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The Influence of Contextual Factors on the Use of New Technologies to Prevent HPV-Related Diseases

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Introduction

Human papillomavirus (HPV) is a common sexually transmitted infection (STI) which may cause external genital warts, cervical cancer, and other anogenital and oral malignancies. New technologies for cervical cancer prevention, including HPV DNA testing and HPV vaccines, have the potential to decrease markedly the substantial morbidity and mortality associated with HPV infection. These technologies will not be effective unless they are delivered effectively and utilized appropriately by adolescents. Adolescents may have difficulty making decisions that optimize the potential health benefits of these technologies for a number of reasons, including 1) poor understanding of HPV infection and its health consequences, 2) immature cognitive and emotional development, and 3) the complexity of new technologies.

Previous research has demonstrated that parents, peers, and health care providers play important roles in adolescent decision-making about reproductive health behaviors. Recently, studies have begun to address the impact of these contextual factors on adolescent decision-making about new cervical cancer technologies. This paper begins with a discussion of the public health impact of HPV infection, a description of new technologies for the prevention of HPV-related diseases, and a summary of the challenges that these technologies present for adolescent decision-making. The paper then summarizes research findings about the influence of contextual factors on adolescent decision-making related to Pap screening, HPV testing, and HPV immunization. The paper ends with a discussion of the implications of current research for health promotion and prevention programs and with a summary of research frontiers.

Public Health Impact of HPV

Human papillomavirus is one of the most common STIs worldwide. It has been estimated that 10-20% of adults 15-49 years of age have molecular evidence of genital HPV infection, 60% have been infected by HPV previously and 15% are currently infected.[1, 2] Classification of HPVs is based on similarities between genomes: different HPV types share less than 90% homology.[3] Almost 120 genotypes have been

described and approximately 40 types infect the genital tract. Genital HPV types are further classified into high-risk and low-risk types based on whether they are or are not associated with cancer.

High-risk HPV types include 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73 and 82.[3, 4] Although HPV infection frequently is transient, those who have persistent infection with high-risk types may develop precancerous cervical lesions (cervical dysplasia) or cervical cancer. Approximately 50% of cervical cancer is caused by type 16, and approximately 20% by type 18.[4] High-risk HPV infection is not only associated with cervical cancer, but also with oral, vulvar, penile and anal cancers.[5-7]

The Pap smear was developed to screen for epithelial cell abnormalities caused by HPV infection which may indicate cervical dypslasia or cervical cancer. Results are categorized according to the type of epithelial abnormality found, and include atypical squamous cells of undetermined significance (ASC-US), atypical squamous cells cannot exclude high-grade squamous intraepithelial lesion (ASC-H), atypical glandular cells (AGC), low-grade squamous intraepithelial lesion (LSIL), high-grade squamous intraepithelial lesion (HSIL), and squamous cell carcinoma.[8] If Pap testing suggests cervical dysplasia, the diagnosis is confirmed with a cervical biopsy specimen. Cervical dysplasia is classified as mild, moderate, or severe cervical intraepithelial neoplasia (CIN) or carcinoma-in-situ.

Conditions associated with high-risk HPV infection are responsible for substantial morbidity and mortality worldwide. Cervical cancer is the second most common cancer among women living in less developed regions of the world, based on age-standardized incidence rates. It is the leading cause of cancer-related mortality among women is those regions, responsible for approximately 230,000 deaths per year (GLOBOCAN 2002 data, http://www-depdb.iarc.fr/globocan/GLOBOframe.htm). In more developed regions of the world, Pap screening and treatment of precancerous lesions have decreased the incidence of cervical cancer dramatically, but it remains the fourth most common cancer diagnosed in women (GLOBOCAN 2002 data, http://www-depdb.iarc.fr/globocan/GLOBOframe.htm). In addition,

marked geographic, racial/ethnic, and socioeconomic disparities in cervical cancer morbidity and mortality persist among U.S. women.[9] For example, relatively high cervical cancer mortality rates have been noted in Caucasian women living in Appalachia, African-American women in the Deep South, and Latino women along the Texas-Mexico border. African American women have more than twice the cervical cancer mortality rate of Caucasian women, and cervical cancer incidence rises with increasing poverty rates in all racial and ethnic groups.[9] These disparities are likely due primarily to disparities in access to and appropriate use of screening technologies such as the Pap test.

Pap screening, follow-up of abnormal results, and treatment of precancerous lesions also is costly. Insinga et al. conducted an observational cohort study of female enrollees of the Kaiser Permanente Northwest health plan to examine the distribution of cervical HPV-related costs. They found that 64% of costs incurred were due to routine Pap screening, 13% to evaluation and treatment of moderate/severe cervical dysplasia, 10% to evaluation and treatment of cancer, 9% to false positive Pap tests, and 4% to mild dysplasia. They estimated that in 1998, cervical HPV-related disease accounted for total U.S. health care costs of $3.4 billion.[10] Finally, screening procedures and follow-up of abnormal Pap results may lead to substantial anxiety and discomfort.[11-14] These psychological and physical costs are difficult to quantify, but may lead to reluctance to participate in future screening and therefore to an increased risk for cervical cancer.[15]

Infection with low-risk HPV types (primarily 6 and 11) may lead to genital warts and recurrent respiratory papillomatosis (RRP).[16] Although population-level prevalence data are not available, experts have estimated that prevalence rates of genital warts range from 1% to 5%.[1, 17] Prevalence rates are substantially higher in specific populations; for example, rates up to 40% have been reported among men and women attending STI clinics.[18-20] Genital warts may be found on the vulva, perineum, perianal area, vagina or cervix in women and on the penis or scrotum in men.[21] Although they generally indicate benign cell proliferation, they may be a marker for exposure to high-risk types or CIN and may cause substantial

physical and psychological morbidity.[14] Topical treatments for genital warts may take weeks to complete and may cause significant discomfort. Surgical procedures are sometimes necessary. Warts also commonly recur after treatment.[22] Vertical transmission of HPV infection from mother to child may cause RRP in young children. Respiratory papillomas may lead to significant airway compromise, and repeated surgical procedures are often necessary to remove them.[23, 24]

The epidemiology and natural history of HPV infection differs in adolescents compared to adults. Age-specific rates of HPV infection are highest in adolescent and young adult compared with adult women, probably due to differences in sexual behaviors such as consistency of condom use and number of sexual partners.[25] In a recent study, investigators demonstrated that over a two-year period, the cumulative prevalence rate of HPV in sexually active adolescent girls was 82%.[26] Many adolescents acquire HPV rapidly after sexual initiation: in a British study, 44% of adolescents had acquired HPV within 3 years of first sexual intercourse.[27] Even in women with only one sexual partner, the risk of acquiring cervical human papillomavirus infection was 46% (95% CI 28%-64%) three years after first intercourse and the median time from first intercourse to first detection of human papillomavirus was three months.[28] Although HPV infection is extremely common in sexually active adolescent girls, it is usually transient. Reported median clearance times are 226 days for high-risk types and 170 days for low-risk types.[26] Abnormal Pap results often regress in adolescents as well. In a sample of adolescents with LSIL, 91% demonstrated regression within 36 months,[29] compared with regression rates of 50 to 65% in adults.[30-32] In addition, cervical cancer is exceedingly rare in adolescents: no cases of invasive cervical cancer were reported in the Surveillance Epidemiology and End Results (SEER) database between 1998 and 2002.(http://seer.cancer.gov/csr/1975_2002/results_merged/sect_05_cervix_uteri.pdf) Although HPV infection tends to be transient in adolescents, the impact of infection during adolescence on the risk for cervical cancer during adulthood is unclear, since it is possible that infection may remain latent and cause later disease even if HPV DNA is no longer detectable.

New Technologies for the Prevention of HPV-Related Diseases

Traditionally, an annual Pap smear was recommended for all sexually active women beginning in late adolescence in order to screen for precancerous cervical lesions. Although Pap screening is responsible for a dramatic reduction in the incidence of and mortality associated with cervical cancer in developed countries such as the U.S., there are several limitations of the Pap smear. First, the sensitivity of a single Pap smear for detection of precancerous lesions is low because cytologic screening is subject to errors in sampling, slide preparation, and interpretation. A recent systematic review demonstrated that the sensitivity of a single Pap smear for detecting abnormalities at least as severe as LSIL ranged from 30% to 87% (mean 47%) and specificity from 86% to 100% (mean 95%).[33] Thus, Pap screening typically was recommended for sexually active women every year in order to increase the sensitivity of screening. Second, the costs associated with Pap screening and follow-up of abnormal results are high as noted previously. Finally, compliance with routine Pap screening and follow-up of abnormal results is poor, particularly in adolescents and those who have poor access to health care.[34, 35]

In response to the limitations of the Pap smear and strong evidence linking HPV infection to cervical cancer, recent research has focused on the development of methods to replace or augment traditional Pap smear screening, including new Pap testing technologies and HPV DNA testing. In addition, vaccines that prevent acquisition of common HPV types may become a highly effective primary prevention strategy in the near future.

<u>New Pap Screening Technologies</u>

In contrast to the traditional Pap smear, in which cells are applied directly to a slide, the ThinPrep® Pap test (Cytyc, Marlborough, MA) utilizes a fluid transport medium to preserve cells. The vial containing the medium is transported to the laboratory, a processor filters out noncellular material in order to eliminate debris, then a representative portion of cells is distributed on a slide in a uniform, even layer. This process may improve the quality of the sample, decreasing errors in interpretation. A more recently-developed but

similar system is the SurePath® liquid-based cytology system (TriPath Imaging, Inc., Burlington, N.C.). The FocalPoint™ slide profiler (TriPath Imaging, Inc., Burlington, N.C.) is an automated cervical cytology system that allows for computerized primary screening of Pap tests. It can also be used for random resampling of normal Pap tests for quality control purposes. All of these technologies enhance or have the potential to enhance the sensitivity of Pap testing, but at additional cost. Additional costs of the new technologies could potentially be mitigated by decreases in the frequency of screening if the new technologies resulted in sufficiently increased sensitivity for the detection of cervical pathology.

HPV DNA Testing

HPV DNA may be detected using a cervical swab, vaginal swab, or supernatant from liquid-based Pap tests. A commercially available test is the Hybrid Capture II (Digene Corporation, Beltsville, MD). A positive test for high-risk HPV DNA is highly sensitive for the detection of moderate and severe CIN.[36-38] Based on the sensitivity of a high-risk HPV test for detection of precancerous lesions and the known limitations of Pap testing, recent guidelines state that HPV DNA testing may be used as an adjunct to Pap screening in women with atypical squamous cells of undetermined significance (ASC-US), in the management of women with abnormal Pap tests, and as a primary screening test (in women over 30 years of age).[39-42] Given that HPV infection and LSIL usually regress and cervical cancer is exceedingly rare in adolescents, new guidelines also recommend delay of Pap screening until approximately three years after sexual initiation in order to minimize unnecessary screening and diagnostic procedures in young women.[40] Evidence is accumulating that supports, in certain circumstances, the use of self-collected vaginal samples for HPV DNA instead of clinician-collected cervical or vaginal samples.[43-46] Self-testing could have significant implications for cervical cancer prevention programs.

HPV Vaccines

Over the past 15 years, remarkable progress has been made in the development of prophylactic HPV vaccines.[47, 48] Two vaccines being evaluated in phase III clinical trials appear to be safe and highly

effective in preventing HPV acquisition and abnormal Pap tests, and are likely to be licensed for clinical use within the next few years.[49, 50] One of these vaccines targets HPV types 6, 11, 16 and 18, and thus is designed to prevent both genital warts and cervical cancer.[50] The other vaccine targets HPV types 16 and 18, and thus is designed to prevent cervical cancer.[49]

Challenges That Technologies Present for Adolescent Health-Related Decision-Making

General challenges

The Institute of Medicine Quality Chasm report highlighted numerous ways in which the current delivery system does not meet the health care needs of the adolescent population.[51] Much can be done to improve the quality, efficiency, and patient centeredness of adolescent health services. Any approach to this problem, however, must include a clear understanding of the challenges related to adolescent health-related decision-making.

The use of new technologies such as liquid-based Pap testing, HPV DNA testing and HPV vaccines has the potential to improve women's reproductive health outcomes from adolescence through adulthood. However, their utilization may present specific challenges for adolescents. Challenges common to all three technologies include 1) making them available to adolescents in a manner that provides the greatest likelihood that they will be utilized, and 2) optimizing the likelihood that adolescents will make the best possible use of the technologies. Focusing on the latter, it will be important to pay attention to educational and developmental issues. A primary requirement is ensuring that adolescents understand HPV infection, Pap testing, and the complex associations between HPV, abnormal Pap tests, and cervical cancer.[52-54] Little is known about adolescents' educational needs or effective strategies for providing education to them about HPV. Providers in a busy clinical setting may have limited time to explain HPV acquisition, sequelae, and prevention strategies to adolescents. Providers who care for children and adolescents, such as pediatricians and family physicians, may lack experience with HPV-related disease, knowledge about

HPV, and understanding of recent screening guidelines, limiting their ability to provide effective counseling to adolescents.[55, 56]

Another fundamental challenge lies in helping adolescents to make informed, healthy decisions about new technologies as they mature cognitively and take on increasing responsibility for their own health care. Adolescents vary greatly in their cognitive and psychosocial development, both of which may impact their ability to make informed decisions about health-related behaviors. As detailed in a recent report, neurobiological research has demonstrated that profound changes occur during adolescence in brain anatomy, biochemistry, and physiology.[57] The prefrontal cortex of the frontal lobe does not fully mature until young adulthood. The prefrontal cortex is responsible for skills such as setting priorities, organizing plans, forming strategies, and allocating attention. In addition, dopamine inputs to the prefrontal cortex increase dramatically during adolescence, which increases the capacity for judgment and impulse control. The authors conclude that ability to plan, make decisions, and imagine possible future consequences of an action are still developing during adolescence. These findings provide a biologic correlate to decades of psychology research about adolescence. They reinforce the notion that adolescents may face challenges making health-related decisions about complex issues with future consequences, such as Pap screening and HPV vaccination.

Pap Testing

The main challenge related to Pap testing among adolescents is ensuring adherence to screening guidelines. In a national sample of nurses' children, only 46% of sexually active adolescent girls reported ever having had a pelvic examination.[58] Similarly, 41% of 15- to 19-year-old sexually active adolescent girls participating in the National Survey of Family Growth reported ever having had a Pap smear.[59] Data from the National Ambulatory Medical Care Survey indicates that based on extrapolated data, only about 12% of sexually active older adolescents had received a Pap test.[60] Kahn et al. examined predictors of Pap smear return among adolescent and young adult women (N=490, mean age 18.3 $\pm$ 2.2 years, 49% black,

23% Hispanic).[35] Although 82% of participants intended to return for a follow-up Pap at baseline, only 30% actually returned. Intention to return was not associated significantly with actual return. One of the main challenges for adolescents in terms of adherence to screening guidelines is that Pap testing requires a speculum examination. Many adolescents find this examination to be painful, embarrassing and inconvenient: these perceptions may be linked to the low rate of compliance with pelvic examinations and Pap testing in adolescents.[15, 61]

Although new screening guidelines will result in fewer adolescents undergoing Pap testing, adherence to current recommendations for screening is important. Adolescent and young adult women, particularly those who are immunocompromised, may develop precancerous lesions such as severe CIN which require treatment to prevent progression to cervical cancer. Establishing appropriate preventive health behaviors such as Pap screening during adolescence may also improve adherence to routine Pap screening in adulthood. Pap screening in adult women is important because it is highly effective in preventing cervical cancer: the majority of adult women who develop cervical cancer either do not have a Pap test within the five years before diagnosis or have never been screened.[62]

HPV Testing

The incorporation of HPV DNA testing into cervical cancer screening guidelines, along with a growing understanding among providers and adolescents about the link between HPV infection and abnormal Pap tests, presents several potential challenges. Many adolescent girls will learn that their abnormal Pap test indicates that they have been exposed to an STI or that they are HPV-positive. In preliminary studies of both adults and adolescents, HPV testing has been associated with anxiety, distress, and perceived stigma.[53, 54, 63, 64] These responses may adversely impact adolescent decisions about future screening and follow-up.[65, 66]

Furthermore, guidelines for appropriate Pap and HPV testing continue to evolve. Recommendations from different organizations sometimes differ, and current guidelines allow for flexibility in decisions about screening and follow-up.[39-42, 67] In the context of different and sometimes inconsistent guidelines, some experts have advocated for shared decision-making regarding choices about cervical cancer screening procedures.[68] However, some adolescents may find it difficult to make an informed choice about such a complex issue given their evolving cognitive development, evidence of poor understanding of HPV infection, and the psychological implications of positive test results.

Finally, the option of self-testing for HPV DNA may present a challenge for adolescents. In the future, self-collected vaginal samples for HPV DNA may be used instead of clinician-collected cervical or vaginal samples.[43-46] Thus, adolescents may be given a choice as to whether they prefer self-collected or clinician-collected HPV specimens. A potential benefit of HPV self-testing is that a speculum examination may not be needed if HPV testing can be used instead of a cervical cytology specimen. Adolescents who find the speculum examination (or even a clinician-collected swab) to be uncomfortable or embarrassing may be more likely to adhere to recommended screening for cervical cancer if it involves self-collected vaginal specimens. In addition, self-collected specimens may allow for testing in non-clinical settings such as within the juvenile justice system or in school-based health centers. The availability of testing outside of physician offices has the potential to dramatically improve screening for HPV but raises issues such as education, counseling, and follow-up of positive results.

Despite the apparent potential for self-testing, some recent evidence indicates that adolescents may have concerns about self-collected specimens. Kahn et al. measured acceptability of self-testing compared to clinician-testing for HPV DNA in urban adolescents.[69] Although acceptability was relatively high both for self- and clinician-testing (before and after testing), participants found self-testing to be less acceptable than clinician-testing and strongly preferred clinician- to self-testing. The differences in acceptability were driven not by comfort of the procedure, but instead by participants' concern about collecting the

specimen themselves. They reported that they trusted the results of clinician-collected more than self-collected specimens and that the clinician-collected specimens were more likely to be obtained correctly and accurately. In contrast, most adult women find self-testing for HPV DNA to be more acceptable than clinician-testing and prefer self- to clinician-testing.[43, 70-72] The findings suggest that adolescents may have less confidence than adults about their ability to self-collect specimens. Efforts to address low screening rates through utilization of self-testing will need to successfully overcome adolescent concerns about taking responsibility for collecting specimens correctly.

HPV Vaccines

Prophylactic HPV vaccines ideally should be administered before sexual initiation, and parental consent will likely be required for vaccination of adolescents less than 18 years of age. Thus, vaccine uptake will depend on acceptability of vaccination to parents as well as adolescents. However, parents may be reluctant to discuss STI vaccines with young adolescents or may be concerned that adolescents who have been vaccinated will practice riskier sexual behaviors because of a false sense of protection or will not participate in STI and Pap screening. Concerns about adverse behavioral consequences of vaccination may be well-founded, considering evidence that some participants in HIV vaccine trials, particularly those who believe they received vaccine, report an increase in sexual risk behaviors.[73] Adolescent concerns about confidentiality or a sense of invulnerability to infection may present additional barriers to vaccination.

Ensuring that adolescents adhere to vaccination guidelines may also present a challenge. Vaccines in development involve a series of three immunizations. Adolescents often do not present for health maintenance visits, and even those who do may not adhere to a schedule of three visits over six months, as was noted with the introduction of the hepatitis B vaccine.[74] The recent introduction of two new vaccines for adolescents may mitigate this concern if the introduction of these vaccines results in improved systems and policies for the delivery of vaccines to adolescents. The most successful policy

option for insuring adherence to childhood vaccination has been state laws mandating vaccination prior to school attendance. Consideration of this policy option as well as others should be part of the process for optimizing the potential of this new technology to improve adolescent health.

Finally, ensuring that women continue regular Pap screening after vaccination, even if it is determined that the interval between screenings can be lengthened safely, could present a challenge. The vaccines in development only prevent acquisition of HPV types 16 and 18, responsible for at most 70% of cervical cancer, so continuation of screening after vaccination will be important.

Influence of Contextual Factors on Adolescent Health Behaviors and Decision-Making Related to Pap Screening, HPV testing, and HPV Immunization: Research Findings

Influence of Contextual Factors on Adolescent Reproductive Health Behaviors

An extensive body of literature addresses the influences of contextual factors on adolescent decision-making concerning reproductive health behaviors such as sexual risk behaviors and contraception. Most studies have focused on the influence of important individuals in adolescents' lives, such as parents and families, health care providers, and peers. Thus, this review will focus on the influence of parents, providers, and peers. However, the social and environmental context of adolescents' lives clearly is much broader, and includes other individuals important to adolescents (e.g. extended family, teachers, sexual partners) organizations (e.g. religious organizations, schools), sociodemographic and economic factors. These factors certainly influence adolescent health-related decision-making as well.

Family-related factors that have been shown to be associated with adolescent sexual and contraceptive behaviors include the contextual and structural features of families (e.g. parental education, marital status); family processes, relationships, or parenting practices (e.g. parental support, supervision); and biologic or hereditary transmission of antecedents to sexual behaviors (e.g. timing of pubertal development).[75] For example, adolescents in single parent families, compared to those living with both

parents, are more likely to have had sexual intercourse.[76] A number of studies have demonstrated that parental warmth, support, parent-child connectedness, parents' values about adolescent sexuality, parent-teen relationship satisfaction, and parent-teen communication are related to adolescent sexual and contraceptive behaviors. Jaccard et al., in a study of 751 African-American adolescents, demonstrated that adolescent perceptions of maternal disapproval of premarital sex and satisfaction with the mother-child relationship were significantly associated with abstinence, less frequent sexual intercourse, and more consistent contraceptive use. Adolescents who reported a low level of satisfaction with their mother were more than twice as likely as those highly satisfied with their relationship to be sexually experienced.[77] In an analysis using data from the Longitudinal Study of Adolescent Health (Add Health), a national school-based study, Jaccard et al. found that adolescent perceptions of maternal approval of birth control were associated with a higher likelihood of contraceptive use. Mother-adolescent relationship satisfaction was associated with a higher probability of birth control use and a lower probability of both sexual intercourse and pregnancy.[78] Other analyses using Add Health data similarly have demonstrated that adolescents' perceptions of maternal attitudes toward sexual intercourse and adolescent satisfaction with the maternal relationship were predictive of sexual intercourse.[79-81] The more disapproving adolescents perceived their mothers to be toward their engaging in sexual intercourse and the more satisfied adolescents were with their relationship with their mothers, the less likely adolescents were to initiate sexual activity or to become pregnant. Relationship satisfaction was also associated with contraceptive use at most recent sexual intercourse. Sieving et al. demonstrated that controlling for the effects of perceived maternal disapproval, stated maternal disapproval did not have an independent relationship with sexual initiation for younger or older teens. Thus, teens' perceived parental values and expectations may be a better predictor of behaviors than actual parental expectations.[80]

Several studies have identified mediating mechanisms that may explain how parental factors influence adolescent sexual behaviors. For example, parent-child closeness is related to possible mediating factors such as teens' attitudes about sexual intercourse, teen depression, impulse control, academic and social

activity, teen substance use, and association with sexually active peers.[82] Parent-child closeness and parental supervision may increase safe sexual behaviors in teens by enhancing educational achievement, providing teens with opportunities to develop social skills, and helping them to acquire a sense of competence and self-worth.[83]

Providers also play a critical role in adolescent reproductive health decisions. Providers have an exceptional opportunity to impact adolescent attitudes and behaviors because many adolescents see a health care provider regularly. O'Connor et al. examined administrative databases of Kaiser Permanente Northwest Division to characterize clinic visits by 14- to 17-year-olds.[84] Of the 22,626 adolescents who were identified, 62% were seen in a primary care clinic within 1 year and almost 83% were seen within 2 years. The authors conclude that primary care visits present an excellent opportunity to reach many teenagers outside of a school setting for short-term educational or prevention initiatives. In addition, most adolescents welcome discussions about sexual health and trust providers' advice, though they express concerns about confidential care. Schuster et al. examined the extent to which adolescents in an urban school district had discussed sexual behavior and risk prevention with a physician, and whether adolescents valued those discussions and trusted physicians to protect their confidentiality. Thirty-nine percent of adolescents reported discussions with physicians about how to avoid getting AIDS, 37% about condom use, 15% about the adolescent's sex life, 13% about how to say no to unwanted sex, and 8% about sexual orientation. Most adolescents (80%-90%) reported that they would find it at least a little helpful to talk with a physician about various sexual matters. Most would trust a physician to keep secret that they asked questions about sex (75%), that they were having sex (65%), or that they were using contraception (68%). However, fewer would trust physicians to keep secret a sexually transmitted disease (44%) or pregnancy (44%).[85]

Finally, perceptions about peer attitudes and behaviors are one of the strongest and most consistent predictors of adolescent sexual risk behaviors, including timing of sexual initiation and sexual activity.[86-

[88] Theories of social influence, such as Social Cognitive Theory[89] and Social Comparison Theory,[90] suggest that peers are influential because adolescents perceive peers as standards for self-evaluation, as role models, or as members of an important social group. Sources of peer influence may include best friends, romantic or sexual partners, friendship networks, and peer networks.[88] Jaccard et al. have recently noted that although numerous studies document that adolescents' risk behaviors are associated with peer behaviors, the associations may be overestimated because they may in part reflect measurement artifacts (e.g. adolescents may be inaccurate in characterizing the behavior and attitudes of their friends due to projection processes) or the fact that adolescents choose friends on the basis of common values, personalities, and life orientations. These values may be associated independently with adolescent behaviors, and thus although there is co-occurrence of risk behavior in adolescents and their peers, the association may not be entirely due to peer influence. The investigators found that after controlling for measurement artifacts and selection effects in a longitudinal study design, the effect of peer sexual activity on an adolescents' sexual activity was significant, but weaker than has been suggested by previous studies.[88]

Given this body of evidence supporting the impact of contextual factors on adolescent reproductive health behaviors, it is reasonable to explore the influence of families, providers and peers on adolescent decision-making about new cervical cancer prevention technologies. Research that focuses on the impact of maternal, provider and peer influences on adolescent Pap screening, HPV testing, and HPV vaccination behaviors is beginning to emerge and is summarized in the following sections.

Influence of Contextual Factors on Pap Screening and HPV Testing

One published study suggested that family factors play a role in adolescent Pap screening behaviors. Kahn et al. examined predictors of return for Pap smear screening or follow-up among adolescent and young adult women (N=490, mean age 18.3 $\pm$ 2.2 years, 49% black, 23% Hispanic).[35] One of the variables independently associated with return was reported family history of cervical cancer (adjusted

odds ratio .28, 95% confidence interval .08-.78). Although the reasons underlying the inverse association between family history of cervical cancer and follow-up are not clear, adult studies suggest that this may be shaped by perceptions of personal risk. Young women who report a family history of cervical cancer may perceive themselves to be at high risk for cancer themselves, and may avoid follow-up appointments because they fear the diagnosis of cancer, wish to avoid medical procedures such as colposcopy, or would prefer not to know if they have cancer because they perceive it to be an incurable disease.[91-93] Other factors might include limited English proficiency or depression.[94, 95]

Providers also influence adolescent Pap screening behaviors. From the standpoint of access to care, women who have a health care provider are more likely to be screened. Data from the 2000 National Health Interview Survey demonstrated that having a usual source of care was a powerful predictor of Pap testing.[96] In addition, provider characteristics and behaviors appear to play a key role in decisions about screening. In the study of adolescent return for Pap testing described previously, likelihood that the doctor would be honest during Pap screening and follow-up visits was associated with return for future Pap testing (adjusted odds ratio 4.07, 95% confidence interval 1.37-17.5).[35] In a qualitative study exploring adolescent girls' understanding and perceptions of Pap smears and barriers to compliance with screening recommendations, participants reported that certain provider characteristics and behaviors presented barriers to Pap screening.[15] For example, participants associated male provider gender and poor provider-adolescent relationship with non-adherence to screening recommendations. Participants also reported that male provider gender and specific provider skills (e.g. gentleness during a pelvic examination and adequate explanation of the procedure) were linked to pain and embarrassment, which in turn were identified as the major barriers to Pap screening. Participants from the study by Kahn et al. recommended strategies to increase awareness of Pap testing and overcome barriers to Pap screening that also were linked to provider behaviors. These included providing in-depth, understandable information about Pap testing, having good communication skills, developing a trusting and consistent relationship with teens, assuring them of confidentiality, and performing the examination gently.

The few studies that have addressed peer influences on Pap screening suggest that peers may have a negative impact on screening. In the previously-described qualitative study, one barrier to Pap screening that was identified by participants' was peers' advice. Participants reported that peers advised them against having a Pap test because of the pain and embarrassment associated with a speculum examination.[15] Millstein et al. similarly found that adolescents' most frequent information source about pelvic examinations was peers, and the most common message adolescents heard from peers was that a pelvic examination was painful.[61]

The previously reported literature focused on Pap testing in adolescents. However, little information is available concerning HPV testing in adolescents because the technology is still relatively new. One study suggests that contextual factors are linked to decisions about Pap and HPV testing in adolescents. The investigators explored the psychosocial and behavioral impact of HPV and Pap testing in 100 sexually active adolescent girls using qualitative methods.[54] Participants' mean age was 17.2 years, 51% were HPV-positive, and 23% had an abnormal Pap test. After participants received an educational protocol about HPV and were informed of their test results, they were interviewed to assess their understanding of and responses to test results. The interview data were then used to create a conceptual framework explaining responses to test results (**Figure 1**). Most participants had little understanding of HPV and Pap tests prior to enrollment in the study as demonstrated by a baseline knowledge assessment, and cognitive understanding of test results varied greatly between participants even after receipt of the standardized educational protocol. Although most participants reported anxiety and distress after receiving an abnormal test result, testing also led to positive responses related to decision-making about future screening behaviors. Nearly all participants said they would return for future Pap screening and HPV testing, noting that screening decreases the risk of cervical cancer, ensures good overall health, and provides an opportunity for further health education. The conceptual framework suggested that contextual factors directly and indirectly influenced decisions to return for screening. These factors included

provider education and counseling about HPV and Pap tests, having experienced cancer within one's family, and relationship factors (e.g. quality of the relationship).

Based on evidence that family, provider and peer factors influence adolescent reproductive health decisions, we designed a study specifically to examine the influence of contextual factors (i.e. maternal, provider, and peer factors) on adolescent decisions regarding several cancer prevention behaviors, including Pap screening. The study uses data from the Growing Up Today Survey, a national cohort study of the adolescent children of nurses participating in the Nurses' Health Study. The study was funded recently by the American Cancer Society and data collection is ongoing, but preliminary results are available concerning the association between maternal communication about Pap screening and adolescent Pap screening behaviors (Frazier and Kahn, unpublished results). Adolescent report of maternal communication about Pap testing was strongly associated with the adolescent's own Pap screening behaviors. Sexually active adolescent girls whose mother had ever told them they should have a Pap test, compared to those whose mother had not, were significantly more likely to report having had a Pap test in the past (1086 [81%] vs. 248 [19%], $p < .0001$). The odds of having ever had a Pap test were 7.69 (95% confidence interval 6.42-9.20) for an adolescent whose mother had told her to have a Pap test, compared to one whose mother had not. Frequency of maternal communication also was associated with adolescent Pap screening. Adolescents whose mothers had talked to them often about having a Pap test, compared to those whose mothers had never talked to them, were more likely to report having had a Pap test in the past (256 [82%] vs. 214 [25%], $p < .0001$). The odds of having ever had a Pap test increased as the frequency of maternal communication increased. Compared to adolescents whose mothers had *never* told them to have a Pap test, the odds of having had a Pap test were 3.32 (95% CI 2.63-4.13) for those whose mothers had discussed Pap tests *once*, 6.11 (95% CI 4.76-7.85) if they had discussed Pap tests *occasionally*, 9.12 (95% CI 6.89-12.1) if they had discussed Pap tests *sometimes*, and 13.5 (95% CI 9.68-18.5) if they had discussed Pap tests *often*. The results were similar when the outcome variable was the adolescent reporting a Pap test within the past year. The results were also similar when analyses were

stratified by adolescent age (< 18 years vs. ≥ 18 years of age) and by mother's history of a pelvic examination (**Table 1**).

Influence of Contextual Factors on Decisions Related to HPV Vaccines

Because HPV vaccines are not yet available for clinical use, few studies have addressed adolescent decisions about their use or contextual issues involved in adolescent decision-making. However, contextual issues will be key factors in effective vaccine uptake. Because physician recommendation may be the most important determinant of immunization status, uptake of HPV vaccines will depend largely upon whether physicians recommend the vaccine to parents and patients. Pediatricians and family physicians will be most influential because the vast majority of preadolescents and early adolescents receive vaccines from physicians in these fields.[97] However, little is known about the process by which physicians adopt new vaccine guidelines or the factors that determine adoption of guidelines.[98] Parents will also be an important determinant of vaccination because parental consent likely will be required for adolescents less than 18 years of age. Thus, recent studies that have addressed provider, parent, and young adults' attitudes about HPV vaccination may be helpful in understanding the contextual factors affecting adolescents' future decision-making about vaccination.

Using data from a national sample of pediatricians, Kahn et al. examined pediatrician characteristics and attitudes associated with intention to recommend the two prophylactic HPV vaccines in development. The mean age of participants (N=513) was 42 years and 57% were female. Participants reported that they were more likely to recommend vaccination to girls vs. boys and older vs. younger children, and to recommend a cervical cancer/genital wart vaccine compared to a cervical cancer vaccine ($p<.0001$). Variables independently associated with intention to recommend a cervical cancer/genital wart vaccine were: higher estimate of the percentage of sexually active adolescents in one's practice (β .084, $p=.002$), number of young adolescents seen weekly (β 1.300, $p=.015$), higher HPV knowledge (β 1.079, $p=.015$), likelihood of following the recommendations of important individuals and organizations regarding

immunization (β .834, p=.001), and fewer perceived barriers to immunization (β -.203, p=.001).[55] In a national study of family physicians, findings were similar. Participants (N=145) reported higher intention to recommend both HPV vaccines to girls vs. boys ($p < .0001$) and to older vs. younger adolescents ($p < .0001$). They were more likely to recommend a cervical cancer/genital wart vaccine than a cervical cancer vaccine to boys and girls ($p < .001$). Variables independently associated with intention to recommend a cervical cancer/genital wart vaccine included: female gender of provider, knowledge about HPV, belief that organizations such as the American Academy of Family Physicians would endorse vaccination, and fewer perceived barriers to vaccination.[56] Similarly, Raley et al. noted that in a national survey of obstetricians/gynecologists, factors important in the decision to recommend an HPV vaccine included recommendation by the American College or Obstetricians and Gynecologists, vaccine efficacy, and patient age: providers reported reluctance to recommend immunization to younger vs. older teens.[99] A study of nurse practitioners demonstrated endorsement by the American Academy of Pediatrics was an important factor in willingness to recommend STI immunization, and that they were reluctant to immunize early adolescents.[100]

Several studies suggest that parents and adolescents generally find HPV vaccines to be acceptable. The most important factors underlying parental attitudes include beliefs about safety, efficacy, and benefits of vaccination. Some parents express concern about an increase in risky sexual behaviors among vaccinated adolescents. Parents and adolescents often do not agree about who should make decisions about vaccination. Bair et al. examined predictors of STI vaccine acceptability among 101 Latino parents for their adolescent children.[101] Participants were given 9 hypothetical vaccine scenarios, each uniquely defined along 4 dimensions related to the disease: severity of disease, vaccine efficacy to prevent disease, sexual transmissibility, and possibility for behavioral prevention. The vast majority of parents strongly endorsed all 9 vaccine scenarios. Parents favored higher efficacy vaccines for potentially fatal infections, and vaccine ratings were not greatly influenced by the availability of behavioral prevention methods. Bair also examined concordance between parental and adolescent attitudes about STI vaccines in Latino

parents and their children (Bair et al., abstract presented at the Pediatric Academic Societies annual meeting, May 16, 2005). STI vaccine acceptability was high among both parents and adolescents, and adolescents believed that they would play an active role in decision-making about STI vaccines. Seventy-one percent of parents compared to 52% of adolescents reported that they would equally share decision-making regarding STI vaccination, while 8% of parents compared to 18% of adolescents thought that the adolescent would be the primary decision-maker. Parents' and adolescents' attitudes about locus of decision-making were not significantly correlated.

Olshen et al. examined parental acceptance of HPV vaccines using qualitative methods.[102] The study sample consisted of 25 parents recruited from an urban adolescent clinic and a suburban private pediatric clinic, who participated in focus groups and individual interviews. The parents were from diverse ethnic backgrounds, and all had at least one child between the ages of 10 and 15 years. Most parents expressed favorable views about HPV vaccines, and all were concerned regarding safety of the vaccine and valued their pediatrician's advice about vaccination. Parental concerns included an increase in unsafe sexual practices among vaccinated adolescents.

Davis et al. conducted a study about acceptance of HPV vaccine among 506 parents of 10- to 15-year-olds recruited from medical and community sites.[103] Parents who wanted the vaccine for their adolescents were significantly more likely to believe that vaccines are effective in preventing disease, to feel that it is important for their children to receive all of their vaccines, to have no fear of vaccines, and to believe that vaccines are helpful (all $p < .01$). Approximately 85% of those who did and those who did not want the vaccine for their child indicated concern about the side effects of vaccines. The most important influences on parental acceptance of the HPV vaccine were a doctor's recommendation and school requirements. Initially, 55% of parents indicated that they wanted the vaccine for their child, 23% did not, and 22% were undecided. After reading an educational fact sheet about HPV and HPV vaccines, 20% of those who initially did not want the vaccine and 65% of those who were undecided changed their minds and wanted

the vaccine. After the intervention, 75% of parents wanted the vaccine, 25% did not, and 5% remained undecided ($p < 0.001$). After the educational intervention, parental acceptance was associated with belief the vaccine was safe ($p < 0.001$) and could not cause HPV infection ($P < 0.001$). Parents who did not want the vaccine, compared to those who did, were more likely to believe that vaccination would encourage early sexual activity ($p < 0.03$). In contrast, Dempsey et al. found that while written educational materials about HPV increased parental knowledge about HPV, they did not affect acceptance of HPV vaccines (Dempsey et al., presented at the Pediatric Academic Societies annual meeting, 5/14/05, Washington, D.C.). Predictors of vaccine acceptability included having a female child, perceiving vaccination as beneficial, perceived child susceptibility to STIs, peer opinions, lack of concern about pain or fear of vaccines, and personal experience with genital warts.

Mays et al. conducted in-depth interviews to examine parental attitudes about accepting vaccines for genital herpes, human immunodeficiency virus, HPV and gonorrhea for their children (aged 8-17).[104] Content analysis of the responses revealed that most of the 34 parents (>70%) approved the administration of all four of the STI vaccines proposed. Parents' reasons for acceptance included wanting to protect their children, being concerned about specific disease characteristics, and previous experience with the infections. Parents who declined the vaccines did so primarily because they perceived their children to be at low risk for the infections or they had low concern about features of the diseases. Most parents thought they should be the decision-maker regarding children receiving an STI vaccine.

Finally, Kahn et al. explored contextual factors related to HPV vaccine acceptability in a sample of young women (N=52, mean age 25 years, range 18-30 years, 35% Black Non-Hispanic, 64% White, Non-Hispanic, 2% Hispanic) who completed a survey assessing knowledge, attitudes about HPV vaccination, and risk behaviors. Forty-eight participants (92%) believed that all people with a family history of cancer should receive an HPV vaccine that would prevent cervical cancer, compared to 32 (62%) who believed that all sexually active individuals should receive the vaccine. Forty-four participants (85%) reported that

they would be extremely or very likely to receive an HPV vaccine themselves, and 43 (83%) that they would make sure their daughter was vaccinated. Of the 43 women who reported that they were likely to receive the vaccine themselves, 39 (90.7%) reported that they would be likely to make sure that their daughter received the vaccine ($p = .004$). Most participants (N=36, 69%) believed that people important to them would approve of their receiving an HPV vaccine. Between 48% and 58% of participants reported that their sexual partner, husband/steady partner, parents, or health care providers would think she should definitely/probably receive the HPV vaccine. These normative beliefs all were associated significantly ($p < .05$) with intention to receive an HPV vaccine.

Utility of Theoretical Frameworks in the Study of Adolescent Health Decision-Making

Theoretical frameworks may be useful in studying the determinants of adolescent health behaviors and decision-making as well as guiding strategies to effect behavioral change. As defined by Glanz et al, a theory is "a set of interrelated concepts, definitions, and propositions that presents a systematic view of events or situations by specifying relations among variables in order to explain and predict events or situations."[105] Theories may be categorized in a number of ways.[105, 106] For example, theories may focus on a specific societal level (individual, interpersonal, group, organizational, community), on individual vs. environmental determinants of behavior, or on cognitive vs. affective determinants of behavior. They may be classified as explanatory theories or change theories.[105] Explanatory theories help describe and identify why a problem exists, guiding the search for modifiable factors such as knowledge, attitudes, and social support. Change theories guide the development of evaluations and interventions.

One limitation of widely-used theories of health behavior is that they may have been developed for use in adults and may not be as relevant for use in adolescents. For example, many theories of health behavior do not take into account adolescent cognitive, social or emotional development. Furthermore, there are a large number of different health behavior theories in the literature, yet a lack of consensus as to which theory is best in explaining particular health-related behaviors. There is also a lack of consensus regarding

terminology for the constructs comprising models, despite the fact that many constructs in different theories of health behavior are similar or virtually identical.[107]

Despite these limitations, theory has been valuable in guiding research about adolescent health behaviors as well as interventions designed to promote healthy decision-making. Research may be most effective if the appropriate theories for a given situation or purpose are chosen. For example, models focused on individual health behavior (e.g. The Health Belief Model, The Transtheoretical Model and Stages of Change, The Theory of Planned Behavior) may be helpful in explaining or guiding interventions to change an individual adolescent's health decisions about behaviors such as Pap screening or HPV vaccination. Models of interpersonal health behavior (e.g. Social Cognitive Theory, Social Support Theory) assume that individuals are embedded in society and are defined in part by interpersonal relationships. These relationships can help individuals develop confidence in their ability to make healthy decisions and are the source of information and support that affect health behaviors. These theories may be particularly useful in understanding the role of families, providers and peers in adolescent decision-making about reproductive health. For example, Sieving et al. used The Theory of Triadic Influence in their study of adolescent sexual behaviors.[80] It suggests that social, attitudinal, and intrapersonal factors influence health-related decisions and behaviors. The theory assumes that an individual's behaviors are shaped in part by perceptions of the health-related attitudes, beliefs, and behaviors of others, and that individuals are motivated to adopt attitudes, beliefs, and behaviors of others with whom they have strong social bonds.

Another approach that has been used to examine health-related behaviors, including Pap screening, is to create integrated or heuristic frameworks based on constructs from more than one theoretical framework.[108, 109] For example, Kahn et al. developed an integrated framework based on a model developed by Gritz et al.[110, 111] to explain compliance with Pap screening in adolescents. The model included constructs derived from the Theory of Planned Behavior, Social Cognitive Theory, the Health

Belief Model, and the Transtheoretical Model/Stages of Change. An integrated model was also useful in predicting intention to return and actual return for Pap screening in a follow-up quantitative study.[35, 112]

Finally, research on adolescent health decision-making may be theory-building. Grounded theory is an example of a qualitative approach that enables an investigator to develop new theory or extend existing theory.[113] This approach may be useful to ensure that theories or frameworks are relevant to adolescents (or subgroups of adolescents) because they are created directly from adolescent narratives.[54]

Implications of Current Research for Health Promotion and Prevention Strategies

Virtually all cervical cancer deaths should be avoidable if at-risk women participate in regular Pap screening and HPV testing and if precancerous lesions detected by screening are treated. Vaccines to prevent HPV infection promise to be a highly effective primary prevention strategy, although the vaccines in development will not replace Pap screening. Thus, goals for health promotion and prevention strategies in adolescents should include increasing adolescent knowledge about cervical cancer prevention technologies; ensuring adherence to recommendations for Pap and/or HPV testing and follow-up of abnormal results; and promoting uptake of HPV vaccines once they are available. These are consistent with Healthy People 2010 goals and objectives (**Table 2**). Strategies to accomplish the goals outlined below take into account the specific challenges these technologies present for adolescents, as well as existing research about the role of contextual factors on adolescent health behaviors and decision-making.

1. Improving awareness and knowledge about cervical cancer prevention technologies among adolescents

Adolescents generally demonstrate poor understanding of HPV infection, cervical cancer screening procedures and guidelines, and new technologies such as HPV DNA testing and HPV vaccines. Thus, the first step in promoting cervical cancer screening (and promoting immunization once HPV vaccines are available) must be to ensure that educational materials and public health messages about these technologies are developed, tested for effectiveness, and made widely available to adolescents.

Educational approaches must be cognitively, developmentally, linguistically and culturally appropriate for the target audience.

2. Increasing adherence to cervical cancer screening protocols and follow-up of abnormal results in adolescents

Several excellent reviews are available that summarize the components of successful interventions to increase cervical cancer screening in adult women.[114-117] These strategies will be valuable for programs that aim to increase adherence in adolescents as well. For example, ensuring that adolescents have a usual source of care will help to maximize utilization of screening services. In addition, comprehensive services that link primary care providers with those who perform Pap/HPV screening and follow-up or treatment of abnormal results are critical to ensure that adolescents do not drop out of the system. Case managers or patient navigators have been used in adults to help with scheduling, keeping appointments, explaining terminology, and assisting with transportation.[9] This model may be particularly helpful for adolescents.

Strategies targeted toward adolescents are also likely to benefit from a focus on contextual influences on adolescent decision-making about screening. For example, parents will likely play a central role in promoting adherence to Pap screening. Parental education about Pap/HPV screening guidelines will be critically important, considering the role that parental communication appears to play in adolescent Pap screening and other reproductive health behaviors. Adult health care providers such as internists, family physicians and gynecologists could play an important role educating mothers about new Pap and HPV testing methods.

Provider factors such as communication and examination skills are also likely to influence adolescent Pap screening behaviors. Although modifying these factors may present challenges, providers can be encouraged or trained to provide in-depth, understandable explanations about Pap/HPV testing and pelvic

examinations, perform examinations gently, and assure teens that care will be confidential. Providers who communicate Pap and HPV test results to adolescents should be aware that some adolescents respond to Pap and HPV results with anxiety, distress, and anticipated stigma (which may impact adversely on decisions about future screening and follow-up), while others respond with a sense of empowerment and self-confidence to prevent future disease. Providers should also be aware that adolescent responses and decisions about future screening are influenced by contextual factors such as provider counseling, family experiences, and beliefs about peer responses. Thus, providers who communicate test results to adolescents should provide accurate information about test results and their implications while minimizing stigma, explore family and peer factors that may adversely affect response to test results, and focus on positive behavioral responses to test results such as empowerment. Providers who communicate effectively may be able to reduce the harmful psychosocial consequences of abnormal test results while helping adolescents to make decisions that will promote positive health outcomes such as return for STI and Pap screening.

In order to communicate effectively, providers must understand new cervical cancer prevention technologies and guidelines. However, many providers who care for children and adolescents, such as pediatricians and family physicians, may be unaware of new cervical cancer screening guidelines for adolescents or unsure how to utilize new technologies such as liquid-based Pap testing or HPV DNA testing. Thus, educational initiatives are needed to improve providers' knowledge about new guidelines and technologies. These initiatives should encourage primary care providers to ask all adolescents about their sexual history, communicate the importance of Pap screening to adolescents who are seeking care for other reasons (e.g. for STI screening), and either perform screening when indicated or refer to other providers if they cannot provide those services. Educational initiatives should also address the difficulty that adolescents may have in making complex medical decisions, and encourage clinicians to provide additional support and counseling if needed.

3. Maximizing uptake of HPV vaccines once available

Once HPV vaccines are available, parents and providers will play critical roles in adolescent uptake of vaccines. Of fundamental importance will be parental education about HPV vaccines. Existing research can help to design evidence-based public health messages as well as to guide strategies for educating parents in clinical settings. These messages should include information about HPV infection, its sequelae, and the safety and efficacy of vaccines. Messages may be more effective if they focus on the benefits of vaccination (e.g. vaccination will protect their child against a serious disease) while addressing parental concerns (e.g. vaccination will lead to riskier sexual behaviors).

Provider attitudes about HPV immunization and recommendations about vaccination will also impact adolescent decision-making about HPV vaccines. Vaccination initiatives directed toward pediatricians, family physicians and other providers that focus on modifiable predictors of intention to vaccinate may facilitate physician adoption of vaccine guidelines and thus ensure vaccine uptake in adolescents. Research suggests that modifiable factors such as knowledge about HPV and attitudes about vaccination, including barriers to vaccination and beliefs about endorsement by professional organizations, are linked to intention to vaccinate. Providers also may benefit from educational materials about HPV vaccines that they can give to parents and adolescents, as well as strategies for addressing common parental and adolescent concerns about HPV vaccination.

Frontier Areas of Research

The National Adolescent Health Information Center recently performed a comprehensive analysis of existing research recommendations related to adolescent health and identified four critical research questions and associated priority areas based on their analysis.[118] The authors identified the study of the social and environmental context of adolescents' lives as one critical question, and stated that family, peer, and provider influences on adolescent health were associated priority areas. They identified the study of health-enhancing and health-risk behaviors as another critical question, and noted that

developing and evaluating interventions to promote healthy behavior and reduce health-risk behavior were associated priority areas. Accordingly, the following frontier areas of research focus on the social and environmental factors in adolescents' lives that may guide strategies to help adolescents make informed, healthy decisions about HPV testing, Pap screening, and HPV vaccination.

1. Adolescent, parent, and provider education about new cervical cancer prevention technologies

Identification of adolescent and parent educational needs about Pap screening, HPV testing, and HPV vaccines is fundamentally important for cervical cancer prevention initiatives. Once needs are identified, educational protocols should be developed for use in different settings (e.g. school-based programs, clinical settings) which are developmentally, linguistically and culturally appropriate. In addition, public health messages should be developed for a wider parental and adolescent audience. Educational protocols and public health messages should be tested rigorously for effectiveness and impact on adolescent use of the technologies. Strategies such as social marketing research may be useful in developing effective public health messages about new technologies.[119]

Providers will be a critical source of information about each of the new technologies, but as noted previously many clinicians who care for children and adolescents have inadequate knowledge about HPV infection and new cervical cancer technologies. Thus, research is needed to determine providers' educational needs and preferred sources of information, to develop strategies for disseminating information to providers, and to assess the impact of education on provider screening practices and vaccine recommendations. The Centers for Disease Control and Prevention has developed evidence-based educational resources for providers and the general public about HPV infection and HPV DNA testing, which are useful models for developing educational protocols (http://www.cdc.gov/std/HPV/default.htm, accessed 8/4/05).

2. Adolescent adherence to cervical cancer screening and follow-up protocols

Research demonstrates that factors such as parent-teen connectedness, relationship satisfaction, and communication are related to adolescent sexual and contraceptive behaviors, and preliminary evidence demonstrates that maternal communication may play an important role in adolescent cervical cancer screening. Further research is needed to sort out the complex relationships between maternal attitudes and screening behaviors; mother-adolescent relationship satisfaction; maternal-adolescent communication about screening; and adolescent attitudes and actual screening behaviors. Longitudinal research designs will be most informative in defining causal pathways and thus in guiding the design of interventions to increase adherence.

Similarly, provider communication and examination skills are important to adolescent adherence, and interventions designed to enhance these skills and assess their impact on adolescent behaviors are needed. Finally, studies are needed to explore the psychological, behavioral, and interpersonal impact of HPV and Pap testing and the role of contextual factors in modifying response to test results. Clinical interventions based on this research could be developed and evaluated in terms of their effectiveness in preventing harmful psychosocial and interpersonal responses to HPV and Pap testing and in promoting healthy sexual behaviors and regular Pap screening.

The importance of parental and provider involvement in adolescent decision-making about cervical cancer screening is underscored by recent neurobiological research suggesting that cognitive skills such as planning and decision-making are largely prefrontal cortex functions that are still maturing during adolescence.[57] Thus, research is needed regarding the appropriate roles of parents or providers in guiding and supporting adolescents' decisions about Pap testing, HPV DNA testing, and follow-up of abnormal results as well as how these roles might change as adolescents mature emotionally and cognitively.

3. Acceptability and Uptake of HPV vaccines

Research is needed to further examine provider and parent acceptance of HPV immunization, especially related to its use in preadolescents or in early adolescents prior to sexual initiation. Little research has focused on adolescent acceptance of HPV vaccines, perceptions of personal risk, or intention to change sexual or screening behaviors after vaccination. Ideally, these studies should be completed before the vaccine is available to ensure optimal vaccine uptake and prevent adverse behavioral effects following vaccination.[9]

Cross-sectional studies have provided information about HPV vaccine acceptability and intention to recommend vaccines among providers. However, the upcoming introduction of HPV vaccines provides a unique opportunity to examine prospectively the process by which physicians become aware of, accept, and ultimately implement new vaccine guidelines. Identification of variables that predict each stage in this process will be important in order to develop targeted interventions designed to modify provider intentions and increase adherence to new HPV vaccine guidelines.

As HPV vaccines are introduced, research is also needed to examine vaccination patterns and to determine factors associated with vaccine uptake among parents and adolescents. This information will be essential not only for the design of future interventions to enhance uptake of HPV and other STI vaccines in development, but also to monitor whether disparities in vaccine uptake occur. In order to assess whether and what type of interventions are needed to prevent adverse behavioral outcomes, prospective studies are needed to determine whether adolescents practice riskier sexual behaviors or demonstrate poorer compliance to Pap screening following vaccination.

Social marketing principles may be useful in designing evidence-based interventions to increase STI vaccine uptake.[119] This approach includes formative research to understand target audiences, designing interventions tailored to the needs and preferences of specific population groups, piloting interventions

before full implementation, and continuously monitoring interventions throughout their implementation.[119]

4. Utility of theoretical approaches in examining adolescent decision-making related to new technologies

Theoretical approaches may be valuable both for exploring the contextual influences on adolescent decision-making about new cervical cancer prevention technologies and for guiding interventions designed to optimize adolescent use of these technologies. Models of individual and interpersonal health behaviors, integrated models, and theory-building models are all approaches that may be useful. Priorities for research would include the use of theoretical approaches in the design of research on adolescent decision-making about new technologies, comparison of the utility and validity of different theories of health behavior to examine decision-making, and development of relevant measures that have been normed and validated in adolescent populations.

5. Exploration of additional contextual factors: individual, organizational, cultural, and socioeconomic

Research is needed regarding contextual factors that remain largely unexplored with respect to adolescent decision-making about Pap testing, HPV testing, and HPV vaccines. These include other individuals (e.g. extended family, teachers, sexual partners), organizations (e.g. religious, educational, and social organizations) and racial, ethnic, and socioeconomic factors. For example, if utilization of new technologies (or alternatively the health impact of these technologies) differs by race, ethnicity, or socioeconomic status, then the introduction of new technologies may widen already marked disparities in cervical cancer incidence and mortality. Therefore, investigators should examine patterns of utilization of new technologies as well as specific barriers to utilization among low-income and/or minority adolescents. Barriers that might be explored include lack of access to reproductive health services, lack of insurance coverage; poor understanding of cervical cancer screening or vaccines; and mistrust of the medical community.[120]

Summary

In summary, new cervical cancer prevention technologies could have a substantial public health impact if utilized appropriately. Although Pap and HPV testing will be used only by the subset of adolescents who are eligible for cervical cancer screening, prophylactic HPV vaccines will be targeted almost exclusively to preadolescents and adolescents. New technologies present a number of challenges for adolescents, who may have difficulty understanding or making decisions about complex screening protocols, as well as adhering to recommendations for Pap screening or HPV vaccination. Emerging research suggests that families, health care providers, and peers may play important roles in adolescent decision-making about these technologies, as they do in adolescent sexual and contraceptive behaviors. Additional research is needed that explores the impact of provider, parent, peer and other contextual factors on adolescent decision-making and takes into account the unique developmental aspects of adolescence. Incorporating the findings of these studies into health promotion and prevention programs may help to improve adolescent knowledge about new technologies and recommendations, increase adherence to cervical cancer screening, and maximize uptake of HPV vaccines.

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Table 1. Association between maternal communication about Pap smears and adolescent Pap screening practices. Analysis stratified by adolescent age (< 18 vs. ≥ 18 years of age) and by maternal history of pelvic exam

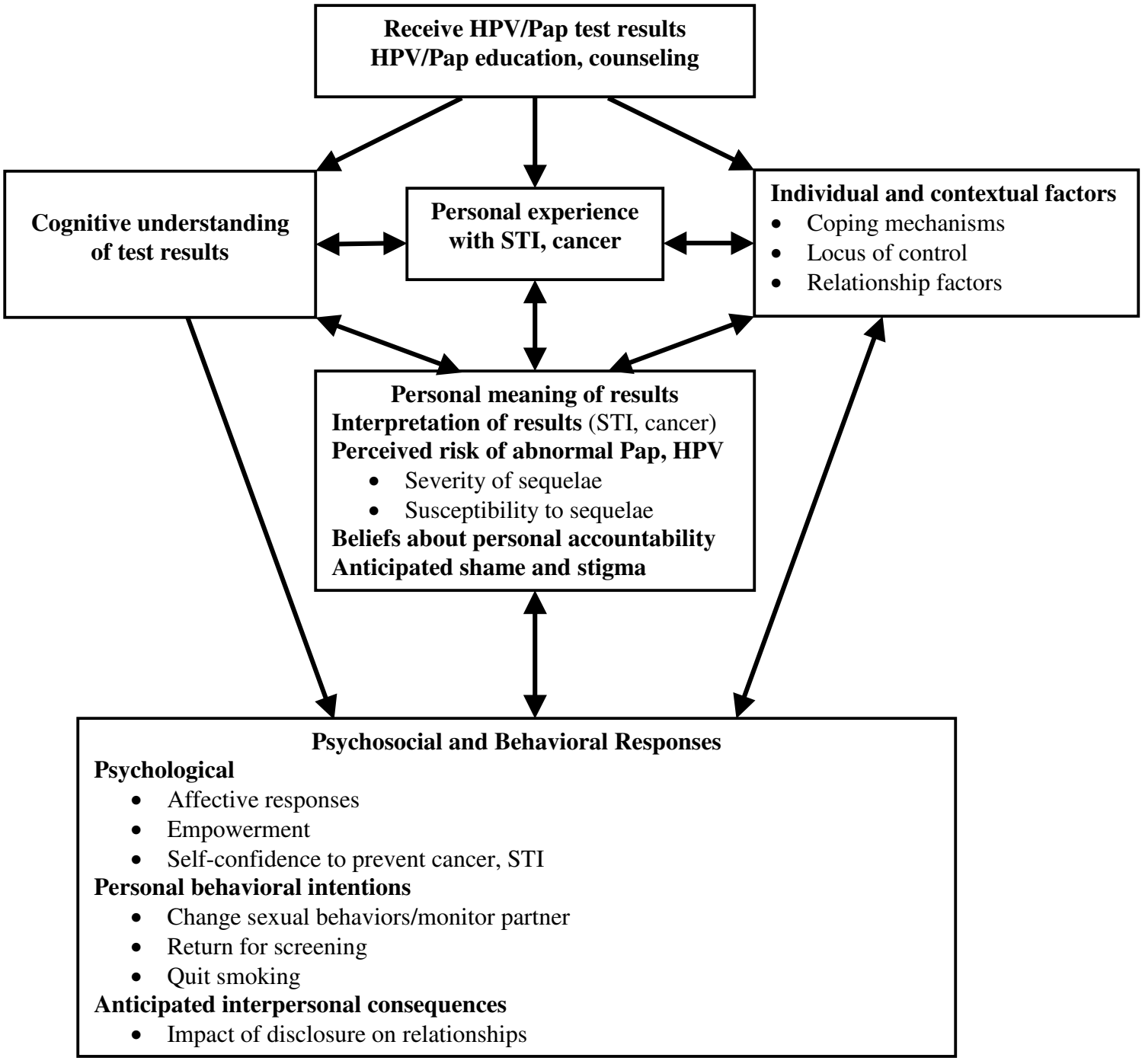
			Adolescent Pap screening practices					
			Adolescent ever had Pap			Adolescent had Pap in past year		
Maternal Communication			OR[1]	95% CI[2]	P value	OR[1]	95% CI[2]	P value
Mother ever told adolescent to have Pap smear	All participants		7.69	6.42-9.21	<.0001	5.31	4.22-6.62	<.0001
	<18 years of age		7.24	4.90-10.80	<.0001	6.42	4.14-10.07	<.0001
	≥18 years of age		7.61	6.17-9.39	<.0001	5.16	4.01-6.69	<.0001
	Mother had pelvic exam		7.92	6.55-9.68	<.0001	5.21	4.10-6.62	<.0001
	Mom did not have pelvic exam		6.30	3.71-10.80	<.0001	5.75	5.05-10.49	<.0001
Frequency with which mother talked to adolescent about Pap smears	All	Once	3.32	2.64-4.15	<.0001	3.53	2.64-4.71	<.0001
		Occasionally	6.11	4.76-7.85	<.0001	5.58	4.06-7.61	<.0001
		Sometimes	9.12	6.89-12.06	<.0001	6.82	4.81-9.68	<.0001
		Often	13.46	9.68-18.54	<.0001	9.78	6.55-14.59	<.0001
	<18 years	Once	5.00	3.06-8.17	<.0001	6.30	3.19-12.43	<.0001
		Occasionally	6.75	3.74-12.18	<.0001	5.64	2.53-12.43	<.0001
		Sometimes	9.68	5.10-18.17	<.0001	9.03	3.46-23.34	<.0001
		Often	16.61	7.54-36.60	<.0001	10.38	3.60-29.96	<.0001
	≥18 years	Once	2.89	2.23-3.74	<.0001	2.97	2.16-4.10	<.0001
		Occasionally	5.70	4.35-7.54	<.0001	5.21	3.67-7.32	<.0001
		Sometimes	8.67	6.30-11.82	<.0001	6.11	4.18-8.94	<.0001
		Often	12.18	8.50-17.46	<.0001	9.12	5.93-14.15	<.0001
	Mother had pelvic exam	Once	3.35	2.64-4.31	<.0001	3.78	2.75-5.21	<.0001
		Occasionally	6.23	4.76-8.17	<.0001	5.53	3.94-7.77	<.0001
		Sometimes	8.94	6.62-12.18	<.0001	6.55	4.53-9.49	<.0001
		Often	13.60	9.68-19.30	<.0001	10.49	6.82-16.12	<.0001
	Mom did not have pelvic exam	Once	3.39	1.75-6.55	.0003	2.53	1.26-5.10	.0088
		Occasionally	4.18	2.03-8.67	.0001	5.47	2.32-12.94	.0001
		Sometimes	12.30	5.00-30.57	<.0001	9.49	3.32-27.11	<.0001
		Often	13.33	4.57-38.47	<.0001	5.31	1.79-15.80	.0027

[1] OR = odds ratio [2] CI = confidence interval

Table 2. Healthy People 2010 goals and associated objectives related to new cervical cancer technologies (www.healthypeople.gov).

Healthy People 2010 Goals		Objectives	
Goal number		Objective number	
3	Decrease new cancer cases and illness, disability and death caused by cancer	3-4	Reduce the death rate from cervical cancer
14	Prevent disease, disability and death from infectious diseases, including vaccine-preventable diseases	14-27	Increase vaccination coverage levels among adolescents
25	Promote responsible sexual behavior, strengthen community capacity, increase access to quality services to prevent STDs and their complications	25-5	Reduce the proportion of adults with HPV

Figure 1. Short-term responses to HPV and Pap test results in adolescent girls.



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