	*HPV testing 97.1% sensitive and 93.3% specific *Cytology 76.6% sensitive and 95.8% specific	2.
Holmquist 2000	2.	3.	1000 women, ages 18 and older	*Prognosis of CC favorable when pt. had benefit of Pap test *Women who never see gynecologist are found to	2.

				have a poor survival rate as a result of invasive CC	
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Appendix B
Discarded Articles

- 1.) Beral, V, Hermon, C, Kay C, Hannaford P, Darby S, Reeves G. Mortality associated with oral contraceptive use: 25 year follow up of cohort of 46,000 women from Royal College of General Practitioners' oral contraception study. *British Medical Journal*. 1999; 318(7176):96-100.
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