CALIFORNIA
HEALTH BENEFITS REVIEW PROGRAM

Analysis of Senate Bill 1245 Health Care Coverage: Cervical Cancer Screening Test

A Report to the 2006–2007 California Legislature
April 7, 2006

CHBRP 06-04

Established in 2002 to implement the provisions of Assembly Bill 1996 (*California Health and Safety Code,* Section 127660, et seq.), the California Health Benefits Review Program (CHBRP) responds to requests from the State Legislature to provide independent analysis of the medical, financial, and public health impacts of proposed health insurance benefit mandates. The statute defines a health insurance benefit mandate as a requirement that a health insurer and/or managed care health plan (1) permit covered individuals to receive health care treatment or services from a particular type of health care provider; (2) offer or provide coverage for the screening, diagnosis, or treatment of a particular disease or condition; or (3) offer or provide coverage of a particular type of health care treatment or service, or of medical equipment, medical supplies, or drugs used in connection with a health care treatment or service.

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A Report to the 2006–2007 California State Legislature

Analysis of Senate Bill 1245
Health Care Coverage: Cervical Cancer Screening Test

April 7, 2006

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PREFACE

This report provides an analysis of the medical, financial, and public health impacts of Senate Bill 1245, a bill that would require health care service plans and health insurance policies to include coverage for testing for the human papillomavirus (HPV) as part of their annual cancer screening benefit. In response to a request from the California Senate Committee on Banking, Finance and Insurance on February 3, 2006, CHBRP undertook this analysis pursuant to the provisions of Assembly Bill 1996 (2002) as chaptered in Section 127600, et seq., of the California Health and Safety Code.

Yali Bair, PhD, Richard Kravitz, MD, and Lisa Ward, MD, all of the University of California, Davis, prepared the medical effectiveness analysis. George Sawaya, MD, provided technical assistance with the literature review and clinical expertise for the medical effectiveness analysis. Linda King, MLS, of UCD conducted the literature search. Nicole Bellows, MHSA, Helen Halpin, PhD, Sara McMenamin, PhD, and Janine Santimauro of the University of California, Berkeley, prepared the public health impact analysis. Miriam Laugesen, PhD, Meghan Cameron, MPH, Nadereh Pourat, PhD, and Gerald Kominski, PhD, of the University of California, Los Angeles, prepared the cost impact analysis. Robert Cosway, FSA, MAAA, of Milliman, provided actuarial analysis. Susan Philip, MPP, of CHBRP staff prepared the background section and synthesized individual sections into a single report. Sarah Ordódy, BA, provided editing services. In addition, a subcommittee of CHBRP's National Advisory Council (see final pages of this report) and a member of the CHBRP Faculty Task Force, Wayne Dysinger, PhD, of the Loma Linda University, reviewed the analysis for its accuracy, completeness, clarity, and responsiveness to the Legislature's request.

CHBRP gratefully acknowledges all of these contributions but assumes full responsibility for all of the report and its contents. Please direct any questions concerning this report to CHBRP:

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TABLE OF CONTENTS

EXECUTIVE SUMMARY

California Health Benefits Review Program Analysis of Senate Bill 1245
Health Care Coverage: Cervical Cancer Screening Test

The California Legislature has asked the California Health Benefits Review Program to conduct an evidence-based assessment of the medical, financial, and public health impacts of Senate Bill 1245. In response to a request from the California Senate Committee on Banking, Finance and Insurance on February 3, 2006, CHBRP undertook this analysis pursuant to the provisions of Assembly Bill 1996 (2002) as chaptered in Section 127600, et seq., of the California Health and Safety Code.

SB 1245 would amend section 1367.66 of the Health and Safety Code and Section 10123.18 of the Insurance Code. These sections of the Health and Safety Code and Insurance Code currently state that "the coverage for an annual cervical cancer screening test… shall include the conventional Pap test and the option of any cervical cancer screening test approved by the federal Food and Drug Administration, upon the referral of the patient's health care provider." SB 1245 would require that the currently mandated cervical cancer screening benefit explicitly include coverage for the HPV (human papillomavirus) test.[1]

There is currently one FDA-approved HPV test available for use in the United States: the Hybrid Capture II High-Risk HPV test.

I. Medical Effectiveness

- HPV has been identified as the single necessary cause of cervical cancer. This means that only in rare cases is cervical cancer diagnosed in women not infected with HPV.

- The use of HPV testing as an adjunct to the conventional Pap test increases the accuracy of the test and improves the efficiency of screening programs.

- A negative result on an HPV test alone or in combination with Pap test screening can identify women at low risk for cervical cancer.

- The use of HPV testing as a triage tool among women who have mild abnormal Pap test results appears to be more effective than traditional repeat Pap testing in identifying women at risk for cervical cancer.

- A positive HPV screen or triage test is less predictive of cervical cancer than a positive Pap and can lead to increased patient anxiety and costs.

[1] Health care service plans, commonly referred to as health maintenance organizations, are regulated and licensed by the California Department of Managed Care (DMHC), as provided in the Knox-Keene Health Care Services Plan Act of 1975. The Knox-Keene Health Care Services Plan Act is codified in the California Health and Safety Code. Health insurance policies are regulated by the California Department of Insurance and are subject to the California Insurance Code.

II. Utilization, Cost, and Coverage Impacts

Coverage

- An estimated 20,144,000 people in California are enrolled in health care plans or have health insurance policies that would be affected by this legislation. An estimated 7,627,000 women between the ages of 18-64 years are among these insured and would specifically be affected by SB 1245.
- An estimated 100% of enrollees currently have coverage for HPV testing as part of their annual cervical cancer screening benefit.
- Coverage is based on currently existing standards of care. HPV testing is generally considered medically necessary for (1) cervical cancer screening among women older than 30 years or (2) women who have an Pap test result indicating atypical squamous cells of undetermined significance (ASC-US).

Utilization

- Currently an estimated 7.1% of women are tested annually for HPV.
- SB 1245 is projected to have no direct impact on the frequency of HPV test usage. This is due to (1) no projected increase in utilization as a result of changes in coverage because coverage levels would remain the same, (2) no projected increase in the number of women demanding the HPV test as a result of the mandate, and (3) no projected changes in practice patterns as a result of the mandate.[2]
- Most health care plans and insurers provide coverage per current medical guidelines. They cover HPV testing services to women over 30 years, or to those who have had an abnormal Pap test.

Annual Expenditures

If SB 1245 were to pass:

- Total private employer premiums would remain the same.
- Individuals who pay for a share of their private employer-based insurance, California Public Employees' Retirement System (CalPERS), or Healthy Families premiums would have the same level of expenditures.
- Premium expenditure on individually purchased insurance would remain the same.
- CalPERS' employer costs would remain the same.
- State expenditures for Medi-Cal HMO members would remain the same.
- Healthy Families state expenditures would remain the same.

[2] While CHBRP projects no change in utilization as a result of the mandate, and therefore no cost and public impacts, Appendix C presents a scenario if SB 1245 were to slightly increase utilization due to potential changes in practice patterns, specifically, *accelerating* the adoption of currently existing clinical guidelines. Appendix C presents the impacts of SB 1245 *if* utilization of the HPV test were to increase by 1 percentage point as a result of the mandate.

- Individuals' out-of-pocket expenditures associated with HPV testing would remain the same.
- Other out-of-pocket costs for HPV testing presently not covered by insurance would remain the same.

Table 1. Summary of Coverage, Utilization, and Cost Effects of SB 1245

	Before Mandate	After Mandate	Increase/ Decrease	% Change After Mandate
Percent of insured women 18-64 with coverage for mandated benefit	100.0%	100.0%	0.0%	0.0%
Number of insured women 18-64 in California with coverage for the benefit	7,627,000	7,627,000	0.0%	0.0%
Percent of insured women 18-64 in California receiving HPV test in a year				
Ages 18-29	6.0%	6.0%	0.0%	0.0%
Ages 30-64	7.4%	7.4%	0.0%	0.0%
Ages 18-64	7.1%	7.1%	0.0%	0.0%
Number of insured women 18-64 in California receiving HPV screen in a year				
Ages 18-29	99,800	99,800	0.0%	0.0%
Ages 30-64	443,800	443,800	0.0%	0.0%
Ages 18-64	543,700	543,700	0.0%	0.0%
Costs				
Average cost per HPV screening	$57	$57	$0	0.0%
Expenditures				
Premium expenditures by private employers for group insurance	$35,792,975,000	$35,792,975,000	$0	0.00%
Premium expenditures for individually purchased insurance	$4,744,086,000	$4,744,086,000	$0	0.00%
CalPERS employer expenditures	$2,330,367,000	$2,330,367,000	$0	0.00%
Medi-Cal state expenditures	$4,334,532,000	$4,334,532,000	$0	0.00%
Healthy Families state expenditures	$644,314,000	$644,314,000	$0	0.00%
Premium expenditures by employees with group insurance or CalPERS, and by individuals with Healthy Families	$11,378,584,000	$11,378,584,000	$0	0.00%
Individual out-of-pocket expenditures (deductibles, copayments, etc.)	$3,837,497,000	$3,837,497,000	$0	0.00%
Expenditures for non-covered services	$0	$0	$0	N/A
Total annual expenditures	$63,062,355,000	$63,062,355,000	$0	0.00%

Source: California Health Benefits Review Program, 2006.
Note: The population includes individuals and dependents in California who have private insurance (group and individual) or are enrolled in public plans subject to the Health and Safety Code, including CalPERS, Medi-Cal, or Healthy Families. All population figures include enrollees aged 0–64 years and enrollees 65 years or older covered by employment-based coverage.
Employees and their dependents who receive their coverage from self-insured firms are excluded because these plans are not subject to mandates.
Key: CalPERS = California Public Employees' Retirement System; HMO = health maintenance organization and point of service plans; PPO = preferred provider organization and fee-for-service plans.

III. Public Health Impacts

- In California, approximately 88.8% of women aged 21 years or older who are enrolled in health plans affected by SB 1245 receive Pap tests at the recommended interval (i.e., within the last 3 years). It is estimated that the rate of HPV infection in the general population is 14.3% and that approximately 7% of those infected with HPV will develop CIN III or cervical cancer. The 5-year survival rate for those diagnosed with cervical cancer is 71%. In California in 2006, an estimated 1,550 cases of cervical cancer and 400 deaths due to cervical cancer are expected.

- Because this mandate is not estimated to increase utilization of the HPV screening test there would be no impact on health outcomes such as number of cervical cancer cases or mortality rates due to cervical cancer.

- There are clear racial disparities in terms of utilization of cervical cancer screening, incidence rates of cervical cancer, and cervical cancer mortality rates. This mandate would not affect cervical cancer screening rates or screening methods. Therefore, we conclude that this mandate will not affect racial disparities in cervical cancer outcomes.

- HPV screening is currently covered for all women enrolled in health care plans affected by this mandate. Accordingly, no increase in utilization of HPV screening is expected as a result of this mandate. Therefore, we conclude that SB 1245 would not affect premature death or its associated economic productivity losses as related to cervical cancer.

INTRODUCTION

Cervical cancer was once the number one cause of cancer deaths among women in the United States. However, the use of the Pap test to routinely screen for cervical cancer has reduced cervical cancer to the 13th cause of cancer-related deaths in women (ACS, 2002). Because cervical cancer is strongly linked to the presence of cancer-causing strains of the human papillomavirus (HPV), there has been significant interest among researchers and clinicians in using a test that detects HPV as an additional tool in cervical cancer screening. Currently there is one HPV test approved by the Food and Drug Administration (FDA) for use in the United States: the Hybrid Capture II High-Risk HPV test, produced by the Digene Corporation.

Current law requires that "the coverage for an annual cervical cancer screening test… include the conventional Pap test and the option of any cervical cancer screening test approved by the federal Food and Drug Administration, upon the referral of the patient's health care provider." SB 1245 would amend current law to *explicitly* require health plans and insurers to "cover the HPV test, upon the referral of the patient's health care provider."[3] For the purposes this analysis, CHBRP interprets this to mean that the HPV test would be covered when providers order the test and they would order such a test when it is medically necessary.[4] According to existing standards of care, which will be discussed in further detail in the *Medical Effectiveness* Section, the HPV test for cervical cancer screening should generally be provided for women older than 30 years or for women who have a Pap test result indicating atypical squamous cells of undetermined significance (ASC-US).

Thirty states currently mandate coverage of cervical cancer screening (BCBSA, 2005). Of those, three states—North Carolina, New Mexico, and Maryland—explicitly require coverage for HPV testing under the cervical cancer screening mandate.

In California, existing law requires the Department of Health Services (DHS) to conduct a "Cervical Cancer Community Awareness Campaign" to provide awareness, assistance, and information regarding cervical cancer to the public. Last year, under Senate Bill 615 (Figueroa), the law was extended to "provide awareness, assistance, and information regarding cervical cancer and the human papillomavirus (HPV)." The efforts are to "include provider education aimed at promoting the awareness of HPV and its link to cervical cancer." Education efforts are to include providing practitioners information regarding prevention, early detection, options for testing, and treatment costs. Furthermore, under the new law, DHS is to collect and study data on age, ethnicity, region, and socioeconomic status to report on the appropriate target audience for its educational campaign. This law goes into effect on January 1, 2007, and it to be funded by voluntary contributions from entities such as foundations or private corporations.

[3] SB 1245 would amend section 1367.66 to the Health and Safety Code and Section 10123.18 of the Insurance Code.

[4] The clause "upon the referral of the patient's health care provider" would require plans to cover the HPV test for cervical cancer screening regardless of plans' utilization review determinations. However, as discussed in the *Utilization, Cost and Coverage* section, this analysis assumes that providers would not have incentives to order the HPV test when it is not medically necessary.

I. MEDICAL EFFECTIVENESS

Cervical Cytology Screening and Human Papillomavirus

Cervical cytology screening, also referred to as Papanicolaou or Pap testing, has significantly reduced cervical cancer rates worldwide. In the United States, the rate of cervical cancer dropped by more than 50% between 1973 and 1994 (Nanda et al., 2000) due to the widespread use of cervical cancer screening programs. Despite the success of these screening programs, the Pap test is subject to variability in sample quality and interpretation (Nanda et al., 2000).

HPV has been identified as the single necessary cause of cervical cancer (Bosch et al., 2002). This means that only in extremely rare cases is cervical cancer diagnosed in women not infected with HPV. This does not mean that all HPV infections cause cancer. There are over 100 strains of HPV, but only a small number of these are known to cause cervical cancer. These "high-risk" strains are often highly prevalent and transient during young adulthood, meaning that they will produce an infection that is ultimately cleared by the body's immune system. The lifetime risk of infection with HPV is estimated to be 80% (2004) and in young women, the rate of infection is nearly 60% over a 3-year period (Einstein and Burk, 2001). The presence of persistent infection with high-risk strains of HPV is considered an important risk factor for the ultimate development of cervical cancer. Thus, identification of persistent infection using a clinical test for HPV may aid in the identification of women at the highest risk for the disease.

Current Cervical Cancer Screening Guidelines

The American College of Obstetrics and Gynecology (ACOG 2003; ACOG 2005a,b), the U.S. Preventive Services Task Force (USPSTF, 2003), and the American Cancer Society (Saslow et al., 2002) recently released updated guidelines for cervical cancer screening and management. According to the most current guidelines, primary screening for cervical cancer should begin at the onset of sexual activity or by 21 years of age. Screening can be accomplished by either a slide-based or liquid-based method of specimen collection. The slide-based, traditional Pap "smear" method allows evaluation of cervical cells. The liquid-based cytology method allows HPV and Pap to be completed on one sample. Women age 30 years and over may receive an HPV test at the time of the Pap test during routine screening, with a 3-year interval between screenings for women with a negative result on both tests and otherwise at low risk of cervical cancer. Expert guidelines differ on when women should discontinue cervical cancer screening. According to the USPSTF guidelines, women aged 65 years or older who have had three normal Pap tests in a row and no history of an abnormal Pap test in the last 10 years may discontinue cervical cancer screening. The American Cancer Society recommends discontinuing screening under these circumstances at age 70, and ACOG does not recommend an upper age limit for screening. Women under 30 years should not receive the HPV test routinely for screening because the prevalence of transient HPV infection is so high in this age group that it is less predictive of women at risk for cervical cancer.

Table 2. Summary of Clinical Guidelines for Use of HPV Testing in Cervical Cancer Screening

Guidelines	Issue Year	Screening Age Range	HPV Screen	HPV Triage	Pap Interval
1. American Cancer Society	2002	Start screening 3 years after onset of sexual activity, or age 21 Discontinue screening at age 70, if otherwise at low risk	HPV with Pap age 30 and over, no more than every 3 years	N/A	Annual with conventional Pap test Every 2 years with liquid-based Pap test Every 2-3 years after age 30, if had 3 consecutive normal results and otherwise at low risk
2. American College of Obstetrics and Gynecology Number 45: Cervical Cytology Screening Number 66: Management of Abnormal Cervical Cytology & Histology Number 61: Human Papillomavirus	2003 #45 2005 # 61 #66	Start screening 3 years after onset of sexual activity, or age 21 Discontinue at physician discretion if low risk; no upper age limit set	HPV with Pap age 30 and over HPV testing no more than every 3 years	Repeat Pap testing, colposcopy, or DNA testing for high-risk types of HPV are all acceptable methods for managing women with ASC-US HPV testing is preferred if liquid-based Pap is used Not recommended for Pap results of LSIL or higher	Under age 30 screen annually Every 2-3 years after age 30, if had 3 consecutive normal results and otherwise at low risk No more than every 3 years if Pap and HPV test both negative (age 30 and over)
3. US Preventive Services Task Force	2002	From onset of sexual activity until age 65 years if cervix not removed	Insufficient evidence for or against use as screening tool	N/A	At least every 3 years if sexually active and have a cervix

Source: California Health Benefits Review Program analysis, 2006.

Management of Abnormal Cervical Screening Results

Further testing is required for women who have an abnormal result on a Pap test, regardless of age. Low-grade abnormalities are found on approximately 5% of Pap screens (ALTS 2003 #2). Women with low-grade abnormalities, such as atypical squamous cells of undetermined significance (ASC-US), have traditionally been referred for repeat Pap testing within 4-6 months after the initial abnormal test. Because many of these low-grade abnormalities are expected to resolve, women may have a normal result upon repeat Pap testing. Women return to annual screening after two consecutive normal screens. If the abnormality remains on the second Pap test, the woman is then referred for colposcopy, which is an examination under magnification that often includes biopsy of the cervix. As an alternative evaluation of ASC-US, current guidelines recommend HPV testing or a repeat Pap test, with HPV testing preferred when liquid-based cytology is used. The HPV test may be conducted immediately upon finding abnormalities on the Pap test, or within 6-12 months of the abnormal Pap test. If the HPV test is positive, women are immediately referred for colposcopy because they are at significantly higher risk of cervical cancer. If the HPV test is negative, women are at little or no increased risk of developing cervical cancer and can return to annual screening. Any woman that is found to have a high-grade lesion on Pap test screening is immediately referred for colposcopy.

Evidence Review Results

This summary of the scientific literature relating to the effectiveness of HPV testing focuses on the use of the HPV test in two clinical settings. Primary screening studies evaluate the use of HPV tests as an adjunct to conventional cytology, or Pap tests. These studies compare the effectiveness of HPV testing in addition to or in place of Pap testing alone as part of the routine cervical cancer screen. Triage studies evaluate the use of HPV testing as a decision-making tool for follow-up of initially abnormal conventional Pap test results. These studies evaluate the use of HPV testing, relative to a repeat Pap test, as a triage mechanism for further follow-up. We summarize the results of this literature review based on these categories.

All research articles listed in this portion of the review use the Hybrid Capture II technology for HPV testing. This is the only FDA-approved HPV test currently available in the United States. A summary of studies evaluating the use of an alternative technology for HPV testing—polymerase chain reaction or PCR test—are included in Appendix B-2. This test is not commercially available for use in clinical settings and is used primarily in research studies. Therefore, we discuss the evidence from these studies only briefly in this report.

Sensitivity, specificity, and predictive value of the HPV test

The accuracy of a screening test for any given disease or condition depends primarily on the test's sensitivity (ability to identify correctly people who have the disease) and the specificity (ability to identify correctly people who do not have the disease). In our review, sensitivity refers to the likelihood that a person with a precancerous condition will have a positive HPV test and specificity refers to the likelihood that a person without a precancerous condition will have a negative HPV test. A highly sensitive test will capture most of the true positives (in this case,

women who have precancer), but at a cost of some false positives (healthy women who falsely return a positive HPV test result). A highly specific test will capture most of the true negatives (healthy women) but at a cost of some false negatives (women with precancer who have a misleadingly negative test result). The most accurate test optimally balances sensitivity and specificity, thus minimizing the false positives (and saving patient anxiety and time and money for further evaluation) and minimizing the false negatives (the risk of missing disease).

The utility of a particular screening test in predicting disease is often referred to as its "predictive value". Positive predictive value (PPV) refers to the likelihood that a person testing positive on the screening test actually has the disease. In other words, this tells us how helpful a positive HPV test is in identifying women with precancer. By contrast, negative predictive value (NPV) refers to the likelihood that a person testing negative on the screening test truly has no disease. The NPV tells us how helpful a negative HPV test is in identifying women who are free of disease.

Table 3. 2001 Bethesda System Terminology for Cervical Cancer Screening Results

Cytology	**Pap Test Findings**
ASC-US	Atypical squamous cells-undetermined significance
ASC-H	Atypical squamous cells-cannot rule out high-grade lesion
AGC	Atypical glandular cells
LSIL	Low-grade squamous intraepithelial lesion
HSIL	High-grade squamous intraepithelial lesion
Histology	**Biopsy Findings**
CIN I	Cervical intraepithelial neoplasia/mild dysplasia
CIN II	Cervical intraepithelial neoplasia/moderate-severe dysplasia Carcinoma in situ
CIN III	Cervical intraepithelial neoplasia/severe dysplasia Carcinoma in situ

Source: Solomon D, Davey D, Kurman R, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. *JAMA*. 2002:287(16):2114-2119.

Figure 1. HPV as Primary Screening (From ACOG, 2005)

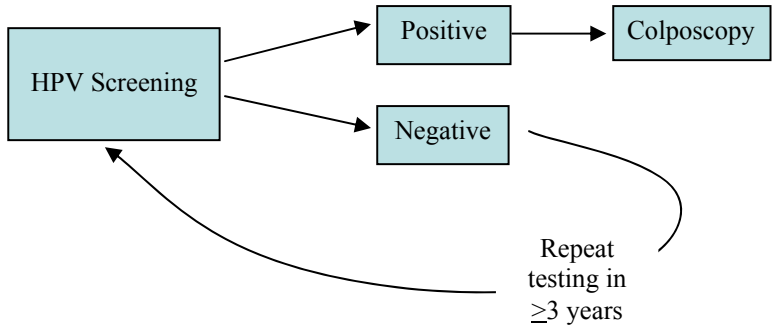


Figure 2. Conventional Cytology with Pap Test Triage (From ACOG, 2005)

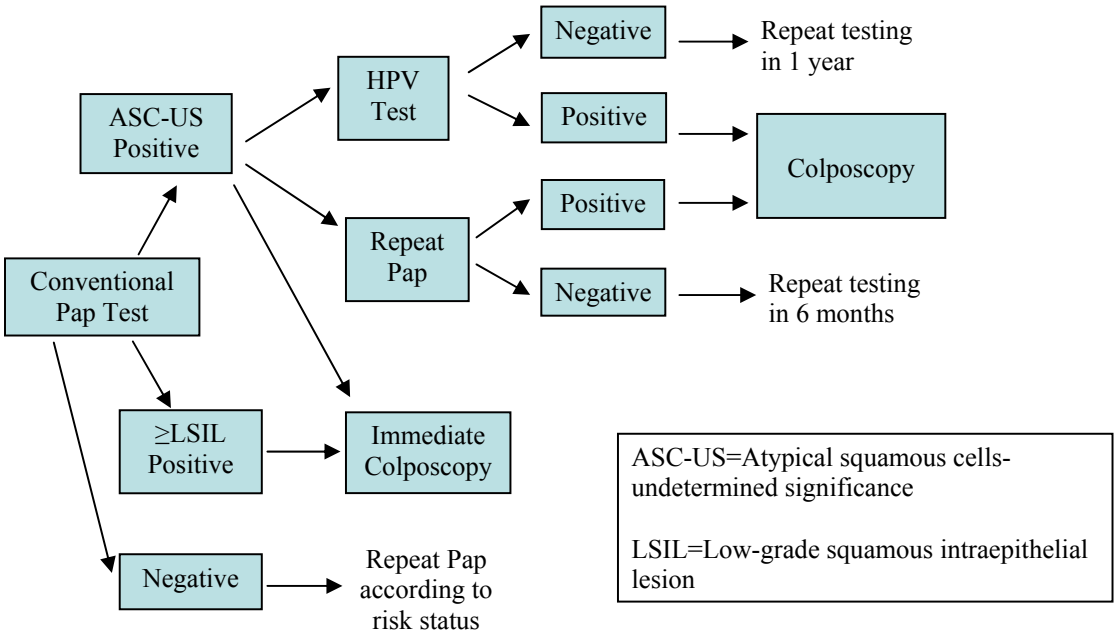
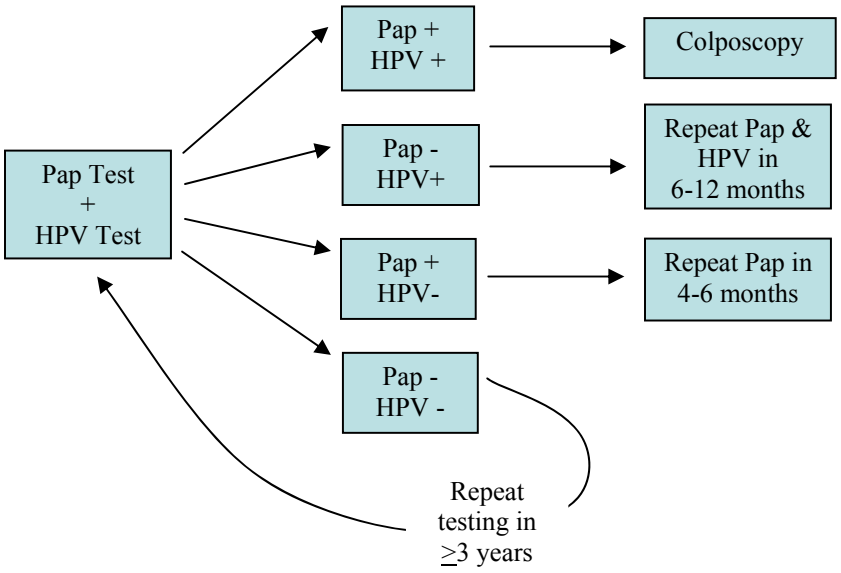


Figure 3. Concurrent Pap & HPV Testing Among Women Aged 30 Years or Older (From ACOG, 2005)



Screening studies

The literature search identified two systematic reviews of the literature in 2003 and three more recently published studies that address the effectiveness of the HPV test in primary screening for cervical cancer. The Lorincz (Lorincz and Richart, 2003) and Franco (Franco, 2003) reviews provide similar estimates for the sensitivity, specificity, and predictive value of the HPV test, relative to conventional Pap test. Studies summarized in both reviews use the identification of cervical intraepithelial neoplasia (CIN) II or higher as the clinical outcome of interest. CIN II and III are the most severe classifications of precancerous cervical lesions. Several studies evaluated the use of the HPV test alone, while others examined the effectiveness of the HPV test combined with the Pap test compared to the Pap test alone. When comparing screening with the Pap test alone versus an HPV test alone, the HPV test increases the sensitivity and slightly decreases the specificity of the screening. This means that more true cases of precancer are identified at the expense of a few missed cases of early cervical abnormality. Carrying out an HPV test and a Pap test concurrently increases the sensitivity and negative predictive value of the test, while slightly decreasing the specificity and positive predictive value. *Overall, compared to traditional Pap test, the addition of the HPV more accurately identifies women at little or no risk of disease.*

A 2004 study by Clavel (Clavel et al., 2004) and colleagues evaluates the predictive value of a negative HPV test for detecting the absence of HSIL (high-grade squamous intraepithelial lesion), an early indicator of precancerous cervical changes. In this study, a negative Pap test result accompanied by a negative HPV test was 99.9% accurate in identifying women without HISL. *Thus, a negative HPV test in combination with a negative Pap test effectively ruled out serious cervical abnormalities.*

A large clinical trial based in India in 2005 (Sankaranarayanan et al., 2005) examines the detection rate between HPV testing alone and conventional cytology alone for identifying CIN II and III. *This study found no difference in detection rate between the two methods when used alone. In this study, the positive predictive value of the HPV test is approximately half that of conventional Pap test.*

The most recent study in this group is a randomized controlled trial based in Finland (Kotaniemi-Talonen et al., 2005). Patients are randomized to screening by Pap test alone, the HPV test alone, or HPV test and Pap test simultaneously. This trial evaluates the accuracy of HPV testing as an adjunct to conventional cytology in identifying CIN I or higher. In this study, use of HPV testing alone decreased both the specificity and positive predictive value of the screening, relative to Pap test alone. Adding HPV to the Pap test made little difference to the specificity, but increased the positive predictive value of the test. In addition, this study estimates that referral for colposcopy increased by 50% among the groups tested for HPV. *Women with CIN II or III were more likely to be accurately identified by the use of Pap with HPV testing than with either test alone. Therefore, fewer false negative cases were identified, but at the expense of more false positive tests.*

Triage studies

We identified several individual studies and one meta-analysis in the literature addressing the use of HPV testing as a triage tool after an initial abnormal Pap result. The meta-analysis by Arbyn and colleagues (Arbyn et al., 2004) evaluates the use of HPV testing, relative to repeat Pap testing, in identifying cases of CIN II or higher. In these studies, the sensitivity of HPV triage was 94%, approximately 14% higher than that of repeat Pap testing. The specificity of HPV triage was almost identical to that for repeat Pap test. HPV triage had a positive predictive value of 22% and a negative predictive value of 99%. *Based on this set of studies, we conclude that HPV triage is more accurate in identifying women at risk for cervical cancer than repeat cytology.*

The first of the individual studies reviewed is a clinical trial conducted by Cuzick and colleagues (Cuzick et al., 2003). This study found that HPV triage is more likely than repeat Pap testing to identify potential cases of CIN II or higher. *The positive predictive value and specificity of HPV testing is slightly lower than that for repeat Pap, indicating that a negative HPV test was more useful than a positive one in accurately identifying disease.* In this study, referral for colposcopy did not differ between the HPV triage group and the repeat cytology group, implying that the increased effectiveness of HPV triage is not due to increased referral for more detailed tests.

Another clinical trial (Lytwyn et al., 2003) evaluates the accuracy of HPV testing in addition to repeat Pap testing compared to repeat Pap testing alone in identifying cases of CIN II or higher. This study found that the HPV and Pap test triage combination had a sensitivity and negative predictive value of approximately 100%. Relative to Pap test alone, the HPV and Pap combination had a lower specificity and slightly lower positive predictive value. *In this study, adding HPV testing to the repeat Pap test among women with initially abnormal findings identified 100% of cases of CIN II or higher.*

We evaluated two studies from the ASCUS-LSIL Triage Study (ALTS) Group (ASCUS-LSIL Triage Study [ALTS] Group 2003a,b). These trials were conducted by the National Cancer Institute in an effort to define the most appropriate management strategy for abnormal cytology results found on Pap tests. Both studies compared the effectiveness of HPV test triage, relative to repeat Pap, in identifying CIN III. *In both studies, HPV testing is more sensitive than repeat Pap test in identifying women with CIN. In both studies, the proportion of patients referred for colposcopy is significantly higher among the HPV triage group than among the group with repeated Pap tests.* This implies that the increased effectiveness of HPV testing in identifying cases of CIN may be due to increased referral for colposcopy verification, rather than intrinsic predictive value. In these studies, patients with initial diagnosis of high grade intraepithelial lesion (HSIL) or more sever abnormalities on Pap test were referred immediately to colposcopy.

The most recent study in this group is a 2005 cohort study conducted in Sweden (Andersson et al., 2005). This study estimated that HPV triage has a higher sensitivity, and similar specificity to repeat cytology for identifying CIN II and III. HPV triage has a positive predictive value of 27% and a negative predictive value of 89%. *In this study, HPV triage is more effective than repeat Pap test in identifying CIN and a negative HPV test is particularly accurate in identifying women with very little risk of disease.*

Studies based on PCR HPV testing technology

PCR tests analyze DNA content of specimens to identify infection with viruses such as HPV. The accuracy of this test depends on the availability of the proper equipment and the technical skills of personnel with adequate training and experience (Castle et al., 2002). We reviewed five studies using the PCR method for detection of HPV. All studies found that the PCR HPV test was more accurate in identifying potential CIN than the conventional Pap test. The sensitivity, specificity, and predictive value of the PCR HPV test is generally lower than that of the Hybrid Capture II HPV test.

Summary of Results

HPV test are an effective addition to cervical cancer screening programs. The use of the HPV test as an adjunct to the conventional Pap test in screening women increases the accuracy of the test and improves the efficiency of screening programs. A positive HPV test is less likely than a positive Pap test to indicate cervical cancer risk. Thus, the most important benefit of HPV testing is its negative predictive value. A negative result on an HPV test alone or in combination with Pap test screening is accurate in identifying women with little or no risk for cervical cancer or precancer, thus allowing for a potentially longer screening interval among these women. The use of HPV testing as a triage tool among women who have mild abnormal cytology results appears to be more efficient than traditional repeat cytology.

The social implications of adding HPV testing to cervical screening may be both positive and negative. The use of HPV testing immediately after the first abnormal Pap test result, rather than a repeat Pap test at a later point in time, may reduce women's anxiety about potentially serious test results. However, HPV testing will also identify HPV infections in women who were previously unaware of this untreatable infection. Women may experience increased anxiety with a diagnosis of a sexually transmitted infection.

II. UTILIZATION, COST, AND COVERAGE IMPACTS

SB 1245 would apply to health care service plans, commonly referred to as health maintenance organizations, regulated and licensed by the California Department of Managed Care (DMHC), as provided in the Knox-Keene Health Care Services Plan Act of 1975. SB 1245 would also apply to health insurance policies regulated by the California Department of Insurance, subject to the California Insurance Code. SB 1245 would require that the currently mandated cervical cancer screening benefit explicitly include coverage for the HPV (human papillomavirus) test.

Present Baseline Cost and Coverage

Current coverage of the mandated benefit

An estimated 20,144,000 people in California are enrolled in health care plans or have health insurance policies that would be affected by this legislation. Of this group, an estimated 7,627,000 women aged 18-64 years would specifically be affected by SB 1245.

CHBRP surveyed the seven largest health plans and insurers in California regarding their coverage levels and criteria for covering HPV testing for cervical cancer screening services. Of those seven, five responded to the survey—representing 91% of privately insured enrollees. The results of this survey suggest that all of the privately insured population have coverage of HPV testing for cervical cancer screening. Plans stated that they cover the HPV test per current standards of care. Plans provided information regarding their internal clinical guidelines. The internal clinical guidelines were consistent with current standards of care which allowed for coverage of the HPV test for (1) cervical cancer screening among women older than 30 years or (2) women who have an abnormal Pap test result indicating atypical squamous cells of undetermined significance (ASC-US).

Coverage of HPV tests as part of the cervical cancer screening benefit is the same across market segments—in HMOs, PPOs, those in the large group, small group, and individual private markets, and in public plans.

Coverage for the publicly insured enrolled in managed care plans subject to the mandate
All enrollees of CalPERS, Medi-Cal Managed Care, and Healthy Families have coverage for HPV testing as part of the cervical cancer screening benefit.

Current utilization levels and costs of the mandated benefit

CHBRP used several data sources to estimate the unit price and utilization of HPV testing services, including the Milliman Health Cost Guidelines, a survey of California large private insurers as discussed, a CDC report on the providers' practice patterns related to HPV testing (CDC, 2005), and data from a scientific study (Goldie et al., 2004).

Unit price
The average unit cost for the HPV DNA test is estimated to be $57. This cost is the marginal cost of testing for HPV in conjunction with a Pap test or during triage testing (when the initial Pap test has abnormal results). We did not include the cost of follow-up visits or treatment (such as for colposcopy) in the case of a positive HPV test in this per-unit cost estimate, as those cost would be *in addition* to the cost of the HPV test.[5]

Current utilization levels
We estimated utilization rates for women who receive the HPV test in conjunction with a Pap test in a given year and for women who receive the HPV test during triage testing—meaning when the Pap test is found to be abnormal. Information to arrive at utilization estimates for California are based on the CDC report which surveyed providers on their knowledge of current clinical guidelines and their practice of ordering HPV tests for their patients (CDC 2005).[6] These estimated utilization rates include:

- The proportion of women who obtain a Pap test in a given year
- The proportion of women who obtain the HPV test in conjunction with a Pap test during the routine cervical cancer screen
- The proportion of women who obtain the HPV test during triage testing when the Pap test is found to be abnormal
- The proportion of women who have an abnormal Pap test requiring follow-up

Applying these rates of testing to the female insured population, we estimate the following utilization levels of the HPV tests: Around 6% of women aged 18-29 are likely to be tested for HPV, or 99,800 women. Around 7.4% of women aged 30-64 would be likely to be tested for HPV, which equals 443,800 women. Averaged across both age groups, the percentage of women receiving testing is estimated to be around 7.1%, or a total of 543,700 women (See Table 4).

The utilization *rates* shown are assumed to be the same across all public and private insured population, including enrollees of Healthy Families, CalPERS, and Medi-Cal. However, we know that rates do in fact vary. Testing for HPV occurs in conjunction with a Pap test or following an abnormal Pap test, so the HPV testing rate depends on the overall frequency and rate of Pap testing. If we compare Pap test utilization, we find that women enrolled in Medi-Cal have a lower rate of testing than privately insured women. Given data limitations, we must assume that the same proportion of women aged 18-64 years are annually tested for HPV as a part of the cervical cancer screening benefit.

For each type of insurance, the total *number* of insured women screened does reflect enrollment variation such as differing age distributions or eligibility criteria. For example, the total number

[5] The estimate is based on a study that estimated costs in 2001 dollars (Goldie et al., 2004). That estimate was updated using the Bureau of Labor Statistics Consumer Price Index deflator.
[6] Self-reported provider use data may not translate directly to utilization by patients since one would need to adjust by the number of patients the responding providers have in their panel, what specialty they practice, etc. However, since this survey (CDC, 2005) was the most recent study available assessing the use of HPV test *after* the approval of the HPV DNA test in 2003 and the clinical guidelines issued by ACS and ACOG (2003), CHBRP relies on this study for these baseline utilization estimates.

of women screened is very low in Healthy Families because the program is limited to women under age 19, so there are only a small number of 18-year-old women who are estimated to receive the Pap test and HPV screening.

The extent to which costs resulting from lack of coverage are shifted to other payers, including both public and private entities.

Normally a lack of coverage could shift costs to other payers. When the level of coverage already is 100%, then shifting costs to public payers in the absence of the mandate is unlikely.

Public demand for coverage

As a way to determine whether public demand exists for the proposed mandate (based on criteria specified under AB 1996 [2002]), CHBRP is to report on the extent to which collective bargaining entities negotiate for, and the extent to which self-insured plans currently have, coverage for the benefits specified under the proposed mandate. Currently, the largest public self-insured plans are CalPERS' PERSCare and PERS Choice PPO plans. These plans include coverage similar to that of the privately insured population. They cover the HPV test as part of the cervical cancer screening benefit per medical guidelines. Based on conversations with the largest collective bargaining agents in California, no evidence exists that unions currently include such detailed provisions regarding a specific screening test during the negotiations of their health insurance policies. In general, unions tend to negotiate for broader contract provisions such as coverage for dependents, premiums, deductible, and coinsurance levels.

Nationally, the Coalition of Labor Union Women (CLUW) is conducting an education campaign to increase women's awareness of the link between HPV and cervical cancer. In addition, they have been proponents of state-level insurance mandates to cover the HPV test. Some proportion of local union members are also members of CLUW. In order to determine whether any local unions or union members are currently engaged in CLUW's efforts, they would need to be surveyed individually.

Impacts of Mandated Coverage

How would changes in coverage related to the mandate affect the benefit of the newly covered service and the per-unit cost?

Benefit of the newly covered service
CHBRP estimates no effect on the average clinical benefit of the service because the 1) there is no estimated change in utilization, and 2) there is no estimated change in the strength of the HPV test. That is, the test's sensitivity or specificity[7] would not change as a result of the mandate.

Unit Cost
Since neither supply nor demand pressures would be expected to change after implementation of the mandate, CHBRP would expect no additional price pressures and, therefore, no change in the per-unit cost of the HPV test.

CHBRP assumes that plans and insurers would continue to negotiate similar reimbursement rates with physicians and the test manufacturer. Therefore, there should be no expected increase in the per-unit cost of the HPV test.

Impact on other Health Care Costs
CHBRP considered whether increased coverage and use of HPV testing services would cause a decrease in other covered health care utilization and costs. No change in health care costs is estimated since there is no estimated change in utilization (see below for discussion on changes in utilization). If there were an increase in utilization, the cost of testing and follow-up visits as a result of positive HPV test results would lead to a net increase in cost, both in the short term and the long term; this includes an increase in premiums. Costs of follow-up visits, for example, include the costs of repeat HPV testing and/or colposcopies. On the other hand, testing and follow-up intervention deters the costs associated with treatment for cervical cancer and mortality associated with cervical cancer. However, over the long term, these dynamics result in a net overall increase in costs (Goldie et al, 2004). Please see Appendix C for an analysis that presents the impacts of SB 1245 if the use of both the concurrent HPV and Pap test screen and the HPV triage screen were to increase by 1 percentage point as a result of the mandate.

The impact of the legislation on health care premiums depends on the assumptions that insurers make regarding the impact of increased HPV test coverage on future health care costs. It is likely that most health plans and insurers increase premiums if they must add newly covered services.[8] In the case of HPV test benefits, there is no increase, since the services are already covered.

CHBRP considered substitution and complementary effects for services. A substitution effect would occur if coverage of a mandated service decreases utilization of a similar service, by shifting those patients to the mandated provider. A complementary effect increases the use of services that are commonly used in conjunction or in addition to the use of the mandated service. Since there is only one FDA-approved HPV test available for use in the United States—the

[7] See the Medical Effectiveness section for explanation of "sensitivity" and "specificity" of the HPV test.
[8] Based on Milliman's experience conducting actuarial analysis for health plans and insurers in California and nationally.

Hybrid Capture II High-Risk HPV test—there are no obvious substitute services. Other services that may be considered before an HPV test is provided (such as a repeat Pap test) are already covered. Therefore, no substitution effects are predicted, because most services that are considered substitutes are already covered. There are no effects anticipated on complementary services provided by other types of providers.

How would utilization change as a result of the mandate?

Predicting market responses to mandates involves consideration of multiple factors. CHBRP considered insurer, provider, and enrollees responses to the mandate. There is uncertainty surrounding how the mandate might influence utilization; however, for the reasons stated below, CHBRP estimates no change in utilization. There are four potential sources of change in utilization: changes in utilization as a result of changes in coverage or lowered prices paid by enrollees; changes in utilization as a result of enrollees demand and awareness; changes in utilization as a result of changes in physicians' practice patterns; and supplier-induced demand.

- *No changes in utilization as a result of changes in coverage or lowered prices:* Normally, lowered prices lead to increased demand. When coverage for a new benefit is added, the price to the patient decreases from the full cost of the service to a partial payment (in the form of out-of-pocket expenditures or coinsurance), leading to higher rates of utilization. Utilization increases *directly* related to mandated benefits legislation would be expected when coverage changes measurably. When the service is already covered by insurers, then a mandate *by itself* is unlikely to increase price-related demand for care. In the case of the HPV test, coverage is not changing, so we do not anticipate changes in utilization.

- *No changes in utilization as a result of member demand and awareness:* Demand for the HPV test could naturally increase over time as consumers become more aware of the test. For example, over the next few years, the Digene Corporation may continue to promote awareness regarding the use of the HPV DNA test. However, this is likely to occur regardless of a mandate to cover the HPV test for the cervical cancer screening. At the present time, there is a general lack of awareness between the clinical link between HPV and cervical cancer. Also, demand for testing for sexually transmitted diseases (STDs) is generally not very high. For example, chlamydia screening rates are around 25% among women aged 16-26 years, even though this test may be administered during a Pap test (NCQA 2006). Even for less invasive tests, utilization changes occur relatively slowly. For example, utilization of mammography (for which coverage is mandated in most states) has increased from 69% of women in 1994 to 76% of women in 2003 by privately insured women, an increase of 8.7%, which is an average growth rate of 0.1% a year (DHHS 2005:306).

- *No changes in utilization as a result of changes in physicians' practice patterns:* CHBRP projects no change in utilization as a result of physician practice patterns as a result of SB 1245. However, it is possible that physician practice patterns change as a result of the increased adoption of HPV testing guidelines. As discussed in the *Medical Effectiveness* section, the guidelines for routinely testing for HPV in women older than 30 years and all women with a Pap test result of ASCUS are still relatively new. We know there is often a delay or a lag time from when clinical guidelines are issued and practice patterns change to adopt those guidelines. Consultation with clinical experts suggested that utilization is unlikely to shift in the short term or in response to the mandate; if there is an increase in HPV testing as a result of physicians "catching up" with clinical guidelines, this would likely occur regardless of the mandate. Appendix C shows the impacts of SB 1245 if utilization were to increase as a result of changes in practice patterns.

- *No likely supplier-induced demand effects:* It has been documented that new reimbursement for technologies or services change provide new opportunities and incentives for physicians to 'induce' demand for services. Assuming a physician is paid on a fee-for-service basis, a new service or procedure offers the potential for physicians to earn additional payments.[9] CHBRP does not expect this additional reimbursement to act as an incentive for utilization for the HPV test because (1) a majority of primary care providers in the state are paid on a capitated basis, (2) the HPV test would be done concurrent with or following a cervical Pap test and the HPV test alone would not require a separate visit, and (3) to the extent that providers would charge a fee associated with the HPV test, the marginal increase in net revenue for all the services incurred during that visit is likely to be small. As a result, most providers do not have an incentive to encourage unnecessary visits.

Utilization in market segments

Averaged across all plan types and baseline levels of coverage, utilization of HPV testing services is estimated to remain the same (see the Present Baseline Cost and Coverage section above). The impact would be the same across all plan types.

To what extent does the mandate affect administrative and other expenses?

CHBRP's model of costs assumes that if health care costs increase as a result of increased utilization or changes in unit costs, there is a corresponding proportional increase in administrative costs. CHBRP assumes that the administrative cost *proportion of premiums* is unchanged. All health care plans and insurers include a component for administration and profit in their premiums. Since CHBRP estimates that this mandate does not increase health care costs, CHBRP also estimates no change in overall administrative costs.

[9] An important source of supplier-induced demand is the price of the test relative to the reimbursement by insurers. For diagnostic tests and medical devices, as well as physician-administered drugs, the physician may be reimbursed for the cost of the test at a level that exceeds the actual cost of purchasing the test or device. Manufacturers may decide to lower the cost for physicians, in order to increase physicians' 'profit' margin on the test. This would encourage physicians to use the test more frequently. CHBRP assumes the same level of profit margin for physicians prescribing the test, because it is difficult to predict whether the Digene Corporation would offer different prices of the HPV test to providers versus insurers.

Impact of the mandate on total health care costs

Total health care costs are not expected to increase as there is no expected change in coverage or utilization.

Costs or savings for each category of insurer resulting from the benefit mandate

SB 1245 would be unlikely to lead to changes in total annual expenditures, for each major category of payer. Total private employer premiums would be likely to remain the same at $35.79 billion per year. Individuals who pay for a share of their employer-based insurance, and individuals paying Healthy Families premiums would have the same expenditures of $11.38 billion per year. Premium expenditure on individually purchased insurance would remain the same at $4.74 billion dollars per year. CalPERS' employer costs would remain the same at $2.33 billion per year. State expenditures for Medi-Cal HMO members would remain the same at $4.33 billion per year. Healthy Families state expenditures would stay the same, at $644 million per year. Out of pocket expenditures associated with HPV testing would remain the same, at $3.84 billion. Other out-of-pocket costs for HPV testing presently not covered by insurance are presently zero and would be expected to remain the same.

Impact on access and health service availability

Due to the lack of effect on premiums or other costs, no impacts are likely on access and health service availability.

III. PUBLIC HEALTH IMPACTS

Present Baseline Health Outcomes

Cervical cancer screening

Both the American Cancer Society and the U.S. Preventive Services Task Force recommend screening for cervical cancer at least once every 3 years starting at age 21 or within 3 years of onset of sexual activity (USPSTF, 2003; Saslow et al., 2002). In the population of women in California ages 21 or older who are enrolled in health insurance plans affected by SB 1245, rates of screening for cervical cancer using Pap tests is very high with 88.8% reporting receiving a Pap test within the last 3 years, 7.5% reporting receiving a Pap test more than 3 years ago, and 3.7% reporting never having had a Pap test (CHIS, 2003). The main reasons reported for not having a Pap test within the past 3 years (or never) include: not knowing that it was needed (11.8%), procrastination or laziness (10.4%), not having any problems (8.9%), and painful or embarrassing (5.7%) (CHIS, 2001).

As estimated in the previous section, approximately 7.1% of women aged 18-64 are tested for HPV as part of their cervical cancer screening benefit. This occurs as part of two different screening strategies: (1) HPV triage (screening for HPV as a follow-up to an abnormal Pap) and (2) concurrent HPV and Pap testing (only recommended for women ages 30 and older).

HPV incidence and prevalence

A literature review was conducted to determine the prevalence and incidence of HPV among women in the United States. There have been no studies to date that estimate prevalence of HPV among Californians. Using national data instead, it is estimated that 20 million Americans are infected with active HPV (i.e., persons with active shedding of HPV DNA), and more than 5.5 million new cases are diagnosed annually (Cates, 1999). It is estimated that 75% of sexually active people will be infected with the HPV virus at some point in their lifetime (Koutsky, 1997). A systematic review of studies in the last decade analyzing the epidemiology of HPV found that the prevalence of HPV ranged from 14% to more than 90% and the reported annual incidence ranged from 7% to 20% (Revzina and DiClemente, 2005). The highest prevalence of HPV was identified among college students and women attending sexually transmitted disease (STD) clinics. The largest and most representative study of HPV prevalence was conducted at Kaiser Permanente among over 20,000 women at least 16 years old. (Sherman et al., 2003). This study reported that the overall prevalence of HPV was 14.3%. Assuming similar rates in California, we can estimate that over 1 million women enrolled in plans affected by this mandate are currently infected with HPV.

Cervical cancer incidence and prevalence

While the majority of HPV infections are cleared by the body, those that are not may lead to cervical cancer. In a large cohort of women studied for a decade, of those who tested positive for HPV at the onset of the study, 7% developed CIN III or cervical cancer at some point over the study period (Sherman et al., 2003). The California Cancer Registry documents cases of cervical

cancer in California. The expected new cases of cervical cancer in 2006 are 1,550 (CCR, 2005). The age-adjusted cervical cancer incidence rate for California is 8.9 per 100,000 women per year in 2002 (CDC, 2005).

Stage at diagnosis and cervical cancer mortality

The aim of cervical cancer screening is to detect the presence of cancer precursors, whose treatment leads to the prevention of cancer. In addition, detecting cancer at an early stage when the survival rates are the highest is another goal of screening. For cervical cancer diagnosed in California, the 5-year survival rates are 91% for localized cancer (the tumor has not spread outside the cervix), 54% for regional cancer (the tumor has spread to the lymph nodes or adjacent tissue), and 16% for distant cancer (the tumor has spread to other parts of the body) (CCR, 2005). Across all three stages, the 5-year survival rate is 71%. Blacks have the lowest percentage (41%) of cervical cancer diagnosed at an early stage (*in situ* or localized), followed by Asians and Pacific Islanders (43%), Hispanics (45%), and Whites (50%) (CCR, 2005). It is estimated that in 2006, 400 women will die from cervical cancer in California (CCR, 2005). The age-adjusted death rate from cervical cancer in California in 2002 was 2.4 deaths per 100,000 women (CDC, 2005).

Impact of the Proposed Mandate on Public Health

Impact on community health

As presented in the Utilization, Cost, and Coverage Impacts section, it is estimated that HPV screening is currently covered for 100% of the 7.6 million women enrolled in health plans that will be affected by this mandate. This implies that physicians are able to order concurrent or follow-up HPV screening for their patient population, and do so according to their own practice preferences. This mandate does not directly change physician practice patterns, and therefore we estimate that this mandate will not stimulate any increase in HPV screening in this population (see Impacts of Mandated Coverage for further explanation).

Depending on the screening strategy (HPV triage or concurrent HPV and Pap testing) and screening interval (every 1, 2, 3, or 4 years), the reduction in lifetime cervical cancer risk varies between 26% to 49% compared to lifetime conventional Pap tests at comparable screening intervals (Goldie et al., 2004). Despite evidence in the medical effectiveness literature that suggests that a shift in cervical cancer screening practices from Pap-only screening to combined HPV and Pap screening would decrease lifetime cervical cancer risks (see Tables C-2 and C-3 in Appendix C), assuming no increase in utilization of HPV screening, we conclude that this mandate will not have any impact on overall public health. We also present two alternate scenarios in Appendix C, in which the utilization of HPV testing increases by 1 percentage point.

Impact on community health where gender and racial disparities exist

A literature review was conducted to determine whether there are racial disparities associated with the prevalence and outcomes of HPV infection documented in the academic literature.

While HPV infection occurs in both men and women, the health effects of HPV–chiefly cervical cancer–are health issues facing women. Therefore, most of the literature on HPV focuses on women's health.

Cervical cancer screening by race/ethnicity
In the population of women in California ages 21 or older who are enrolled in health insurance plans affected by SB 1245, rates of recommended screening for cervical cancer using Pap tests varies across race and ethnicity with Asians reporting the lowest rate of having a Pap test within the last 3 years (79.3%) compared to Latinos (91.2%), whites (90.2%), and blacks (89.6%) (CHIS, 2003).

HPV incidence & prevalence by race/ethnicity
Among women, racial differences have been reported in the literature with regards to HPV prevalence. Researchers have found that black women are more likely to be infected with HPV compared to white women (Burk et al., 1996; Khan et al., 2005; Shields et al., 2004; Stone et al., 2002). Hispanic women have also been found to have a higher prevalence of HPV compared to non-Hispanic women (Burk et al., 1996; Peyton et al., 2001).

Cervical cancer incidence & prevalence by race/ethnicity
Nationally, Black women have higher incidence and prevalence rates of cervical cancer compared to all other races/ethnicities (Krieger et al., 1999; Morgan et al., 1996; CDC, 2005; Newmann and Garner, 2005; Patel et al. 2005). Additionally, other minority groups, particularly Hispanic women, have been found to have higher incidence and prevalence rates of cervical cancer compared to non-Hispanic Whites (Krieger et al., 1999; Napoles-Springer et al., 1996; CDC, 2005; Patel et al., 2005). In California, the age-adjusted incidence rate of cervical cancer among Hispanics in 2002 was estimated as 14.8 per 100,000 women, for whites as 9.3 per 100,000 women, and for Blacks as 7.5 per 100,000 women (CDC, 2005). Although the CDC does not include incidence rates for Asian and Pacific Islanders, the California Cancer Registry estimated the age-adjusted rate for cervical cancer for Asian and Pacific Islander women in California to be approximately 8.0 per 100,000 women in 2002 (CCR, 2005).

Stage at diagnosis and cervical cancer mortality by race/ethnicity
Other research has also reported racial disparities across the nation in cervical cancer. Compared to white women, Black women have been found to present with more advanced stages of cervical cancer (Howell et al., 1999; Leath et al., 2005; Morgan et al., 1996; Schwartz et al., 2003) and have poorer survival rates (Howell et al., 1999; Mundt et al., 1998; Patel et al., 2005). Some research has found that Hispanic women have poorer survival rates compared to non-Hispanic White women (Napoles-Springer et al., 1996; NCI, 2005). Cervical cancer mortality rates vary by race and ethnicity in California. In California, the age-adjusted death rate for Hispanics in 2002 is estimated as 3.6 per 100,000 women, for Blacks as 3.4 per 100,000 women, and Whites as 2.4 per 100,000 women (CDC, 2005). Cervical cancer death rates between 1988 and 2001 decreased slightly for non-Latino whites, non-Latino blacks, and Filipinas but stayed the same for Latinas, presumably due to screening interventions (Cockburn and Deapen, 2004). Also, mortality rates for cervical cancer decreased by about half among Chinese and Korean women, though not significantly for Koreans (Cockburn and Deapen, 2004).

Several authors have suggested that much of the racial disparities found in cervical cancer might be attributed to differences in income and socioeconomic status and that racial disparities were substantially lessened once other socioeconomic variables were controlled for (Brooks et al., 2000; Krieger et al., 1999; Schwartz et al., 2003).

While there clearly are racial disparities in terms of utilization of cervical cancer screening, incidence rates of cervical cancer, and cervical cancer mortality rates, this mandate will not have any effect on cervical cancer screening rates or screening methods. Therefore, we conclude that this mandate will have no impact on cervical cancer gender and racial disparities.

Reduction of premature death and the economic loss associated with disease

A literature review was conducted to determine the extent that HPV results in premature death and economic loss to California and whether SB 1245 might have an impact on these outcomes. In order to quantify the reduction of premature death due to a health insurance benefit mandate the following must be true: mortality must be a relevant health outcome, the impact of the mandated benefit must be established in the medical effectiveness literature, and the mandate must increase the number of utilizers (through either increased coverage or increased utilization).

Mortality as a relevant outcome
HPV is responsible for almost all cervical cancer cases (Walboomers et al., 1999). In California, approximately 400 women are expected to die in 2006 from cervical cancer (CCR, 2005). Since 1975, the percentage of women dying of cervical cancer has been steadily decreasing. From 1996 to 2002, the annual percentage change for women dying of cervical cancer in the United States was –3.8% (NCI, 2005).

Impact of cervical cancer screening on mortality
As presented in the analysis on the impact on community health (section above) a shift in provider practice pattern in cervical cancer screening from Pap only to Pap in combination with the HPV screen (either simultaneously or as triage) has the potential to reduce lifetime risk of cervical cancer. Tables C-2 and C-3 in Appendix C present a summary of the reduction of lifetime cervical cancer risk among women with different screening intervals. Depending on the screening strategy (triage or concurrent HPV/Pap) and screening interval, the reduction in lifetime cervical cancer risk varied between 26% to 49% compared to lifetime conventional Pap tests at comparable screening intervals (Goldie et al., 2004).

Change in utilization of HPV screening
As described in the *Utilization, Cost, and Coverage Impacts* section, the population of women enrolled in health plans affected by the mandate currently have coverage for HPV screening. Therefore, the passage of SB 1245 would not increase the utilization of HPV screening in this population. Despite evidence that HPV screening has the potential to reduce the incidence of cervical cancer and related mortality in California, we conclude that SB 1245 would not affect premature death related to cervical cancer.

Economic loss

In order to quantify the reduction of the economic loss associated with disease associated with the passage of a benefit mandate the following must be true: the indirect cost of illness must be established in the scientific literature and the mandate must increase the number of utilizers (through either increased coverage or increased utilization).

The economic loss associated with cervical cancer consists of the direct costs discussed in the section *Utilization, Cost, and Coverage Impacts* and the indirect costs related to a reduction in productivity due to premature mortality. For HPV screening and cervical cancer, the productivity losses are due to lost workdays for women. Based on a review of literature by Insinga et al., there is limited economic research quantifying these indirect costs. Insinga et al., did conclude that based on available data and given the mortality rates of cervical cancer over the past 30 years, the annual indirect costs of cervical cancer are likely to be in the billions of dollars and exceed direct medical costs by a factor of several times. A recent analysis in California reported a present value for the lost wages and housekeeping services of women dying from cervical cancer of $351,000 per cervical cancer death in 1998 dollars (Max et al., 2003). Furthermore, this study stated that the 452 deaths reported from cervical cancer in California in 1998 amounted to 12,989 person-years lost, or 28.7 years per death at an overall loss of $159 million to the economy. These $159 million indirect costs are three times the amount of direct costs calculated in this study. Lastly, since almost two thirds (64%) of the deaths due to cervical cancer occur among women under age 65, these deaths to younger women represent more than four fifths (82%) of the person-years lost and almost all (97%) of the losses in productivity (Max et al., 2003).

As mentioned previously, the population of women enrolled in health plans affected by the mandate currently have coverage for HPV screening. Therefore, the passage of SB 1245 would not increase the utilization of HPV screening in this population. Despite evidence that HPV screening has the potential to reduce the incidence of cervical cancer and related economic productivity losses in California, we conclude that SB 1245 would not affect lost productivity related to cervical cancer.

TABLES

Table 4. Annual Rates and Total Numbers of Women Tested for HPV, by Age, California, 2006

By Age Group	Percentage of insured women aged 18-64 years in California receiving HPV test in a year	Number of insured women aged 18-64 years in California receiving HPV test in a year
Ages 18-29	6.0%	99,800
Ages 30-64	7.4%	443,800
Combined, ages 18-64	7.1%	543,700

Source: California Health Benefits Review Program analysis, 2006.
Note: Insured women refer to women covered through private employer and individually purchased insurance, and public programs (Healthy Families, CalPERS, and Medi-Cal).

Table 5. Baseline (Premandate) Per-Member Per-Month Premium and Expenditures in California by Insurance Type, 2006

	Large Group		Small Group		Individual		CalPERS	Medi-Cal		Healthy Families	
	HMO	**PPO**	**HMO**	**PPO**	**HMO**	**PPO**	**HMO**	**HMO 65 and Over**	**HMO Under 65**	**HMO**	**Total Annual**
Population currently covered (in thousands)	8,237	1,827	2,593	1,215	984	1,030	782	339	2,423	714	20,144
Average portion of premium paid by employer	$202.76	$292.75	$189.45	$235.81	$0.00	$0.00	$248.33	$265.00	$112.00	$75.20	$43,102,188,000
Average portion of premium paid by employee	$62.47	$77.87	$74.62	$49.58	$257.58	$137.75	$43.82	$0.00	$0.00	$4.80	$16,122,670,000
Total premium	$265.23	$370.62	$264.07	$285.39	$257.58	$137.75	$292.16	$265.00	$112.00	$80.00	$59,224,858,000
Covered benefits paid by member (deductibles, copays, etc.)	$9.39	$50.08	$15.90	$42.40	$15.68	$32.14	$10.35	$0.00	$0.00	$2.18	$3,837,497,000
Benefits not covered	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0.00	$0
Total expenditures	$274.62	$420.70	$279.97	$327.79	$273.26	$169.89	$302.51	$265.00	$112.00	$82.18	$63,062,355,000

Source: California Health Benefits Review Program, 2006.
Note: The population includes individuals and dependents in California who have private insurance (group and individual) or are enrolled in public plans subject to the Health and Safety Code, including CalPERS, Medi-Cal, or Healthy Families.
All population figures include enrollees aged 0-64 years, except the Medi-Cal population, which includes dually eligible Medicare/Medi-Cal recipients of all ages.
Employees and their dependents that receive their coverage from self-insured firms are excluded because these plans are not subject to mandates.
(1) This represents what all individuals in a plan pay to cover the cost of this service. It represents the total expenditures per service multiplied by the quantity utilized, divided by the number of members in each plan, divided by 12 months.
(2) All values include all health care benefits, except expenditures by individuals on the mandated benefit.
(3) HMO category includes point of service (POS) members.
(4) PPO category includes fee-for-service enrollees
Key: HMO = health maintenance organization; PPO = preferred provider organization. CalPERS = California Public Employees' Retirement System.

Table 6. California Cervical Cancer Screening, Incidence, and Mortality

Race	Screening Rate, 2003 (% of women 21 and over who received a Pap test within 3 years)	Age-Adjusted Incidence Rate, 2002 (per 100,000 women per year)	Age-Adjusted Death Rate, 2002 (per 100,000 women per year)
All races	88.8	8.9	2.4
White	90.2	9.3	2.4
Black	89.6	7.5	3.4
Hispanic	91.2	14.8	3.6
Asian/Pacific Islander	79.3	NA	NA
American Indian/Alaskan Native	84.2	NA	NA

Source: California Health Benefits Review Program, 2006.
Screening rates are from direct analysis of California Health Interview Survey (CHIS, 2003).
Age-adjusted incidence and mortality rates are directly from the Centers for Disease Control and Prevention and National Cancer Institute (CDC, 2005).

APPENDICES

Appendix A-1: Literature Review Methods

Appendix A-1 describes the literature search for studies on the medical effectiveness of human papillomavirus (HPV) testing in cervical cancer screening.

This appendix also discusses the outcomes used in analysis of the mandate. To "grade" the evidence for all outcome measures, the CHBRP effectiveness team uses a system with the following categories:

1. Favorable (statistically significant effect): Findings are uniformly favorable, and many or all are statistically significant.
2. Pattern toward favorable (but not statistically significant): Findings are generally favorable, but there may be none that are statistically significant.
3. Ambiguous/mixed evidence: Some findings are significantly favorable, and some findings with sufficient statistical power show no effect.
4. Pattern toward no effect/weak evidence: Studies generally find no effect, but this may be due to a lack of statistical power.
5. No effect: There is statistical evidence of no clinical effect in the literature with sufficient statistical power to make this assessment.
6. Unfavorable: No findings show a statistically significant benefit, and some show significant harms.
7. Insufficient evidence to make a "call": There are very few relevant findings, so it is difficult to discern a pattern.

Studies were identified from PubMed (January 1985-January 2005), Cochrane Library, and CINAHL databases. Only English language studies were included in the analysis. The initial search terms were "HPV" or "papillomavirus".

The *Medical Subject Headings* (MeSH) terms used by the librarian in the PubMed search were:

Uterine Cervical Neoplasms *(by site)*
Cervical Intraepithelial Neoplasia *(by histological type)*
Uterine Cervical Dysplasia *(uterine diseases)*

Papillomavirus Infections
- Warts
  - Condylomata Acuminata
  - Epidermodysplasia Verruciformis

Papillomavirus, Human
- Human papillomavirus 11
- Human papillomavirus 16
- Human papillomavirus 18
- Human papillomavirus 6

DNA Probes, HPV

Mass Screening
Primary Prevention
Diagnosis
Early Diagnosis
Vaginal Smears
Diagnostic Errors
    False Positive Reactions
    False Negative Reactions
Cytodiagnosis
/prevention and control *(*subheading)
/diagnosis *(subheading)*

Costs and Cost Analysis
    Cost Allocation
    Cost-Benefit Analysis
    Cost Control
        Cost Savings
    Cost of Illness
    Cost Sharing
        Deductibles and Coinsurance
        Medical Savings Accounts
    Health Care Costs
        Direct Service Costs
        Drug Costs
        Employer Health Costs
        Hospital Costs
    Health Expenditures
        Capital Expenditures
/economics *(subheading)*

Publication types:
Meta-analysis
Practice Guideline
Randomized Controlled Trial
Clinical Trial
Cohort Study
Systematic Review

Substance Names:
Hybrid Capture II

Additional key words (found in title or abstract) were used to identify recent articles that had not yet been assigned MeSH tems: (* = truncation symbol) are:

HPV
Papillomavirus
Cervi*
intraepithel*
CIN*
ASCUS
SIL
Test*
Screen*
Diagno*
Swab*
Scrap*
Smear*
DNA probe
Hybrid capture
Cytolog*
Ctyodiagnos*

At least two reviewers screened the title and abstract of each citation returned by the literature search to determine eligibility for inclusion. Full-text articles were obtained and reviewers reapplied the initial eligibility criteria.

A large number of publications were identified through the literature search. The analysis focused on the most recent systematic reviews of the literature in addition to any clinical trials or cohort studies meeting the inclusion criteria, but published after the systematic reviews. The analysis also includes a comprehensive summary of the most recent evidence-based clinical guidelines for the use of HPV testing in two clinical settings: primary cervical screening using HPV and Pap testing, and the use of HPV as a triage tool for decision-making after abnormal initial cervical screening results. Studies published before the systematic reviews and those included in the reviews were excluded from the analysis. In addition, publications relating to diseases other than cervical cancer were excluded from the analysis.

At least one systematic review was identified for the use of HPV testing, with respect to cervical cancer screening and triage of abnormal cervical screening. In addition, we identified a smaller number of more recent clinical trials and cohort studies evaluating the effectiveness of HPV testing in cervical cancer screening and triage.

Appendix A-2: Common Terminology

Adenocarcinoma refers to cancer in the cells that line the inside of the cervix and the uterus. These cells meet up with squamous cells, a second, distinct type of cell that covers the outside of the cervix . Adenocarcinoma, or cancer in the more internal cells, is the most common type of gynecologic cancer.

CIS or Carcinoma in situ are cancerous cells that have not yet invaded the surrounding tissue. This diagnosis is included in the CIN II/III category until it develops into invasive cancer.

Colposcopy is a visual examination of the cervix using a magnification instrument. This procedure is used in order to more closely evaluate cervical tissue and to guide the process of obtaining a cervical biopsy.

Cytology refers to cervical cancer screening, more commonly known as the Pap (Papanicolaou) test or Pap smear. This test is based on a sample of cells from the surface of the cervix, which are then analyzed for abnormalities using microscopic techniques.

Dysplasia refers to a precancerous condition. In the case of cervical cancer, dysplasia is characterized by abnormal growth of the layer of cells that covers the cervix.

HPV or Human Papillomavirus is the virus that has many strains known to cause cervical cancer.

Hybrid Capture refers to the most current method of testing for the presence of high risk strains of HPV.

PCR or Polymerase Chain Reaction refers to an alternate method for detecting the presence of HPV DNA.

Squamous cells refer to the cell type that is found on the external part of the cervix; they are commonly sampled during cervical cancer screening.

Table A-2. 2001 Bethesda System Terminology for Cervical Cancer Screening Results

Cytology	**Pap Test Findings**
ASC-US	Atypical squamous cells-undetermined significance
ASC-H	Atypical squamous cells-cannot rule out high-grade lesion
AGC	Atypical glandular cells
LSIL	Low-grade squamous intraepithelial lesion
HSIL	High-grade squamous intraepithelial lesion
Histology	**Biopsy Findings**
CIN I	Cervical intraepithelial neoplasia/mild dysplasia Mild abnormalities that rarely develop into cancer
CIN II	Cervical intraepithelial neoplasia/moderate-severe dysplasia Carcinoma in situ More severe abnormalities that may progress to cancer if left untreated
CIN III	Cervical intraepithelial neoplasia/moderate-severe dysplasia Carcinoma in situ Most severe abnormality, with highest likelihood of progressing to cancer

Source: Solomon D, Davey D, Kurman R, et al. The 2001 Bethesda System: terminology for reporting results of cervical cytology. *JAMA*. 2002:287(16):2114-2119.

Terms related to screening test performance

Sensitivity refers to the ability of the test to identify correctly those people who have the disease.

Specificity refers to the ability of the test to identify correctly those people who do not have the disease.

PPV or Positive Predictive Value refers to the likelihood that a person testing positive on the screening test actually has the disease.

NPV or Negative Predictive Value refers to the likelihood that a person testing negative on the screening test is truly negative for disease.

Appendix B-1: Summary of Published Studies on the Medical Effectiveness of HPV Testing for Cervical Cancer Screening

Tables B-1 (a-c) provide a summary of published studies informing the findings on the medical effectiveness of human papillomavirus (HPV) testing of cervical cancer screening. In this context, the use of HPV testing is evaluated in two clinical settings: HPV testing used concurrently with Pap testing in primary screening for cervical cancer (screening studies); and HPV testing as a decision-making tool after abnormal initial cervical screening results (triage studies). Unless otherwise indicated, these studies use the one FDA-approved HPV test available for use in the United States: the Hybrid Capture II High-Risk HPV test, produced by the Digene Corporation. Studies using polymerase chain reaction (PCR) technology for HPV testing are summarized separately and are not included in the medical effectiveness analysis of this report, as this is not a technology that is widely used in clinical practice. PCR is not an FDA-approved method of HPV testing in the United States.

Table B-1a. Screening Studies

Name, Year	**Type of Study**	**Interventions Studied**	**Clinical Outcome(s)**
Kotaniemi-Talonen et al., 2005	Clinical trial	Pap alone HPV alone Pap + HPV	CIN I or higher
Sankaranarayanan et al., 2005	Cohort study	Pap alone HPV alone	CIN II or III
Clavel et al., 2004	Cohort study	Pap alone Pap + HPV	HSIL
Franco, 2003 Review (Excluding PCR studies)	Systematic review	Pap alone HPV alone Pap + HPV	CIN II or higher
Lorincz et al., 2003 Review (Excluding PCR studies)	Systematic Review	Pap alone HPV alone Pap + HPV	CIN II or higher

CIN=Cervical intraepithelial neoplasia; HPV=Human papillomavirus; HSIL=High-grade squamous intraepithelial lesion; Pap=Papanicolaou (Pap) test

Table B-1b. Triage Studies

Name, Year	Type of Study	Interventions Studied	Clinical Outcome(s)
Andersson et al., 2005	Cohort study	Repeat Pap HPV triage	CIN II or III
Arbyn et al., 2005 **Meta analysis**	Meta analysis	Repeat Pap HPV triage	CIN II or higher
ALTS Group 2003	Clinical trial	Repeat Pap HPV triage	CIN III
ALTS Group 2003	Clinical trial	Repeat Pap HPV triage	CIN III
Lytwyn et al., 2003	Clinical trial	Repeat Pap Pap + HPV triage	CIN II or higher
Cuzick et al., 2003	Clinical trial	Repeat Pap HPV triage	CIN II or higher

CIN=Cervical intraepithelial neoplasia; HPV=Human papillomavirus; Pap=Papanicolaou (Pap) test

Table B-1c. Studies Using PCR Technology for HPV Testing

Name, Year, Citation	Type of Study	Interventions Studied	Clinical Outcome(s)
Screening studies			
Cuzick et al., 1995 Lancet 345:1533-6 From Franco review	Clinical trial	Pap alone HPV alone	CIN II or III
Schneider et al., 2000 Int J Cancer 89: 529-34 From Lorincz and Franco reviews	Clinical trial	Pap alone HPV alone	CIN II or III
Kjaer et al., 2002 BMJ 325: 572-8 From Lorincz review	Clinical trial	HPV alone	CIN II or III
Kulasingam et al., 2002 JAMA 288: 1749-57 From Lorincz review	Clinical trial	Pap alone HPV alone	CIN III
Triage study			
Carozzi et al., 2005 Cancer 105: 2-7	Clinical trial	Pap alone HPV alone	CIN II

CIN=Cervical intraepithelial neoplasia; HPV=Human papillomavirus; Pap=Papanicolaou (Pap) test

Appendix B-2: Screen Studies

Table B-2a. Screening Studies

Name, Year	Sensitivity	Specificity	PPV	NPV	Other Findings	Clinical Outcome	Strength of Evidence: Does HPV testing improve the likelihood of identifying women at risk for cervical cancer?
Kotaniemi-Talonen et al., 2005		Pap 99.6% HPV/Pap 99.3% HPV 92.1%	Pap 44.2% Pap/HPV 50.8% HPV 8.0%		Referral Rate for colpo 50% higher in HPV arm	CIN I or higher	Yes–Pap with HPV identifies more true positive cases of CIN I or higher than either test alone **FAVORABLE**
Sankaranarayanan et al., 2005			Pap 19% HPV 10.9%		No difference in detection rate for CIN II and III Pap 1% HPV 0.9%	CIN II or III	No–Same identification rate as Pap **NO EFFECT**
Clavel et al., 2004			1.1% HPV	Pap 99.2% HPV/Pap 99.9%		HSIL	Yes–The combination of negative Pap and negative HPV results in almost 100% identification of women with little or no risk for cervical cancer **FAVORABLE**
Franco, 2003 Review (Excluding PCR studies)	Pap 27-88% HPV 62-100% Pap/HPV 89%	Pap 89-99% HPV 41-95% Pap/HPV 90%		Pap/HPV 100%		CIN II or higher	Yes–Pap with HPV identifies more true positive cases of CIN II or higher than either test alone **FAVORABLE**
Lorincz et al., 2003 Review (Excluding PCR studies)	Pap 38-94% HPV 63-100% Pap/HPV 76-100%	Pap 78-99% HPV 73-96% Pap/HPV 68-95%	Pap 3-37% HPV 4-23% Pap/HPV 6-16%	Pap 98.4-99.8% HPV 98.2-100% Pap/HPV 99.3-100%		CIN II or higher	Yes–Pap with HPV identifies more true positive cases of CIN II or higher than either test alone **FAVORABLE**

S=Statistically significant difference; NS=No statistically significant difference; PPV=Positive predictive value; NPV=Negative predictive value; Colpo=Colposcopy; CIN=Cervical intraepithelial neoplasia; HSIL=High-grade squamous intraepithelial lesion; Pap=Papanicolaou (Pap) test; HPV=Human papillomavirus

Table B-2. Triage Studies

Name, Year	Sensitivity	Specificity	PPV	NPV	Other findings	Outcome(s)	Does HPV testing improve the likelihood of identifying women at risk for cervical cancer?
Andersson et al., 2005	Repeat Pap 61% HPV triage 82%	Repeat Pap 34% HPV triage 39%	27% HPV	89% HPV		CIN II or III	Yes–Relative to repeat Pap, HPV testing identifies more women at risk for cervical cancer **FAVORABLE**
Arbyn et al., 2005 Meta analysis	HPV triage 94% HPV sensitivity 14% higher than repeat Pap	HPV triage 62% HPV specificity almost identical to repeat Pap	HPV 22%	HPV 99%		CIN II or higher	Yes–HPV triage had a higher detection rate than repeat Pap and the capability to identify almost 100% of women with little or no risk for cervical cancer **FAVORABLE**
ALTS Group 2003	Repeat Pap 54.6% HPV triage 72.3%				Colposcopy referral: Repeat Pap 12.3% HPV 55.6%	CIN III	Yes–Relative to repeat Pap, HPV testing identifies more women at risk for cervical cancer, but increased colpo referral **FAVORABLE**
ALTS Group 2003	Repeat Pap 48.4% HPV triage 65.9%				Colposcopy referral: Repeat Pap 18.8% HPV 85.3%	CIN III	Yes–Relative to repeat Pap, HPV testing identifies more women at risk for cervical cancer, but increased colpo referral **FAVORABLE**
Lytwyn et al., 2003	Repeat Pap 63.6% HPV/Pap 100%	Repeat Pap 71.4 % HPV/Pap 46.4 %	Repeat Pap 28% HPV/Pap 19.6%	Repeat Pap 91.8% HPV/Pap 100%		CIN II or higher	Yes–HPV/Pap detects 100% cases CIN2+ while Pap alone detected 64% cases CIN II or higher No significant difference in loss to f/u for HPV/Pap versus colpo (note this data not shown) **FAVORABLE**
Cuzick et al., 2003	Repeat Pap 76.6% HPV triage 97.1%	Repeat Pap 95.8% HPV triage 93.3%	Repeat Pap 15.8% HPV triage 12.8%			CIN II or higher	Yes–Relative to repeat Pap, HPV testing identifies more women at risk for cervical cancer, and does not increase colpo referral **FAVORABLE**

S=Statistically significant difference; NS=No statistically significant difference; PPV=Positive predictive value; NPV=Negative predictive value; Colpo=Colposcopy; CIN=Cervical intraepithelial neoplasia; HSIL=High-grade squamous intraepithelial lesion; Pap=Papanicolaou (Pap) test; HPV=Human papillomavirus

Table B-2c. Studies using PCR technology for HPV testing

Name, Year, Citation	Sensitivity	Specificity	PPV	NPV	Outcome(s)	Does HPV testing improve the likelihood of identifying women at risk for cervical cancer?
Screening Studies						
Cuzick et al., 1995 Lancet 345:1533-6 From Franco review	Pap 46% HPV 75%	Pap 96% HPV 96%			CIN II or III	Yes–HPV testing identifies more true positive cases of CIN II or III than Pap **FAVORABLE**
Schneider et al., 2000 Int J Cancer 89: 529-34 From Lorincz and Franco reviews	Pap 20% HPV 89%	Pap 99% HPV 94%	Pap 71% HPV 36%	Pap 97.5% HPV 99.6%	CIN II or III	Yes–HPV testing identifies more true positive cases of CIN II opr III than Pap **FAVORABLE**
Kjaer et al., 2002 BMJ 325: 572-8 From Lorincz review	HPV 93%				CIN II or III	Yes–HPV testing identifies more true positive cases of CIN II or III than Pap **FAVORABLE**
Kulasingam et al., 2002 JAMA 288: 1749-57 From Lorincz review	Pap 50-61% HPV 80-88%	Pap 82-86% HPV 79-87%		Pap 99.5% HPV 98.5%	CIN III	Yes–HPV testing identifies more true positive cases of CIN III than Pap **FAVORABLE**
Triage Study						
Carozzi et al., 2005 Cancer 105: 2-7	HPV 96.4-100%		HPV 30.76-32.14%	HPV 98.73-100%	CIN II or higher	Yes–Relative to repeat Pap, HPV testing identifies more women at risk for cervical cancer **FAVORABLE**

S=Statistically significant difference; NS=No statistically significant difference; PPV=Positive predictive value; NPV=Negative predictive value; Colpo=Colposcopy; CIN=Cervical intraepithelial neoplasia; HSIL=High-grade squamous intraepithelial lesion; Pap=Papanicolaou (Pap) test; HPV=Human papillomavirus

Appendix C: Analysis Presenting an Adjusted Utilization Assumption: A Scenario Presenting Potential Cost and Public Health Impacts of SB 1245

As discussed in *Section II: Utilization, Cost and Coverage*, CHBRP projects no increase in utilization as a result of SB 1245. However this section presents potential impacts *if* utilization were to increase by a small margin as a result of the mandate.

- *Changes in utilization as a result of changes in coverage:* As stated, CHBRP would expect no changes in utilization as a result of change in coverage. The cervical cancer screening benefit is already covered on an annual basis and the largest plans and insurers indicate that they meet the requirements of SB 1245 currently by covering HPV tests for cervical cancer screening per existing guidelines.

- *Changes in utilization as a result of changes in member demand and awareness:* We would also not expect changes in utilization of the HPV test as part of the cervical cancer screening benefit due to increase member demand as a result of the mandate. For example, over the next few years, the Digene Corporation may continue to promote awareness regarding the use of the HPV DNA test. However, this is likely to occur regardless of a mandate to cover the HPV test for the cervical cancer screening. At present time, there is a general lack of awareness between the clinical link between HPV and cervical cancer. As mentioned in the *Introduction* there may be an increase in awareness as a result of the education campaign to be conducted under SB 615 (Figueroa) to take effect January 1, 2007. In addition, *if* the HPV vaccine, currently under review by the FDA was to be approved, and the relevant pharmaceutical company was to launch an advertising campaign, there would also be an increase in awareness of the link between HPV and cervical cancer. The passage of SB 1245 may have an impact in *accelerating* the demand for the HPV test and the take-up rate of the test, but the various potential causes of such an increase are difficult to separate.

- *Changes in utilization as a result of changes in physicians' practice patterns:* CHBRP projects no change in utilization as a result of physician practice patterns *as a result of SB 1245.* However, it is possible that physician practice patterns change as a result of the increased adoption of HPV testing guidelines. As discussed in the *Medical Effectiveness* section, the guidelines for routinely testing for HPV women over the age of 30 and all women with a Pap test result of ASCUS are still relatively new. We know there is often a delay or a lag time from when clinical guidelines are issued and practice patterns change to adopt those guidelines. SB 1245 may serve to *accelerate* the adoption of these guidelines but this is difficult to ascertain.

- *Supplier-induced demand:* As discussed in the *Utilization, Cost, and Coverage* section, there is no evidence to suggest that providers would have incentives to order the HPV test unnecessarily, given the highly rates of capitation among providers and the marginal reimbursement would be for the HPV test alone (and not for an additional visit).

For these reasons, CHBRP offers an analysis in a scenario where utilization would increase slightly—adjusting the utilization assumption from zero to 1 percentage point increase in utilization. The resulting cost and public health impacts, including long-term impacts, are summarized below.

Utilization, Cost, and Coverage Impacts

This section will discuss the estimated cost impacts *in the short term* in 2007 given the scenario in which utilization increases slightly. Except where noted, assumptions and baseline costs of this analysis are the same in the scenario as in the main cost analysis. For example, as in the cost analysis, 100% of enrollees have coverage for medically necessary HPV testing. Medically necessary is defined as a woman having an abnormal Pap or being older than 30 years. Likewise, the unit costs of testing would be the same: $57.

However, in order to illustrate how a higher rate of increase of utilization would impact costs, this scenario models the cost effects if use of both the concurrent HPV and Pap test screen and the HPV triage screen were to increase by 1 percentage point. Women who have an HPV test will either be tested in the course of a routine Pap test (concurrent testing) or as a follow-up test after an earlier abnormal test result. Follow-up screening is also known as HPV triage screening. Per clinical guidelines, we assume all women aged 18-64 years would receive an HPV test after an abnormal Pap test; however, concurrent use of HPV testing during a routine Pap test would only be done after age 30.

Utilization impacts in the short term

Table C-1 shows the impacts of SB 1245 if an increased number of women aged 18-64 years were to fall under the HPV screening strategy based on existing clinical guidelines. If an additional 1% of women were to fall under the HPV triage strategy (1% of 7,627,000 = 76,000), then a subset of those would (1) have a Pap test within a year, (2) have an abnormal pap result, (3) be eligible for the HPV test, and obtain an HPV test *within the next year*. Table C-1 shows that those aged 18-64 years under the HPV triage strategy who would obtain an HPV test in the next year would increase from 7.1% to 7.2%. This increase is slight because follow-up testing for an abnormal Pap result is currently high. This increase could potentially be attributable to utilization that moves from follow-up (or repeat) Pap testing in the case of an abnormal Pap directly to HPV testing.

If an additional 1% of women aged 30-64 years were to fall under the HPV concurrent testing strategy (1% of 6,000,000 = 60,000), then a subset of those would (1) have a Pap test within a year, (2) have the HPV test concurrent with that Pap test. Table C-1 shows that those aged 30-64 under the HPV concurrent strategy who would obtain an HPV test in the next year would increase from 7.1% to 7.8%. As stated above, this increase could be attributable to a potential increase in providers "catching-up" with current clinical guidelines and ordering HPV tests concurrent with Pap tests at a higher rate for those age 30-64.

Impact on other health care costs

As mentioned above, this cost impact analysis does not include the marginal cost associated with follow-up visits as a result of a HPV-positive result, colposcopy, and treatment of cervical cancer in the long term. Nor is the cost savings for avoided cervical cancer mortality included here. However, both of these long term impacts are discussed in the Public Health Impacts section below.

Costs or savings for each category of insurer in the short term

Total annual expenditures for all public and private payers would increase by $3,772,000, an increase of 0.01%. The impact on costs is shown in Table C-1. Analyzed by each payer, the costs would be distributed as follows:

- Total private employer premiums would likely increase by $2,047,000 per year, or 0.01%.
- Premium expenditure on individually purchased insurance would likely increase by $415,000 per year, or 0.01%.
- CalPERS' employer costs would likely increase by $130,000 per year, or 0.01%.
- State expenditures for Medi-Cal HMO members would likely increase by $294,000 per year, or 0.01%.
- Healthy Families state expenditures would likely remain the same, at $644 million.
- Individuals who pay for a share of their private employer-based insurance, CalPERS, or Healthy Families premiums would likely ay an additional $657,000 per year, an increase of 0.01%.
- Out-of-pocket expenditures associated with HPV testing would likely increase by $229,000, or 0.01%.
- Other out-of-pocket costs for HPV testing presently not covered by insurance are presently zero and would be expected to remain the same.

Impact on access and health service availability

The overall increase in health expenditure as a result of increased utilization of HPV testing is likely to be 0.01%. This increase is not large enough to suggest an impact on the purchasing behavior of individuals or the provision of services in such a way as to change access or availability of the HPV test for cervical cancer screening.

Table C-1. Summary of Cost Impacts in the Short-Term, Based on Utilization Increase in Triage and concurrent use of HPV

	HPV Test during triage		**HPV Test concurrent with Pap Test**	
	Increase/Decrease	**Increase/Decrease**	**% Change After Mandate**	**% Change After Mandate**
% of insured women aged 18-64 years with coverage for mandated benefit	0	0	0.0%	0.0%
Number of insured women aged 18-64 years in California with coverage for the benefit	0	0	0.0%	0.0%
Utilization				
Increase in the number of women aged 18-64 years in HPV screening strategies (1)				
HPV test during triage (2)	76,000	0	0.0%	2.2%
HPV test concurrent with Pap (3)	0	60,000	13.8%	0.0%
% of insured women aged 18-64 years in California receiving HPV screen in a year				
Ages 18-29 (4)	0.05%	0.0%	0.0%	0.8%
Ages 30-64	0.05%	0.86%	11.6%	0.7%
Ages 18-64	0.05%	0.67%	9.4%	0.7%
Number of insured women aged 18-64 years in California receiving HPV screen in a year				
Ages 18-29 (4)	800	0.0%	0.0%	0.8%
Ages 30-64	3,100	51,100	11.5%	0.7%
Ages 18-64	3,900	51,100	9.4%	0.7%

Source: California Health Benefits Review Program analysis, 2006.

Table C-1. Summary of Cost Impacts in the Short-Term, Based on Utilization Increase in Triage and Concurrent use of HPV (cont.)

	HPV Test During Triage		HPV Test Concurrent with Pap Test		Total
	Increase/ Decrease	% Change After Mandate	Increase/ Decrease	% Change After Mandate	Total Increase/ Decrease
Costs					
Average cost per HPV screening	$0	0.0%	$0	0.0%	$0
Expenditures					
Premium expenditures by private employers for group insurance	$142,000	0.0004%	$1,905,000	0.01%	$2,047,000
Premium expenditures for individually purchased insurance	$29,000	0.0006%	$386,000	0.01%	$415,000
CalPERS employer expenditures	$9,000	0.0004%	$121,000	0.01%	$130,000
Medi-Cal state expenditures	$26,000	0.0006%	$268,000	0.01%	$294,000
Healthy Families state expenditures	$0	0.0000%	$0	0.00%	$0
Premium expenditures by employees with group insurance or CalPERS, and by individuals with Healthy Families	$46,000	0.0004%	$611,000	0.01%	$657,000
Individual out-of-pocket expenditures (deductibles, copayments, etc.)	$16,000	0.0004%	$213,000	0.01%	$229,000
Expenditures for non-covered services	$0	0.0%	$0	N/A	$0
Total annual expenditures	$268,000	0.0004%	$3,504,000	0.01%	$3,772,000

Source: California Health Benefits Review Program, 2006.

(1) The utilization increase of 1 percentage point is applied to all women from ages 18-64 who would be eligible for screening. In other words, per clinical guidelines they would be included as part of an HPV screening strategy—1 percentage additional women for HPV test triage and 1 percentage additional women for HPV test concurrent with the Pap test. Adjustments are made for how many would be expected to receive a Pap test in the short term—within the next year.

(2) "Triage screening" means HPV testing for those women who have an abnormal Pap test. About 55 million Pap tests are performed each year in the United States. Of these, approximately 3.5 million (6%) are abnormal and require medical follow-up (NCI, 2005). If a Pap were performed with conventional cytology, a woman would be asked to have a return office visit for the HPV test; if the Pap were performed with liquid-based cytology, the physician can order the HPV test directly. Approximately 51% of providers report ordering the HPV test either by asking for a follow-up visit for the HPV test or ordering the test directly (CDC, 2005).

(3) "Concurrent testing" means that the HPV test is performed along with the Pap test for cervical cancer screening. 21% of providers report conducting concurrent testing—with 29% doing so "always" or "usually" for women over 30 (CDC, 2005).

(4) Per clinical guidelines, an increase in HPV test concurrent with the Pap test would not apply for women under age 30

Public Health Impacts

While CHBRP projects no change in utilization as a result of the mandate, and therefore no changes in public health outcomes as a result of SB 1245, this section presents potential impacts if utilization were to increase by a small margin as a result of the mandate. This section also presents the net lifetime costs associated with HPV testing and associated follow-up treatment, and reductions in cervical cancer cases.

As discussed, this alternate scenario presents the public health impact of a 1 percentage point increase in each of the two different combined HPV and Pap screening strategies (HPV and Pap primary screen and HPV triage screen) in comparison to Pap testing alone. Goldie et al. (2004) present absolute lifetime cervical cancer risk and lifetime costs for four different screening intervals (every 1, 2, 3, or 4 years) and four different screening strategies (lifetime conventional Pap; liquid-based Pap with reflex HPV testing, lifetime; conventional Pap until age 30, HPV and Pap after age 30; and liquid Pap until age 30, HPV and Pap after age 30). As shown in Tables C-2 and C-3, these numbers were used in combination with the distribution of current Pap screening intervals to calculate a weighted average of reduction in lifetime cervical cancer risk and increase in lifetime costs across all screening intervals. This weighted average was then applied to the population numbers presented in Table C-1 to produce specific estimates of reduction of cervical cancer cases and increase in lifetime costs, presented below.

It is estimated that 7.6 million women are in health insurance plans affected by this mandate. Therefore, a hypothesized 1 percentage point increase in HPV triage screening would result in 76,000 more women shifting from lifetime conventional Pap tests to lifetime HPV triage screening. A shift from lifetime conventional Pap screening to HPV triage would result in a 29% reduction in lifetime cervical cancer risk and a 9% increase in lifetime costs. In this scenario, for each increase by 1 percentage point in the rate of women screened for cervical cancer using the HPV triage screening strategy (compared to lifetime conventional Pap tests), over the lifetime of the 76,000 women newly subject to this screening strategy, this would result in a reduction in cervical cancer cases from 290 to 205 with an associated cost increase of 14.3 million dollars.

It is estimated that 6.0 million women age 30 or older are in health plans affected by this mandate. Therefore, a hypothesized 1 percentage point increase in HPV primary screening would result in 60,000 more women shifting from lifetime conventional Pap tests to HPV/Pap primary screen at age 30 and older. A shift in the rate of HPV/Pap primary screening in women ages 30 and older (compared to lifetime conventional Pap tests) would result in a 39% reduction in lifetime cervical cancer risk and a 45% increase in lifetime costs. For each increase by 1 percentage point in the rate of women screened for cervical cancer with Pap and HPV concurrent screening (compared to lifetime conventional Pap tests) over the lifetime of the 60,000 women newly subject to this screening strategy, this would result in a reduction in cervical cancer cases from 224 to 137 with an associated cost increase of 57.6 million dollars.

Table C-2. Lifetime Cervical Cancer and Lifetime Costs with Alternative Cervical Cancer Screening Strategies: *Strategy 1: Lifetime HPV Triage*

		Lifetime Cervical Cancer Risk		**Lifetime Costs of Cervical Cancer Screening**	
Pap Screen Frequency	Distribution*	Lifetime Conventional Pap**	Lifetime Triage HPV testing**	Lifetime Conventional Pap**	Lifetime Triage HPV testing**
Annually	65.8%	0.0034	0.0025	$2,457	$2,653
Every 2 years	11.1%	0.0041	0.0028	$1,536	$1,707
Every 3 years	8.2%	0.005	0.0032	$1,196	$1,358
Every 4 years	5.7%	0.0061	0.0038	$1,009	$1,163
4+ years/never	9.1%	NA			
Total***	100%	0.0038	0.0027	$2,140	$2,327
Overall Change			-29%		+9%

Table C-3. Lifetime Cervical Cancer and Lifetime Costs with Alternative Cervical Cancer Screening Strategies: *Strategy 2: Pap until age 30, Pap and HPV as Primary Screen for ages 30 and Older*

		Lifetime Cervical Cancer Risk		**Lifetime Costs of Cervical Cancer Screening**	
Pap Screen Frequency	Distribution*	Lifetime Conventional Pap**	HPV and Pap (30+)**	Lifetime Conventional Pap**	HPV and Pap (30+)**
Annually	71.1%	0.0034	0.0022	$2,457	$3,575
Every 2 years	11.1%	0.0041	0.0023	$1,536	$2,151
Every 3 years	7.8%	0.005	0.0026	$1,196	$1,647
Every 4 years	5.1%	0.0061	0.0031	$1,009	$1,377
4+ years/never	5.0%	NA			
Total***	100%	0.0038	0.0023	$2,168	$3,133
Overall Change			-39%		+45%

Sources:

* Analysis of the 2001 California Health Interview Survey (CHIS, 2001)

** From Goldie et al., 2004, Table 2

*** Weighted average based on distribution of screening frequency

Appendix D: Cost Impact Analysis: Caveats and Assumptions

This appendix describes caveats and assumptions used in conducting the cost impact analysis, including those presented in Appendix C. For additional information on the cost model and underlying methodology, please refer to the CHBRP Web site, http://www.chbrp.org/costimpact.html.

The cost analysis in this report was prepared by Milliman and University of California, Los Angeles (UCLA), with the assistance of CHBRP staff. Per the provisions of AB 1996 (California Health and Safety Code, Section 127660, et seq.), the analysis includes input and data from an independent actuarial firm, Milliman. In preparing cost estimates, Milliman and UCLA relied on a variety of external data sources. The *Milliman Health Cost Guidelines* (HCG) were used to augment the specific data gathered for this mandate. The HCGs are updated annually and are widely used in the health insurance industry to estimate the impact of plan changes on health care costs. Although this data was reviewed for reasonableness, it was used without independent audit.

General Caveats and Assumptions

The expected costs in this report are not predictions of future costs. Instead, they are estimates of the costs that would result if a certain set of assumptions were exactly realized. Actual costs will differ from these estimates for a wide variety of reasons, including:

- Prevalence of mandated benefits before and after the mandate different from our assumptions.
- Utilization of mandated services before and after the mandate different from our assumptions.
- Random fluctuations in the utilization and cost of health care services.

Additional assumptions that underlie the cost estimates presented here are:

- Cost impacts are only shown for people with insurance.
- The projections do not include people covered under self-insurance employer plans because those employee benefit plans are not subject to state-mandated minimum benefit requirements.
- Employers and employees will share proportionately (on a percentage basis) in premium rate increases resulting from the mandate. In other words, the distribution of premium paid by the subscriber (or employee) and the employer will be unaffected by the mandate.

There are other variables that may affect costs, but which Milliman did not consider in the cost projections presented in this report. Such variables include, but are not limited to:

- Population shifts by type of health insurance coverage. If a mandate increases health insurance costs, then some employer groups or individuals may elect to drop their coverage. Employers may also switch to self-funding to avoid having to comply with the mandate.
- Changes in benefit plans. To help offset the premium increase resulting from a mandate, enrollees or insured may elect to increase their overall plan deductibles or copayments. Such changes would have a direct impact on the distribution of costs between the health

plan and the insured person, and may also result in utilization reductions (i.e., high levels of patient cost sharing result in lower utilization of health care services). Milliman did not include the effects of such potential benefit changes in its analysis.

- Adverse selection. Theoretically, individuals or employer groups who had previously foregone insurance may now elect to enroll in an insurance plan postmandate because they perceive that it is to their economic benefit to do so.
- Health plans may react to the mandate by tightening their medical management of the mandated benefit. This would tend to dampen our cost estimates. The dampening would be more pronounced on the plan types that previously had the least effective medical management (i.e., FFS and PPO plans).
- Variation in existing utilization and costs, and in the impact of the mandate, by geographic area and delivery system models. Even within the plan types we modeled (HMO/POS and PPO/FFS), there are variations in utilization and costs within California. One source of difference is geographic. Utilization differs within California due to differences in the health status of the local commercial population, provider practice patterns, and the level of managed care available in each community. The average cost per service would also vary due to different underlying cost levels experienced by providers throughout California and the market dynamic in negotiations between health plans and providers.
- Both the baseline costs prior to the mandate and the estimated cost impact of the mandate could vary within the state due to geographic and delivery system differences. For purposes of this analysis, however, we have estimated the impact on a statewide level.

Mandate-Specific Caveats and Assumptions

- CHBRP assumes that the populations with and without coverage are similar with respect to their mix of severity of illness, and associated demand for HPV testing services.

Appendix E: Information Submitted by Outside Parties for Consideration for CHBRP Analysis

CHBRP policy includes analysis of information submitted by outside parties, and places an open call to all parties who want to submit information during the first two weeks of the CHBRP review.

The following articles were submitted by the Office of Senator Liz Figueroa on February 21, 2006. These articles were considered as part of this analysis where appropriate.

ACOG . Practice Bulletin Number 66: Clinical Management Guidelines for Obstetrician-Gynecologists. Management of abnormal cervical cytology and histology. 2005:106(3): 645-64.

Association of Reproductive Health Professionals (ARHP). Advances in Cervical Cancer Prevention. Clinical Proceedings. 2003:1-22.

Goldie SJ, Kim JJ, Wright TC. Cost-effectiveness of human papillomavirus DNA testing for cervical cancer screening in women aged 30 years or more. Obstetrics & Gynecology. 2004:103(4):619-31.

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Waxman A, et al. Cervical Cytology Screening. ACOG Practice Bulletin: Clinical Management Guidelines for Obstetrician-Gynecologists No. 45. August 2003:1-7.

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For information on the processes for submitting information to CHBRP for review and consideration please visit: http://www.chbrp.org/requests.html

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A group of faculty and staff undertakes most of the analysis that informs reports by the California Health Benefits Review Program (CHBRP). The CHBRP **Faculty Task Force** comprises rotating representatives from six University of California (UC) campuses and three private universities in California. In addition to these representatives, there are other ongoing contributors to CHBRP from UC. This larger group provides advice to the CHBRP staff on the overall administration of the program and conducts much of the analysis. The CHBRP **staff** coordinates the efforts of the Faculty Task Force, works with Task Force members in preparing parts of the analysis, and coordinates all external communications, including those with the California Legislature. The level of involvement of members of CHBRP's Faculty Task Force and staff varies on each report, with individual participants more closely involved in the preparation of some reports and less involved in others.

As required by CHBRP's authorizing legislation, UC contracts with a certified actuary, Milliman, to assist in assessing the financial impact of each benefit mandate bill. Milliman also helped with the initial development of CHBRP's methods for assessing that impact.

The **National Advisory Council** provides expert reviews of draft analyses and offers general guidance on the program to CHBRP staff and the Faculty Task Force. CHBRP is grateful for the valuable assistance and thoughtful critiques provided by the members of the National Advisory Council. However, the Council does not necessarily approve or disapprove of or endorse this report. CHBRP assumes full responsibility for the report and the accuracy of its contents.

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The California Health Benefits Review Program is administered by the Division of Health Affairs at the University of California, Office of the President, under Wyatt R. Hume, DDS, PhD, Acting Provost and Senior Vice President for Academic Affairs.