THE EFFECTIVENESS OF COMBINED ECTOCERVICAL SCRAPING AND ENDOCERVICAL ASPIRATION AS A SCREENING METHOD FOR CERVICAL AND ENDOMETRIAL CANCER IN WOMEN OVER FORTY YEARS OF AGE

by

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A Thesis

Presented to
The University of Oregon Health Sciences Center
School of Nursing
in partial fulfillment
of the requirements for the degree of
Master of Nursing

June 1981

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This study was supported by a traineeship from the United States Public Health Service Grant Number 5A11 NU00250-02.

Acknowledgements

I wish to express my appreciation to my thesis advisor, Dr. Charold Baer, for her support, advice and encouragement in carrying out this research. I would like to thank Dr. Mary Ann Curry and Ms. Katherine Crabtree for their support and editorial assistance.

I am grateful to the Research Department of Kaiser Foundation Hospitals for allowing me to conduct this study at their agency. I especially would like to thank Dr. B. Mengelberg, Ms. Shirley Marcy, Dr. Knox, Ms. Arlene Garrison and Ms. Donna Burnett for their assistance and participation in this study.

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CHAPTER I

Introduction

The purpose of this retrospective study was to evaluate the use of endocervical aspiration, in conjunction with ectocervical scraping, in the cytologic screening of women over forty years of age for cervical and endometrial carcinoma and their precursor lesions. This study examined whether combined ectocervical scraping and endocervical aspiration provided more precise data regarding the state of health/disease of the cervical and endometrial epithelium than that provided by the ectocervical scraping alone.

In recent years, there has been an increased emphasis on disease prevention and early recognition of asymptomatic disease (Frame & Carlson, 1975; Sackett, 1975; Whitby, 1974). Primary care providers consider prevention and early detection of disease one of their main obligations in health care delivery. Prevention and early detection are means of minimizing subsequent complications of a disease state. This may be accomplished through health maintenance exams which are designed to: 1) identify high risk individuals for a particular disease; and 2) screen for the presence of an asymptomatic disease state.

Screening, as defined by the Commission on Chronic Illnesses, is "the presumptive identification of unrecognized disease or defect by the application of tests, examinations or other procedures which can be applied rapidly" (Whitby, 1974, p. 819). The function of screening tests is not diagnostic, but only to differentiate those individuals that may have some disorder from those that don't, in order that more definitive diagnostic procedures can be undertaken.

Screening can be carried out on whole populations or major subgroups (mass screening), or it can be undertaken with selected subgroups of the population who have been identified as being at high risk for a disease process (selective screening). It can consist of an isolated procedure, such as a blood pressure measurement, tuberculin skin test, or Pap smear; or it may involve more comprehensive testing including multiphasic screening with a complete history and physical exam.

With the increased interest in screening, it is becoming apparent that many of the screening procedures and programs have not been properly validated or critically appraised (Frame & Carlson, 1975). To be worthwhile, a screening test must be able to separate normal from abnormal. In addition, it must be considered sensitive and specific for the disease under study (Whitby, 1974; Wilson & Cantab, 1963). Cochrane and Holland (1971) suggest that ethical, scientific and financial justification of the worth of screening tests be required before their adoption into medical practice. Also, there must be evidence that the screening can adequately detect disease or its precursors, and that subsequent treatment can alter the natural history of the disease. In addition, the incidence of the disease in the population must be such that the cost of screening is justified.

Wilson and Jungner (1968), in their review of screening practices, have advocated that individual screening programs be evaluated according to the following basic principles or criteria:

1. The condition sought should be an important health problem.
2. There should be an accepted treatment for patients with recognized disease.

3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case finding should be a continuing process and not a "once and for all" project. (p. 27).

This study dealt with screening for cervical and endometrial carcinoma. Uterine cancer is still a major problem throughout the world. It is becoming apparent that this is a changing disease. Over the past twenty years there has been a significant decrease in the incidence and mortality of cervical cancer. With this decrease, endometrial carcinoma is becoming the most common uterine neoplasm seen. Only recently has there been evidence that the incidence of endometrial carcinoma is rising. With the changing nature of this disease there is growing need for the improved detection of endometrial carcinoma and its precursor lesions.

According to the criteria established by Wilson and Jungner (1968), cervical and endometrial carcinoma would appear to be diseases for which screening is desirable: 1) they represent important health problems; 2) the natural history of these two cancers has been well studied; and 3) eradication of these carcinomas has been shown to influence survival rates.

The Papanicolaou smear, which has been so successful in detecting cervical cancer and its precursor lesions, may not be as useful for the detection of endometrial cancer. In addition, in women over forty years of age, the ectocervical scraping (the technique most widely used for obtaining the Pap smear) may not be as sensitive as desired for a screening test for cervical cancer in this age group. This is due to the endocervical location of the squamocolumnar junction in 80% of these women, thus making it difficult to obtain ectocervical and endocervical cells (Ostergard, 1977). In this population therefore, a more suitable cervical smear may be obtained by a combination of ectocervical scraping and endocervical aspiration.

Endometrial biopsy or cytology, done on an outpatient basis, is the most sensitive screening procedure for endometrial carcinoma now available. However, this screening procedure is considered unacceptable by many patients, costly, and too time consuming to be employed for widespread screening. Reagan and Ng (1973) have proposed that a sample obtained by aspirating the endocervical canal may serve as an alternative method for widespread screening for this carcinoma and its precursor lesions. Characteristic cellular changes, seen in endometrial cells when endometrial carcinoma and its precursors are present, are

noted to some extent in spontaneously desquamated endometrial cells found in endocervical aspirates. However, at the present time endocervical aspiration would not be considered a highly sensitive screening procedure for endometrial carcinoma.

In considering that women over forty years of age should be screened for cervical cancer and its precursor lesions by ectocervical scraping and endocervical aspiration, the opportunity exists for further evaluation of the endocervical aspirate as a screening tool for endometrial atypia in this age group. With continued research and education in the area of endometrial cytology, detection rates may improve for this cancer and its precursors. As nurses are involved with screening for these two diseases, they need to be aware of the most suitable procedure to employ to insure early detection of these diseases.

Statement of the Problem

Screening of the general population for the presence of asymptomatic disease is becoming an increasingly popular practice. However, many screening procedures and programs are introduced and accepted as 'routine practice' before their worth has been established. Ongoing evaluation of these practices is a responsibility of health care providers. Criteria have been established to assist health care providers to identify those disease states for which screening is worthwhile (Wilson & Jungner, 1968).

Women over forty years of age are at risk for developing cervical and endometrial carcinoma. However, the ectocervical scraping may not provide a suitable cervical smear to adequately screen this age group for cervical cancer and its precursors. In addition, cervical cytology (vaginal pool smears and ectocervical scrapings) has not been shown

to be an effective screening procedure for endometrial carcinoma and its precursors.

It has been proposed that the combined use of ectocervical scraping and endocervical aspiration may provide for a more complete cytologic evaluation of women over forty years of age for cervical and endometrial carcinoma and their precursors. Endocervical aspiration is a relatively simple procedure to perform, requiring the same expertise on the part of the practitioner as that required to obtain an ectocervical scraping. As the sample is comprised of spontaneously desquamated cells and the sampling method does not entail the forceful dislodgement of the tissue (as does a biopsy), patient discomfort is minimal. The laboratory cost of this cytology sample is comparable to that of an ectocervical scraping ($14.00 for each cytology specimen at the agency utilized in this study). This is the only additional expense incurred by including this procedure in the gynecologic exam. This additional health care cost is justified if the combined sampling technique permits earlier detection of the disease, thus decreasing treatment costs and minimizing subsequent complications of the disease state. However, before including an endocervical aspiration as a routine part of the cytologic examination in women over forty, its effectiveness as a screening method for detecting cervical and endometrial epithelial changes needs to be established.

Purpose of the Study

The purpose of this retrospective study was to evaluate the use of endocervical aspiration, in conjunction with ectocervical scraping, in the cytologic screening of women over forty years of age for cervical and endometrial carcinoma and their precursor lesions. This study

examined whether combined ectocervical scraping and endocervical aspiration provided more precise data regarding the state of health/disease of the cervical and endometrial epithelium than that provided by the ectocervical scraping alone.

Implications of the Study

Health care providers are directly involved with disease prevention and early detection of asymptomatic disease. Much of their practice deals with screening a healthy population that is at risk for a variety of disease states. As health care providers assume primary care roles, they must also assume some of the responsibility for ongoing evaluation and validation of screening procedures and programs in their practice.

The findings of this study will assist health care providers to determine whether the endocervical aspirate should be included in their screening procedure for cervical and endometrial cancer in women over forty years of age. Additionally, the results will indicate whether all women over forty will benefit from this procedure or whether this procedure is only feasible for women of selected age groups over forty.

If combined ectocervical scraping and endocervical aspiration is shown to provide more precise data regarding normal and abnormal changes in the cervical and endometrial epithelium, then it may also be a more complete procedure to employ in followup visits of women with known or treated atypia.

Review of the Literature

Cancer of the Cervix

Since the development of the Papanicolau Smear, in the 1940's, cancer of the uterine cervix has been one of the most widely screened

diseases in the United States and around the world. The use of cervical cytology has increased over the past twenty years, so that today the Pap smear is regarded as a routine screening procedure. With this widespread use, much data has been accumulated so that the natural history, risk factors, and incidence and mortality rates have been extensively studied. Knowledge of these factors is needed to evaluate whether cervical cancer screening programs are effective in preventing or detecting early disease and to identify the population at greatest risk.

Anatomy of the cervix. The cervix is the lower part of the uterus and it is divided from the corpus of the uterus by the internal os, which is a fibromuscular junction. The endocervical canal joins the uterine cavity with the vagina, beginning at the level of the internal os and extending to the vagina at the level of the external os. This canal is normally about three cm. long and seven mm. in width at its widest point (Jordan & Singer, 1976). (See Figure 1).

Histologically, the cervical epithelium consists of squamous and columnar epithelium joining together at the squamocolumnar junction. The location of the squamocolumnar junction is variable, assuming an ectocervical location in a large percentage of adolescents and an endocervical location in the perimenopausal and post menopausal female (Jordan & Singer, 1976; Kolstad & Stafl, 1972; Ostergard, 1977). This junction usually consists of an area of squamous metaplasia, termed the transformation zone, in which the columnar epithelial cells are gradually replaced by squamous cells. The changes in the position of the squamocolumnar junction may be dependent on humoral and local

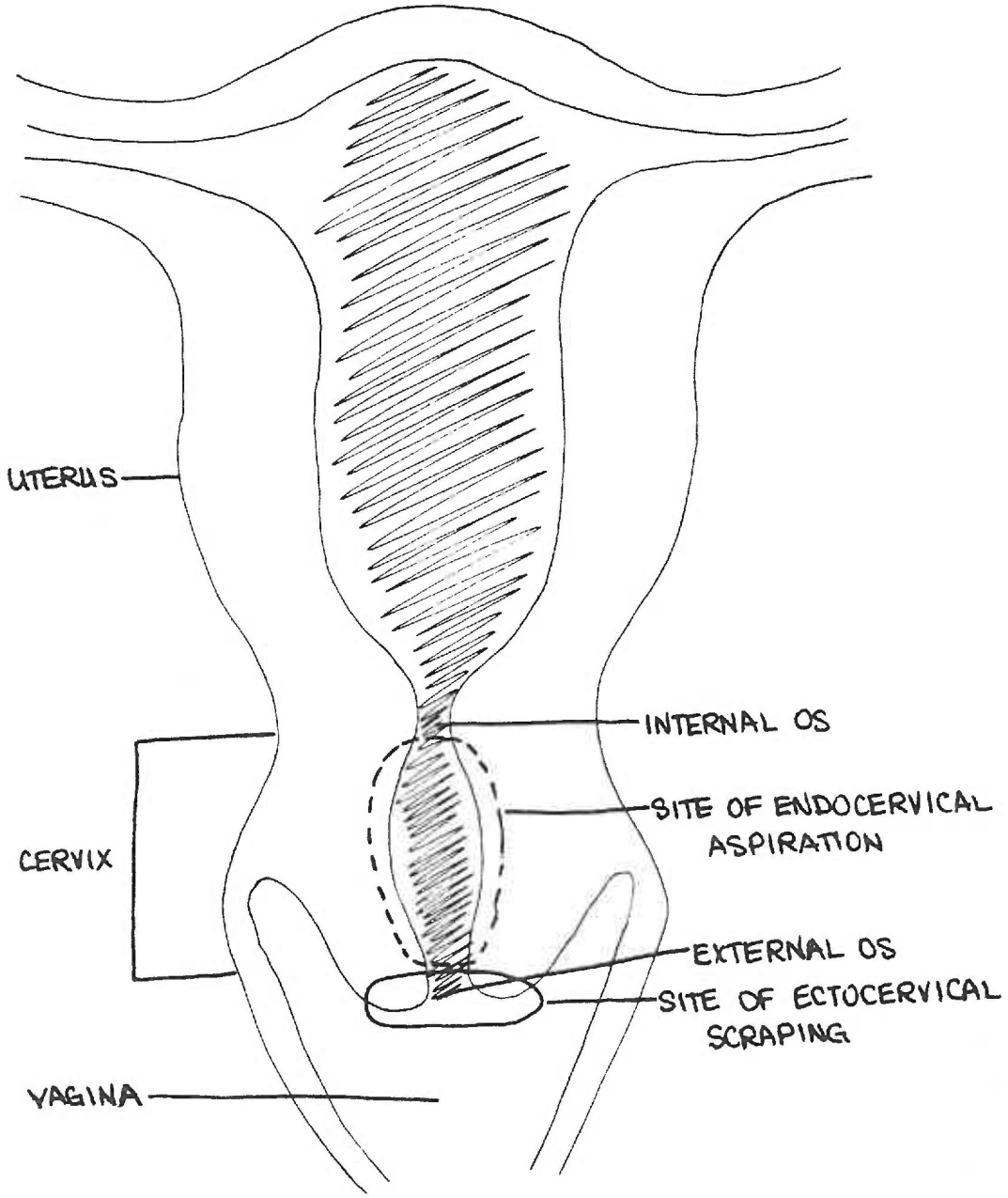

FIGURE 1: THE UTERUS

factors (Kolstad & Stafl, 1972). According to a study by Ostergard (1977), increasing age, gravidity, and parity are associated with endocervical squamocolumnar junctions, with age being the most powerful indicator of the location of the junction. He noted the junction in the endocervix in 80 percent of women over the age of forty.

Natural history of cervical cancer. The natural history of carcinoma of the cervix, from benign to malignant changes, has been well documented over the past years, due to the high incidence of neoplasia occurring at this site and the easy accessibility of the cervix for cytologic and histologic study. Ninety-five percent of cervical neoplasms are squamous cell carcinomas, with the remaining 5% being either adenocarcinomas or adenoacanthomas (mixed squamous and adeno patterns). Squamous cell carcinomas and adenoacanthomas begin at or near the squamocolumnar junction and adenocarcinomas arise in the endocervical glands (Robbins, 1974).

The current evidence suggests that there is a continuum of cellular changes seen in the cervical epithelium, ranging from normal epithelium to invasive carcinoma with dysplasia (mild to severe) and carcinoma in situ occurring between the two extremes (Guzick, 1978; Robbins, 1974; Task Force Report, 1976). Richart and Barron (1969), in a followup study of patients with cervical dysplasia (very mild to severe), observed a constant progression rate from one grade of dysplasia to a higher grade and they concluded that dysplasia is a significant lesion which will progress in a large majority of cases to carcinoma in situ (CIS). While there is agreement that the dysplasias and CIS represent precancerous lesions of the cervix, not all of these lesions become invasive cervical cancer (ICC). Some regress to normal while

others persist or are removed by the biopsies necessary for histological diagnosis. Guzick (1978) has recently reviewed the evidence concerning the relationship of CIS to ICC and has concluded that CIS does progress to ICC in fifty to seventy percent of the cases. In addition, it is rare to find a case of ICC that was not preceded by a CIS stage (Guzick, 1978; Robbins, 1974; Task Force Report, 1976).

Epidemiological studies concerning carcinoma of the cervix suggest that this disease is a slowly progressive one, with many years separating early dysplasia and ICC. In a prospective study by Richart and Barron (1969), the average progression time for all dysplasias to reach CIS was 44 months, with a range from 12 months to 86 months. Much of the information regarding the duration of CIS has been extrapolated from incidence data of CIS and ICC. The peak ages for CIS and ICC are ages 25-34 and 45-49 respectively. This indicates a 10 to 25 year course (Kim, Rigal, Patrick, Walters, Bennett, Nordin, Claybrook & Parekh, 1978; Task Force Report, 1976). Once invasive cervical carcinoma is present, the average time it takes to develop into a clinical lesion is five years (Kashgarian & Dunn, 1970).

Carcinoma of the cervix is categorized according to stages. These stages are determined by the extent of invasion into the surrounding environment. Following, are the stages as defined by and included in the International Classification of Carcinoma of the Cervix:

Stage 0 Carcinoma in situ, intraepithelial carcinoma

Stage I Carcinoma confined to the cervix

Stage Ia Microinvasive carcinoma (early stromal invasion)

Stage Ib All other cases of Stage I

Stage II The carcinoma extends beyond the cervix but has not extended to the pelvic wall. The carcinoma involves the vagina, but not the lower third of the vagina.

Stage III The carcinoma has extended to the pelvic wall. In rectal examination there is no cancer-free space between the tumor and the pelvic wall. The tumor involves the lower third of the vagina.

Stage IV The carcinoma has extended beyond the true pelvis or has clinically involved the mucosa of the bladder or rectum. This stage includes distant metastases (Nelson, Averette, Richart, 1975, p. 144).

Benefits from treatment. Knowing that most cases of cervical cancer develop from dysplasia and CIS, early detection and eradication of these lesions will help prevent the subsequent development of ICC. In those in whom ICC is detected, the stage at which the lesion is first discovered can influence the prognosis. This can be illustrated by the five year survival rates for the various stages. These survival rates are: Stage 0=100%; Stage I=80-90%; Stage II=75%; Stage III=55%; and Stage IV=10-15% (Robbins, 1974). Thus, detection and treatment of the early stages of ICC is important in maintaining survival.

Incidence and mortality. Over the past twenty years, the overall incidence of CIS and ICC combined has not significantly changed. However, over this same time period, there has been a progressive increase in the number of cases of CIS and a reciprocal decrease in the number of cases of ICC (40-60%). The overall incidence of ICC (calculated on females age 20 and older) has declined from 29.7-35/100,000 cases in the mid 1950's to 12.7-15.7/100,000 in the early 1970's, while the

incidence of CIS has increased from 7-19.5/100,000 cases to 35-45/100,000 in the same time period (Christopherson, Lundin, Mendez, & Parker, 1976; Kim, et al., 1978). As noted earlier, the peak ages for occurrence of these two lesions are different, with CIS occurring with greater frequency in those under the age of 40, and ICC having a higher incidence in women over 40.

Coinciding with the decrease in incidence, there has also been a decline in the mortality from cervical cancer, from 14/100,000 to 5-7/100,000 cases in the time period noted above (Christopherson, et al., 1976; Kim, et al., 1978). The greatest decrease in morbidity and mortality has been noted in women under the age of 50.

While declining incidence and mortality figures tend to support the widely held belief that screening for cervical cancer has been successful in identifying and treating this disease in its early stages (Christopherson, et al., 1976; Cramer, 1975; Kim, et al., 1978), it is difficult to validate because of other intervening variables that may have been operating in the long time period studied. However, in a review of studies evaluating the efficacy of cervical cancer screening programs, the view that cervical cytology is responsible for the decline is supported (Guzick, 1978). Guzick noted that incidence and mortality rates were lower among screened women than unscreened women, higher in geographic areas and occupational groups having less screening, and declining in many centers that had constant or increasing rates before screening was introduced.

Risk factors for cervical cancer. A number of studies have been done to identify risk factors for cervical cancer. These studies have resulted in the identification of a large number of highly correlated

variables that have been implicated in the etiology of this type of cancer. Rotkin (1973), in a comparison review of many of these studies, identified two factors that had a high correlation with the development of cervical cancer. Those factors were: 1) early onset of coitus (less than 20 years of age, but an even more significant factor if less than 17 years of age); and 2) sexual intercourse with an increased number of partners.

Currently, the research into a viral etiology of cervical cancer looks promising. The herpes simplex (type II) virus is being implicated as an initiating or promoting carcinogenic agent that can be transmitted during coitus (Jordan & Singer, 1976; Robbins, 1974; Rotkin, 1973). Whatever the carcinogenic agent may be, the likelihood of it being transmitted to a female would increase with multiple sexual partners. Also, the cervical epithelium of the adolescent is highly vulnerable to cell transformation and the chances of a carcinogenic agent initiating epithelial changes would be maximal at this time (Rotkin, 1973).

Cervical Cancer Detection

Before the introduction of the Pap smear in the 1940's, cervical cancer was detected by histological diagnosis in those women who had clinically evident carcinoma. With the use of cervical cytology, it is now possible to screen for precancerous lesions and pre-clinical carcinoma of the cervix and to obtain histological confirmation in atypical cases. Currently, the American Cancer Society recommends that asymptomatic females over the age of 20 and sexually active females under 20 have a Pap smear every three years after two initial annual Pap smears are negative (American Cancer Society Report, 1980).

The overall accuracy of cervical smears in detecting abnormalities of the cervix is influenced by several factors: the cellular specimen obtained; the preparation of the specimen for study; and the skill of the cytologist or cytopathologist in interpreting cervical cytology. Errors in any of these areas can result in a false negative Pap smear (Frost, 1969; Richart, 1964). Richart (1964) defines a false negative test as a "negative cytological examination of a patient with a known neoplasm or of a patient who is found to have a neoplasm within a short time after the smear is taken" (p. 723). Absolute rates for false negative results in cervical cytology are impossible to obtain, as it would entail obtaining histological confirmation of large numbers of negative cytology reports. Therefore, false negative rates are usually calculated by rescreening a group of women within a short time period, or by comparing the histologic diagnosis obtained at biopsy with the cytologic diagnosis in a population with known positive cytology (Berget, Olsen, & Poll, 1977; Luthy, Briggs, Buyco, & Schenbach, 1978; Richart, 1964; Richart & Vaillant, 1965; Sedlis, Walters, Balin, Hontz, & Sciuto, 1974).

The adequacy of the cellular specimen can influence the false negative rate. The cellular content of the smear varies according to the technique used to obtain it (Reagan & Lin, 1967). Therefore, the false negative rate is variable, depending on the technique employed. The methods used for obtaining a Pap smear include: vaginal pool aspiration or scrapings, ectocervical scrapings, endocervical sampling and vaginal irrigation (Frost, 1969). False negative rates for these techniques reported in the literature differ from study to study. Frost (1969), in reviewing rates for vaginal pool smears, found a

false negative rate between 6-42% for ICC and 12-69% for CIS. For the vaginal irrigation method, false negative rates are noted in 11-48% of cases, with this method being more sensitive for ICC than for dysplasia and CIS (Reagan & Lin, 1967). False negative rates for ectocervical scrapings have been reported between 4-35% (Berget, et al., 1977; Coppleson, 1960; Luthy, et al., 1978; Richart & Vaillant, 1965; Sedlis, et al., 1974), and for endocervical sampling, 0-18% (Frost, 1969; Richart & Vaillant, 1965). The ectocervical scraping is the technique most widely used (Garite & Feldman, 1978; Richart & Vaillant, 1965; Shingelton, Gore, Straughn, Austin, & Littleton, 1976).

Since one in eight cases of CIS and early cervical neoplasms may be confined to hidden areas of the endocervical canal, a suitable cervical smear should include both endocervical (columnar epithelial cells) and ectocervical (squamous epithelial cells) material (Bourne & Beilby, 1976; Frost, 1969; Gondos, Marshall, & Ostergard, 1972; Weid, 1955). Gondos, et al. (1972) conducted a study to determine the frequency of finding endocervical cells in smears obtained by scraping the external os. In their series of 1883 patients, 90.3% showed endocervical and/or metaplastic cells. However, when the results were further analyzed by age, they found that the frequency of finding endocervical cells in ectocervical smears decreased with advancing age. These results correspond to the variable anatomic location of the squamocolumnar junction in the cervix due to age, with the cells shifting upward into the endocervical canal with increasing age (Ostergard, 1977). In two additional studies of ectocervical scrapings, 25-69% of the smears were found to contain endocervical cells (Bounds, Grubb, Metaxas, & Vessey, 1976; Bourne & Beilby, 1976). The results

of these studies are summarized in Table 1.

Tovell, Banogan, and Nash (1976), in studying the site of lesions in 254 patients with cervical intraepithelial neoplasia (dysplasia and CIS) and microinvasive carcinoma, found 7.9% of the lesions confined to the endocervical canal. The mean age of the women with endocervical lesions was 46.9 years compared with 30.8 years for ectocervical lesions only, and 35.3 years for ectocervical and lower canal lesions. Twenty-four percent of the women in this study over the age of 40 were found to have lesions limited to the endocervical canal.

Several studies have demonstrated the superiority of combined ectocervical and endocervical sampling techniques in the early detection of cervical cancer, and in reducing the false negative rate of cervical cytology from 1-11 percent (Frost, 1969; Garite & Feldman, 1978; Reagan & Lin, 1967; Richart, 1964; Richart & Vaillant, 1965). Reagan and Lin (1967) reported that with combined sampling, they were able to detect cellular abnormalities in 99.2% of 131 samples, and in 93.1% of the samples the cellular interpretation correlated with the histopathologic diagnosis. In the study by Richart and Vaillant (1965) on combined ectocervix and endocervix sampling, false negative rates were reduced from 17% to 2% for cervical dysplasia and from 4% to zero for CIS and ICC, when compared with any single technique.

Contrary to this view of the superiority of the combined sampling, Shingleton, et al. (1975) reported that the endocervical smear detected a lesion missed by the ectocervical smear in only 2.9% of the patients. However, the mean age of the population under study was 29.1 years, with only 14% over 45 years of age, and as shown by Tovell, et al. (1976)

Table 1

Frequency of Finding Endocervical Cells
in Ectocervical Scraping Smears

Year	Study	(age of subject)	N	Endocervical Cells Present
1972	Gondos, et al.	Below 45	1753	92.5%
		45-54	70	64%
		55-64	39	62%
		65 and over	21	52%
1976	Bourne & Beilby	Armovical Spatula		
		Below 24	3706	40%
		25 and over	2965	37%
		Ayre Spatula		
		Below 24	2443	25%
		25 and over	2206	25%
1976	Bounds, Grugg, Metaxas & Vessey	Armovical Spatula		
		All ages	491	69%
		Ayre Spatula		
		All ages	491	42.2%

Note: Type of spatula used to obtain the ectocervical scraping specimen can influence the adequacy of the specimen.

lesions in this age groups are usually limited to the ectocervix.

Endocervical sampling can be obtained by endocervical aspiration or endocervical swab, both techniques containing naturally exfoliated cells and cells that have been dislodged by the instrument. Shingelton, et al. (1975), in a comparative study of the two techniques, found that endocervical aspiration smears and endocervical swab smears were almost identical in their ability to detect atypical epithelium of the endocervix. However, the number of unsatisfactory smears was 3.5% with the swab technique as compared to .4% with the endocervical aspiration smears. This may be explained by the fact that dry cotton swabs were used in this study and these instruments have been shown to trap a large number of cells (Rubio, 1977).

For cervical cytology to be a valid screening tool, it must be sensitive and specific in its ability to detect abnormalities of the cervical epithelium. As false negative rates are higher for earlier lesions (Garite & Feldman, 1978), the technique chosen for screening this disease must be one that has been shown to have the lowest false negative rate to insure detection of precancerous and early cancerous lesions of the uterine cervix.

Endometrial Carcinoma

With the decreasing incidence of cervical cancer, endometrial carcinoma is recognized as the most common uterine neoplasm, especially in women over fifty years of age (Cramer & Cutler, 1974). Cervical cytology, which has contributed to a reduction in morbidity and mortality for cervical cancer, has had little effect on endometrial carcinoma. If an attempt is to be made to decrease the incidence of

endometrial carcinoma, screening techniques other than the Pap smear must be used and evaluated.

Anatomy of the uterus. The uterus is composed of three separate layers: 1) the serosa or outer peritoneal covering; 2) the myometrium, three layers of smooth muscle fibers; and 3) the endometrium or mucous membrane lining the cavity. The endometrium is made up of tubular glands lined by simple columnar epithelium which extend the full thickness of the mucosa, connective tissue stroma, and microvasculature (Kistner, 1979).

The ovarian hormones, estrogen and progesterone, are responsible for the cyclic structural modifications that the endometrium undergoes (menstrual cycle). The menstrual cycle consists of three phases: menstrual phase (day 1-4); proliferative phase (day 5-14); and the secretory phase (day 15-28). During the menstrual phase, the endometrium undergoes involution and the functional layer (compact and spongy layer) becomes necrotic and desquamation of this layer occurs. After the menstrual phase, cellular proliferation takes over, with reconstruction of the endometrial glands and epithelial lining. This occurs under the influence of estrogen. The secretory phase begins after ovulation and is dependent on estrogen and progesterone. During this phase, with glandular secretion, the endometrium reaches its average maximum thickness of 5 mm. (Junqueira, Carneiro, & Contopoulos, 1977).

Normally, endometrial cells resulting from physiological shedding are noted in cytology smears obtained during the first half of the menstrual cycle. The presence of endometrial cells in the second half of the cycle or at any time in the postmenopausal period can result from abnormal endometrial desquamation (Ng, Reagan, & Cechner, 1973; Reagan &

Ng, 1973).

Natural history of endometrial carcinoma. Endometrial carcinoma is the general term for carcinomas arising from the endometrial lining of the uterus. There are three major types of endometrial carcinoma: adenocarcinoma; adenocanthoma (benign appearing squamous portion and a malignant appearing glandular portion); and mixed adenosquamous (malignant appearing squamous and glandular components). Endometrial adenocarcinoma is the most common lesion, seen in 85% of the cases (Robbins, 1974).

As with cervical epithelium, there are progressive cellular changes seen in the endometrium of the uterus, ranging from normal epithelium and stroma to endometrial carcinoma. Endometrial hyperplasias and adenocarcinoma in situ occur between these two extremes. Endometrial hyperplasia is a broad term encompassing cystic hyperplasia, adenomatous hyperplasia and atypical adenomatous hyperplasia.

Retrospective studies, consisting of review of prior biopsies of known cases of endometrial carcinomas, have led investigators to believe that adenomatous hyperplasia, atypical adenomatous hyperplasia and adenocarcinoma in situ (CIS) represent precursors of endometrial carcinoma. Atypical adenomatous hyperplasia and CIS represent more severe atypia than does adenomatous hyperplasia (Foster & Montgomery, 1965; Gore & Hertig, 1966; Ng, et al., 1973; Reagan & Ng, 1973; Sherman, 1978; Wentz, 1974). These atypical lesions have been found to occur in 69-100% of biopsies obtained months or years prior to the development of the cancer (Foster & Montgomery, 1966; Gore & Hertig, 1966; Sherman, 1978).

Prospective studies on the relationship of endometrial hyperplasia to endometrial carcinoma have also provided evidence that precursor lesions do exist. Sherman (1978) followed 204 women with adenomatous hyperplasia (106), atypical adenomatous hyperplasia (91), and CIS (6) for two to fifteen years without treatment. Thirty-eight percent of the women developed endometrial carcinoma, 42% had persistent hyperplasia and only 20% of the lesions reverted to a benign state. It is significant that the more advanced the lesion, the greater the tendency to advance to carcinoma. In a similar study by Wentz (1974), 115 patients with persistant, untreated atypia were followed for two to eight years with the following results: 26.7% of those with adenomatous hyperplasia, 81.8% with atypical hyperplasia and 100% of the patients with CIS progressed to invasive adenocarcinoma during this time frame.

The duration of the precursor lesions of endometrial carcinoma has not been well-documented. In the prospective studies cited, these lesions were present from two to fifteen years after initial identification until carcinoma was diagnosed. Foster and Montgomery (1965), reporting on a study by Gusberg, noted an average duration for adenomatous hyperplasia of 5.7 years before cancer was diagnosed. Data from the Third National Cancer Survey (1969-70) lists the mean age of women with invasive endometrial cancer as 60.2 years compared with 53.3 years for women with CIS (Cramer & Cutler, 1974). Thus, an average duration of seven years for a CIS lesion of the endometrium could be inferred.

Endometrial carcinoma is categorized according to stages. The following are the stages as classified by the Federation of Gynaecology

and Obstetrics Cancer Committee (1971):

Stage 0 Carcinoma in situ

Stage 1 Carcinoma confined to the corpus

Stage 1a The length of the uterine cavity is 8 cm or less

Stage 1b The length of the uterine cavity is greater than 8 cm

Stage II The carcinoma involves the corpus and the cervix

Stage III The carcinoma had extended outside the uterus but not outside the true pelvis

Stage IV The carcinoma has extended outside the true pelvis or has obviously involved the mucosa of the bladder or rectum. (Malkasian, 1978, p. 997).

Benefits from treatment. As with cervical cancer, early detection and eradication of the precursor and in situ lesions of endometrial carcinoma will help prevent the subsequent development of this cancer. Five and ten year survival rates vary according to the stage of the carcinoma when initially diagnosed. Refer to the display below.

	Five-Year Survival	Ten-Year Survival
Stage 0	100%	
Stage Ia	83%	72%
Stage Ib	79%	73%
Stage II	75%	58%
Stage III	59%	52%
Stage IV	13%	9% (Malkasian, 1978)

Endometrial carcinoma is a disease for which early detection and treatment can affect the outcome and increase the chances for survival.

Incidence and mortality. The reported incidence of endometrial carcinoma indicated little change in regional and national surveys conducted up to 1970 (Cramer & Cutler, 1974; Cramer, Cutler, & Christine, 1974). However, recent reports indicate that the incidence has increased significantly since 1970. Although actual rates vary from region to region, the overall trend is upward with incidence rates increasing from 16-28/100,000 women in 1970 to 18.2-40/3.100,000 women (age 20 or older) in 1975 (Kim, et al., 1978; Marrett, Elwood, Meig, & Flannery, 1978; Weiss, Szekely, & Austin, 1976). This change was most apparent in the 50-75 year age group, the population most at risk for this disease.

Mortality rates for endometrial carcinoma have changed little over the years. Kim, et al. (1978) report that the death rate has remained constant over the last two decades at 12-13/100,000 women. Marrett, et al. (1978) have noted a slight decline in the death rate in their population (mean of all ages over 20), from 4.6/100,000 to 4.0/100,000.

There are several theories being offered to explain the recent increase in incidence rates. These include: the increasing number of older females in the population who are more susceptible to this form of cancer, detection of lesions at earlier stages of development, more precise histological criteria, and the increasing use of exogenous estrogens since 1970 (Kim, et al., 1978; Marrett, et al., 1978; Weiss, et al., 1976).

Risk factors for endometrial carcinoma. Knowledge of risk factors for endometrial carcinoma is important in order to identify the population

that will benefit most from screening programs for this disease. Several risk factors for this type of cancer have been documented. They include: age, obesity, nulliparity, early menarche, late menopause, diabetes, hypertension and exogenous estrogen administration (Antunes, Stolley, Roshenshein, Davies, Tonascia, Brown, Burnett, Rutledge, Pokempner, & Carcia, 1979; Elwood, Cole, Rothman, & Kaplan, 1977; Gusberg, 1976; Kjellgren, 1977; MacMahon, 1974).

As noted by incidence data, most cases of endometrial cancer occur in women over the age of 50 and predominately in the 50-70 year age group. Obese females also have an increased risk, probably due to an increased conversion rate of adrenal androstenedione to estrone by adipose tissue (Elwood, et al., 1977; Gusberg, 1976). A history of being 21-50 pounds overweight at age 25-29 is associated with a three-fold greater risk of developing endometrial cancer, while those more than 50 pounds overweight have a ten-fold greater risk (MacMahon, 1974). The rates for nulliparous females are twice as high as for females with one child, and three times as high as those with five children. Additionally, early menarche (before age 12) is associated with a 1.6 times greater risk (Elwood, et al., 1977) and menopause after the age of 52 carries a 2.4 times greater risk when compared with women whose menopause occurred before age 49 (MacMahon, 1974). Diabetic females are found to have a reported risk of 2.4 to 2.8 times that of non-diabetic females while a history of hypertension increases the risk of developing endometrial cancer by 1.5 times (Elwood, et al., 1977; MacMahon, 1974).

Currently, the most controversial and widely studied risk factor for developing endometrial carcinoma is exogenous estrogen administration.

The controversy centers around the methodology employed in various studies reporting that women treated with exogenous estrogen are four to eight times more likely to develop endometrial carcinoma than other women (Berger & Fowler, 1977). However, a recent study which addressed the criticisms of previous studies also found a correlation between exogenous estrogen administration and endometrial carcinoma (Antunes, et al., 1979). These latter findings suggest that the overall risk of endometrial carcinoma is six-fold for estrogen users when compared to non users. Long term users (greater than 5 years) had a fifteen-fold increase in risk.

Endometrial Cancer Detection

With the increasing frequency of endometrial carcinoma, there is a growing need for improved detection of this cancer and its precursor lesions. Only by detecting and eradicating the precursors can the frequency of endometrial carcinoma be reduced. The optimal screening procedure then, would be one which would identify the precursors in addition to the obvious cancers.

Outpatient endometrial biopsy, obtained by several different techniques, is regarded as the most sensitive screening procedure now available (Cohen & Gusberg, 1975; Ng, 1974; Reagan & Ng, 1973). However, universal screening with endometrial biopsy is not advocated for several reasons. These include: 1) the time, expertise and cost involved in obtaining and processing the endometrial tissue; 2) lack of acceptance by the patient to have this procedure done on a routine basis, due to discomfort; and 3) the presence of cervical stenosis in a large number of women in the age group at risk, thus preventing

the passage of the instrument into the endometrial cavity (Ng, 1974; Pomerance & Hall, 1978). Additionally, with the introduction of the biopsy instrument into the uterine cavity there is risk of uterine perforation, bleeding, and infection. However, for women with multiple risk factors for developing endometrial cancer, periodic screening by endometrial biopsy is advocated (Burk, Lehman, & Wolf, 1974; Cohen & Gusberg, 1975; Jafari, 1978).

Cervical cytology, so effective in detecting cervical cancer and its precursors, is not equally effective in detecting endometrial carcinoma and its precursors. Studies on the accuracy of vaginal pool smears, once considered adequate for the detection of endometrial carcinoma, have reported wide ranges of accuracy. False negative rates reported in the literature vary between 28-53% (Cohen & Gusberg, 1975; Jafari, 1978; Vuopala, 1977; Ng, 1974). The vaginal fornix is not considered a suitable environment for preservation of spontaneously desquamated cells from the endometrium, with the number of cells being limited in quantity and often deteriorated (Reagan & Ng, 1973). Ecto-cervical scraping, the most widely used technique for obtaining a Pap smear, has a false negative rate between 30-45% (Jafari, 1978; Joelsson, 1977; Ng, 1974; Reagan & Ng, 1973).

Only recently have criteria been established to identify the characteristic cellular changes seen in endometrial hyperplasias and CIS of the endometrium, the precursor lesions of endometrial carcinoma (Reagan & Ng, 1973). In the past, tissue for histologic study was needed to establish the presence of endometrial hyperplasias and CIS (Jafari, 1978). While cytologic samples taken directly from the

endometrium would provide an optimum cellular sample, this technique is too time consuming to be considered as a widespread screening procedure. Reagan and Ng (1973) propose that a sample obtained by aspirating the endocervical canal may be an alternative screening method for determining endometrial atypia, especially in view of its occasional use for detecting cervical cancer.

This sample is easily obtained, relatively inexpensive, and usually provides an adequate number of preserved, spontaneously desquamated endometrial cells satisfactory for detection of endometrial carcinoma and its precursors. The cervical mucous provides a more favorable environment than does the vaginal fornix and it also acts as a trap for these endometrial cells. As the severity of the endometrial lesions increases, the number of abnormal cells found per slide also increases. This is due to the decreased matual adhesiveness exhibited by cancer cells when compared with normal cells (Ng et al., 1973; Robbins, 1974).

In their study of 163 women with confirmed precursors of endometrial carcinoma, Reagan and Ng (1973) were able to detect an abnormality in 117 (71.8%) of the cases by endocervical aspiration. The accuracy with this technique increased as the severity of the lesions progressed, with 80% of those with CIS of the endometrium detected by endocervical aspiration. The overall false negative rate in this study was 28%.

In a separate study dealing with the identification of endometrial carcinoma by endocervical aspiration, these same investigators found differing accuracy rates for the variants of endometrial cancer; 75.5% of the adenocarcinomas (N=208), 76% of the adenoacanthomas,

(N=75), and 92.5% (N=40) of the mixed adenosquamous cancers of the endometrium were identified by endocervical aspiration.

False negative rates reported in the literature for detection of endometrial carcinomas vary between 23-28% (Vuopala, 1977; Reagan & Ng, 1973). These rates are comparable to those reported by Reagan and Ng (1973).

As stated previously, the value of the endocervical aspirate lies in its ability to provide a sample containing an adequate number of preserved, abnormal endometrial cells for cytologic study. The presence of these abnormal cells is highly suggestive of an endometrial lesion. However, the presence of normal appearing endometrial cells can also be suggestive of endometrial atypia if they are found in samples obtained during the second half of the menstrual cycle or in the postmenopausal period. At these times physiological shedding should not occur (Ng et al., 1974). Ng et al. (1974) conducted a study to evaluate endometrial changes (by histological techniques) in 696 women found to have this abnormal desquamation of normal appearing endometrial cells in endocervical aspirations. Their results are illustrated in Table 2. Thus, the presence of these cells appears to be highly significant. It is also noted that the frequency of finding endometrial cancer and its precursor lesions in these cases increased with age.

There remains a wide margin of error in the detection of endometrial carcinoma and its precursors by endocervical aspiration. The ability to detect cellular changes in the endometrial cells requires great expertise on the part of cytologists and cytopathologists. At the present level of sophistication, endocervical aspiration would not be considered a highly sensitive screening procedure. However, as

Table 2

Endometrial Changes in Women with Abnormal Desquamation of Normal Appearing Endometrial Cells in Endocervical Aspiration Smear (Ng et al., 1974)

Age	N	Histological Diagnosis		
		Normal Endometrium	Endometrial Hyperplasia	Endometrial Adenocarcinoma
20-39	195	99%	1%	0%
40-49	237	90.7%	7.2%	2.1%
50-59	188	84.6%	11.2%	4.2%
60 and over	76	68.4%	18.4%	13.2%

endometrial cytology is a relatively new field, it is Ng's (1974) opinion that detection rates can improve with continued research and education in this area.

Conceptual Framework

One role of the primary care practitioner (nurses and physicians) is to screen for the presence of asymptomatic disease in a population at risk for a particular disease. The primary care practitioner must have a clear understanding of the factors that can influence the effectiveness of any screening program. These include: 1) the significance of the disease as a health problem; 2) the natural history of the disease; 3) accepted treatment for the disease screened; 4) risk factors for the disease; 5) accuracy of the screening test; 6) acceptability of the screening test to the population screened; 7) cost of the screening; and 8) ongoing evaluation of the screening procedure or program. These factors should be considered when screening programs and practices are established and/or evaluated.

This study dealt with health screening, specifically, the screening for cervical and endometrial cancer and their precursor lesions, by primary care practitioners. Cervical and endometrial cancer are diseases for which screening would be desirable because of the following: 1) they represent important health problems; 2) the natural history of these two cancers has been well studied; 3) treatment has been shown to influence survival rates; and 4) risk factors for the two cancers have been documented. Women over forty years of age are still at risk for developing cervical cancer and nearing the age when they are at risk for developing endometrial cancer. Therefore, this age group may benefit from screening for both of these cancers. Figure 2 presents a Health Screening Model demonstrating the role of health

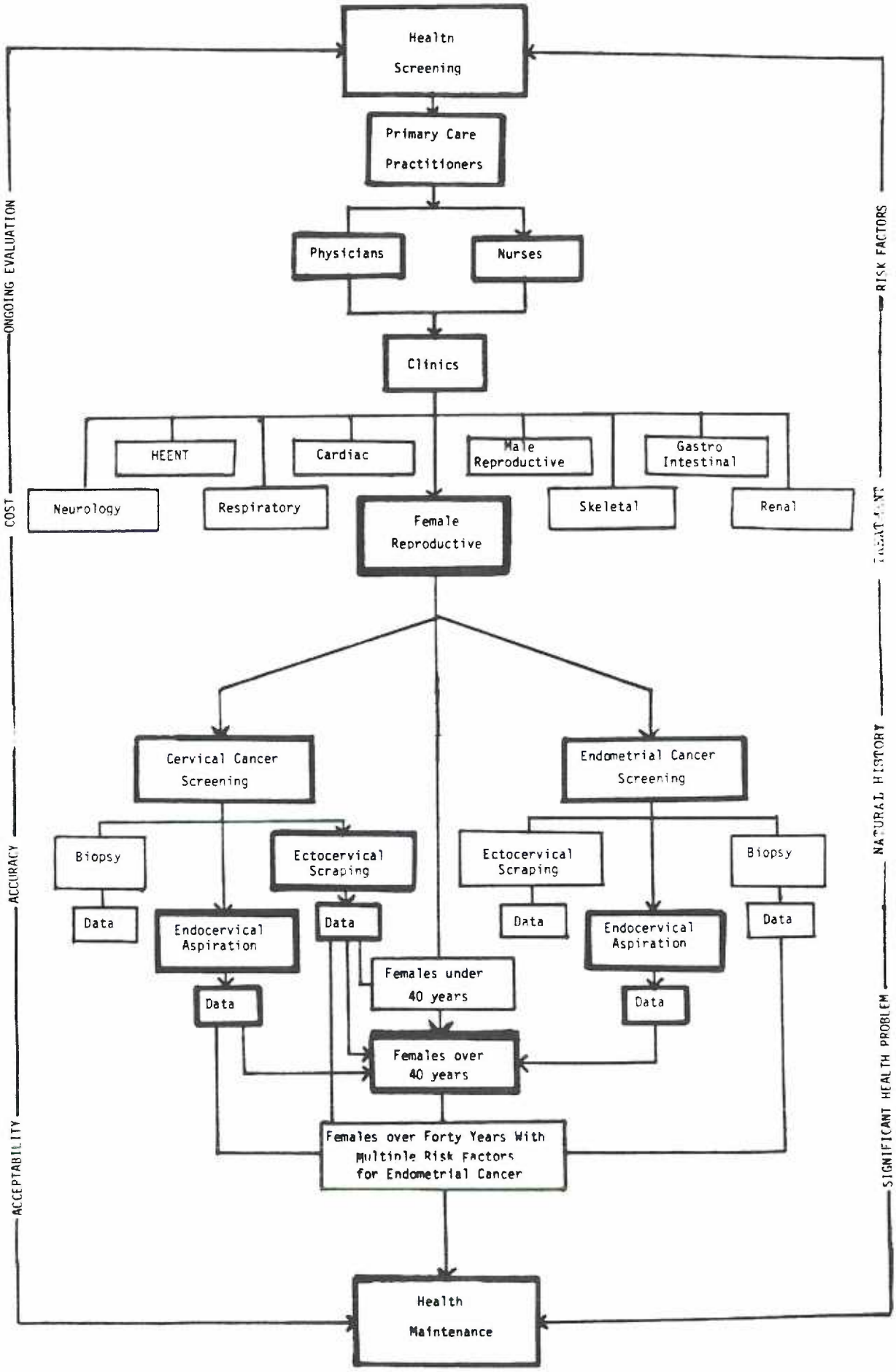

Figure 2: Health Screening Model

screening in providing health maintenance. Screening for cervical and endometrial cancer in women over forty years of age is highlighted in this model.

Primary care practitioners need to be aware of the most suitable procedure to employ for widespread screening of women in this age group for these two cancers. The most suitable screening test should be one that: can be applied rapidly at relatively low cost; is acceptable to the population; and will provide adequate and accurate information regarding the state of health/disease of the cervical and endometrial epithelium.

As depicted in the Health Screening Model, the ectocervical scraping alone may not provide a suitable cellular specimen to adequately screen women over forty for cervical cancer. Women in this age group may best be screened for this cancer by combined ectocervical scraping and endocervical aspiration because of the endocervical location of the squamocolumnar junction in 80% of women over forty and the high incidence of endocervical lesions in women over forty who have cervical cancer.

Additionally, endocervical aspiration may yield a suitable cellular specimen to screen for endometrial cancer in women over forty. Ideally, screening for this cancer should be done by direct endometrial sampling, but this procedure is not considered acceptable for widespread screening and is reserved for women with multiple risk factors for developing endometrial cancer.

As endocervical aspiration is a relatively simple procedure to perform, causing no increase in discomfort to the patient or significant increase in time to collect the specimen, it may be a highly

acceptable procedure to the population screened. The cost of including endocervical aspiration in the screening procedure would be increased because of the additional laboratory fee for processing and interpreting the specimen. Therefore, an evaluation of the effectiveness of the combined sampling procedure is needed to decide if the additional health care cost is justified.

Thus, given the significance of these two diseases as health problems, knowledge of their natural histories, identification of risk factors for their development, knowledge of benefit from treatment, and accuracy and acceptability of screening methods at relatively low cost, it may be feasible to screen for both cervical and endometrial cancer in women over forty years of age by combined ectocervical scraping and endocervical aspiration. However, the effectiveness of the combined sampling procedure should be evaluated to determine if the additional health care cost is justified.

Hypotheses

Therefore, given that combined ectocervical scraping and endocervical aspiration may be the most suitable procedure for screening for cervical and endocervical cancer in women over forty years of age, and that the adequacy of the endocervical aspiration smear may be influenced by the age of the woman, the following hypotheses have been generated.

Hypothesis 1. The combined use of an ectocervical scraping and an endocervical aspiration, as the screening method for cervical and endometrial carcinoma and their precursor lesions in women over forty years of age, will provide more precise data regarding the state of

health/disease of the cervical and endometrial epithelium than that provided by the ectocervical scraping alone.

Hypothesis 2. The adequacy of the cellular specimen obtained by endocervical aspiration is not influenced by the age of the subject.

Operational Definitions

Ectocervical scraping: Specimen obtained by scraping the squamocolumnar junction area in entirety (360°). If this junction is not visualized, it is standard procedure to then scrape the area around the external os.

Endocervical aspiration: Specimen obtained from the endocervical canal by placing a disposable plastic suction cannula into the cervical canal and aspirating the contents with a 10cc syringe.

More precise data: The numerical rating assigned to the combined ectocervical scraping and endocervical aspiration specimen will be greater than the numerical rating of the ectocervical scraping alone. This numerical rating will be obtained by application of the Cytology Conversion Scale (Appendix C).

Adequate cellular specimen: A specimen obtained by endocervical aspiration is considered adequate if endocervical cells are present in the specimen.

Atypia's reported on cytology report

Metaplasia: Reversible change from one adult cell type to another permitted adult cell type. A permitted cell type is a benign cell type which represents a physiologic response to an injurious agent (Robbins, 1974).

Dysplasia: Atypical proliferation and growth of cells, usually epithelial cells, in response to chronic irritation or inflammation (Robbins, 1974).

Endometrial hyperplasia: "Abnormal endometrial proliferation which results in both an increase in the number of glands and atypical patterns of gland growth" (Robbins, 1974, p. 1230).

Carcinoma in situ: Cancers that are confined to their original location and which have not invaded the basement membrane into surrounding tissues.

CHAPTER II

Methodology

Setting

This study was conducted at a Health Maintenance Organization (HMO) located in the Portland-Vancouver-Salem area. The OB-GYN department of this HMO served as the setting for the study. This particular setting was chosen because a small number of the OB-GYN practitioners routinely obtain an endocervical aspiration, in addition to an ectocervical scraping, for their cytologic screening of women over forty years of age.

This agency provides comprehensive health care services for approximately 250,000 plan members and it operates eleven outpatient clinics in these areas. Four of the outpatient clinics offer gynecological services to female health plan members. Within these four clinics, there are 26 OB-GYN practitioners (physicians and nurse practitioners) who screen their patients for cervical and endometrial atypia.

The patients receiving care in the OB-GYN department have either personally chosen their practitioner; been assigned to a practitioner by an appointment clerk, or been referred by another practitioner within the health plan. Routinely, patients visiting an OB-GYN physician are experiencing a gynecologic problem, while those visiting an OB-GYN nurse practitioner are usually healthy females seeking preventative health care services.

Sample

The sample for this study was a convenience sample of 139 subjects.

All subjects had an ectocervical scraping and an endocervical aspiration performed by either one of two OB-GYN physicians or an OB-GYN nurse practitioner employed by the agency. These three practitioners have routinely used these two cytologic screening procedures on patients who are forty years of age and older. All three practitioners have been using these techniques for at least three years. The number of practitioners collecting the specimens may be considered a limitation of this study, due to possible individual variation in collecting and processing the cellular specimens. However, utilizing three practitioners provided a larger sample which may be more representative of women receiving these preventative health care services.

The following criteria were used to select subjects for the sample.

1. The subjects were women forty years of age or older.
2. Only women with intact uteri were included. This excluded only women who had had a hysterectomy. It did not exclude women who had undergone various surgical procedures involving the uterus, such as: cryosurgery, D&C, cervical conization, etc.
3. The subject had an ectocervical scraping and an endocervical aspiration obtained at the same visit. (See Appendix A for protocol for obtaining specimens).
4. Specimens were obtained between March 1, 1979 and March 1, 1980.

This setting did not provide a sample that was representative of all the female health plan members over forty years of age. Many of

the subjects included presented to the OB-GYN clinic because of a gynecologic problem. However, as each subject was compared only with herself to test the first hypothesis, it was felt that the subject selection process used did not influence these results. A one calendar year for subject inclusion was considered an adequate time frame in which to provide a representative sample of patients visiting the health care practitioners.

Design and Procedure

This was a retrospective study which was approved by the Committees for the Protection of Human Subjects at the study agency and at the University of Oregon Health Sciences Center School of Nursing. The data analyzed were drawn from cytology reports of the ectocervical scraping and the endocervical aspiration obtained from each of the subjects between March 1, 1979 and March 1, 1980. The results of the ectocervical scraping and the endocervical aspiration were reported on separate cytology slips. (Appendix B, Cytology Report). This investigator had no knowledge of the identification of the subjects. That portion of the cytology report identifying the subject's name and chart number was deleted prior to the investigator receiving the data. The ectocervical scraping report and the endocervical aspiration report for each individual subject were attached to each other and identified as subject number 1, subject number 2, etc.

Independent variables

1. Type of procedure employed to screen for cervical and endometrial carcinoma and their precursor lesions in women over forty years of age.

a. Ectocervical Scraping

b. Combined Ectocervical Scraping and Endocervical Aspiration

2. Age of the subject

Dependent variables

1. The amount of data obtained regarding the state health/disease of the cervical and endometrial epithelium by each of the procedures.
2. The ability of the endocervical aspirate to provide an adequate cellular specimen of the endocervical epithelium, i.e., provide endocervical cells for interpretation.

Hypothesis 1. To determine whether combined ectocervical scraping and endocervical aspiration provided more precise data than did the ectocervical scraping alone, the cytology reports for each procedure, on each subject, were studied. The data reported by each type of procedure was assigned a numerical rating which reflected the amount of data reported by each procedure. This rating was obtained by use of the Cytology Conversion Scale (Appendix C).

The Cytology Conversion Scale was designed to convert the nominal scale data presented on the cytology report to ordinal scale data, by the assignment of a numerical rating. The use of this scale assumed an underlying continuum of reported changes in the cervical and endometrial epithelium, from normal to malignant, with the assigned rating increasing as the severity of the atypia increased. Data from specimens reported as inadequate were considered at the beginning of this continuum.

When specimens were reported as inconclusive, there was usually a question as to the severity of the atypia. Therefore, in any cases that fell into this category, the less severe interpretation was considered in assigning the rating. Additionally, the rating reflected the extent of follow-up and/or treatment that was suggested by the cellular interpretation. For example, in the atypia benign category there were two ratings. The interpretations assigned a rating of three (3) usually required a repeat cytology exam in six to twelve months, while those assigned a rating of four (4) usually required a repeat cytology exam in three months or biopsy of the tissue for histologic confirmation.

The presence of normal endocervical cells and the presence of normal endometrial cells during the first part of the cycle was also included in this scale as this provided information regarding the state of health of the epithelium. Additionally, a suitable cervical smear should include endocervical cells.

The cellular specimens obtained by ectocervical scraping and endocervical aspiration from a subject were interpreted by the same cytologist. Therefore, a difference in the interpretation of cellular changes in the two specimens was less likely to occur due to observer bias. The following is a discussion of how the Cytology Conversion Scale was used to assign a numerical rating to the interpretation presented by each type of procedure. A typical report may contain the following data.

Ectocervical Scraping	Endocervical Aspiration
Atypia benign	Atypia benign
mild dysplasia	mild dysplasia
	Endocervical cells present

In the example above the ectocervical scraping reported mild dysplasia, which is classified as an atypia benign change. No other data was reported. Using the Cytology Conversion Scale, the rating that was assigned to this interpretation is four (4). The subject's endocervical aspiration also showed mild dysplasia. In addition, this specimen also contained endocervical cells, which the ectocervical scraping did not show. Therefore, the interpretation reported by combined ectocervical scraping and endocervical aspiration was mild dysplasia with endocervical cells present. Using the Cytology Conversion Scale the rating that was assigned to this interpretation is six (6), four points for reporting mild dysplasia plus two points for endocervical cells being present.

Hypothesis 2. Cervical stenosis can make direct endometrial sampling difficult in post menopausal women, thus, it was felt that it may also be difficult to obtain adequate cellular material with endocervical aspiration in this age group. To determine whether age was a determinant of the ability of the endocervical aspirate to provide an adequate cellular specimen, the subjects were arbitrarily divided into the following age groups: 40-49; 50-59, and 60 and over. The presence of endocervical cells in the endocervical aspirate was used as the criterion for an adequate specimen.

Data Analysis

To test the hypothesis that the combined sampling procedure provides more precise data than does the ectocervical scraping alone, the Wilcoxon matched-pairs signed ranks test was used. The rating assigned to each procedure, for all subjects, provided the data for this analysis.

This test is a nonparametric test, designed for use with repeated measures on the same individuals, utilizing ordinal scale data. It is considered one of the most powerful statistical tests in this category (Downie & Starry, 1977). The alpha level chosen for this analysis was .01.

A 2X3 contingency table using the Chi Square statistic was used to determine if there was a significant difference in the adequacy of the cellular specimen by age group, at an alpha level of .05.

CHAPTER III

Results

This study was designed to describe the effectiveness of combined ectocervical scraping and endocervical aspiration as a screening method for cervical and endometrial cancer in women over forty years of age. The analysis of data includes a description of the sample, a descriptive analysis of the smear results and the findings related to the hypotheses under investigation.

Analysis of Data

Description of the Sample

The sample was comprised of 139 subjects. It was a convenience sample in that it included all patients who fit the criteria for subject selection and who had an ectocervical scraping and an endocervical aspiration performed between March 1, 1979 and March 1, 1980 by one of three practitioners. Sixty of the subjects were seen by two physicians while 79 subjects were screened by one nurse practitioner.

All data used in the following analyses were obtained from cytology reports that were stored by each of the three practitioners during the study period of March 1, 1979 to March 1, 1980. The cytology reports, with the subject's name and chart number deleted, were provided to this investigator by the three practitioners after approval was obtained from the study agency's Committee for the Protection of Human Subjects.

Subjects ranged in age from 40-76 years. Fifty-one percent (N=71) of the subjects were in the 40-49 year age range, thirty-eight

percent (N=53) were in the 50-59 year age range, and eleven percent (N=15) were 60 years of age and older.

Information on gravidity was obtained from 133 subjects. Nine percent (N=12) of these subjects had never been pregnant, thirty percent (N=40) had had one or two pregnancies, forty percent (N=53) had had three or four pregnancies, and twenty-one (N=28) of these subjects had been pregnant five times or more.

Fifty-two percent (N=73) of the subjects were premenopausal, 43% (N=59) were post-menopausal and no information regarding menopausal status was provided for 5% (N=7). Table 3 presents a distribution of the subjects by their menopausal status.

Table 3

Frequency Distribution of Subjects by Menopausal Status

	Post Menopausal Years			
Premenopausal	1-4	5-9	10 or more	No Data Available
N=73 (52%)	N=19 (14%)	N=21 (15%)	N=19 (14%)	N=7 (5%)

Only four subjects were noted to be on any form of hormone therapy. The hormone therapy for those subjects is summarized in Table 4.

Table 4

Distribution of Subjects by Hormone Therapy

Subject number (N=4)	Medication	Dosage	Frequency
7	Topical estrogen	not available	not available
24	Estrogen Provera	.625 mgm 10 mgm	day 1-21 day 20-25
36	Diethyl-stilbesterol	not available	not available
56	Estrogen	.625 mgm	not available

Presence of Endocervical Cells in Ectocervical Scraping, Endocervical Aspiration and Combined Sampling Smears

All subjects had an ectocervical scraping and an endocervical aspiration performed during the same visit. Of the 139 ectocervical scraping smears obtained, 46% (N=64) had endocervical cells present. Endocervical cells were present in 76% (N=106) of the 139 endocervical aspiration smears. When both ectocervical and endocervical smears were considered together as a combined sampling smear, 83% (N=115) of the smears were found to contain endocervical cells. Seventeen percent (N=24) of the subjects had no endocervical cells present on either the ectocervical scraping or the endocervical aspiration smear. Six percent (N=9) had endocervical cells present on the ectocervical scraping smear only. Table 5 summarizes this information. The combined sampling procedure did significantly increase the yield of smears containing endocervical cells.

Table 5

Presence of Endocervical Cells in Ectocervical Scraping, Endocervical Aspiration and Combined Sampling Smears

Endocervical Cells	Ectocervical Scraping	Endocervical Aspiration	Combined Sampling
Present	N=64 (46%)	N=106 (76%)	N=115 (83%)
Absent	N=75 (54%)	N=33 (24%)	N=24 (17%)

Presence of Endocervical Cells in Smears in Relation to Age, Gravidity, and Post Menopausal Status

The presence or absence of endocervical cells in the ectocervical scraping smear, endocervical aspiration smear, and the combined sampling smear was further analyzed by the age, gravidity, and post menopausal status of the subject. Tables 6, 7, and 8 present this information.

As indicated by the data presented in the tables, the combined sampling technique does increase the overall yield of smears having endocervical cells when compared with ectocervical scraping smears. This increase does not appear to be significantly affected by the age, gravidity, or post menopausal status of the subjects.

The gravidity of the subjects does appear to influence the presence of endocervical cells in the three types of smears. Those subjects who had never been pregnant had a lower percentage of smears that contained endocervical cells than subjects who had had one or more pregnancies.

Table 6

Presence of Endocervical Cells in Ectocervical Scraping, Endocervical Aspiration, and Combined Sampling Smears in Relation to Age of the Subject

Type of Smear	Endocervical Cells	Age		
		40-49	50-59	60 and over
Ectocervical Scraping Smear	Present	N=34 (48%)	N=25 (47%)	N=4 (37%)
	Absent	N=37 (52%)	N=28 (53%)	N=11 (73%)
Endocervical Aspiration Smear	Present	N=57 (80%)	N=42 (80%)	N=10 (67%)
	Absent	N=14 (20%)	N=11 (20%)	N=5 (33%)
Combined Sampling Smear	Present	N=61 (86%)	N=45 (85%)	N=11 (73%)
	Absent	N=10 (14%)	N=8 (15%)	N=4 (27%)

Table 7

Presence of Endocervical Cells in Ectocervical Scraping Endocervical Aspiration, and Combined Sampling Smears in Relation to Gravidity of the Subject

Type of Smear	Endocervical Cells	Gravidity			
		0	1-2	3-4	5 or more
Ectocervical Scraping Smear	Present	N=3 (25%)	N=17 (42%)	N=24 (45%)	N=15 (53%)
	Absent	N=9 (75%)	N=23 (58%)	N=29 (55%)	N=13 (47%)
Endocervical Aspiration Smear	Present	N=6 (50%)	N=34 (85%)	N=42 (80%)	N=22 (79%)
	Absent	N=6 (50%)	N=6 (15%)	N=11 (20%)	N=6 (21%)
Combined Sampling Smear	Present	N=6 (50%)	N=34 (85%)	N=46 (87%)	N=26 (93%)
	Absent	N=6 (50%)	N=6 (15%)	N=7 (13%)	N=2 (7%)

Table 8

Presence of Endocervical Cells in Ectocervical Scraping, Endocervical Aspiration, and Combined Sampling Smears in Relation to Post Menopausal Status of the Subjects

Type of Smear	Endocervical Cells	Post-Menopausal Years		
		1-4	5-9	10 or more
Ectocervical Scraping Smear	Present	N=8 (42%)	N=9 (43%)	N=5 (26%)
	Absent	N=11 (58%)	N=12 (57%)	N=14 (74%)
Endocervical Aspiration Smear	Present	N=16 (84%)	N=17 (81%)	N=11 (58%)
	Absent	N=3 (16%)	N=4 (19%)	N=8 (42%)
Combined Sampling Smear	Present	N=16 (84%)	N=17 (81%)	N=12 (63%)
	Absent	N=3 (16%)	N=4 (19%)	N=7 (37%)

As post menopausal years increased, there was a decrease in the number of smears that yielded endocervical cells. However, this decrease was not significant at the .05 level when this data was analyzed by use of the Chi Square statistic.

Presence of Endometrial Cells in Smears

Endometrial cells were present in nine of the 139 combined smears taken. As depicted in Table 9, the endometrial cells were always present in the ectocervical scraping smear of these subjects, but were found in only four of the endocervical aspirates of these nine subjects.

Seven of the nine smears contained normal endometrial cells, present in smears taken before day 12 of the menstrual cycle. Subject number 24 had normal endometrial cells present in both smears in the post menopausal period. The ectocervical scraping smear of subject number 77 contained atypical endometrial cells on day 39 of her menstrual cycle, while her endocervical aspiration smear did not contain endometrial cells.

Additionally, there were five subjects who had smears taken before day 12 of their menstrual cycle and neither smear contained endometrial cells. These data appear in Table 10. Normally the time period before day 12 of the menstrual cycle is when physiological shedding occurs and thus endometrial cells could be expected to be seen in the cytology smears.

Table 9

Presence of Endometrial Cells in Ectocervical Scraping and Endocervical Aspiration Smears

Subject number (N=9)	Age	Ectocervical Scraping Smear	Endocervical Aspiration Smear
12	42	Normal endometrial cells present-day 5 of menstrual cycle	Inadequate smear
21	41	Normal endometrial cells present-day 5 of menstrual cycle	No endometrial cells present
24	51	Endometrial cells present-5 years post menopausal	Endometrial cells present-5 years post menopausal
43	43	Normal endometrial cells present-day 2 of menstrual cycle	Normal endometrial cells present-day 2 of menstrual cycle
70	45	Normal endometrial cells present-day 4 of menstrual cycle	Normal endometrial cells present-day 4 of menstrual cycle
77	46	Atypical endometrial cells present-day 39 of menstrual cycle	No endometrial cells present
128	40	Normal endometrial cells present-day 10 of menstrual cycle	No endometrial cells present
132	43	Normal endometrial cells present-day 8 of menstrual cycle	No endometrial cells present
139	45	Normal endometrial cells present-day 2 of menstrual cycle	Normal endometrial cells present-day 2 of menstrual cycle

Table 10

Cytology Smears Obtained During Period of Physiological Shedding That Did Not Contain Endometrial Cells

Subject Number (N=5)	Age	Day of Menstrual Cycle Smears were Obtained
31	47	Day 5
46	42	Day 10
62	40	Day 11
99	43	Day 11
118	45	Day 11

Cytologic Interpretation by Age Group

Table 11 contains the cytologic interpretation, of cervical epithelial changes, reported by combined sampling according to the age of the subjects. Fifty-two percent of the smears obtained from subjects in the 40-49 year age group, 68% from the 50-59 years age group, and 80% from the subjects 60 years of age and older were negative. Twenty-four percent of the smears from both the 40-49 year age group and the 50-59 year age group reported reactive endocervical cells, while 13% of the smears obtained from subjects 60 years of age and older showed these changes. Only 8% of the subjects from the 50-59 year age group and 7% of the 60 and over year age group displayed active metaplastic cells, while 31% of the smears of 40-49 year old subjects had these changes present. Three of the smears obtained from subjects in the 40-49 year age group, and two smears from the 50-59 year age group

Table 11

Cytologic Interpretation of Combined Sampling Smears by Age

Age	Cytologic Interpretation					
		Reactive Endocervical	Active	Dysplasia		
	Negative	Cells	Metaplasia	Mild	Mod.	Severe
40-49 (N=71)	N=37 (52%)	N=17 (24%)	N=22[a] (31%)	N=1 (1.4%)	N=1[b] (1.4%)	N=1 (1.4%)
50-59[c] (N=50)	N=34 (68%)	N=12 (24%)	N=4[d] (8%)	N=2 (4%)		
60+ (N=15)	N=12 80%	N=2 (13%)	N=1 (7%)			

a. Category includes 8 subjects also included in reactive endocervical cells category

b. This subject also included in reactive endocervical cells category

c. Three subjects from this age group not included in this analysis due to lack of data on the cytology report

d. Category includes 2 subjects also included in reactive endocervical cells category

showed dysplasic changes. No smears taken from subjects 60 years and older displayed these changes.

Inadequate Smears

There were 278 cytologic smears taken from the 139 subjects in this study. Eight smears were reported as providing inadequate cellular material for cytologic interpretation. All eight smears were endocervical aspiration smears. Two of the inadequate smears were taken from women in the 40-49 year age group, four from the 50-59 year age group, and two from women 60 years of age and older. Six of the eight subjects with inadequate endocervical aspirations were post menopausal, while two of the subjects were premenopausal. There was no significant difference in the percentage of inadequate smears performed by each of the three practitioners.

Findings Related to the First Hypothesis

The first hypothesis, which states that the combined use of an ectocervical scraping and an endocervical aspiration, as the screening method for cervical and endometrial carcinoma and their precursor lesions in women over forty years of age, will provide more precise data regarding the state of health/disease of the cervical and endometrial epithelium than that provided by the ectocervical scraping alone, was supported by the findings of this study. This hypothesis was tested in the following manner. The ectocervical scraping and the combined ectocervical scraping and endocervical aspiration smear interpretation, for each subject, were assigned a rating by application of the Cytology Conversion Scale (Appendix C) to the data reported by each procedure. The Wilcoxon matched-pairs signed ranks test was used to determine

if there was a significant difference in the ratings assigned to the two procedures. Refer to Appendix D for presentation of the data used for this analysis. The z statistic of -6.62 obtained was significant at the .01 level.

Much of the difference between the two procedures was due to the ability of the endocervical aspiration to provide endocervical cells for cytologic interpretation. As indicated in Table 12, in 13 cases the endocervical aspirate reported data that was not provided by the ectocervical scraping. In one case (subject number 19) this additional data reported by the endocervical aspiration was of significant consequence to warrant further investigation by direct tissue biopsy.

Findings Related to the Second Hypothesis

The second hypothesis, which states that the adequacy of the cellular specimen obtained by endocervical aspiration is not influenced by the age of the subject was supported. To test this hypothesis, the Chi Square statistic was used. The subjects were categorized according to the following age groups: 40-49; 50-59; 60 and older. The presence of endocervical cells in the endocervical aspiration smear was used as the criterion for an adequate smear. Refer to Table 6 for the data used in this analysis. A chi-square value of 1.71 was not significant at the .05 level.

Table 12

Cases in Which the Endocervical Aspiration Smear Reported Data Not Reported by the Ectocervical Scraping Smear

Subject number (N=13)	Age	Ectocervical Scraping Interpretation	Endocervical Aspiration Interpretation
13	56	Negative	Reactive endocervical cells
14	48	Negative	Active metaplasia Reactive endocervical cells
17	42	Reactive endocervical cells	Active metaplasia
19*	43	Atypical endocervical cells (atypia-benign)	Severe dysplasia
23	42	Reactive endocervical cells	Reactive endocervical cells Active metaplasia
33	47	Negative	Reactive endocervical cells
47	46	Negative	Hyperchromatic, slightly hyperplastic endocervical cells (atypia-benign)
54	50	Negative	Reactive endocervical cells
55	46	Active metaplasia	Reactive endocervical cells
59	51	Negative	Reactive endocervical cells
71	41	Negative	Active metaplasia
116	44	Negative	Active metaplasia Reactive endocervical cells
127	41	Negative	Reactive endocervical cells

CHAPTER IV

Discussion

The combined ectocervical scraping and endocervical aspiration was shown to provide more precise data than the ectocervical scraping alone in the sample under study. However, much of the difference in the ratings assigned to each procedure was due to the presence of endocervical cells in 83% of the combined smears as compared to 46% of the ectocervical scraping smears. This is significant, though, in that a suitable cervical smear should include both ectocervical and endocervical cells for interpretation (Bourne & Beilby, 1976; Frost, 1969; Gondos, et al., 1972; Weid, 1955). In 13 cases the inclusion of the endocervical aspirate provided additional cytologic information, regarding cervical epithelial changes, that was not provided by the ectocervical scraping alone. However, in only one of the 13 cases was the additional information of significant consequence to warrant followup.

The endocervical aspiration smear did not provide any information regarding the state of health/disease of the endometrial epithelium that was not provided by the ectocervical scraping. In this sample, the ectocervical scraping yielded a greater number of smears containing endometrial cells than did the endocervical aspiration smear. These results were contrary to the viewpoint of Reagan and Ng (1973) who postulated that the cervical mucous present in the endocervical canal provides a favorable environment and acts as a trap for spontaneously desquamated endometrial cells.

The studies conducted by Reagan and Ng dealt with populations known to have endometrial lesions and/or large populations selected

on the basis of endometrial cells being present in endocervical aspiration smears (Ng, et al., 1974; Reagan & Ng, 1973). They did not deal with the overall ability of endocervical aspiration to provide endometrial cells for cytologic interpretation at times when physiologic shedding should be occurring in a normal population; i.e., before day 12 of the menstrual cycle. The present study was an attempt to determine the frequency of finding endometrial cells, at a time when physiological shedding is usually observed. In this study, only 25% of the endocervical aspirations obtained during the first half of the mentstual cycle included endometrial cells for interpretation as compared with 58% of the ectocervical scraping smears. It may be that the ectocervical scraping smear removed cervical mucous which may have contained trapped endometrial cells, thus limiting the ability of the endocervical aspiration smear to obtain endometrial cells.

Cervical stenosis makes direct endometrial sampling difficult in post menopausal women, thus, it was felt that the post menopausal state might also influence the ability of the endocervical aspirate to provide endocervical cells. However, this was not supported by the current study. There was no significant difference in the number of endocervical smears containing endocervical cells in relation to age of the subjects.

Gondos, et al. (1972) found that the frequency of finding endocervical cells in ectocervical scraping smears decreased with advancing age. In their study, 92% of smears taken from women under the age of 45 contained endocervical cells as compared with 52%-64% of smears

taken from women over 45 years of age. This study supports that finding. There was a minimal decrease in the percentage of ectocervical scraping smears containing endocervical cells as age increased. However, because this study did not include subjects under the age of 40, it is not possible to compare the magnitude of the decrease with the study conducted by Gondos, et al.

Gravidity and parity were equally noted by Ostergard (1977) to be indicators of the location of the squamocolumnar junction. He found that an increase in gravidity and parity was associated with an increased likelihood of an endocervical location of the squamocolumnar junction. One could infer from these results that with advancing gravidity and parity, the ectocervical scraping's ability to obtain endocervical cells would be impaired. Such an inference was not supported by the results obtained in this study. In the present study, the ability of the ectocervical scraping to yield endocervical cells increased with advancing gravidity. Only 25% of non gravid subject's ectocervical scrapings contained endocervical cells as compared with 42-53% of subjects with gravidity of one or greater. These conflicting results may have been due to the small number (N=12) of non gravid subjects in the sample.

When the combined sampling smears were analyzed according to the degree of cervical cellular atypia reported by age group, it was found that as age increased, cellular atypia decreased (Table 11, page 54, summarizes these findings). Only 52% of the combined sampling smears obtained from subjects 40-49 years of age were reported as negative, while 68% and 80% of the smears obtained from subjects 50-59 years and 60 and over, respectively, were reported as negative. This difference

corresponds to reported incidence data for cervical epithelial changes which indicates that women under forty are at higher risk for these changes, and that the risk decreases as age increases.

While the findings of this study do support the hypothesis that the combined sampling procedure does provide more precise data than does the ectocervical scraping, the results must be viewed with caution. This investigator was not able to determine the false negative and false positive rates of the procedures under study, so no statement can be made as to the influence of combined sampling on these rates.

The two principal conclusions to be drawn from this study are that in women over forty: 1) the combined sampling procedure does seem to significantly increase the yield of smears containing endocervical cells, thus providing evidence of proper sampling for cervical cancer detection; and 2) the endocervical aspiration smear does not seem to be a sensitive screening test for endometrial cancer and its precursor lesions.

Since women over forty years of age are not considered at high risk for developing cervical cancer, the question may arise as to whether the additional health care cost for obtaining, processing, and interpreting the endocervical aspiration smear is justified. An alternative to the cost of processing and interpreting two separate smears would be to combine the two specimens obtained, on a single slide. There is evidence that the diagnostic accuracy of multiple preparations on a single slide is the same as the multiple preparations on individual slides (Frost, 1969).

Women over forty years of age are at risk for developing endo-

metrial cancer. However, at the present time an acceptable, accurate, and low cost screening test for mass screening of women in this age group, for this cancer, does not seem to exist. This fact is supported by the present study. Therefore, selective screening of women with multiple risk factors for developing endometrial cancer should be carried out by using a direct endometrial sampling screening procedure. Knowledge of the relative importance of the various risk factors, as indicators of the need for endometrial sampling, is needed by health care providers to identify the population that would benefit most by this form of screening.

The present study emphasizes the need for primary care practitioners to participate in ongoing evaluation of their screening practices. They must be aware of the strengths and limitations of the screening tests employed in their practice. Additionally, they must be knowledgeable of the disease being screened, i.e., have an adequate understanding of: 1) the significance of the disease as a health care problem; 2) the natural history of the disease; 3) treatment for the disease; and 4) the risk factors for developing the disease.

Limitations of the Study

A limitation of the study was that this investigator had no control over the procedures under study, i.e., the collecting, processing, and interpreting of the smears. Individual variation in any of these three phases could have influenced the actual results. However, there was no significant difference noted in the quality of the smears obtained by the three practitioners participating in the study as determined by the number of adequate and inadequate smears performed

by each. Additionally, the normal and abnormal smears were classified according to which of the six cytologists interpreted them. No significant difference was observed in the number of normal and abnormal smears reported by each cytologist.

Also, the results obtained from testing the first hypothesis must be viewed with caution, as the acceptance of this hypothesis implied that the combined sampling smear was more effective than the ectocervical scraping smear in screening women over forty years of age for both cervical and endometrial cancer. In reality, it was shown to be more effective for cervical cancer screening only.

CHAPTER V

Summary, Conclusions, and Recommendations

Summary

Screening of the general population for the presence of asymptomatic diseases is becoming an increasingly common practice. Many screening procedures are accepted as 'routine practice' before their worth has been established. Primary care providers have as their responsibility the ongoing evaluation and critical appraisal of these screening practices.

The purpose of this study was to evaluate the effectiveness of combined ectocervical scraping and endocervical aspiration as a screening method for cervical and endometrial cancer and their precursor lesions in women over forty years of age. A convenience sample of 139 subjects was used for this study. Each subject had an ectocervical scraping and an endocervical aspiration performed at the same visit by one of three practitioners participating in the study. The two specimens obtained from each subject were interpreted by the same cytologist. The ectocervical scraping smear and the combined ectocervical scraping and endocervical aspiration smears were each assigned a rating by this investigator, reflecting the amount of data reported by each procedure. Additionally, the presence of endocervical cells and endometrial cells in the different specimens was studied.

The findings of the study support the hypothesis that the combined sampling procedure provides more precise data regarding the state of health/disease of the cervical and endometrial epithelium than that

provided by the ectocervical scraping alone. Further examination of the data revealed that much of the difference in the ratings assigned to the data obtained by the two procedures was due to the high yield of endocervical cells from the combined sampling procedure. In addition, the combined sampling procedure did not provide more precise data regarding the state of health/disease of the endometrial epithelium than that which was provided by the ectocervical scraping alone. The results also indicated that the endocervical aspiration was equally effective in obtaining endocervical cells in all age groups under study.

Conclusions

The following conclusions can be drawn from the findings of this study.

1. The advantage of using combined ectocervical scraping and endocervical aspiration in screening women over forty years of age, for cervical cancer and its precursor lesions, lies in the ability of the endocervical aspirate to provide more cytologic material for interpretation, i.e., endocervical cells.
2. The endocervical aspiration smear did not provide more precise data regarding the state of health or disease of the endometrial epithelium than that provided by the ectocervical scraping alone.
3. The ability of the endocervical aspirate to yield endocervical cells for cytologic interpretation is not significantly influenced by age.

Recommendations for Further Study

Based on the findings of this study the following recommendations are made.

1. Repeat the study, using subjects under the age of 40 years, to determine if combined ectocervical scraping and endocervical aspiration provides more precise data regarding the state of health/disease of the cervical epithelium than does the ectocervical scraping alone.
2. Conduct a comparative study of the following two endocervical sampling technqiues: endocervical aspiration smears and endocervical swab smears.
3. Conduct a study, using a larger population, to determine the frequency of finding endometrial cells in endocervical aspiration smears obtained during the first half of the menstrual cycle, when physiological shedding occurs.
4. Develop an assessment tool designed to identify women at high risk for endometrial cancer who would benefit from screening for this disease by direct endometrial sampling.

The implementation of these recommendations will provide health care practitioners with an expanded knowledge base to enable them to make informed decisions regarding their screening practices and procedures.

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APPENDIX A

Protocol for Obtaining and Processing Cellular Specimens

Protocol for Obtaining and Processing Cellular Specimens

1. A vaginal speculum is inserted into the vagina to properly visualize and position the cervix for inspection and collection of cellular samples.
2. The squamocolumnar junction is identified. A wooden cervical scraper is used to scrape the squamocolumnar junction in entirety (360°). If this junction is not visualized, it is standard procedure to then scrape the area around the external os.
3. This cellular specimen is spread uniformly on a labeled glass slide with the cervical scraper and is fixed immediately in a 95% alcohol solution.
4. Next, a specimen is obtained from the endocervical canal by placing a disposable plastic suction cannula into the cervical canal and aspirating the contents with a 10cc syringe.
5. The contents of the cannula are expelled onto a labeled glass slide, spread uniformly with the edge of the cannula, and immediately fixed in a 95% alcohol solution.
6. These specimens are sent to the cytology lab with a requisition which includes the following data (also see Appendix B):

    Age

    Source of the specimen

    Last menstrual period (LMP)

    Obstetrical History

    Current hormonal history

    Presence or absence of an intrauterine device

    Menopausal status

    Pertinent clinical information

These specimens are interpreted by cytologists.

Abnormal specimens are referred to cytopathologists for final interpretation.

7. The final cytologic interpretation is noted on the cytology report by checking the appropriate cytologic impression category, i.e. negative, atypia benign, suspicious, malignant, inadequate or inconclusive. Several possible interpretations exist for some of the categories listed (see Appendix C). If a cellular specimen falls into the atypia benign, suspicious, malignant or inconclusive category, the actual interpretation is handwritten in by the cytologist.
8. The cytology report is then returned to the practitioner for follow-up as indicated.

Credentials of cytologists

This organization's cytology department employs six full- and part-time cytologists. All of the cytologists have completed two years of college plus one year of cytology training at the University of Oregon Health Sciences Center. Their average number of years working for this organization is 5.5 years (range: six months to ten years).

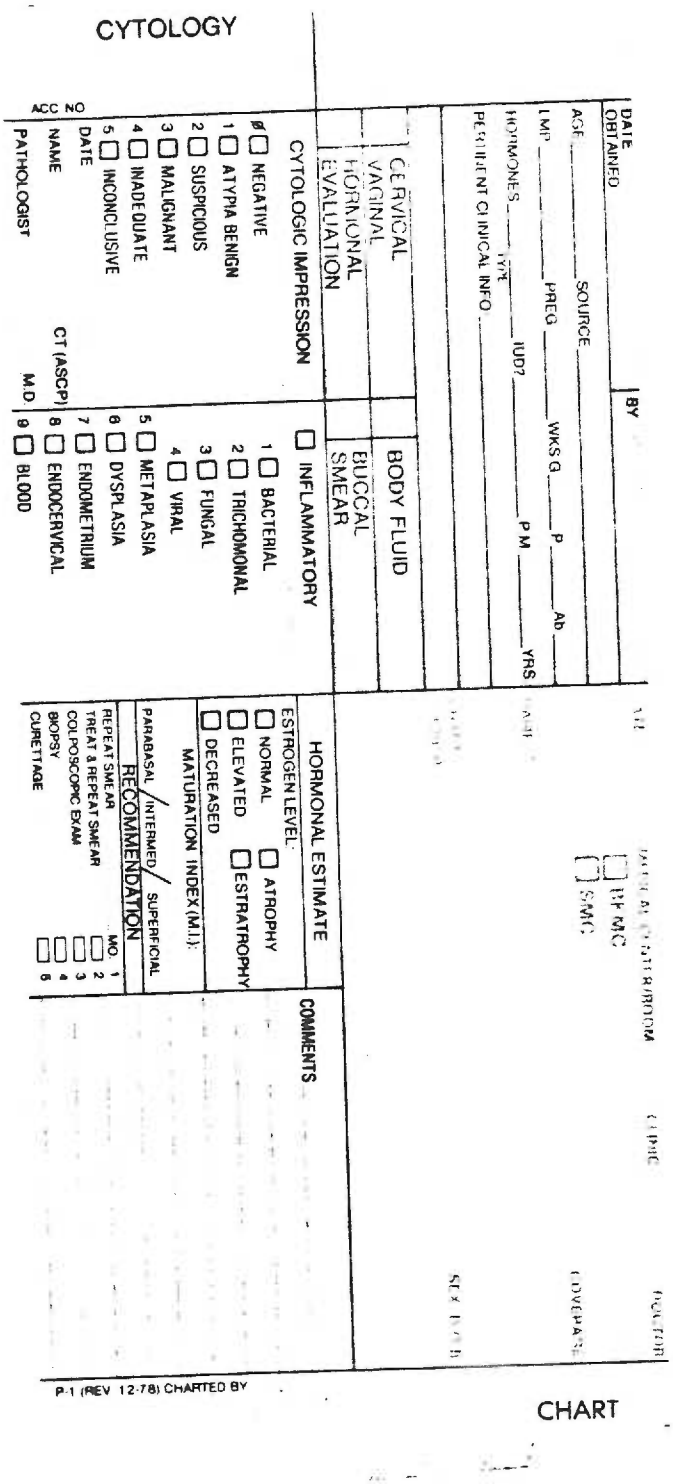
Quality Control

Ten percent of all GYN cytology slides screened are rescreened by the cytopathologists. Additionally, slides are reviewed when there is a discrepency between cellular interpretation and histologic diagnosis.

APPENDIX B

Cytology Report

Cytology Report



APPENDIX C

Cytology Conversion Scale

Cytology Conversion Scale

Reportable Data	Rating
Inadequate	0
Negative includes squamous metaplasia	1
Endocervical Cells (normal) Present	2
Endometrial Cells (normal, present before day 12 in the premenopausal female)	2
Atypical Benign	
1. reactive changes of any cell type	3
2. active squamous metaplasia	3
3. Mild dysplasia	4
4. moderate dysplasia	4
5. mild endometrial hyperplasia	4
6. appearance of endometrial cells on or after day 12 of the menstrual cycle or anytime in the post menopausal period	4
Suspicious	
1. severe dysplasia	5
2. severe endometrial hyperplasia	5
3. endocervical atypia suspicious of endocervical adenoma	5
Malignant	
1. carcinoma in situ of the cervix	6
2. adenocarcinoma in situ of the endometrium	6
3. squamous cell carcinoma of the cervix	7
4. endocervical adenoma	7
5. adenocarcinoma of the endometrium	7

APPENDIX D

Raw Data Used for Wilcoxon Matched-Pairs Signed Ranks Test

Raw Data Used for Wilcoxon Matched-Pairs Signed Ranks Test

Subject Number	Age	Assigned Rating: Ectocervical Scraping	Assigned Rating: Combined Sampling	Difference	Rank
1	64	3	3	0	0
2	53	3	5	2	24.5
3	41	5	5	0	0
4	50	5	5	0	0
5	42	5	5	0	0
6	40	1	3	2	24.5
7	58	1	1	0	0
8	58	3	3	0	0
9	51	5	5	0	0
10	59	6	6	0	0
11	48	1	3	2	24.5
12	42	5	5	0	0
13	56	1	5	4	54
14	48	5	8	3	59.5
15	45	5	5	0	0
16	57	1	3	2	24.5
17	47	5	8	3	49.5
18	46	8	8	0	0
19	43	6	7	1	1
20	49	8	8	0	0
21	41	7	7	0	0
22	51	1	3	2	24.5
23	42	5	8	3	49.5
24	51	6	6	0	0
25	45	5	5	0	0
26	44	4	9	5	57.5
27	52	1	3	2	24.5
28	59	3	3	0	0
29	44	1	1	0	0
30	52	5	5	0	0
31	47	6	6	0	0
32	51	3	3	0	0
33	47	1	5	4	54
34	49	1	1	0	0
35	45	6	8	2	24.5
36	42	3	3	0	0
37	48	1	3	2	24.5
38	49	1	3	2	24.5
39	50	3	5	2	24.5
40	74	1	3	2	24.5
41	47	1	3	2	24.5
42	56	1	1	0	0
43	43	5	5	0	0
44	48	8	8	0	0

Subject Number	Age	Assigned Rating: Ectocervical Scraping	Assigned Rating: Combined Sampling	Difference	Rank
45	53	3	3	0	0
46	42	3	3	0	0
47	46	3	5	2	24.5
48	64	5	5	0	0
49	53	1	1	0	0
50	54	1	3	2	24.5
51	50	1	3	2	24.5
52	51	1	3	2	24.5
53	56	1	3	2	24.5
54	50	3	5	2	24.5
55	56	5	8	3	49.5
56	49	1	1	0	0
57	50	5	5	0	0
58	55	1	1	0	0
59	51	1	5	4	54
60	74	1	3	2	24.5
61	64	3	3	0	0
62	40	5	5	0	0
63	43	1	3	2	24.5
64	53	3	3	0	0
65	43	1	3	2	24.5
66	58	1	3	2	24.5
67	57	1	1	0	0
68	53	5	5	0	0
69	43	3	3	0	0
70	45	5	5	0	0
71	41	1	5	4	54
72	76	1	3	2	24.5
73	40	1	3	2	24.5
74	56	1	1	0	0
75	53	3	3	0	0
76	40	1	1	0	0
77	46	6	6	0	0
78	54	1	3	2	24.5
79	56	3	3	0	0
80	44	3	3	0	0
81	43	5	5	0	0
82	41	1	3	2	24.5
83	40	3	5	2	24.5
84	44	1	3	2	24.5
85	67	1	1	0	0
86	64	1	3	2	24.5
87	49	3	3	0	0
88	59	1	3	2	24.5
89	41	3	5	2	24.5
90	53	3	3	0	0

Subject Number	Age	Assigned Rating: Ectocervical Scraping	Assigned Rating: Combined Sampling	Difference	Rank
91	59	9	9	0	0
92	56	5	5	0	0
93	41	1	1	0	0
94	46	5	5	0	0
95	57	1	3	2	24.5
96	50	8	8	0	24.5
97	49	3	3	0	0
98	41	1	1	0	0
99	43	3	3	0	0
100	58	3	3	0	0
101	47	3	3	0	0
102	41	3	3	0	0
103	41	3	3	0	0
104	45	1	3	2	24.5
105	52	3	3	0	0
106	42	1	1	0	0
107	62	5	5	0	0
108	60	1	3	2	24.5
109	42	5	5	0	0
110	64	1	1	0	0
111	63	3	3	0	0
112	43	1	1	0	0
113	51	3	5	2	24.5
114	53	1	3	2	24.5
115	44	6	6	0	0
116	44	3	8	5	57.5
117	53	3	3	0	0
118	45	1	3	2	24.5
119	53	1	3	2	24.5
120	41	3	3	0	0
121	56	1	3	2	24.5
122	59	3	3	0	0
123	40	1	3	2	24.5
124	45	3	3	0	0
125	66	1	3	2	24.5
126	45	3	5	2	24.5
127	41	1	5	4	54
128	40	5	5	0	0
129	53	5	5	0	0
130	59	1	1	0	0
131	64	1	3	2	24.5
132	43	1	1	0	0
134	45	1	1	0	0
135	52	3	3	0	0
136	57	1	1	0	0
137	48	1	3	2	24.5
138	62	3	3	0	0
139	45	9	11	2	24.5

AN ABSTRACT OF THE THESIS OF

MARY C. BAUER

For the MASTER OF NURSING

Date Receiving this Degree: June, 1981

Title: The Effectiveness of Combined Ectocervical Scraping and Endocervical Aspiration as a Screening Method for Cervical and Endometrial Cancer in Women over Forty Years of Age

Approved: [redacted]
Charold L. Baer, R.N., Ph.D. Thesis Advisor

Screening of the general population for the presence of asymptomatic disease has become an increasingly common practice. Criteria have been established to determine which diseases are worthy of screening. This study dealt with determining the effectiveness of combined ectocervical scraping and endocervical aspiration as a screening method for cervical and endometrial cancer in women over forty years of age.

This retrospective study used the data obtained from cytology reports of ectocervical scrapings and endocervical aspirations that had been done on women over forty years of age from March 1, 1979 to March 1, 1980. The sample was a convenience sample comprised of 139 subjects who had these procedures performed at the same visit by one of three practitioners employed by the agency involved in the study.

The findings supported the hypothesis that the combined sampling procedure would provide more precise data regarding the state of health or disease of the cervical and endometrial epithelium than that provided by ectocervical scraping alone. Further examination of

the data revealed that much of the increased precision of the data collected was due to the high yield of endocervical cells from the combined sampling procedure. The combined sampling procedure did not provide more precise data regarding the state of health/disease of the endometrial epithelium than was provided by the ectocervical scraping alone. The endocervical aspiration was found to be equally effective in obtaining endocervical cells in all age groups under study.