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CALIFORNIA
HEALTH BENEFITS REVIEW PROGRAM

Analysis of Assembly Bill 1774
Health Care Coverage:
Gynecological Cancer Screening Tests

A Report to the 2007–2008 California Legislature
April 7, 2008

CHBRP 08-05



The California Health Benefits Review Program (CHBRP) responds to requests from the State Legislature to provide independent analyses of the medical, financial, and public health impacts of proposed health insurance benefit mandates and proposed repeals of health insurance benefit mandates. In 2002, CHBRP was established to implement the provisions of Assembly Bill 1996 (California Health and Safety Code, Section 127660, et seq.) and was reauthorized by Senate Bill 1704 in 2006 (Chapter 684, Statutes of 2006). The statute defines a health insurance benefit mandate as a requirement that a health insurer or managed care health plan (1) permit covered individuals to obtain 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.

A small analytic staff in the University of California's Office of the President supports a task force of faculty from several campuses of the University of California, as well as Loma Linda University, the University of Southern California, and Stanford University, to complete each analysis within a 60-day period, usually before the Legislature begins formal consideration of a mandate bill. A certified, independent actuary helps estimate the financial impacts, and a strict conflict-of-interest policy ensures that the analyses are undertaken without financial or other interests that could bias the results. A National Advisory Council, drawn from experts from outside the state of California and designed to provide balanced representation among groups with an interest in health insurance benefit mandates, reviews draft studies to ensure their quality before they are transmitted to the Legislature. Each report summarizes scientific evidence relevant to the proposed mandate, or proposed mandate repeal, but does not make recommendations, deferring policy decision making to the Legislature. The State funds this work through a small annual assessment on health plans and insurers in California. All CHBRP reports and information about current requests from the California Legislature are available at the CHBRP Web site, www.chbrp.org.

A Report to the 2007–2008 California State Legislature

Analysis of Assembly Bill 1774 Health Care Coverage: Gynecological Cancer Screening Tests

April 7, 2008

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PREFACE

This report provides an analysis of the medical, financial, and public health impacts of Assembly Bill 1774, a bill to mandate the coverage of screening and diagnostic tests for the purpose of assisting or facilitating the diagnosis of gynecological cancers. In response to a request from the California Assembly Committee on Health on February 6, 2008, the California Health Benefits Review Program (CHBRP) undertook this analysis pursuant to the provisions of Senate Bill 1704 (Chapter 684, Statutes of 2006) as chaptered in Section 127600, et seq. of the California Health and Safety Code.

Edward Yelin, PhD, Janet Coffman, MPP, PhD, Mi-Kyung (Miki) Hong, MPH, and Wade Aubry, MD, all of the University of California, San Francisco, prepared medical effectiveness analysis section. Bruce Abbott, MLS, of the University of California, Davis, conducted the literature search. Cheryl Saenz, MD, of the University of California, San Diego, provided technical assistance with the literature review and expert input on the analytic approach. Helen Halpin, ScM, PhD, and Nicole Bellows, PhD, of the University of California, Berkeley, prepared the public health impact analysis and related portions of the introduction. Susan Ettner, PhD, and Meghan Cameron, MPH, all of the University of California, Los Angeles, prepared the cost impact analysis. Jay Ripps, FSA, MAAA, of Milliman, provided actuarial analysis. Cynthia Robinson, MPP, of CHBRP staff prepared the background section and synthesized the individual sections into a single report. Cherie Wilkerson, BA, provided editing services. A subcommittee of CHBRP's National Advisory Council (see final pages of this report) and a member of the CHBRP Faculty Task Force, Ted Ganiats, PhD, of the University of California, San Diego, 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:

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Susan Philip, MPP
Director

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EXECUTIVE SUMMARY

California Health Benefits Review Program Analysis of Assembly Bill 1774: Health Care Coverage: Gynecological Cancer Screening Tests

The California Legislature requested the California Health Benefits Review program (CHBRP) to conduct an evidence-based assessment of the medical, financial, and public health impacts of Assembly Bill (AB) 1774 Health Care Coverage: Gynecological Cancer Screening Tests, as amended on March 5, 2008. This bill would mandate coverage of “any test necessary for the screening and diagnosis of gynecological cancers when ordered by a physician, nurse practitioner, or certified nurse midwife in whose judgment the test would assist or facilitate the diagnosis of cancer.” AB 1774 would add Section 1367.655 to the Health and Safety Code, and Section 10123.182 to the Insurance Code.

Gynecological cancers are cancers of the female reproductive tract, including the cervix, endometrium, fallopian tubes, ovaries, uterus, vagina, and vulva. The three most common types of cancer—uterine or endometrial, ovarian, and cervical—account for 90% of all gynecological cancers.

AB 1774 is intended to address the problem of late diagnoses, when these cancers in particular are far less treatable. According to a recent press release from the bill author Assemblymember Sally Lieber, “the common Pap test does not detect ovarian or uterine cancer. Additional tests are readily available to diagnose them, but they are underutilized.”

Current law requires health plans and insurers to cover all generally medically accepted cancer screening tests; an annual cervical cancer screening test, including the conventional Pap test and the human papillomavirus (HPV) screening test; and diagnostic services.

Health plans and health insurers cover gynecological cancer screening tests for women subject to their medical necessity criteria. The standards used by plans to determine medical necessity appear to be broadly consistent with evidence-based clinical guidelines issued by the U.S. Preventive Services Task Force and American Cancer Society.

CHBRP initially assumed the bill, modeled on the current cervical cancer statute, would be interpreted by regulatory agencies as preserving the right of insurers to determine medical necessity prior to authorizing services. However, discussions with state regulators and state and federal agencies that administer publicly financed health insurance programs did not support this interpretation.

Because the bill has no precedent in current law, both the Department of Managed Health Care (DMHC) and the California Department of Insurance (CDI) view the phrase “in whose judgment” as reflecting a legislative intent to move discretion over whether a test is needed, and therefore a covered benefit, from the health plan and insurer to the individual medical providers. State and federal agencies that administer programs for Medi-Cal, Managed Risk Medical Insurance Board programs, and the California Public Employees’ Retirement System (CalPERS) were also consulted, and their interpretation of the bill was consistent with those of the

regulatory agencies. Conversations with the bill author staff also indicated it was the bill author's intent to allow health care providers to use their judgment and not be "second-guessed" by health plans.¹ Consultations with legal counsel suggested that the interpretation of the bill language would end up being adjudicated in the courts. CHBRP assumes for the sake of this analysis that under AB 1774, screening would be "medically necessary" for a woman if a provider made that determination. It is possible that, following enactment of this legislation, there would be litigation over this matter, and courts might rule that the bill language does not preclude health plans and health insurers from applying medical necessity criteria for making coverage determinations. In this event, the resulting costs would be different from CHBRP cost estimates.

Medical Effectiveness

The medical effectiveness review for AB 1774 focused on the three gynecological cancers that account for 90% of all gynecological cancers in California: cervical cancer, ovarian cancer, and endometrial cancer.

Cervical Cancer

Screening Asymptomatic Women at Average Risk (no previous history of abnormal cervical cytology or cervical lesions)

- There is a preponderance of evidence that, among asymptomatic women who are sexually active and have not had a hysterectomy, screening with conventional cytology (i.e., Pap test) reduces the incidence of cervical cancer, because this test can detect precancerous lesions. Treatment of precancerous lesions can prevent a woman from developing cervical cancer. In addition, conventional cytology can reduce morbidity and mortality from cervical cancer by detecting cancerous lesions at an early stage at which treatment is most likely to be successful.
- A preponderance of the evidence suggests that liquid-based cytology is no more accurate than conventional cytology for screening asymptomatic women for cervical cancer, regardless of whether it is performed alone or in conjunction with DNA testing for the human papillomavirus (HPV).
- The evidence of the accuracy of the following tests for screening asymptomatic women for cervical cancer relative to conventional cytology is ambiguous:
 - HPV DNA test versus conventional cytology
 - Multimodal screening with the HPV DNA test and conventional cytology versus conventional cytology alone

¹ Personal communication with Barry Steinhart, Office of Assemblymember Lieber, February 12, 2008.

Screening Asymptomatic Women at High Risk (due to abnormal cytology and/or previous history of cervical lesions)

- The available evidence suggests that the HPV DNA test and conventional cytology are equally accurate for identifying women with abnormal cytology (i.e., abnormal Pap test) who should undergo further testing with colposcopy (and biopsy if necessary) to determine whether they have cervical cancer or precancerous lesions.
- The evidence of relative accuracy of the following tests and technologies for identifying women with abnormal cytology who should receive further testing is ambiguous:
 - Liquid-based cytology versus conventional cytology
 - HPV DNA test plus conventional cytology versus conventional cytology alone
- The preponderance of evidence suggests that using the HPV DNA test to triage women with abnormal cytology on either an initial or a repeat test more accurately identifies women who need further testing than performing conventional cytology alone.

Ovarian Cancer

Screening Asymptomatic Women at Average Risk (no familial risk history)

- There is insufficient evidence to determine the effectiveness of providing genetic tests for mutations associated with increased risk of ovarian cancer (i.e., *BRCA1* and *BRCA2* mutations) to women who do not have a family history (i.e., hereditary risk) of ovarian cancer.
- The preponderance of evidence suggests that screening asymptomatic women at average risk for ovarian cancer with transvaginal ultrasound and/or the CA-125 blood test can detect ovarian cancer at an earlier stage.
- However, there is insufficient evidence to determine whether screening asymptomatic women at average risk for ovarian cancer reduces morbidity and mortality over the long term.
- Screening asymptomatic women at average risk for ovarian cancer might increase harms due to surgery and complications thereof.

Screening Asymptomatic Women at High Risk (with familial risk history)

- The available evidence suggests that, among asymptomatic women at increased risk for ovarian cancer due to age and/or family history of ovarian cancer, annual screening with transvaginal ultrasound is accurate and may increase survival over the short term.

- There is insufficient evidence to determine whether multimodal screening of asymptomatic women with a family history of ovarian cancer using transvaginal ultrasound and CA-125 yields more accurate results than screening with transvaginal ultrasound alone.

Endometrial Cancer

Screening Asymptomatic Women at Average Risk (those not presenting with abnormal uterine bleeding)

- No studies of the effectiveness of screening asymptomatic women for endometrial cancer were identified.

Diagnosing Women With Symptoms That May Indicate Cancer (those presenting with abnormal uterine bleeding)

- There is insufficient evidence to determine whether pelvic or transvaginal ultrasound can accurately diagnose endometrial hyperplasia or carcinoma among women with abnormal uterine bleeding.
- The preponderance of evidence suggests that endometrial biopsy and hysteroscopy can accurately diagnose endometrial carcinoma among women with abnormal uterine bleeding.

Utilization, Cost, and Coverage Impacts

Summarized below is one set of estimates of possible utilization and cost effects using assumptions based on the judgment of expert physician consultants, opinions solicited from physicians in community-based practice, and relevant literature.

As mentioned, CHBRP is following the opinion of the legal counsel and regulatory agencies in interpreting AB 1774 as removing the carrier's ability to apply medical necessity requirements in their coverage determinations for gynecological cancer diagnostic and screening tests. Public programs subject to AB 1774, such as Medi-Cal managed care, would also lose their ability to deny coverage for tests based on medical necessity criteria. Because CHBRP cannot project the *actual* changes in utilization that would result from prohibiting health plans from applying medical necessity guidelines for coverage determinations, estimates are provided instead for one plausible scenario that *might* occur if the bill were to pass.

CHBRP emphasizes that the utilization and cost figures presented in this report are merely an illustration of what could happen as a result of the passage of the bill, not a projection of what will happen. The impact of AB 1774 on utilization could vary substantially, depending on a number of factors that include patient demand in conjunction with provider financial incentives and competitive market pressures. Furthermore, if carriers mounted a successful court challenge to the interpretation of the bill that re-established their legal authority to include medical necessity requirements in their coverage determinations, utilization in the long run would be unlikely to change as a result of the bill, since carriers are generally already covering all medically appropriate tests.

Coverage

- CHBRP's cost analysis focuses on women 18 years and older because children under 18 are unlikely to be screened for gynecological cancer. CHBRP estimates that 8,433,000 females aged 18 and over are currently covered by health plans that would be subject to AB 1774.
- Based on its survey of major California health plans, CHBRP estimates that 100% of privately and publicly insured 18- to 64-year-old females currently have coverage for screening and diagnostic tests for gynecological cancers, subject to medical necessity requirements of the health plans.
- Tests currently being covered by health plans include diagnostic tests for symptomatic women and screening tests for asymptomatic women for which there is evidence of medical effectiveness (for example, those recommended by the U.S. Preventive Services Task Force and the American Cancer Society).
- With the exception of Pap tests for all women and HPV DNA tests for women of certain ages, privately as well as publicly funded health plans do not generally cover screening tests for average-risk, asymptomatic women, with the stated reason that there is no evidence of medical effectiveness for these tests. Health plans generally cover the screening tests recommended for high-risk, asymptomatic women.

Utilization

- As diagnostic tests, screening tests for certain high-risk, asymptomatic women, Pap tests for all women and HPV DNA tests for women of certain ages are already covered, the impact of AB 1774 on utilization would likely be limited to other gynecological cancer screening tests for average-risk, asymptomatic women.
- In the scenario modeled in this analysis, CHBRP assumed use of "first-line" screening tests ranged from 0% to 40%, depending on the test and subpopulation. Under this scenario, utilization of screening tests in the first year post-mandate would increase by about 1,565,000 for transvaginal ultrasound, 945,000 for endometrial biopsy, 232,000 for *BRCA1/2* genetic mutation tests, and 244,000 for HNPCC genetic mutation tests. Other selected screening tests would experience lower utilization increases.
- Because each woman would need to have genetic testing only once in her lifetime, utilization of these tests would likely diminish significantly in the years following the bill's passage as more of the population underwent such testing. Eventually demand for these tests among adult women would be satisfied and only subsequent cohorts of girls turning 18 would require new testing.

Costs

- Based on the assumed utilization increases in the scenario being modeled, total annual health care expenditures (including total premiums and out-of-pocket expenditures) could increase by \$2.72 billion, or 3.43%, as a result of AB 1774.
- The estimates presented for this scenario do not include the cost of surgical complications resulting from false-positive screens that lead to unnecessary surgery; however, these costs are not anticipated to have a material impact on the overall cost of the bill.
- The estimates also exclude potential savings due to earlier diagnosis. Based on the medical effectiveness literature, early detection associated with screening tests not already covered would be relatively rare and limited to ovarian cancer.
- Over half of the potential increase in costs is driven by the assumed use of genetic testing for endometrial and ovarian cancers, as the cost model assumes that approximately 3% of all women would receive these tests in the first year post-mandate and the tests cost \$2,300-\$3,300 each. The cost of this genetic testing would likely diminish substantially over time, as fewer women remain who have never been tested. About one-seventh of the cost is attributable to dilation and curettage surgery for women whose endometrial biopsies were inconclusive or otherwise required follow-up. Over one-quarter of the cost is due to transvaginal ultrasound screening and follow-up for false positives.
- CHBRP estimates that under the scenario presented in the cost section, total premiums paid by all private employers in California could increase by about \$1.63 billion per year, or 3.46%.
- Total premiums for individually purchased insurance could increase by about \$287 million, or 4.67%. The share of premiums paid by individuals for group or public insurance could increase by \$437 million, or 3.41%.
- Premiums paid by CalPERS could increase by about \$91 million, or 3.09%. Medi-Cal expenditures could increase by \$77 million, or 1.90%. Healthy Families is not expected to experience an increase in costs.
- Individual out-of-pocket expenditures could increase by \$202 million, or 3.60%. The extent to which this increase would be offset by a decrease in expenditures for screening tests currently paid entirely out of pocket is unknown; however, it is unlikely that large numbers of women are currently receiving noncovered gynecological cancer screening tests because these tests are generally expensive and their use for asymptomatic, average-risk women is not recommended by any national medical organization.
- Based on the scenario being modeled, CHBRP estimates that across all markets, approximately 82,000 commercially insured individuals could lose coverage due to the premium increases resulting from the mandate.

- There is a dearth of evidence with regard to the cost effectiveness of gynecological cancer screening tests for average-risk, asymptomatic women, but it seems unlikely that general population screening using tests currently not covered would be cost effective when medical effectiveness has not yet been demonstrated.

Public Health Impacts

- The positive health outcomes intended by AB 1774 are those associated with the detection of gynecological cancers at an earlier stage, primarily increased survival and decreased morbidity due to early treatment. Another positive outcome is the reduction in stress and anxiety related to gynecological cancers for those who receive reassuring results.
- There are also potential harms associated with AB 1774. False-positive results generate unnecessary stress and anxiety, and result in complications from follow-up procedures. Additionally, false negatives could result in delayed treatment once symptoms emerge.
- Based on the scenario for increased utilization, no cases of cervical cancer are expected to be detected early due to increased HPV DNA testing among women 18–29 years old. However, approximately 4,600 women are expected to have false-positive results, which could result in stress and anxiety.
- Based on the scenario for increased utilization, ovarian cancer screening of the average-risk population due to AB 1774 is expected to result in the detection of early-stage cancer for 470 women over 3 years. More than 30,000 women are expected to have false-positive results for the initial screen, and another 6,600 women are expected to have unnecessary surgeries due to increased screenings. Of the 6,600 unnecessary surgeries, approximately 330 are expected to have complications, such as hemorrhage and infection.
- Since no studies were found to discuss the accuracy or effects of endometrial cancer tests for asymptomatic women, the health effects of the estimated increase in utilization of tests for endometrial cancer are unknown.
- Since AB 1774 is not expected to result in increased utilization of proven medically effective gynecological screening and diagnostic tests where racial disparities exist, it is not expected to have an impact on racial disparities related to gynecological cancers.
- Since insurers typically cover the gynecological tests that have been found to be medically effective, AB 1774 is not expected to substantially reduce premature death among women. However, for the 470 women expected to have early-stage ovarian cancer detected due to AB 1774, this could potentially improve survival.
- Overall, at present, there are over \$500 million in indirect costs associated with gynecological cancers in California. AB 1774 could potentially decrease lost productivity costs by increasing survival for women with earlier detected ovarian cancer. There could also be some lost productivity costs associated with false positives and the time necessary to get follow-up tests and procedures; particularly for the estimated 330 women projected to have complications from surgery.

- Based on the scenario that approximately 82,000 people could lose coverage due to increased premiums associated with AB 1774, there are potential long-term health impacts associated with the loss of insurance. In California, uninsured individuals report poorer health, more psychological distress, and more delays in receiving treatments.

Table 1. Summary of Coverage and Potential Utilization and Cost Impacts of AB 1774

	Before Mandate	After Mandate	Increase/ Decrease	Change After Mandate
Coverage				
Number of individuals affected by mandate—women aged 18–64 yrs	8,433,000	8,433,000	—	0%
Percentage of individuals with coverage for cervical cancer tests				
Diagnostic testing for symptomatic women	100%	100%	0%	0%
Routine screening tests for high-risk, asymptomatic women	100%	100%	0%	0%
Routine screening tests for average-risk, asymptomatic women	100%	100%	0%	0%
Percentage of individuals with coverage for ovarian cancer tests				
Diagnostic testing for symptomatic women	100%	100%	0%	0%
Routine screening tests for high-risk, asymptomatic women	100%	100%	0%	0%
Routine screening tests for average-risk, asymptomatic women	0%	100%	100%	N/A
Percentage of individuals with coverage for endometrial cancer tests				
Diagnostic testing for symptomatic women	100%	100%	0%	0%
Routine screening tests for high-risk, asymptomatic women	100%	100%	0%	0%
Routine screening tests for average-risk, asymptomatic women	0%	100%	100%	N/A
Utilization and cost				
Number of tests/procedures used by average-risk, asymptomatic women				
Pap smears	792,000	792,000	—	0%
HPV DNA test	83,000	311,000	228,000	275%
Colposcopy	—	8,000	8,000	N/A
Transvaginal ultrasound	—	1,565,000	1,565,000	N/A
CA-125 blood test	—	175,000	175,000	N/A
Laparoscopy	—	6,000	6,000	N/A
Laparotomy	—	2,000	2,000	N/A
<i>BRCA1/2</i> genetic test	—	232,000	232,000	N/A
<i>BRCA1/2</i> genetic test—genetic counseling	—	232,000	232,000	N/A
Endometrial biopsy	—	945,000	945,000	N/A
Dilation and curettage	—	71,000	71,000	N/A
HNPCC genetic test	—	244,000	244,000	N/A
HNPCC genetic test—genetic counseling	—	244,000	244,000	N/A

Table 1. Summary of Coverage and Potential Utilization and Cost Impacts of AB 1774 (Cont'd)

	Before Mandate	After Mandate	Increase/ Decrease	Change After Mandate
Average cost per test/procedure, selected tests/procedures				
Pap tests	\$41.12	\$41.12	—	0%
HPV DNA test	\$68.80	\$68.80	—	0%
Colposcopy	\$235.05	\$235.05	—	0%
Transvaginal ultrasound	\$363.14	\$363.14	—	0%
CA-125 blood test	\$45.14	\$45.14	—	0%
Laparoscopy	\$3,667.16	\$3,667.16	—	0%
Laparotomy	\$3,010.29	\$3,010.29	—	0%
<i>BRCA1/2</i> genetic test	\$3,292.02	\$3,292.02	—	0%
<i>BRCA1/2</i> genetic test—genetic counseling	\$42.27	\$42.27	—	0%
Endometrial biopsy	\$164.31	\$164.31	—	0%
Dilation and curettage	\$2,788.57	\$2,788.57	—	0%
HNPCC genetic test	\$2,298.70	\$2,298.70	—	0%
HNPCC genetic test—genetic counseling	\$42.27	\$42.27	—	0%
Expenditures				
Premium expenditures by private employers for group insurance	\$47,088,966,000	\$48,717,926,000	\$1,628,960,000	3.46%
Premium expenditures for individually purchased insurance	\$6,158,288,000	\$6,445,780,000	\$287,492,000	4.67%
Premium expenditures by individuals with group insurance, CalPERS, Healthy Families, AIM or MRMIP	\$12,819,308,000	\$13,256,253,000	\$436,945,000	3.41%
CalPERS employer expenditures ^a	\$2,942,984,000	\$3,033,831,000	\$90,847,000	3.09%
Medi-Cal state expenditures ^b	\$4,044,192,000	\$4,121,111,000	\$76,919,000	1.90%
Healthy Families state expenditures ^c	\$644,074,000	\$644,074,000	\$0	0.00%
Individual out-of-pocket expenditures (deductibles, copayments, etc.)	\$5,602,060,000	\$5,803,857,000	\$201,797,000	3.60%
Out-of-pocket expenditures for non- covered services	N/A	N/A	N/A	N/A
Total annual expenditures^e	\$79,299,872,000	\$82,022,832,000	\$2,722,960,000	3.43%

Source: California Health Benefits Review Program, 2008.

Notes: The population includes employees and dependents covered by employer-sponsored insurance (including CalPERS), individually purchased insurance, and public health insurance provided by a health plan subject to the requirements of the Knox-Keene Health Care Service Plan Act of 1975. All population figures include enrollees aged 0–64 years and enrollees 65 years or older covered by employer-sponsored insurance. Premium expenditures by individuals include employee contributions to employer-sponsored health insurance and member contributions to public health insurance.

^aOf the CalPERS employer expenditure, about 60% of the increase, or \$54,508,000, would be State expenditures for CalPERS members who are State employees.

^bMedi-Cal state expenditures for members under 65 years of age include expenditures for Major Risk Medical Insurance Program (MRMIP) and Access for Infants and Mothers (AIM) program.

^cCHBRP assumes that utilization and cost impacts will be negligible for Healthy Families. Only 2% of Healthy Families enrollees are women aged 18 years and above, and even those enrollees are 18- and 19-year-olds.

This includes administrative expenses of \$11,324,000,000 before mandate and \$11,723,000,000 after the mandate, an increase of \$399,000,000.

Key: CalPERS=California Public Employees' Retirement System.

INTRODUCTION

The California Legislature requested the California Health Benefits Review program (CHBRP) to conduct an evidence-based assessment of the medical, financial, and public health impacts of Assembly Bill (AB) 1774 Health Care Coverage: Gynecological Cancer Screening Tests, as amended on March 5, 2008. This bill would mandate coverage of “any test necessary for the screening and diagnosis of gynecological cancers when ordered by a physician, nurse practitioner, or certified nurse midwife in whose judgment the test would assist or facilitate the diagnosis of cancer.” AB 1774 would add Section 1367.655 to the Health and Safety Code, and Section 10123.182 to the Insurance Code.

Gynecological cancers make up approximately 12% of all cancer in women and 11% of all cancer deaths. Gynecological cancers are cancers of the female reproductive tract, including the cervix, endometrium, fallopian tubes, ovaries, uterus, vagina, and vulva. The three most common types of cancer—uterine or endometrial, ovarian, and cervical—account for 90% of the gynecological cancers.

The bill is intended to address the problem of late diagnoses. The intent of bill is to “increase the number of women whose cancers are diagnosed at Stage 1.” At Stage 1, “these diseases are most treatable and curable . . . early diagnosis means dramatically increased survival rates.” According to the bill author, “the common Pap test does not detect ovarian or uterine cancer. Additional tests are readily available to diagnose them, but they are underutilized. This bill doesn’t dictate any type of treatment or testing by doctors, or call for the coverage of experimental therapies. It makes medically recognized, reliable tests more widely available to the women who can benefit from them.” (Lieber, 2008)

Current Law

Requirements in current law address both screening and diagnostic tests. For screening, current law requires health plans and insurers are to cover:

- all generally medically accepted cancer screening tests;² and
- an annual cervical cancer screening test upon the referral of the patient’s physician and surgeon, a nurse practitioner, or certified nurse midwife, providing care to the patient and operating within the scope of practice otherwise permitted for the license. Coverage for this test includes the conventional Pap test and the Federal Drug Administration (FDA)-approved human papillomavirus (HPV) screening test.³

With the exception of the cervical cancer screening tests, current law does not specify what cancer screening tests are “generally medically accepted.” Most health plans and insurers cover screening tests ordered by a health care provider subject to meeting the health plan, insurer, or medical groups’ criteria for “medical necessity.” Medical necessity criteria are typically based on recommendations of the U.S. Preventive Services Task Force (USPSTF) or American Cancer Society (ACS) guidelines.

² Health and Safety Code, Section 1367.665, Insurance Code Section 10123.20

³ Health and Safety Code, Section 1367.66 and Insurance Code Section 10123.18

All health care service plans regulated by the Department of Managed Health Care are required to provide diagnostic services as part of the minimum “basic health care services” benefit. Diagnostic services are those “diagnostic laboratory services, diagnostic and therapeutic radiological services, and other diagnostic services, which shall include, but not be limited to, electrocardiography and electroencephalography.”⁴ Health insurance products regulated by the California Department of Insurance have no statutory minimum services, except specific mandated benefits. Nonetheless, health insurance products generally cover physician and hospital services and medical tests.

Populations Affected

AB 1774 will primarily affect insured women under age 65 years. Table 2 details the 2008 expected new cases and expected deaths for the under age 65 population in California. For all gynecological cancers (cervical, uterine, ovarian, vaginal, vulva, and other cancers of the female genital system), there are 4,717 new cases expected and 1,119 expected deaths. Looking at the three most common gynecological cancers (cervical, uterine, and ovarian), the greatest number of expected new cases are from uterine cancer, and the greatest number of expected deaths are from ovarian cancer.⁵

Table 2. Female Genital System Cancer: Expected New Cases and Expected Deaths in Under 65 Population for 2008⁶

Gynecological Cancers	Expected New Cases	Expected Deaths
Female genital system	4,717	1,119
Cervical	1,158	270
Uterine (primarily endometrial)	1,952	198
Ovarian	1,210	577

Sources: American Cancer Society, California Division and Public Health Institute, California Cancer Registry (CCR). *California Cancer Facts and Figures, 2008*.

Notes: The total new expected cases and deaths for 2008 were multiplied by proportion of cases and deaths that were under age 65 years from 1988–2002. For the female genital system category, the total new expected cases and deaths were multiplied by proportion of ovarian, cervical, and uterine cancer cases and deaths that were under age 65 from 1988–2002.

In California, it is estimated that the percentage of the female population under age 65 years with a cervical cancer diagnosis is approximately 0.16%. For uterine cancer, the estimated prevalence is approximately 0.18%, and for ovarian cancer the estimated prevalence is 0.09% (CHIS, 2005; SEER, 2004).⁷

Key Assumptions for CHBRP Analysis

Two assumptions are made for the purpose of this analysis: (1) determinations of medical necessity would be made exclusively by health care providers, (2) screening tests would be a

⁴ Health and Safety Code, Section 1345(b)(3); Title 28 California Code of Regulations, Section 1300.67(i)(d).

⁵ Most, but not all, of these cancers are endometrial cancers.

⁶ Although AB 1774 would primarily affect females under 65 years, some females over 65 who are eligible for both Medicare and Medi-Cal and are enrolled in Medi-Cal managed care plans may also be affected by the mandate.

⁷ Prevalence estimates were generated by applying the age-specific limited duration prevalence rates for women 20-64 (SEER, 2004) to the estimated number of women in each age category within the privately insured Californian population (CHIS, 2005).

covered benefit for all women, regardless of risk factors or symptoms, and (3) screening tests for initial diagnosis are the focus of concern rather than tests ordered to monitor the progression of a disease in a person with a confirmed diagnosis.

Determinations of Medical Necessity by Health Care Providers

Under the proposed mandate, health plans and insurers would be required to provide coverage for any test necessary for the screening and diagnosis of gynecological cancers when ordered by a physician, nurse practitioner, or certified nurse midwife. The bill is silent as to whether the health plan, health insurer, or medical group is precluded from conducting utilization management reviews based on their own medical necessity criteria for the purpose of making coverage determinations.

In existing law, there are examples of bills that do not address the right of the insurer to evaluate the health care provider's judgment. Under the cervical cancer screening test mandate, for example, insurers must provide coverage "upon referral" of a health care provider.

CHBRP initially assumed the bill, modeled on the current cervical cancer statute, would be interpreted by regulatory agencies as preserving the right of insurers to determine medical necessity prior to authorizing services. However, discussions with state regulators and state and federal agencies that administer publicly financed health insurance programs did not support this interpretation.

Because the bill has no precedent in current law, both the Department of Managed Health Care (DMHC) and the California Department of Insurance (CDI) view the phrase "in whose judgment" as reflecting a legislative intent to move discretion over whether a test is needed, and therefore a covered benefit, from the health plan and insurer to the individual medical providers. State and federal agencies that administer programs for Medi-Cal, Managed Risk Medical Insurance Board programs, and CalPERS were also consulted and their interpretation of the bill was consistent with those of the regulatory agencies. Conversations with the bill author staff also indicated it was the bill author's intent to allow health care providers to use their judgment and not be "second-guessed" by health plans⁸. Consultations with legal counsel suggested that the interpretation of the bill language would end up being adjudicated in the courts.

Based on these discussions, CHBRP assumes, for the purpose of this analysis, that all women will have access to coverage for screening tests, as long as it was considered necessary "in the judgment" of the health care provider.

Screening and Diagnostic Tests Would Be a Covered Benefit for All Women, Regardless of Risk Factors or Symptoms

All female enrollees in plans subject to AB 1774 would be covered for screening tests ordered by a health care provider because every woman is at risk for gynecological cancer. The risk level varies from average to high risk depending on whether a woman has one or more risk factors for these cancers. Factors that place a woman at risk for ovarian cancer include family history and having a mutation of the *BCRA1* or *BCRA2* gene. Risk factors for cervical cancer include having

⁸ Personal communication with Barry Steinhart, Office of Assemblymember Lieber, February 12, 2008.

the HPV virus, family history, smoking, and having HIV or chlamydia. Risk factors for endometrial cancer include family history, obesity, and tamoxifen treatment for breast cancer. Some women in the covered population are asymptomatic, whereas others have symptoms of a gynecological cancer. For example, women with symptoms for ovarian cancer present to their health care provider with persistent bloating, pelvic or abdominal pain, difficulty eating or feeling full quickly, and urgent or frequent urination. Symptoms of cervical cancer include abnormal uterine bleeding, abnormal vaginal discharge, and pain during intercourse. Abnormal uterine bleeding is the primary symptom of endometrial cancer.

CHBRP assumes the bill will have minimal effect on symptomatic women and women at high risk because health plans and insurers currently cover the tests for these populations consistent with the recommendations of the U.S. Preventive Services Task Force and American Cancer Society. CHBRP assumes the bill would primarily affect coverage of screening tests for asymptomatic women who are not at high risk of developing the cancer.

Screening and Diagnostic Tests to Facilitate Initial Diagnosis

Screening refers to testing for a condition before a person has symptoms. Diagnostic tests are procedures that are used to confirm whether a person has cancer.

Because the intent of the bill is to cover those tests necessary to facilitate an initial diagnosis of cancer, this report will focus on those FDA-approved screening and diagnostic tests which are available to health care providers to assist in the early diagnosis of these diseases rather than those tests used to monitor a disease once a diagnosis has been confirmed.

State Activities Related to Screening for Gynecological Cancers

The Cancer Detection Section of the California Department of Public Health administers a statewide program, “Every Woman Counts,” to provide screening and treatment for breast and cervical cancer. The program provides screening for cervical cancer to the uninsured.

The California Department of Health Services (DHS) conducts a “Cervical Cancer Community Awareness Campaign” to provide awareness, assistance, and information regarding cervical cancer and the human papillomavirus (HPV).”

Thirty states currently mandate coverage of cervical cancer screening (BCBS 2007). Five states have enacted laws mandating coverage of ovarian cancer tests for surveillance or monitoring of women who are at risk of ovarian cancer and/or for women who have ovarian cancer. These states typically define “at risk” as women with a family history of cancer (MHBAC, 2007).

Federal Activities Related to Screening for Gynecological Cancers

At the federal level, there are ongoing efforts by the gynecologic cancer community in the legislative arena that are aimed at encouraging additional government support of gynecologic cancer research, education and training: These include:

- Johanna’s Law: The Gynecologic Cancer Education and Awareness Act of 2005 (H.R. 1245/S.1172). On January 12, 2007, President Bush signed into law this bill that funds a

national campaign to raise awareness about gynecologic cancers among women and their health care providers. Administered through Centers for Disease Control and Prevention and the Office of Women's Health at the Public Health Service, this campaign is intended to educate women about early warning signs of gynecologic cancers.

- Ovarian and Cervical Cancer Awareness Act of 2007 (HR 2468) introduced on May 23, 2007: Amends Johanna's Law to revise requirements for a national public awareness campaign regarding gynecologic cancers to: (1) require the Secretary of Health and Human Services specifically to increase awareness and knowledge of ovarian and cervical cancers; and (2) expand such campaign to include public service announcements targeted to low-income women.
- Ovarian Cancer Biomarker Research Act of 2008 (S2569/HR3689). To amend the Public Health Service Act to authorize the Director of the National Cancer Institute to make grants for the discovery and validation of biomarkers for use in risk stratification for, and the early detection and screening of, ovarian cancer.

Analytic Approach

This report provides an analysis of the medical, financial, and public health impacts of AB 1774. The Medical Effectiveness section of this report focuses on the accuracy of the screening and diagnostic tests and outcomes associated with screening tests for all asymptomatic women, as well as literature on diagnostic tests for symptomatic women because research has not been conducted on screening tests for asymptomatic women. The Utilization, Cost, and Coverage section examines the impact of a possible scenario where women would have coverage for any gynecological cancer test for which they could obtain orders from a physician, nurse practitioner, or certified nurse midwife, even if the test was not considered to be medically necessary per health plans medical necessity criteria. The Public Health section of this report examines the possible benefits and harms for women stemming from the scenario illustrated in the Utilization, Cost, and Coverage section.

MEDICAL EFFECTIVENESS

The medical effectiveness review for AB 1774 focused on the three most common types of gynecological cancers: cervical cancer, ovarian cancer, and endometrial or uterine cancer. As indicated in the Introduction, these cancers account for 90% of all gynecological cancers in California. The tests used to screen for and diagnose these three cancers are also used for screening and diagnosis of other, less common gynecological cancers.

As indicated in the Introduction, the medical effectiveness review examined the literature on tests that are used to screen for and/or diagnose gynecological cancers.⁹ Literature on tests performed as part of a diagnostic “workup” on women with an initial diagnosis of a gynecological cancer were not included nor was literature on treatments for gynecological cancers.

Literature Review Methods

A literature search was performed to retrieve studies of the accuracy of screening tests used to screen or diagnose women for gynecological cancers and studies of the impact of screening on morbidity and mortality from these cancers. The following databases that index peer-reviewed literature were searched: PubMed (MEDLINE and other PubMed records), the Cochrane Database of Systematic Reviews, the Cumulative Index of Nursing and Allied Health Literature, Web of Science (Science Citation Index and Social Science Citation Index), DynaMed, Global Health, and EconLit. The National Guideline Clearinghouse and the Health Technology Assessments Database produced by the Centre for Reviews and Dissemination were also searched. In addition, the Web sites maintained by the National Comprehensive Cancer Network, the National Institute of Clinical Excellence, the Scottish Intercollegiate Guideline Network, and the U.S. Preventive Services Task Force (USPSTF) were searched to identify evidence-based guidelines for screening and diagnosis of gynecological cancers.

Studies with the following research designs were included: meta-analyses, systematic reviews, evidence-based guidelines, randomized controlled trials (RCTs), nonrandomized studies with comparison groups, and studies that compared the accuracy of a screening or diagnostic test to a reference standard. The search was limited to studies published in English. The timeframes for the literature searches varied across the three cancers. For cervical cancer, the search was limited to studies published from 2005 to present, because the California Health Benefits Review Program (CHBRP) previously reviewed literature on screening and diagnostic tests for cervical cancer published from 1985 through 2005 for a report on DNA testing for the human papillomavirus (HPV) that was issued in 2006 (CHBRP, 2006). For ovarian cancer, the search was limited to studies published from 2004 to present, because CHBRP previously reviewed literature on screening and diagnostic tests for cervical cancer published from 1985 through 2003 for a report on ovarian cancer screening that was issued in 2004 (CHBRP, 2004). For endometrial cancer, a topic CHBRP has not previously addressed, the search encompassed literature published from 1995 to present.

⁹ Screening may be provided to all women, women in a certain age group, or targeted to those with a family history or other factors suggesting they may be at above-average risk. Unless otherwise specified, screening in this report will refer to all women in the age range screened, not just those at high risk.

Thirty-three pertinent studies were identified, retrieved, and reviewed. A more thorough description of the methods used to conduct the medical effectiveness review and the process used to grade the evidence for each outcome measure is presented in Appendix B: Literature Review Methods. Appendix C includes tables that describe the studies that CHBRP reviewed and their findings.

Outcomes Assessed

In order for a screening test for a gynecological cancer to be effective, the test must be able to detect the cancer at a sufficiently early stage that treatment can reduce the risk of death, the severity of illness, and/or the duration of symptoms. In addition, the test should accurately distinguish women who have the cancer from women who do not have it. The rate of false-positive tests should be low to minimize the number of women who do not have a cancer who undergo treatment unnecessarily. Avoiding unnecessary treatment is especially important for gynecological cancers because abdominal surgery to remove affected organs is the first-line treatment for these cancers. Premenopausal women who have these organs removed can no longer bear children. False-negative rates should also be low to ensure that women who have a gynecological cancer have an opportunity to obtain treatment when the cancer is at an early stage.

Most studies of the accuracy of screening and diagnostic tests compare the test(s) they are evaluating to a reference standard. In studies of gynecological cancers, the reference standard is usually histology of tissue obtained from a biopsy (i.e., tissue analyzed by a pathologist under a microscope). Histology is used as a reference standard because it is a highly accurate means for diagnosing cancer. Some studies also compare two or more tests to one another as well as the reference standard.

A variety of statistics are used to assess the accuracy of screening and diagnostic tests. The statistics reported in the studies that CHBRP reviewed are described below.

Sensitivity is the probability that a test result will be “positive” if a person *has* the disease.

Specificity is the probability that a test result will be “negative” if a person *does not have* the disease.

Likelihood ratio is a statistical test that indicates the validity of a screening or diagnostic test. It is a ratio of the likelihood that the result of a test for a given disease would be expected in a person who has the disease to the likelihood that the same result would be expected in a person who does not have the disease. A likelihood ratio of 1.0 signifies that a test for a given disease has no ability to predict whether a person has the disease (i.e., ratio of 1:1).

Positive Predictive Value (PPV) is the proportion of persons with positive test results who are correctly diagnosed. It is a function of the specificity of a test and the prevalence of the disease in the population tested. The PPV of a test is always lower for diseases that have a low prevalence than for those that have a high prevalence regardless of the specificity of the test.

Negative Predictive Value (NPV) is the proportion of persons with negative test results who are correctly diagnosed. NPV is a function of the sensitivity of a test and the prevalence of disease in the population tested. Regardless of the sensitivity of a test, the NPV rises as the prevalence of the disease in the population decreases.

Relative Sensitivity is the ratio of the sensitivity of the test being evaluated to the sensitivity of the test to which it is being compared (e.g., HPV DNA test vs. Pap test for cervical cancer screening). A relative sensitivity of 1.0 signifies that the tests are equally sensitive (i.e., ratio of 1:1).

Relative Positive Predictive Value (Relative PPV) is the ratio of the PPV of the test being evaluated to the PPV of the test to which it is being compared. A relative PPV of 1.0 signifies that the PPVs of the tests are equal (i.e., ratio of 1:1).

Study Findings

Cervical Cancer

Conventional cytology (i.e., Pap test) has been used for many years to screen asymptomatic women for cervical cancer. A systematic review conducted for the USPSTF in 2003 concluded that the preponderance of evidence from multiple nonrandomized studies indicates that routinely screening asymptomatic women under age 65 who are sexually active and have a cervix (i.e., have not had a hysterectomy) with conventional cytology reduces morbidity and mortality from cervical cancer (USPSTF, 2003).¹⁰

Repeat testing with conventional cytology is often used to confirm abnormal findings from an initial test and determine whether further diagnostic testing is warranted. If abnormal findings are confirmed, a colposcopy is performed. *Colposcopy* is an outpatient procedure that does not require anesthesia. A colposcope, a lighted, magnifying instrument, is used to illuminate the vagina and cervix. A vinegar solution is applied to the vagina and cervix so that any abnormal tissue will turn white, which permits a physician to see it more clearly. If a physician finds abnormal tissue during colposcopy, he or she will excise a tissue specimen for biopsy. The tissue specimen is then examined by a pathologist under a microscope.

Conventional cytology and colposcopy with biopsy can detect lesions at a precancerous stage.¹¹ These lesions can be removed on an outpatient basis under local anesthetic, obviating the need to perform a hysterectomy, a major abdominal surgery, in which the female reproductive organs are removed. Even if lesions are cancerous, most women can be treated successfully with hysterectomy if they are detected at an early stage in which the cancer is localized in the cervix (USPSTF, 2003). Cervical cancer grows slowly, which increases the likelihood that routine screening will detect precancerous lesions or localized cancer.

¹⁰ There is limited direct evidence to indicate the optimal ages for starting and stopping cervical cancer screening as well as the appropriate interval for screening. The USPSTF found indirect evidence that most of the benefits of cervical cancer screening can accrue by screening women at least every 3 years commencing at age 21 or within 3 years of onset of sexual activity (whichever comes first) (USPSTF, 2002). Current law in California requires health plans to provide coverage for annual screening for cervical cancer.

¹¹ Further details on the classification of precancerous lesions and other types of abnormal cytology are presented in CHBRP's 2006 report on cervical cancer screening (CHBRP, 2006).

There is a preponderance of evidence from multiple nonrandomized studies that screening asymptomatic women under age 65 and who are sexually active and have not had a hysterectomy with conventional cytology (Pap test) reduces morbidity and mortality from cervical cancer.

Most recent studies of screening and diagnostic testing for cervical cancer have focused on newer technologies for identifying women with cervical cancer. These studies can be divided into two major groups: studies of liquid-based cytology and studies of DNA testing to identify women who have the human papillomavirus (HPV).

In conventional cytology, a tissue specimen from a woman's cervix is placed directly on a slide for analysis, whereas in *liquid-based cytology*, the sample is immersed in a liquid. The rationale for liquid-based cytology is that using a liquid medium could improve the sensitivity of Pap tests (i.e., increase the probability that a positive test result indicates that a woman has cervical cancer or precancerous lesions) and decrease the proportion of specimens that are unsatisfactory for assessment.

HPV is the most important risk factor for developing cervical cancer. Although HPV infection is asymptomatic and clears on its own among most women, some women contract "high-risk" strains of HPV that, if undetected, can lead to the development of precancerous lesions on the cervix. If precancerous lesions are not identified and treated, they can become cancerous. Approximately two-thirds of all cervical cancers are caused by HPV 16 and 18 (ACS, 2007).¹²

Some of these studies have investigated the use of liquid-based cytology and/or HPV DNA testing as primary screening tools for use in place of conventional cytology. Others have evaluated the effectiveness of newer technologies for identifying women with *abnormal cytology* (i.e., women who have had an abnormal Pap test) who should receive a colposcopy (and biopsy if the colposcopy finds abnormalities). These studies compared repeat testing with conventional cytology to testing with newer technologies alone or in combination with conventional cytology. A number of studies did not specify whether the women who participated in the study had abnormal cytology or combined asymptomatic women with abnormal cytology and women who had not been previously screened (Abulafia et al., 2003; CHBRP, 2006; Coste et al., 2003; Karnon et al., 2004; Klinkhamer et al. 2003; USPSTF, 2003). In light of this limitation, the discussion of the literature on cervical cancer testing will focus on those studies for which the population studied consisted solely of either asymptomatic women at average risk for cervical cancer or asymptomatic women at high risk due to abnormal cytology. All studies used colposcopy and/or histology as a reference standard. None assessed the impact of these newer technologies on morbidity or mortality from cervical cancer.

Screening of Asymptomatic Women

Liquid-based cytology. Three studies compared the accuracy of liquid-based cytology to conventional cytology for screening asymptomatic women at average risk for cervical cancer (Kirschner et al., 2006; Mattosinho de Castro Ferraz et al., 2004; Ronco et al., 2006a; Ronco et

¹² A vaccine for cervical cancer was recently approved by the Food and Drug Administration. Further information about this vaccine can be found in a report on vaccination for cervical cancer that CHBRP issued in 2007 (CHBRP, 2007).

al., 2006b).¹³ The preponderance of evidence from these studies suggests that liquid-based cytology and conventional cytology have equal sensitivities for detection of neoplasia¹⁴ (i.e., are equally accurate for identifying women who have abnormal cytology). One study found no difference in the percentage of women with false-positive results (Kirschner et al., 2006). However, the PPV for liquid-based cytology is lower than the PPV for conventional cytology (relative PPV = 0.6) (Ronco et al., 2006a; Ronco et al., 2006b).

The preponderance of evidence suggests that liquid-based cytology and conventional cytology are equally accurate for screening asymptomatic women for cervical cancer.

HPV DNA test. One meta-analysis and two individual studies compared the accuracy of the HPV DNA test to conventional cytology for screening asymptomatic women at average risk for cervical cancer (Koliopoulos et al. 2007; Mayrand et al., 2007; Ronco et al., 2006a; Ronco et al., 2006b). These studies found that the PPVs and NPVs of HPV DNA testing and conventional cytology were similar for identifying women for whom a diagnosis of neoplasia (\geq CIN 2)¹⁵ was confirmed by colposcopy and biopsy. In other words, the tests correctly identified similar percentages of women with positive and negative test results.

The preponderance of evidence suggests that the HPV DNA test and conventional cytology are equally accurate for screening asymptomatic women for cervical cancer.

Multimodal screening. Two studies have examined multimodal strategies for screening asymptomatic women at average risk for cervical cancer (Mayrand et al., 2007; Ronco et al., 2006a; Ronco et al., 2006b). Mayrand and colleagues (2007) compared HPV DNA testing and conventional cytology to conventional cytology alone for detection of high-grade neoplasia (\geq CIN 2+). The study found that the two screening methods had similar specificity and NPV, but that screening with both HPV DNA testing and conventional cytology had greater sensitivity and a lower PPV than screening with conventional cytology alone. Ronco and colleagues (2006a and 2006b) compared HPV DNA testing and liquid-based cytology to conventional cytology for detection of high-grade neoplasia (\geq CIN 2+). The sensitivities of the two screening methods were similar, but among women aged 25–34 years, PPV was higher for HPV DNA testing and liquid-based cytology to conventional cytology than for conventional cytology.

One study investigated the impact of performing both HPV DNA testing and conventional cytology and using abnormal findings on one test to triage women who had abnormal findings on the other test to either repeat testing or further diagnostic workup with colposcopy (Mayrand et al., 2007). The authors found that using the HPV DNA test to triage women for whom conventional cytology identified high-grade neoplasia (\geq CIN 2+) increased the PPV of screening and had an equally high NPV. They reported similar findings for the use of conventional cytology (finding of \geq CIN 2+) to triage women who test positive. In other words,

¹³ Ronco and colleagues published two articles that report findings from a single RCT. One article presented findings for all women enrolled in the study (Ronco et al., 2006a). The other article reported findings for women aged 25 to 34 years (Ronco et al., 2006b).

¹⁴ The term *dysplasia* is sometimes used instead of neoplasia.

¹⁵ \geq CIN 2 indicates that a woman has histology consistent with *cervical intraepithelial neoplasia/moderate or carcinoma in situ*. In the United States, results of conventional and liquid-based cytology tests are reported using the 2001 Bethesda System Terminology (CHBRP, 2006).

using the HPV DNA test to triage women who had high-grade neoplasia or using conventional cytology to triage women who have HPV increased the percentage of women with positive tests who are diagnosed accurately.

The preponderance of evidence suggests that performing both the HPV DNA test and either conventional or liquid-based cytology increases the percentage of women with positive tests diagnosed accurately, if the results of one test are used to triage women with abnormal findings on the other test.

Screening Asymptomatic Women at High Risk (due to abnormal cytology and/or previous history of cervical lesions)

As indicated previously, some studies have examined the use of liquid-based cytology and/or HPV DNA testing to determine which women with abnormal cytology (i.e., an abnormal Pap test) should receive further testing with colposcopy (and biopsy if the colposcopy yields abnormal findings) and which can be managed by repeating conventional cytology at more frequent intervals. These studies compared repeat testing with conventional cytology to testing with these newer technologies alone or in combination with conventional cytology.

Liquid-based cytology. Two nonrandomized studies have assessed the accuracy of liquid-based cytology for detecting cervical lesions (LSIL+)¹⁶ among women with abnormal cytology or a history of previous cervical lesions (Hussein et al., 2005; Longatto Filho et al., 2005). The studies compared performing liquid-based cytology to repeat testing with conventional cytology. The authors reported that the PPVs and NPVs for liquid-based cytology and conventional cytology were similar. In other words, the tests correctly diagnose similar percentages of persons with positive and negative test results.

The preponderance of evidence from two nonrandomized studies suggests that liquid-based cytology alone may be no more accurate than conventional cytology alone at identifying women with abnormal cytology who need a colposcopy to determine whether they have cervical cancer or precancerous lesions.

HPV DNA test. Two nonrandomized studies evaluated the effectiveness of using the HPV DNA test to identify women with abnormal cytology who should be referred for colposcopy in lieu of repeat testing with conventional cytology (Lee et al., 2004; Monsonego et al., 2006). These studies found that the PPVs of the HPV DNA test and repeat conventional cytology for high-grade neoplasia (\geq CIN 2+) were similar and that the HPV DNA test had a higher NPV. In other words, both the tests correctly identified a similar percentage of women with positive results who required further testing with colposcopy and biopsy, but the HPV DNA test correctly identified a larger percentage of women who could be managed with repeat conventional cytology.

¹⁶ Under the 2001 Bethesda System Terminology, the classification LSIL indicates that a woman has cytology that indicates the presence of a low-grade squamous intraepithelial lesion (CHBRP, 2006).

The available evidence from two nonrandomized studies suggests that the HPV DNA test may be more accurate than conventional cytology alone at identifying women with abnormal cytology who should undergo colposcopy.

Multimodal screening. One meta-analysis and two nonrandomized studies have examined multimodal strategies for determining which women with abnormal cytology should be referred for further testing with colposcopy and biopsy (Arbyn et al., 2005; Lee et al., 2004; Saqi et al., 2006). One nonrandomized study assessed the accuracy of performing both the HPV DNA test and conventional cytology relative to conventional cytology alone to determine whether further testing was necessary (Lee et al., 2004). The findings of this study are inconclusive. Performing both the HPV DNA test and conventional cytology increases the number of women with negative test results who are correctly returned to screening relative to conventional cytology alone (i.e., increases NPV), but decreases the percentage of women with positive test results who are correctly referred for further testing with colposcopy and biopsy (i.e., decreases PPV).

One meta-analysis synthesized findings from studies of the accuracy of performing both conventional cytology and the HPV DNA test on women with abnormal cytology and then using the results of the HPV DNA test to determine whether further testing with colposcopy was warranted (Arbyn et al., 2005). The authors analyzed the relative sensitivity and specificity of the two strategies for identifying women with high-grade neoplasia (\geq CIN 2+). They concluded the two strategies had similar specificity and that using the HPV DNA test to triage women who have abnormal findings upon repeat conventional cytology has a slightly higher sensitivity (relative sensitivity = 1.14). In other words, there is a slightly higher probability that women with positive results for both repeat conventional cytology and the HPV DNA test are correctly referred for colposcopy and biopsy than if the determination were based on repeat conventional cytology alone.

One nonrandomized study assessed the accuracy of performing both liquid-based cytology and the HPV DNA test on women with abnormal cytology and then using the results of the HPV test to determine whether referral for colposcopy was warranted (Saqi et al., 2006). The sensitivity, specificity, PPV, and NPV for this testing strategy were high.

There is clear and convincing evidence that performing both conventional cytology and the HPV DNA test on women with abnormal cytology and then using the results of the HPV DNA test to determine whether colposcopy should be performed yields slightly more accurate decisions about further testing than if decisions are based solely on repeat conventional cytology. There is insufficient evidence to ascertain the accuracy of other multimodal strategies for determining whether further testing with colposcopy is warranted.

Ovarian Cancer

Ovarian cancer is difficult to diagnose because many women do not become symptomatic until the cancer has reached an advanced stage. In addition, the symptoms of ovarian cancer are also symptoms of other non-cancerous conditions, such as digestive disorders and urinary tract infections. It was not until 2007 that experts on ovarian cancer reached a consensus on four symptoms that, if they exist together, suggest that a woman may have an early-stage ovarian

cancer. These symptoms are: bloating, pelvic or abdominal pain, feeling full quickly or having difficulty eating, and frequent or urgent need to urinate (ACS, 2007).

Another challenge of ovarian cancer is that a definitive diagnosis often cannot be made without performing surgery on the affected ovary. Due to the position of the ovaries in the body, this major abdominal surgery must be performed in a hospital under general anesthesia. In addition, in premenopausal women, removal of the ovaries leads to early menopause, which prevents them from bearing children.

The difficulty in diagnosing ovarian cancer at an early stage without major surgery has led researchers to study strategies for screening asymptomatic women for ovarian cancer or risk factors associated with it. The strongest risk factor for ovarian cancer is family history (i.e., hereditary risk). Genetic tests can be performed to determine whether a woman has a mutation of the *BCRA1* or *BCRA2* gene that further increases her risk of ovarian cancer.¹⁷ Age is also a risk factor for ovarian cancer in that the prevalence of ovarian cancer increases with age. Some studies have assessed the effectiveness of screening asymptomatic women with these risk factors, whereas others have examined the effectiveness of screening asymptomatic women at average risk or all women regardless of risk. In all studies of cancer screening tests, the reference standard was histology obtained during a surgical procedure for ovarian cancer.

Screening of Asymptomatic Women at Average Risk

Genetic testing for *BCRA1* or *BCRA2* mutations. The U.S. Preventive Services Task Force contracted with the Oregon Evidence-based Practice Center to prepare a systematic review of studies on the effectiveness of risk assessment, genetic counseling, and testing for *BCRA1* or *BCRA2* mutations (Nelson et al., 2005). Most of the studies identified by this systematic review examined the effectiveness of screening women with existing cancer or a strong family history of cancer. The authors concluded that there is insufficient evidence to ascertain the benefits and harms of screening asymptomatic women at average risk for ovarian cancer for these mutations. A simulation that used data obtained through the systematic review to estimate the impact of genetic testing for *BCRA1* or *BCRA2* mutations suggested that providing genetic testing to a hypothetical cohort of 100,000 women at all levels of risk for ovarian cancer would prevent only 31 cases of ovarian cancer (Nelson et al., 2005). The yield for a cohort of 100,000 at average risk would be lower (14 cases), whereas yields would be higher for women at moderate or high risk due to family history of ovarian cancer (230 and 530 cases, respectively). Although genetic testing for these mutations does not prevent ovarian cancer per se, some women who know that they have them choose to undergo prophylactic surgery to remove their ovaries, which eliminates their risk of developing ovarian cancer.

There is insufficient evidence to ascertain the benefits and harms of screening asymptomatic women at average risk for ovarian cancer for mutations of the <i>BCRA1</i> or <i>BCRA2</i> gene.

CA-125 blood test. Other studies have investigated the accuracy of screening asymptomatic women using a blood test to ascertain the level of CA-125, a protein that is more frequently found in ovarian cancer cells than in other cells. However, having a high CA-125 level does not

¹⁷ Having the *BCRA1* mutation increases a woman's lifetime risk for ovarian cancer from 2% to 26%, and having the *BCRA2* mutation increases lifetime risk to 10% (Nelson et al., 2005; NIH, 2002).

necessarily mean that a woman has ovarian cancer, because a woman's CA-125 level may be elevated due to another cancer or a benign condition, such as endometriosis, or to physiological changes during the menstrual cycle (Bosse et al., 2006). A feasibility study for an RCT assessed the accuracy of using the CA-125 blood test to screen asymptomatic women who were postmenopausal and at average risk for ovarian cancer (Menon et al., 2005). The findings of this study suggest that screening for an elevated level of CA-125 can accurately detect ovarian cancer at an earlier stage than it can be detected in the absence of screening. Of 6,532 women screened, 16 underwent surgery and 5 were diagnosed with ovarian cancer (number of women screened per cancer detected = 1,306). The PPV was 19% (Menon et al., 2005). However, the study provides insufficient evidence that screening with the CA-125 test is beneficial, because findings for women who were screened were not compared to findings for a control group of unscreened women.

Evidence from a single nonrandomized study suggests that CA-125 may accurately detect ovarian cancer in postmenopausal women at an earlier stage than it can be detected in the absence of screening, but there is insufficient evidence to determine whether screening with CA-125 reduces morbidity and mortality.

Transvaginal ultrasound. Transvaginal ultrasound is another technology used to screen asymptomatic women for ovarian cancer. A transducer (i.e., a probe) is inserted into the vagina to provide an image of the pelvic organs and detect abnormalities in them. Two systematic reviews and one nonrandomized study with a comparison group published subsequent to the systematic views examined the accuracy of transvaginal ultrasound for screening asymptomatic women at average risk for ovarian cancer (Fung et al., 2004; USPSTF, 2004; van Nagell et al., 2007). PPVs ranged from 0% to 15.6%. The authors of these studies concluded that the preponderance of evidence suggests that transvaginal ultrasound can accurately detect ovarian cancer at an earlier stage than it can be detected in the absence of screening.

The number of women who needed to be screened to detect one case of ovarian cancer varied widely across the studies, as did the number of surgeries performed per cancer detected. In the three studies in which one or more cancers were detected, the number needed to screen ranged from 497 to 3,350. The number of surgeries performed per cancer detected ranged from 7 to 36 (Fung et al., 2004; van Nagell et al., 2007). No cancers were detected in two studies with samples of 435 and 500 women (Fung et al., 2005). The study that reported the most detailed data on stage of cancer at diagnosis reported that of 51 ovarian cancers diagnosed through screening, 55% were stage 1, 16% were stage 2, 12% were stage 3, and 14% were metastases from other cancers (van Nagell et al., 2007). The study also found that nine cancers were detected among women with negative transvaginal ultrasound screens who developed symptoms, all of which were stage II or stage III cancers.

Two studies have assessed the impact of screening with transvaginal ultrasound on morbidity and mortality from ovarian cancer. One study compared the 2- and 5-year survival rates of women enrolled in the study who developed ovarian cancer to survival rates of women with ovarian cancer who had not been screened. The authors reported that the 2- and 5-year survival rates were higher for women who had been screened (van Nagell et al., 2007). However, the survival rate was not calculated separately for women at increased risk for ovarian cancer due to

family history and for postmenopausal women at average risk.¹⁸ An earlier study, discussed in the systematic review by Fung and colleagues (2004), found that screening did not improve long-term survival. That study found no difference in ovarian cancer mortality between women who were screened and a control group of unscreened women over a 15-year period following the completion of a screening program.

The preponderance of evidence suggests that transvaginal ultrasound can accurately detect ovarian cancer at an earlier stage than it can be detected in the absence of screening and may improve short-term survival rates, but does not improve long-term survival.

Multimodal screening. Two systematic reviews and one RCT published subsequently evaluated the accuracy of multimodal screening of asymptomatic women at average risk using both transvaginal ultrasound and the CA-125 blood test (Fung et al., 2004; Lacey et al., 2006; USPSTF, 2004). One large, multi-site study conducted in the United States assessed the use of both the CA-125 test and transvaginal ultrasound to screen women aged 55 to 74 years without a family history of ovarian cancer (Lacey et al., 2006). Among 27,687 women screened, 860 surgeries were performed and 47 women were diagnosed with ovarian cancer (number needed to screen to detect one case of cancer = 483; surgeries per cancer detected = 18). The PPV of screening was low (1.1%).

Fung and colleagues' (2004) systematic review discussed findings from three studies in which women were initially screened with transvaginal ultrasound and those with positive results were referred for CA-125 testing. In the two studies that reported PPVs, the PPVs were 6.9% and 9.1%. The number of women who needed to be screened to detect one case of cancer ranged from 478 to 2,343. In the two studies that reported the number of surgeries performed, the numbers of surgeries per cancer diagnosed via screening were 11 and 15 (Fung et al., 2004).

This systematic review also reported findings from five studies in which all women were screened with the CA-125 test and those with positive results were referred for further screening with transvaginal ultrasound. The PPVs reported by these studies ranged from 0% to 26.8%. In the studies in which at least one cancer was detected, the number of women who needed to be screened to detect one case of cancer ranged from 667 to 2,000. Among studies that reported the number of surgeries performed, the number of surgeries per cancer detected via screening ranged from 4 to 6 (Fung et al., 2004). Only one of these studies compared outcomes for women who were screened to outcomes for a control group of unscreened women. That study found that women who were screened were more likely to have their cancers diagnosed at an early stage and had longer median survival following diagnosis (73 months versus 42 months) (Fung et al., 2004).

One systematic review examined studies of the potential benefit of adding color Doppler imaging to transvaginal ultrasound for screening asymptomatic women at average risk (Fung et al., 2004). The rationale for adding color Doppler imaging to transvaginal ultrasound is that it might enable physicians to more clearly visualize the pelvic organs. The systematic review

¹⁸ Van Nagell and colleagues' study (2007) enrolled premenopausal and postmenopausal women who had a family history of ovarian cancer as well as postmenopausal women who did not have a family history of this cancer. The authors reported sensitivity, specificity, PPV, and NPV separately for the two groups of women but did not report survival rates separately.

identified three studies in which women were screened consecutively or sequentially with transvaginal ultrasound and color Doppler imaging. The PPVs reported by these studies ranged from 10.5% to 33.3% and the number of women who needed to be screened to detect one case of cancer ranged from 1,253 to 2,953 (Fung et al., 2004).

The authors of the systematic reviews concluded that the preponderance of evidence suggests that screening asymptomatic women with both transvaginal ultrasound and the CA-125 test can accurately detect ovarian cancer at an earlier stage than it can be detected in the absence of screening (Fung et al., 2004; USPSTF, 2004). However, it is unclear whether multimodal screening is more accurate than screening with either transvaginal ultrasound or the CA-125 test alone. The variations in PPVs among studies of each of the screening strategies are so wide that it is difficult to determine whether any one strategy yields more accurate results than the others. In all cases, the numbers of women who needed to be screened to detect one case of cancer were large, and many women underwent unnecessary diagnostic workups and surgeries due to false-positive results.

Evidence of the accuracy of screening asymptomatic women at average risk with both transvaginal ultrasound and the CA-125 test relative to screening with either test alone is ambiguous. Evidence of the impact on accuracy of adding color Doppler imaging to transvaginal ultrasound is also ambiguous.

Screening of Asymptomatic Women at Increased Risk

Four studies have investigated the accuracy of transvaginal ultrasound alone or in combination with the CA-125 blood test to screen women at elevated risk for ovarian cancer due to family history (Bosse et al., 2006; Lacey et al., 2006; van Nagell et al., 2007; Woodward et al., 2007).

Transvaginal ultrasound. One nonrandomized study examined the use of transvaginal ultrasound alone to screen women at elevated risk for ovarian cancer due to family history (van Nagell et al., 2007). The study found that transvaginal ultrasound is highly accurate for identifying women at increased risk who do not have ovarian cancer and is moderately accurate for identifying women at increased risk who have ovarian cancer. The authors compared the 2- and 5-year survival rates of women enrolled in the study who developed ovarian cancer to women with ovarian cancer who had not been screened. They reported that the 2- and 5-year survival rates were higher for women who had been screened (van Nagell et al., 2007). However, the survival rate was not calculated separately for women at increased risk for ovarian cancer due to family history and for postmenopausal women at average risk.

The available evidence suggests that transvaginal ultrasound is highly accurate for identifying women at increased risk who do not have ovarian cancer, is moderately accurate for identifying women who have ovarian cancer, and may improve short-term survival.

Multimodal screening. One RCT and two nonrandomized studies assessed the accuracy of multimodal screening for women at increased risk for ovarian cancer due to family history with both transvaginal ultrasound and the CA-125 test (Bosse et al., 2006; Lacey et al., 2006; Woodward et al., 2007). One study (Bosse et al., 2006) reported that multimodal screening had high sensitivity and specificity (i.e., was highly accurate at identifying both women with and women without ovarian cancer), whereas another reported only moderate sensitivity and

specificity (Woodward et al., 2007). The PPVs also varied across studies. These three studies provide insufficient evidence that multimodal screening is more accurate than screening with transvaginal ultrasound alone for women at increased risk of ovarian cancer.

The numbers needed to screen to detect one case of ovarian cancer were smaller among studies of multimodal screening for women at increased risk than among studies of multimodal screening for women at average risk. Whereas the numbers of women at average risk who needed to be screened to detect one case of ovarian cancer ranged from 478 to 2,953 (Fung et al., 2004), the numbers of women at increased risk who needed to be screened ranged from 240 to 341 (Bosse et al., 2006; Lacey et al., 2006). However, the numbers of surgeries performed per ovarian cancer diagnosed via screening were generally higher, ranging from 10 to 30 surgeries per cancer diagnosed (Bosse et al., 2006; Woodward et al., 2007).

There is insufficient evidence to determine whether screening women with both transvaginal ultrasound and the CA-125 test yields more accurate results than screening with transvaginal ultrasound alone.

Diagnosis of Symptomatic Women

No studies of the effectiveness of diagnostic tests for ovarian cancer were identified that had been published since the previous CHBRP report on ovarian cancer was issued.

Endometrial Cancer

Endometrial cancer refers to cancer of the endometrium (i.e., the lining of the uterus). The primary symptom of endometrial cancer is abnormal uterine bleeding. However, abnormal uterine bleeding is also a symptom of several benign conditions, such as polyps and fibroids. Most women with abnormal bleeding have one of these benign conditions (Gupta, et al., 2002). Endometrial cancer is more easily diagnosed in postmenopausal women than premenopausal women, because any uterine bleeding in postmenopausal women is abnormal. Among premenopausal women, additional assessment is needed to distinguish women with abnormal uterine bleeding due to a benign or cancerous endometrial condition from women who have irregular menstrual cycles. The survival rate for endometrial cancer is high regardless of whether asymptomatic women are screened because most women experience symptoms of abnormal bleeding while the cancer is at an early stage (ACS, 2007).

Screening of Asymptomatic Women at Average Risk (those not presenting with abnormal uterine bleeding)

The literature search retrieved no studies of the accuracy and effectiveness of screening asymptomatic women for endometrial cancer. One meta-analysis included studies that enrolled both asymptomatic and symptomatic women as well as studies that enrolled only symptomatic women, but did not report findings separately for asymptomatic women (Dijkhuizen et al., 2000).

There is insufficient evidence to determine whether there are any effective tests for screening asymptomatic women for endometrial cancer.

Diagnosis of Symptomatic Women

Two meta-analyses and three systematic reviews of studies of the accuracy of diagnostic tests for endometrial cancer were retrieved (Clark et al., 2002a; Clark et al., 2002b; Dijkhuizen et al., 2000; Farquhar et al., 2003; Gupta et al., 2002). All five syntheses assessed studies that compared findings from diagnostic tests to histology.

One meta-analysis and one systematic review examined the accuracy of transvaginal or transabdominal ultrasound to diagnose endometrial cancer by measuring the thickness of the endometrial lining (Farquhar et al., 2003, Gupta et al., 2002). Researchers are interested in evaluating the accuracy of ultrasound for diagnosing endometrial cancer because it is less invasive than performing an endometrial biopsy to obtain a tissue sample for histological examination. The systematic review concluded that the evidence regarding the diagnostic accuracy of ultrasound for endometrial carcinoma and hyperplasia in premenopausal women is ambiguous (Farquhar et al., 2003). The meta-analysis concluded that among postmenopausal women, ultrasound accurately diagnoses women who do not have endometrial pathology, but does not accurately distinguish between women with benign and cancerous conditions (Gupta et al., 2002).

Evidence of the accuracy of ultrasound for diagnosing endometrial cancer in premenopausal women with abnormal uterine bleeding is ambiguous. However, there is evidence that ultrasound can accurately identify postmenopausal women with abnormal uterine bleeding who do not have endometrial cancer.

One meta-analysis and one systematic review assessed the diagnostic accuracy of endometrial sampling relative to histology obtained through more invasive procedures such as dilatation and curettage, hysteroscopy, or hysterectomy (Clark et al., 2002a; Dijkhuizen et al., 2000). Endometrial sampling is performed by inserting a small, hollow tube into the uterus through the vagina and cervix. Gentle suction is used to remove a sample of the endometrium for biopsy. Both the meta-analysis and the systematic review concluded that endometrial sampling is a highly accurate procedure for diagnosing endometrial cancer, which suggests that performing endometrial sampling could help target more invasive diagnostic procedures toward women most likely to have endometrial pathology. The meta-analysis reported that this endometrial sampling is more accurate in postmenopausal women than in premenopausal women (Dijkhuizen et al., 2000).

Two systematic reviews investigated the diagnostic accuracy of hysteroscopy relative to histology obtained through hysterectomy (Clark et al., 2002b; Farquhar et al., 2003). A hysteroscopy is a procedure performed under anesthesia in which a hysteroscope, a long, narrow tube with a built-in viewing device is inserted in the uterus. A physician uses a hysteroscopy to view the uterus and carry out a biopsy. Both systematic reviews found clear and convincing evidence that hysteroscopy is an accurate diagnostic procedure for endometrial cancer.

There is a preponderance of evidence that both endometrial sampling and hysteroscopy are effective procedures for diagnosing endometrial cancer.

Summary of Findings

Cervical Cancer

Screening Asymptomatic Women at Average Risk (no previous history of abnormal cervical cytology or cervical lesions)

- There is a preponderance of evidence that, among asymptomatic women who are sexually active and have not had a hysterectomy, screening with conventional cytology (i.e., Pap test) reduces the incidence of cervical cancer, because this test can detect precancerous lesions. Treatment of precancerous lesions can prevent a woman from developing cervical cancer. In addition, conventional cytology can reduce morbidity and mortality from cervical cancer by detecting cancerous lesions at an early stage at which treatment is most likely to be successful.
- A preponderance of evidence suggests that liquid-based cytology is no more accurate than conventional cytology for screening asymptomatic women for cervical cancer, regardless of whether it is performed alone or in conjunction with DNA testing for the human papillomavirus (HPV).
- The evidence of relative accuracy of the following tests for detecting cervical cancer among asymptomatic women is ambiguous:
 - HPV DNA test versus conventional cytology
 - Multimodal screening with the HPV DNA test and conventional cytology versus conventional cytology alone

Screening Asymptomatic Women at High Risk (due to abnormal cytology and/or previous history of cervical lesions)

- The available evidence suggests that the HPV DNA test and conventional cytology are equally accurate for identifying women with abnormal cytology (i.e., abnormal Pap test) who should undergo further testing with colposcopy (and biopsy if necessary) to determine whether they have cervical cancer or precancerous lesions.
- The evidence of relative accuracy of the following tests and technologies for identifying women with abnormal cytology who should receive further testing is ambiguous:
 - Liquid-based cytology versus conventional cytology
 - HPV DNA test plus conventional cytology versus conventional cytology alone
- The preponderance of evidence suggests that using the HPV DNA test to triage women with abnormal cytology on either an initial or a repeat test is more accurate than performing conventional cytology alone for determining which women should receive further testing.

Ovarian Cancer

Screening Asymptomatic Women at Average Risk (no familial risk history)

- There is insufficient evidence to determine the effectiveness of providing genetic tests for mutations associated with increased risk of ovarian cancer (i.e., *BRCA1* and *BRCA2* mutations) to women who do not have a family history (i.e., hereditary risk) of ovarian cancer.
- The preponderance of evidence suggests that screening asymptomatic women at average risk for ovarian cancer with transvaginal ultrasound and/or the CA-125 blood test can detect ovarian cancer at an earlier stage.
- However, there is insufficient evidence to determine whether screening asymptomatic women at average risk for ovarian cancer improves long-term morbidity and mortality
- Screening asymptomatic women at average risk for ovarian cancer would increase harms due to surgery and complications thereof.

Screening Asymptomatic Women at High Risk (with familial risk history)

- The available evidence suggests that among asymptomatic women at increased risk for ovarian cancer due to age and/or family history of ovarian cancer, annual screening with transvaginal ultrasound is accurate and may increase survival over the short term.
- There is insufficient evidence to determine whether multimodal screening of asymptomatic women with a family history of ovarian cancer using transvaginal ultrasound and CA-125 is yields more accurate results than screening with transvaginal ultrasound alone.

Endometrial Cancer

Screening Asymptomatic Women at Average Risk (those not presenting with abnormal uterine bleeding)

- No studies of the accuracy of screening tests for endometrial cancer or the impact of screening for endometrial cancer on morbidity or mortality were identified.

Diagnosing Women with Symptoms That May Indicate Cancer (those presenting with abnormal uterine bleeding)

- There is insufficient evidence to determine whether pelvic or transvaginal ultrasound can accurately diagnose endometrial hyperplasia or carcinoma among women with abnormal uterine bleeding.
- The preponderance of evidence suggests that endometrial biopsy and hysteroscopy can accurately diagnose endometrial carcinoma among women with abnormal uterine bleeding.

UTILIZATION, COST, AND COVERAGE IMPACTS

An estimated 22,362,000 people in California are enrolled in health care plans or have health insurance policies that would be affected by AB 1774. Of this group, an estimated 8,433,000 women 18 years and over would specifically be affected by this legislation.

This section presents the current, or baseline, coverage and costs of services used to screen and diagnose gynecological cancers. It then describes the estimated impact of AB 1774 on coverage and one set of estimates of possible utilization and cost effects, based on a plausible scenario developed with input from expert physician consultants, physicians in community-based practice, and relevant literature. The scenario is discussed below in *How Will Utilization Change as a Result of the Mandate?* The detailed assumptions used for the scenario are shown at the end of Appendix D.

For purposes of utilization and cost analysis, the California Health Benefits Review Program (CHBRP) made the simplifying assumption to focus only on three types of gynecological cancer: cervical, endometrial, and ovarian. Vaginal cancer uses the same screening tests as cervical cancer. Vulvar cancers are rare (340 new cases and 65 deaths per year). Fallopian tube cancers are also rare. Uterine cancers are predominantly endometrial. Other uterine cancers are sarcomas, which do not lend themselves to the same screening tests.

Present Baseline Cost and Coverage

Current Coverage of Mandated Benefit

CHBRP surveyed the largest major health plans and insurers regarding coverage. Responses to this survey represented 75.0% of the California Department of Insurance (CDI)-regulated and 85.4% of Department of Managed Health Care (DMHC)-regulated market. Overall, 84.0% of the privately insured market was represented. Although it is possible that the current coverage provisions for all enrollees in California differ from the survey-based coverage estimates, CHBRP has no reason to believe that such differences would have a material impact on the conclusions in this report, especially given the consistency of responses across health plans.

The results of this survey suggest that 100% of the privately and publicly insured population have coverage of gynecological cancer diagnostic tests for women with cancer symptoms or prior abnormal screening test results. In addition, 100% of the privately and publicly insured population have coverage for certain gynecological cancer screening tests for asymptomatic women, depending on the woman's risk factors for developing the cancer and medical appropriateness criteria. Coverage of gynecological cancer tests is the same across market segments—in health maintenance organizations (HMOs), preferred provider organizations (PPOs), those in the large-group, small-group, and individual private markets.

The standards used by plans to determine medical appropriateness and hence coverage of screening tests for symptomatic women and certain subgroups of asymptomatic women at high risk of developing these cancers appear to be broadly consistent with evidence-based clinical guidelines issued by the U.S. Preventive Services Task Force and American Cancer Society. Therefore, the bill would primarily affect coverage of screening tests for asymptomatic women at

average (i.e., low) risk of developing the cancer for which the test is screening, with the exception of Pap tests and human papilloma virus (HPV) DNA tests for women of certain ages (typically 30 years and over), which are already covered. Table D-1, in Appendix D, provides further details regarding current evidence-based standards of care and private health plan coverage of screening tests among asymptomatic women.

Coverage of diagnostic and screening tests in publicly financed insurance programs is consistent with the approach taken by the private plans. CalPERS Basic HMO members are covered for annual pelvic exams, Pap tests, and HPV screening tests, and all routine diagnostic testing and laboratory services recommended by the U.S. Preventive Services Task Force (USPSTF). CalPERS covers routine HPV testing starting from age 21 or 3 years after onset of sexual activity.

Health plans that provide services for enrollees in Medi-Cal managed care must provide all “medically necessary covered services” required of Medi-Cal and the basic scope of benefits required of all DMHC-regulated health plans. For asymptomatic, healthy adults, Medi-Cal managed care plans use the standards set by the USPSTF to determine the provision of clinical preventive services. Health plans are required to cover diagnostic, treatment and follow-up services that are medically necessary given the findings of risk factors.¹⁹

Although health plan contracts with the Department of Health Care Services (DHCS) require plans to ensure that the medical necessity of covered services be determined through utilization management procedures, these requirements would be superseded by the language in the proposed mandate, allowing medical necessity to be determined by the health care provider.

Beneficiaries enrolled in programs administered by the Major Risk Medical Insurance Board (MRMIB)—Major Risk Medical Insurance Program (MRMIP), Access for Infants and Mothers (AIM), and Healthy Families—are covered for benefits similar to those enrolled in DMHC-regulated managed care health plans.²⁰ Like other private and public HMO plans, routine testing is covered, subject to the health plan’s medical necessity requirements.

In the sections that follow, CHBRP focuses exclusively on the utilization and cost associated with screening tests for asymptomatic, average-risk women, since AB 1774 is not expected to affect coverage or utilization of diagnostic tests for symptomatic women or screening tests for high-risk women.

Current Utilization Levels and Costs of the Mandated Benefit

The following estimates were based on a large dataset of national commercial claims data that includes the inpatient and outpatient utilization and expenditures of 7 million people, with adjustments made to reflect the California population and market conditions. National datasets were used because their sample size is larger than California data, thus allowing for more precise statistical estimates.

¹⁹ Standard contract for commercial plans participating in the Medi-Cal Managed Care Program, 2006.

²⁰ MRMIB requires that participating plans comply with all requirements of the Knox-Keene Health Care Service Plan Act of 1975, including amendments as well as its application regulations; Title 10, CCR, Chapter 5.8, Article 3, Section 2699.6700(a).1

Current utilization levels

Currently, an estimated 792,000 Pap tests and 83,000 HPV tests are being performed annually in California. With these exceptions, no other gynecological cancer screening tests are covered for asymptomatic, average-risk women, so covered utilization of other screening tests for this population is zero. It is conceivable that some asymptomatic, average-risk women pay entirely out of pocket for additional screening tests; however, such utilization is likely to be of trivial magnitude, since these tests would fall outside of evidence-based clinical guidelines and are unlikely to be regarded as worth the price.

Unit price

The average prices of the screening tests considered most likely to experience increased utilization as a result of AB 1774 are shown in Table 1 and summarized here:

- Cervical cancer
 - Pap test \$41
 - HPV DNA test \$69
 - Colposcopy \$235
- Ovarian cancer
 - Transvaginal ultrasound \$363
 - CA-125 blood test \$45
 - Laparoscopy \$3,667
 - Laparotomy \$3,010
 - *BRCA1/2* genetic testing plus counseling \$3,334
- Endometrial cancer
 - Endometrial biopsy \$164
 - Dilation and curettage \$2,789
 - HNPCC genetic testing plus counseling \$2,341

These prices include professional fees for the test plus facility charges (when applicable) but assume that screening tests would be ordered during the woman's regular preventive visits to the doctor, so the cost of the screening tests does not include additional office visit charges.

Current premiums and expenditures

The pre-mandate per member per month (PMPM) premiums and expenditures in different market segments are detailed in Table 3. To summarize briefly:

- 2008 health insurance premiums for the population affected by AB 1774 are projected to total \$73.7 billion. Average premiums PMPM vary by market segment, from \$85.17 for Healthy Families to \$402.17 for CDI-regulated large group plans.

- Employers pay the majority of these premium costs (\$54.7 billion), with the remainder being paid by the employees.
- Total expenditures were \$79.3 billion, with the difference between premiums and expenditures being the \$5.6 billion that consumers paid out of pocket for services through deductibles and copayments.
- The amount spent out of pocket on uncovered gynecological cancer screening tests could not be ascertained, but as explained above, is unlikely to be substantial.

The Extent to Which Costs Resulting From Lack of Coverage Are Shifted to Other Payers, Including Both Public and Private Entities

As explained above in Current Coverage of the Mandated Benefit, public programs take the same general approach to covering gynecological cancer screening tests for average-risk, asymptomatic women that the private plans do, namely covering only tests for which there is evidence of medical appropriateness. Because Medi-Cal and other public insurance programs are no more generous in their coverage than the private plans, opportunities for cost-shifting would appear to be minimal. Similarly, CHBRP is unaware of any publicly funded clinics that would apply different criteria for the provision of these tests than those used by the health plans.

Public Demand for Coverage

As a way to determine whether public demand exists for the proposed mandate (based on criteria specified under SB 1704 [2007]), 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 those preferred provider organization (PPO) plans offered by CalPERS. These plans provide coverage similar to that of the privately self-insured plans. CalPERS PPO plans are administered by Blue Cross. The plans cover screening and diagnostic tests that are medically necessary as defined by Blue Cross of California’s Medical Policy. For cancer screening tests, Blue Cross’s Medical Policy relies on American Cancer Society’s Cancer Detection guidelines. Based on conversations with the largest collective bargaining agents in California, CHBRP concluded that unions currently do not include cancer screening tests in their health insurance policy negotiations. In general, unions negotiate for broader contract provisions such as coverage for dependents, premiums, deductibles, and coinsurance levels.²¹

Impacts of Mandated Coverage

How Will Changes in Coverage Related to the Mandate Affect the Benefit of the Newly Covered Service and the Per-Unit Cost?

Impact on Per-Unit Cost

It is conceivable that as a result of the elimination of utilization management, AB 1774 would result in a sharp increase in utilization of gynecological cancer screening tests among average-

²¹ Personal communication with the California Labor Federation and member organizations on March 25, 2008.

risk, asymptomatic women. If so, the per-unit cost of certain gynecological cancer screening tests could rise, depending on the nature of the test and the time frame. Tests performed in the hospital rather than the doctor's office (e.g., laparotomy, laparoscopy, and dilation and curettage) are more likely to experience price increases, particularly in the short run, due to the potential for capacity constraints. For tests that could be performed in either setting (e.g., transvaginal ultrasound), a shift may occur over time from hospital outpatient departments to physicians' offices. Over the long run, inflationary pressures due to increased demand are less likely, as supply expands in response to market opportunities. Important exceptions are tests for genetic mutations associated with high risk of developing certain gynecological cancers (e.g., HNPCC and *BRCA1/2*). These tests are patented by Myriad (www.myriad.com/), so monopoly power could allow the company to increase price as demand for their services grows.

How Will Utilization Change as a Result of the Mandate?

If insurers retained discretion over whether tests were needed, utilization would be expected to remain unchanged as a result of AB 1774. As noted above in Current Coverage of the Mandated Benefit, plans are already covering gynecological cancer diagnostic tests for symptomatic women and medically appropriate screening tests for asymptomatic women. As described below in Impact on Access and Health Service Availability, no evidence exists to suggest that medically appropriate gynecological cancer tests are currently being denied coverage. The screening tests not currently covered have not been shown to be medically effective, so would continue to be denied if carriers were still allowed to use evidence-based guidelines to determine coverage. Although media campaigns to educate the public about the need for such tests could increase utilization of tests already being covered, these campaigns are likely to be mounted even if the bill did not pass, so their effects could not necessarily be attributed to the mandate. Moreover, in the absence of benefit changes, raising awareness alone may be insufficient to ensure that women will obtain necessary tests (Burack et al., 1998).

The bill language, however, has been interpreted to allow health care providers exclusive rights to determine medical necessity so that carriers would no longer be allowed to apply their medical necessity requirements to coverage determinations. Women would have coverage for any gynecological cancer test for which they could obtain orders from a physician, nurse practitioner, or certified nurse midwife, even if the test did not meet the medical necessity criteria of the health plans and insurers.

AB 1774 could therefore result in the adoption of a community-based, rather than evidence-based, standard of care. A significant number of asymptomatic, average-risk women may want additional screening tests if tests are being reimbursed by insurers, despite the lack of evidence regarding effectiveness. The extent to which patients will demand such tests will depend in part on knowledge and fears about gynecological cancers. Media coverage about these cancers has been significant, and in particular, many women are concerned about ovarian cancer (Fung et al., 2004), which is generally diagnosed at a late stage and has a poor prognosis. Many women obtain routine gynecological cancer screening tests as a way to seek reassurance (Whynes et al., 2007).

In discussing the phenomenon of what he terms “over-enthusiastic implementation” of cancer screening programs resulting from economic incentives, Whynes (2004) notes that “The

public—the subjects of screening—is ignorant of cancer etiology and is terrified by the disease: . . . To the layman, cancer is insidious, arbitrary, and probably incurable. Therefore, faced with this ‘enemy,’ any defense would appear better than none, especially if the physician is supportive. The public’s faith in screening is evidenced by the popular protests which emerge when the worth of screening programs is questioned.” Many women may not understand medical effectiveness research and the potential harms associated with false-positive test results. Rolnick et al. (1999) found that the majority of female patients were skeptical about the change in their HMO’s guidelines from annual to triennial Pap tests, despite the fact that the new guidelines were evidence-based. Philips, Whyne, and Avis (2006) note that “It is known that, owing to low levels of knowledge of cancer and screening in the general population, women both over-estimate the risk of disease and the efficacy of screening.”

Given likely patient demand for tests not currently covered, the increase in utilization resulting from AB 1774 would depend critically on the willingness of health care professionals to provide (or order) gynecological cancer screening tests for asymptomatic, average-risk patients in the absence of an evidence base supporting the use of these tests for such women. Although some physicians may decline to provide screening tests, CHBRP believes it likely that the majority would be unwilling to refuse patient requests, or may even offer women the tests without solicitation. Insurance would now pay for the tests, and the legislative mandate would be seen as a sanction to provide them. Some physicians might also perceive financial incentives to provide tests, particularly if they practice in fee-for-service settings and the tests can be done in the physician’s office. Financial incentives to provide tests may be attenuated in managed care settings where individual physicians or provider groups are paid on a salaried or subcapitated basis. However, even physicians who do not have a direct financial incentive to “induce demand” might be reluctant to turn down patient requests, faced with competitive market pressures and the need to maintain their patient base.

Equally important may be the fear of medical malpractice suits if the law requires health plans to pay for screening for gynecological cancers, and a community-based standard is set. A physician might be concerned that he or she would be found liable if a patient whose cancer was diagnosed at a late stage sued for negligence on the grounds that the physician failed to perform a screening test that could have detected the cancer earlier, even if the medical evidence suggests that use of the test for asymptomatic, average-risk women does not lead to significantly earlier diagnoses.

Some researchers have suggested that providers already screen average-risk women more intensively than recommended by guidelines (Fung et al., 2004). Saint et al. (2005) asserted that “Most US obstetricians/gynecologists screen low-risk women often and indefinitely, despite national guidelines designed to minimize screening harms resulting from overtesting.” Herman et al. (1996) found that nearly all OB/GYNs and a large majority of primary care physicians recommend annual breast and cervical cancer screening for their female patients of all ages, regardless of risk. Noller et al. (2003) concluded that most providers are reluctant to abandon annual testing for low-risk women, despite the lack of evidence supporting it. Sirovich and Welch (2004) estimated that the 25–33 million women who currently receive annual Pap tests may be screened too often, given their low risk. Finally, Rappaport et al. (2004) found evidence that physicians are eager adopters of new screening tests that have not been shown to improve outcomes relative to the existing technology, particularly in the presence of commercial marketing campaigns. These studies suggest that physicians might not take over the gatekeeper

role if insurance carriers were to stop managing utilization of gynecological cancer screening tests.

Scenario to estimate possible impact on utilization of eliminating utilization review to determine medical necessity for coverage determinations

CHBRP is unable to project the changes that would result from the passage of AB 1774, because it is impossible to predict with any certainty how the elimination of the medical necessity requirements currently imposed by health plans and insurers would affect utilization and costs. However, to illustrate the magnitude of the *possible* impact of AB 1774 on utilization and costs of gynecological cancer screening tests, CHBRP developed a hypothetical scenario based on input from expert physician consultants, physicians in community practice, and relevant literature. Although the scenario reflects only one of the many possible outcomes of this bill, it is considered to be a plausible example of the potential impact of AB 1774.

To provide a broad overview, simplified screening algorithms were developed for each of the three types of gynecological cancer considered (cervical, endometrial, and ovarian), selecting certain tests as the “first-line” screening procedures likely to be used and others as the follow-up tests that would be administered to women who receive abnormal results on the initial screen. For example, screening of asymptomatic, average-risk women for endometrial cancer was assumed to start with an endometrial biopsy; women for whom the biopsy did not obtain an adequate specimen or who otherwise require follow-up were assumed to then receive dilation and curettage. Only the follow-up tests and procedures considered to be “unnecessary” (e.g., those performed due to false-positive test results) were included in the cost estimates. In addition, some women may ask to be tested for a genetic mutation associated with high rates of endometrial cancer, even though they have no family history to suggest that they are at high risk for the mutation.

By making reasonable assumptions about the increases in utilization rates of each of these screening tests and follow-up procedures if AB 1774 passed, we can calculate the cost of the particular scenario being evaluated, using the unit costs of each test or procedure. Specific details of the model assumptions (e.g., the clinical algorithms, definitions of the population of potential users of screening tests, and assumed utilization rates for each test and population) can be found in Appendix D: Cost Impact Analysis: Data Sources, Caveats, and Assumptions. Depending on the test and subpopulation, assumed use of “first-line” screening tests ranged from 0% to 40%. Some of the factors likely to affect the utilization rate of each screening test in the post-mandate period include:

- General awareness of the cancer (e.g., ovarian cancer has received much publicity as the “silent killer”).
- Perceived health benefits and risks associated with the screening test.
- Invasiveness of the test; all else equal, less invasive tests (e.g., transvaginal ultrasound) ought to experience greater demand than more invasive tests (e.g., endometrial biopsy).

- Current utilization rates of other cancer screening tests that might serve as substitutes (e.g., women may be less likely to demand HPV tests, and providers less likely to give them, because Pap tests are already covered, especially given the greater effectiveness of Pap tests).
- The likelihood that the women who most want screening tests are already able to get coverage for them; for example, ovarian cancer symptoms are sufficiently vague that health plans are unlikely to be able to disprove their existence if a woman cites symptoms as a reason for requesting coverage for an ovarian cancer test.
- The extent to which the test can be provided in the physician's office using equipment already available, thereby giving the physician a financial incentive to induce demand; for example, many OB/GYNs already own ultrasound machines and could perform transvaginal ultrasounds quite easily if screening of asymptomatic, average-risk women became routine.
- Whether the provider practices in a managed care or fee-for-service environment, and the extent to which the managed care plan or provider group offers incentives to the individual physician for limiting utilization.

CHBRP assumes that patients in managed care will experience smaller increases in utilization than those in fee-for-service plans because provider groups are usually subcapitated and the cost of screening tests comes out of the group's capitation payment. For staff-model HMOs, we assume that new utilization of medically inappropriate screening tests will be lower than for other managed care plans, because physicians are salaried and there is typically more widespread dissemination and adoption of treatment guidelines. We assume that screening rates among Medi-Cal managed care beneficiaries under 65 years will be similar to those of staff-model HMOs, but for different reasons. Medi-Cal managed care beneficiaries are believed to have problems of access to primary and specialty care due to low reimbursement rates.²² Although in theory, Medi-Cal would be required to pay for these screening tests, reimbursement rates could be set so low that providers would be unwilling to provide the tests to patients. For this reason, it seems unlikely that utilization would increase as much for Medi-Cal Managed Care as for plans for the privately insured. Based on expert opinion, Medi-Cal beneficiaries 65 years and over are assumed to experience even smaller utilization increases under AB 1774 than those under 65 because they are likely to receive fewer endometrial biopsies and transvaginal ultrasounds.

Based on the scenario outlined in Appendix D, utilization of the selected screening tests and procedures in the first year post-mandate would increase as follows (Table 1):

- 228,000 HPV tests
- 8,000 colposcopies
- 1,565,000 transvaginal ultrasounds
- 175,000 CA-125 blood tests

²² *Medi-Cal Redesign, Updated Medi-Cal Redesign Fact Sheet, August 2005.*

- 6,000 laparoscopies
- 2,000 laparotomies
- 232,000 *BRCA1/2* genetic tests with genetic counseling
- 945,000 endometrial biopsies
- 71,000 dilation and curettage procedures
- 244,000 HNPCC genetic tests with genetic counseling

To What Extent Does the Mandate Affect Administrative and Other Expenses?

The mandate will likely increase the administrative expenses for health plans because of the increase in gynecological cancer screening test claims. CHBRP assumes that the administrative costs *as a proportion of premiums* remain unchanged. Health care plans and insurers include a component for administration and profit in their premiums. The estimated impact of this mandate on premiums includes the assumption that plans and insurers will apply their existing administration and profit loads to the marginal increase in health care costs produced by the mandate. Therefore, to the extent that gynecological cancer screening test claims will increase, administrative costs will increase commensurately.

In addition to the increase in administrative costs reflected in the CHBRP model, health plans may have to modify insurance contracts, provider manuals, internal policy and guideline documents, and member materials to reflect the new rules regulating coverage of gynecological cancer screening tests for asymptomatic women. .

Impact of the Mandate on Total Health Care Costs

Based on the assumed utilization increases in the scenario being modeled, total annual health care expenditures (including total premiums and out-of-pocket expenditures) could increase by \$2.72 billion, or 3.43%, as a result of AB 1774 (Table 1). The increases in total PMPM expenditures range from 0% to 6.75%, based on the market segment (Table 4).

Over half of the increase in costs is driven by the assumed use of genetic testing for endometrial and ovarian cancers, as the CHBRP model assumes that approximately 3% of all women would receive these tests in the first year post-mandate, and the tests cost around \$2,300-\$3,300 each. About one-seventh of the cost is attributable to dilation and curettage surgery for women whose endometrial biopsies were inconclusive or otherwise required follow-up. Over one-quarter of the cost is due to transvaginal ultrasound screening and follow-up screening for false positives.

CHBRP emphasizes that these cost figures could either underestimate or overestimate the true impact of the bill. For example, supply and demand could respond more vigorously than anticipated to the change from an evidence- to community-based standard of care for determining coverage. The CHBRP cost model does not include the cost of complications associated with invasive testing (e.g., laparotomies or laparoscopies) or unnecessary treatment in

response to false-positive screening results. Although the number of women with false-positive test results is anticipated to be small, the per-woman costs associated with unnecessary treatment and/or complications could be large. In addition, the CHBRP scenario includes only a subset of screening tests considered to be the most likely ones used for the newly covered population of asymptomatic, average-risk women. Utilization of other screening tests may also go up, potentially increasing costs further.

On the other hand, the numbers may overstate annual utilization after the first few years post-mandate. In particular, the genetic tests would only have to be performed once during each woman's lifetime, and it is likely that most women who want these tests will request them as soon as they are covered, so eventually demand would be exhausted (except among new cohorts of young adult women) and the rate of genetic testing would decline substantially. Furthermore, if carriers were able to reinstate their right to conduct utilization management through court challenges to the interpretation of the bill, utilization and costs would be likely to revert back to essentially the same levels as before.

These figures do not include the costs and benefits of treating women whose cancer was detected earlier than it otherwise would have been, as a result of getting screened. The medical effectiveness literature suggests that for cervical and endometrial cancer, the newly covered tests for average-risk, asymptomatic women would not affect time to diagnosis. For ovarian cancer, there is some evidence that screening may detect cancer earlier, but early detection is rare (see the Medical Effectiveness and Public Health sections). Whether treatment is more or less expensive if detection occurs later rather than earlier is ambiguous. First, research is inconclusive with regard to whether earlier detection translates into improved morbidity and mortality. Second, costs could actually be higher in the first year post-mandate because the cost of treating cancer is being incurred sooner rather than later. Third, some women with undetected cancer may end up dying before receiving intensive and/or long-term treatment for their cancer, so women whose cancer is diagnosed earlier might actually incur higher treatment costs. (Note that CHBRP does not attempt to place a dollar value on life-years saved for inclusion in the cost models; however, the potential benefit in terms of reduced mortality is discussed in the Public Health section that follows.)

Costs or Savings for Each Category of Insurer Resulting From the Benefit Mandate

Table 1 provides a summary of the potential impact of AB 1774 on premiums paid by private and public employers and employees under the possible scenario described earlier. Highlights from this table include the following:

- Total annual premiums paid by all private employers in California affected by AB 1774 would increase by about \$1.63 billion, or 3.46%.
- Premium expenditures for individually purchased insurance would increase by \$287 million, or 4.67%.
- The portion of premiums for employment-based insurance that is paid by employees would increase by \$437 million, or 3.41%.

- Total annual premiums paid by CalPERS would increase by \$91 million, or 3.09%.
- Total annual premiums paid by Medi-Cal, AIM, and MRMIP would increase by \$77 million, or 1.90%.
- Total annual premiums paid by the Healthy Families program would not be expected to change.

The projected impact of AB 1774 on PMPM total premiums (including both the employer and individual shares) by market segment is as follows (Table 4):

- \$10.56 (3.60%) for the DMHC-regulated large-group market
- \$10.29 (2.56%) for the CDI-regulated large-group market
- \$11.24 (3.31%) for the DMHC-regulated small-group market
- \$9.54 (2.66%) for the CDI-regulated small-group market
- \$11.65 (3.96%) for the DMHC-regulated individual market
- \$10.86 (6.75%) for the CDI-regulated individual market
- \$10.93 (3.09%) for CalPERS
- \$1.44 (0.79%) for Medi-Cal managed care 65 and over
- \$2.43 (2.01%) for Medi-Cal managed care under 65, AIM, and MRMIP
- \$0.00 (0.00%) for Healthy Families

Changes in coverage as a result of premium increases

Due to the possibility that AB 1774 could lead to large increases in utilization and costs, it must be considered whether increases in premiums resulting from the mandate might induce some individuals to drop coverage. When estimating the effects of mandates on premiums and cost, CHBRP assumes that the number of insured in each market segment remains stable. However, we consider the secondary impact of increases in premiums on the number of insured dropping coverage when premium increases exceed 1%.

Using CHBRP's method for estimating the impact on the uninsured,²³ of the 22,362,000 commercially insured individuals subject to the mandate, an estimated 82,000 could drop coverage as a result of the mandate if the CHBRP scenario were an accurate projection of what would happen in the absence of utilization management. It is unlikely that any of the newly

²³ See www.chbrp.org/documents/uninsured_020707.pdf for more information on CHBRP's methods for calculating the number of uninsured as a result of premium changes.

uninsured would be eligible for Medi-Cal because if they were, it is likely they would have opted for Medi-Cal coverage rather than paying a share of premiums for employer-sponsored insurance or paying the full premium for individual coverage. In addition to the drop in the number of commercially insured individuals, the increased costs for the public programs could provide an impetus to change their eligibility requirements or engage in other new cost-containment measures.

Impact on Long-Term Costs

As noted above, CHBRP has not included long-term costs associated with any unnecessary treatment and/or complications resulting from false-positive test screens, or possible benefits associated with earlier detection. Although the magnitude of the costs associated with false-positive screens is unknown, they are potentially significant. Based on a sample of women 55 to 74 years of age who were not previously diagnosed with ovarian cancer, Buys et al. (2005) show that there were 3.4 surgeries for every invasive cancer diagnosed among women who tested positive on both a transvaginal ultrasound and a CA-125 blood test. Lafata et al. (2004) estimate that women who have false-positive results on transvaginal ultrasound incur \$4,900 more in medical expenditures in the year following screening than those with negative results. Part of this additional expenditure may have been due to follow-up screening costs, which the CHBRP cost estimate already takes into account. Nonetheless, it is possible that the costs associated with our utilization scenario for AB 1774 would have been higher if we had been able to calculate the cost of medical complications. Although it is also possible that early detection would have produced some cost savings, only ovarian cancer screening demonstrates a significant impact on the time until diagnosis among asymptomatic, average-risk women, and even then, the rate of cancer detection is low (see estimates in the Public Health section that follows).

A review of the literature on the cost-effectiveness of gynecological cancer screening tests produced very few studies that look at the population of interest for the current analysis, namely asymptomatic, average-risk women. The bulk of the research has focused on surveillance of women who have already had cancer, testing of high-risk women (e.g., genetic tests for women with a family history), or cervical cancer screening for the general population. In all of these cases, the tests are already being covered, so the literature does not add to our understanding of whether AB 1774 would provide good value for the money that might be spent providing screening tests to asymptomatic, average-risk women who otherwise would not be covered for these tests. It seems unlikely, however, that tests for which medical effectiveness has not yet been demonstrated (and for which the harms may outweigh the benefits) would prove to be cost-effective; indeed, the reason for the lack of cost-effectiveness literature on this topic may be that researchers generally analyze costs only for services already known to be medically effective.

The handful of studies that discuss the cost of screening tests not already covered in California suggest that screening asymptomatic, average-risk women may not be cost-effective. For example, in a review of the evidence on screening post-menopausal women for ovarian cancer, Fung et al. (2004) conclude that “The benefits of screening in terms of lives saved, pain, and suffering do not appear to be outweighed by the social costs of unnecessary investigations and treatments.” However, Fung et al. did not attempt to quantify these social costs. An examination of women age 40 years and over who were shedding normal endometrial cells in Pap tests found

that endometrial sampling was not cost-effective, as no asymptomatic premenopausal women were found to have significant endometrial pathology through screening and the costs were high (Kapali et al., 2007). A review of the economic evidence on genetic testing for ovarian and other cancers found that when used for population screening, it cost up to \$2.6 million for each HNPCC mutation detected, and \$138,280 per *BRCA1* mutation found. The cost per quality-adjusted life year (QALY) associated with population testing for the *BRCA1* mutation was \$1.6 million. (For comparison, thresholds for determining cost-effectiveness cited in the literature typically range from \$50,000 to \$200,000 per QALY.)

Impact on Access and Health Service Availability

Access to screening and diagnostic tests has not emerged as a problem for the insured. Tests are available, although coverage is dependent on the health plan's determination of medical necessity. Health Consumer Alliance (HCA) administers consumer assistance programs to help low-income people with health access issues in California. Of the 56,000 persons HCA has assisted since 1998, about 865 have a problem related to "tests." Medi-Cal eligibility and service issues predominate HCA's work on behalf of individual clients, so it not clear whether those with private insurance have access issues.

DMHC's HMO Help Center has logged over 30,000 complaints since its inception in 2001, of which 41 are complaints related to positron emission tomography (PET) and computed tomography (CT) scans for gynecological cancers.²⁴ Lack of case detail precludes CHBRP from drawing any conclusions on what procedures are being denied. Patients who dispute health plan denials because procedures are not considered medically necessary or they are considered experimental or investigations, can appeal disputes to the California Independent Medical Review (IMR). Out of 6,231 IMR decisions rendered since 2001, 11 disputes were related to screening and diagnostic tests, principally appeals of health plan denials for the PET scan combined with a CT either for diagnosis or monitoring the disease process in the treatment phase.

²⁴ Personal communication with S. Lowenstein, DMHC, March 4, 2008.

Table 3. Baseline (Pre-mandate) Per Member Per Month Premium and Expenditures by Insurance Plan Type, California, 2008

	Large Group		Small Group		Individual		CalPERS	Medi-Cal Managed Care		Healthy Families Managed Care	Total Annual
	DMHC-Regulated	CDI-Regulated	DMHC-Regulated	CDI-Regulated	DMHC-Regulated	CDI-Regulated		65 yrs and Over	Under 65 yrs		
Population currently covered											
Average portion of premium paid by employer	11,721,000	342,000	3,256,000	728,000	1,299,000	812,000	815,000	172,000	2,532,000	685,000	22,362,000
Average portion of premium paid by employee	\$238.92	\$315.18	\$245.82	\$296.00	\$0.00	\$0.00	\$300.92	\$181.00	\$120.01	\$78.35	\$54,695,911,000
Total premium	\$54.60	\$86.99	\$93.75	\$62.26	\$294.46	\$160.95	\$53.10	\$0.00	\$0.80	\$6.81	\$19,001,902,000
Member expenses for covered benefits (deductibles, copays, etc.)	\$293.53	\$402.17	\$339.57	\$358.26	\$294.46	\$160.95	\$354.02	\$181.00	\$120.81	\$85.17	\$73,697,813,000
Member expenses for benefits not covered	\$15.78	\$45.50	\$24.95	\$95.56	\$50.61	\$39.36	\$18.26	\$0.00	\$0.56	\$2.32	\$5,602,060,000
Total expenditures	\$309.30	\$447.67	\$364.52	\$453.82	\$345.07	\$200.31	\$372.28	\$181.00	\$121.36	\$87.49	\$79,299,873,000

Source: California Health Benefits Review Program, 2008.

Note: The population includes individuals and dependents in California who have private insurance (group and individual) or public insurance (e.g., CalPERS, Medi-Cal, Healthy Families, AIM, MRMIP) under health plans or policies regulated by DMHC or CDI. All population figures include enrollees aged 0–64 years and enrollees 65 years or older covered by employment-based coverage. The total annual expenditures expressed in this table vary from Table 1 in this report due to rounding.

^aOf these CalPERS members, about 60%, or 489,000, are state employees whose cost is borne by the General Fund.

Key: CalPERS=California Public Employees' Retirement System; HMO=health maintenance organization and point of service plans.

Table 4. Potential Post-Mandate Impacts on Per Member Per Month and Total Expenditures by Insurance Plan Type, California, 2008

	Large Group		Small Group		Individual		CalPER S	Medi-Cal Managed Care		Healthy Families Managed Care ^b	Total Annual
	DMHC-Regulated	CDI-Regulated	DMHC-Regulated	CDI-Regulated	DMHC-Regulated	CDI-Regulated		65 yrs and Over	Under 65 yrs		
Population covered	11,721,000	342,000	3,256,000	728,000	1,299,000	812,000	815,000	172,000	2,532,000	685,000	22,362,000
Average portion of premium paid by employer	\$8.60	\$8.07	\$8.14	\$7.88	\$0.00	\$0.00	\$9.29	\$1.44	\$2.42	\$0.00	\$1,796,236,000.00
Average portion of premium paid by employee	\$1.96	\$2.23	\$3.10	\$1.66	\$11.65	\$10.86	\$1.64	\$0.00	\$0.02	\$0.00	\$724,927,000.00
Total premium	\$10.56	\$10.29	\$11.24	\$9.54	\$11.65	\$10.86	\$10.93	\$1.44	\$2.43	\$0.00	\$2,521,163,000.00
Member expenses for covered benefits (deductibles, copays, etc.)											
Member expenses for benefits not covered	\$0.57	\$1.16	\$0.83	\$2.54	\$1.97	\$2.66	\$0.56	\$0.00	\$0.01	\$0.00	\$201,797,000.00
Total expenditures	\$11.13	\$11.46	\$12.07	\$12.08	\$13.62	\$13.52	\$11.49	\$1.44	\$2.45	\$0.00	\$2,722,960,000.00
Percentage impact of mandate											
Insured premiums	3.60%	2.56%	3.31%	2.66%	3.96%	6.75%	3.09%	0.79%	2.01%	0.00%	3.42%
Total expenditures	3.60%	2.56%	3.31%	2.66%	3.95%	6.75%	3.09%	0.79%	2.01%	0.00%	3.43%

Source: California Health Benefits Review Program, 2008.

Note: The population includes individuals and dependents in California who have private insurance (group and individual) or public insurance (e.g., CalPERS, Medi-Cal, Healthy Families, AIM, MRMIP) under health plans or policies regulated by DMHC or CDI. All population figures include enrollees aged 0–64 years and enrollees 65 years or older covered by employment-based coverage. The total annual expenditures expressed in this Table vary from Table 1 in this report due to rounding.

^aOf these CalPERS members, about 60%, or 489,000, are state employees whose cost is borne by the General Fund.

^bCHBRP assumes that utilization and cost impacts will be negligible for Healthy Families. Only 2% of Healthy Families enrollees are aged 18 years and above, and even those enrollees are 18- and 19-year olds who are unlikely to receive the additional tests and procedures covered under AB 1774.

Key: CalPERS=California Public Employees' Retirement System; HMO=health maintenance organization and point of service plans.

PUBLIC HEALTH IMPACTS

Impact of the Proposed Mandate on the Public’s Health

AB 1774 aims to mandate coverage for screening and diagnostic tests associated with gynecological cancers. Because diagnostic tests for symptomatic women and screening tests for high-risk, asymptomatic women are already being covered by insurance, the only increases in utilization of gynecological tests are screening tests for average-risk, asymptomatic women. As mentioned in the previous sections of this report, gynecological screening tests are not 100% accurate, and the outcomes associated with screening tests include both the intended outcomes and the unintended outcomes attributed to erroneous results.

Table 5 describes the scope of health and psychological outcomes associated with gynecological cancer screens²⁵. In the first cell, the “true positives” are represented where the screening resulted in an identification of an individual with cancer. This cell represents one of the primary intents of AB 1774, to detect gynecological cancers in asymptomatic women with the hope that the cancer is detected at an earlier stage so that survival is improved and treatment is less severe (NCI, 2008). Another positive outcome associated with screening programs is represented in cell four, where “true negative” results can reduce stress and anxiety related to gynecological cancers (Andersen et al., 2007; Brain et al., 2004).

In addition to these positive outcomes, there are also potential harms associated with false-positive and false-negative results. “False-positives” are represented in cell two, where an individual does not have cancer; however, a positive screening result could generate unnecessary stress and anxiety as well as complications arising from unnecessary follow-up procedures (Andersen et al., 2007; Meeuwissen et al., 2005; Stirling et al., 2005). Although less discussed in the literature, there is also the potential for harms associated with false negatives (cell three), where individuals with false-negative results may delay treatment when symptoms emerge (Petticrew et al., 2001).

Table 5. Summary of Health Outcomes Associated With Gynecological Screenings

	Individual Has Cancer	Individual Does Not Have Cancer
Positive screening results	1. <i>True positive</i> Early detected cancer and possibility of increased survival	2. <i>False positive</i> Unnecessary stress/anxiety and complications from follow-up
Negative screening results	3. <i>False negative</i> Possibility of reduced follow-up to later symptoms	4. <i>True negative</i> Reduced stress/anxiety

Based on the scenario described in the previous section, the utilization of gynecological screening tests could increase substantially, thus yielding the following health outcomes:

²⁵ Table 5 represents a simplified analysis of the outcomes associated with gynecological screenings for demonstration purposes. In practice, screens do not typically come back “positive” or “negative” but rather vary according to the specific test, and results often indicate whether results are in a normal range or whether they are elevated and require further testing.

Cervical cancer

According to the scenario described in the previous section, an increased in utilization of the human papilloma virus (HPV) DNA tests for women aged 18–29 years could be expected. Within this population, the HPV strains that can lead to cervical cancer are highly prevalent with a 3-year risk of infection at nearly 60% for young women (Einstein and Burk, 2001). In most cases, the HPV infection is cleared by the body's immune system. If the HPV infection is detected in women older than 30 years, however, it is an important risk factor for a future development of cervical cancer. Due to the high prevalence of HPV in women under 30, the fact that most HPV infections will clear on their own, and the extremely low prevalence of cervical cancer in women under 30, it is not recommended that women in this age range receive HPV DNA screening tests unless they have abnormal Pap test results. Since the increase in HPV tests are expected to be among women 18–29 years already using Pap tests, the estimated increased 228,000 HPV tests are not expected to detect any additional cervical cancers in women 18–29.

Based on the scenario of increased HPV testing among women 18–29 years, no cases of cervical cancer would be detected early due to increased HPV DNA testing. However, approximately 4,600 women would have false-positive results, which could result in stress and anxiety²⁶.

Ovarian cancer

The medical effectiveness review found that the screening of asymptomatic women at average risk for ovarian cancer can detect ovarian cancer at an earlier stage. One systematic review (Fung et al., 2004) found that for every 10,000 women participating in an annual screening program for 3 years, 3 women will be diagnosed at early-stage disease. Using these projections and the scenario of increased in utilization of ovarian cancer screening, 470 women could have early-stage ovarian cancer detected due to AB 1774 in the first 3 years. Although short-term survival rates are higher for early-stage ovarian cancer compared to late stages, at present there is insufficient evidence to determine the extent to which screening would improve morbidity and mortality for this population.

Increases in screening could also generate false-positive results and thus could produce unnecessary anxiety and stress. Based on the scenario of increased utilization, in the first year, more than 30,000 women would have false-positive results for the initial screen²⁷. Additionally, over 6,600 women would have unnecessary surgeries due to increased screenings²⁸. Of the unnecessary surgeries, approximately 330 could complications such as hemorrhage and infection²⁹.

²⁶ The number of false-positive HPV tests was calculated using the estimated prevalence of HPV 60% in the 18–29 population (Einstein and Burk, 2001) and the 95% specificity of the HPV DNA test (Goldie et al, 2004).

²⁷ The number of false-positive initial ovarian cancer tests were calculated using the estimated ovarian cancer prevalence of 0.094% in the general population and a specificity of 98% for the transvaginal ultrasound (see Table C-2-b-ii).

²⁸ The number of unnecessary surgeries was calculated by taking the cost projection of total laparoscopies and laparotomies, and subtracting the cancers that would be detected, according to Fung et al., 2004. Half of the cancers are expected to be early-stage cancers.

²⁹ The 300 expected complications are based on a projected 5% complication rate, provided by a content expert.

Endometrial cancer

As detailed in the Medical Effectiveness section, the tests associated with endometrial cancer are primarily performed on women with abnormal uterine bleeding, and no studies were identified on the accuracy of screening tests or the morbidity and mortality impact of screening for asymptomatic women. As such, the effects of the estimated increase in utilization of tests for endometrial cancer are unknown.

The Impact on the Health of the Community Where Gender and Racial Disparities Exist

A literature review and examination of existing data sources were conducted to describe racial disparities in prevalence, outcomes, and treatment associated with gynecological cancers. Tables 6 and 7 detail the age-adjusted incidence rates and mortality rates for gynecological cancers in California. Across all cancers of the female genital system, white women have a higher age-adjusted incidence, whereas black women have a higher age-adjusted mortality rate. Specifically, black women have higher mortality for cervical and uterine cancer compared to white women. Hispanic women have the highest incidence rates for cervical cancer, more than double that of white women. Additionally, Hispanic women also have a higher incidence of vaginal cancer (CCR, 2008).

Table 6. California Age-Adjusted Incidence Rate per 100,000 Women (2000–2004)

Demographic Group	Female Genital System	Cervical	Ovarian	Uterine
All races	51.60	8.91	13.35	21.47
Non-Hispanic white	54.61	7.11	14.80	23.67
Non-Hispanic black	44.94	8.65	9.53	18.79
Hispanic	49.71	14.42	11.88	16.94
Non-Hispanic Asian/Pacific Islander	37.49	8.38	10.12	15.58

Source: California Cancer Registry. Age-Adjusted Cancer Incidence Rates.

Table 7. Age-Adjusted Mortality Rate per 100,000 Women (2000–2004)

Demographic Group	Female Genital System	Cervical	Ovarian	Uterine
All races	16.17	2.51	9.06	1.67
Non-Hispanic white	16.90	1.91	10.29	1.72
Non-Hispanic black	19.18	4.05	7.17	3.07
Hispanic	15.71	3.93	7.63	1.36
Non-Hispanic Asian/Pacific Islander	10.74	2.63	5.35	1.07

Source: California Cancer Registry. Age-Adjusted Cancer Mortality Rates.

For cervical cancer, researchers have found that compared to white women, black women are initially diagnosed with more advanced-stage cancer (Howell et al., 1999; Morgan et al., 1996; Schwartz et al., 2003). This difference in stage does not appear to be due to similar disparities in

cervical cancer screening, since black women have been found to have the same or higher cervical cancer screening rates compared to white women (CHIS, 2005; De Alba et al., 2005; Newmann and Garner, 2005). The reasons behind the racial differences in gynecological cancer mortality remain uncertain, with some studies positing that racial differences disappear once controlling for stage of cancer, equal treatment, and socioeconomic measures (Morgan et al., 1996; Schwartz et al. 2003).

Since AB 1774 is not expected to result in increased utilization of proven medically effective gynecological screening and diagnostic tests where racial disparities exist, it is not expected to have an impact on racial disparities related to gynecological cancers.

The Extent to Which the Proposed Service Reduces Premature Death and the Economic Loss Associated With Disease.

The primary intention of AB 1774 is to reduce premature death by identifying gynecological cancers at early stages when survival rates are substantially higher. Since insurers typically cover the gynecological tests that have been found to be medically effective, AB 1774 is not expected to substantially reduce premature death among women. However, as mentioned previously, 470 women would be expected to have early-stage ovarian cancer detected due to AB 1774 and this could potentially yield improved survival; however, there is insufficient evidence to determine whether screening reduces mortality for this population.

Gynecological cancers result in a substantial economic loss to society. The economic loss estimates most relevant to AB 1774 come from Max et al., 2003, who detailed the direct and indirect (lost productivity) costs of cervical, ovarian, and uterine cancer in California. Table 8 details the estimated economic costs associated with these gynecological cancers in women under 65 years old. Overall, there are over \$500 million in indirect costs associated with gynecological cancers, with the highest indirect costs attributed to ovarian cancer, followed by cervical and uterine cancer (Max et al., 2003).³⁰

Table 8. Estimated Direct and Indirect Costs Associated With Gynecological Cancers for Women Under 65 (\$ 000’s)

Cancer Type	Direct Costs	Indirect Costs	Total Costs
Cervical	\$51,353	\$199,517	\$250,870
Ovarian	\$63,934	\$232,850	\$296,784
Uterine	\$38,370	\$72,070	\$110,440
All gynecological	\$153,657	\$504,437	\$658,094

Source: Max et al., 2003.

AB 1774 could have two potential impacts on the indirect costs associated with gynecological cancers. First, if AB 1774 resulted in decreased mortality, this would lower indirect costs. At present, however, there is insufficient evidence to suggest that AB 1774 will reduce mortality in this population. There could be also be some lost productivity costs associated with false

³⁰ Max et al. (2003) reported costs in 1998 dollars, which were adjusted to 2008 dollars using the Consumer Price Index. The direct costs for women under 65 years was calculated using the total direct costs multiplied by the fraction of hospital costs that were for women under 65.

positives and the time necessary to get follow-up tests and procedures; particularly for the estimated 330 women projected to have complications from surgery (Lafata et al., 2004).

Long-Term Impacts

According to the scenario described in the Utilization, Cost, and Coverage Impacts section, AB 1774 could raise insurance premiums to the extent that approximately 82,000 people would lose insurance coverage. The consequences of being uninsured have been well documented by the Institute of Medicine's Committee on the Consequences of Uninsurance.³¹ Uninsured adults without insurance are more likely to delay getting needed care and do not receive the care they need. In California, uninsured individuals report poorer health, more psychological distress, and more delays in receiving treatment (CHIS, 2005).

³¹ See www.iom.edu/Object.File/Master/17/736/Fact%20sheet%20overview.pdf

APPENDICES

Appendix A: Text of Bill Analyzed

BILL NUMBER: AB 1774 AMENDED
BILL TEXT

AMENDED IN ASSEMBLY MARCH 5, 2008

INTRODUCED BY Assembly Members Lieber and De Leon
(Coauthors: Assembly Members Dymally, Evans, Fuentes and Laird)
(Coauthor: Senator Cedillo)

JANUARY 14, 2008

An act to add Section 1367.655 to the Health and Safety Code, and to add Section 10123.182 to the Insurance Code, relating to health care coverage.

LEGISLATIVE COUNSEL'S DIGEST

AB 1774, as amended, Lieber. Health care coverage: ~~uterine and ovarian~~ *gynecological* cancer screening tests.

Existing law, the Knox-Keene Health Care Services Plan Act of 1975, provides for the licensure and regulation of health care service plans by the Department of Managed Health Care and makes a willful violation of the act a crime. Existing law also provides for the regulation of health insurers by the Department of Insurance.

Under existing law, a health care service plan and a health insurer are deemed to provide coverage for all generally medically accepted cancer screening tests.

This bill would specifically require that a health care service plan contract and a health insurance policy be deemed to provide coverage for ~~annual uterine and ovarian cancer screening tests~~ *any test necessary for the screening and diagnosis of gynecological cancers when ordered by a physician, nurse practitioner, or certified nurse midwife*, as specified.

Because the bill would specify an additional requirement for a health care service plan, the willful violation of which would be a crime, it would impose a state-mandated local program.

The California Constitution requires the state to reimburse local agencies and school districts for certain costs mandated by the state. Statutory provisions establish procedures for making that reimbursement.

This bill would provide that no reimbursement is required by this act for a specified reason.

Vote: majority. Appropriation: no. Fiscal committee: yes.
State-mandated local program: yes.

THE PEOPLE OF THE STATE OF CALIFORNIA DO ENACT AS FOLLOWS:

SECTION 1. Section 1367.655 is added to the Health and Safety Code, to read:

1367.655. ~~(a)~~ - Every individual or group health care service plan contract, except for a specialized health care service plan contract, that is issued, amended, or renewed, on or after January 1, 2009, shall be deemed to provide coverage for ~~annual uterine and ovarian cancer screening tests, including, but not limited to, the appropriate blood tests, a transvaginal ultrasound, and a rectovaginal pelvic examination consistent with good professional practice.~~ *any test necessary for the screening and diagnosis of gynecological cancers when ordered by a physician, nurse practitioner, or certified nurse midwife in whose judgment the test would assist or facilitate the diagnosis of cancer.*

SEC. 2. Section 10123.182 is added to the Insurance Code, to read:

10123.182. (a) Every individual or group policy of health insurance that is issued, amended, or renewed, on or after January 1, 2009, shall be deemed to provide coverage for ~~annual uterine and ovarian cancer screening tests, including, but not limited to, the appropriate blood tests, a transvaginal ultrasound, and a rectovaginal pelvic examination consistent with good professional practice.~~ *any test necessary for the screening and diagnosis of gynecological cancers when ordered by a physician, nurse practitioner, or certified nurse midwife in whose judgment the test would assist or facilitate the diagnosis of cancer.*

(b) This section shall not apply to Medicare supplement, vision-only, dental-only, or Champus-supplement insurance, or to hospital indemnity, accident-only, or specified disease insurance that does not pay benefits on a fixed-benefit, cash payment only basis.

SEC. 3. No reimbursement is required by this act pursuant to Section 6 of Article XIII B of the California Constitution because the only costs that may be incurred by a local agency or school district will be incurred because this act creates a new crime or infraction, eliminates a crime or infraction, or changes the penalty for a crime or infraction, within the meaning of Section 17556 of the Government Code, or changes the definition of a crime within the meaning of Section 6 of Article XIII B of the California Constitution.

Appendix B: Literature Review Methods

Appendix B describes methods used in the medical effectiveness literature review for AB 1774, a bill that would require health plans and health insurance policies to provide coverage for any tests for the screening and diagnosis of gynecological cancers that a physician, nurse practitioner, or certified nurse midwife believes would aid in early detection of gynecological cancer progression and earlier diagnostic evaluation.

Gynecologic cancers are cancers of the female reproductive tract, including the cervix, endometrium, fallopian tubes, ovaries, uterus, vagina, and vulva. CHBRP focuses this review of the literature on the effectiveness of screening and diagnostic tests for endometrial, ovarian and cervical cancers, because they comprise 90% of all gynecological cancers. In addition, the tests that are used to screen and diagnose women for these three cancers are also used to screen and diagnose women for other, less common gynecological cancers. AB 1774 would require health plans to cover *all* tests currently available for gynecological cancers, regardless of whether they are recommended in national guidelines, such as those issued by the U.S. Preventive Services Task Force (USPSTF) and the American Cancer Society (ACS).

A medical librarian conducted a literature search to retrieve literature on the following topics: the accuracy of screening and diagnostic tests; the effects of screening on mortality, morbidity, and quality of life; the differential outcomes in screening effectiveness between women at high risk versus average risk; and harms associated with screening (e.g., increased anxiety, unnecessary tests and procedures, surgical complications). The literature search was limited to literature syntheses (i.e., meta-analyses, systematic reviews, evidence-based guidelines) and individual studies with comparison groups (e.g., randomized controlled trials, cohort studies, case-control studies, and comparisons of a test with a reference standard). Editorials and letters to the editor were included if they directly addressed research findings.

The search for literature pertaining to cervical cancer screening was limited to articles and reports published from 2005 to present, because CHBRP had conducted a thorough review of literature published prior to that date for its 2006 report on cervical cancer screening. Similarly, the search for literature pertaining to ovarian cancer screening was limited to articles and reports published from 2004 to present, because CHBRP had conducted a thorough review of the literature published prior to that date for its 2004 report on ovarian cancer screening. Literature pertaining to endometrial cancer screening included articles and reports published from 1995 to present. Only studies that enrolled females were included, because cervical, endometrial, and ovarian cancers affect the female reproductive system. Study populations included all adult women, because women of all ages can become diseased with cervical, endometrial, or ovarian cancer.

The following databases that index peer-reviewed literature were searched: PubMed, Web of Science, EconLit, the Cochrane Library (including the Cochrane Database of Systematic Reviews and the Cochrane Register of Controlled Clinical Trials), CINAHL, and the Social Science Citation Index. Web sites maintained by the following organizations that publish systematic reviews and evidence-based guidelines, along with databases that provide public

information were searched: American College of Obstetricians and Gynecologists, American College of Physicians Information and Education Resource (ACP PIER), Agency for Healthcare Research and Quality (including the U.S. Preventive Services Task Force), British National Collaborating Center for Women's and Children's Health, Database of Abstracts of Reviews of Effects, DynaMed, Institute for Clinical Systems Improvement, International Network of Agencies for Health Technology Assessment, Global Health Technology Assessments Database (HTA), National Comprehensive Cancer Network (NCCN), National Guideline Clearinghouse, National Institutes of Health, UpToDate, and the World Health Organization.

The literature search yielded a total of 466 abstracts on the effectiveness of ovarian, endometrial, and cancer screening tests in the facilitation of a diagnosis. At least two reviewers screened the title and abstract of each citation returned by the literature search to determine eligibility for inclusion. The reviewers obtained the full text of articles that appeared to be eligible for inclusion in the review and reapplied the initial eligibility criteria. Thirty-two studies met the inclusion criteria and were included in the medical effectiveness review.

In making a “call” for each outcome measure, the team and the content expert consider the number of studies as well the strength of the evidence. To grade the evidence for each outcome measured, the team uses a grading system that has the following categories:

- Research design
- Statistical significance
- Direction of effect
- Size of effect
- Generalizability of findings

The grading system also contains an overall conclusion that encompasses findings in these five domains. The conclusion is a statement that captures the strength and consistency of the evidence of an intervention's effect on an outcome. The following terms are used to characterize the body of evidence regarding an outcome.

- Clear and convincing evidence
- Preponderance of evidence
- Ambiguous/conflicting evidence
- Insufficient evidence

The conclusion states that there is “clear and convincing” evidence that an intervention has a favorable effect on an outcome, if most of the studies included in a review are well-implemented randomized controlled trials and report statistically significant and clinically meaningful findings that favor the intervention.

The conclusion characterizes the evidence as “preponderance of evidence” that an intervention has a favorable effect if most but not all five criteria are met. For example, for some interventions the only evidence available is from nonrandomized studies or from small RCTs with weak research designs. If most such studies that assess an outcome have statistically and clinically significant findings that are in a favorable direction and enroll populations similar to

those covered by a mandate, the evidence would be classified as a “preponderance of evidence favoring the intervention.” In some cases, the preponderance of evidence may indicate that an intervention has no effect or has an unfavorable effect.

The evidence is presented as “ambiguous/conflicting if their findings vary widely with regard to the direction, statistical significance, and clinical significance/size of the effect.

The category “insufficient evidence” of an intervention’s effect is used where there is little if any evidence of an intervention’s effect.

Search Terms

The following MeSH terms and keywords were used to search PubMed, Cochrane Library, EconLit, Web of Science and relevant web sites to locate studies pertinent to AB 1774:

Brenner tumor
carcinoma, endometrioid
cost
costs
cost analysis
cost effective
diagnos*
diagnosis
diagnostic*
differential
economic
endometrial neoplasms
endometrial stromal tumors
fallopian tube neoplasms
genital neoplasms, female
granulosa cell tumor
luteoma
mass screening
Meigs Syndrome
observer variation
ovarian neoplasms
predict*
predictive value of tests
prevention and control
sarcoma, endometrial stromal
scor*
sensitiv*
sensitivity and specificity
Sertoli-Leydig cell tumor
uterine cervical neoplasms
uterine neoplasms

vaginal neoplasms
vulvar neoplasms

* indicates that a term was truncated to maximize the number of publications retrieved.

Appendix C: Description of Studies on Medical Effectiveness of Screening and Diagnostic Testing for Cervical, Ovarian, and Endometrial Cancers

Appendix C describes the meta-analyses, systematic reviews, and individual studies on screening and diagnostic tests for cervical, ovarian, and endometrial cancers that were analyzed by the medical effectiveness team. Table C-1-a through C-1-c presents information regarding the type of study, topic studied, population of the study, and the location at which a study was conducted. Table C-1-a describes studies of tests for cervical cancer, table C-1-b describes studies of tests for ovarian cancer, and table C-1-c describes studies of tests for endometrial cancer. Tables C-2-a through C-2-c list studies that assessed topics pertinent to the evaluation of the effectiveness of screening and diagnostic tests for cervical, ovarian, and endometrial cancers, respectively.

Table C-1. Characteristics of Published Studies on the Accuracy of Cervical, Ovarian, and Endometrial Cancer Screening Tests

Citation	Type of Trial	Screening Tests vs. Diagnostic Reference Standard	Population Studied	Location
Abulafia et al., 2003	Systematic review	Liquid-based cytology (ThinPrep) vs. histology, clinical diagnosis from surgery or expert consensus Conventional cytology (Pap test) vs. histology, clinical diagnosis from surgery, or expert consensus	Population demographics not reported	N/A ³²
Arbyn et al., 2005	Meta-analysis	HPV DNA triage testing ³³ vs. colposcopy and histology Repeat Pap testing vs. colposcopy and histology	Women with abnormal cytology (index Pap test with atypical squamous/glandular cells of unspecified significance [ASCUS/AGUS])	N/A
California Health Benefits Review Program, 2006	Systematic review	HPV DNA testing vs. colposcopy and histology HPV DNA testing + conventional cytology (Pap test) vs. colposcopy and histology	Population demographics not reported	N/A

³² Location is not reported for systematic reviews and meta-analyses because they synthesize results from multiple studies conducted in multiple locations

³³ HPV DNA triage testing is the protocol of using HPV DNA testing as a decision-making tool for follow-up of initially abnormal conventional Pap test results

Citation	Type of Trial	Screening Tests vs. Diagnostic Reference Standard	Population Studied	Location
		HPV DNA triage testing vs. colposcopy and histology		
		Repeat Pap testing vs. colposcopy and histology		
		Conventional cytology (Pap test) vs. colposcopy and histology		
Coste et al., 2003	Cross sectional study	Liquid-based “monolayer” cytology vs. colposcopy and histology	Asymptomatic without previous cytology results and asymptomatic women with abnormal cytology	France
		HPV DNA testing vs. colposcopy and histology		
		Conventional cytology (Pap test) vs. colposcopy and histology		
Hussein et al., 2005	Split sample study	Liquid-based cytology (Thinprep) vs. colposcopy and histology	Women with abnormal cytology	United Kingdom
		Conventional cytology (Pap test) vs. colposcopy and histology		
Karnon et al., 2004	Systematic review	Liquid-based cytology vs. histology	High-risk and average-risk women ³⁴	N/A
		Conventional cytology (Pap test) vs. histology		
Kirschner et al., 2006	Retrospective comparison with historic controls	Liquid-based cytology (Surepath) vs. colposcopy and histology	Asymptomatic women aged 23–59 years	Denmark
		Conventional cytology (Pap test) vs. colposcopy and histology		
Klinkhamer et al., 2003	Systematic review	Liquid-based cytology (Surepath) vs. histology or expert consensus	Asymptomatic without previous cytology results and asymptomatic women with abnormal cytology	N/A
		Liquid-based cytology (Thinprep) vs. histology or expert consensus		
		Conventional cytology (Pap test) vs. histology or expert consensus		

³⁴ Not specifically defined because the systematic review pooled studies that enrolled populations with varying demographic characteristics

Citation	Type of Trial	Screening Tests vs. Diagnostic Reference Standard	Population Studied	Location
Koliopoulos et al., 2007	Meta-analysis	HPV DNA testing vs. colposcopy and histology Conventional cytology (Pap test) vs. colposcopy and histology	Asymptomatic women aged 18-70 years	N/A
Lee et al., 2004	Prospective case series	HPV DNA testing vs. colposcopy and histology HPV DNA testing + conventional cytology (Pap test) vs. colposcopy and histology Conventional cytology (Pap test) vs. colposcopy and histology	Women with abnormal cytology	Korea
Longatto Filho et al., 2005	Split sample study	Liquid-based cytology (DNA-Citoliq System) vs. colposcopy and histology Conventional cytology (Pap test) vs. colposcopy and histology	Women with abnormal cytology and/or previous history of cervical lesion) aged 14-86 years	Brazil
Mattosinho de Castro Ferraz et al., 2004	Cross sectional study	Liquid-based cytology (universal collection medium) vs. colposcopy and histology Conventional cytology (Pap test) vs. colposcopy and histology	Asymptomatic women	Brazil
Mayrand et al., 2007	Randomized control trial	HPV DNA testing vs. colposcopy/biopsy and histology Conventional cytology (Pap test) with HPV triage vs. colposcopy/biopsy and histology HPV DNA testing with conventional cytology (Pap test) triage vs. colposcopy/biopsy and histology Conventional cytology (Pap test) + HPV DNA testing vs. colposcopy/biopsy and histology	Asymptomatic women aged 30-69 years	Canada

Citation	Type of Trial	Screening Tests vs. Diagnostic Reference Standard	Population Studied	Location
Monsonogo et al., 2006	Prospective case series	Conventional cytology (Pap test) vs. colposcopy/biopsy and histology	Women with abnormal cytology	France
Ronco et al., 2006a	Randomized control trial	<p>Conventional cytology (Pap test) vs. biopsy and histology</p> <p>HPV DNA testing vs. colposcopy and histology</p> <p>Liquid-based cytology vs. colposcopy and histology</p> <p>Liquid-based cytology + HPV DNA testing vs. colposcopy and histology</p> <p>Conventional cytology (Pap test) vs. colposcopy and histology</p>	Asymptomatic women aged 25–60 years	Italy
Ronco et al., 2006b	Randomized control trial	<p>HPV DNA testing vs. colposcopy and histology</p> <p>Liquid-based cytology vs. colposcopy and histology</p> <p>Liquid-based cytology + HPV DNA testing vs. colposcopy and histology</p> <p>Conventional cytology (Pap test) vs. colposcopy and histology</p>	Asymptomatic women aged 25–34 years	Italy
Saqi et al., 2006	Prospective case series	Liquid-based cytology (Thinprep) with HPV triage vs. biopsy and histology	Women with abnormal cytology (atypical glandular cells [AGC]) aged 17–86 years	United States (New York, New York)
USPSTF, 2003	Systematic review	<p>HPV DNA testing vs. diagnostic histology</p> <p>HPV DNA triage testing vs. diagnostic histology</p> <p>Conventional cytology (Pap test) vs. diagnostic histology</p>	Population demographics not reported	N/A

Table C-1-b. Characteristics of Published Studies on the Accuracy of Ovarian Cancer Screening Tests in the Detection of Ovarian Cancer

Citation	Type of Trial	Screening Test vs. Diagnostic Reference Standard	Population Studied	Location
Nelson et al., 2005	Systematic review	Risk assessment, genetic counseling and mutation testing vs. surgical diagnostic findings	Asymptomatic women	N/A
Bosse et al., 2006	Prospective case series	Transvaginal ultrasound + CA-125 vs. surgical diagnostic findings	Asymptomatic women aged 30–70 years with a hereditary risk for ovarian cancer (family history of ovarian cancer or test positive for genetic mutation, i.e., <i>BRCA1</i> or <i>BRCA2</i>)	Germany
Buyse et al., 2005	Randomized control trial	Transvaginal + CA-125 vs. ultrasound Transvaginal + CA-125 vs. CA-125 repeat Transvaginal + CA-125 vs. chest radiograph Transvaginal + CA-125 vs. surgery (including laparotomy) Transvaginal + CA-125 vs. Computed Tomography (CT) scan Transvaginal + CA-125 vs. Magnetic Resonance Imaging (MRI) Transvaginal + CA-125 vs. needle aspiration, culdocentesis, or paracentesis Transvaginal + CA-125 vs. Intravenous Pyelogram (IVP) Transvaginal + CA-125 vs. barium enema	Asymptomatic women aged 55–74 years with no prior diagnosis of lung, colorectal, or ovarian cancer and some with familial risk history	United States
Fung et al., 2004	Systematic review	CA-125 + ultrasound vs. surgical diagnostic findings Ultrasound alone vs. surgical diagnostic findings Ultrasound + color Doppler imaging vs. surgical diagnostic findings	Asymptomatic postmenopausal women not at increased risk for ovarian cancer, (i.e., no family history of ovarian cancer) unless specified	N/A ³⁵

³⁵ Location is not reported for systematic reviews because they synthesize results from multiple studies conducted in multiple locations.

Citation	Type of Trial	Screening Test vs. Diagnostic Reference Standard	Population Studied	Location
Lacey et al., 2006	Randomized control trial	<p>Transvaginal + CA-125 vs. ultrasound</p> <p>Transvaginal + CA-125 vs. CA-125 repeat</p> <p>Transvaginal + CA-125 vs. chest radiograph</p> <p>Transvaginal + CA-125 vs. surgery (including laparotomy)</p> <p>Transvaginal + CA-125 vs. CT scan</p> <p>Transvaginal + CA-125 vs. MRI</p> <p>Transvaginal + CA-125 vs. needle aspiration, culdocentesis, or paracentesis</p> <p>Transvaginal + CA-125 vs. IVP</p> <p>Transvaginal + CA-125 vs. barium enema</p>	Asymptomatic women aged 55–74 years with no prior diagnosis of lung, colorectal, or ovarian cancer, and some with familial risk history	United States
Menon et al., 2005	Randomized control trial	CA-125 vs. surgical diagnostic findings	Asymptomatic postmenopausal women ≥ 50 years with no increased risk of ovarian cancer due to familial genetic predisposition, and more than 12 months of amenorrhea, following a natural or surgical menopause or more than 12 months of hormone replacement therapy commenced for menopausal symptoms	United Kingdom
USPSTF, 2004	Systematic review	<p>Transvaginal ultrasound alone vs. surgical diagnostic findings</p> <p>Transvaginal ultrasound + CA-125 vs. surgical diagnostic findings</p> <p>Transvaginal ultrasound + color Doppler imaging vs. surgical diagnostic findings</p>	Asymptomatic women	N/A
van Nagell et al., 2007	Retrospective case series	Transvaginal ultrasound vs. surgical diagnostic findings	Asymptomatic women ≥ 50 years and asymptomatic women aged ≥ 25 years with a documented family history	United States. (Kentucky)
Woodward et al., 2007	Retrospective audit	Transvaginal ultrasound + CA-125 vs. surgical diagnostic findings	Asymptomatic women with a family history of ovarian cancer	UK

Table C-1-c. Characteristics of Published Studies on the Accuracy of Diagnostic Procedures in the Detection of Endometrial Cancer

Citation	Type of Trial	Diagnostic Test vs. Diagnostic Reference Standard	Population Studied	Location
Clark et al., 2002a	Systematic review	Outpatient endometrial biopsy vs. endometrial histology obtained from inpatient sampling	Premenopausal or postmenopausal women with abnormal uterine bleeding	N/A
Clark et al., 2002b	Systematic review	Hysteroscopy vs. endometrial histological findings	Premenopausal or postmenopausal women with abnormal uterine bleeding	N/A
Dijkhuizen et al., 2000	Meta-analysis	Endometrial sampling vs. histological findings at dilation and curettage (D&C), hysteroscopy, and/or hysterectomy	Premenopausal or postmenopausal women who were asymptomatic or had abnormal uterine bleeding	N/A
Farquhar et al., 2003	Systematic review	Transvaginal ultrasound (TVS), transabdominal or transvaginal sonohysterography (TVSH), and diagnostic hysteroscopy (with biopsy) vs. histopathology in combination with either hysteroscopy or hysterectomy	Premenopausal women with menstrual symptoms suggestive of underlying uterine pathology	N/A
Gupta et al., 2002	Meta-analysis	Pelvic ultrasonography vs. hysteroscopy and/or endometrial sampling	Postmenopausal women with uterine bleeding	N/A

Table C-2. Summary of Findings From Published Studies on the Accuracy of Cervical, Ovarian, and Endometrial Cancer Screening Tests

Table C-2-a-i. Summary of Findings From Published Studies on the Accuracy of Cervical Cancer Screening Tests in the Detection of Cervical Cancer Among Asymptomatic Women

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>Liquid-based cytology vs. histology</p> <p>Test accuracy of liquid-based cytology (LBC) in detecting cervical lesions or neoplasia relative to conventional cytology (Pap test) among asymptomatic women</p>	<p>1 retrospective comparison; 1 randomized control trial; 1 cross sectional study</p>	<p>LBC³⁶: Sensitivity³⁷ = 75.3% Specificity³⁸ = 86.4% PPV³⁹ = 74.4% NPV⁴⁰ = 87.0%</p> <p>Pap⁴¹: Sensitivity = 81.8% Specificity = 85.2% PPV = 74.1% NPV = 90.1%</p> <p>% of false positive⁴² cases decreased from 2.7% to 2.5% after switch from Pap to LBC</p> <p>Relative sensitivity^{43, 44} of LBC to Pap test is 1.0</p> <p>Relative PPV⁴⁵ of LBC to Pap test is 0.6 (statistically significant)</p>	<ul style="list-style-type: none"> Generalizable: studies evaluated asymptomatic women in developed countries 	<ul style="list-style-type: none"> Evidence from three studies suggests that screening with liquid-based cytology is equally effective at detecting cervical lesions vs. Pap test (relative sensitivity = 1.0); however, liquid-based cytology is less effective in correctly diagnosing patients with a positive test result

³⁶ Statistic from cross sectional study, Mattosinho de Castro Ferraz et al., 2004.

³⁷ Sensitivity to the disease is the probability that if the person has the disease, the test will be "positive."

³⁸ Specificity of the test to the disease is the probability that the test indicates 'negative' if the person does not have the disease.

³⁹ PPV (positive predictive value) = proportion of patients with positive test results who are correctly diagnosed.

⁴⁰ NPV (negative predictive value) = proportion of patients with negative test results who are correctly diagnosed.

⁴¹ The term "Pap" refers to conventional cervical cytology tests.

⁴² Statistic from retrospective comparison, Kirschner et al., 2006.

⁴³ Statistic from randomized control trial, Ronco et al., 2006a and 2006b

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>HPV DNA testing vs. colposcopy and histology</p> <p>Test accuracy of HPV DNA testing in detecting cervical lesions (HSIL+)⁴⁶ and neoplasia (\geq CIN 2+)⁴⁷ relative to conventional cytology (Pap test) among asymptomatic women</p>	<p>1 meta-analysis; 2 randomized control trials</p>	<p>HPV (\geq CIN 2+): Sensitivity = 90.0%–94.6% Specificity = 86.5%–94.1% PPV = 6.4% NPV = 100%</p> <p>Pap (\geq CIN 2+): Sensitivity = 55.4%–72.7% Specificity = 91.9%–96.8% PPV = 7.1% NPV = 99.8%</p> <p>Relative sensitivity⁴⁸ of HPV to Pap test is 1.43 among women 25–60 years of age (\geq CIN 2+, not statistically significant)</p> <p>Relative PPV⁹ of HPV to Pap test is 0.58 among women 25–60 years of age (\geq CIN 2+, statistically significant)</p> <p>Relative sensitivity⁹ of HPV to Pap test is 1.58 among women 25–34 years of age (\geq CIN 2+, statistically significant)</p>	<ul style="list-style-type: none"> Generalizable: studies evaluated asymptomatic women in developed countries or multiple locations 	<ul style="list-style-type: none"> Clear and convincing evidence suggests that screening with HPV DNA testing is more effective at determining those with cervical neoplasia vs. Pap test upon a positive test result Clear and convincing evidence suggests HPV DNA testing is less effective in determining those <i>without</i> cervical neoplasia vs. Pap test upon a negative test result Preponderance of the evidence suggests that HPV DNA testing is less effective in correctly diagnosing patients with a positive test result among women 25–60 years of age (\geq CIN2+)

⁴⁴ Relative sensitivity is the ratio of the alternative screen sensitivity (e.g., LBC) to that of the reference screen sensitivity (e.g., Pap test). Relative sensitivity of 1.0 signifies that the sensitivity of both screens is equivalent (1:1 ratio).

⁴⁵ Relative PPV (positive predictive value = proportion of patients with positive test results who are correctly diagnosed) is the ratio of the alternative screen PPV (e.g., LBC) to that of the reference screen PPV (e.g., Pap). Relative PPV of 0.6 signifies that the reduced loss of PPV for LBC technique is 40%

⁴⁶ HSIL = cytology result of high-grade squamous intraepithelial lesion.

⁴⁷ \geq CIN 2 = biopsy result of cervical intraepithelial neoplasia/moderate-severe or carcinoma in situ or more severe disease.

⁴⁸ Statistics are from the same randomized control trial, however the 2 age cohorts (25–60 years and 25–34 years) are analyzed in two separate publications, Ronco et al., 2006a and 2006b

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
		Relative PPV ⁹ of HPV to Pap test is 0.78 among women 25–34 years of age (\geq CIN 2+, not statistically significant)		
HPV DNA testing + conventional cytology (Pap test) vs. colposcopy/biopsy and histology				
Test accuracy of HPV DNA testing combined with conventional cytology (Pap test) in detecting cervical neoplasia (\geq CIN 2+) relative to conventional cytology alone	1 randomized control trial	<p>HPV + Pap: Sensitivity = 100% Specificity = 92.5% PPV = 5.5% NPV = 100%</p> <p>Pap: Sensitivity = 56.4% Specificity = 97.3% PPV = 8.5% NPV = 99.8%</p> <p>Relative sensitivity of HPV + Pap to Pap test alone is 1.77</p> <p>Relative specificity of HPV + Pap to Pap test alone is 0.95</p> <p>Relative PPV of HPV + Pap to Pap test alone is 0.65</p> <p>Relative NPV of HPV + Pap to Pap test alone is 1.0</p>	<ul style="list-style-type: none"> Generalizable: study evaluated asymptomatic women aged 30–69 years in a developed country 	<ul style="list-style-type: none"> Preponderance of the evidence suggests that HPV DNA testing + Pap testing is less effective in correctly diagnosing patients with a positive test result vs. Pap testing alone
HPV DNA testing + liquid-based cytology vs. colposcopy and histology				
Test accuracy of HPV DNA testing combined with	1 randomized control trial	Relative sensitivity of HPV+LBC to Pap test is 1.02 among women	<ul style="list-style-type: none"> Generalizable: study evaluated 	<ul style="list-style-type: none"> Preponderance of the evidence suggests that

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>liquid-based cytology (LBC) in detecting cervical neoplasia (\geq CIN 2+) relative to conventional cytology (Pap test) alone among asymptomatic women</p>		<p>25–60 years of age (not statistically significant)</p> <p>Relative PPV of HPV+LBC to Pap test is 1.66 among women 25–60 years of age (statistically significant)</p> <p>Relative sensitivity of HPV+LBC to Pap test is 1.29 among women 25–34 years of age (not statistically significant)</p> <p>Relative PPV of HPV+LBC to Pap test is 0.94 among women 25–34 years of age (not statistically significant)</p>	<p>asymptomatic women aged 25–60 years in a developed country</p>	<p>HPV DNA testing + LBC is more effective in correctly diagnosing patients with a positive test result vs. conventional cytology (Pap test) alone (by 66%)</p>
<p>Conventional cytology (Pap test) with HPV triage vs. colposcopy/biopsy and histology</p>				
<p>Accuracy of HPV triage following conventional cytology (Pap test) in identifying cervical lesions (HSIL+) and neoplasia (\geq CIN 2+) relative to conventional cytology among asymptomatic women</p>	<p>1 randomized control trial; 1 systematic review</p>	<p>Pap + HPV triage (\geq CIN 2+): Sensitivity = 53.8% Specificity = 98.7% PPV = 14.9% NPV = 99.8%</p> <p>Pap + HPV triage (HSIL+): Sensitivity = 85% Specificity = 60% NPV = 97%</p> <p>Pap (\geq CIN 2+): Sensitivity = 56.4%</p>	<ul style="list-style-type: none"> Generalizable: studies evaluated asymptomatic women aged 30–69 years in a developed country 	<ul style="list-style-type: none"> Preponderance of the evidence suggests that HPV triage following Pap testing is more effective in correctly diagnosing patients with a positive test result vs. Pap testing alone

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>HPV DNA testing with conventional cytology (Pap test) triage vs. colposcopy/biopsy and histology</p> <p>Accuracy of conventional cytology (Pap test) triage following HPV DNA testing in identifying cervical neoplasia (\geq CIN 2+) relative to conventional cytology alone among asymptomatic women</p>	<p>1 randomized control trial</p>	<p>Specificity = 97.3% PPV = 8.5% NPV = 99.8%</p> <p>HPV + Pap triage: Sensitivity = 53.8% Specificity = 99.1% PPV = 21.4% NPV = 99.8%</p> <p>Pap: Sensitivity = 56.4% Specificity = 97.3% PPV = 8.5% NPV = 99.8%</p> <p>Relative sensitivity of HPV + Pap triage to Pap test alone is 0.95</p> <p>Relative specificity of HPV + Pap triage to Pap test alone is 1.0</p> <p>Relative PPV of HPV + Pap triage to Pap test alone is 2.5</p> <p>Relative NPV of HPV + Pap triage to Pap test alone is 1.0</p>	<ul style="list-style-type: none"> Generalizable: study evaluated asymptomatic women aged 30–69 years in a developed country 	<ul style="list-style-type: none"> Preponderance of the evidence suggests that conventional cytology triage following HPV DNA testing is more effective in correctly diagnosing patients with a positive test result vs. conventional cytology alone

Table C-2-a-ii. Summary of Published Studies on the Accuracy of Cervical Cancer Screening Tests in the Detection of Cervical Cancer Among Women at Increased Risk Due to Abnormal Cytology (i.e., Abnormal Pap Test)

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>Liquid-based cytology vs. histology</p> <p>Test accuracy of liquid-based cytology (LBC) in detecting cervical lesions (LSIL⁴⁹ and HSIL+) and neoplasia (\geq CIN2+) relative to conventional cytology (pap test) among women at increased risk</p>	<p>1 systematic review; 2 split sample studies</p>	<p>LBC: Sensitivity = 91.27%–92% Specificity = 70.86%–76% PPV = 29.26%–57% NPV = 96%–98.4%</p> <p>Pap: Sensitivity = 72.81%–83% Specificity = 82%–85.24% PPV = 39.34%–62% NPV = 93%–95.97%</p>	<ul style="list-style-type: none"> Not generalizable: studies evaluated symptomatic high-risk women with abnormal cytology 	<ul style="list-style-type: none"> Preponderance of the evidence suggests that screening with liquid-based cytology is more effective at determining those <i>with</i> cervical lesions/neoplasia vs. Pap test upon a positive test result among symptomatic and/or high-risk women Preponderance of the evidence suggests liquid-based cytology is less effective in determining those <i>without</i> cervical lesions/ neoplasia vs. Pap test upon a negative test result among this population The evidence suggests that liquid-based cytology is equally effective in correctly diagnosing patients with a positive test result among symptomatic and/or high-risk women

⁴⁹ LSIL = cytology result of low-grade squamous intraepithelial lesion.

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>HPV DNA testing vs. colposcopy/biopsy and histology</p> <p>Test accuracy of HPV DNA testing in detecting cervical neoplasia (\geq CIN 2+) relative to conventional cytology (Pap test) among women at increased risk</p>	<p>2 prospective case series</p>	<p>HPV: Sensitivity = 89.6%–92.4% Specificity = 52.4%–54.3% PPV = 49.3%–67.7% NPV = 82.9%–93.2%</p> <p>Pap: Sensitivity = 76.3%–84.6% Specificity = 49.2%–65.8% PPV = 52.8%–64.2% NPV = 74.8%–84.7%</p>	<ul style="list-style-type: none"> Not generalizable: studies evaluated symptomatic women with abnormal cytology 	<ul style="list-style-type: none"> The evidence from two studies suggests that HPV DNA testing is more effective in correctly diagnosing patients with a negative test result among this population
<p>HPV DNA testing + conventional cytology (Pap test) vs. colposcopy and</p>				

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>histology</p> <p>Test accuracy of HPV DNA testing combined with Pap testing in detecting cervical neoplasia (\geq CIN 2+) relative to conventional cytology (Pap test) alone among women at increased risk</p>	<p>1 prospective case series</p>	<p>HPV + Pap: Sensitivity = 97.8% Specificity = 36.7% PPV = 43.6% NPV = 97.3%</p> <p>Pap: Sensitivity = 76.3% Specificity = 65.8% PPV = 52.8% NPV = 84.7%</p> <p>Relative sensitivity of HPV + Pap to Pap test alone is 1.28</p> <p>Relative specificity of HPV + Pap to Pap test alone is 0.56</p> <p>Relative PPV of HPV + Pap to Pap test alone is 0.83</p> <p>Relative NPV of HPV + Pap to Pap test alone is 1.15</p>	<ul style="list-style-type: none"> • Not generalizable: study evaluated symptomatic women with abnormal cytology 	<ul style="list-style-type: none"> • Evidence from a single study suggests that HPV DNA test + Pap testing is less effective in correctly diagnosing patients with a positive test result vs. Pap testing alone in this population • Evidence from a single study suggests that HPV DNA test + Pap testing is more effective in correctly diagnosing patients with a negative test result vs. Pap testing alone in this population
<p>Conventional cytology (Pap test) with HPV triage vs. colposcopy and histology</p>				
<p>Accuracy of HPV triage following conventional cytology (Pap test) in identifying cervical neoplasia (\geq</p>	<p>1 meta-analysis</p>	<p>Relative sensitivity of HPV triage to repeat Pap is 1.14</p>	<ul style="list-style-type: none"> • Not generalizable: study evaluated symptomatic women 	<ul style="list-style-type: none"> • Preponderance of the evidence suggests that HPV triage is slightly

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
CIN 2+) relative to repeat conventional cytology triage among women at increased risk		Relative specificity of HPV triage to repeat Pap is 0.99		<p>more effective at determining those <i>with</i> cervical neoplasia vs. repeat Pap triage upon a positive test result among symptomatic women</p> <ul style="list-style-type: none"> • Preponderance of the evidence suggests that HPV triage is equally effective in determining those <i>without</i> cervical neoplasia vs. repeat Pap triage upon a negative test result in this population
Liquid-based cytology with HPV triage vs. biopsy and histology				
Accuracy of HPV triage following liquid-based cytology in identifying cervical neoplasia-associated lesions (ASCUS ⁵⁰ , LSIL, HSIL, AIS ⁵¹) among women at increased risk	1 prospective case series	Sensitivity = 97.4% Specificity = 91% PPV = 86% NPV = 98%	<ul style="list-style-type: none"> • Not generalizable: study evaluated symptomatic women 	<ul style="list-style-type: none"> • Evidence from one study suggests that HPV triage following liquid-based cytology is effective among symptomatic women

⁵⁰ ASCUS = Cytology result of atypical squamous cells-undetermined significance

⁵¹ AIS = Cytology or histology result of adenocarcinoma in situ

Table C-2-a-iii. Summary of Published Studies on the Accuracy of Cervical Cancer Screening Tests in the Detection of Cervical Cancer Among Asymptomatic and Women at Increased Risk Due to Abnormal Cytology (i.e., Abnormal Pap Test)

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>Liquid-based cytology vs. histology Test accuracy of liquid-based cytology (LBC) in detecting cervical lesions (LSIL+) and neoplasia (\geq CIN 1+)⁵² relative to conventional cytology (Pap test) among asymptomatic and women at increased risk</p>	<p>1 systematic review; 1 cross sectional study</p>	<p>LBC (\geq CIN1+): Sensitivity = 92% Specificity = 58% Pap (\geq CIN1+): Sensitivity = 95% Specificity = 60%</p> <p>Relative sensitivity of LBC to Pap (LSIL+): 1.12–1.36</p> <p>Relative specificity of LBC to Pap (LSIL+): 0.99–1.0</p>	<ul style="list-style-type: none"> • Somewhat generalizable: population demographics not reported 	<ul style="list-style-type: none"> • Evidence from 2 studies suggests that screening with liquid-based cytology is more effective at determining those <i>with</i> cervical lesions (LSIL+) vs. Pap test upon a positive test result in this population • Evidence from 2 studies suggests that liquid-based cytology is equally effective in determining those <i>without</i> cervical lesions (LSIL+) vs. Pap test upon a negative test result among this population • Preponderance of the evidence suggests that screening with liquid-based cytology is equally effective as Pap test at detecting cervical neoplasia (\geqCIN1+) in this population
<p>HPV DNA testing vs. colposcopy and histology Test accuracy of HPV DNA testing in detecting cervical neoplasia (\geq CIN 1+) relative to conventional cytology (Pap</p>	<p>1 cross sectional study</p>	<p>HPV: Sensitivity = 82% Specificity = 74%</p>	<p>Generalizable: study conducted in a developed country</p>	<ul style="list-style-type: none"> • Evidence from a single study suggests that screening with HPV DNA testing is less effective at determining those <i>with</i> cervical neoplasia vs. Pap test upon a positive test result in this

⁵² \geq CIN1+ = biopsy result of cervical intraepithelial neoplasia/mild dysplasia.

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
test) among asymptomatic and women at increased risk		Pap: Sensitivity = 95% Specificity = 60% Relative sensitivity of HPV test to Pap: 0.86 Relative specificity of HPV test to Pap: 1.23		population; however, HPV DNA testing is more effective in determining those <i>without</i> cervical neoplasia vs. Pap test upon a negative test result

Table C-2-a-iv. Summary of Published Studies on the Accuracy of Cervical Cancer Screening Tests in the Detection of Cervical Cancer Among Populations for Whom Level of Risk Is Unspecified

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>Liquid-based cytology vs. histology</p> <p>Test accuracy of liquid-based cytology (LBC) in detecting cervical lesions and neoplasia relative to conventional cytology (Pap test) findings among populations for whom level of risk is unspecified</p>	<p>1 systematic review</p>	<p>LBC: Sensitivity = 76% Specificity = 86%</p> <p>Pap: Sensitivity = 68% Specificity = 79%</p>	<ul style="list-style-type: none"> Generalizability cannot be assessed because the population is unspecified 	<ul style="list-style-type: none"> Clear and convincing evidence suggests that screening with liquid-based cytology is more effective at determining those <i>with</i> cervical lesions and neoplasia vs. Pap test upon a positive test result Clear and convincing evidence suggests that liquid-based cytology is more effective in determining those <i>without</i> cervical lesions and neoplasia vs. Pap test upon a negative test result
<p>HPV DNA testing vs. histology</p> <p>Test accuracy of HPV DNA testing in detecting cervical neoplasia (\geq CIN 1+) relative to conventional cytology (Pap test) among populations for whom level of risk is unspecified</p>	<p>1 systematic review</p>	<p>HPV: Sensitivity = 62%–100% Specificity = 41%–96% PPV = 1.1%–23% NPV = 98.2%–100%</p> <p>Pap: Sensitivity = 27%–94% Specificity = 78%–99% PPV = 3%–44.2% NPV = 98.4%–99.8%</p>	<ul style="list-style-type: none"> Generalizability cannot be assessed because the population is unspecified 	<ul style="list-style-type: none"> Evidence of the effectiveness of HPV DNA testing to detect cervical neoplasia relative to conventional cytology (Pap test) is ambiguous
<p>HPV DNA testing + conventional cytology (Pap test) vs. histology</p>				

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>Test accuracy of HPV DNA testing combined with Pap testing in detecting cervical neoplasia (\geq CIN 2+) relative to conventional cytology (Pap test) alone among populations for whom level of risk unspecified</p>	<p>1 systematic review</p>	<p>HPV + Pap: Sensitivity = 76%–100% Specificity = 68%–95% PPV = 6%–16% NPV = 99.3%–100%</p> <p>Pap: Sensitivity = 27%–94% Specificity = 78%–99% PPV = 3%–37 % NPV = 98.4%–99.8%</p>	<ul style="list-style-type: none"> Generalizability cannot be assessed because population is unspecified 	<ul style="list-style-type: none"> Preponderance of the evidence suggests that screening with HPV DNA testing + Pap is more effective at determining those <i>with</i> cervical neoplasia vs. Pap test upon a positive test result in this population
<p>Conventional cytology (Pap test) with HPV triage vs. histology</p> <p>Accuracy of HPV triage following Pap testing in identifying cervical neoplasias (\geq CIN 2+) relative to conventional cytology (Pap test) repeat triage among populations for whom level of risk unspecified</p>	<p>1 systematic review</p>	<p>Pap + HPV triage: Sensitivity = 65.9%–97.1% Specificity = 39%–93.3% PPV = 12.8%–19.6% NPV = 100%</p> <p>Pap repeat triage: Sensitivity = 48.4%–76.6% Specificity = 34%–95.8% PPV = 15.8%–28% NPV = 91.8%</p>	<ul style="list-style-type: none"> Generalizability cannot be assessed because the population is unspecified 	<ul style="list-style-type: none"> Preponderance of the evidence suggests that HPV triage following Pap testing is more effective at determining those <i>with</i> cervical neoplasia vs. Pap repeat triage upon a positive test result in this population

Table C-2-b-i. Summary of Published Studies on the Accuracy of Ovarian Cancer Screening Tests in the Detection of Ovarian Cancer among Women in Multiple Risk Groups

Risk assessment, genetic counseling, and mutation testing vs. diagnostic findings (surgery)

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>Identification of women at risk for developing ovarian cancer associated with <i>BRCA1</i> or <i>BRCA2</i> mutations and its impact on ovarian cancer incidence and mortality</p>	<p>1 systematic review</p>	<p>In a hypothetical cohort of 100,000 women, 13 cases of ovarian cancer among average risk women, 16 cases of ovarian cancer among moderate risk women, and 2 cases among high risk women would be prevented if all were tested for <i>BRCA</i> mutation⁵³.</p> <p>Total cases of cancer prevented with testing = 31/100,00</p>	<ul style="list-style-type: none"> Generalizable: study evaluated asymptomatic women at multiple levels of risk with a genetic predisposition Genetic mutations increase a woman's lifetime risk for ovarian cancer to 26% (<i>BRCA1</i>) and 10% (<i>BRCA2</i>)⁸ 	<ul style="list-style-type: none"> Insufficient evidence to suggest that genetic testing for <i>BRCA1</i> or <i>BRCA2</i> mutations for women without increased risk family history is effective; fair evidence to suggest that routine referral and genetic testing of low-risk women would result in adverse consequences

⁵³ See Nelson et al., 2005, for a complete analysis of this cohort.

Table C-2-b-ii. Summary of Published Studies on the Accuracy of Ovarian Cancer Screening Tests in the Detection of Ovarian Cancer Among Asymptomatic, Average-Risk Women

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>Transvaginal ultrasound vs. surgical diagnostic findings</p> <p>Test accuracy of transvaginal ultrasound in detecting ovarian cancer among asymptomatic women with average-risk status (i.e., no familial history of disease or distant relation to an affected relative)</p>	<p>2 systematic reviews; 1 retrospective case series</p>	<p>Sensitivity = 88% (95% CI, 47%–100%)</p> <p>Specificity = 97%–99%</p> <p>PPV: range = 0%–15.6%</p> <p>NPV = NR</p> <p>Number of surgeries per cancer diagnosed (number of false positives per 1 true positive; range): 10–36</p>	<ul style="list-style-type: none"> Somewhat generalizable: studies evaluated asymptomatic women ≥ 50 years in alignment with general population demographic 	<ul style="list-style-type: none"> Preponderance of the evidence suggests that screening with transvaginal ultrasound can detect ovarian cancer at an earlier stage than can be detected in the absence of screening; evidence suggests that earlier detection has a small effect on mortality from ovarian cancer
<p>CA-125 vs. surgical diagnostic findings</p> <p>Test accuracy of CA-125 screening in detecting ovarian cancer among asymptomatic women with average risk status (i.e., no familial history of disease or distant relation to an affected relative)</p>	<p>1 randomized control trial</p>	<p>Sensitivity = NR</p> <p>Specificity = 99.8% (95% CI, 99.7%–99.9%)</p> <p>PPV: range = 19%</p> <p>NPV = NR</p>	<ul style="list-style-type: none"> Somewhat generalizable: studies evaluated asymptomatic women ≥ 50 years in alignment with general population demographic 	<ul style="list-style-type: none"> Preponderance of the evidence suggests that screening with CA-125 can detect ovarian cancer at an earlier stage than can be detected in the absence of screening; evidence suggests that earlier detection has a small effect on mortality from ovarian cancer
<p>Transvaginal ultrasound + CA-125 vs. surgical diagnostic</p>				

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>findings</p> <p>Test accuracy of transvaginal ultrasound + CA-125 in detecting ovarian cancer among asymptomatic women with average risk status (i.e, no familial history of disease or distant relation to an affected relative)</p>	<p>2 systematic reviews; 1 randomized control trial</p>	<ul style="list-style-type: none"> Sequence: CA-125 followed by ultrasound Sensitivity = 79%–100% Specificity = 100% PPV: range = 1.1%–26.8% NPV = NR Number of surgeries per cancer diagnosed (number of FP per 1 TP); range: 3.7–5.6 Sequence: ultrasound followed by CA-125 PPV: range = 6.9%–9.1% Number of surgeries per cancer diagnosed (number of FP per 1 TP); range: 11–15 	<ul style="list-style-type: none"> Somewhat generalizable: studies evaluated asymptomatic women \geq 40 years in alignment with general population demographic 	<p>Preponderance of the evidence suggests that screening with transvaginal ultrasound + CA-125 can detect ovarian cancer at an earlier stage than can be detected in the absence of screening; evidence suggests that earlier detection has a small effect on mortality from ovarian cancer</p>
<p>Ultrasound + color Doppler imaging vs. surgical diagnostic findings</p>	<p>1 systematic review</p>	<p>Sensitivity = NR</p>	<ul style="list-style-type: none"> Somewhat generalizable: 	<ul style="list-style-type: none"> The evidence of the effectiveness of adding color Doppler imaging to
<p>Test accuracy of ultrasound + color Doppler imaging in detecting ovarian</p>				

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
cancer among asymptomatic women with average-risk status (i.e., no familial history of disease or distant relation to an affected relative)		Specificity = NR PPV: range = 10.5%–33.3% NPV = NR Number of surgeries per cancer diagnosed (number of FP per 1 TP); range: 3–10	studies evaluated asymptomatic women \geq 40 years in alignment with general population demographic	ultrasound screening as an enhancement for the detection of ovarian cancer is ambiguous

Table C-2-b-iii. Summary of Published Studies on the Accuracy of Ovarian Cancer Screening Tests in the Detection of Ovarian Cancer Among Asymptomatic, High-Risk Women

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>Transvaginal ultrasound vs. surgical diagnostic findings</p> <p>Test accuracy of transvaginal ultrasound in detecting ovarian cancer among asymptomatic women with familial history of disease or elevated risk age status</p>	<p>1 retrospective case series</p>	<p>Sensitivity = 85%</p> <p>Specificity = 98.7%</p> <p>PPV= 14.01%⁵⁴</p> <p>PPV: moderate risk = 1.2%⁵⁵</p> <p>PPV: high risk = 0.7%⁶</p> <p>NPV = 99.99%</p> <p>Survival of ovarian cancer patients in the annually screened population: 89.9 ± 10.1% at 2 years 77.2 ± 22.8% at 5 years</p>	<ul style="list-style-type: none"> • Somewhat generalizable: study evaluated asymptomatic, high-risk women with genetic predisposition • Genetic mutations increase a woman's lifetime risk for ovarian cancer to 26% (<i>BRCA1</i>) and 10% (<i>BRCA2</i>)⁵⁶ 	<ul style="list-style-type: none"> • Evidence from two studies suggests that transvaginal ultrasound, when performed annually, detects ovarian cancer at an earlier stage and decreases case-specific ovarian cancer mortality; transvaginal ultrasound is less effective in detecting ovarian cancers in women with ovaries of normal size
<p>Transvaginal ultrasound + CA-125 vs. surgical diagnostic findings</p> <p>Test accuracy of transvaginal ultrasound + CA-</p>	<p>1 prospective</p>	<p>Sensitivity =</p>	<ul style="list-style-type: none"> • Somewhat 	<ul style="list-style-type: none"> • Insufficient evidence to

⁵⁴ Statistic from the case series, Van Nagell et al., 2007

⁵⁵ Statistic from the randomized control trial, Lacey et al., 2006

⁵⁶ Statistics cited from Nelson et al., 2005

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
125 in detecting ovarian cancer among asymptomatic women with a hereditary risk factor for ovarian cancer	case series; 1 retrospective audit; 1 randomized control trial	66.7%–100% Specificity = 82.9%–98.7% PPV= 1.5%–10% NPV= 99.8%–100%	generalizable: study evaluated asymptomatic, high-risk women with genetic predisposition <ul style="list-style-type: none"> Genetic mutations increase a woman's lifetime risk for ovarian cancer to 26% (<i>BRCA1</i>) and 10% (<i>BRCA2</i>)⁸ 	suggest that ovarian cancer multimodal screening is accurate and effective for women at high risk

Table C-2-c. Summary of Findings from Studies of the Accuracy of Diagnostic Procedures in the Detection of Endometrial Cancer in Asymptomatic or Symptomatic Premenopausal or Postmenopausal Women

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
<p>Gynecologic ultrasound vs. endometrial histological findings</p> <p>Diagnostic test accuracy of endometrial thickness measurement⁵⁷ by gynecologic ultrasound⁵⁸ for predicting endometrial carcinoma and/or hyperplasia</p>	1 systematic review; 1 meta-analysis	<ul style="list-style-type: none"> • Carcinoma⁵⁹ Sensitivity: range = 33%–100% Specificity: range = 79%–99% • Likelihood ratio⁶⁰ for diagnosing endometrial disease Endometrial thickness ≤ 4 mm Positive test = 2.17 (95% CI 1.73–2.73) Negative test = 0.07 (95% CI 0.04–0.11) Endometrial thickness ≤ 5 mm Positive test = 2.62 (95% CI 2.03–3.38) Negative test = 0.15 (95% CI 0.09–0.27) 	<ul style="list-style-type: none"> • Somewhat generalizable: studies evaluated symptomatic women ; one review population comprised of premenopausal³ women, one review population comprised of postmenopausal⁴ Women. Results may not generalize to asymptomatic women. 	<ul style="list-style-type: none"> • Insufficient evidence that ultrasonic measurement of endometrial thickness is diagnostically accurate for the detection of endometrial hyperplasia or carcinoma
<p>Endometrial biopsy/sampling vs. endometrial histological findings</p> <p>Test accuracy of endometrial biopsy in diagnosing</p>	1 systematic review; 1	<ul style="list-style-type: none"> • Statistically significant • Carcinoma 	<ul style="list-style-type: none"> • Somewhat generalizable: studies 	<ul style="list-style-type: none"> • Preponderance of the evidence suggests that

⁵⁷ Increased thickness of the endometrium is indicative of hyperplasia, which may be a precursor of carcinoma.

⁵⁸ Gynecological ultrasound includes pelvic and transvaginal ultrasonography.

⁵⁹ Statistics cited from Farquhar et al., 2003

⁶⁰ Statistics cited from Gupta et al., 2002

Comparison/Outcome	Research Design	Findings	Generalizability	Conclusion
endometrial disease (carcinoma and/or hyperplasia) in asymptomatic women and women with abnormal uterine bleeding	meta-analysis	Sensitivity = 68%–81% (P = 0.61) Specificity = 99.7%–99.9% (P = 0.01) • Likelihood ratio ⁶¹ for diagnosing cancer: Positive test = 66.48% (95% CI 30.04–147.13) Negative test = 0.14 (95% CI 0.0–0.27)	evaluated premenopausal or postmenopausal women, who were either symptomatic or asymptomatic	endometrial biopsy/sampling has high accuracy in diagnosing endometrial cancer
Hysteroscopy vs. endometrial histological findings				
Test accuracy of hysteroscopy in diagnosing endometrial disease (carcinoma and/or hyperplasia) in women with abnormal uterine bleeding	2 systematic reviews	• Carcinoma ⁶² Sensitivity = 86.4% (95% CI, 84.0% - 88.6%) Specificity = 99.2% (95% CI, 99.1%-99.3%) • Hyperplasia or Carcinoma ² Sensitivity = 78% (95% CI, 76.3% - 79.6%) Specificity = 95.8% (95% CI, 95.6%-96.1%)	• Somewhat generalizable: studies evaluated premenopausal or postmenopausal women with abnormal bleeding; results may not generalize to asymptomatic women	• Clear and convincing evidence that hysteroscopy is accurate in diagnosing endometrial cancer in women with abnormal uterine bleeding

⁶¹ The likelihood ratio indicates by how much a given biopsy finding raises or lowers the probability of having cancer. With a positive test result, a likelihood ratio ≥ 1 increases the probability that cancer will be present. With a negative test result, a likelihood ratio ≤ 1 decreases the probability that cancer is present.

⁶² Statistics are cited from Clark et al., 2002b

Appendix D: Cost Impact Analysis: Data Sources, Caveats, and Assumptions

This appendix describes data sources, as well as general and mandate-specific caveats and assumptions used in conducting the cost impact analysis. For additional information on the cost model and underlying methodology, please refer to the CHBRP Web site, www.chbrp.org/costimpact.html.

The cost analysis in this report was prepared by the Cost Team which consists of CHBRP task force members and staff, specifically from the University of California, Los Angeles, and Milliman Inc. (Milliman). Milliman is an actuarial firm, and it provides data and analyses per the provisions of CHBRP authorizing legislation.

Data Sources

In preparing cost estimates, the Cost Team relies on a variety of data sources as described below.

Private Health Insurance

1. The latest (2005) California Health Interview Survey (CHIS), which is utilized to estimate insurance coverage for California's population and distribution by payer (i.e., employment-based, privately purchased, or publicly financed). The biannual CHIS is the largest state health survey conducted in the United States, collecting information from over 40,000 households. More information on CHIS is available at www.chis.ucla.edu/
2. The latest (2007) California Employer Health Benefits Survey is utilized to estimate:
 - size of firm,
 - percentage of firms that are purchased/underwritten (versus self-insured),
 - premiums for plans regulated by the Department of Managed Health Care (DMHC) (primarily health maintenance organizations (HMOs)),
 - premiums for policies regulated by the California Department of Insurance (CDI) (primarily preferred provider organizations (PPOs)), and
 - premiums for high deductible health plans (HDHP) for the California population covered under employment-based health insurance.

This annual survey is released by the California Health Care Foundation/National Opinion Research Center (CHCF/NORC) and is similar to the national employer survey released annually by the Kaiser Family Foundation and the Health Research and Educational Trust. Information on the CHCF/NORC data is available at: <http://www.chcf.org/topics/healthinsurance/index.cfm?itemID=133543>.

3. Milliman data sources are relied on to estimate the premium impact of mandates. Milliman's projections derive from the Milliman Health Cost Guidelines (HCGs). The HCGs are a health care pricing tool used by many of the major health plans in the United States. See www.milliman.com/expertise/healthcare/products-tools/milliman-care-

[guidelines/index.php](#). Most of the data sources underlying the HCGs are claims databases from commercial health insurance plans. The data are supplied by health insurance companies, Blues plans, HMOs, self-funded employers, and private data vendors. The data are mostly from loosely managed healthcare plans, generally those characterized as preferred provider plans or PPOs. The HCGs currently include claims drawn from plans covering 4.6 million members. In addition to the Milliman HCGs, CHBRP's utilization and cost estimates draw on other data, including the following:

- The MEDSTAT MarketScan Database, which includes demographic information and claim detail data for approximately 13 million members of self-insured and insured group health plans.
- An annual survey of HMO and PPO pricing and claim experience, the most recent survey (2006 Group Health Insurance Survey) contains data from seven major California health plans regarding their 2005 experience.
- Ingenix MDR Charge Payment System, which includes information about professional fees paid for healthcare services, based upon approximately 800 million claims from commercial insurance companies, HMOs, and self-insured health plans.

These data are reviewed for applicability by an extended group of experts within Milliman but are not audited externally.

4. An annual survey by CHBRP of the seven largest providers of health insurance in California (Aetna, Blue Cross of California, Blue Shield of California, CIGNA, Health Net, Kaiser Foundation Health Plan, and PacifiCare) to obtain estimates of baseline enrollment by purchaser (i.e., large and small group and individual), type of plan (i.e., DMHC- or CDI-regulated), cost-sharing arrangements with enrollees, and average premiums. Enrollment in these seven firms represents 93.9% of enrollees in full-service health plans regulated by DMHC and 82.1% of lives covered by comprehensive health insurance products regulated by CDI.

Public Health Insurance

5. Premiums and enrollment in DMHC- and CDI-regulated plans by self-insured status and firm size are obtained annually from CalPERS for active state and local government public employees and their family members who receive their benefits through CalPERS. Enrollment information is provided for fully funded, Knox-Keene licensed health care service plans covering non-Medicare beneficiaries—which is about 75% of CalPERS total enrollment. CalPERS self-funded plans—approximately 25% of enrollment—are not subject to state mandates. In addition, CHBRP obtains information on current scope of benefits from health plans' evidence of coverage (EOCs) publicly available at www.calpers.ca.gov.
6. Enrollment in Medi-Cal managed care (Knox-Keene licensed plans regulated by DMHC) is estimated based on CHIS and data maintained by the Department of Health Care Services (DHCS). DHCS supplies CHBRP with the statewide average premiums negotiated for the Two-Plan Model, as well as generic contracts which summarize the

current scope of benefits. CHBRP assesses enrollment information online at www.dhs.ca.gov/admin/ffdmb/mcss/RequestedData/Beneficiary%20files.htm.

7. Enrollment data for other public programs—Healthy Families, Access for Infants and Mothers (AIM), and the Major Risk Medical Insurance Program (MRMIP)—are estimated based on CHIS and data maintained by the Major Risk Medical Insurance Board (MRMIB). The basic minimum scope of benefits offered by participating plans under these programs must comply with all requirements of the Knox-Keene Act, and thus these plans are affected by changes in coverage for Knox-Keene licensed plans. CHBRP does not include enrollment in the Post-MRMIB Guaranteed-Issue Coverage Products as these individuals are already included in the enrollment for individual health insurance products offered by private carriers. Enrollment figures for AIM and MRMIP are included with enrollment for Medi-Cal in presentation of premium impacts. Enrollment information is obtained online at www.mrmib.ca.gov/. Average statewide premium information is provided to CHBRP by MRMIB staff.

General Caveats and Assumptions

The projected cost estimates 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 may be different from CHBRP assumptions.
- Utilization of mandated services before and after the mandate may be different from CHBRP assumptions.
- Random fluctuations in the utilization and cost of health care services may occur.

Additional assumptions that underlie the cost estimates presented in this report are:

- Cost impacts are shown only for people with insurance and only for the first year after enactment of the proposed mandate.
- The projections do not include people covered under self-insured employer plans because those 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.
- For state-sponsored programs for the uninsured, the state share will continue to be equal to the absolute dollar amount of funds dedicated to the program.
- When cost savings are estimated, they reflect savings realized for one year. Potential long-term cost savings or impacts are estimated if existing data and

literature sources are available and provide adequate detail for estimating long-term impacts. For more information on CHBRP's criteria for estimating long-term impacts please see:

www.chbrp.org/documents/longterm_impacts_final011007.pdf

- Several recent studies have examined the effect of private insurance premium increases on the number of uninsured (Chernew et al., 2005; Hadley, 2006; Glied and Jack, 2003). Chernew et al. estimate that a 10-percent increase in private premiums results in a 0.74 to 0.92 percentage point decrease in the number of insured, whereas Hadley (2006) and Glied and Jack (2003) estimate that a 10-percent increase in private premiums produces a 0.88 and 0.84 percentage point decrease in the number of insured, respectively. The price elasticity of demand for insurance can be calculated from these studies in the following way. First, take the average percentage point decrease in the number of insured reported in these studies in response to a 1-percent increase in premiums (about -0.088), divided by the average percentage of insured individuals (about 80 percent), multiplied by 100 percent, i.e., ($\{[-0.088/80] \times 100\} = -0.11$). This elasticity converts the *percentage point* decrease in the number of insured into a *percentage* decrease in the number of insured for every 1-percent increase in premiums. Because each of these studies reported results for the large-group, small-group, and individual insurance markets combined, CHBRP employs the simplifying assumption that the elasticity is the same across different types of markets. For more information on CHBRP's criteria for estimating impacts on the uninsured please see: http://www.chbrp.org/documents/uninsured_020707.pdf.

There are other variables that may affect costs, but which CHBRP 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 and 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, health plan members 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). CHBRP 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 post-mandate 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 the CHBRP cost estimates. The

dampening would be more pronounced on the plan types that previously had the least effective medical management (i.e., 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 CHBRP modeled (HMO—including HMO and point of service [POS] plans—and non-HMO—including PPO and fee for service [FFS] policies), there are likely variations in utilization and costs by these plan types. Utilization also 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, CHBRP has estimated the impact on a statewide level

Bill Analysis-Specific Caveats and Assumptions

The simplified scenario used to model possible utilization and cost increases associated with AB 1774 was developed based on the opinions of expert physician consultants and community-based physicians, as well as relevant literature. The scenario makes the following assumptions.

Cervical cancer

- Pap tests are already covered for asymptomatic, average-risk women, so utilization of this test would not increase.
- HPV DNA testing is not always covered for asymptomatic, average-risk women under 30 years of age, so utilization would increase for newly covered women.
- The subgroup of women potentially subject to increased use of HPV tests is operationalized as women aged 18–29 years who do not have cervical cancer and who had a negative Pap test in the past year; based on estimates from the literature, this is approximately 48% of all women aged 18 to 29.
- CHBRP assumes that the number of women in this age group who have had total hysterectomies is zero.
- Women with dysplasia are assumed to have already been taken out of the denominator for screening due to abnormal Pap tests.
- CHBRP assumes that of these potential users, 40% of those in CDI-regulated plans will receive an HPV test in the first year post-mandate (25% for staff-model HMO enrollees and Medi-Cal managed care/AIM/MRMIP beneficiaries; 35% for other managed care enrollees).
- Of those receiving an HPV test, 2.9% will receive a positive test result and go on to receive a colposcopy. All women with positive test results (not just those with false positives) are included in the cost calculations because in the absence of the mandate,

women with negative Pap tests would not be given colposcopies, even if they were HPV-positive.

- In the years following the first post-mandate year, the rate of HPV testing would likely fall because it is generally only performed once every 3 years for women aged 30 years and over, and it is unlikely that women under 30 would receive it more frequently. Furthermore providers are currently using HPV tests to screen young women prior to giving them the new HPV vaccine; in the long run, however, that source of demand should diminish as most women will have already been vaccinated. Costs associated with HPV testing could therefore be overestimated.
- Increased utilization of other cervical cancer screening tests is not included in the model, which may lead to an underestimate of costs.

Endometrial Cancer

- Currently, no endometrial cancer screening test is covered for asymptomatic, average-risk women, so utilization of these tests would increase for newly covered women.
- The subgroup of women potentially subject to increased use of these tests is operationalized as women over 18 years who do not have endometrial cancer and who have not had a hysterectomy; based on estimates from the literature, this is approximately 87% of all women aged 18 to 64 and 79% of women 65 and over.
- CHBRP assumes that of these potential users, 10% would be tested for the HNPCC genetic mutation plus receive genetic counseling in the first year post-mandate (0% for staff-model HMO enrollees and Medi-Cal managed care of all ages/AIM/MRMIP beneficiaries; 5% for other managed care enrollees). Note that in later years, this rate would fall as fewer women would remain who had not yet been tested.
- CHBRP also assumes that of these potential users, 20% would receive an endometrial biopsy as an initial screening test (5% for Medi-Cal managed care 65 and over; 10% for staff-model HMO enrollees and Medi-Cal managed care under 65/AIM/MRMIP beneficiaries; 15% for other managed care enrollees).
- Of those receiving an endometrial biopsy, 7.5% would go on to receive dilation and curettage, because the biopsy did not obtain an adequate specimen or otherwise required followup. All dilation and curettage procedures would be performed in an outpatient hospital setting, thereby incurring facility charges in addition to professional fees.
- Increased utilization of other endometrial cancer screening tests is not included in the model, which may lead to an underestimate of costs.

Ovarian Cancer

- Currently no ovarian cancer screening test is covered for asymptomatic, average-risk women, so utilization of these tests would increase for newly covered women.
- The subgroup of women potentially subject to increased use of these tests is operationalized as women 18 years and over who do not have ovarian cancer, who have not had an oophorectomy, and who do not have at least three symptoms of ovarian cancer (which would qualify them for coverage even in the absence of the mandate); based on

estimates from the literature, this is approximately 83% of all women aged 18 to 64 and 80% of women 65 and over.

- CHBRP assumes that of these potential users, 10% would be tested for the *BRCA1/2* genetic mutation and receive genetic counseling in the first year post-mandate (0% for staff-model HMO enrollees and Medi-Cal managed care of all ages/AIM/MRMIP beneficiaries; 5% for other managed care enrollees). Note that in later years, this rate would fall as fewer women would remain who had not yet been tested.
- CHBRP also assumes that of these potential users, 30% would receive a transvaginal ultrasound (TVU) as an initial screening test (5% for Medi-Cal managed care 65 and over; 20% for staff-model HMO enrollees and Medi-Cal managed care under 65/AIM/MRMIP beneficiaries; 25% for other managed care enrollees). TVU was chosen as the “first-line” screening test because it has greater sensitivity than CA-125 blood tests (Fung et al., 2004).
- 90% of TVUs will be performed in an outpatient hospital setting; the other 10% would be performed in a physician’s office.
- Of those receiving a transvaginal ultrasound, 11.2% would go on to receive a CA-125 blood test due to false-positive (1.2%) or indeterminate (10%) TVU results.
- Half of the women receiving a CA-125 blood test would require a special blood draw; the other half would have their blood drawn as part of other testing, so no additional costs would be incurred.
- 0.58% of all of the women receiving the initial TVU screening would have double false-positive results (false positive on the TVU followed by false positive on the CA-125 blood test) and require a follow-up surgical test; three-quarters of these women would receive a laparoscopy and one-quarter would receive a laparotomy. All of these surgical operations would be performed in an outpatient hospital setting.
- Increased utilization of other ovarian cancer screening tests is not included in the model, which may lead to an underestimate of costs.

Table D-1. Comparison of Guidelines for Gynecological Cancer Screening of Asymptomatic Women With Private Health Plan Coverage

	U.S. Preventive Services Task Force Recommendations	ACS Guidelines	Examples of guidelines used by private insurance carriers
Cervical	<p>Cervical cytology (Pap test) in women who have been sexually active and have a cervix.</p> <p>Recommendation against routine screening of average-risk women over age 65 years if they have had adequate recent screening with normal Pap tests, or women who have had a total hysterectomy for benign disease.</p> <p>Insufficient evidence to recommend for or against routine use of HPV testing as a primary screening test or new screening technologies (e.g., liquid based cytology).</p>	<p>Screening test recommended: Pap test</p> <p>No recommendation for HPV DNA test</p>	<p>Screening tests covered for asymptomatic women with and without risk factors:</p> <ul style="list-style-type: none"> • Annual Pap test, pelvic exams, or other FDA-approved cervical screening and HPV screening tests • Annual Pap tests (conventional or liquid-based) with automated cervical cancer slide interpretation systems (except for women with absent cervix or complete hysterectomy for benign disease) HPV DNA testing used in combination with Pap test for screening of women aged 30 years and older (every 3 years if both results negative). • Annual Pap test, pelvic exams, and HPV DNA testing used in combination with Pap test for screening of women aged 30 years and older covered for asymptomatic women with and without risk factors. • Additional screening tests for asymptomatic women with risk factors: liquid-based cytology, colposcopy, biopsy, endocervical curettage. • Determination of medical necessity by provider. • Tests covered at greater frequency for women with risk factors.

Ovarian	U.S. Preventive Services Task Force Recommendations	ACS Guidelines	Examples of guidelines used by private insurance
<p>Recommendation against routine screening, either by measurement of CA-125 levels or by transvaginal ultrasound.</p> <p>Rationale: Early detection would only have a small effect on mortality from ovarian cancer. Harms of screening outweigh the potential benefits.</p>	<p>Transvaginal ultrasonography and CA-125 blood tests are not recommended for ovarian cancer screening of women without known strong risk factors.</p>	<p>Screening tests covered for asymptomatic women without risk factors:</p> <ul style="list-style-type: none"> • Annual pelvic exam • Determination of medical necessity by provider. • No coverage guidelines used for ovarian cancer screening since there are no generally accepted tests for ovarian cancer in asymptomatic women with average risk. • Use same coverage guidelines used for cervical cancer screening since there are no generally accepted tests for ovarian cancer in asymptomatic women with average risk. <p>Screening tests covered for asymptomatic women with risk factors:</p> <ul style="list-style-type: none"> • For asymptomatic women with risk factors: CA-125 measurement if history of ovarian cancer • Annual or semi-annual measurements of CA-125 for patients with known <i>BRCA1</i> or <i>BRCA2</i> mutation or in patients with at least one first degree relative with a history of ovarian cancer. Genetic testing for <i>BRCA1/2</i> and HNPCC women with family history. • Transvaginal ultrasonography for women with <i>BRCA2</i> mutation. • Blood tests (e.g., CA-125), transvaginal or transabdominal ultrasonography with or without color Doppler imaging, rectovaginal pelvic exam, fine needle aspiration cytology, <i>BCRA1/2</i> gene testing. • Determination of medical necessity by provider. 	

Endometrial	U.S. Preventive Services Task Force Recommendations	ACS Guidelines	Examples of guidelines used by private insurance
	<p>Has not issued any recommendations</p>	<p>Currently, there are no tests that can detect endometrial cancer early in asymptomatic women at average risk.</p> <p>Women with or at risk for hereditary nonpolyposis colon cancer (HNPCC) should be offered yearly testing with endometrial biopsy starting at age 35.</p>	<p>Screening tests covered for asymptomatic women without risk factors:</p> <ul style="list-style-type: none"> ● Pap test ● Determination of medical necessity by provider. ● No coverage guidelines used for endometrial cancer screening since there are no generally accepted tests for ovarian cancer in asymptomatic women with average risk. ● Use same coverage guidelines used for endometrial cancer screening since there are no generally accepted tests for ovarian cancer in asymptomatic women with average risk. <p>Screening tests covered for asymptomatic women with risk factors:</p> <ul style="list-style-type: none"> ● Determination of medical necessity by provider. ● No coverage guidelines used for endometrial cancer screening since there are no generally accepted tests for ovarian cancer in asymptomatic women with average risk. ● Use same coverage guidelines used for endometrial cancer screening since there are no generally accepted tests for ovarian cancer in asymptomatic women with average risk. ● Endometrial biopsy, hysteroscopy with dilation and curettage, sonohysterography, and transvaginal ultrasonography.

Note: In addition to screening tests for asymptomatic women, plans cover diagnostic tests for all women with symptoms (e.g., abnormal vaginal bleeding for endometrial cancer; pelvic mass, or combinations of symptoms such as bloating, frequent urination, etc. for ovarian cancer). Besides use of internal guidelines, plans also refer to national guidelines such as the USPTF and ACS.

Appendix E: Information Submitted by Outside Parties

In accordance with CHBRP policy to analyze information submitted by outside parties during the first two weeks of the CHBRP review, the following parties chose to submit information.

No information was submitted directly by interested parties for this analysis.

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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California Health Benefits Review Program Committees and Staff

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 the CHBRP 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 the CHBRP authorizing legislation, UC contracts with a certified actuary, Milliman Inc. (Milliman), to assist in assessing the financial impact of each benefit mandate bill. Milliman also helped with the initial development of CHBRP 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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