January 2005

Examination of Current Clinical Guidelines of HMOs Regarding Management of Women with Cervical Cytological Abnormalities: Phase I

Final Report

Prepared for

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ABSTRACT

Since the early 1990s, there has been a proliferation of practice guidelines and recommendations among Federal agencies and professional health organizations with respect to cervical cancer screening. However, the Centers for Disease Control and Prevention (CDC) remains concerned about variations in the management of women with abnormal Pap tests by geographic location and provider type. This study explores whether or not there is concordance between (1) recommendations of the United States Preventive Services Task Force (USPSTF), American College of Obstetricians and Gynecologists (ACOG), and American Cancer Society (ACS) for cervical cancer screening and follow-up and (2) the policies of health management organizations (HMOs), hereafter referred to as managed care organizations (MCOs). Because of the exploratory nature of the study, we selected 9 MCOs from the original 29 we had identified. We selected three each of large (5 million or more members), medium-sized (1 to 4 million members), and small (less than 1 million members) organizations, which also represented various types of coverage and geographic locations. Three MCOs actively participated in the study through interviews, e-mail correspondence, and sharing of guidelines and materials. We reviewed and summarized cervical cancer screening guidelines and recommendations from Federal agencies and professional health organizations, and selected tracer features to compare with the MCO policies. When we compared MCO policies with USPSTF, ACOG, and ACS recommendations, we noted a concerted effort on the part of the MCOs to keep abreast of clinical practice norms and to disseminate current information regarding cervical cancer screening to providers and members/patients. Because our sample consists of only three MCOs, albeit large national organizations, the information we gathered cannot in any way be generalized to all MCOs. Our study sheds light on three MCOs' awareness of USPSTF, ACOG and ACS recommendations and how they have developed and communicated policies for screening of cervical cancer to their physicians.

1. OVERVIEW

The purpose of this study is to (1) explore managed care organization (MCO) policies for practice guidelines related to cervical cancer screening and follow-up of abnormal findings and (2) assess MCO policy concordance with the United States Preventive Services Task Force (USPSTF), American College of Obstetricians and Gynecologists (ACOG), and American Cancer Society (ACS) recommendations. We identified representative MCOs in terns of size (lives covered), geographic location, and provider type. We contacted the organizations to obtain their clinical polices and patient education materials with respect to cervical cancer screening. We reviewed USPSTF, ACOG, and ACS recommendations and identified tracer features of these recommendations to compare them with the recruited MCOs' clinical policies.

2. BACKGROUND

2.1 Overview of Current Guidelines for Cervical Cancer Screening and Follow-up

In 2002, the American Cancer Society estimated that approximately 13,000 new cases of invasive cervical cancer would be diagnosed and that nearly 4,100 women would die of cervical cancer the following year (American Cancer Society, 2002a). Since the early 1990s, there has been a proliferation of practice guidelines and recommendations among Federal agencies and professional health organizations. However, the Centers for Disease Control and Prevention (CDC) remains concerned about variations in the management of women with abnormal Pap tests by geographic location and provider type. This concern is mirrored in a study by Casalino and associates (2003), which found that 50 percent of the physician organizations studied used four or fewer of the 16 care management protocols that were in place for four chronic diseases (asthma, congestive heart failure, depression, and diabetes).

Pap smears have been the primary diagnostic tool for cervical cancer screening in asymptomatic women. Cells are removed from the cervix by brushing or scraping the cervix during a pelvic examination and then placing the cells on one or more glass slides. The slides are sent to an accredited laboratory to be stained, examined under a microscope, and interpreted. The Pap test can detect precancerous changes or cancer of the cervix and vagina. Recently, new technologies for screening or preparing the Pap smear have been approved by the Food and Drug Administration (FDA). Human papillomavirus (HPV) has been associated with development of cervical intraepithelial neoplasia (CIN) and invasive cancer of the cervix. HPV testing has been proposed as an adjunctive test in women with atypical squamous cells of undetermined significance (ASC-US), to identify those at highest risk for cervical cancer. HPV has also been proposed as a primary screening test to be performed simultaneously with Pap smear screening.

The efforts of the Agency for Healthcare Research and Quality (AHRQ), formerly Agency for Health Care Policy and Research, and the landmark studies of the Institute of Medicine (IOM) (1990, 1992) resulted in the proliferation of practice guidelines. In 1994, the American Society of Clinical Oncology (ASCO) began assembling expert panels to develop evidence-based oncology practice guidelines in several areas (Somerfield et al., 2000) and the Institute for Clinical Systems Improvement (ICSI) released its first cervical cancer screening guidelines, which were revised in June 2002. The USPSTF, which first released guidelines for cervical cancer screening in 1996, revised them in January 2003 (AHRQ, 2003). In September 2001, the American Society for Colposcopy and Cervical Pathology (ASCCP) hosted a consensus conference to develop evidence-based guidelines for the management of women with cervical cytological abnormalities and cervical cancer precursors. This conference came about, in part, because of a need for clear, unbiased guidelines delineating the best use of new technologies for early detection of cervical cancer. To ensure that the guidelines would reflect the needs of the broad range of clinicians who provide cervical cancer screening, representatives from 29 participating professional health organizations and Federal agencies were invited to attend. Resulting guidelines were released in April 2002 (Wright et al., 2002).

Recently, the American College of Obstetricians and Gynecologists (ACOG) revised its cervical cancer screening guidelines for annual pelvic exams and annual Pap tests (ACOG, 2004a) and clarified its recommendations on cervical cancer screening in adolescents (ACOG, 2004b). In August of this year, the ICSI updated a previous version of its algorithm for cervical cancer screening (ICSI, 2004). Finally, Miller et al. (2003) challenged screening intervals based on results from a matched case-control study of invasive squamous cell cervical cancer patients who were long-term members of a large health maintenance organization.

2.2 Managed Care Organization Models

Managed care is a complex system that involves the active coordination of, and arrangement for, the provision of health services and coverage of health benefits. The most common types of MCOs include health maintenance organizations (HMOs), preferred provider organizations (PPOs), and exclusive provider organizations (EPOs). Managed care usually involves three key components: oversight of the medical care given; contractual relationships and organization of the providers giving care, and covered benefits tied to managed care rules (MCOL, 2004). It is important to note that most working-age women in this country who have insurance are likely to be covered by some kind of managed care program.

2.3 Adoption and Dissemination of Clinical Guidelines

Social scientists have focused on the diffusion of innovations for some time (Rogers, 1995; Schroeder et al., 1986). For this study, we defined innovation as a technology or practice that an organization uses for the first time whether or not other organizations have used it (Emmons et al., 2000; Klein et al., 2001; Rogers, 1995). The innovation we are discussing

here is adoption and dissemination of clinical guidelines for cervical cancer screening and follow-up.

Health care is rich in evidence-based innovations such as clinical guidelines, which often disseminate slowly, if at all. Although clinical science provides the rationale for choosing the best drugs, surgery, diagnostic strategies, and other elements of care, major gaps in knowledge persist (Ellis et al., 1995). Berwick (2003) noted that several clusters of influence determine the rate with which an innovation spreads. The **perception of the innovation** is the most powerful force that leads to adoption because the more knowledge individuals have about the expected consequences of the innovation; the more likely they are to adopt it. The **characteristics of the people** who adopt the change and its **compatibility with their values and beliefs** also enhance adoption. This is particularly important against the backdrop of our discussion because only a minority of physician groups routinely use formal, scientific protocols and guidelines in their practices (Casalino et al., 2003). Finally, the **context** of the innovation, especially with regard to leadership and management, affects its adoption**.**

Based on these factors, we would expect that the adoption of cervical cancer screening policies by physicians in a given MCO would increase proportionately with the active development and dissemination of the policy and with clear support from the MCO's leadership.

3. APPROACH

The aim of this project is to explore whether or not there is concordance between (1) recommendations of the USPSTF, ACOG, and ACS for cervical cancer screening and follow-up and (2) the policies of health management organizations (HMOs), hereafter referred to as managed care organizations (MCOs).[1]

3.1 Identifying Managed Care Organizations

Using the National Directory of Managed Care Organizations, 4th edition (Harris, 2003), we generated a list of 29 MCOs in the United States. Next, we systematically classified them according to (1) size, i.e., number of enrollees/lives covered; (2) geographic service area; (3) type of coverage; (4) products offered; and (5) model (individual practice association [IPA], network, etc.). Two tables in *Appendix A* summarize these characteristics.

3.2 Recruiting Managed Care Organizations

To determine which of the 29 MCOs would best serve our purposes, we searched the Internet, gathering as much information as possible about each organization. Together with the CDC task manager (TM) we identified three each large (5 million or more members), medium-sized (1 to 4 million members), and small (less than 1 million members) organizations, which also represented various types of coverage and geographic locations. Because of the exploratory nature of this study, we limited the number of MCOs to nine, which together incorporated the range of characteristics of interest (see *Table 1*).

While contacting the MCOs to enlist their participation, we encountered organizations in which the Medical Director's position was not filled and others that were in the process of merging or being bought out. Officials from several MCOs took time to review the project and opted not to participate. *Table 2* summarizes their responses to our contacts. Nevertheless, we have had direct contact with the MCOs on our list and have conducted a series of in-depth conversations with three MCOs: Aetna Inc. (hereafter called Aetna), UnitedHealth Group (UHG), and Kaiser Permanente—Kaiser Foundation Health Plan (Kaiser).

[1] Health ***management*** organizations (HMOs) are entities that use certain concepts or techniques to manage the accessibility, cost, and quality of health care. By using the term MCO in this report, there should be no confusion with the term health ***maintenance*** organization (also HMO), which refers specifically to a health care system that assumes or shares both the financial and delivery risks associated with providing comprehensive medical services to a voluntarily enrolled population.

Table 1. Characteristics of Nine Recruited MCOs. Shading indicates the MCOs interviewed.

	Aetna Inc.	UnitedHealth Group Inc.	Kaiser Permanente—Kaiser Foundation Health Plan	Humana Inc.	Mid Atlantic Medical Services, Inc.	Sierra Health Services	AmeriGroup Corp	Cariten Healthcare	Mayo Health Plan
Enrollment	14,000,000	8,520,000	8,400,000	6,631,400	1,800,000	1,282,100	510,000	447,017	8,247
Data for year	2002	2002	2002	2002	2001	2001	2002	2001	1999
Large	✓	✓	✓	✓					
Medium					✓	✓			
Small							✓	✓	✓
For profit (Yes/No)	Yes	Yes	No	Yes	No Listing	Y	No Listing	Yes	Yes
Model*	IPA	Network	Salaried Providers	IPA	IPA	Group	No Listing	IPA	IPA
Type of coverage	Commercial, Medicare, Medicaid	Commercial, Individual, Medicare, Medicare +, Medicaid	Commercial, Individual, Medicare, Medicaid	Commercial, Individual, Medicare, Medicare +, Medicaid	Commercial, Individual, Medicare, Medicare +, Medicaid	Commercial, Medicaid Medicare, Military Health Services	Medicaid, SCHIP	Commercial, Medicare, Medicare + Medicaid	Commercial, Medicare
Plan types*	HMO, PPO POS	HMO, PRO, POS, UR	HMO	HMO, PPO, POS, EPO, ASO	HMO, PPO, POS	HMO, PPO, POS, ASO, UR	HMO	HMO, PPO, POS, ASO	TPA
Location	National	National	National	National	National	National	National	National	National
Number of states	50	No Listing	10	50	7	3	5	1	3

* ASO = administrative services only; EPO = exclusive provider organization; HMO = health maintenance organization; IPA = individual practice association; POS = point of service; PPO = preferred provider organization; TPA = third-party administrators; UR = utilization review.

Source: The National Directory of Managed Care Organizations, 4th edition.

Table 2. Recruitment of MCOs

Managed Care Organizations	Number of Contacts	Participation (Yes/No)	If No, Reason
Aetna Inc.	16	Yes	
UnitedHealth Group Inc.	23	Yes	
Kaiser Permanente—Kaiser Foundation Health Plan	11	Yes	
Humana, Inc.	7	No	Medical Director has left the organization. The position is currently unfilled and there was no one with whom we could speak
Mid Atlantic Medical Services, Inc.	6	No	Merged with UnitedHealth Group
Sierra Health Services	6	No	"Sierra is not interested in participating in this study"
AMERIGROUP Corporation	7	No	"I [Medical Director] have discussed the information with our Medical Directors, and at this time we are unable to participate"
Cariten Healthcare	6	No	No Response
Mayo Health Plan	9	No	Unable to identify an appropriate contact in the organization.

3.3 Guideline Review

Through the National Guidelines Clearinghouse (http://www.guideline.gov), we accessed cervical cancer screening guidelines disseminated by Federal agencies and professional health organizations. Through a series of discussions with the CDC TM and our consultant Dr. Katherine Hartmann, we determined to focus on tracer features of screening guidelines as a starting point for our review (*Figure 1*). Please note that we did not address current discussions about alternatives to conventional cervical cytology smears in this review.

Figure 1. Tracer Features of Screening Guidelines

- Age at first Pap test screening
- Pap test screening up to age 30
- Pap test screening 30 years through age 64
- Pap test and HPV screening 30 years through age 64
- Pap test screening ceases

Table 3. Pap Test Screening Guidelines

	Organization		
	American Cancer Society (ACS)	**American College of Obstetricians and Gynecologists. (ACOG)**	**U.S. Preventive Services Task Force (USPSTF)**
Title	American Cancer Society Guidelines for the Early Detection of Cervical Neoplasia and Cancer (ACS, 2002b)	Cervical Cytology Screening (ACOG, 2003)	Screening for Cervical Cancer: Recommendations and Rationale (USPSTF, 2003)
Screening Begins	Approximately 3 years after the onset of vaginal intercourse and no later than 21 years of age.	Approximately 3 years after first sexual intercourse or by age 21, whichever comes first.	3 years after onset of sexual activity or at age 21, whichever comes first.
Screening to age 30	Annually with conventional cervical cytology smears OR every 2 years using liquid-based cytology.	Annual screening.	
Screening 30 years of age or older: Pap test only	At or after age 30, women who have three consecutive normal Pap tests may be screened every 2 to 3 years, unless they have a history of *in utero* DES* exposure, are HIV-positive,* or are immunocompromised.	If a woman over 30 has three consecutive negative Pap tests, screen with cervical cytology alone every 2 to 3 years.	
Screening 30 years of age or older: Pap test and HPV* DNA test	If FDA approved, should NOT be more often than every 3 years.	Using combination of cervical cytology and FDA-approved test for high risk types of HPV, once both tests are negative, screen with both tests every 3 years. If only one test is negative more frequent screening will be necessary.	Evidence is insufficient to recommend for or against HPV testing as a primary test for cervical cancer.
Screening Ceases	Women who are 70 and older with an intact cervix and who have had three or more documented consecutive normal tests within the 10-year period to age 70 may elect to cease cervical cancer screening.	Physicians determine on an individual basis when an older woman can stop having cervical cancer screening based on medical history and monitoring of patient.	No routine screening for women over 65 provided they have had adequate screening with normal Pap test results.

* DES = diethylstilbesterol; HIV = human immunodeficiency virus; HPV = human papillomavirus.

Table 3 summarizes screening guidelines for the ACS, ACOG, and USPSTF. (Recommendations of the American Society for Cytopathology (ASCP) are not included because they are focused on laboratory practices and deal with sampling, handling, and analyzing specimens.) The three organizations are in agreement regarding when cervical cancer should begin—3 years after the onset of vaginal intercourse or by 21 year of age, whichever comes first. With regard to screening for women up to age 30, ACS recommends annual screening with conventional Pap test OR screening every 2 years using liquid-based cytology. Although ACOG recommends annual screening for cervical cancer, it does not

specify testing method for women to age 30. There is basic agreement between ACS and ACOG regarding screening with only a Pap test for women 30 and older—namely, women who have had three consecutive normal Pap tests may be screened every 2 to 3 years. When HPV testing is added to the mix, all three organizations qualify their recommendations. ACS indicates that HPV testing need not take place more often than every 3 years. ACOG addresses screening with a combination of Pap and HPV DNA tests, indicating that once both Pap and HPV DNA tests are negative, screening with both tests can occur every 3 years. If only one test is negative, the recommendation is for more frequent screening. USPSTF contends that the evidence is insufficient to recommend for or against the use of HPV testing for primary screening for cervical cancer. Opinions also diverge regarding when cervical cancer screening should cease. ACS recommends that women 70 years of age or older with an intact cervix and three or more documented consecutive normal Pap tests within the previous 10-year period may elect to cease cervical cancer screening. ACOG recommends that physicians determine when to stop cervical cancer screening based on the medical history and monitoring of the patient. USPSTF recommends no routine screening for women over 65 provided they have had adequate previous screening with normal Pap test results.

3.4 Data Collection

To assist us in categorizing National Managed Care Organizations as well as guidelines for cervical cancer screening, that have recently been disseminated by governmental, scientific and professional organizations, we designed two Microsoft Access databases to facilitate consistent data capture. In preparation for contacting the MCOs, we developed a recruitment kit that included a scripted interview that enabled us to be consistent in our presentations. Once we identified the appropriate person in the organization, we e-mailed to him or her Fact Sheet and a personalized support letter from CDC's TM. Because MCOs are complex, organizations often in a state of flux, we also developed a tracking log to keep a record of our contacts. (See *Appendix B*)

4. FINDINGS

When we compared their guidelines with USPSTF, ACOG, and ACS recommendations, we noted a concerted effort to keep abreast of clinical practice norms and to disseminate current information regarding cervical cancer screening to providers and members/patients. The remainder of this section compares and contrasts how these three MCOs developed their clinical guidelines for cervical cancer screening and health education materials on the topic, and describes the process by which these materials were disseminated.

4.1 MCO Policies

Although each of the three MCOs we interviewed approached guideline development in its own way, all of them had incorporated USPSTF, ACOG and/or ACS recommendations into their clinical policies (see *Table 4*).

Table 4. Concordance of MCO Screening Tracer Features with ACOG, ACS, and USPSTF Recommendations

Tracer Feature	Aetna	UnitedHealth Group	Kaiser Permanente
Screening Begins	ACOG, ACS, USPSTF	ACOG, ACS, USPSTF	ACOG, ACS, USPSTF
Screening to age 30	ACOG	ACOG, ACS	ACOG
Screening 30 years of age or older: Pap test only	ACOG	ACOG, ACS	ACOG
Screening 30 years of age or older: Pap test and HPV* DNA test	ACOG	ACOG, ACS	ACOG
Screening Ceases	ACOG	no information	ACOG

Aetna reported that USPSTF recommendations are the starting point for its cervical cancer screening guidelines; however, it also references ACOG and ACS recommendations. *Cervical Cancer Screening and Follow-up of Abnormal Cytology Results; Clinical Policy Bulletin 0443* is included in *Appendix C*. This bulletin is based on a review of currently available clinical information including clinical outcome studies in the peer-reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health profession organizations, views of physicians practicing in relevant clinical areas, and other relevant factors. The bulletin concludes with a comprehensive bibliography of references for cervical cancer screening and follow-up, including international citations.

Generally UHG considers USPSTF guidelines as its gold standard. In the case of Pap tests and HPV-DNA tests, it follows ACOG and ACS guidelines. UHG develops Technology Assessments, which are approved by both its Medical Policy and Medical Technology Assessment Committees. The Technical Assessments serve as general reference resources for UHG providers. In 2004, three Technology Assessments dealing with use of technologies for HPV and atypical cells, cervical cancer, and its precursor lesions were completed.

Kaiser develops its clinical guidelines through a consensus process that includes convening a panel of Kaiser clinical specialists and guideline methodologists. The panel begins by characterizing the issue at hand and then conducts a primary evidence-based literature search. Through an iterative process in which panel members report findings to their respective chief groups (in this case OB/GYN specialists), it reaches consensus about the clinical policy. This course of action takes several months. *Clinical Practice Guidelines—Cervical Cancer Screening and Follow-up of Abnormal Cytological Results*, developed through this process, and accompanying *Algorithms* are presented in *Appendix E*.

4.2 Disseminating MCO Policies

As with guideline development, each of the three MCOs disseminates policy and health education information about cervical cancer screening guidelines in its own way.

During the summer of 2003, Aetna sent a health education information packet, *Cervical Cancer Screening Educational Materials: New Screening Strategy for Cervical Cancer*, to tens of thousands of its providers, including obstetrics/gynecology (OB/GYN) specialists and "high-volume" primary care physicians. The packet (see *Appendix C*) included (1) a cover letter reminding physicians of current screening tools and emphasizing ACS and ACOG endorsement, (2) a flyer that summarized updated cervical cancer screening guidelines for health care professionals, (3) a series of patient health education flyers and posters, and (4) a return postcard asking providers to comment on the usefulness of the materials. Aetna is currently in the process of tabulating responses. In addition to distributing information in mailings, Aetna discusses the cervical cancer screening guidelines at regional quality assurance meetings where it reviews clinical policies and answers provider questions.

UHG guidelines are not disseminated per se; rather, when test results or interventions for any of their patients differ from the gold standard (e.g., follow-up for a positive Pap test result is not carried out), providers receive a clinical profile (including patient name, ID, and phone number).

Kaiser's clinical practice guidelines are disseminated to its providers in several ways. A bound copy of all guidelines is published every other year and distributed to specialists within the system and to a tailored distribution list of networks and other outreach organizations. They are also available for Kaiser Clinicians on Kaiser's Intranet system.

4.3 Health Education Materials for Members

Aetna develops and publishes its own health information materials, which it considers as private intellectual property. Aetna uses USPSTF as its primary information source and,

depending on the topic, confers with other regulatory and health professional agencies such as CDC or the National Institutes of Health (NIH). For the cervical cancer screening materials, Aetna consulted ACOG and worked closely with CDC to be sure that its core messages about cervical cancer screening are correct. Aetna distributes its health education materials via providers. Included in the packet as described above (*Appendix C*) was a patient health education flyer in English and Spanish, *Cervical Cancer Screening: Ask Your Doctor about Two Important Tests*. Finally, Aetna sends preventive health reminders to its members annually. A reminder about the Pap test is part of its message to women. A series of health education materials dealing with Pap tests for various age groups is also available to the general public on the Internet at http://womenshealth.aetna.com.

UHG obtains health education materials for its consumer Web site from three sources (Dr. R. Justman, personal communication, November 17, 2004): (1) Healthwise publishes the Healthwise Handbook and offers online consumer advice; (2) Optum offers a Reminders Program, which includes reminders about getting Pap tests; and (3) Best Treatments from the *British Medical Journal*. See *Appendix D* for the UHG health education materials regarding Pap tests.

Kaiser develops its own health education materials. *Provider Information—Frequently Asked Questions* is a two-page quick reference for clinicians that summarizes clinical practice guidelines for cervical cancer screening. Materials for patients include *When Should You Get a Pap Test and Why?, Human Papillomavirus, New Improvement in Cervical Cancer Prevention for Women Age 30 and Over,* and a document in English, Spanish, and Chinese entitled *DNA Pap: What Women Should Know About Cervical Cancer Prevention Using Pap Smears and HPV Testing*. Copies of these materials are in *Appendix E*.

5. DISCUSSION AND IMPLICATIONS

Clearly, the MCOs discussed here are vastly different from one another. Aetna, an independent practice association, and UHG, a network that offers services through six businesses operating in all 50 states and internationally, are for-profit operations. In contrast, Kaiser Permanente, with salaried providers, is the nation's largest nonprofit health plan.

In their examination of clinical guideline adoption and adherence, Biuso (2004) and Cabana et al. (1999) offered insight into barriers to clinical policy adoption among clinicians. In our discussion, we will concentrate on two clusters of influence discussed in Section 2.3—perception of innovation (Knowledge and Awareness of Cervical Cancer Screening Guidelines) and context (Managed Care Organizations)—and characteristics of those who adopt and adhere to guidelines.

5.1 Knowledge/Awareness of Cervical Cancer Screening Guidelines

The more knowledge individuals have about expected consequences of an innovation, the more likely they are to adopt that change. Hence, getting the message about cervical cancer screening guidelines out to providers is crucial. Rodgers (1995, p. 168) calls this "reduction of uncertainty." With that in mind, we would expect that Kaiser, through its iterative process for developing clinical guidelines and its formal distribution system, increases the probability of adoption of and adherence to clinical guidelines among its providers. Similarly Aetna, with its Clinical Policy Bulletin regarding cervical cancer screening and its extensive mailing to OB/GYN specialists and high volume primary care physicians should also positively impact adoption of and adherence to clinical guidelines. Because UHG is a very large, diversified network of health care providers, dissemination of information in this organization is more diffuse. Nevertheless, it advocates for USPSTF and ACOG recommendations and develops Technology Assessments which are available to its providers online.

5.2 Managed Care Organizations as Context

We define context as management practices that encourage and support, or discourage and impede, the actual process of spread of information (Berwick, 2003). How organizations or social systems deal with and promulgate change impacts that change. Rogers (1995, p. 372) identifies three types of leadership styles "optional," "collective," and "authority" and emphasizes that no one style is best in all circumstances or for all innovations.

Both Aetna and Kaiser employ a collective management style in the development and dissemination of its guidelines. At Aetna, the Medical Director of the Women's Health Department championed cervical cancer screening guidelines. Working closely with CDC to stay on message, and building on USPTF and ACOG recommendations, Aetna developed and published materials that it then distributed to providers and made available on the Internet to the general public. Similarly, Kaiser's Medical Assessment Department led the development and promulgation of cervical cancer screening guidelines within its

organization. In contrast, UHG employs what Rogers terms an authority style as it notifies its providers when their patients' test results or interventions differ from the gold standard—e.g., follow-up for positive Pap test results is not carried out. In this way UHG physicians are both made aware of clinical practice guidelines and admonished to adhere to them.

5.3 Characteristics of Individuals Who Adopt/Adhere to Guidelines

The third cluster of influence Berwick (2003) identified is characteristics of individuals who adopt/adhere to guidelines. This includes such things as the personalities of individuals who adopt an innovation. Cabana and associates (1999) reviewed 76 published studies describing barriers to adherence to clinical practice guidelines. They emphasized that physician adherence is critical in translating recommendations into improved outcomes, and pointed out that lack of awareness of or familiarity with guidelines affects physician adoption of guidelines. Further, physician attitudes, such as lack of agreement, self-efficacy, outcome expectancy, and the inertia of previous practice are also potential barriers to adopting an innovation. The scope of this study did not permit us to take a close look at provider characteristics and adherence to cervical cancer screening guidelines.

5.4 Limitations

Because our sample consists of only three MCOs, although they are large, national organizations, the information we gathered cannot be generalized to other MCOs. For this study, we had no data on very poor women who may access health services through Medicaid or older women who may access health services through Medicare. However, we recognize that most of the working-age women in this country who have insurance are likely to be covered by some kind of managed care plan.

With the exception of Kaiser with its salaried physicians, we also recognize that physicians contract with multiple plans so that the impact of one plan on a particular physician's adoption of guidelines may be limited (Dr. J. Armstrong, Director of Women's Health Department, Aetna; personal communication; May 5, 2004). Finally, our findings do not provide a clear understanding of clinical practice within the three MCOs. Nor do they allow us to differentiate screening practice and follow-up for diverse and underserved populations.

5.5 Implications and Next Steps

This study sheds light on three MCOs' awareness of ACS, ACOG, and USPSTF recommendations and how these MCOs have developed and communicated policies for cervical cancer screening to their physicians. By modifying and expanding the original study, in collaboration with CDC's Division of Cancer Prevention and Control (DCPC) and UnitedHealth Group (UHG), we will gain a better understanding of provider adherence to those policies.

We will begin by conducting a quantitative analysis of the treatment received by a large sample of women during the first year following an abnormal Pap test. The women will be drawn from a UHG research database that includes enrollment, physician, facility, and

laboratory claims data. In consultation with DCPC and RTI, UHG is developing the database containing the cohort and analytic variables that will be used in this analysis.

During the next stage of the project, we will conduct a qualitative analysis by reviewing selected charts to answer questions about the treatment received by women with cervical cytological abnormalities and cervical disease. Results of the study will be disseminated through publications in peer-reviewed journals.

Additional research might address guideline-related, patient-related, and environmental barriers to physician adoption and adherence. Such studies would help fill in the gap between knowledge and practice.

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Appendix A

Characteristics of Managed Care Organizations

Table A-1. Classification of Managed Care Organizations: Lives Covered and Geographic Region

MCO Name	Enrollment		Geographic Region				
	Lives Covered	Year	Nat'l	West	Midwest	Northeast	South
Aetna Inc.—Corporate Headquarters, Hartford	25,800,000	2002	✓				
Aetna Inc.—Corporate Headquarters, Blue Bell	14,400,000	2002	✓				
CIGNA HealthCare—Corporate Headquarters	14,318,000	2001	✓				
UnitedHealth Group—Corporate Headquarters	8,520,000	2002	✓				
Kaiser Permanente—Kaiser Foundation Health Plan, Inc.	8,400,000	2002		✓	✓		✓
Humana Inc.—Corporate Headquarters	6,631,400	2002	✓				
Health Net Inc.—Corporate Headquarters	5,300,000	2002		✓		✓	✓
PacifiCare Health Systems—Corporate Headquarters	3,226,000	2002		✓			✓
Aetna Inc. of Central and Eastern Pennsylvania	3,057,818	1999				✓	
Great West One Health Plan	2,600,000	2001	✓				
Mid Atlantic Medical Services Inc. (MAMSI)—Corporate Headquarters	1,800,000	2001				✓	✓
Oxford Health Plans Inc.—Corporate Headquarters	1,500,000	2002				✓	
Sierra Health Services Inc.—Corporate Headquarters	1,282,100	2001		✓			
Health Net Inc.—Northeast Corporate Headquarters	1,006,370	2001				✓	
AMERIGROUP Corporation	510,000	2002			✓		✓
Cariten Healthcare	447,017	2001	✓				
Aetna Health Plans of Mid-Atlantic	427,000	2000					✓
Molina Healthcare Inc.	405,454	2001		✓			
Coventry Health Care Inc.—Kansas City	144,210	2001			✓		
Aetna Inc.—Pennsylvania Region	95,566	2001				✓	
Coventry Health Care Inc.—Iowa	90,526	2001			✓		
AmCare—Corporate Headquarters	76,631	2000					✓

Table A-1. Classification of Managed Care Organizations: Lives Covered and Geographic Region (continued)

MCO Name	Enrollment		Geographic Region				
	Lives Covered	Year	Nat'l	West	Midwest	Northeast	South
Coventry Health Care Inc.—Louisiana	60,298	2001					✓
Coventry Health Care Inc.—Georgia Inc.	54,218	2001					✓
Coventry Health Care Inc.—Nebraska	44,507	2001			✓		
Coventry Health Care Inc.—Wichita	43,238	2001			✓		
AmeriHealth Insurance Company	12,822	2001					✓
Mayo Health Plan	8,247	1999		✓			✓
Mutual of Omaha Companies—Corporate Headquarters	not listed	not listed	✓				

Source: The National Directory of Managed Care Organizations, 4th edition
West: Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, Wyoming
Midwest: Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin
Northeast: Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Puerto Rico, Rhode Island, Vermont
South: Alabama, Arkansas, Delaware, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, Washington DC, West Virginia

Table A-2. Classification of Managed Care Organizations: Model, Coverage, and Plan Type

MCO Name	Model	Coverage[1]						Plan Type[1]		
		Com	Indv	Mcare	Supp Mcare	Mcaid	EPO	HMO	POS	PPO
Aetna Inc.—Corporate Headquarters—Hartford	IPA	✓						✓	✓	✓
Aetna Inc.—Corporate Headquarters—Blue Bell	IPA	✓		✓				✓	✓	✓
CIGNA HealthCare—Corporate Headquarters	Network	✓	✓	✓	✓	✓		✓	✓	✓
UnitedHealth Group—Corporate Headquarters	Network	✓	✓	✓	✓	✓		✓	✓	✓
Humana Inc.—Corporate Headquarters	IPA	✓	✓	✓	✓	✓		✓	✓	✓
Health Net Inc.—Corporate Headquarters	Network	✓	✓	✓	✓	✓		✓	✓	✓
PacifiCare Health Systems—Corporate Headquarters	not listed	✓		✓				✓	✓	✓
Aetna Inc. of Central and Eastern Pennsylvania	IPA	✓	✓	✓		✓	✓	✓	✓	✓
Great West One Health Plan	Mixed	✓						✓	✓	✓
Oxford Health Plans Inc.—Corporate Headquarters	IPA	✓	✓	✓		✓		✓		✓
Sierra Health Services Inc.—Corporate Headquarters[2]	Group	✓		✓	✓			✓	✓	✓
Health Net Inc.—Northeast Corporate Headquarters	IPA	✓						✓	✓	✓
Aetna Health Plans of Mid-Atlantic	IPA	✓						✓	✓	✓
Molina Healthcare Inc.	not listed	✓						✓		
Coventry Health Care Inc.—Kansas City	Mixed	✓		✓				✓	✓	✓
Aetna Inc.—Pennsylvania Region	IPA			✓				✓	✓	✓
Coventry Health Care Inc.—Iowa	IPA	✓		✓		✓		✓	✓	✓
AmCare—Corporate Headquarters	IPA	✓	✓			✓		✓		✓
Coventry Health Care Inc.—Louisiana	IPA	✓						✓	✓	✓
Coventry Health Care Inc.—Georgia Inc.	IPA	✓						✓	✓	✓

(continued)

Table A-2. Classification of Managed Care Organizations: Model, Coverage, and Plan Type (continued)

MCO Name	Model	Coverage[1]							Plan Type[1]	
		Com	Indv	Mcare	Supp Mcare	Mcaid	EPO	HMO	POS	PPO
Coventry Health Care Inc.—Nebraska	IPA	✓						✓	✓	
Coventry Health Care Inc.—Wichita	IPA	✓						✓	✓	✓
AmeriHealth Insurance Company	IPA	✓			✓			✓	✓	✓
Mayo Health Plan	IPA	✓								
Mutual of Omaha Companies—Corporate Headquarters	Mixed	✓	✓							✓
Kaiser Permanente—Kaiser Foundation Health Plan, Inc.	Salaried providers	✓	✓	✓		✓		✓		
Mid Atlantic Medical Services Inc. (MAMSI)—Corporate Headquarters	IPA	✓	✓	✓	✓	✓		✓	✓	✓
AMERIGROUP Corporation	not listed					✓		✓		
Cariten Healthcare	IPA	✓		✓	✓	✓		✓	✓	✓

[1]None of the companies list indemnity coverage or Medicare Plus plans. Com = commercial; Indv = individual; Mcare = Medicare; Supp Mcare = supplemental Medicare; Mcaid = Medicaid; EPO = exclusive provider organization; HMO = health maintenance organization; POS = point of service; PPO = preferred provider organization

[2]Sierra Health Services Inc. lists Federal Employee Health Benefit Plan (FEHBP) coverage.

Source: The National Directory of Managed Care Organizations, 4th edition.

Appendix B

Participant Recruitment Tool Kit

- **Script for Initial Contact**
- **Fact Sheet**
- **CDC Letter of Support**
- **MCO Tracking Form**

First contact (recruiting) MCOs

We will begin by contacting Medical Directors for the prioritized 9 MCOs listed in our spread sheet. If there is a new medical director or a quality assurance person, try to reach them. If you have to go through a "gate keeper" be sure to get his/her name and provide as much information as necessary as per script below. Be sure to enter account code 08633.003 when you make these calls and use respective tracking form for the MCOs.

Script

Hello my name is _____, and I'm calling from Research Triangle Institute in North Carolina. We are one of the leading non-profit research organizations in the country in the fields of health and medicine, environmental protection, technology commercialization, education, and decision support systems.

We have been contracted by the Centers for Disease Control and Prevention to examine Managed Care Organizations' policies and practice with regard to screening and follow-up for abnormal Pap tests.

Our overall approach will focus on examining practice standards and guidelines in nine national Managed Care Organizations that represent various sizes (enrollment), numbers/types of plans, regions and populations served. We will be comparing MCO guidelines with those put forth by national provider organizations and national agencies like ACS and NCI. We have reviewed over 100 MCOs and have narrowed our list. *Name of MCO* is one of the organizations we'd like to include in our study.

I am calling to day to find out if *name of MCO* might be interested in participating in this project. Participation in the project would

- Require minimal time and effort.
- First, we would ask you to provide us with copies of your policy/recommendation/guidelines and any patient education information about screening for and disease management of cervical cancer.
- We will then review the materials and
- call you for a short discussion (15-20 minutes) about the materials and your organization's policy and practice.
- Finally our conversation will be summarized in a draft report, which we will then ask you to review for accuracy. You will receive a copy of this report.

Your report along with reports from the 8 other MCOs will then be submitted to CDC.

Does *name of MCO* have written formal policies about screening and follow-up for abnormal Pap tests?

If no: (Be sure that you are talking to someone who knows whether or not there is a policy.) Thank you for your time

If yes: Using the tracking form probe for the regional offices, plan types, and products

Do you have any questions?

Offer to send fact sheet about the project and to call back if necessary.

Confirm contact information – and find out who will be sending the materials we requested. Get their contact information also.

Thank you for your time – we look forward to working with you.

IMPORTANT: enter correct contact information in tracking form and note details from contact in the order they occur. Be sure to include date for contact. See examples below

11/05 Called John Doe MCO Med Director at 202 202 2202

11/05 left message for John Doe at 202 202 2202

11/06 John Doe returned message asked for Fact sheet.

11/06 John Doe indicated by phone that MCO is interested in participating and referred to Mary Jane at 202 202 2203.

11/06 Mary Jane will be sending policy and education materials to RTI

11/14 Reminder call to Mary Jane – she will send today

11/16 MCO Materials received and archived.

Fact Sheet

Examine Current Clinical guidelines of MCOs Regarding the Management of Women with Cervical Cytological Abnormalities

Purpose: The Centers for Disease Control and Prevention (CDC) seeks to gain an overall picture of current recommendations for follow-up of abnormal results in national managed care organizations (MCOs). RTI has been contracted by CDC to review national consensus guidelines developed by governmental agencies and professional/patient associations e.g. National Cancer Institute, American Cancer Society, and American College of Obstetricians and Gynecologists. Although recommendations from these guidelines are not mandatory, they are followed by many physicians and some managed care organizations have adopted their own standards and protocols for screening and follow-up. RTI will compare and contrast the national guidelines with screening and follow-up policies for cervical cancer in targeted national managed care organizations.

Research Design & Methods: Our overall approach will focus on examining practice standards and protocols in nine targeted national MCOs that represent various sizes (enrollment), numbers/types of plans, regions and populations served. In Phase I, we will collect policies/recommendations from the targeted organizations and compare them with national guidelines. In Phase II we will discuss our observations with respective Medical Directors (or designee) and get input as to our understanding of their policies. During our conversations with the MCO representatives we will also explore how guidelines do/do not vary with respect to patient population served, region, or organization size. Additionally we will identify differences between centralized and regional policies in the same MCO and the extent to which policies are aligned with identified national policies. In Phase III we will confirm our findings with the respective MCOs. Summary of our findings will be submitted to CDC.

About RTI: RTI International, one of the leading non-profit research organizations in the country, is dedicated to conducting innovative, multidisciplinary research that improves the human condition. With a worldwide staff of more than 1,950 people, RTI International is active in the fields of health and medicine, environmental protection, technology commercialization, education, and decision support systems.

Participating Organizations: Managed Care Organizations will be recruited based on criteria listed above as well as their interest in the project.

Funding Agency: Centers for Disease Control and Prevention (CDC)

Award Period: August 1, 2003 – October 1, 2004

Questions: For more information contact: Linda G. Pucci, BSN, MPH 919-316-3442 lpucci@rti.org

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

May 5, 2004

Dr. Cheryl Pegus
AETNA Inc.
980 Jolly Road
Mail Stop U12S
Blue Bell, PA 19422

Dear Dr. Pegus:

We are writing to enlist your participation in a study funded by the Centers for Disease Control (CDC) that is being implemented by RTI International, a not-for-profit research firm based in the Research Triangle Park, North Carolina. See attached Fact Sheet. The goal of this study is to examine current managed care clinical recommendations/policies for screening and follow-up of women with cervical cytological abnormalities. Your involvement in the study would require a minimum of time and effort.

We selected 9 MCO's to represent various sized organizations (measured in enrollment), as well as regions of the country, types of plans and special populations served. As one of the chosen 9 MCO's, we very much need your participation.

An RTI associate will be contacting you to ask your help in collecting your organization's policy or recommendations for Pap test and any patient education materials you are distributing. The materials will be reviewed and summarized and the associate will then contact you for a brief conversation to fill in gaps and confirm the information.

This is an important study, and your participation is crucial in obtaining a national picture of MCO recommendations and practice guidelines for cervical cancer screening. Thank you in advance for your consideration and help.

Sincerely,

Vicki Benard

Vicki Benard, PhD
Center for Disease Control and Prevention
Division of Cancer Prevention and Control
4770 Buford Hwy NE, MS K-55
Atlanta, GA 30341

Participant ☐ Yes ☐ NO
If no, give reason.

MCO Corporate Name

Street Address

City State ZIP

Medical Director

Phone Fax

email

Medical Director assistant

Phone Fax

email

Referral Contact

Phone Fax

email

Referral Contact

Phone Fax

email

Referral Contact

Phone Fax

email

Referral Contact

Phone Fax

email

Referral Contact

Phone Fax

email

Products Offered by name

Types of Plans

Contact date	Tracking notes

Appendix C

Aetna Materials

- **Clinical Policy Bulletin 0443**
- **Physician Survey**
- **Patient Flyer in English**
- **Patient Flyer in Spanish**
- **Cover Letter**
- **Physician Flyer**
- **Poster**

We want you to know™
Aetna
Close this window

Clinical Policy Bulletins

Number: 0443
Subject: Cervical Cancer Screening

Important Note

This Clinical Policy Bulletin expresses Aetna's determination of whether certain services or supplies are medically necessary. Aetna has reached these conclusions based upon a review of currently available clinical information (including clinical outcome studies in the peer-reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). Aetna expressly reserves the right to revise these conclusions as clinical information changes, and welcomes further relevant information. ***Each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their providers will need to consult the member's benefit plan to determine if there are any exclusions or other benefit limitations applicable to this service or supply.*** The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (i.e., will be paid for by Aetna) for a particular member. The member's benefit plan determines coverage. Some plans exclude coverage for services or supplies that Aetna considers medically necessary. If there is a discrepancy between this policy and a member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid members. CMS's Coverage Issues Manual can be found on the following website: http://cms.hhs.gov/manuals/pub06pdf/pub06pdf.asp.

Policy

I. Aetna considers annual cervical cancer screening with conventional or liquid-based Papanicolaou (Pap) smears a medically necessary preventive service. Aetna considers Pap smear screening *not* medically necessary for women who have undergone complete hysterectomy for benign disease (e.g., no evidence of cervical neoplasia or cancer) or have absent cervix.

Note: Medically necessary cervical cancer screening is covered under plans that cover routine physical exams, routine gynecological exams and/or routine Pap smears. Please check benefit plan descriptions for details.

II. Diagnostic Pap smears are considered medically necessary when *any* of the following conditions is met:

1. Pap smear is accompanied by a diagnosis of a malignancy of the female genital tract (i.e., cervix, ovary, vagina, or uterus); *or*
2. There is a description of symptoms or a disease requiring diagnosis by a Pap smear, for example:

    a. Vaginal tumor
    b. Chronic cervicitis

c. Abnormal vaginal bleeding or discharge; *or*

3. Following gynecological surgery for cancer; *or*
4. Member has been exposed to diethylstilbesterol (DES); *or*
5. Member has any of the following risk factors for cervical cancer:

   a. Immunosuppression
   b. History of cervical, vaginal or vulvar cancer
   c. HIV infection
   d. History of genital HPV infection
   e. Previously abnormal Pap smear
   f. Previous sexually transmitted disease
   g. Multiple sexual partners.

III. Aetna considers automated liquid-based thin-layer slide preparation methods (ThinPrep® PapTest™, SurePrep™ Liquid Based Pap Test, AutoCyte PREP System™) medically necessary as an alternative to conventional Pap smears when the criteria for conventional Pap smears are met.

IV. Note: Aetna considers automated cervical cancer slide interpretation systems (e.g., FocalPoint Slide Profiler (formerly AutoPap), PAPNET) to be an integral part of the Pap smear. Slide interpretation systems (whether human or automated) of some or all Pap smears are considered part of the laboratory's quality control methods.

V. Aetna considers human papilloma virus (HPV) DNA testing to be medically necessary for the following indications:

   1. HPV DNA testing is considered medically necessary for assessment of women with ASCUS (atypical squamous cells of undetermined significance), using the Hybrid Capture II technique. This is consistent with the National Cancer Institute's interim guidelines for managing abnormal cervical cytology as well as the position of the American Society of Colposcopy and Cervical Pathology for the management of ASCUS.
   2. The use of a combination Pap smear and HPV DNA screening is considered medically necessary for screening women aged 30 years and older. If this combination is used, it is not considered medically necessary to rescreen women who receive negative results on both tests more frequently than every 3 years. This policy is consistent with guidelines from the American College of Obstretricians and Gynecologists (2003).

VI. Aetna considers HPV testing to be experimental and investigational when used as a primary screening test for cervical cancer in women younger than 30 years of age. According to evidence-based guidelines from the U.S. Preventive Services Task Force (2003), the medical literature does not support HPV testing as a screening test for cervical cancer for younger individuals whose cervical cytology is normal or is unknown. In addition, HPV testing is not considered medically necessary for members with definitively positive cervical cytology.

VII. Aetna considers cervicography or speculoscopy (Pap-Sure) to be experimental and investigational for the screening or diagnosis of cervical cancer because of a lack of adequate large prospective randomized controlled clinical trials related to their use.

Background

Pap smears consist of cells removed from the cervix, which are specially prepared for microscopic examination. The cells are removed by brushing or scraping the cervix during a pelvic examination and then placing the cells on one or more glass slides. Each slide typically contains hundreds of thousands of cells. All Pap smears should be sent to an accredited laboratory to be stained, examined under a microscope, and interpreted. The test is used as the principal screening test to detect cervical cancer in asymptomatic women. It can detect precancerous changes or cancer of the cervix or vagina. A Pap test will only rarely detect cancer of the ovaries or endometrial cancer. It can also find some infections of the cervix and vagina.

The American Cancer Society, National Cancer Institute, American College of Obstetricians and Gynecologists, American Medical Association, and the American Academy of Family Physicians recommend that all women who are or have been sexually active, or who have reached age 18, should have annual Pap smears. The recommendation allows less frequent Pap testing after 3 or more annual smears have been normal, at the discretion of the physician. For women who have had repeated negative tests, the marginal gain from screening more often than every 3 years decreases sharply. However, because of the difficulty in identifying patients at increased risk for cervical cancer, most physicians will recommend a Pap test be performed at least once a year.

After age 65, there is no clear consensus on the need for Pap smears in women who have had previous adequate screening. The American Academy of Family Physicians recommends that at age 65, screening may be discontinued if there is documented evidence of previously negative smears; however, these recommendations are currently under review. The American College of Physicians (ACP) recommends Pap smears every 3 years for women aged 20-65, and every 2 years for women at high risk. The ACP also recommends screening women aged 66-75 every 3 years if not screened in the 10 years before age 66.

Pap testing need not be performed for women who had a hysterectomy for benign disease; however, women who had a hysterectomy performed in which the cervix was left intact probably still require screening. However, a recent study by Sirovich and Welch (2004) indicated that many US women who have undergone hysterectomy are undergoing Pap smear screening despite the U.S. Preventive Services Task Force's recommendation that Pap smear screening is unnecessary for women who have undergone a complete hysterectomy for benign disease.

Repeat Pap smears may be indicated 3-4 months following local treatment of vaginal infection/inflammation, and 2-3 months following a Pap test suggestive of mild dyskaryosis or if the initial Pap smear results were unsatisfactory due to inadequate sampling.

To decrease the number of false-negative Pap smears, new technologies for screening or preparing the Pap smear have been approved by the Food and Drug Administration (FDA). The FocalPoint (TriPath) rescreens Pap smears read as normal, and then tries to identify the false-negative interpretation errors. The ThinPrep® PapTest™ (Cytyc), and AutoCyte "PREP" System™ (TriPath) are new automated liquid-based thin layer slide preparation techniques

Automated System (FocalPoint, PAPNET)

Computerized re-screening (e.g., PapNet, TriPath Imaging Inc.) is designed to automate re-screening of Pap smears initially read as negative by a cytotechnologist. Algorithm-based prescreening (e.g., FocalPoint (formerly AutoPap), TriPath Imaging Inc.) identifies slides that exceed a selected probability for containing abnormal cells.

It is not known whether automated rescreening methods are more effective than human rescreening in detecting more cervical cancers. An Agency for Healthcare Research and Quality technology assessment of cervical cancer screening techniques (McCrory, et al., 1999) concluded that there is substantial uncertainty about the estimates of sensitivity and specificity of computerized rescreening technologies compared with conventional Pap testing, which in turn results in substantial uncertainty about the estimates of the effectiveness and cost-effectiveness of these techniques. "Although it is clear that both thin-layer cytology and computerized rescreening technologies provide an improvement in effectiveness at higher cost, the imprecision in estimates of effectiveness makes drawing conclusions about the relative cost-effectiveness of thin-layer cytology and computerized rescreening technologies problematic."

A technology assessment for the Minnesota Health Technology Advisory Committee (1999) concluded:

> Studies of these methods demonstrate that computer-assisted cervical cancer screening and rescreening modestly improves detection of false-negative smears as compared with

> conventional manual screening. The majority of false-negative smears detected are low-grade squamous intraepithelial lesions (LGSIL), reactive or reparative changes, or atypical squamous cells of undetermined significance (ASCUS) rather than the more serious premalignant or malignant lesions. Some studies have shown that computer-assisted Pap smear screening may marginally improve health outcome for some patients. The net health benefits of computer-assisted screening have not been proven. Studies examining the cost-effectiveness of the new technologies indicate that the cost-benefit of computer-assisted rescreening technologies is less favorable than any manual rescreening alternatives.

The American College of Obstetricians and Gynecologists (1998) concluded:

> Despite the recent FDA approvals of new Pap test screening techniques (ThinPrep, AutoPap, PAPNET), these technologies do not represent the current standard of care in cervical cancer screening .... While the new techniques improve on the sensitivity of the Pap test, their routine use cannot be recommended based on costs and the lack of sufficient data demonstrating whether they reduce the incidence of or improve the survival rate from invasive cervical cancer.

An assessment of algorithm-based screening and rescreening technologies conducted by the Research Triangle Institute Evidence-Based Practice Center for the Agency for Healthcare Research and Quality (Hartmann, et al., 2002) concluded that "[o]verall, the quality of this literature is poor for the purposes of making decisions about choice of screening systems in US populations. No randomized trials or prospective cohort studies relate use of a screening modality over time to outcomes for individual women. The cost-effectiveness of use of new technologies has only been estimated, not measured directly."

More recently, the U.S. Preventive Services Task Force (USPSTF, 2003) reached the following conclusions regarding Pap rescreening techniques:

> The USPSTF concludes that the evidence is insufficient to recommend for or against the routine use of new technologies to screen for cervical cancer. The USPSTF found poor evidence to determine whether new technologies, such as liquid-based cytology, computerized rescreening, and algorithm based screening, are more effective than conventional Pap smear screening in reducing incidence of or mortality from invasive cervical cancer. Evidence to determine both sensitivity and specificity of new screening technologies is limited. As a result, the USPSTF concludes that it cannot determine whether the potential benefits of new screening devices relative to conventional Pap tests are sufficient to justify a possible increase in potential harms or costs.

Automated Liquid-Based Thin-Layer Slide Preparation (ThinPrep, AutoCyte PREP)

With the ThinPrep System, a conventional Pap smear is not performed. Using a spatula and a brush or a cervical broom, the cervical area is sampled and the devices are rinsed in a fixative solution. The slide is then automatically made in the laboratory, which decreases the possibility of air-drying artifacts. It is then stained and read by a technician or a cytopathologist.

AutoCyte PREP System is another liquid-based thin-layer sample preparation system that automatically prepares and stains cytology slides.

A standardized method of reporting cytology findings was developed by the National Cancer Institute called the "Bethesda System". In the Bethesda System, potentially premalignant squamous lesions fall into three categories: *atypical squamous cells of undetermined significance (ASCUS), low-grade squamous intraepithelial lesions (LSIL), and high-grade squamous intraepithelial lesions (HSIL)*. Low-grade squamous intraepithelial lesions include CIN 1 (mild dysplasia) and the changes of HPV, termed *koilocytotic atypia*. High-grade squamous intraepithelial lesions include CIN 2 and CIN 3 (moderate

dysplasia, severe dysplasia, and carcinoma in *situ*). Other classification systems in use include the Dysplasia/CIN System and the Papanicolaou System.

SurePath (formerly known as the AutoCyte Prep) is a liquid-based cytology system that uses centrifugation to separate cells from obscuring material.

An assessment for the European Cervical Cancer Screening Network's Guidelines for Quality Assurance in Cervical Cancer Screening (Nieminen, 2003) summarized the current evidence for automated cervical cancer screening and re-screening systems:

> There are several articles published concerning the performance of automation assisted screening. They show generally a better sensitivity with at least same specificity than conventional screening. Most of these articles have been retrospective (quality control) and/or relatively small numbers of smears have been studied. However, randomised, prospective public health trials in primary screening setting have been published very few. The show equal or slightly better performance compared to manual conventional screening …. When implementing the new methods, it is needed to carefully ascertain and evaluate the performance of the method in primary (public health) screening up to the final invasive end points with randomised prospective studies.

Wain (1997) has commented that "[t]he performance of automated techniques in quality assurance should be assessed against other methods of quality assurance, such as random re-screening of a mandated proportion of smears, directed re-screening of 'high-risk' groups and 'rapid re-screening'."

In its updated guidelines on cervical cancer screening, the American Cancer Society expert review panel (Saslow, et al., 2002) only considered screening technologies with sufficient published clinical data, and excluded automated screening from its consideration.

HPV Testing

Human papillomavirus (HPV) has been associated with the development of cervical intraepithelial neoplasia (CIN) and invasive cancer of the cervix. Recent prospective studies have shown that abnormal Pap smears that are HPV positive are much more likely to be associated with abnormal colposcopic findings than abnormal Pap smears that are HPV negative.

HPV testing has been proposed as an adjunctive test in women with ASCUS to identify those at highest risk for cervical cancer, who should go on to receive definitive colposcopy. HPV testing of patients with ASCUS can be used to identify patients at highest risk of underlying cervical dysplasia, and minimize the number of unnecessary colposcopic examinations in women who have no disease.

HPV testing has also been proposed as a primary screening test to be performed simultaneously with Pap smear screening. Digene Corp. received FDA approval for a test that combines the Pap smear with a genetic exam for 13 oncogenic strains of HPV. Aetna, however, does not cover HPV testing as a screening test for cervical cancer for women less than 30 years of age because the evidence is insufficient to determine whether HPV screening reduces the incidence of or mortality from invasive cervical cancer. Aetna's policy is consistent with recently updated recommendations of the U.S. Preventive Services Task Force (USPSTF) (2003). The USPSTF concluded that the evidence is insufficient to recommend for or against the routine use of human papillomavirus (HPV) testing as a primary screening test for cervical cancer. The USPSTF found "poor evidence to determine the benefits and potential harms of HPV screening as an adjunct or alternative to regular Pap smear screening."

The American College of Obstetricians and Gynecologists (2003) concluded, based on "limited and inconsistent scientific evidence" that the use of a combination of cervical cytology and HPV DNA screening is appropriate for women aged 30 years and older. According to ACOG (2003), if this combination is used, women who receive negative results on both tests should be rescreened no more

frequently than every 3 years. ACOG's recommendation was based on the results of studies that demonstrated that women aged 30 years and older who had both negative cervical cytology test results and negative high-risk type HPV-DNA test results were at extremely low risk of developing CIN 2 or CIN 3 during the next 3-5 years (Sherman, 2003; Schiffman, 2000; Belinson, 2001; Petry, 2003). ACOG guidelines explain that any woman aged 30 years or older who receives negative test results on both cervical cytology screening and HPV DNA testing should be rescreened no more frequently than every 3 years. The ACOG guidelines state that the combined use of these modalities has been shown to increase sensitivity but also decrease specificity and increase cost. However, ACOG estimated that the increase in screening interval will offset the cost of this new screening regimen.

The ACOG guidelines (2003) state that the combination of cytology and HPV DNA screening should be restricted to women aged 30 years and older because transient HPV infections are common in women younger than 30 years, and a positive test result may lead to unnecessary additional evaluation and treatment.

Published studies of cervical cancer screening using a combination of cytology and HPV DNA tests have predominantly employed conventional Pap smears for assessment of cervical cytology. Although there are no studies directly comparing the screening performance of HPV-cytology combination testing using a conventional Pap versus liquid-based cervical cytology, available indirect evidence suggests that there is no clinically significant difference in the screening performance of HPV-cytology combination testing regardless of whether conventional or liquid-based cervical cytology is used (Lörincz and Richart, 2003).

The National Cancer Institute is currently sponsoring a multicenter 5-year clinical trial directed at determining the role of HPV testing in the management of cervical disease. Interim guidelines for the management of abnormal cytologic findings in the cervix were developed at a workshop sponsored by the NCI, which concluded that HPV testing can be used as an adjunctive test to help identify patients at low or high risk of developing CIN and cancer. The American Society of Colposcopy and Cervical Pathology has also issued guidelines for the management of ASCUS which incorporated HPV testing and typing to determine which women with ASCUS should undergo colposcopy.

Cervicography and Speculoscopy

Cervicography is procedure in which the cervix is swabbed with an acetic acid solution to identify acetowhite changes in the cervix. With Cervicography, a photograph of the cervix is taken with a special camera (Cerviscope), and is sent to trained technicians for evaluation (National Testing Laboratories, St. Louis, MO). The technicians determine whether the visual image is most compatible with normal, atypia/metaplasia, intraepithelial neoplasia, or cancer. In contrast, speculoscopy (PapSure) uses a chemiluminescent light to aid naked-eye or minimally magnified visualization of acetowhite changes on the cervix. Both Cervicography and speculoscopy have been used as an adjunct to Pap smear for cervical cancer screening and as a triage method to identify which patients with low grade atypical Pap smears need further evaluation by colposcopy and biopsy. According to practice guidelines from the American Society of Colposcopy and Cervical Pathology (ASCCP), "there have been insufficient large scale controlled studies related to their use in the triage of LGISL [low grade squamous intraepithelial lesion] to recommend either for or against their use" (Cox, et al., 2000). An International Academy of Cytology (IAC) Task Force (van Niekerk, et al., 1998) concluded that "[t]he role of cervicography, or high resolution photography, as a screening device remains to be defined." The IAC Task Force also noted that "[t]here are, at present, insufficient data for the evaluation of speculoscopy…." The U.S. Preventive Services Task Force (1996) concluded that "[t]here is insufficient evidence to recommend for or against routine screening with cervicography …., although recommendations against such screening can be made on other grounds."

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August 31, 2004

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Physician Survey

Let us know if our educational efforts are useful!

Your feedback helps us improve our efforts to provide meaningful information to you and your patients. Please take a moment to answer a few questions — your responses are confidential.

PLEASE RESPOND BY MAY 1, 2004.

1. Prior to this mailing, were you aware of the updated recommendations to use combination HPV DNA test and Pap smear as a primary cervical cancer screening option for women age 30 and older? ❑ Yes ❑ No

2. If yes, how and from whom did you hear of this recommendation? (Check all that apply.)

   A. ❑ E-mail ❑ Website
   ❑ Journal or newsletter ❑ Other

   B. ❑ ACOG ❑ ACS ❑ Aetna ❑ Digene
   ❑ Health plan other than Aetna
   ❑ Other

3. Are you aware that the recommended interval for cervical cancer screening in women age 30 and older whose HPV DNA test and Pap smear are negative is every 3 years? ❑ Yes ❑ No

4. Are you planning to discuss the combination HPV DNA test and Pap smear as a cervical cancer screening option with your patients who are age 30 and older? ❑ Yes ❑ No

5. Will you share the information contained in this mailing with your patients? ❑ Yes ❑ No

6. In general, do you find the educational materials (fact sheets, posters, quick guides/guidelines) that Aetna sends useful in supporting or influencing your clinical practice activities? ❑ Yes ❑ No

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Cervical Cancer Screening

Ask your doctor about TWO important tests.

Screening for cervical cancer with a Pap smear along with an HPV DNA test is now recommended for women age 30 and over.

- Nearly all cervical cancer is caused by a virus — HPV (human papillomavirus). HPV is a sexually transmitted disease. There are many types of HPV, but only certain types are associated with cervical cancer.
- Almost every woman will have HPV at some point in her lifetime. In fact, HPV is very common in women younger than age 30, and the virus almost always goes away on its own. **Most women with HPV never get cervical cancer.**
- HPV is less common in women over 30, but if the virus is present, it may have been there a while. **Women with a persistent HPV infection — an infection that doesn't clear up on its own** — are at higher risk for getting cervical cancer.
- **Like the Pap smear, the HPV DNA test uses cells collected from your cervix. The HPV DNA test can be done at the same time as your Pap smear.**
- Knowing if you have HPV can help determine your risk of developing cervical cancer. This helps you and your doctor decide how often you should be screened.
- **If you are 30 or older and your Pap smear and HPV DNA test are both negative (normal), you should wait three years before being checked again for cervical cancer.**
- If your HPV DNA test is positive, your doctor will check you more frequently for cervical cancer. Testing positive does not mean you or your partner have done anything wrong.
- An annual exam with your gynecologist is still important, regardless of your HPV status. Even if you can safely wait three years between tests, remember to visit your doctor once a year for a clinical breast examination, blood pressure screening and other routine, preventive medical needs.

CERVICAL CANCER SCREENING RECOMMENDATIONS of the American Cancer Society and American College of Obstetricians and Gynecologists

3 years after you begin having vaginal intercourse, or at age 21

> Start annual Pap smears

Under age 30

> Annual Pap smear

Age 30 and over

> Pap smear plus HPV DNA test every 3 years if results are normal (no abnormalities)

OR

> Annual Pap smear (or Pap smear every 1 to 3 years after 3 consecutive years of normal results)

Information obtained from the following sources: 1) American Cancer Society. Cancer Facts and Figures 2003. Atlanta (GA):ACS;2003. 2) Cervical cytology screening. ACOG Practice Bulletin No. 45. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2003:102; 417-27.

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Pruebas de detección del cáncer cervical

Pregunte a su médico sobre DOS pruebas importantes.

Actualmente, se recomienda que las mujeres de 30 años de edad o más se sometan a una exploración para cancer cervical con un papanicolau, junto con una prueba de ADN de PVH.

- Prácticamente todo cáncer cervical es causado por un virus — el PVH (papillomavirus humano). Hay muchos tipos de PVH, sin embargo sólo ciertos tipos están asociados al cáncer cervical.
- Casi todas las mujeres tendrán el PVH en algún punto de sus vidas. De hecho, el PVH es muy común en las mujeres menores de 30 años, y casi siempre el virus desaparece por sí solo. **La mayoría de las mujeres con PVH jamás tendrá cáncer cervical.**
- El PVH es menos común en mujeres de más de 30 años de edad; pero si el virus está presente, es posible que hace tiempo que lo tiene. **Las mujeres con una infección persistente de PVH — una infección que no desaparece sola — tienen mayor riesgo de tener cáncer cervical.**
- **Como el papanicolau, la prueba de ADN de PVH utiliza células retiradas del cervix. La prueba de ADN de PVH puede hacerse al mismo tiempo que su papanicolau.**
- **El saber si usted tiene PVH puede ayudar a determinar su riesgo de desarrollar cáncer cervical.** Esto ayuda a usted y a su médico a decidir con qué frecuencia se le debe realizar una prueba.
- **Si usted tiene 30 años de edad o más y su prueba de ADN de PVH y papanicolau tienen ambos resultados negativos (normal), debe esperar tres años para su próxima prueba de detección de cáncer cervical.**
- Si su prueba de ADN de PVH es positiva, su médico le hará chequeos más frecuentes de detección para cáncer cervical. Que su prueba tenga resultado positivo no significa que usted o su compañero haya hecho nada incorrecto.
- **Un examen anual con su ginecólogo aún es importante, independiente de su situación de PVH.** Aunque usted pueda, sin peligro, esperar tres años entre pruebas; recuerde visitar a su médico una vez al año para un examen clínico de mamas, chequeo de presión sanguínea y otras necesidades médicas preventivas y de rutina.

RECOMENDACIONES PARA PRUEBAS DE DETECCIÓN DEL CÁNCER CERVICAL

según la Sociedad Americana del Cáncer y el Colegio Americano de Obstetras y Ginecólogos

3 años después de haber comenzado a tener relaciones sexuales vaginales, o a los 21 años de edad

> Iniciar papanicolaus anuales

Menor de 30 años

> Papanicolau anual

30 años o más

> Papanicolau más prueba de ADN de PVH cada 3 años si los resultados son normales (sin anormalidades)

O

> Papanicolau anual (o papanicolau cada 1 a 3 años después de 3 años consecutivos de resultados normales)

Información obtenida de las siguientes fuentes: 1) Sociedad Americana del Cáncer Datos y números del cáncer 2003. Atlanta (GA):ACS;2003. 2) Detección citológica cervical. ACOG Boletín de Práctica No. 45. Colegio Americana de Obstetras y Ginecólogos. *Obstet Ginecol* 2003:102; 417-27.

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980 Jolly Road
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January 2004

Dear Physician and Practice Associates:

It is well known among medical experts that human papillomavirus (HPV) is the primary cause of cervical cancer, and that testing for HPV plays an important role in cervical cancer screening. Many women, however, do not understand the relationship between HPV and cervical cancer.

We want to work with you to change this.

Now there is a new test that can improve on the sensitivity of the Pap smear and help women know their risk for cervical cancer. The HPV DNA test, in combination with a Pap smear, has been approved by the FDA as a primary cervical cancer screening tool for women ages 30 and older.

Both the American Cancer Society and the American College of Obstetricians and Gynecologists (ACOG) support HPV DNA testing, along with a Pap smear, for cervical cancer screening in this age group. In addition, **women over age 30 who have both a normal Pap smear and no evidence of HPV infection should be screened for cervical cancer no more frequently than once every three years**, according to ACOG. Aetna's clinical policy for cervical cancer screening coverage is consistent with these recommendations. As a reminder, Aetna covers HPV DNA testing in combination with the Pap smear for primary cervical cancer screening for women ages 30 and older. Annual gynecologic examinations, including pelvic exams, are still recommended and continue to be covered for Aetna members.*

Please read and share the enclosed materials with your patients.

Aetna developed the enclosed educational materials to help update you on new cervical cancer screening guidelines and advances and to help ensure that your patients are more fully educated about HPV and its role in the development of cervical cancer. Additional information can be found at:

- American Cancer Society: www.cancer.org
- American College of Obstetricians and Gynecologists: www.acog.org
- American Society for Colposcopy and Cervical Pathology: www.asccp.org
- National HPV & Cervical Cancer Public Education Campaign: www.cervicalcancercampaign.org

Let us know if our educational efforts are useful.

Your feedback helps us improve our efforts to provide meaningful information to you and your patients. After you have read through the materials, please take a moment to complete the brief, postage-paid survey card. Thank you for your support and involvement in this important women's health initiative.

Sincerely,

Joanne Armstrong, M.D.
Senior Medical Director
Women's Health

C204
Enclosures

*Please call the Member Services number on your patient's ID card for specific provisions for coverage and exclusions.

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Updated Cervical Cancer Screening Guidelines

For Health Care Professionals

The combined use of a Pap smear and an HPV DNA test is a recommended primary cervical cancer screening option for women ages 30 and older.[1,2]

- Human papillomavirus (HPV) is a recognized risk factor for cervical cancer. Persistence of oncogenic strains of the virus is important to the development of cervical cancer.[3]
- The increased sensitivity of the HPV DNA test, when coupled with a traditional Pap smear, is more reliable than a Pap smear alone in determining which women are at risk of developing cervical disease.[3]
- Due to the transient nature of HPV infection in women under 30, combination testing is not appropriate in this age group.
- Aetna covers primary HPV DNA screening in conjunction with either conventional Pap smears or liquid-based cytology. The clinical efficacy of the HPV DNA testing is comparable when done with conventional Pap smears or liquid-based testing. Aetna's clinical policy for cervical cancer screening coverage is consistent with these recommendations.
- **The recommended testing interval when both Pap smear and HPV DNA test are negative is every three years.[1] There are no additional benefits to more frequent testing. Aetna's clinical policy for cervical cancer screening coverage is consistent with these recommendations.**
- HPV DNA testing as a follow-up to an ASC-US Pap smear result is appropriate for women of all ages to help determine if further evaluation is needed.[1]
- Women should continue visiting their physicians annually, regardless of their test results, for routine preventive health maintenance and care.

CERVICAL CANCER SCREENING RECOMMENDATIONS

of the American Cancer Society and American College of Obstetricians and Gynecologists[1,2]

3 years after onset of vaginal intercourse, or at age 21

> Start annual Pap smears

Under age 30

> Annual Pap smear

> Follow-up ASC-US with reflex HPV test

Age 30 and over

> Pap smear plus HPV DNA test every 3 years if results are negative

> May select annual or biennial Pap smear alone

> If results are discordant, refer to published guidelines in *JAMA*[4]

[1]American Cancer Society. Cancer Facts and Figures 2003. Atlanta (GA): ACS; 2003.

[2]Cervical cytology screening. ACOG Practice Bulletin No. 45. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2003; 102: 417-27.

[3]Clavel et al. Human Papillomavirus Testing in Primary Screening for the Detection of High-grade Cervical Lesions. *Brit J Cancer* 2001; 89: 1616-23.

[4]Wright et al. 2001 Consensus Guidelines for the Management of Women with Cervical Cytological Abnormalities. *JAMA* 2002; 287: 2120-9.

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Cervical Cancer Screening Just Got Better

If you are 30 years or older, ask your doctor about getting a Pap smear and an HPV DNA test at the same time.

Nearly all cervical cancer is caused by a virus — HPV (human papillomavirus). There are many types of HPV, but only certain types are associated with cervical cancer.

ASK YOUR DOCTOR ABOUT TWO IMPORTANT TESTS

> PAP SMEAR

Looks for any cell changes in your cervix that are not normal.

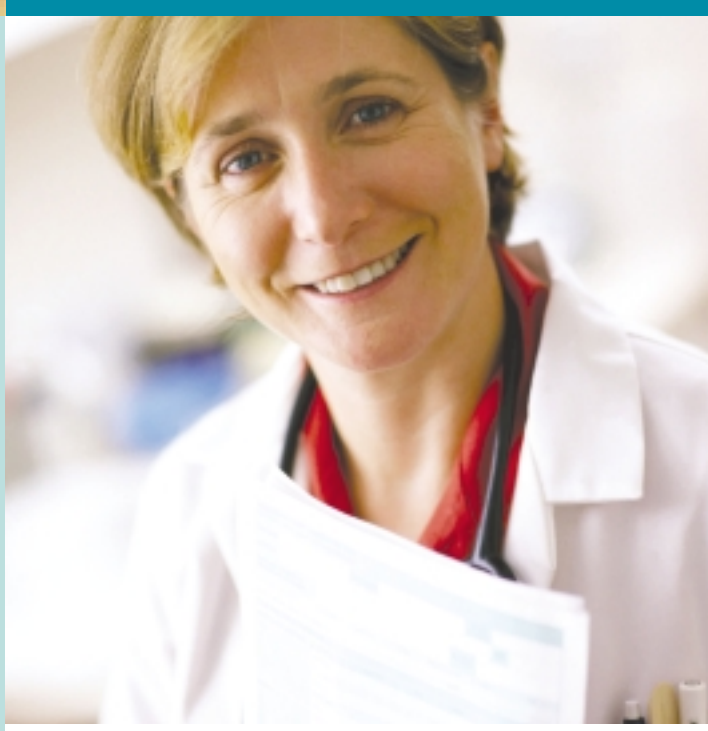
> HPV DNA TEST

Checks for the types of the virus that can lead to cervical cancer.

Getting both tests together makes it more likely that any abnormal cells will be found.

If your Pap smear and HPV DNA test are negative, you don't need to be checked for cervical cancer for **another three years**.

Give yourself the best protection against cervical cancer.
Talk to your doctor TODAY about having both a Pap smear and an HPV DNA test.



Information obtained from the following sources: 1) American Cancer Society. Cancer Facts and Figures 2003. Atlanta (GA):ACS;2003. 2) Cervical cytology screening. ACOG Practice Bulletin No. 45. American College of Obstetricians and Gynecologists. *Obstet Gynecol* 2003:102; 417-27.

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Appendix D

UnitedHealth Group Materials

Pap Test In-Depth (Web page)

myuhc.com

UnitedHealthcare
A UnitedHealth Group Company

Welcome Client Name:
Today is November 29, 2004

Tests & Treatments

Pap Test In-Depth

healthwise
for every health decision

Pap Test

Test Overview

The Pap test is used to screen women for cancer of the cervix. Named for George Papanicolaou, the doctor who designed the test, the Pap test reliably detects early abnormal cell changes that could lead to cervical cancer. In the United States, the use of the Pap test as a screening tool for cervical cancer has dramatically increased cure rates. You should have your first Pap test within 3 years of the onset of sexual intercourse or at age 21. You should continue to have regular Pap tests until you are 65 to 70 years of age and have had 3 normal Pap tests within the last 10 years. The frequency for having Pap tests depends on your age and risk factors for cervical cancer.

During a Pap test, a small sample of cells from the surface of the cervix is collected by a health professional. The sample is then spread or smeared on a slide (Pap smear) or mixed in a liquid fixative and sent to a lab for examination under a microscope. The cells are examined for abnormalities that may indicate cancer or changes that could lead to cancer.

Cervical cancer has well-defined stages, and the chance of a cure is much higher when it is detected before it has spread from the cervix to other parts of the body.

Several factors, such as having mutiple partners, having human immunodeficiency virus (HIV), and having sexual intercourse before 18 years of age, increase a woman's risk of developing cervical cell changes that can lead to cancer of the cervix.

Why It Is Done

A Pap test is done to screen for cancerous and precancerous cells of the cervix.

My Plan Summary

Client Name:
Group #:
Plan:

Eligibility Information
Copay Summary
Deductible/Out of Pocket

You should have your first Pap test within 3 years of the onset of sexual intercourse or at age 21. You should continue to have regular Pap tests until you are 65 to 70 years of age and have had 3 normal Pap tests within the last 10 years. The frequency for having Pap tests depends on your age and risk factors for cervical cancer. Talk with your health professional about how often you should have a Pap test.

How To Prepare

Do not use douches, tampons, vaginal medications, or vaginal sprays or powders for at least 24 hours before having a Pap test.

Schedule the test for a time when you are not having your menstrual period, because the presence of blood cells may interfere with test results. The best time to schedule the test is during the early part of your menstrual cycle, 8 to 12 days from the start of your last menstrual period.

Tell your health professional whether you have had an abnormal Pap test in the past.

You will be asked to empty your bladder just before the test, both for your own comfort and to help the health professional with the examination.

Talk to your health professional about any concerns you have regarding the need for the test, its risks, or how it will be done. Complete the medical test information form to help you understand the importance of this test.

How It Is Done

You will need to take off your clothes below the waist and drape a paper or cloth covering around your waist. You will then lie on your back on an examination table with your feet raised and supported by stirrups. This allows the health professional to examine your vagina and genital area. You may want to wear socks to keep your feet warm while they are in the stirrups.

The health professional will insert a lubricated vaginal speculum into your vagina. The speculum gently spreads apart the vaginal walls, allowing the inside of the vagina and the cervix to be examined.

Your health professional will collect several samples of cells from your cervix using a cotton swab, brush (cytobrush or cervix brush), or a small spatula. Cells are collected from the visible part of the cervix as well as from its opening (endocervical canal). In women who do not have a cervix, cells from the vagina are collected. The cells are smeared on a slide or mixed in a liquid fixative and sent to a lab for examination under a microscope.

How It Feels

You may feel some discomfort when the speculum is inserted, especially if your vagina is irritated, tender, or narrow. You may also feel pulling or pressure when the sample of cervical cells is being collected.

You will feel more comfortable during your Pap test if you and the health professional are relaxed. Breathing deeply and having a light conversation with your health professional may help you relax. Holding your breath or tensing your muscles will increase your discomfort.

You may have a small amount of vaginal bleeding after this test, and you may want to use a sanitary napkin or pantiliner to protect your clothes from any spotting.

Risks

A Pap test poses no direct risks to your health.

Results

Results from a Pap test are usually available in 1 to 2 weeks.

Classification systems

In the United States, the Bethesda system (TBS) of classifying Pap tests was developed by the National Cancer Institute to provide more detailed information about Pap test results. This system improves communication between the health professional who does the Pap test and the laboratory specialist (cytologist) who examines the cervical cells. It provides information about the quality of the cell sample and the types of cell changes found.

While the Bethesda system (TBS) is widely used in North America to classify abnormal cells, other classification systems may still be used in other parts of the world.

Normal

The sample of cells collected from the cervix was adequate (cells from the surface of the cervix and inside the cervix are present) and no abnormal cells were detected.

Abnormal

Abnormal cells were seen or not enough cells were collected from the surface of the cervix and inside the cervix (inadequate sample).

See illustrations of cervical cancer and the progression of cancer of the cervix.

What Affects the Test

- Failure to apply the preservative to the slide immediately after the cells of the cervix are spread on it can cause the cells to dry out and interfere with test results.
- Menstrual blood on the slide can interfere with the examination of the cervical cells and may interfere with test results.
- A vaginal infection can interfere with Pap test results.
- A Pap test done within 24 hours of douching or using vaginal lubricants or medications may provide inaccurate results because the products may wash away or coat the

cells on the surface of the cervix.
- The health professional may not obtain an adequate sample of the abnormal area of the cervix, or the sample may contain too few cells, which may give a false-negative test result.

What To Think About

- A normal Pap test result does not rule out dysplasia or cervical cancer.
- Depending on the results, an abnormal Pap test may be followed immediately by a test that looks at the cervix through a magnifying instrument (colposcopy) or by a repeat Pap test within 3 to 6 months. If severe abnormal cells or cervical cancer is suspected, colposcopy should be done soon after the Pap test results are ready. If the abnormality is minor, repeat Pap tests may be done to monitor any changes in the cervix. If the Pap test indicates an infection, treatment may be started. Just over half of the minor abnormalities found by a Pap test may disappear without treatment. For more information, see the medical test Colposcopy and Cervical Biopsy.
- A small sample of tissue from the cervix may be collected (for biopsy) to follow up on Pap tests that remain abnormal. Colposcopy and a cervical biopsy may also be done during the same examination. For more information, see the medical test Colposcopy and Cervical Biopsy.
- A Pap test alone cannot confirm the presence cervical cancer. Other tests, such colposcopy and cervical biopsy, are needed to diagnose cervical cancer. Even if Pap test results show evidence of cancer, there is a 20% chance that cancer is not present.
- False-negative and false-positive test results sometimes occur with Pap tests. The reliability of Pap test results depends on how well the sample is collected, the size and severity of the abnormality, and the quality of the lab work when examining the Pap smears.
- Some new testing methods, such as AutoCyte-Screen (automated review of a negative Pap smear) and ThinPrep (liquid collection and processing method for cervical cell specimens) are being studied to see whether they increase the reliability of Pap testing at a reasonable cost.
- Since Pap smears are not 100% accurate, it is very important for women to have them done regularly. Over time, repeat Pap tests with normal results make it very unlikely that a problem has been missed.
- Some health professionals test for human papillomavirus (HPV) when a woman's Pap test is classified as atypical squamous cells of undetermined significance (ASC-US) to determine whether she should have a repeat Pap test or colposcopy.
- A Pap test is not used to screen for sexually transmitted diseases (STDs) or cancer other than cervical cancer.

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Last Updated December 10, 2003

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Appendix E

Kaiser Materials

Clinical Practice Guidelines—Cervical Cancer Screening & Follow-up of Abnormal Cytological Results

Provider Information—Frequently Asked Questions (2003 Clinical Practice Guidelines for Cervical Cancer Screening)

Clinical Practice Guidelines—Algorithms for Cervical Cancer Screening & Follow-up of Abnormal Cytological Results

Patient Education

- **When Should You Get a Pap Test and Why?**
- **Human Papillomavirus (HPV)**
- **New Improvement in Cervical Cancer Prevention for Women Age 30 and Over**
- **DNA Pap: What Women Should Know about Cervical Cancer Prevention: Using Pap Smears and HPV Testing (in English, Spanish, and Chinese)**

CLINICAL PRACTICE GUIDELINES

November 2002

Cervical Cancer Screening & Follow-up *of* Abnormal Cytology Results

Endorsed by:
Chiefs of Obstetrics & Gynecology
Chiefs of Medicine

Introduction

Due to widespread screening, cervical cancer is relatively uncommon in industrialized nations. In the United States in 1995, there were 16,000 cases diagnosed and 4,800 deaths. The annual incidence is approximately 10/100,000. There are 80-100 invasive cervical cancer cases every year in Northern California. In countries where screening is not available, cervical cancer is by far the most common cancer in women, as well as the most common cause of death from cancer in women.

Summary *of* Recommendations & New Developments

Screening

Evaluation of cervical cytology specimens should be done using the Bethesda 2001 Guidelines. Changes in the categories have led to new recommendations for follow-up.

Cervical cancer screening should begin at three years after the onset of vaginal intercourse or age 21, whichever is earlier. Historical risk factors (other than immunosuppression) are not useful and should not be used to recommend earlier screening.

Women under 30 may safely be screened at two-year intervals. After two normal annual Pap tests, women under 30 can extend the screening interval to 24 months without increased risk of invasive cancer. Annual Pap screening is acceptable, but associated with unnecessary tests, visits, and procedures and does not confer additional protection from cancer in this age group.

Pap test plus HPV DNA is recommended for women age 30 and over. If both tests are negative, they do not need to be repeated for three years. If HPV is positive and Pap negative, retesting in one year with Pap plus HPV is recommended. Annual screening with Pap alone is acceptable but results in unnecessary visits, tests, and procedures. Biennial screening with Pap alone is acceptable only if the patient understands the increase in cancer risk incurred in exchange for fewer visits and procedures.

Follow-up *of* Abnormal Cytology

HPV DNA testing is recommended for triage of ASC-US Pap results. Co-collection of an HPV tube at the same time as the Pap test is preferred where reflex testing is available. Other options include immediate colposcopy or repeat Pap testing twice, at six-month intervals.

ASC-H results should be evaluated by colposcopy and endocervical curettage (ECC). HPV testing for triage adds little information since >80 % may be positive.

LSIL results should be evaluated by colposcopy and ECC, with the exception of adolescents and post-menopausal women, who may undergo colposcopy and ECC or may be followed with HPV testing at twelve months or repeat Pap testing at six-month intervals times two.

HSIL and AGC results should be evaluated by colposcopy and ECC in all cases. Women with AGC smears should have endometrial biopsy if over age 40 or clinical suspicion of endometrial cancer.

Appropriate follow-up for a variety of abnormal results consists of HPV testing alone at one year, or repeat Pap testing at six and twelve months with repeat colposcopy for any abnormal results (ASC-US, HPV positive or worse.)

New Developments

Human papillomavirus (HPV) is responsible for nearly all cases of invasive cervical cancer. Yet, the vast majority of women infected with oncogenic HPV will never develop invasive cervical cancer or its precursors.

Transient HPV carriage is *normal* and does not represent a *disease*. In most women, clearance of HPV occurs within a short time, averaging eight months in one series.

Prolonged productive carriage of high-risk HPV is required for the development and maintenance of CIN2/3. Persistence of CIN2/3 over time (average ten years) is associated with the development of invasive cervical cancer.

The risk of invasive cancer is very low for women under 30 (5% of the cervical cancers in KPNC), and screening does very little to change that risk.

In contrast, women age 30 and over experience 95% of the cervical cancers in KPNC and screening can prevent most of these cancers.

Results of NCI's landmark ASC-US and Low Grade Triage Study (ALTS) have defined the natural history, optimal evaluation, and follow-up of cervical dysplasia. Follow-up recommendations for the most common categories of dysplasia have changed considerably based on these results.

New guidelines from the American Society of Colposcopy and Cervical Pathology (ASCCP) and the American Cancer Society (ACS) support continued integration of HPV testing into clinical practice, including screening, starting at age 30, with Pap plus HPV testing every three years. In addition, they support major changes in follow-up recommendations for the most common categories of dysplasia based on the ALTS trial.

The recommendations contained in this guideline were developed using an evidence-based and consensus approach, and include review of the scientific literature, analysis of KPNC clinical practice outcomes, and examination of the guidelines and recommendations from other organizations. The clarification of optimal screening practices, intervals, and methods are active areas of ongoing research, and continuing changes in clinical practice should be anticipated.

Information and input from KPNC played a part in the development of the Bethesda 2001, ASCCP and ACS recommendations. With rare exceptions appropriate to our practice and population, this Guideline follows these recommendations.

Visit the Clinical Library at http://cl.kp.org for a version of the guideline with complete references.

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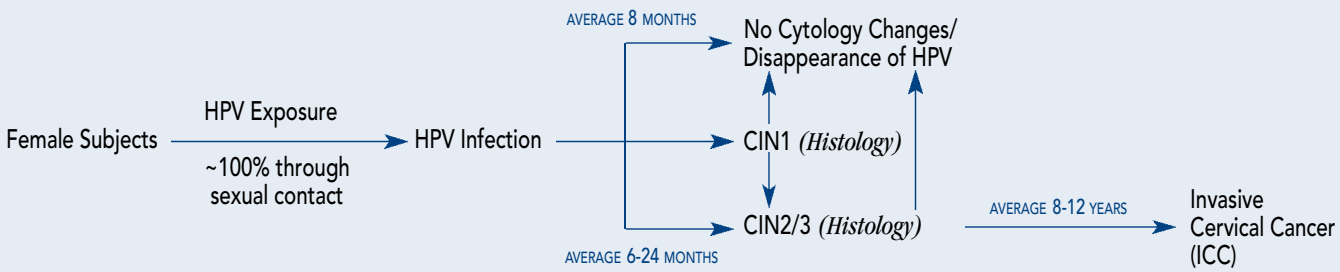
Figure 1. Natural History *of* Cervical Carcinogenesis



Development *of* Cervical Cancer

The presence of an oncogenic (also called high-risk) strain of the human papillomavirus (HPV) is a necessary but not sufficient condition for the development of virtually 100% of cervical cancers. *The presence of or testing for low-risk HPV has no relevance to cervical cancer prevention. References to HPV hereafter may be assumed to indicate high-risk HPV.* The time course, molecular changes, and risk of cancer associated with the various high-risk subtypes are sufficiently similar that there is currently no clinical utility to knowing which high-risk type is present.

HPV is transmitted almost exclusively through sexual contact, and acquiring HPV is a very common event within a short time after the initiation of sexual activity. HPV may produce no cytologic abnormalities, or may manifest as cytologic squamous intraepithelial lesions (SIL) or histologic cervical intraepithelial neoplasias (CIN). The vast majority of women with HPV never develop invasive cervical cancer (ICC) or its precursors–high-grade cervical intraepithelial neoplasia (CIN2/3), or adenocarcinoma in situ (AIS). In most women, clearance of HPV occurs within a short time, averaging eight months in one series.

Cytologic LSIL or histologic CIN1 is not a cancer precursor, per se, but rather the appearance of squamous cells that are making HPV. This is simply a marker for risk of subsequent development of CIN2/3 as any other indication of HPV would be.

Prolonged productive carriage of HPV is required for the development and maintenance of CIN2/3, and persistence of HPV over time is associated with the development of invasive cervical cancer. When progression to CIN2/3 follows, it frequently does so within 24 months. Most cases of CIN2/3 that progress have a sojourn time averaging 8 to12 years prior to the onset of ICC. This period is referred to as the "detectable preclinical phase."

It should be noted that due to a small number of women who experience rapid progression, invasive squamous cancer of the cervix could not be eradicated even with a perfect screening test and 100% compliance with annual screening.

Cervical Cancer Screening Goals

- Reduce the incidence of cervical cancer, and thereby reduce the morbidity associated with treatment, including loss of fertility
- Reduce mortality related to cervical cancer
- Reduce the burden of screening on the patient and the provider

In order to achieve these goals, the task of the clinician at each screening visit is twofold:

- Exclude with the greatest possible certainty the presence of CIN2/3 or cancer
- Define the interval to the next screening

Methods of achieving goals:

- Development and implementation of guideline recommendations
- Patient education
- In/outreach to under-screened members and maintenance of access to screening
- Incorporation of Bethesda 2001 categories and criteria in Pap test cytology reporting
- Continued assessment and monitoring of outcomes

CERVICAL CANCER SCREENING

Highlights *of the* Bethesda 2001 System

Bethesda 2001 advanced the practice of cervical cytology by eliminating previous categories of equivocal results that had no clinical relevance and by providing the practitioner with stratification of risk to guide specific evaluation steps for some of the remaining equivocal categories. The provider interested in the details of the data and rationale underlying these changes is referred to the article announcing and describing them (Solomon 2002), and to the web site *bethesda2001.cancer.gov.*

- A normal test is now called NIL (No Intraepithelial Lesion). *Benign cellular changes, reactive changes, metaplasia, inflammation* and all similar designations become part of NIL, reflecting the fact that the purpose of Pap tests is to detect CIN. Associated findings (trichomonas, atrophy, etc.) will be reported but do not make the test abnormal.
- The designation *satisfactory but limited by* is abolished. Tests are either satisfactory for interpretation or not. Smears without endocervical cells are satisfactory for interpretation.
- ASC-US has been collapsed from three categories *[favor neoplasia, favor reactive,* and *not otherwise specified (NOS)]* into two categories: ASC-US and ASC-H (ASC-US rule out HSIL).
- AGC-US has been changed to AGC NOS, AGC *favor neoplastic* and AIS (adenocarcinoma in situ).

Screening Recommendations

Screening Methods

- Conventional cytology is an acceptable method for cervical cancer screening
- Testing for high-risk oncogenic human papillomavirus (HPV) is complementary to cytology when cytology is equivocal or when screening with high negative predictive value is important.
- Testing for high-risk HPV may be performed for the following indications (from the ASCCP and ACS guidelines):
  - Clarification of minimally abnormal cytology–ASC-US in all age groups, follow-up of LSIL in adolescents and postmenopausal women;

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- Follow-up after non-correlating cytology and colposcopy: ASC-US HPV positive, ASC-H or LSIL smear and a subsequent negative colposcopy;
- Follow-up of untreated CIN1;
- Test of cure and assessment of subsequent risk after treatment of dysplasia;
- In women age 30 and over; to focus annual screening on the 10%-15% who are actually at risk for high-grade dysplasia and cancer.

RATIONALE. *Conventional Cytology.* The conventional Papanicolau (Pap) test was introduced more than 50 years ago, and is credited with the dramatic decrease in incidence and mortality from cervical cancer since its introduction. Despite the admirable progress made where screening is available, there is a significant false negative rate for conventional Pap tests which results in occurrence of ICC in screened women.

The review of cervical cancer screening conducted by the Agency for Healthcare Research & Quality (AHRQ), at the request of the American College of Obstetricians and Gynecologists (ACOG), concluded that if one insists on biopsy proven CIN as the endpoint, the sensitivity of the conventional Pap test is 51%. Most CIN is low grade and subject to regression, although data from ALTS revealed little if any regression of CIN3 over a two-year follow-up period. At the same time, sensitivity of cytology for CIN3 or cancer may be as low as 50%. *(See Table 1)* The traditional response to this dilemma has been frequent testing. Frequent testing is less than optimal both from the standpoint of patient convenience and resource utilization. Also, there is evidence that sequential Pap test results are not independent, i.e., a lesion that is difficult to detect cytologically remains so on subsequent Pap tests.

Cytologic screening has had little impact on the incidence of adenocarcinoma of the cervix. This suggests that cervical cytology is of limited efficacy for the detection of adenocarcinoma precursors, and assessments of the efficacy of screening apply to squamous neoplasia only. On the other hand, there is evidence from the KPNC population and elsewhere that once invasive cancer is present, cytologic screening can detect adenocarcinomas before symptoms are present in some cases, and that adenocarcinomas detected by cytologic screening are associated with lower stage and increased survival.

Monolayer ("liquid medium") cytology preparations have been introduced in recent years for the purpose of improving the sensitivity of conventional cytology. A review of eight prospective studies comparing direct-to-vial use of one monolayer preparation versus conventional dry slide cytology demonstrates a doubling of cytologic LSIL and HSIL diagnoses. An additional benefit is that reflexive testing for sexually transmitted diseases (HPV, chlamydia, and gonorrhea) can be conducted from the residual liquid where adequate fluid remains after cytology (approximately 95% of specimens). Monolayer gynecologic cytology is not presently performed in KPNC laboratories.

Human papillomavirus testing (for high-risk types) is complementary to cytology, and currently available to TPMG physicians. It provides two pieces of information, one concerning the risk that CIN2/3 or cancer is present currently, and the other regarding risk of the subsequent development of CIN2/3. Both are relevant to the clinician's task—to exclude CIN2/3 and define the interval to the next screening. High-risk HPV testing is more sensitive but less specific than conventional cytology for the detection of CIN2/3+. Hence, it is useful when cytology is equivocal or high negative predictive value is important.

The combination of negative HPV testing and normal cervical cytology is of greater value than historical risk factors or previous negative smears in predicting patients at low risk of having or developing high grade CIN or cancer in the ensuing 2 to 3 years. These patients may be screened at intervals greater than one year.

Initiation *of* Screening

- Cervical cancer screening should begin approximately three years following the onset of vaginal intercourse or age 21, whichever is earlier. The critical importance of appropriate preventive health care for adolescents is recognized, but cervical cancer screening should not be the basis for initiating gynecologic care.

TABLE 1. SENSITIVITY *of* PAP & HPV TESTING *for* BIOPSY DIAGNOSIS *of* CIN3 *or* CANCER

POPULATION	N	PREVALENCE OF CIN3+ (%)	SENSITIVITY (%) PAP ALONE	HPV ALONE	HPV & PAP
UK	9761	0.52	90.2	94.1	98.0
Mexico	6115	1.26	58.4	94.8	97.4
Costa Rica	6176	1.10	82.3	93.6	96.8
S. Africa	2925	3.66	84.1	89.7	92.5
China	1936	2.17	97.6	100.0	100.0
Baltimore	1040	0.19	50.0	100.0	100.0
Germany	7592	0.36	51.6	96.3	100.0

FIGURE 2. NEGATIVE PREDICTIVE VALUES (NPV) *of* CERVICAL CANCER SCREENING TESTS

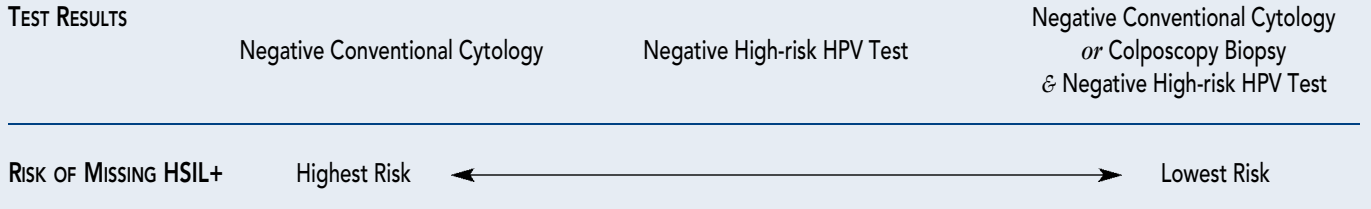

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Table 2. Relative Risk *of* Invasive Squamous Cancer *of the* Cervix *by* Screening Interval

	1 Year	2 Years	3 Years
All Cases	1.0	1.7 (P=.013 vs 1 Yr)	2.1 (P=.007 vs 1 Yr)
Ever Abnormal Pap	1.0	2.1 (P=.02 vs 1 Yr)	2.2 (P=.005 vs 1 Yr)
Two Negative Paps	1.0	2.2 (P=.02 vs 1 Yr)	3.6 (P=.004 vs 1 Yr)

Figure 3. Age Specific Incidence Rates *of* Cervical Cancer Before & After *the* Introduction *of* Screening

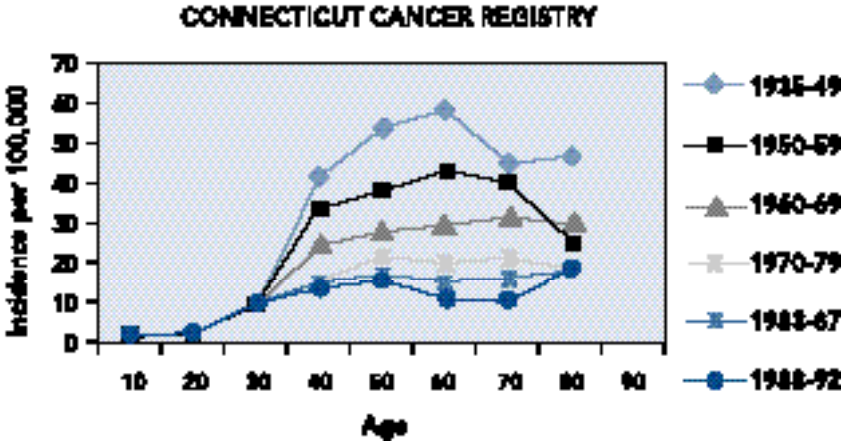
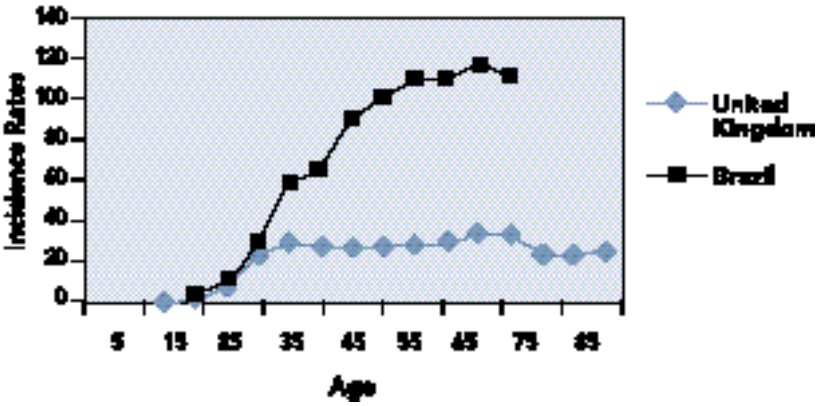


Figure 4. Age Specific Incidence Rates *of* Cervical Cancer *in* Brazil & *the* United Kingdom



- In young women who are HIV-infected or immunosuppressed, screening should be initiated at the onset of vaginal intercourse.

Rationale. Risk of cervical dysplasia is related to the number of years since first intercourse, rather than chronological age. As CIN2/3 must be present for an average of ten years prior to the onset of ICC, cancer is *extremely* rare before age 25. Risk of squamous ICC for compliant members, with a minimum of three Pap tests before age 25, is so small that it cannot be estimated accurately from the data presently available. The SEER reported incidence is 0/100,000/year for ages 10-19 for 1995-1999, which is consistent with KPNC data.

Screening Intervals

Screening intervals cannot be meaningfully addressed in the absence of the discussion of methods. Intervals and methods interact to determine cancer risk and the number of visits and procedures required to achieve a given level of risk reduction.

Women Under the Age of 30

- *Recommended:* Screening by conventional cytology every two years (biennial screening) after two or more consecutive negative Pap tests within the past five years.
- *Acceptable:* Annual cytology screening, should the patient choose this option after a discussion of the risk and benefits of more frequent screening.

Women Aged 30 and Over

- *Recommended:* Screening intervals should be based upon cytology and HPV test results.
  - Women with negative cytology and HPV tests should be rescreened at 30-36 months
  - Women with negative cytology and positive HPV tests should be rescreened by both tests at one year
- *Acceptable:* Annual cytology screening, should the patient choose this option after a discussion of the risk and benefits of more frequent screening.
- *Acceptable:* Biennial cytology screening after two or more consecutive negative Pap tests within the previous five years is acceptable only if the patient understands the increase in cancer risk incurred in exchange for fewer visits and procedures.
- Women in whom initial cervical cancer screening was performed by cytology alone should be screened annually for two years to compensate for the small but real possibility of an initial false negative Pap test before moving to a longer screening interval.
- Women 30 years of age or more who initiate screening with cytology and HPV testing may proceed directly to the interval appropriate to their cytology and HPV results.

Women 65 years and over

- Screening may be discontinued for women age 65 and over who have had three consecutive negative Pap tests (at intervals of one year or greater) in the past ten years and no history of anogenital warts, CIN2/3, or invasive cancer of the cervix, vagina, or vulva.
- Screening should be continued indefinitely if a history of anogenital warts, CIN2/3, or invasive cancer of the cervix, vulva, or vagina is present. Until more data are available, women who test positive for HPV may elect to continue screening.

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Rationale for Screening Recommendations for Women Under the Age of 30

For women under the age of 30, there has been no change in cervical cancer incidence associated with the introduction of cytologic screening, and there are so few cancers that risk cannot be reliably measured at different intervals. Figure 3 graphs records of the Cancer Registry of the State of Connecticut and Figure 4 compares age specific incidence rates of Brazil, where relatively little cytologic screening is done, to the United Kingdom, which has a government administered screening system with computerized call and recall. Incidence rates in the two figures with widely different screening practices are virtually superimposable up to the age of 30 and diverge widely thereafter.

With no clear evidence that any screening program can decrease cancer risk below the age of 30, the benefits of less frequent screening (fewer visits, biopsies, LEEPs, etc) outweigh the risks.

Rationale for Screening Recommendations for Women Starting at Age 30

KPNC embarked on an effort to examine interval extension in the 1980s and 1990s. The study by Miller et al., had a sample size significantly larger than earlier studies, and demonstrated that risk of ICC doubles between a one-year and a two to three-year screening interval. These changes are not affected by history of a previous abnormal smear or multiple previous negative smears. At the same time, annual screening in women of this age group increases the risk of false positive results, leading in turn to patient anxiety and unnecessary visits, tests and procedures.

- Biennial screening is associated with a significant increase in risk of cervical cancer as opposed to annual cytology, or cytology plus HPV testing.
- There is small but real possibility of an initial false negative Pap test before moving to a longer screening interval. False negative rates for conventional Pap tests in previously unscreened women with ICC are 10% or less, resulting in a <10% chance of not having the cancer detected by the first two annual Pap tests.
- The negative predictive value of the Pap test and HPV DNA for CIN2/3+ approaches 100%, eliminating the need for repetitive testing at short intervals.

The ability to focus annual screening on patients who are actually at risk for cervical cancer is based on the timeline of cervical carcinogenesis depicted in Figure 1, the interrelationship and negative predictive value of the combination of Pap and HPV tests depicted in Table 1, and the ensuing text. Other observations that underlie this approach may be summarized as follows:

- Prevalence of high risk HPV infection peaks in the twenties at between 25% and 35% and falls to 10%-15% by age 30.
- In KPNC, 75% of the Pap tests done in the Regional Lab and 95% of our cancers are in women 30 years of age and older.
- Given the anticipated average 10-year interval from CIN2/3 to ICC, an immunocompetent woman who has a negative Pap and HPV test can acquire HPV the following day and develop CIN2/3 within a matter of weeks and still be safe from ICC at a 30-36 month screening interval.
- Frequent screening with tests with poor positive predictive value places unnecessary burdens on patients and providers.
- The issue of when a woman should undergo colposcopy for persistent HPV(+)/cytology(-) screens remains unresolved. At present, data is not sufficient to recommend colposcopy for members who are HPV(+)/cytology(-).

When a patient is seeking more frequent screening, or additional testing that is without apparent benefit (such as Pap plus HPV annually), the provider should discuss the risks and benefits of different screening intervals and methods.

Like all powerful tools, combined testing must be used correctly to be beneficial. There are some important "Don'ts" associated with combined testing.

- Don't test women under 30 with both tests
- Don't do both tests every year in women who are negative for cytology and HPV: there is no benefit to the patient
- If the provider and/or the patient are not interested at testing at intervals of 30-36 months, don't do both tests
- Don't colposcope women for a HPV positive/cytology negative result
- Don't treat (LEEP, cryotherapy, etc.) on the basis of a positive HPV test alone in the absence of proven CIN
- Don't tell a woman she must use condoms because of a positive HPV test
- Don't blame! HPV status is not a reliable guide to sexual behaviors

Screening Rationale in Women 65 Years and Older

In the Northern California Kaiser Permanente population, as in the U.S. at large (SEER dataset), older women bear a disproportionate burden of cervical disease: 25% of our cases and 40% of our deaths are in women over the age of 65. Older women participate in screening less frequently and *"an older woman's screening history is the most important variable in deciding whether a Pap test is indicated"* (Mandelblatt 1986). Most organizations recommend that screening for older women be decreased in intensity or discontinued, but the criteria for making this decision are widely variable. Our recommendation is based on a number of studies: a Swedish study indicating that women over age 70 with only one normal Pap test in the last 10 years have an incidence of ICC of 3/100,000/year, the U.S. Office of Technology Assessment model of cancer screening in the elderly woman, the most recent Canadian National Workshop on Screening for Cancer of the Cervix, and by data from our own membership.

Data regarding long-term risk of cervical dysplasia and cancer in patients with anogenital warts are sparse. Until better information is available, continued follow-up is justified due to a reported 19% ten-year cumulative risk of CIN2/3.

Risk Factors & Screening Intervals

- Women should be screened at the recommended intervals regardless of the presence or absence of historical high or low-risk factors, unless immunosuppressed.
- *High-Risk:* Available evidence does not permit definition of an immunocompetent group that will benefit from more frequent screening.
- *Low-Risk:* Patients and their physicians frequently lack the information necessary to identify the patient who is truly "low-risk."

Rationale for Risk Factors

- **High-Risk.** The vast majority of an individual's risk of cervical cancer is attributable to her sexual behavior and that of her partner(s). Sexual contact with more partners occurring at an earlier age leads to increased risk, presumably due to increased opportunity for transmission of HPV and other sexually transmitted diseases, which may act as cofactors. Smoking is a recognized cofactor, and there is evidence that genetic susceptibility may also be important, as may the use of oral contraceptives. However, there is no evidence

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that these risk factors change the rate of progression to ICC (sojourn time) and hence the efficacy of screening. As a consequence, "the epidemiologic indicators of risk (such as multiple sexual partners) are of little value in selecting women for screening" (Miller 1996).

Screening of "high-risk" women is a practical problem not because of inefficacy of cervical cytology, but because women at greatest risk are precisely those least likely to avail themselves of preventive health care services, including cervical cancer screening.

- **Low-Risk.** The sexual behavior and history of the patient's male partner(s) contribute as much or more to her risk as any one of the factors listed above. This association is present for both squamous and adenocarcinoma cell types. As the patient or her physician sometimes cannot reliably determine the partner's behavior and history, the difficulty in accurately defining a "low-risk" group is intuitively apparent.

Screening Intervals *with* Special Considerations

- *Oral Contraceptives:* A woman's choice of contraceptive methods should not influence her screening interval.
- *Screening Lesbian Women:* All women should participate in cervical cancer screening, regardless of sexual orientation, history of heterosexual intercourse, or recency of sexual activity.
- *HIV Positivity/Immunosuppression:* Immunosuppressed women should be screened at least annually with cervical cytology.
- *Screening Following Hysterectomy for Benign Conditions:*
  - Screening may be discontinued following a total hysterectomy for benign conditions (cervix removed) in women with no history of CIN2/3 or cancer of the cervix, vagina, or vulva.
  - Women with a history of CIN2/3 or whose history is uncertain should continue cytologic screening until three consecutive normal smears are obtained (at intervals of one year or greater) in a ten-year period, following which screening may be discontinued.
  - Screening should be continued indefinitely if a *history of invasive cancer* is present.
  - Screening post hysterectomy, if indicated, should be conducted with cytology alone. HPV testing may be useful for triage of minimally abnormal cytology.

Rationale for Special Considerations

- *Oral Contraceptives.* Preliminary reports have suggested a link between the use of oral contraceptives and an increased risk of carcinoma of the cervix in patients who are HPV DNA positive. Excess risk was not present in HPV negative women. However, there is currently no evidence that oral contraceptives change the transit time from HSIL to invasive cancer, and hence a recommendation for more frequent screening to prevent squamous cancer is not warranted at this time.
- *Screening Lesbian Women*. The common perception that lesbian women are at minimal risk for cervical dysplasia and cancer is not supported by clinical experience and contributes to underscreening. Prior heterosexual intercourse is reported by 75%-90% of lesbians, providing ample opportunity for HPV transmission. HPV and all grades of CIN have also been reported in women who have no history of intercourse with men.
- *HIV Positivity/Immunosuppression:* Annual screening cervical cytology is consistent with the recommendations of the CDC and other major organizations.

  Severe immunosuppression, as present in some women with HIV, women with Hodgkin's disease, or those taking immunosuppressive medications, is the single risk factor for CIN and cancer wherein patients *may* benefit from more frequent screening. Unlike other risk factors, immunosuppression may shorten the sojourn time and reduce the efficacy of screening. There is no outcome information available that permits precise recommendations.

  Shorter screening intervals may prove beneficial under two circumstances:
  - If HSIL in severely immunosuppressed women can be effectively treated. Currently available evidence for women with HIV is not reassuring, with very high recurrence rates noted at short follow-up intervals (39%-59%).
  - If detection and treatment of HSIL changes either longevity or quality of life in severely immunosuppressed women. For women with HIV, no direct evidence is available. However, the high mortality associated with invasive cervical cancer in this population (100% in one series) suggests that dysplasia treatment, if effective, may change longevity. Recently published modeling supports this assertion, finding that annual Pap tests in HIV positive women provides a 2.1 month gain in quality-adjusted life expectancy at the modest cost of $12,800 per life year saved.

  Cytology is adequate for screening of HIV infected women. High false negative rates for conventional dry slide cytology have been reported in HIV-infected women and renal transplant recipients, but they are no higher than those found in the general population when analysts insist on histologic endpoints. These observations prompted trials of colposcopic screening, with the majority finding that cytology is the best choice for screening of HIV infected women.
- ***Screening Following Hysterectomy***. When patients with hysterectomy *for benign disease* desire screening it is recommended that practitioners discuss the extremely low incidence of post-hysterectomy squamous carcinoma of the vagina and the significant false positive rate of Pap tests. Between 1988 and 1994, there were 14 cases of invasive squamous cancer of the vagina post-hysterectomy among our members, and 13 out of 14 of these women were alive at a median follow-up of 37 months post diagnosis (range 7 to 89 months). Assuming that 12% of the female membership during that time period had a hysterectomy, the estimated incidence of post-hysterectomy squamous carcinoma of the vagina was 1.4/100,000/year, and mortality 0.1/100,000/year (given the follow-up intervals noted above). Information regarding the history of cervical dysplasia is not available for the vaginal cancer cases from our membership, but the literature suggests that such a history may identify roughly half of the cases of invasive cancer of the vagina post-hysterectomy.

  In women with a *previous history of CIN2/3*, the recommendation to stop screening following hysterectomy (unlike older women with a similar history and an intact cervix) is motivated by the extreme rarity of vaginal cancer, and by the very low yield of screening in this situation. Following hysterectomy, 98% of women with a history of CIN will remain negative after 5 years of annual cytologic screening and 96.5% will be have remained negative after 20 years.

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Specimen Collection Recommendations

Sampling Technique & Specimen Adequacy

When both cytology and HPV specimens are taken utilizing separate sampling instruments, the cytology specimen should be collected first to minimize contamination with blood. Collection of specimens utilizing the brush provided with the HPV tube should involve contact of the brush with the T-zone. After the insertion of the brush in the cervical os, three full 360-degree rotations are recommended. Adequate sampling of the T-zone is essential for reliable results from either cytology or HPV testing. This requires insertion of the sampling brushes into the endocervical canal in older women.

Endocervical Cells & Specimen Adequacy

Absence of endocervical cells on an otherwise normal Pap test is not an indication to repeat the Pap test.

Some years ago, the observation was made on review of Pap tests believed to be "false negative" that more lacked endocervical cells (EC) than tests from the general population. It was concluded that Pap tests lacking EC were "inadequate" and it was inferred that they should be repeated. Some older prospective trials comparing sampling tools noted higher percentages of abnormal Pap tests with better sampling of the endocervix. Recent experience using cervical histology as the endpoint demonstrates similar correlation of cytology and histology, similar neoplasia detection rates, and similar risk of subsequent dysplasia independent of the presence or absence of EC. Repeating Pap tests lacking EC has not increased the detection of CIN.

Outside Pap Tests

New Kaiser Permanente members should be screened (rescreened) within KPNC.

KPNC and others have demonstrated that self-reporting of Pap test intervals is not reliable. Written documentation of outside Pap test results is frequently unavailable to the Kaiser Permanente clinician, and there is no assurance that quality control of the outside lab meets our rigorous standards.

FOLLOW-UP OF ABNORMAL CYTOLOGY RESULTS

The object of these recommendations is not to define the only acceptable pattern of follow-up for each of the various cytologic abnormalities. All follow-up algorithms represent compromises between missed disease on the one hand, and patient time, discomfort or risk, and expenditure of resources on the other.

The only randomized, prospective clinical trial defining the consequences of different options for evaluation and follow-up choices is the ASC-US and Low-grade Triage Study (ALTS). Recommendations are based on most current available information reflecting the results of the recent Consensus Conference of the ASCCP sponsored by the National Cancer Institute. The rationale for these recommendations is summarized here briefly but can be found in detail in the original publications.

Highlights *of the* ALTS Trial Results

The ALTS trial (Solomon 2001) demonstrated only modest reproducibility of cytologic and histologic diagnoses, making the addition of objective (molecular) methods valuable, both for quality control and enhancement of clinical guidance.

The risk of CIN2/3+ at 2 years is virtually identical for women with ASC-US HPV (+), or LSIL Pap tests and any colposcopy less than CIN2/3. Whether the colposcopy result is negative or CIN1 is irrelevant to subsequent risk.

Because of low reproducibility of HSIL cytology, the ASCCP has recommended cytology review before proceeding with surgical treatment when there is a negative satisfactory colposcopy and endocervical curettage (ECC).

In follow-up of patients with minor abnormalities the best compromise between sensitivity for CIN2/3+ and the number of follow-up tests or procedures is to perform a single HPV test at 12 months and colposcope the positive results, or two Pap tests at 6-month intervals and evaluate any abnormal result with colposcopy. The sensitivity of the schemes is similar, but a single visit and HPV test refers fewer women to colposcopy than the combination of two visits and two Paps. *Adding cytology to HPV testing at 12 months refers more patients to colposcopy but does not increase pick-up of CIN2/3 and hence is not indicated.* Note that this recommendation is based on optimized Pap smears: monolayer cytology read at least twice by national experts. To achieve sensitivity similar to HPV testing using conventional cytology would probably require three repeat visits and Paps using conventional cytology, as previously recommended for ASC-US.

Table 3. Agreement Between University Cytopathologists & First Quality Control Reviewer: ALTS Trial

Cytology	ASC-US	633/1473	43%
	LSIL	908/1335	68%
	HSIL+	204/433	47%
Histology	CIN 1	378/887	43%
	CIN2/3+	370/481	77%

Recommendations

Unrecognized Cytologic & Histologic Diagnoses

Pap test diagnoses that the clinician does not recognize or that do not occur within the Bethesda system should prompt communication with the interpreting pathologist, and if necessary, a request for a revised report including a Bethesda diagnosis. Narrative interpretation of cervical cytology or diagnostic categories specific to the interpreting pathologist or facility do not permit the patient to benefit from the exam. Continued efforts at provider education will be required to encourage reporting of a single Bethesda 2001 diagnostic category for every cervical specimen.

Atypical Squamous Cells–Undetermined Significance (ASC-US)

- Reflexive testing for HPV is preferred where available.
- ASC-US HPV(+): Perform colposcopy; if negative, then retest with HPV testing alone at twelve months or with cytology twice at six-month intervals. Repeat colposcopy for cytology of ASC-US HPV(+) or worse, or for a positive HPV test.
- ASC-US HPV(-): Repeat screening in twelve months; additional ASC-US HPV negative Pap tests do not require colposcopy.
- ASC-US and HPV status unknown: Recall for HPV testing, or for colposcopy, or re-Pap at six-month intervals times two; if a re-Pap is ASC-US HPV(+) or worse, perform colposcopy. Postmenopausal women with no contraindications to estrogen therapy may receive a course of intravaginal estrogen with the first repeat Pap a week after completion of treatment and a second repeat Pap six months thereafter.

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Rationale. Studies performed by Kaiser Permanente Northern California, Kaiser Permanente Southern California, NCI, and elsewhere have demonstrated that testing for the presence of high-risk HPV among women with ASC-US tests is a more accurate form of triage than cytologic follow-up. In Northern California, 89% of the histologic HSIL+ was found in the 39% ASC-US/HPV+ results. The corresponding sensitivity in the ALTS trial was 96%.

The circumstances under which specimens are collected and the way in which the information is used will depend on the services available and the preferences of the clinicians at a given facility. Schemes that involve reflexive testing (specimen available without calling the patient back), either from a monolayer cytology vial, or from a separate vial collected with every Pap test (stored and tested only on those women with ASC-US Pap tests) provide triage information without requiring another patient visit and as a consequence are the preferred approach.

Triage by repeating cytology twice is less attractive than HPV triage for the following reasons:

- The likelihood of an abnormal first repeat Pap test is ~40% in our population and other populations. By the time that a patient has had three repeat Pap tests, the likelihood of an abnormal is estimated at approximately 66%. As a consequence, Pap test follow-up consumes more resources and compromises access to a greater degree than any other triage scheme, including 100% colposcopy. In addition, assessment of compliance with repeat cytology by examination of KPNC computerized databases suggests substantial loss to follow-up in actual practice.
- Follow-up Pap tests are notoriously unreliable. False negative rates for CIN2/3 of 25%-70% have been reported.
- The recommendation for two repeat cytologies is based on the sensitivity of liquid medium preparations read by experts in the experimental setting of the ALTS trail, which included 100% cytology review by the authors of the Bethesda system. This level of sensitivity is unlikely in daily practice using fractional quality control review of dry slides.

Atypical Squamous Cells–Rule Out HSIL (ASC-H)

- Colposcopy and ECC are recommended; if colposcopy is negative, then retest with HPV testing alone at 12 months or with cytology twice at 6-month intervals.
- Repeat colposcopy for any abnormal results.
- *Follow-up with repeat Pap tests (without colposcopy or HPV triage) is not acceptable for ASC-H.*

Rationale for ASC-H. In populations other than Kaiser Permanente ASC-H is associated with a risk of CIN2/3 at colposcopy of 24%-94%, between that of an LSIL and an HSIL smear. A preliminary evaluation of the histologic correlates of this diagnosis indicates that this is also true in our lab: biopsies for evaluation of an ASC-H smear demonstrated CIN2/3 in >30% of cases and 1% of ICC. HPV testing is not the preferred choice for ASC-H because >80% of women with ASC-H tests will have a positive test if results in actual practice reflect those in the research setting. If HPV testing is performed the negative predictive value is the same as for other ASC designations: those patients who don't harbor HPV are at little risk for CIN2/3 and may be rescreened at 12 months. In addition, the realistic assessment of the reproducibility of cytology and histology noted in the ALTS trial suggests that ASC-H outside of the experimental setting may not have the same histologic correlates or HPV prevalence.

Atypical Glandular Cells *of* Undetermined Significance (AGC)

Atypical Squamous *&* Glandular Cells *of* Undetermined Significance (ASGC)

Adenocarcinoma In Situ (AIS)

Initial Evaluation

- Age <40: Colposcopy, ECC*; Endometrial biopsy (EMB) if abnormal bleeding, obese, diabetic, oligoovulatory, or clinical suspicion of endometrial cancer.
- Age >40: Colposcopy, ECC and EMB.
- Stenotic cervix (preventing endocervical evaluation): Cervical dilation and endocervical sampling or LEEP and ECC.

*ECC may be performed by obtaining a separate vigorous endocervical brush specimen. The brush specimen is at least as sensitive as the ECC, perhaps more so, but runs the risk of an ASC-US result. Patients with ASC-US brush ECCs should be called back for traditional curettage.

Rationale. At 0.5%, our AGC rate is 2 to 3 times higher than other reported populations, yet the rate of underlying disease (HSIL, ACIS and cancer identified by AGC Paps) is identical to other populations at 45-65/100,000 tests. Accordingly, histologic HSIL+ is found in only 12.5% of our AGC patients, versus 22%-34% in other reports. Recommendations for evaluation and follow-up, therefore, take these patterns specific to our practice into account, and are consistent with the current ASCCP Guideline.

Evaluation of the role of HPV testing in AGC/ASGC patients is in progress. Detection of all five AIS cases in the 39 HPV positives out of 136 AGC patients in the recent study here suggests that there will be a role for HPV assays in the management of these patients. Unpublished follow-up data on this cohort suggest that the yield of conization in patients with AGC/ASGC Pap test who have a negative colposcopy and ECC, and a negative HPV test, is likely to be very low. However, because of the insensitivity of ECC, it seemed prudent to perform additional follow-up of women who were initially histologically negative prior to making a recommendation. This work is currently in progress.

Evaluation *of an* LSIL *or* HSIL Pap Test

- Colposcopy with endocervical sampling, and biopsy of visible lesions, with the following exceptions:
  - Postmenopausal women or adolescents with an LSIL Pap may be followed without colposcopy, if desired: Retest with HPV testing alone at twelve months or with cytology twice at six-month intervals. Repeat colposcopy for any abnormal results.
  - Postmenopausal women without contraindications to estrogen therapy may also be given a course of intravaginal estrogen before their repeat Pap tests.
  - Pregnancy. *See following.*

Rationale for LSIL or HSIL. CIN2/3+ is detected at colposcopy in approximately 17% of our KPNC members with LSIL tests and 70% of those with HSIL cytology. Therefore, the Ob/Gyn Chiefs have recommended evaluation with colposcopy and ECC for most of these women. The preference for immediate colposcopy in most women with LSIL is based on the high prevalence of HPV and of CIN2/3+, not inaccuracy on the part of the HPV test. Further evaluation may demonstrate that the HPV positive percent in post menopausal women with LSIL Pap tests is low enough that primary triage with HPV makes sense. Since some CIN1 and occasionally CIN2 is associated with low-risk HPV types, a percentage of negative HPV tests in women with CIN1 and occasionally CIN2 is expected.

In the hands of an experienced colposcopist, "see and treat" using LEEP for women with HSIL tests has been shown to be efficacious and cost effective.

Follow-up of LSIL and CIN1 is the most vexatious problem in cervical cancer screening after ASC-US triage. Incidence of LSIL is high, particularly in young women whose risk of ICC is very low

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(see Cervical Cancer Screening, page 2). LSIL is a reliable marker for the presence of oncogenic HPV. In our population, 84% of such patients are positive by Hybrid Capture II. The ALTS Group has reported the same observation: 83% of their LSIL patients were oncogenic HPV positive. The clinical consequence of this observation is an elevated risk of future diagnosis of CIN2/3. This increased risk continues for at least 10 years, follow-up tests are notoriously insensitive, and loss to follow-up is large. Postponing the HPV test to 12 months following the LSIL Pap affords time for spontaneous resolution of HPV infection and identifies women with prolonged carriage and therefore risk of CIN2/3. The option of follow-up for adolescents with LSIL tests with cytology or HPV testing without initial colposcopy is predicated on the very high spontaneous resolution rates of abnormal tests and CIN1 in these women and the negligible risk of missed invasive cancer. Endocervical sampling, as noted above, is an essential component of the evaluation of abnormal cytology.

The option of avoiding colposcopy in the postmenopausal woman is based on the fact that the likelihood of CIN2/3 in the postmenopausal woman with an LSIL Pap is markedly lower than in the premenopausal state. Only 58% of these women (over age 40) with LSIL Paps were HPV positive in our population and that number falls to 45% over the age of 50. That is low enough to warrant considering HPV triage as an option in this group. As in other settings, the negative predictive value of HPV testing for CIN2/3 remains high.

Evaluation *of* Abnormal Pap Tests During Pregnancy

- ASC-US and LSIL: Colposcopic evaluation may be delayed until >6 weeks postpartum.
- AGC/ASGC and HSIL: Evaluate colposcopically during pregnancy, though it is recognized that ECC will have to be delayed until >6 weeks postpartum.

Rationale. Spontaneous regression rates of HSIL CIN2/3 are substantial and progression of HSIL CIN2/3 to ICC during pregnancy is extremely rare. ICC is uncommonly associated with ASC-US or LSIL, and the optimal management of early invasive cancer in pregnancy is cesarean delivery and treatment of the ICC at or after delivery. Hence the only utility of the evaluation of abnormal Pap tests in pregnancy is to diagnose ICC already present so as to permit decisions about treatment and in early cases to optimize the route of delivery.

Other Cytology Findings

Normal Endometrial Cells *on* Pap Tests

- Asymptomatic and no clinical suspicion of endometrial cancer (obese, diabetic, oligoovulatory): No evaluation required.
- Symptomatic or clinical suspicion: Endometrial biopsy.

Rationale. Endometrial cells are commonly present on Pap tests (12% incidence overall in one report, including 0.6% in postmenopausal women). Reporting of normal endometrial cells on Pap tests creates a management dilemma for the clinician. Traditional wisdom dictates endometrial biopsy for all such women, motivated by reports of endometrial cancer rates of 13%-17% with this finding. This policy must be considered in light of the fact that age, obesity, and unopposed estrogens are also strongly associated with malignancy in this group, and that nearly all of the reported cancers were in women with abnormal bleeding. The incidence of cancer in asymptomatic women is reported at 0%-2%. Gomez-Fernandez, et al., reported 44 asymptomatic women with endometrial cells on pap who were followed without evaluation for a minimum of three years. During this time 0/44 subjects developed malignancy, suggesting limited clinical relevance to this cytologic finding in the asymptomatic woman.

Psammoma Bodies *on* Pap Tests

- Asymptomatic, normal pelvic exam, and no malignant cells on Pap test: perform pelvic ultrasound and endometrial biopsy.
- Symptomatic, abnormal pelvic exam, or malignant cells on Pap test: evaluate as indicated.

Rationale. Psammoma bodies on Pap tests are extremely rare (0.0016-0.0030%). There are 59 cases in the world's literature from 1964-1999, of which 27 were associated with benign conditions (notably endosalpingiosis) and 32 with malignant diagnoses. Age was strongly associated; the average age for malignant results was 56, versus average age 39 for benign results. Many of the patients with malignancy were either symptomatic or had an abnormal pelvic exam or malignant cells in addition to Psammoma bodies on their Pap test. The most recent and largest series (15 cases from 1,026,725 Pap tests) contained only three patients with malignancies, all three of whom were symptomatic.

Further Follow-up *after* Colposcopy

Evaluation after *an* ASC-US HPV Positive *or* LSIL Pap Test *&* *a* Subsequent Normal Colposcopy

- Negative satisfactory or unsatisfactory, colposcopy (including vagina) and ECC.
- Retest with HPV testing alone at 12 months or with cytology twice at 6-month intervals.
- Repeat colposcopy for any abnormal result.

Rationale. It is recognized that this represents more intensive follow-up for women with a negative colposcopy than recommended in the last edition of the Guideline. The change in recommendations is motivated by the ALTS results noted above.

Endocervical sampling, as noted above, is an essential component of the evaluation of abnormal cytology.

The role for HPV testing is indicated by the ALTS experience and by the publication of Fait, et al., who performed Hybrid Capture and LEEP on 166 women who had ASC-US or LSIL tests followed by a negative colposcopy. High-risk HPV was present in 34/166, 21 of 166 women harbored CIN2/3, and 20 of the 21 were among the 34 women who were HPV positive.

Evaluation After *an* Initial AGC *or* ASGC Pap *&* Negative Colposcopy

- AGC NOS and ASGC NOS–Repeat cytology and ECC at 6-month intervals times four prior to returning to routine screening.
- AGC or ASGC favor neoplasia, or AIS–Diagnostic excisional procedure, preferably a cold-knife conization.

Rationale for negative initial evaluation. Given that AGC has been reported to herald cancers of the colon, pancreas and ovary, a complete physical exam and consideration of sigmoidoscopy is encouraged. Recurrent AGC NOS with a negative evaluation may prompt consideration of pelvic ultrasound, and/or dilation and curettage (D&C), and/or cold knife conization as clinically indicated. The prevalence of disease in our AGC population does not warrant the blanket recommendation of Duska, et al., conization of all patients with a negative initial evaluation for a single AGC NOS Pap test.

However, the risk of adenocarcinoma in situ, or invasive adenocarcinoma associated with recurrent AGC NOS, a single AGC favor neoplastic, or an AIS smear, justifies the recommendation of a diagnostic excisional procedure if appropriate

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initial evaluation is negative. Conization is recommended because of the importance of margin status in defining further treatment, which may be obscured by cautery artifact in LEEP specimens.

Evaluation after *an* HSIL Pap Test *& a* Subsequent Normal Colposcopy

- Negative satisfactory colposcopy (including vagina) and negative ECC or inadequate colposcopy: Consider review of cytology. If review is not elected or upholds the HSIL diagnosis, then LEEP.
- Adequate colposcopy, LSIL histology, and negative ECC: Consider review of cytology. If review is not elected or upholds the HSIL diagnosis, then LEEP or follow as untreated CIN1.

RATIONALE. Both the risk of undiagnosed CIN2/3+ and the risk of incident disease are higher following HSIL than LSIL, prompting the recommendation of more aggressive initial evaluation. Consideration of review of HSIL tests prior to surgical procedures is recommended by the ASCCP in light of the data from ALTS: a second cytopathologist rereading smears with an HSIL diagnosis resulted in agreement in <50% of cases *(see Table 3)*. Note also that 3% of HSIL tests were reread as normal.

Prevalence of missed CIN2/3 or ICC varies widely with the experience of the colposcopist. Estimates of the risk of incident disease range from 22% CIN (all Grades) including 15.9% CIN2/3 at a median follow-up of 10.6 years to 43% CIN at an average follow-up of 14 months. The brevity of the interval suggests substantial missed prevalent disease.

RECOMMENDATIONS *on the* MANAGEMENT *of* CERVICAL INTRAEPITHELIAL NEOPLASIAS (CIN)

Management *of* CIN1

- *Satisfactory Colposcopy:* Observation is preferred in the compliant patient. Retest with cytology twice at 6-month intervals or with HPV testing alone at 12 months. Repeat colposcopy for any abnormal result. Rescreen again in 12 months if colposcopy is normal. If treatment is undertaken, timing and modality should be determined by patient and provider preferences.
- *Unsatisfactory Colposcopy:* A diagnostic excisional procedure is preferred. Exceptions may be made for pregnant patients and adolescents. Ablative procedures are not recommended.

RATIONALE. CIN1 is by far the most common dysplastic abnormality diagnosed in cervical cancer screening. Transient CIN1 is a frequent consequence of HPV infection, and is endemic in young, sexually active women. Most patients will resolve CIN1 spontaneously, however a minority (11% in Ostor's review) will be found subsequently to harbor CIN2/3. This occurs as a consequence of missed CIN2/3 at colposcopy, subsequent infection with different HPV types, and presumably, progression.

LSIL is associated with the presence of detectable oncogenic HPV in 83% of patients in the ALTS population, and CIN1 carries similar risk. ALTS follow-up studies indicate that the risk of a woman with CIN1 followed without treatment subsequently developing CIN2/3 is similar to the risk of a woman with an ASC-US/HPV+ or LSIL test and negative colposcopy developing CIN2/3. Either a CIN1 biopsy or a normal biopsy in that setting is associated with the same risk at two years. This observation prompts the recommendation for follow-up with similar modalities and schedules.

Diagnosis of CIN2/3 is highly correlated with productive high-risk HPV infection whether or not CIN1 or LSIL is diagnosed prior to CIN2/3. The recommendations above are therefore an attempt at a balance between overtreatment and the desire to minimize loss to follow-up or progression of the disease. The recommendation to treat persistent CIN1 is consistent with the data of Nobbenhuis, et al., and with ACOG recommendations.

Management *of* CIN2/3

- *Satisfactory Colposcopy:* Ablation or excision of the entire transformation zone. Excisional procedures have the advantage of permitting pathologic examination to exclude early invasive cancer.
- *Unsatisfactory Colposcopy*: A diagnostic excisional procedure is preferred. Ablative procedures are not recommended.
- *Special Circumstances*
  - Pregnancy–Treatment should be deferred to the postpartum period unless excision is required to rule out invasive cancer.
  - Adolescents–CIN2 may be followed similar to CIN1 in the compliant adolescent.

RATIONALE. The proportion of women with CIN2/3 and an unsatisfactory colposcopy harboring ICC has been reported to be as high as 7%. The rate of spontaneous regression of CIN2/3 in pregnancy/delivery is high: one series reports regression in 69% of 153 patients and no progression to ICC. Recognizing the low risk of ICC and the substantial risk of bleeding and premature labor associated with excisional procedures during pregnancy motivates the recommendation for observation.

A similar sort of risk/benefit calculation underlies the recommendation concerning CIN2 in adolescents. Histologic diagnoses are poorly reproducible, risk of progression to ICC approaches zero and substantial regression of CIN2 (unlike CIN3) is observed, particularly in younger patients.

TEST *of* CURE: RECOMMENDATIONS FOR FOLLOW-UP *of* TREATMENT *of* SILs, AIS

Follow-up *of* Women Treated *for* Squamous Intraepithelial Lesions

FOLLOWING TREATMENT OF LSIL:

- Restart cytologic screening (two negative annual Pap tests before biennial screening, if biennial screening is elected) or
- Women 30 and older who have a negative Pap test and a negative HPV test may be rescreened in 30-36 months.

FOLLOWING TREATMENT OF HSIL:

- Two Pap tests, at 6 and 12 months, or a Pap and HPV test at 6 months, with colposcopy if either is positive, then
- Annual cytologic screening for at least ten years thereafter, preferably for life.

RATIONALE. A correctly interpreted biopsy showing an intraepithelial dysplastic lesion indicates that HPV infection has occurred. For most women, particularly younger women with low grade SILs, this is a self-limited condition.

Histologic CIN1 is a manifestation of HPV infection that occurs with an incubation period of months from exposure (similar to cutaneous and genital warts). It has been demonstrated during follow-up of untreated CIN1 by Nobbenhuis, et al., that the only patients who subsequently develop histologic CIN2/3 during follow-up are (a subset of) those who continue to express the virus for more than 6 months after diagnosis of "mild to moderate dyskaryosis". The same group has demonstrated that persistence of high-risk HPV after treatment of dysplasia identifies those women at risk for recurrence.

Most of the literature concerning the risk of subsequent dysplasia and ICC concerns women with CIN2/3, for whom risk is significant despite treatment. Risk of invasive cancer following treatment of CIN2/3 is independent of treatment modality and is quite uniform in different populations at 85-123/100,000/year. This represents a risk approximately 12 times that of

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our 8/100/000/year KPNCR population. While loss to follow-up or inadequate follow-up in treated women can be substantial, it must be stressed that the majority of cases of ICC that have been reported post treatment occur in women who have had what is believed to represent adequate follow-up. *There is no follow-up scheme that can reduce the risk of ICC to zero following treatment of SILs. There will be cases of ICC in women whose treatment is perfectly adherent to this or any other guideline. This cannot be prevented and does not indicate an error in practice or recommendations.*

The risk of ICC following treatment of CIN2/3 is quite constant over time, and this elevated risk exists for as long as it has been measured (at least 10 years), and hence, any response to that risk should ideally persist for at least ten years. In women who have margins on their LEEP or cone specimen involved by dysplasia, cytologic follow-up without retreatment is adequate.

Extension of screening intervals for women with a history of treatment for CIN2/3 and negative Pap and HPV tests is not presently recommended pending additional data.

Follow-up *of* Women Treated *for* Adenocarcinoma In Situ (AIS)

- In the compliant patient who desires future fertility:
  - Document discussion of potential risk;
  - Pap test and ECC every six months.
- At the completion of childbearing: hysterectomy.

RATIONALE. A systematic review by Krivak, et al., found that of 154 women with AIS and clear margins on conization or LEEP, 40/154 (26%), harbored additional AIS on a subsequent cone or hysterectomy, and 3/154 (1.9%) were found to have unsuspected invasive cancer. Both conventional cytology and endocervical curettage have high false negative rates. Negative cone margins do not reliably exclude the presence or subsequent development of invasive adenocarcinoma despite regular negative cytologic surveillance. The risk of invasive cancer persists >10 years post diagnosis. Because of the extreme rarity of this condition, trials of the application of HPV testing may never be done.

Online Resources

- NATIONAL ORGANIZATIONS/RECOMMENDATIONS
  - American Cancer Society *(www.cancer.org)*
  - American Society for Colposcopy and Cervical Pathology *(www.asccp.org)*
  - Bethesda 2001 *(bethesda2001.cancer.gov)*
- HPV INFORMATION
  - National HPV & Cervical Cancer Resource Center *(www.ashastd.org)*
  - Women's Cancer Network *(www.wcn.org)*
  - National Cervical Cancer Coalition *(www.nccc-online.org)*
  - National HPV & Cervical Cancer Public Education Campaign *(www.cervicalcancercampaign.org)*
  - National Women's Health Resource Center *(www.healthywomen.org)*
  - The HPV Test *(www.thehpvtest.com)*

Acronyms

AIS	Endocervical Adenocarcinoma in Situ
ACOG	American College of Obstetricians and Gynecologists
ACS	American Cancer Society
AGC	Atypical Glandular Cells
AHRQ	Agency for Healthcare Research & Quality
ALTS	ASC-US and Low Grade Triage Study
ASC-H	Atypical Squamous Cells rule out High-grade SIL
ASC-US	Atypical Squamous Cells of Undetermined Significance
ASCCP	American Society for Colposcopy and Cervical Pathology
CIN	Cervical Intraepithelial Neoplasias (histologic) Grades 1, 2 & 3
ECC	Endocervical Curettage
EMB	Endometrial Biopsy
HPV	Human papillomavirus
HSIL	High-Grade Squamous Intraepithelial Lesions (cytologic), equivalent to CIN2/3
ICC	Invasive Cervical Cancer
LEEP	Loop Electrosurgical Excision Procedure (aka, LLETZ, LETZ)
LSIL	Low-Grade Squamous Intraepithelial Lesions (cytologic), equivalent to CIN1
NIL	Negative for Intraepithelial Lesion or malignancy
NOS	Not Otherwise Specified
SIL	Squamous Intraepithelial Lesions (cytologic)

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Available on the Clinical Library: *http://cl.kp.org*

Clinical Practice Guideline for *Cervical Cancer Screening & Follow-up of Abnormal Cytology Results*

- Version with complete References
- PDF version

Algorithms for *Cervical Cancer Screening & Follow-up of Abnormal Cytology Results* (PDF version)

Patient Information on Cervical Cancer Screening

- Patient Flyer distributed by Medical Assistants
- What Women should know About the DNA Pap
- Templates for Patient Results Letters (2)

Physician & Other Provider Information

- Provider Information Sheet–Frequently Asked Questions
- Quick Reference for Medical Assistants

Berkeley Regional Laboratory Information

- Sample Laboratory Requisition Form and Instructions

From Regional Health Education

- When Should you Get A Pap Test and Why?
- Human Papilloma Virus (HPV)
- Genital Warts
- What Are Gynecologic Cancers?

Contact Information

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TPMG Quality & Operations Support
1800 Harrison Street, 4th Floor
Oakland, CA 94612
510-625-6650 or tie-line 8-428-6650.

To obtain more information about KPNC Clinical Practice Guidelines, printed copies, or permission to reproduce any portion, please contact TPMG Quality & Operations Support, or send an e-mail message to *clinical.guidelines@kp.org*.

KPNC Clinical Practice Guidelines and implementation tools can be viewed on-line on the Kaiser Permanente Northern California intranet at *http://cl.kp.org*.

CME Credit. Continuing Education Credit for physicians and nurses is available for review of this guideline. The CME Pre-Test and Post-Test is available on-line at *http://cl.kp.org* or by calling 510-625-6650 or tie-line 8-428-6650.

This website is accessible only from the Kaiser Permanente computer network.

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The Permanente Medical Group (TPMG) Clinical Practice Guidelines have been developed to assist clinicians by providing an analytical framework for the evaluation and treatment of selected common problems encountered in patients. These guidelines are not intended to establish a protocol for all patients with a particular condition. While the guidelines provide one approach to evaluating a problem, clinical conditions may vary significantly from individual to individual. Therefore, the clinician must exercise independent judgment and make decisions based upon the situation presented. While great care has been taken to assure the accuracy of the information presented, the reader is advised that TPMG cannot be responsible for continued currency of the information, for any errors or omissions in this guideline, or for any consequences arising from its use.

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Provider Information

Frequently Asked Questions

2003 Clinical Practice Guideline for Cervical Cancer Screening

1. **How is this version different? Just tell me the important stuff!**

   *Start Pap smears **3 years** after onset of vaginal intercourse or age 21*

   Age <30

   - *Recommended: 2 Annual negatives, then Pap every 2 years (biennial)*
   - *May select annual Pap*

   Age 30+

   - ***Recommended**: Pap plus HPV q 3 years*
   - ***Re-screen** Pap negative/HPV positive with **both tests in 1 year***
   - *May select annual or biennial Pap alone*

   *Follow-up for a variety of common situations is 2 Paps at 6 month intervals **or one HPV test at 12 months.***

   - *ASC-US HPV positive and a negative colposcopy*
   - *ASC-H and a negative colposcopy*
   - *LSIL and a negative colposcopy*
   - *Adolescents with LSIL managed without colposcopy*
   - *HPV infection is often transient, even high-risk types.*

2. **Does this mean that if I use Pap plus HPV I can't see my patients more often than every 3 years?**

   *No ! You can see them whenever they need it. Just don't Pap them more frequently if they are negative on both tests. This is not being done to save appointments, but because it's a **better, more reliable** screen, and avoids many of the false positives seen with Paps alone, and which lead to unnecessary follow-ups and procedures.*

3. **Why not do both tests every year?**

   *It's adverse for both patients and practitioners: More tests, procedures, anxiety and cost without additional cancer protection. **There is no additional safety associated with the detection of transient infection (i.e. CIN1).** Only the detection of potentially precancerous lesions (CIN2/3) is valuable. And, we will drown the lab and turnaround will be bad for everybody if this practice is widespread. Besides, the yearly Pap, especially combined with HPV triage of ASC-US, remains a reliable screening test for precancerous lesions.*

4. **Suppose my patient gets HPV right after her negative Pap and HPV. How can she be safe for 3 years?**

   *Remember the time course – **10 years (average) from HSIL to cancer!***

   Remember also that this applies to the immunocompetent woman. Women on chronic/repeat courses of steroids, transplant drugs, chemo or women who are HIV+ need different screening.

5. **How do I talk to my patients about testing?**

   We do a Pap smear to test for abnormal cells on your cervix just like we always did, and a DNA test to decide when you need to be tested again.

   This new method is better: more accurate, less tests and biopsies, and is safer than annual dry slide Paps. Mention that this is FDA approved, consistent with recommendations of American Cancer Society and ASCCP, and KP is the first health plan to offer it for free while other insurance companies often charge up to $50 for the additional test.!

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6. **How do I talk to my patients who want annual Paps (or biennial at age 30+)? Or both tests every year? Or monolayer cytology (Thin-Prep)?**

   Annual Paps*: Tell them that this means more tests and biopsies that are really not needed, and less protection from cancer. After that, do what they want & go on*

   Both tests every year*: Politely decline. Tell them that if they have already decided to be tested yearly they don't need HPV to find out if they need to be tested yearly. Be persistent.*

   Monolayer cytology*: Research shows that once you add HPV testing to Pap smears the advantage of monolayer cytology goes away.*

7. **How can you say that Pap plus HPV is safer than dry slides?**

   You really know who needs annual screening, who may be at risk over the next few years.
   Knowledge of HPV positive result decreases loss to annual follow-up
   Future: Colposcopy of women with repeated HPV positive Pap negative results. How long to wait to colpo? 1 year, 2 years, longer? Research in progress – stay tuned

8. **How do I talk to my patients who are upset because they equate a positive HPV test with STDs like gonorrhea or syphilis?**

   Talk to them at the time of testing to prepare them. Go through the info:
   Cumulative lifetime risk of (high risk) HPV infection is at least 75%, probably higher.
   This doesn't mean that your partner has been unfaithful !! (very important)
   May have been acquired 50 or more years ago, and not necessarily through intercourse
   No, you don't have to tell anybody
   There is no treatment – there doesn't need to be – this is a normal consequence of having ever had sex (with men or women) and is not a disease.
   Condoms have little if anything to do with transmission!

9. **What do I do if they still want more information?**
   Give them the patient information brochure and suggest the Web!

   National HPV & Cervical Cancer Resource Center
   www.ashastd.org
   Women's Cancer Network
   www.wcn.org
   National Cervical Cancer Coalition
   www.nccc-online.org
   National HPV & Cervical Cancer Public Education Campaign
   www.cervicalcancercampaign.org
   National Women's Health Resource Center
   www.healthywomen.org
   The HPV Test
   www.thehpvtest.com

10. **Are there pitfalls of Pap plus HPV that I need to avoid?**

- *Don't use both tests on women under 30*
- *Don't do both tests at intervals <30 months (if both are negative)*
- *Don't feel you have to do a Pap just because the woman is there for a visit. Follow the intervals.*
- *Don't do both tests or extend intervals on immunosuppressed women*
- *Don't colpo women for a single HPV positive / cytology negative result (or maybe even for multiple results)*
- *Don't treat a woman for a positive HPV test in the absence of CIN*
- *Don't blame! A positive HPV test does not mean that their partner has been unfaithful!*
- *Don't tell women that they need to use condoms because they are HPV positive*

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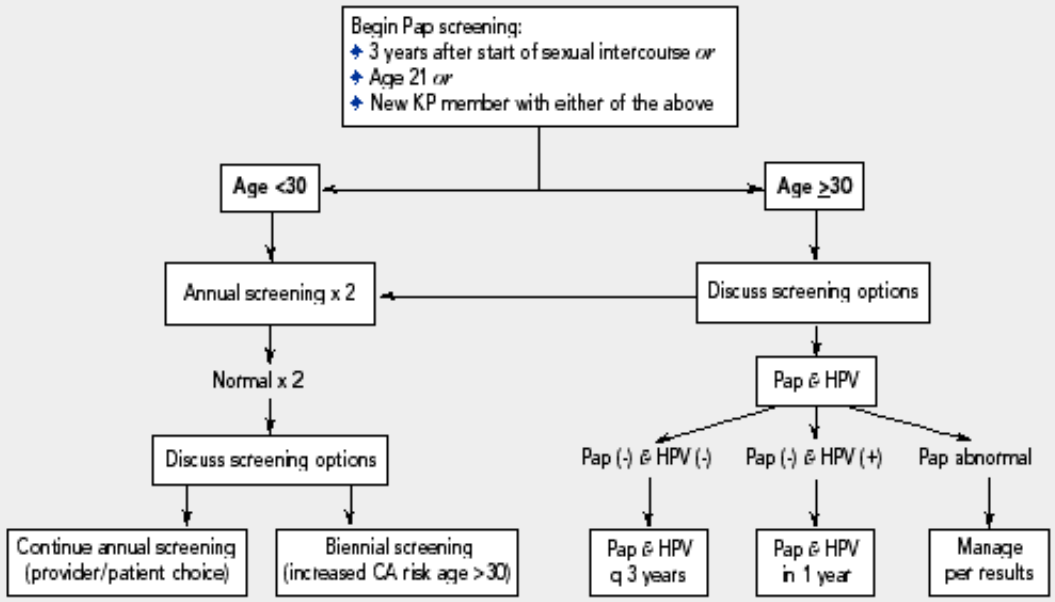
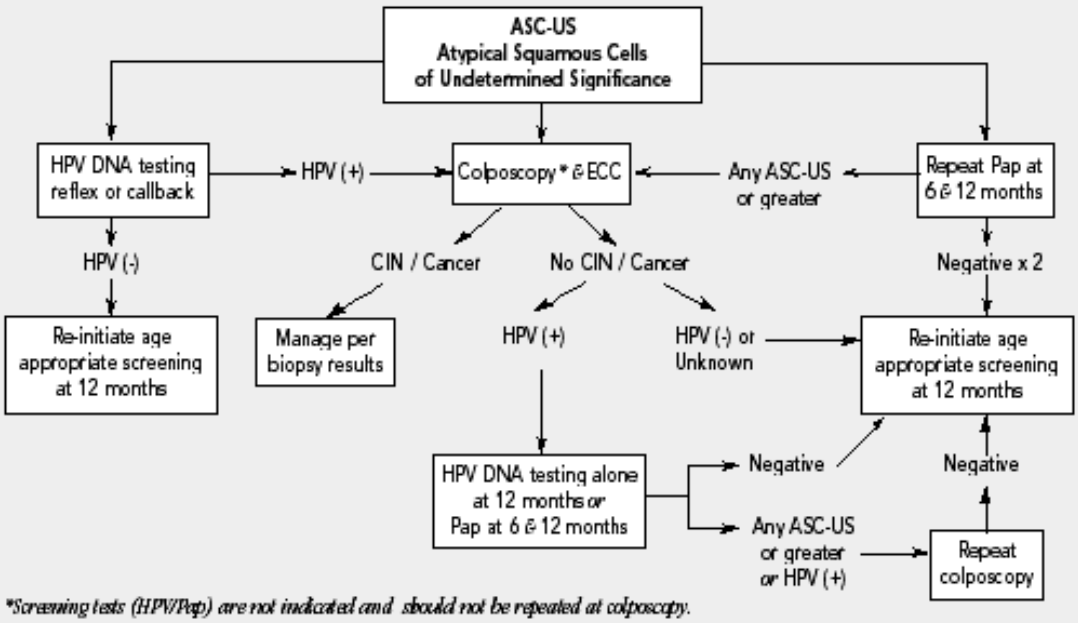
ALGORITHMS *for* CERVICAL CANCER SCREENING & *the* FOLLOW-UP *of* ABNORMAL CYTOLOGY RESULTS

CERVICAL CANCER SCREENING*



** For HIV positive or immunosuppressed women, see guideline.*

FOLLOW-UP *of* ASC-US



**Screening tests (HPV/Pap) are not indicated and should not be repeated at colposcopy.*

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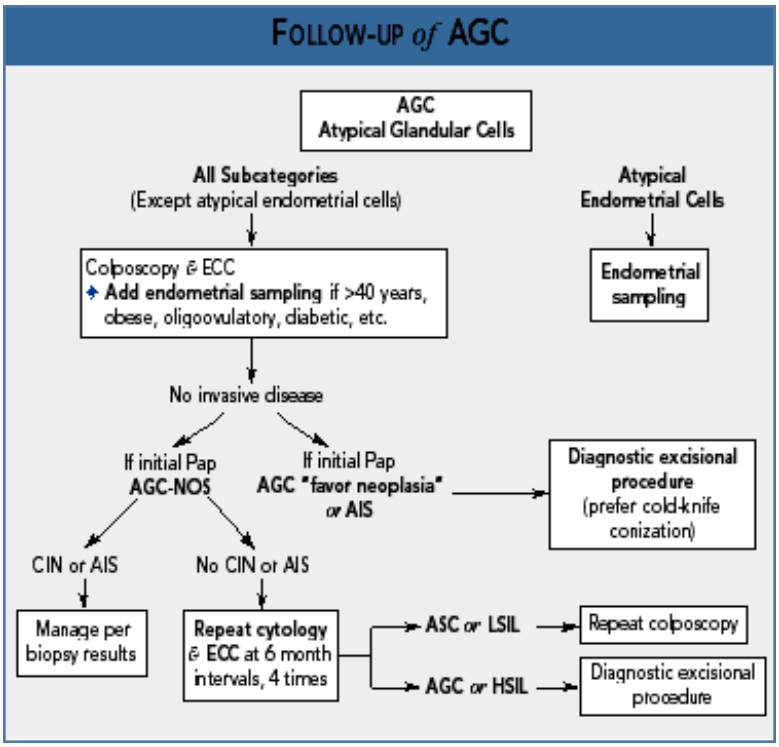

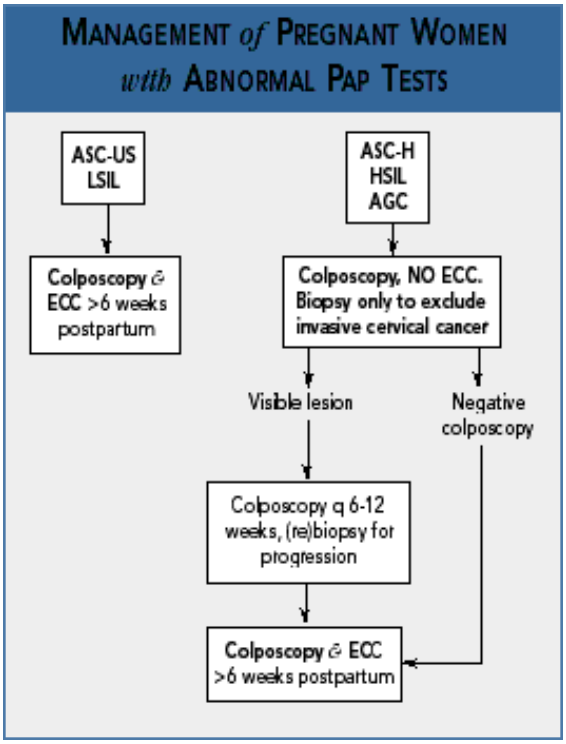

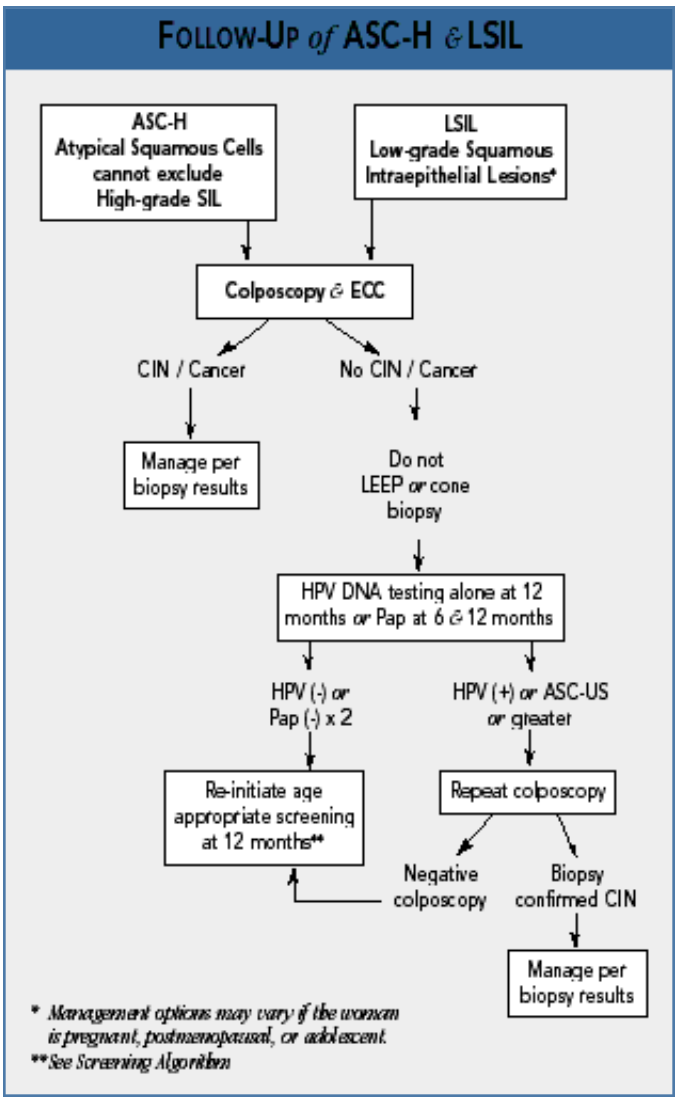

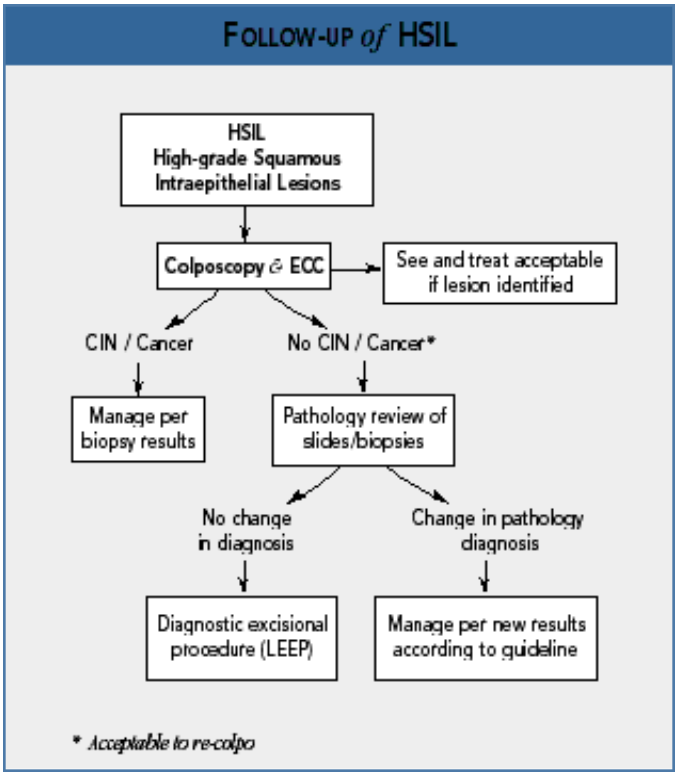

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When Should You Get a Pap Test and Why?

A Pap test can detect precancerous changes on the cervix, which can usually be treated with simple office procedures.

A Pap test—often called a Pap smear—is a quick test that can help find early signs of cervical cancer. Your doctor or nurse practitioner gently removes cells from your cervix (the part of the uterus or womb at the top of the vagina) during a pelvic exam. The cells are sent to a lab to see if they are cancerous or might turn into cervical cancer.

Most Pap tests are negative, which means that the cells are normal and healthy. If there are changes in the cells on your cervix, you may need further testing to find out if you have precancerous changes.

Why is it important to get a Pap test?

A Pap test can detect precancerous changes on the cervix, which can usually be treated with simple office procedures. Because of the Pap test, there are now many fewer deaths from cervical cancer.

How does a woman get cervical cancer?

Scientists think that the Human Papillomavirus (HPV) causes most types of cervical cancer.

HPV is a common sexually transmitted virus. Sometimes it can cause genital warts, though most people with HPV have no visible symptoms. There are many types of HPV, and most of them are harmless. A few types of HPV are associated with cervical cancer.

Smoking may also contribute to the development of cervical cancer in women who have HPV. If you are a smoker and would like to quit, talk to your medical professional, or go to your health education department for more information. Kaiser Permanente can help you quit.

How can I protect myself from cervical cancer?

The best way to protect yourself from cervical cancer is to get regular Pap tests. Precancerous changes are present for years in most women who eventually develop cervical cancer. Cervical cancer is preventable if precancerous cell changes are detected and treated early, before cervical cancer develops.

HPV can be spread during sex and through skin-to-skin contact. Often, genital HPV cannot be prevented by condom use. However, condom use is recommended in order to prevent other sexually transmitted diseases.

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Women should go to the doctor or clinic if there are any visible signs of genital warts, such as unusual bumps or skin changes on or near the vagina, vulva, anus, or groin (where the genital area meets the inner thigh). You should also see your doctor if there is any unusual itching, pain, or bleeding. Men should go to the doctor or clinic if there are any unusual bumps or skin changes on the penis, scrotum, or groin.

Who should get a Pap test?

You should get a Pap test regularly if any one of the following applies:

- you have been sexually active for 3 years or more
- you are over 21 years old
- you have had an abnormal Pap test
- you have had cancer of the cervix, vulva, or vagina
- you have had genital warts

How often should you get a Pap test?

Kaiser Permanente recommends that women under the age of 30 get a Pap test every two years (after having had two normal yearly Pap tests in a row). Cervical cells become cancerous very slowly. A Pap test every two years can find changes in cells early on, which can usually be treated during an office procedure before the cancer can spread. At age 30 and over, you should have Pap plus HPV testing. If both tests are negative, you are safe from cervical cancer for three years. If your HPV test is positive, you need to have a Pap plus HPV test every year until your HPV becomes negative. This does not mean you can't see your doctor more often, it just means that you do not need testing for cervical cancer more often.

You should also get a Pap test if any one of the following applies:

- you are a new member
- you have recently returned to Kaiser Permanente, and have not had a Pap test at Kaiser Permanente in the past two years
- you have never had a Pap test

If you had a Pap test that was abnormal, you and your doctor or nurse practitioner will decide how often you need to get a Pap test.

If you have bleeding between periods, pelvic pain, or other symptoms, you should see your doctor or nurse practitioner.

You may be wondering . . .

Do I need to get a Pap test if I do not have sexual intercourse?

It is recommended that all women who are between the ages of 21 and 65 (and have not had a hysterectomy) have Pap tests.

When can I stop having Pap tests?

You can stop having Pap tests at age 65 if:

- you have had at least three normal Pap tests in the past ten years; *or*
- if you have had a total hysterectomy (where your cervix was removed) *and* you have no history of:
  - ✓ cancer (of the cervix, vulva or vagina)
  - ✓ genital warts.

  If you had a partial hysterectomy and you still have your cervix, you should continue to have Pap tests.

Other resources

- Call your local Kaiser Permanente facility and ask for the Health Education Department to learn more about quit smoking programs
- Check your *Kaiser Permanente Healthwise Handbook*
- Call the Kaiser Permanente Healthphone at 1-800-33-ASK ME (TTY: 1-800-777-9059)
- Visit our Web site at *www.kp.org*
- Call NCI cancer information at 1-800-422-6237

This information is not intended to diagnose health problems or to take the place of medical advice or care you receive from your physician or other medical professional. If you have persistent health problems, or if you have further questions, please consult your doctor.

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915800013 (Rev. 3-03), RL 7.3

Human Papillomavirus (HPV)

Think about it

Talk about it

Protect yourself and your partner

Human Papillomavirus (HPV) is the most common sexually transmitted disease (STD) in the United States. Over 20 million women and men are infected at any one time, but most don't know it. There are many types of HPV, and most of them are harmless.

Currently, there is no cure for HPV. However, there are treatments for the diseases caused by HPV, such as genital warts and precancerous cells on the cervix.

Most people with HPV have no symptoms and will not develop any problems from the infection. Typically, within 12 months after infection occurs, the virus is no longer detectable. Infection with some types of HPV can cause genital warts. Other types of HPV can be associated with cervical and anal cancer, but this is rare. These types usually don't cause warts. Often, a person will be infected with more than one type of HPV.

How is HPV transmitted?

HPV is spread through skin-to-skin contact, usually during sex. It is generally passed from one partner to another during vaginal and anal sex, and occasionally can infect the throat from oral sex.

HPV is spread easily during sex, even if condoms are used, and even if no genital warts are present. The virus lives in the skin of infected people usually in areas such as the penis, scrotum, and vagina. Condoms do not offer much protection against HPV because the virus can often be in areas that the condom doesn't cover. Still, it is a good idea to use them because there are other STDs that condoms do prevent, such as chlamydia, gonorrhea, HIV, and hepatitis B and C. The only definite way to protect yourself from HPV is not to have sex.

How do I know if I have HPV?

Usually the only way to know if you have HPV is if genital warts appear or from an abnormal Pap test.

If a woman has an abnormal Pap test, follow-up testing may be needed to determine if HPV is the cause.

How can I protect myself from HPV?

Since HPV is so common and so easy to transmit, most sexually active people will have HPV infections at some point in their lives. In most people, these infections will not cause any serious problems.

Both men and women should do self-exams for warts and unusual bumps around the vagina and anus. If you are a woman, the best thing you can do to protect yourself from having an HPV infection that progresses into cervical cancer is to get regular Pap tests. If you are 30 years old or older, HPV testing is also helpful to determine how often you need a Pap test.

What are genital warts?

Some types of HPV can cause genital warts. Genital warts usually appear as cauliflower-like bumps or flat pink, red or flesh-colored patches inside the vagina, on the lips around the vagina, on the penis or scrotum, around the anus, or occasionally on the belly or thighs. The affected area can itch, or feel irritated, but sometimes the warts do not cause any discomfort at all. Often, an outbreak of genital warts may occur when the immune system is weakened. If a person is infected with HPV, it may take several months or even years for the warts to appear. Your doctor or nurse practitioner can usually identify warts during an office visit.

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What is the treatment for genital warts?

Although there is no cure for HPV, there are different treatments for genital warts. Your doctor or nurse practitioner may recommend surgical removal, freezing the warts, laser treatment, or putting medication on the warts. It often takes several visits to completely remove the warts. Once the warts are gone, the virus may still be present, and passing it to your partner is still possible.

Sometimes genital warts clear up without treatment after a few months. However, they can sometimes grow and spread through the genital area. If you think you have genital warts, talk to your doctor or nurse practitioner.

How is HPV linked to cancer?

Some types of HPV are known to cause cervical cancer in women and anal cancer in women and men. Most people who are infected with HPV will not get cancer.

For women, the most important thing you can do to protect yourself from cervical cancer is to get regular Pap tests. Pap tests can detect pre-cancerous cells on the cervix. If results reveal abnormal cells then follow-up tests are needed.

Smoking may also contribute to the development of cervical cancer in women who have HPV. If you are a smoker and would like to quit, talk to your doctor or nurse practitioner or call your local Kaiser Permanente Health Education Department for more information.

Both men and women who have anal sex should be aware of the symptoms of anal HPV infection. These may include bleeding from the rectum during bowel movements or during anal sex, unusual bumps around the anus, or pain during anal sex. If you have any of these symptoms, or if you have had anal warts in the past, talk to your doctor or nurse practitioner.

What about HPV and pregnancy?

HPV does not affect a woman's ability to get pregnant and is rarely a concern during pregnancy. In some women who have HPV, pregnancy may cause an outbreak of genital warts. Pregnancy can also cause warts to grow larger than usual. In rare cases, if large warts obstruct the birth canal, a Caesarian section may be necessary. This is unlikely to happen if you are receiving regular prenatal care and treatment for your warts.

What should I tell my partner if I have been diagnosed with HPV?

HPV can be a difficult topic to discuss with a partner because, aside from not having sex, there is no reliable way to prevent HPV transmission. When you tell your partner you have HPV, you may want to let him or her know that this is a very common virus that many sexually active people carry, and that, in most people, it does not cause serious problems. Remember: It is important to use condoms to prevent the transmission of other STDs. You may also want to ask your doctor or nurse practitioner about being tested for other STDs

What if I'm under 18?

If you are 12 years old or older, you can get a Pap test and be seen, evaluated, and treated for STDs (and other sexual health concerns), without a parent's permission. California State law requires that Kaiser Permanente must protect your privacy.

Other resources

Web sites

- Kaiser Permanente
  www.kp.org
- National HPV and Cervical Cancer Prevention Resource Center
  www.ashastd.org/hpvccrc

Phone numbers

- Kaiser Permanente Healthphone
  1-800-33-ASK ME
  (TTY: 1-800-777-9059)
- National STD Hotline
  1-800-227-8922
- National HPV Hotline
  (919) 361-4848

Kaiser Permanente Healthwise Handbook.

Visit your local facility's Health Education Department for books, videos, classes, and additional resources.

This information is not intended to diagnose health problems or to take the place of medical advice or care you receive from your physician or other medical professional. If you have persistent health problems, or if you have further questions, please consult your doctor.

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915800045 (Rev. 04-03), RL 8.5

Women's Health

New Improvement In Cervical Cancer Prevention For Women Age 30 and Over

New technology now enables us to check for the HPV virus that is associated with cervical precancer and cancer at the same time as your Pap smear. When this test is done along with a Pap smear in women age 30 and older, the two together are *much* more accurate than Pap smears alone in determining whether you are at risk for developing cervical precancer or cancer. If both tests are negative, you can be confident that your risk of cervical cancer over the next 5-10 years is *extremely* low and you don't need a repeat Pap for another three years. If your HPV test is positive then yearly Pap smears should be done, even if your Pap is normal.

If your immune system is depressed, then HPV testing is not helpful for you to know how often you need a Pap smear. Please inform your provider if you have been taking steroids like Prednisone by mouth for more than a month, are taking transplant drugs or chemotherapy, or have HIV infection. Any of these can depress your immune system.

We are proud to be one of the first Health Plans in the country to offer this advance in preventive medical care to our Members.

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DNA Pap

What Women Should Know About

Cervical Cancer Prevention Using Pap Smears and HPV Testing

In the United States, 13,000 women are diagnosed with cervical cancer each year, and 4,100 women die. However, cervical cancer can usually be prevented through early detection of pre-cancerous changes. The traditional screening test for cervical cancer is the Pap test. HPV DNA testing is a new and exciting addition to the Pap test.

What is the Pap test?

The Pap test detects changes in the cells of the cervix. These changes are most commonly harmless, but can be precancerous, or cancer. The test is done by using a small spatula to collect a sample of cells from the surface of the cervix. Then the cells are put on a slide and examined under a microscope

What is HPV (Human Papillomavirus)?

HPV is a virus that most humans carry at some time in their lives. There are approximately 100 types of HPV. Some HPV types cause warts, some cause mild changes in cervical cells that do not turn into cancer, and some cause pre-cancerous changes. Occasionally, having HPV for many years can lead to cancer of the cervix, vagina, vulva (area around the opening of the vagina) or anus.

The types of HPV that are found in the genital areas are usually sexually transmitted. Experts estimate that over 20 million Americans currently harbor the virus. In some age groups, as many as one-third of people have HPV at any one time. Virtually all humans who have ever been sexually active will have the virus at least once. This is normal, it is not dangerous, and does not represent “disease”.

In almost all cases, a healthy immune system will keep the virus (including the cancer-related types) under control or clear it completely. Only a tiny fraction of women with HPV develop cervical cancer if not treated. However, if HPV is persistent over many years, there is a greater chance of developing cell changes that may lead to cervical cancer.

Who carries HPV?

Anyone who has ever had sexual relations may have gotten HPV. It is estimated that nearly everyone will carry genital HPV at some time in their life, if only briefly.

What are the signs of HPV?

In most cases, HPV is harmless and has no symptoms. However, it may cause changes in the cervical cells. These changes can be identified in your Pap test. Some of these abnormalities are mild and need no treatment. Some of the more severe abnormalities could lead to cervical cancer if not treated but this process takes many years.

Low-risk, non-cancer causing types of HPV also cause genital warts.

Signs of HPV infection can appear weeks, months, or even decades after initial infection, so it is possible to have HPV for a long time without knowing it. Also, women who get HPV during their teenage years may not show cervical cell changes until their thirties or forties – or later – or may never develop any abnormality at all.
Only in very rare cases does the presence of HPV lead to cervical cancer.

Why is the HPV test useful?

The HPV DNA Test can detect the presence of any of 13 types of HPV that are related to cervical cancer. The HPV test helps us know which women really do need yearly Pap tests and which women can safely extend the screening interval to 3 years.

If I have a negative Pap and HPV test, how can I be safe for 3 years? What if I get HPV the next day?

Normally, cervical cell changes occur extremely slowly. It takes an average of 10 years to move from the most severe precancerous changes to cancer.

How is the HPV DNA test done?

It is done at the same time as the Pap test by using a small soft brush to collect cervical cells which are sent to the laboratory.

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What is the DNA Pap?

The DNA Pap combines HPV DNA testing with the Pap test, for routine cervical cancer screening. It is useful in women age 30 and over. A normal Pap test with a negative HPV DNA Test means you can be very confident (>99.9%,) that you do not have precancerous cervical changes or cancer. Research shows that one normal DNA Pap result provides better reassurance of no cervical cancer or precancer in the next several years than three normal annual Pap tests.

The **American Cancer Society** recommends that DNA Pap may be safely used to screen women age 30 and over, **and if negative, the test does not need to be repeated for 3 years**. Kaiser Permanente is one of the first organizations to offer this new, more accurate testing to women.

Why is the DNA Pap only for women age 30 and over?

HPV is very common. Cervical cancer is very, very rare, and when it does occur, it almost always does so in women age 30 and over. So many women under age 30 have HPV that adding the HPV test to the Pap isn't helpful.

After age 30, HPV is much less common. Many women who test positive for HPV got the virus years previously, and their immune system hasn't cleared it. So they need annual Pap tests. That makes the HPV test useful.

What if I have a normal Pap result, and my HPV test is positive?

A positive HPV test with a normal Pap result does *not* mean you will develop cervical precancer or cancer. Your doctor will recommend yearly Pap testing for you in order to detect any changes in the cervical cells while they can be easily treated.

Why shouldn't I have both tests every year?

If you are already planning to have a Pap test every year you don't need the HPV test to find out if you need a Pap every year. The Pap test remains an excellent screening test for cervical cancer, but many women who have an abnormal Pap don't have precancerous changes. One of the benefits of combined testing is to reassure women who are negative on both tests that they can very safely have DNA Pap screening every three years. This means fewer tests and visits and biopsies without increasing cancer risk, and agrees with the recommendations of the American Cancer Society and national experts.

Should women under age 30 ever be tested for HPV?

Not if their Pap test is normal. But HPV DNA testing is extremely helpful for women of all ages who have inconclusive Pap test results. Each year, over two million women receive such results known as ASC-US (atypical squamous cells of undetermined significance). Again, a negative HPV DNA test can assure that the woman has no cervical disease. A positive test only means that more frequent Pap testing should be done.

Can HPV infections be treated?

While there is currently no treatment available for the virus itself, treatments do exist for the problems HPV can cause, such as cervical cell changes or genital warts. Your healthcare provider can discuss appropriate treatment options for those conditions with you, if you need them.

Key Points to Remember:

- Almost all women will have HPV at some point, but very few will develop cervical cancer. When a woman's immune system is working normally, only HPV infection that is persistent over many years can lead to cervical cancer.
- If you are age 30 or older, HPV testing can be helpful to know how often you need screening for cervical cancer. If you are under 30, presence of HPV is expected, and testing is only helpful if you have some types of abnormal Pap smear.
- Don't blame**!** Your HPV status is ***not*** a reliable indicator of you or your partner's sexual behavior.

Resources on HPV and Cervical Cancer

National HPV & Cervical Cancer Resource Center
www.ashastd.org

Women's Cancer Network
www.wcn.org

American Cancer Society
www.cancer.org

National Cervical Cancer Coalition
www.nccc-online.org

National HPV & Cervical Cancer Public Education Campaign
www.cervicalcancercampaign.org

National Women's Health Resource Center
www.healthywomen.org

The HPV Test
www.thehpvtest.com

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Lo que las mujeres deben saber acerca de

La Prueba Papanicolaou y la prueba del HPV ADN

En los Estados Unidos, 13,000 mujeres son diagnosticadas con cáncer cervical cada año, y 4,100 mujeres mueren a causa del mismo. Sin embargo, el cáncer cervical puede usualmente ser prevenido a través de la detección temprana de los cambios precancerosos. La prueba tradicional de detección para el cáncer cervical es la prueba de Papanicolaou (prueba de Pap). La prueba del HPV ADN es una nueva y emocionante adición a la prueba de Pap.

¿Qué es la prueba de Papanicolaou?

La prueba de Pap detecta cambios en las células de la cérvix. Estos cambios con mayor frecuencia son inocuos, pero pueden ser precancerosos o ser cáncer. La prueba se hace usando una pequeña espátula para recoger una muestra de células de la superficie de la cérvix. Luego, las células se ponen en una lámina de vidrio y se examinan bajo un microscopio.

¿Qué es el HPV (Virus del papiloma humano)?

El HPV (abreviatura en inglés) es un virus que la mayoría de los seres humanos portan en algún momento de sus vidas. Hay aproximadamente 100 tipos del HPV. Algunos tipos del HPV causan verrugas, algunos causan cambios leves en las células cervicales que no se convierten en cáncer, y otros causan cambios precancerosos. Ocasionalmente, el portar el HPV por muchos años puede llegar a producir cáncer de la cérvix, vagina, vulva (área alrededor de la abertura de la vagina) o en el ano.

Los tipos del HPV que se encuentran en las áreas genitales usualmente son de transmisión sexual. Los expertos estiman que más de 20 millones de estadounidenses actualmente portan el virus. En algunos grupos de edad, hasta una tercera parte de la gente tiene el HPV en algún momento. Virtualmente todos los seres humanos que han sido alguna vez sexualmente activos tendrán el virus por lo menos una vez. Esto es normal, no es peligroso, y no representa una "enfermedad".

En casi todos los casos, un sistema inmunológico saludable mantendrá el virus bajo control (incluyendo los tipos relacionados con el cáncer) o lo eliminará por completo. Sólo una pequeñísima fracción de mujeres con el HPV llegarán a tener cáncer cervical si no se tratan. Sin embargo, si el HPV es persistente en el curso de muchos años, hay una probabilidad mayor de llegar a tener los cambios celulares que pueden llevar al cáncer cervical .

¿Quién porta el HPV?

Cualquier persona que alguna vez haya tenido relaciones sexuales puede haber contraído el HPV. Se estima que casi todo el mundo portará el HPV genital en algún momento de su vida, aunque sea brevemente.

¿Cuáles son las señales del HPV?

En la mayoría de los casos, el HPV es inocuo y no presenta síntomas. Sin embargo, puede causar cambios en las células cervicales. Estos cambios pueden ser identificados en su prueba de Pap. Algunas de estas anormalidades son leves y no necesitan tratamiento. Algunas de las anormalidades más serias podrían llegar a producir cáncer cervical si no se tratan, pero este proceso toma muchos años.

Los tipos de bajo riesgo, no cancerosos del HPV también pueden causar verrugas genitales.

Las señales de infección del HPV pueden aparecer semanas, meses o hasta décadas después de la infección inicial, de modo que es posible tener el HPV por largo tiempo sin saberlo. También, las mujeres que contraen el HPV durante sus años de adolescencia puede que no muestren cambios en las células cervicales hasta los treinta o cuarenta años, o más tarde, o tal vez nunca lleguen a tener ninguna anormalidad.

Sólo en muy pocos casos la presencia del HPV llega a producir cáncer cervical.

¿Por qué es útil la prueba del HPV?

La prueba para ADN del HPV puede detectar la presencia de cualesquiera de 13 tipos del HPV que están relacionados con el cáncer cervical. La prueba del HPV nos ayuda a saber qué mujeres en verdad necesitan una prueba de Pap anual y qué mujeres pueden con seguridad extender a 3 años el intervalo de la prueba de detección.

Si tengo una prueba de Pap y una prueba del HPV negativas, ¿cómo puedo estar segura por 3 años? ¿Qué pasa si contraigo el HPV al día siguiente?

Normalmente, los cambios de las células cervicales ocurren de una manera extremadamente lenta. Toma un promedio de 10 años para pasar de los cambios precancerosos más a graves al cáncer.

¿Cómo se hace la prueba para ADN del HPV?

Se hace al mismo tiempo que la prueba de Pap, usando un cepillo pequeño y suave para obtener células cervicales, las cuales se envían al laboratorio.

¿Qué es una prueba para ADN por medio de una prueba de Pap?

La prueba para ADN por medio de una prueba de Pap combina la prueba para ADN del HPV con la prueba de Pap para la detección rutinaria del cáncer cervical. Es una prueba útil para mujeres de 30 años y mayores. Una prueba normal de Pap con una prueba negativa para ADN del HPV significa que usted puede estar muy

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confiada (más del 99.9%) de que usted no tiene cambios cervicales precancerosos o cáncer.

Las investigaciones muestran que un resultado normal de la prueba para ADN por medio de una prueba de Pap proporciona mayor confianza de que no habrá durante los próximos años un cáncer cervical o un precáncer que tres pruebas anuales normales de Pap.

La **American Cancer Society** recomienda que la prueba para el ADN por medio de la prueba de Pap puede ser usada seguramente para hacer pruebas de detección en mujeres de 30 años y mayores, **y si la prueba es negativa, no tiene que ser repetida por 3 años**. Kaiser Permanente es una de las primeras organizaciones que ofrece esta nueva y más exacta prueba a las mujeres.

¿Por qué es la prueba para ADN por medio de una prueba de Pap sólo para mujeres de 30 años y mayores de 30?

El HPV es muy común. El cáncer cervical es muy, muy poco frecuente, y cuando sí ocurre, casi siempre ocurre en mujeres de 30 años y mayores. Hay tantas mujeres menores de 30 años que tienen el HPV, que añadir la prueba de HPV a la de Papanicolaou no es útil.

Después de los 30 años, el HPV es mucho menos común. Muchas mujeres que resultan positivas para el HPV contrajeron el virus en los años anteriores, y su sistema inmunológico no lo ha eliminado. Por lo tanto, necesitan pruebas anuales de Pap. Eso hace que la prueba de HPV sea útil.

¿Qué pasa si tengo un resultado normal en una prueba de Pap y mi prueba de HPV es positiva?

Una prueba de HPV positiva con un resultado normal de una prueba de Pap *no* significa que usted llegará a tener precáncer o cancer. Su doctor le recomendará una prueba anual de Pap para poder así detectar cualquier cambio en las células cervicales cuando todavía se pueden tratar con facilidad.

¿Por qué no debo hacerme ambas pruebas anualmente?

Sin usted ya está planeando hacerse una prueba de Pap anual, usted no necesita la prueba del HPV para saber si necesita una prueba de Pap anual. La prueba de Pap sigue siendo una excelente prueba de detección para el cáncer cervical, pero muchas mujeres que tienen una prueba de Pap anormal no tienen cambios precancerosos. Uno de los beneficios de las pruebas combinadas es reasegurar a las mujeres que resultan negativas en ambas pruebas de que no correrán ningún riesgo si tienen la prueba para ADN por medio de una prueba de Pap cada tres años. Esto significa menos pruebas y citas y biopsias, sin aumentar el riesgo de cáncer, y está de acuerdo con las recomendaciones de la American Cancer Society y con los expertos nacionales.

¿Deben las mujeres menores de 30 años hacerse alguna vez la prueba para el HPV?

No, si su prueba de Papanicolaou es normal. Pero la prueba para ADN por medio de una prueba de Pap es extremadamente útil para las mujeres de todas las edades que tengan unos resultados inconcluyentes en la prueba de Pap. Cada año, más de dos millones de mujeres reciben los resultados llamados en inglés ASC-US (células escamosas atípicas de significado no determinado). De nuevo, un resultado negativo en una prueba para ADN por medio de una prueba de Pap puede asegurar que la mujer no tiene un mal cervical. Un resultado positivo de una prueba solamente significa que la prueba de Pap se debe hacer más frecuentemente.

¿Pueden ser tratatadas las infecciones del HPV?

Aunque actualmente no hay un tratamiento disponible para el virus mismo, sí existen tratamientos para los problemas que puede causar el HPV, tales como cambios en las celulas cervicales o verrugas genitales. Su proveedor de salud puede comentar con usted cuáles son las opciones de tratamiento apropiadas para estas afecciones, si usted las necesita.

Puntos clave para recordar:

- Casi todas las mujeres tendrán el HPV en algún momento de su vida, pero muy pocas llegarán a tener cáncer cervical. Cuando el sistema inmunológico de una mujer está trabajando normalmente, sólo una infección del HPV que sea persistente en el curso de muchos años puede llegar a producir cáncer cervical .
- Si usted tiene 30 años o más, la prueba del HPV puede ser útil para saber con qué frecuencia necesita hacerse una prueba de detección para el cáncer cervical. Si usted es menor de 30 años, la presencia del HPV es algo esperado y las pruebas sólo son útiles si usted tiene algunos tipos de resultados anormales en la prueba de Pap.
- ¡No acuse a nadie**!** Su estatus de HPV ***no*** es un indicador confiable del comportamiento sexual suyo o de su pareja.

Recursos acerca del HPV y el cáncer cervical

National HPV & Cervical Cancer Resource Center
www.ashastd.org

American Cancer Society
www.cancer.org

National Cervical Cancer Coalition (NCCC)
Información en español
www.nccc-online.org

National Women's Health Resource Center
www.healthywomen.org

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DNA子宮頸抹片檢驗

婦女須知

預防子宮頸癌
使用子宮頸抹片檢驗和HPV測試

在美國，每年有13,000婦女被診斷有子宮頸癌，而有4,100婦女會死於子宮頸癌。但是，通過及早發現癌症之前的改變，子宮頸癌通常是可以預防的。傳統檢驗子宮頸癌的方法是用子宮頸抹片檢驗。HPV DNA測試是抹片檢驗以外，一個新的和令人振奮的檢驗方法。

什麼是子宮頸抹片檢驗？

子宮頸抹片檢驗是檢查子宮頸細胞的改變。這些改變很多時都是無害的，但亦可能屬癌症前期的，或是癌症。這個檢驗通常是用小的刮刀，從子宮頸收集一些細胞樣本，然後放在顯微鏡的玻璃片下觀察。

什麼是HPV（Human Papillomavirus人類乳突病毒）？

HPV是一種大部份人在生命某個時段都帶有的病毒。約有100種類的HPV。有些HPV導致肉疣，有些導致子宮頸細胞有輕微的改變但不會變癌，而有時則會導致癌症前期的改變。偶爾，多年帶有HPV可能導致子宮頸癌、子宮癌、外陰癌（在陰道口的部位）或肛門癌。

在生殖器部位發現的HPV種類，通常是因性交而感染的。專家估計超過二千萬美國人現時帶有此病毒。在一些年齡層裡，差不多有三分一人在任何同一時候帶有HPV。幾乎所有曾有性事的人，最少有一次帶有HPV。這是正常的，也不危險，並不代表是「疾病」。

在大部份情形下，一個健康的免疫系統可控制或完全清除病毒（包括與癌症有關的種類）。只有少部份帶有HPV的婦女，如沒有接受治療，則會發展為子宮頸癌。但是，如有HPV已多年，則細胞的改變可導致子宮頸癌的機會將會增加。

什麼人帶有HPV？

任何人曾有性關係者均可能帶有HPV。估計差不多每個人在他們生命中有一段時期均帶有生殖型HPV，即使為期非常短暫。

HPV有什麼徵兆？

在大部份情況下，HPV感染是無害也沒有徵狀的。但是，它可以導致子宮頸細胞的改變。子宮頸抹片檢驗可以找出這些改變。此類改變有時是輕微的，無須治療。有些較為嚴重的病變，如不治療的話，可以導致子宮頸癌，但這個過程需時多年。

無風險、無致癌類型的HPV，亦可以導致生殖器部位生肉疣。

HPV的徵兆可以在初步感染後幾個星期、幾個月、甚至數十年後才出現，所以人們可能帶有HPV多年而不自知。此外，如婦女在他們年輕時期得到HPV，可能要到三十或四十多歲時——甚或更遲——才會出現子宮頸細胞的改變，或甚至完全沒有發展至不正常的地步。

只有非常少有的情況下，HPV才會導致子宮頸癌。

為什麼HPV測試有用？

HPV DNA測試可以檢測到十三種與子宮頸癌有關的HPV。HPV測試幫助我們知道哪些婦女是真正需要做每年的子宮頸抹片檢驗，而哪些婦女可以安全地將檢驗期延至每三年一次。

如我的子宮頸抹片檢驗和HPV測試都是陰性（正常），我可能保持三年安全嗎？如果我第二天就感染到HPV呢？

通常子宮頸細胞的改變極為緩慢。從最嚴重的癌症前期發展至癌症，平均要十年的時間。

如何做HPV DNA測試？

它是在做子宮頸抹片檢驗時同時做的，用一個小的軟刷來收集子宮頸細胞然後送到化驗室化驗。

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什麼是 DNA 子宮頸抹片檢驗？

DNA子宮頸抹片檢驗是結合HPV DNA測試和子宮頸抹片檢驗的定期的子宮頸癌篩檢。這對三十歲或以上的婦女甚為有用。正常的子宮頸抹片檢驗加上HPV DNA 測試陰性，意指你可以非常放心(>99.9%)你沒有癌症前期改變或癌症。研究指出一個正常的DNA子宮頸抹片檢驗結果比連續三年的子宮頸抹片檢驗（每年一次）都正常，提供未來數年沒有子宮頸癌或癌症前期的更佳保證。

美國防癌協會建議DNA子宮頸抹片檢驗，可以安全地使用在三十歲或以上的婦女身上，**如檢驗是陰性的，則三年內無須再檢驗。**凱薩醫療機構是最早為婦女提供此新的和更準確檢驗的機構之一。

為什麼 DNA 子宮頸抹片檢驗只適用於三十歲或以上的婦女？

HPV是非常常見的，而子宮頸癌則非常、非常少見。當子宮頸癌出現時，差不多都是發生在三十歲或以上的婦女。三十歲以下的婦女有很多有HPV，在子宮頸抹片檢驗加上HPV測試並無幫助。

三十歲以後，HPV較少見。很多檢驗有HPV感染的婦女，都是早年前感染上HPV的，而她們的免疫系統沒有將之消除，所以他們需要每年做子宮頸抹片檢驗，這時同時做HPV測試就更有幫助。

如果我的子宮頸抹片檢驗正常，但 HPV 測試是陽性的，那怎辦？

HPV測試呈陽性而子宮頸抹片檢驗正常並不表示你有子宮頸癌症前期變化或子宮頸癌。你的醫生將建議你每年做一次子宮頸抹片檢驗以檢查子宮頸細胞是否有改變，以便及早治療。

為什麼我不應每年做兩種檢驗？

如果你已計劃每年做子宮頸抹片檢驗，你就無須每年做HPV測試。子宮頸抹片檢驗仍是檢查子宮頸癌的卓越方法，但很多婦女雖有不正常的抹片檢驗結果，卻無癌症前期的改變。結合兩種檢驗的好處之一是確保兩個檢驗均呈陰性的婦女可以非常安全地每三年才做一次DNA子宮頸抹片檢驗，也就是說你到醫院來的次數減少，做組織檢查次數也可以減少而不會有增加得到癌症的風險，這與美國防癌協會及全國的專家所建議是一致的。

三十歲以下的婦女是否應做 HPV 測試？

如果她們的子宮頸抹片檢驗是正常的，則無須做HPV測試。但如子宮頸抹片檢驗結果沒有結論時，則做HPV DNA測試對所有年齡的婦女來說均十分有助。每年有超過二百萬婦女的子宮頸抹片檢驗結果得到像稱為ASC-US（未能決定重要性之非典型扁平細胞）的診斷。此時，如HPV DNA測試結果是陰性的，可以保證婦女無子宮頸病變。而陽性的結果只是指應做更頻繁的子宮頸抹片檢驗而已。

HPV 感染是否可以治療的呢？

雖然現在並沒有可以治療此病毒的方法，但對HPV導致的問題則有治療方法，例如子宮頸細胞改變或生殖部位肉疣。如你有需要，你的醫療服務者可以和你討論此類情況之適當治療。

要記得的重點：

- 幾乎所有婦女在某段時期均帶有HPV，但很少繼續發展成為子宮頸癌。當婦女的免疫系統正常時，只有持續多年的HPV感染才可導致子宮頸癌。
- 如你在三十歲或以上，HPV測試可以幫助你知道應隔多久做子宮頸癌篩檢。如你在三十歲以下，你應預期會有HPV，但除非你的子宮頸抹片檢驗有某類不正常時，做HPV檢驗才會有所幫助。
- 不要責怪什麼！你的HPV狀況***不是***一個你或你伴侶性行為的可靠指標。

HPV 和子宮頸癌資源

全國HPV和子宮頸癌資源中心
www.ashastd.org

婦女防癌網絡
www.wcn.org

美國防癌協會
www.cancer.org

全國子宮頸癌聯盟
www.nccc-online.org

全國HPV及子宮頸癌公共教育活動
www.cervicalcancercampaign.org

全國婦女健康資源中心
www.healthywomen.org

HPV檢驗
www.thehpvtest.com

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Appendix F

Acronyms

ACRONYMS

ACOG	American College of Obstetricians and Gynecologists
ACS	American Cancer Society
AHRQ	Agency for Healthcare Research and Quality
ASCCP	American Society for Colposcopy and Cervical Pathology
ASCO	American Society of Clinical Oncology
ASCP	American Society of Cytopathology
ASC-US	atypical squamous cells of undetermined significance
ASO	Administrative services only
CDC	Centers for Disease Control and Prevention
CIN	cervical intraepithelial neoplasia
DES	diethylstilbesterol
EPO	exclusive provider organization
FDA	Federal Drug Administration
FEHBP	Federal Employee Health Benefits Plan
HIV	human immunodeficiency virus
HMO	health *maintenance* organization
HPV	human papillomavirus
ICSI	Institute for Clinical Systems Improvement
IPA	independent practice association
MAMSI	Mid Atlantic Medical Services Inc.
MCO	managed care organization
NIH	National Institutes of Health
OB/GYN	obstetrics/gynecology
OMB	Office of Management and Budget
POS	point of service
PPO	preferred provider organization
TPA	third-party administration
UHG	UnitedHealth Group
UR	utilization review
USPSTF	United States Preventive Services Task Force