

# California Health Benefits Review Program

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Analysis of California Assembly Bill 2342  
BRCA Gene Mutations: Screening, Counseling,  
and Testing

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A Report to the 2017–2018 California State Legislature

April 16, 2018

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# Key Findings:

## Analysis of California Assembly Bill 2342

### BRCA Gene Mutations: Screening, Counseling, and Testing

Summary to the 2017–2018 California State Legislature, April 16, 2018



## AT A GLANCE

The version of California Assembly Bill 2342 analyzed by CHBRP would require that plans and policies provide coverage for breast cancer susceptibility gene (BRCA) screening, and if indicated, genetic counseling and genetic testing for women who meet certain criteria.

1. CHBRP estimates that, in 2019, of the 23.4 million Californians enrolled in state-regulated health insurance, 23.4 million of them will have insurance subject to AB 2342.
2. **Benefit coverage.** CHBRP estimates that AB 2342 would not change benefit coverage because coverage at baseline is 100%. The bill would not be likely to exceed the essential health benefits (EHBs).
3. **Utilization.** Due to 100% baseline coverage for screening, genetic counseling and testing for BRCA gene mutations, CHBRP estimates there will be no measurable change in utilization of these services.
4. **Expenditures.** CHBRP estimates no change in expenditures as utilization will remain steady.
5. **Medical effectiveness.** Regarding **screening**, there is a preponderance of evidence that familial risk screening tools are effective in accurately identifying women at risk for a BRCA mutation. Regarding **counseling**, there is a preponderance of evidence that genetic counseling before testing improves risk perception accuracy, decreases breast-cancer related worry and decreases intention to pursue genetic testing among women unlikely to be mutation carriers. Regarding **testing**, the diagnostic accuracy of BRCA mutation genetic tests — or the tests' ability to correctly identify mutation carriers - appears to be well established.
  - a. CHBRP finds insufficient evidence to conclude whether screening, counseling, and testing for BRCA gene mutations leads to reduced incidence of BRCA-related cancer or reduced mortality due to the lack of studies addressing this question.
6. **Public health.** Because utilization is not expected to change, CHBRP estimates no measurable public health impact.
7. **Long-term impacts.** It appears unlikely that AB 2342 will have long-term cost or public health impacts due to existing coverage for BRCA screening, counseling, and testing as a grade "B" U.S. Preventive Services Task Force (USPSTF) recommended service. If the Affordable Care Act is repealed or altered, AB 2342 would preserve coverage in California for BRCA screening, counseling, and testing.

## CONTEXT

*BRCA1* and *BRCA2* are cancer susceptibility genes that create tumor suppressor proteins.<sup>1</sup> Individuals with inherited mutations in these genes experience an increased risk of developing some types of cancer, including breast and ovarian cancer. BRCA gene mutations can impact both men and women's risk of developing certain kinds of cancer.

## BILL SUMMARY

The bill requires that health care service plans and policies provide coverage for **screening for risk of BRCA genetic mutations** for women who have not been diagnosed with a BRCA-related cancer and are asymptomatic, but may have an increased risk for mutations in breast or ovarian cancer susceptibility genes. AB 2342 requires plans and policies to provide coverage for BRCA screening for asymptomatic women who meet one or more of the following family history criteria:

1. Breast cancer diagnosis before 50 years of age.
2. Bilateral breast cancer.
3. Breast and ovarian cancer.
4. Presence of breast cancer in at least one male family member.
5. Multiple cases of breast cancer in the family.
6. At least one family member with two types of BRCA-related cancer.
7. Ashkenazi Jewish ancestry.

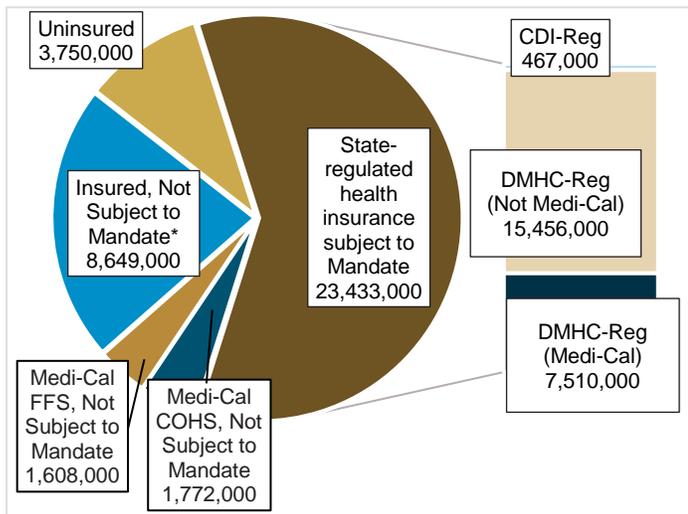
Following use of a generally accepted screening tool to identify family history that may be associated with an increased risk for mutations in *BRCA1* or *BRCA2* genes, AB 2342 requires that plans and policies also cover genetic counseling and genetic testing, if indicated. For women who receive positive screening results, the bill requires that plans and policies provide coverage for **genetic counseling**. If indicated after counseling, AB 2342 also requires coverage for BRCA mutation **genetic**

<sup>1</sup> Refer to CHBRP's full report for full citations and references.

**testing.** The full text of AB 2342 can be found in Appendix A.

Figure 1 notes the number of Californians with health insurance that would be subject to AB 2342, those with insurance coverage not subject to AB 2342, and Californians that are uninsured.

**Figure 1.** Health Insurance in CA and AB 2342



Source: California Health Benefits Review Program, 2018.

Notes: \*Medicare beneficiaries, enrollees in self-insured products, etc.

Key: CDI = California Department of Insurance; COHS = County Organized Health Systems; DMHC = Department of Managed Care; FFS = Fee-for-Service.

## IMPACTS

### Benefit Coverage, Utilization, and Cost

The Affordable Care Act (ACA) requires that certain preventive services be covered without cost sharing for private nongrandfathered plans (individual, small group, and large group).

Based on the recommendation of the U.S. Preventive Services Task Force (USPSTF), nongrandfathered group and individual health insurance plans and policies are required to cover, without cost sharing, screening, genetic counseling, and testing, if indicated, for women whose family history is associated with an increased risk for *BRCA1* or *BRCA2* gene mutations.

### Benefit Coverage

CHBRP estimates 100% of enrollees with health insurance that would be subject to AB 2342 have coverage for screening of family history risk for breast cancer susceptibility genes (*BRCA*), genetic counseling, and *BRCA* mutation testing.

Current coverage of *BRCA* family history screening, genetic counseling, and testing was determined by a survey of the largest (by enrollment) health insurers in California. Responses to this survey represent 78% of enrollees in privately funded health insurance market that can be subject to state mandates, 59% of enrollees with coverage through a Medi-Cal Managed Care Plan.

### Utilization

Because an estimated 100% of enrollees have coverage for the benefits outlined in AB 2342, CHBRP estimates no measurable change in utilization following enactment of AB 2342. Because AB 2342 will not lead to a change in benefits for health plans, CHBRP assumes health plans will not invest in new marketing or documentation changes that may raise provider awareness or education.

### Expenditures

AB 2342 would result in no measurable change in total net annual expenditures, premiums, or enrollee expenses for covered and/or noncovered benefits.

Among publicly funded DMHC-regulated health plans, CHBRP estimates no impact on Medi-Cal Managed Care. Because AB 2342 does not apply to Medi-Cal Fee-for-Service or Medi-Cal County Organized Health Systems, CHBRP estimates no impact on these market segments.

### CalPERS

CHBRP estimates no measurable impact projected on CalPERS plans.

### Number of Uninsured in California

CHBRP estimates no measurable impact on the number of people who are uninsured in California.

## Medical Effectiveness

Although there is no direct evidence that the clinical pathway outlined in AB 2342 — familial risk screening, genetic counseling, and then genetic testing — leads to reductions in the incidence of BRCA-related cancer, cancer-related mortality, or all-cause mortality, there is indirect evidence supporting that each of these activities, as well as risk-reducing interventions for women identified as *BRCA1* or *BRCA2* mutation carriers, are effective. Through CHBRP’s review of the 2013 systematic review to inform the USPSTF, as well as studies published since 2012, CHBRP finds evidence that:

- Familial risk screening tools can accurately identify women at risk for BRCA mutations.
- Genetic counseling before genetic testing improves risk perception accuracy and decreases intention to pursue testing among women unlikely to be BRCA carriers.
- Positive BRCA mutation test results accurately predicts the risk of developing BRCA-related cancer.
- Risk-reducing interventions (intensive screening, medications, and surgery) can mitigate some BRCA-related cancer risk, particularly for BRCA-related breast cancer, leading to reduced incidence of breast cancer and mortality.

## Public Health

Although the continuum of screening services for BRCA gene mutations — family-history based risk screening, genetic counseling, and genetic testing — is medically effective, CHBRP concludes that passage of AB 2342 would have no short-term public health impact on breast

cancer outcomes or disparities in screening among women in California due to no population level changes in coverage or utilization for BRCA screening services.

## Long-Term Impacts

It appears unlikely that AB 2342 will have long term cost or public health impacts due to existing coverage for BRCA screening, counseling and testing as a grade “B” USPSTF recommended service. If the Affordable Care Act is repealed or altered, it is possible that AB 2342 would preserve coverage for BRCA screening, counseling and testing.

## Essential Health Benefits and the Affordable Care Act

Nongrandfathered individual and small group plans are required to cover essential health benefits, including preventive services with a grade “A” or “B” from the US Preventive Services Task Force (USPSTF). At the time of this report’s publication, the USPSTF recommends (with a grade “B”) that primary care providers screen women who have a family history of BRCA-related cancer (i.e., family members with breast, ovarian, tubal, or peritoneal cancer). The risk requirements described in AB 2342 include several similar family history risk requirements, but also include Ashkenazi Jewish ancestry independent of family history. The USPSTF also recommends with a grade “B” that women who screen positive should then receive genetic counseling and, if indicated, genetic testing for BRCA gene mutations. The USPSTF recommendation does not apply to men.

AB 2342 would not require coverage for a new state benefit mandate, but would rather define the risk requirements for screening for *BRCA1* and *BRCA2* gene mutations. The bill requirements appear not to exceed the definition of EHBs in California.

A Report to the California State Legislature

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April 16, 2018

**California Health Benefits Review Program**  
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The California Health Benefits Review Program (CHBRP) was established in 2002. As per its authorizing statute, CHBRP provides the California Legislature with independent analysis of the medical, financial, and public health impacts of proposed health insurance benefit-related legislation. The state funds CHBRP through an annual assessment on health plans and insurers in California.

An analytic staff based at the University of California, Berkeley, supports a task force of faculty and research staff from multiple University of California campuses to complete each CHBRP analysis. A strict conflict-of-interest policy ensures that the analyses are undertaken without bias. A certified, independent actuary helps to estimate the financial impact. Content experts with comprehensive subject-matter expertise are consulted to provide essential background and input on the analytic approach for each report.

More detailed information on CHBRP's analysis methodology, authorizing statute, as well as all CHBRP reports and other publications are available at [www.chbrp.org](http://www.chbrp.org).

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**Table 1.** AB 2342 2019 Impacts on Benefit Coverage, Utilization, and Cost

	Baseline and Postmandate
<b>Benefit Coverage</b>	
Total enrollees with health insurance subject to state benefit mandates (a)	23,433,000
Total enrollees with health insurance subject to AB 2342	23,433,000
Percentage of enrollees with health insurance subject to AB 2342	100%
Number of enrollees with health insurance fully compliant with AB 2342	23,433,000
Percentage of enrollees with health insurance fully compliant AB 2342	100%
<b>Utilization and Cost</b>	
Number of female enrollees with a family history of breast or ovarian cancer using genetic counseling or BRCA testing <sup>(a)</sup>	20,000
Counts of service (total)	64,000
Genetic counseling	15,000
BRCA testing	49,000
Utilization per 1,000 Covered Enrollees (total)	2.73
Genetic counseling	0.65
BRCA testing	2.08
Average Cost/Unit (both services)	\$1,034
Genetic counseling	\$161
BRCA testing	\$1,307
Average Cost Sharing/Unit (both services)	\$21
Genetic counseling	\$3
BRCA testing	\$26
PMPM (both services)	\$0.2354
Genetic counseling	\$0.0088
BRCA testing	\$0.2267

Source: California Health Benefits Review Program, 2018.

Notes: (a) CHBRP estimates are derived from MarketScan 2016. CHBRP is unable to ascertain from MarketScan data the results of family history risk screening or testing, and thus reports only utilization and costs of services of those with a family cancer history and no personal diagnosis of cancer.; thus, utilization is presented for women with a family history of breast or ovarian cancer (degree of relative not specified).

Key: CalPERS HMOs = California Public Employees' Retirement System Health Maintenance Organizations; CDI = California Department of Insurance; DMHC = Department of Managed Healthcare Services.

## POLICY CONTEXT

The California Assembly Committee on Health has requested that the California Health Benefits Review Program (CHBRP)<sup>2</sup> conduct an evidence-based assessment of the medical, financial, and public health impacts of AB 2342, BRCA Gene Mutations: Screening, Counseling, and Testing.

### Bill-Specific Analysis of AB 2342, BRCA Gene Mutations: Screening, Counseling, and Testing

#### BRCA Gene Mutations

*BRCA1* and *BRCA2* are cancer susceptibility genes that create tumor suppressor proteins (NCI, 2018). Individuals with inherited mutations in these genes experience an increased risk of developing some types of cancer, including breast and ovarian cancer. BRCA gene mutations can impact both men and women's risk of developing certain kinds of cancer.

#### Bill Language

AB 2342 would require that health care service plans and health insurance policies provide coverage for breast cancer susceptibility gene (BRCA) screening, and if indicated, genetic counseling and genetic testing for women who meet certain criteria.

The bill requires that plans and policies cover **screening** for women who have not been diagnosed with a BRCA-related cancer and are asymptomatic, but may have an increased risk for mutations in breast or ovarian cancer susceptibility genes. Per the bill language, this applies to asymptomatic women who meet one or more of the following family history criteria:

1. Breast cancer diagnosis before 50 years of age.
2. Bilateral breast cancer.
3. Breast and ovarian cancer.
4. Presence of breast cancer in at least one male family member.
5. Multiple cases of breast cancer in the family.
6. At least one family member with two types of BRCA-related cancer.
7. Ashkenazi Jewish ancestry.

Following use of a generally accepted screening tool to identify family history that may be associated with an increased risk for mutations in *BRCA1* or *BRCA2* genes, AB 2342 requires that plans and policies also cover genetic counseling and genetic testing, if indicated. For women who receive positive screening results, the bill requires that plans and policies provide coverage for **genetic counseling**. If indicated after counseling, AB 2342 also requires coverage for BRCA **genetic testing**. The full text of AB 2342 can be found in Appendix A.

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<sup>2</sup> CHBRP's authorizing statute is available at <http://chbrp.org/faqs.php>.

## Relevant Populations

If enacted, AB 2342 would apply to the health insurance of approximately 23.4 million enrollees (60% of all Californians).<sup>3</sup> This represents 100% of the 23.4 million Californians who will have health insurance regulated by the state that may be subject to any state health benefit mandate law — health insurance regulated by the California Department of Managed Health Care (DMHC) or the California Department of Insurance (CDI). If enacted, the law would apply to the health insurance of enrollees in DMHC-regulated plans and CDI-regulated policies, exempting specialized health care service plans.

## Interaction With Existing Requirements

Health benefit mandates may interact and align with the following federal and state mandates or provisions.

### Federal Policy Landscape

#### *Affordable Care Act*

A number of Affordable Care Act (ACA) provisions have the potential to or do interact with state benefit mandates. Below is an analysis of how AB 2342 may interact with requirements of the ACA as presently exists in federal law, including the requirement for certain health insurance to cover essential health benefits (EHBs).<sup>4</sup>

Any changes at the federal level may impact the analysis or implementation of this bill, were it to pass into law. However, CHBRP analyzes bills in the current environment given current law and regulations.

#### Federally Selected Preventive Services

Under the Affordable Care Act Preventive Services requirement (Section 2713 of the Public Health Service Act), nongrandfathered group (small and large) and individual health insurance plans and policies are required to cover certain preventive services without cost sharing when delivered by in-network providers and as soon as 12 months after a recommendation appears in any of the following:<sup>5</sup>

- The United States Preventive Services Task Force (USPSTF) A and B recommendations;
- The Health Resources and Services Administration (HRSA)-supported health plan coverage guidelines for women's preventive services;
- The HRSA-supported comprehensive guidelines for infants, children, and adolescents, which include:
  - The Bright Futures Recommendations for Pediatric Preventive Health Care; and

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<sup>3</sup> Although AB 2342 is related to care for women enrollees only, the bill would apply to all state-regulated health insurance, not just the state-regulated insurance of women enrollees.

<sup>4</sup> The ACA requires nongrandfathered small-group and individual market health insurance — including, but not limited to, qualified health plans sold in Covered California — to cover 10 specified categories of EHBs. Resources on EHBs and other ACA impacts are available on the CHBRP website: [http://www.chbrp.org/other\\_publications/index.php](http://www.chbrp.org/other_publications/index.php).

<sup>5</sup> A resource on this ACA requirement is available on the CHBRP website: [www.chbrp.org/other\\_publications/index.php](http://www.chbrp.org/other_publications/index.php).

- The recommendations of the Secretary's Advisory Committee on Heritable Disorders in Newborns and Children; and
- The Advisory Committee on Immunization Practices (ACIP) recommendations that have been adopted by the Director of the Centers for Disease Control and Prevention (CDC).

At the time of this report's publication, the USPSTF recommends with a grade "B" that primary care providers screen women who have a family history of BRCA-related cancer (i.e., family members with breast, ovarian, tubal, or peritoneal cancer) with a screening tool designed to identify family history that may be associated with an increased risk for potentially harmful mutations in the *BRCA1* or *BRCA2* genes. Women who receive a positive screening result should then be offered genetic counseling, and if indicated, BRCA genetic testing (USPSTF, 2013).

The population relevant to this USPSTF recommendation includes asymptomatic women who have not been diagnosed with a BRCA-related cancer but who have family member(s) with breast, ovarian, tubal (fallopian tube), or peritoneal cancer. The recommendation states that women with one or more family members with a known potentially harmful mutation in the *BRCA1* or *BRCA2* genes should be offered genetic counseling and testing. This recommendation does not apply to men.

Based on the grade "B" rating, nongrandfathered group and individual health insurance plans and policies are currently required to cover, without cost sharing, screening, genetic counseling, and genetic testing, if indicated, for women whose family history is associated with an increased risk for *BRCA1* or *BRCA2* gene mutations (CMS, 2015).

It should be noted that for women whose family history is *not* associated with an increased risk, the USPSTF recommends against routine genetic counseling or BRCA testing; the panel grades routine counseling or testing a grade "D" (USPSTF, 2013).

### Essential Health Benefits

State health insurance marketplaces, such as Covered California, are responsible for certifying and selling qualified health plans (QHPs) in the small-group and individual markets. QHPs are required to meet a minimum standard of benefits as defined by the ACA as essential health benefits (EHBs). In California, EHBs are related to the benefit coverage available in the Kaiser Foundation Health Plan Small Group Health Maintenance Organization (HMO) 30 plan, the state's benchmark plan for federal EHBs.<sup>6,7</sup>

States may require QHPs to offer benefits that exceed EHBs.<sup>8</sup> However, a state that chooses to do so must make payments to defray the cost of those additionally mandated benefits, either by paying the purchaser directly or by paying the QHP.<sup>9,10</sup> State rules related to provider types, cost sharing, or

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<sup>6</sup> The U.S. Department of Health and Human Services (HHS) has allowed each state to define its own EHBs for 2014 and 2015 by selecting one of a set of specified benchmark plan options. CCIO, Essential Health Benefits Bulletin. Available at: [cciio.cms.gov/resources/files/Files2/12162011/essential\\_health\\_benefits\\_bulletin.pdf](http://cciio.cms.gov/resources/files/Files2/12162011/essential_health_benefits_bulletin.pdf).

<sup>7</sup> H&SC Section 1367.005; IC Section 10112.27.

<sup>8</sup> ACA Section 1311(d)(3).

<sup>9</sup> State benefit mandates enacted on or before December 31, 2011, may be included in a state's EHBs, according to the U.S. Department of Health and Human Services (HHS). Patient Protection and Affordable Care Act: Standards Related to Essential Health Benefits, Actuarial Value, and Accreditation. Final Rule. Federal Register, Vol. 78, No. 37. February 25, 2013. Available at: [www.gpo.gov/fdsys/pkg/FR-2013-02-25/pdf2013-04084.pdf](http://www.gpo.gov/fdsys/pkg/FR-2013-02-25/pdf2013-04084.pdf).

<sup>10</sup> However, as laid out in the Final Rule on EHBs HHS released in February 2013, state benefit mandates enacted on or before December 31, 2011, would be included in the state's EHBs and there would be no requirement that the state defray the costs of those state mandated benefits. For state benefit mandates enacted after December 31, 2011, that are identified as exceeding EHBs, the state would be required to defray the cost.

reimbursement methods would *not meet* the definition of state benefit mandates that could exceed the EHBs.

AB 2342 would not require coverage for a new state benefit mandate, but would rather specify the risk requirements for screening for *BRCA1* and *BRCA2* gene mutations. At the time of this report's publication, the USPSTF recommends with a grade "B" that primary care providers screen women who have a family history of BRCA-related cancer (i.e., family members with breast, ovarian, tubal, or peritoneal cancer). The risk requirements described in AB 2342 include several similar family history risk factors, but also include Ashkenazi Jewish ancestry regardless of family history as one possible risk requirement for being screened for BRCA gene mutations. The USPSTF also recommends with a grade "B" that women who screen positive should then receive genetic counseling and, if indicated, genetic testing for BRCA gene mutations. The USPSTF recommendation does not apply to men.

California's EHBs are based on the state's benchmark plan, and the benchmark plan is a small-group plan that is required to cover services outlined in the ACA preventive services requirement. This includes services with an "A" or "B" grading from the USPSTF, such as the "B" graded BRCA-related services described previously. As such, the benchmark plan is required to cover these services without cost sharing to meet the preventive services requirement. The bill requirements appear not to exceed the definition of EHBs in California.

## California Policy Landscape

### *California law and regulations*

CHBRP is unaware of similar mandates at the state level related to BRCA gene mutations. More broadly, Section 1367.6 of the California Health and Safety Code and Section 10123.8 of the California Insurance Code require coverage for screening for, diagnosis of, and treatment for breast cancer in DMHC-regulated plans and CDI-regulated policies.

### *Other California programs*

The Every Woman Counts (EWC) program provides free breast and cervical cancer screenings and diagnostic services to underserved populations (DHCS, 2017b). It is the state equivalent of a national program, the National Breast and Cervical Cancer Early Detection Program (NBCCEDP) of the Centers for Disease Control and Prevention. The Breast and Cervical Cancer Treatment Program provides cancer treatment to women with household incomes at or below 200% of the Federal Poverty Level, who are under 65 years of age and with no other source of insurance, who have been diagnosed with breast or cervical cancer and require treatment (DHCS, 2017a).

Because these programs are administered under the Medi-Cal Fee-for-Service program, which is not impacted by this bill, and because they focus largely on patient populations that are uninsured, CHBRP considered these programs to be outside the scope of this bill, which impacts insurance coverage requirements.

### *Similar requirements in other states*

Several states have considered or are considering bills related to coverage of BRCA screening, genetic counseling, and/or genetic testing, including Hawaii, Kentucky, Maine, New Mexico, and Oregon. Oregon passed a bill focused on reproductive health that also required screening to determine whether

counseling related to the *BRCA1* or *BRCA2* gene mutations is indicated.<sup>11</sup> The bill was signed into law by Oregon Governor Kate Brown, and became effective August 15, 2017.<sup>12</sup>

## Medicaid Coverage of BRCA Screening, Counseling, and/or Testing

States with expanded Medicaid programs are required to cover preventive services for adults who became newly eligible under the Affordable Care Act's Medicaid expansion. This includes services outlined in the USPSTF recommendations with a grade A or grade B, such as screening, genetic counseling, and genetic testing for *BRCA1* and *BRCA2* gene mutations in women with a family history of BRCA-related cancer. However, states are not required to cover the same set of preventive services for adults enrolled in a traditional Medicaid program prior to Medicaid expansion (Gates et al., 2014). Still, 37 states, including California, cover genetic testing for *BRCA1* and *BRCA2* in their traditional Medicaid program (Walls et al., 2016).

## Other Considerations

Apart from federal and state policy considerations, there are important market considerations for services related to BRCA gene mutations.

Recent literature has already documented an increase in BRCA testing from 2013 to 2014, thought to be associated with the following events in 2013: 1) increased market competition following a Supreme Court decision that eliminated a testing monopoly; 2) clarification of the Affordable Care Act preventive services requirements that BRCA testing and genetic counseling qualified as a preventive service with elimination of cost sharing (based on the USPSTF recommendation); 3) celebrity publicity regarding BRCA risks (Weren et al., 2017). However, incomplete provider knowledge, lack of provider referrals, and lack of familiarity with family history patterns as appropriate indications for BRCA evaluation have been cited as the primary sources of underutilization of genetic counseling and BRCA testing (Armstrong et al., 2015; Bellcross et al., 2011; Hamilton et al., 2017; Nair et al., 2017).

Another consideration is the presence of BRCA tests marketed to consumers, particularly following the Supreme Court decision eliminating a market monopoly on such tests.

In March of 2018, the Food and Drug Administration approved direct-to-consumer marketing of a BRCA test that detects three specific *BRCA1/BRCA2* gene mutations (out of thousands of possible BRCA gene mutations) that are common in people of Ashkenazi Jewish ancestry, but not the general population (FDA, 2018).

## Analytic Approach and Key Assumptions

Because the bill is limited to care for women enrollees, the CHBRP analysis focuses on medical effectiveness evidence, cost and utilization, and public health considerations as they relate to women. The impacts on men are outside the scope of this report.

The bill language states that relevant health care service plans and health insurance policies shall “provide breast cancer susceptibility gene (BRCA) screening, genetic counseling, and testing services under the circumstances described.” CHBRP assumes that this language indicates that health insurance

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<sup>11</sup> Enrolled Oregon House Bill 3391 (HB 3391-B).

<https://olis.leg.state.or.us/liz/2017R1/Downloads/MeasureDocument/HB3391>. Accessed March 3, 2018.

<sup>12</sup> Enrolled Oregon House Bill 3391 (HB 3391-B).

<https://olis.leg.state.or.us/liz/2017R1/Downloads/MeasureDocument/HB3391>. Accessed March 3, 2018.

plans and policies shall provide *coverage* for the mentioned services, and not that the plans and policies would provide such services in place of health care providers.

CHBRP assumes that the relevant population for this bill includes women 18 to 64 years old with state-regulated health insurance coverage. Genetic testing is not recommended for patients under 18 as it would not change management (increased screening and risk reduction treatments do not start until age 18)<sup>13</sup> and there are concerns related to informed consent of minors (Nelson, 2013). The majority of women aged 65 and older are Medicare beneficiaries.

The report examines the baseline utilization of screening, genetic counseling, and genetic testing for *BRCA1* and *BRCA2* gene mutations.

Although there are several BRCA-related cancers, for the purposes of the cost and utilization projections, this report focuses on breast and ovarian cancer because they are the most common BRCA-related cancers.

Among nongrandfathered group and individual health insurance plans and policies, BRCA screening, counseling, and genetic testing are currently covered without cost sharing through the federal preventive services requirement. Based on USPSTF guidelines, this is relevant for women with at least one family member with breast, ovarian, or other types of BRCA-related cancer. Because this requirement already applies to nongrandfathered group and individual health insurance plans and policies, CHBRP assumes that the bill has the potential to only impact coverage for grandfathered plans.

Lastly, direct-to-consumer marketed BRCA genetic tests are considered to be outside the scope of this analysis. Because the bill language outlines the clinical pathway to be followed for mandated insurance coverage, we did not consider the impact of direct-to-consumer genetic testing, which may occur without risk assessment or genetic counseling. Furthermore, plans and policies may have contracts in place to complete BRCA genetic tests which may exclude direct-to-consumer BRCA genetic tests.

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<sup>13</sup> Personal communication, Patricia Ganz, MD, University of California, Los Angeles. April 1, 2018.

## BACKGROUND ON BRCA-ASSOCIATED HEREDITARY BREAST AND OVARIAN CANCER SYNDROME

This *Background* section provides context for understanding the scope and impact of BRCA-related hereditary breast and ovarian cancer (HBOC) syndrome among women in California and the pathway for genetic testing. Although BRCA gene mutations have been implicated in many types of cancers in both men and women, the **coverage for screening, genetic counseling, and testing mandated in AB 2342 is limited to women with a specific familial risk (defined below) for breast and ovarian cancer.** Therefore, information on BRCA-related cancers in men and non-breast or non-ovarian cancers will not be presented in this report; it should be noted, however, that cancers in men and non-breast, non-ovarian cancers must be considered by health care providers in screening, counseling and testing.

### What Is Hereditary Breast and Ovarian Cancer Syndrome?

HBOC is characterized by an inherited risk for breast and ovarian cancers that occurs at younger ages or with greater frequency than in the average population. HBOC is most commonly caused by harmful mutations in the *BRCA1* and *BRCA2* genes (or BRCA, generally) that can be passed down by both men and women.

It is not uncommon for persons with HBOC to have several generations of family members affected by these cancers because BRCA gene mutations exhibit an autosomal dominant pattern of transmission. This means that offspring and siblings have a 50% chance of inheriting the gene mutation from a parent who carries the gene mutation(s), thereby becoming gene mutation carriers themselves. In the United States, 10% to 20% of persons with breast and ovarian cancer have a close relative<sup>14</sup> who has also had one of these cancers (Wooster and Weber, 2003).

Specific high-risk BRCA mutations that are clustered among certain ethnic groups, known as *founder mutations*, have also been implicated in hereditary breast and ovarian cancer susceptibility. There are known founder mutations for persons of Ashkenazi Jewish ancestry, African Americans, U.S. Hispanics, and among persons from the Netherlands, Iceland, and Sweden (Peshkin and Isaacs, 2018).

### Lifetime Cancer Risk and the Prevalence of BRCA Gene Mutations

BRCA gene mutations can substantially increase a person's lifetime risk for breast or ovarian cancer relative to the general population. Whereas the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program estimates that the lifetime risk of developing breast cancer among women aged 70 years and older in the general population is 7%, the risk of breast cancer increases to 45% to 65% with clinically significant *BRCA1/2* gene mutation. Comparatively, the lifetime risk for ovarian cancer at age 70 years and older in the general population is 0.7%; however, women aged 70 and older with BRCA mutations have a 17% to 39% chance of developing ovarian cancer (Antoniou et al., 2003; Howlader, 2017).

Estimates of BRCA gene mutation prevalence in the *general population* (otherwise known as the carrier rate) range from 1:300 (0.3%) to 1:500 (0.2%) women. It should be noted that groups with known founder

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<sup>14</sup> Guidelines issued by the American College of Obstetricians and Gynecologists (ACOG) and the National Comprehensive Care Network (NCCN) define a close family member as a first-degree relative (parents, siblings, children), second-degree relative (grandparents, aunts/uncles, nieces/nephews, grandchildren and half-siblings), or third-degree relative (great-grandparents, great-aunts/great-uncles, great-grandchildren, and first cousins).

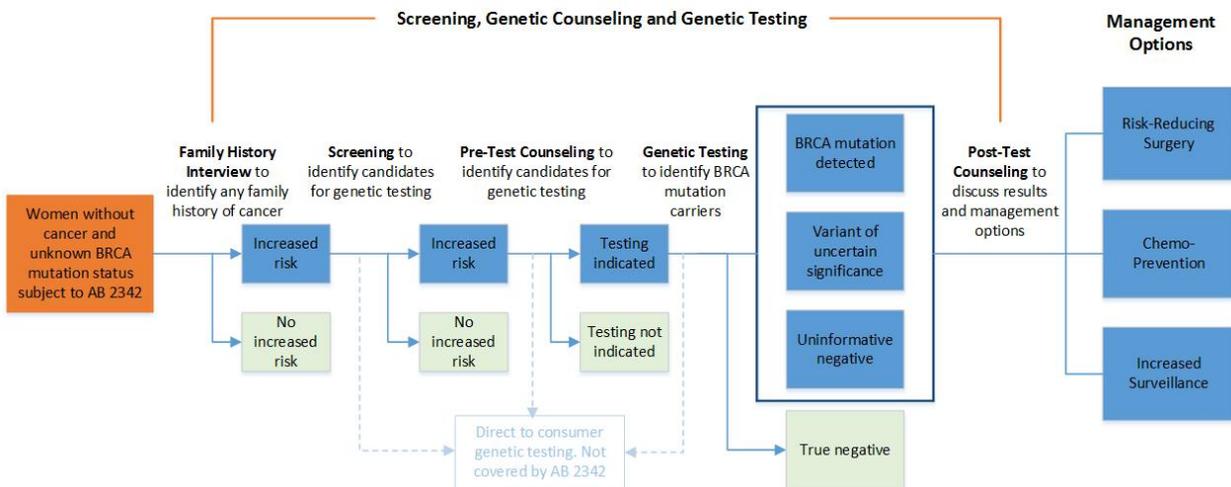
mutations often demonstrate a higher prevalence of *BRCA1/2* mutations relative to the general population. For instance, the prevalence of BRCA gene mutations among persons of Ashkenazi Jewish ancestry has been estimated to be 1:40 (2.5%) (Manchanda et al., 2014).

Estimates of HBOC prevalence among the *populations diagnosed with breast and ovarian cancers* may be more clinically useful. Using this method, large population-based studies from the United Kingdom and Australia observed that 12% of breast cancers and 14% of ovarian cancers were attributable to BRCA gene mutations (Alsop et al., 2012; Copson et al., 2018). The American Cancer Society estimates that in 2018, there will be approximately 29,360 new cases of female breast cancer and 2,540 new cases of ovarian cancer in California (Siegel et al., 2018); therefore, CHBRP estimates that 3,523 cases of breast cancer and 356 cases of ovarian cancer diagnosed in California in 2018 will be attributable to *BRCA1/2* gene mutations.

## BRCA Gene Mutation Detection and Management

AB 2342 mandates coverage for the continuum of services that comprise the detection pathway (Figure 1) for BRCA gene mutations: familial risk screening, genetic counseling prior to genetic testing, and genetic testing for BRCA gene mutations. Although the bill language does not clearly differentiate between pre-test and post-test counseling, post-test genetic counseling is commonly recommended for BRCA tests because the results can be complex and difficult to interpret (Kolor et al., 2017). These activities, and the clinical management options for confirmed BRCA gene mutations, are described in the following five subsections.

**Figure 2.** Clinical Pathway for HBOC Detection and Management



### Screening for HBOC Risk

Screening (also known as risk assessment) for HBOC generally occurs in primary care settings and involves a two-step assessment of personal cancer risk conferred by individual and family characteristics.

In the first step, patients are assessed for their general cancer risk as part of a primary care family history. During a standard family history interview, providers ask whether patients have family member with cancer, the specific types of cancer, primary cancer sites, which family members were affected, relatives with multiple types of primary cancer, and the age at diagnosis and sex of affected family members (Moyer, 2014). Guidelines issued by ACOG and the National Cancer Care Network (NCCN) state that a

family member must be a first-, second-, or third-degree relative to confer sufficient risk indicating the need for additional assessment.

If it is determined from the initial screen that a patient has at least one family member with breast, ovarian, or other types of BRCA-related cancers, guidelines issued by the United States Preventive Services Task Force (USPSTF) and the NCCN recommend that providers administer a brief familial risk stratification tool (step two) to determine whether a patient's risk for HBOC is sufficient to necessitate in-depth genetic counseling (Daly et al., 2017; Moyer, 2014).

Many BRCA-specific risk stratification tools exist, but the USPSTF recommends the use of one of the five tools listed in Table 4 in Appendix E because they are the easiest to administer in primary care settings and have all been determined to be successful predictors of who should be referred to genetic counseling (see the *Medical Effectiveness* section for more information on the effectiveness of these tools). The tools are a mixture of clinical risk scoring tools and checklists that assign risk scores based on an accumulation of points or number of checks that reflect the degree of relationship a patient has to a family member with cancer and other clinical indicators associated with BRCA gene mutation risk. Scores over a defined threshold indicate the need for referral to genetic counseling. It should be noted that the degree of familial relationship required to meet the minimum risk threshold is not consistent between risk stratification tools and ranges from first-degree relatives only, to first-, second-, and third-degree relatives.

Key family history criteria for risk stratification and counseling referral include:

- Breast cancer diagnosis in a family member prior to age 50 years;
- Bilateral breast cancer in the same family member;
- Both breast and ovarian cancer in the family;
- Presence of breast cancer in one or more male family members;
- Multiple cases of breast cancer in the family;
- At least one family member with two primary types of BRCA-related cancer;
- Family history of early onset pancreas, melanoma or prostate cancer; and
- Ashkenazi Jewish ancestry (Daly et al., 2017; Moyer, 2014).<sup>15</sup>

Family history-based risk assessment activities may exclude certain patients from progressing through the screening process who are at substantially increased risk. In the United States, some groups with high rates of HBOC, such as persons of Ashkenazi Jewish or U.S. Hispanic ancestry, are often carriers of BRCA mutations, but *do not have a family history that indicates increased risk for HBOC* (Peshkin and Isaacs, 2018). Results from population studies and randomized trials of BRCA testing among Ashkenazi Jewish persons indicate that only about half of the BRCA mutations present in this population are identified by family history screening (Gabai-Kapara et al., 2014; Manchanda et al., 2014). In light of this research, researchers recommend that patients with known ancestry risk should be tested regardless of family cancer incidence (Manchanda et al., 2014; Weitzel et al., 2013).

## Genetic Counseling

Genetic counseling is recommended by the USPSTF, ACOG, and NCCN as a critical component of the risk assessment process for *BRCA1/2* gene mutations and may involve a pre- and post-test session.

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<sup>15</sup> Jewish ancestry is only assessed in two (RST and PAT) of the five recommended tools.

Whenever possible, genetic counseling should be performed by a credentialed genetic counselor; however, primary care providers, obstetricians/gynecologists, oncologists, nurse practitioners and physician assistants with training in cancer genetics may also provide this service (Peshkin and Isaacs, 2017). In-person genetic counseling is the current standard of care, but randomized controlled trials have shown tele-counseling (via telephone or videoconference) and electronic decision aids also to be safe and effective methods for delivering genetic counseling (Schwartz et al., 2014; Wakefield et al., 2008).

### *Pre-test genetic counseling*

The purpose of pre-test counseling is to provide patients with a more in-depth genetic risk assessment and to discuss the implications of the possible outcomes of genetic testing. Tools such as kindred analysis and mathematical modeling may be used to construct personalized comprehensive familial risk profiles to provide patients with an estimate of their future cancer risk and the chance that they will test positive for gene mutations (Peshkin and Isaacs, 2017). In addition to risk assessment, counselors also use decision aids to frame discussions about the benefits and limitations of genetic testing, as well as the potential impacts (psychological and social) that a positive result may have on the patient and their relatives.

It is estimated that 55% of women who receive genetic counseling decide to pursue genetic testing (Michigan Department of Community Health, 2012). Among a large cohort of patients who decided not to pursue testing following a genetic counseling session, the most common reasons for no testing were not being the best candidate in their family (29.2%), not being clinically indicated for testing (26.7%), and inadequate insurance coverage (14.9%) (Michigan Department of Community Health, 2012). It should be noted that this survey was performed prior to the key aspects of the Affordable Care Act were enacted stipulating coverage for the continuum of services included in BRCA screening and testing.

### *Post-test genetic counseling*

The results of genetic testing are generally presented and reviewed with the patient in a post-test genetic counseling session. Although tests for *BRCA1/2* mutations are known to be highly accurate at detecting specific mutations, genetic testing is complex and must be interpreted in the context of a patient's family history. In particular, patients who receive testing and do not have a confirmed family history of a gene mutation are likely to receive results that require careful interpretation. During this session, individuals also receive counseling on the importance of informing and testing other high-risk family members; receive information about available support infrastructure, such as support groups and clinical trials; and discuss risk-reducing management options (described below), if needed (NCCN, 2017).

## **Genetic Testing**

### *Genetic testing panels*

The extent and type of *BRCA1/2* gene mutation testing that a person receives is based on their known familial or ancestral risk. When possible, it is recommended that testing begin with a relative who has been diagnosed with breast or ovarian cancer so as to increase the likelihood of receiving useful results by targeting mutation testing to the known or suspected causative mutations found in the relative with diagnosed breast or ovarian cancer. Depending on the amount of genetic risk information that is obtained from family assessment, providers will recommend one of three testing options (assessed with a blood or saliva sample):

- **Specific *BRCA1/2* Mutation Testing.** Individuals who have a relative with a confirmed *BRCA1/2* mutation, or from ethnic groups with well-established founder mutations (for example, women of

Ashkenazi Jewish descent), can be tested for specific harmful gene mutations using a primary *BRCA1/2* sequencing assay. Tests for the three most common *BRCA* gene mutations present among persons of Ashkenazi Jewish descent are also commercially available at a reduced cost.

- **Full *BRCA1/2* Gene Sequencing.** Individuals without a confirmed family or ancestral mutation may require full *BRCA1/2* gene sequencing to check for less common or novel mutations, including inherited large gene deletions or duplications called large gene rearrangements (LRs). It is estimated that LRs account for almost 24% of mutations identified in persons with high pre-test mutation indications (Judkins et al., 2012).
- **Multigene Panel Testing.** Individuals without a confirmed family or ancestral *BRCA1/2* mutation and who have family members with other types of cancers or a family history of non-HBOC hereditary cancer syndromes that may be influenced by several genes may be offered multigene panel testing. This testing modality simultaneously analyzes sets of genes that have been implicated in family cancers (NCCN, 2017). In recent years, multigene testing has become the preferred method of testing for hereditary cancer syndromes; this shift in clinical practice has been influenced by recent studies indicating that multigene panel testing may identify *BRCA1/2* mutations beyond those that were detected by single-gene testing or mutations on other genes known to be associated with breast cancer risk (Kurian et al., 2014; Walsh et al., 2006), and studies showing that multigene testing is more cost-effective and efficient when more than one gene could be responsible for an inherited cancer syndrome (Hall et al., 2016; Walsh et al., 2011).

In addition to the three types of tests described above, the U.S. Food and Drug Administration (FDA) has recently authorized a limited direct-to-consumer (DTC) testing option that tests for the three *BRCA1/2* mutations that are most common among persons with Ashkenazi Jewish heritage. However, there are over 1,000 known *BRCA1/2* mutations, and the limited panel approved by the FDA does not test for the most common mutations present in the general population; therefore, it is recommended that patients consult with a health care provider before initiating this test. It is important to note that DTC genetic tests do not fall within the scope of AB 2342, because the bill requires provider-delivered screening and genetic counseling prior to *BRCA1/2* testing.

### *Genetic testing results*

Genetic testing for *BRCA1/2* yields four possible results: (1) true positive, (2) true negative, (3) uninformative negative, and (4) variant of uncertain significance. These results, and their implications, are described in Table 2. Data collected from a genetic counseling database in Michigan state indicate that 91.6% of individuals undergoing genetic testing for *BRCA1/2* mutations from 2008 to 2012 received either a true or uninformative negative, 3.9% had a positive test result, and 4.5% had a variant of unknown significance (Michigan Department of Community Health, 2012).

**Table 2.** Possible Clinical Results of *BRCA1/2* Genetic Testing

Test Result	Definition	Implications of Test Result
True positive	Harmful mutation is detected in either the <i>BRCA1</i> or <i>BRCA2</i> gene	Individual is at increased risk of developing breast or ovarian cancer and will need to select a management strategy to minimize their risk. This person's children will have a 50% risk of inheriting this mutation.
True negative	No harmful <i>BRCA1</i> or <i>BRCA2</i> gene mutations in an individual who has relatives with confirmed harmful <i>BRCA1</i> or <i>BRCA2</i> gene mutations.	Individual's risk of developing breast and ovarian cancer is similar to the general population, and they cannot pass the mutation down to their children.
Uninformative negative	No harmful mutations identified in an individual with a family history that suggests the possibility of having an inherited mutation, but there is no confirmed family cancer mutation.	Cancer risk relative to the general population is unknown. A harmful familial mutation could be present but was not identified because: (1) it cannot be detected by the test that was performed, (2) it occurs on a gene that was not tested, or (3) no one with breast or ovarian cancer in the family has been tested. The tested individual could also be a true negative, but it is not possible to know because mutations have not been confirmed in other family members. More comprehensive testing may be recommended.
Variant of uncertain significance	A mutation in the <i>BRCA1/2</i> or another gene is identified, but it is unknown whether the mutation is harmful.	Cancer risk relative to the general population is unknown. It is possible that this result could be reclassified if clinical evidence becomes available regarding the mutation's relationship to breast or ovarian cancer. Individuals should discuss risk-reducing clinical management strategies with their provider.

Source: CHBRP, 2018 (informed by Peshkin and Isaacs, 2017, and NCCN, 2017).  
 Key: *BRCA1/2* = Breast Cancer Susceptibility Gene 1 and 2

### Risk-Reducing Management Strategies

For women who are confirmed or suspected *BRCA1/2* mutation carriers, cancer risk-reducing management strategies include intensive screening for cancer with imaging or blood tests, prophylactic surgery, and preventive medication (Isaacs and Peshkin, 2016). These strategies and recommendations for use are described below; information regarding the uptake of these services from a cohort study (N = 465) of women who participated in genetic counseling and testing at a major U.S. cancer center (Schwartz et al., 2012) is also presented.

### *Intensive screening*

Because *BRCA1/2* mutations are associated with early onset of breast and ovarian cancer, early and more frequent screening with enhanced imaging techniques is recommended by the NCCN for women who are *BRCA* mutation carriers.

Breast cancer screening should include annual clinical breast examinations beginning at age 18 years and semiannual examinations at age 25 years; in addition, the NCCN recommends that female *BRCA1/2* carriers initiate annual mammography or breast magnetic resonance imaging (MRI) between the ages of 25 and 29 years, based on the earliest age of cancer onset in the family (NCCN, 2017). Almost half (46%) of women *BRCA1/2* carriers and a third (27%) of respondents with uninformative test results reported receiving at least one screening MRI from 1998 to 2005 (Schwartz et al., 2012).

Recommendations regarding screening for ovarian cancer are mixed: currently, the NCCN recommends semiannual screening with transvaginal ultrasound (TVUS) and carbohydrate antigen 125 (CA-125) blood testing beginning at age 30 years (NCCN, 2017); however, ACOG and the USPSTF do not recommend long-term ovarian cancer screening due to a lack of proven mortality and survival benefit with either of the available screening methods in average- or high-risk populations (ACOG, 2017; Moyer, 2014). Among surveyed *BRCA* carriers, 56% reported a CA-125 test and 46% reported having a TVUS in the prior year (Schwartz et al., 2012).

### *Prophylactic surgery*

The NCCN recommends two prophylactic surgeries for women with confirmed *BRCA1/2* mutations: bilateral risk reduction mastectomy (RRM) and bilateral risk-reducing salpingo-oophorectomy (RRSO).

RRM, with or without breast reconstruction, involves the almost total removal of breast tissue.<sup>16</sup> The NCCN recommends discussing RRM based on a carrier's individual cancer risks in the context of their family history. Almost half (48.5%) of female *BRCA1/2* carriers opted for RRM in one study (Schwartz et al., 2012).

RRSO involves the removal of both ovaries and fallopian tubes, and is recommended for women who have completed childbearing and should be performed before age 40 years (Isaacs and Peshkin, 2016)<sup>17</sup>. In a cohort study of U.S. women, 65% of women carriers reported obtaining RRSO following genetic testing (Schwartz et al., 2012).

### *Preventive medications*

For women with *BRCA1/2* mutations who opt to forgo risk-reducing surgeries, the NCCN recommends the use of selective estrogen receptor modulators (SERMs), either tamoxifen or raloxifene, to reduce the risk for breast cancer. In a cohort study of women who received genetic testing, only 17% of women with confirmed *BRCA1/2* mutations reported using tamoxifen or raloxifene for cancer risk reduction (Schwartz et al., 2012).

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<sup>16</sup> RRM does not completely eliminate the risk of developing breast cancer because it is not possible to remove all breast tissue.

<sup>17</sup> Following RRSO, women are still at increased risk for peritoneal carcinoma; therefore, follow-up screening with CA 125 is recommended.

## Provider-Related Barriers to Genetic Services for BRCA Mutations

### *Lack of referral and provider awareness*

Recent studies indicate that lack of referral to genetic counseling or genetic testing from health care providers accounts for a substantial portion of women for whom genetic testing is indicated but do not receive this service. Among women participating in the national ABOUT study (a study of commercially insured women) who underwent genetic testing without prior genetic counseling, the most common reason given for not seeking genetic counseling was lack of a provider recommendation for this service (Armstrong et al., 2015). Similarly, Bellcross et al. (2013) found that although 90% of patients who had a family history of breast and ovarian cancer that met the USPSTF high-risk criteria disclosed their risk status to their physicians, only 20% received a referral to a genetic counselor, and only 8% underwent genetic testing for BRCA mutations. Moreover, evidence suggests that referrals vary with provider specialty. In the ABOUT study, patients referred to genetic testing by obstetricians, gynecologists, and family practice physicians were significantly less likely to use genetic counseling compared to patients who received referrals from oncologists (Armstrong et al., 2015).

Lack of referral to genetic counseling or genetic testing from a physician may be a reflection of a provider's level of awareness of the USPSTF evidence-based recommendations for referral. A systematic review of genetic testing–related knowledge among primary care providers (PCPs) found that PCPs consistently reported a lack of confidence in their genetic testing–related knowledge, with 54% of providers in one study reporting a lack of confidence in breast cancer risk referral criteria (Hamilton et al., 2017). To that end, Bellcross et al. (2011) found that, although a majority of PCPs responding to a survey were aware of genetic testing for BRCA, and many had ordered a test in the prior year, only 19% were able to correctly identify all of the USPSTF increased risk criteria for BRCA mutations when presented with practice scenarios. This is consistent with a study of primary care provider adherence to *BRCA1/2* testing referral guidelines in which Trivers et al. (2011) found that only 41% of providers recommended appropriate counseling and testing when presented with a practice scenario involving high-risk patients.

### *Limited supply of genetic counselors*

Although in-person counseling with credentialed genetic counselors is recommended by the USPSTF and NCCN for women at high risk for hereditary breast and ovarian cancer syndrome, there is currently an inadequate supply of genetic counselors to meet the demand for their services (Berg et al., 2018; Hoskovec et al., 2018). Commercial claims data indicate that, between 2009 and 2014, the demand for BRCA testing among privately insured women aged 18 to 64 years increased by 2.3 times in urban areas and 3.0 times in rural areas (Kolor et al., 2017); and in 2016, there were almost twice the number of job openings for genetic counselors as there were graduates from genetic counseling programs in North America (Berg et al., 2018). There is a lack of U.S.-based data on the appropriate genetic counselor to care population ratio, but the U.K. Association of Genetic Counselors and Nurse recommends 1 counselor per 100,000 persons. Using this standard, a recent workforce modeling study determined that the United States would need 3,293 genetic counselors engaged in direct patient care to meet demand in 2018; currently, there are only 2,588 counselors working in patient care environments, accounting for a shortage of 704 genetic counselors (Hoskovec et al., 2018).

Although primary care providers may provide genetic counseling after cancer genetics training, CHBRP did not identify literature describing the frequency or impact of this practice; however, it stands to reason that some women would likely have access to genetic counseling through their PCP in the absence of a credentialed genetic counselor.

## Disparities<sup>18</sup> and Social Determinants of Health<sup>19</sup> in BRCA Screening and Intervention Uptake

Per statute, CHBRP includes discussion of disparities and social determinants of health (SDoH) as it relates to screening for HBOC. Whereas, disparities are differences between groups (e.g., race/ethnicity, gender, age) that are modifiable, social determinants of health (SDoH) are factors outside of the traditional medical care system that influence health status and health outcomes (e.g., income, education, geography, etc.) and may contribute to disparities.

### Disparities

CHBRP found literature suggesting that there may be disparities in the receipt of genetic counseling and testing, as well as in the uptake of effective risk-reducing management strategies by race/ethnicity, educational attainment, and insurance type.

### *Race/ethnicity*

Early evidence from a cohort of commercially insured women with early-onset breast cancer diagnoses (n=1,474) showed that black and Hispanic women were significantly less likely to use genetic testing than white women (66% and 48% less likely, respectively) between 2004 and 2007 (Levy et al., 2011). In two more recent companion studies of disparities in BRCA-related genetic counseling, testing, and management uptake, Cragun et al. (2015; 2017) surveyed women living in Florida who were diagnosed with invasive breast cancer at age 50 years or younger between 2009 and 2012. In the first study, black women who were surveyed about their participation in genetic counseling (n = 440) all met national criteria for genetic counseling; however, only 37% were referred to counseling (Cragun et al., 2015). Although all participants in the second study (N = 1,622) met the risk criteria for counseling and testing established in clinical guidelines, compared with non-Hispanic whites (NHW), black women were 16.6 times less likely to have discussed genetic testing with a health care provider (p < 0.0001) and primarily Spanish-speaking Hispanic women were almost 2 times less likely to have discussed testing with a provider. Consequently, black women were less likely to report undergoing genetic testing (36.1%) compared with NHWs (64.5%), English-speaking Hispanics (69%), and Spanish-speaking Hispanics (49.6%). Overall, black women were 5.6 times less likely to undergo genetic testing than NHWs; there were no significant differences in testing between Spanish-speaking Hispanics and NHWs. Among study participants who underwent testing and were confirmed BRCA carriers, black women reported significantly lower uptake of risk-reducing salpingo-oophorectomy [RRSO] (p = 0.025) and mastectomy [RRM] (p = 0.008) as compared with NHWs and Hispanics. Proportionally, only 21.8% of black women received RRSO compared with 76.6% of NHWs, whereas uptake of RRM was recorded in 68.8% of black BRCA carriers versus 95.7% among white carriers (Cragun et al., 2017).

Despite the strong evidence presented in the aforementioned studies, disparities in BRCA counseling and testing observed among women with invasive breast cancer in Florida have not been confirmed in other

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<sup>18</sup> Several competing definitions of “health disparities” exist. CHBRP relies on the following definition:

Health disparity is defined as the differences, whether unjust or not, in health status or outcomes within a population. Wyatt et al., 2016.

<sup>19</sup> CHBRP defines social determinants of health as conditions in which people are born, grow, live, work, learn, and age. These social determinants of health (economic factors, social factors, education, physical environment) are shaped by the distribution of money, power, and resources and impacted by policy (adapted from Healthy People 2020, 2015; CDC, 2014). See CHBRP’s SDoH white paper for further information:

[www.chbrp.org/analysis\\_methodology/docs/Incorporating Relevant Social Determinants of Health in CHBRP Analyses Final to WEBSITE 033016.pdf](http://www.chbrp.org/analysis_methodology/docs/Incorporating_Relevant_Social_Determinants_of_Health_in_CHBRP_Analyses_Final_to_WEBSITE_033016.pdf).

studies of patient and provider behaviors. In a national, commercially insured cohort recruited for the ABOUT study (Armstrong et al., 2015), no racial/ethnic disparities were observed among the participants who were deemed to be eligible for genetic testing or among those who received genetic testing without a prior genetic counseling session; rather, differences in genetic counseling qualification and rates were primarily attributed to personal history of breast cancer and the specialty of the clinician ordering the test (Armstrong et al., 2015). Additionally, in a study of provider adherence to BRCA practice guidelines, no significant differences in race/ethnicity were observed in provider referrals for high-risk women when physicians were presented with race-coded practice scenarios (Trivers et al., 2011).

### *Educational attainment*

Findings from the previously described ABOUT study indicate that, compared with commercially insured women who had not attended college, women with some college education were significantly more likely to have used genetic counseling prior to genetic testing for BRCA (odds ratio [OR], 1.69; 95% confidence interval [CI], 1.36 to 2.10;  $p < 0.001$ ) (Armstrong et al., 2015). Additionally, results from two cohort studies of high-risk women in Florida that examined BRCA-related genetic counseling and testing utilization showed that women with some college education were significantly more likely to receive referrals to genetic counseling (OR, 2.1; 95% CI, 1.3 to 3.3), discuss genetic testing with a provider (OR, 1.63; 95% CI, 1.19 to 2.23), and participate in genetic testing (OR, 1.71; 95% CI, 1.31 to 2.24) as compared with women who did not attend college (Cragun et al., 2015; 2017).

### *Insurance type*

Privately insured women in the previously described Florida cohorts were almost three times more likely to undergo genetic counseling (OR, 2.8; 95% CI, 1.7 to 4.6) and genetic testing (OR, 2.88; 95% CI, 2.04 to 4.07) for BRCA mutations as compared with uninsured or publicly insured women (Cragun et al., 2015; 2017); however, these women were recruited prior to the Affordable Care Act, which mandates coverage for preventive services that receive A or B grades by the USPSTF. As discussed in the *Policy Context* section, BRCA-related screening services received a B grade in 2013 and is therefore covered at no cost in all nongrandfathered U.S. health insurance plans. Anecdotal evidence suggests that certain insurance plans may only cover one test and thereby provide inadequate coverage,<sup>20</sup> but CHBRP did not find studies supporting this issue as it might relate to insurance type.

## **Social Determinants of Health**

CHBRP found literature indicating that geographic location and health literacy may contribute to disparities in utilization of genetic testing and risk-reducing management strategies for BRCA gene mutations.

### *Geographic location*

Genetic counselors commonly work at major academic medical centers, and less commonly in rural areas (Buchanan et al., 2016). Evidence from qualitative studies suggests that access to in-person genetic counseling may be limited by structural barriers such as transportation to these services, appointment availability, and the need for childcare, particularly among persons living in geographically remote areas (Anderson et al., 2012; Brandt et al., 2008; Kne et al., 2017; Trivers et al., 2011).

In an analysis of BRCA testing insurance claims from 2009 to 2014 among women with employer-sponsored insurance, aged 18 to 64 years, BRCA testing rates were higher among women located in

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<sup>20</sup> Personal communication, Patricia Ganz, MD, University of California, Los Angeles. March 2, 2018.

urban areas compared to women living in more rural locations throughout the 5-year study period; study authors determined that this difference accounted for approximately 6,600 missed tests among women living in rural areas (Kolor et al., 2017). In addition, a regional sub-analysis of the claims data showed that whereas BRCA testing increased nationally over the study period, testing gains among enrollees in western states were greater for enrollees living in urban areas compared with enrollees in rural locations; this difference in rates may indicate that western states are not providing sufficient access to genetic testing in rural areas (Kolor et al., 2017). Among enrollees with confirmed BRCA mutations, women living in rural areas were significantly less likely to have used genetic counseling within 90 days of testing or intensive breast cancer screening (with mammography or MRI) within 1 year of genetic testing as compared with women in urban areas between 2009 and 2014; there were no significant differences in rates of mastectomy (Kolor et al., 2017). It is unclear to what extent the geographic differences noted in this study are the result of differences in demand, access, or provider behaviors; however, a study of physician referral compliance found that primary care providers were less likely to recommend guideline-compliant counseling and testing for high-risk women in rural areas as compared with urban areas (24.8% vs. 44.1%;  $p = 0.003$ ) (Trivers et al., 2011).

### *Health literacy*

In qualitative studies examining underutilization of genetic counseling and testing among women at high risk for BRCA-related cancers, lack of knowledge regarding personal cancer risk and testing relevance, the importance or nature of genetic tests, and genetic-testing related insurance practices were among the top reasons patients gave for not pursuing genetic counseling or testing when recommended by a health care provider (Anderson et al., 2012; Kne et al., 2017; Shaw et al., 2017). In the most recent U.S.-based study, Kne et al. (2017) recruited three focus groups of women who did not use genetic counseling from a cohort of women who were referred to genetic counseling after screening positive for increased BRCA mutation risk at a large health center in Minnesota; in the focus group meetings participants were asked to discuss factors that contributed to their decision not to undergo genetic counseling. The majority of women in all three groups expressed a lack of knowledge about the process of counseling and the role of genetic counselors, many stated that the amount of information received at the point of referral did not clearly communicate the relative importance of genetic counseling in general. Participants in two of the focus groups did not think that their personal cancer risk was high enough to warrant counseling, despite having screened positive for family cancer risk. Finally, patients did not pursue recommended genetic counseling because they were unsure whether they had insurance coverage for genetic testing; however, most patients had not attempted to call their insurers regarding coverage for these services (Kne et al., 2017). Given that these focus groups were conducted after the implementation of the ACA and update to USPSTF recommendations on BRCA screening in 2014, this finding supports a lack of knowledge about important insurance coverage policies for these services.

Studies of BRCA screening-related knowledge among black women — who are, as described previously, significantly less likely than whites and Hispanics to use recommended genetic services — indicate that lack of knowledge and understanding regarding BRCA-related genetic services was associated with suboptimal utilization (Hurtado-de-Mendoza et al., 2017; Sheppard et al., 2014). Findings from a focus group conducted among black women who had at least one first-degree family member with breast or ovarian cancer showed that overall knowledge of genetic counseling and testing for BRCA was low: not a single participant had any knowledge of these services prior to the focus group. Comparatively, women with a breast cancer diagnosis who participated in other focus groups were more likely to have both heard of genetic counseling services and expressed interest in using them (Sheppard et al., 2014). These findings are supported by results from a telephone survey of black women at risk for hereditary breast and ovarian cancer that found that women who engaged with recommended genetic counseling or testing reported significantly higher breast cancer genetics knowledge prior to attendance at a counseling session.

## MEDICAL EFFECTIVENESS

As discussed in the *Policy Context* section, AB 2342 requires all DMHC-regulated plans and CDI-regulated policies to cover screening, genetic counseling, and genetic testing for BRCA gene mutations in women who have not been diagnosed with BRCA-related cancer and do not have signs or symptoms of the disease, but who may have an increased risk based on one or more specified family risk factors. Additional information on BRCA mutations and BRCA-related cancers is included in the *Background* section.

The medical effectiveness review summarizes evidence<sup>21</sup> from 2012 to present on the benefits and harms associated with screening, genetic counseling and genetic testing for BRCA mutations. This review also covers the effectiveness and harms of risk-reducing interventions that may take place after genetic testing, including intensive screening, risk-reducing medications, and risk-reducing surgery. Although AB 2342 does not explicitly cover these interventions, they may occur as part of the clinical pathway following genetic testing.

### Research Approach and Methods

Studies of screening, genetic counseling, and genetic testing for BRCA gene mutations were identified through searches of PubMed, the Cochrane Library, Web of Science, EconLit, Business Source Complete, the Cumulative Index of Nursing and Allied Health Literature, and PsycINFO. Websites maintained by the following organizations that produce and/or index meta-analyses and systematic reviews were also searched: the Agency for Healthcare Research and Quality (AHRQ), the International Network of Agencies for Health Technology Assessment (INAHTA), the National Health Service (NHS) Centre for Reviews and Dissemination, the National Institute for Health and Clinical Excellence (NICE), and the Scottish Intercollegiate Guideline Network. The search was limited to abstracts of studies published in English.

The medical effectiveness review searched the literature from 2012 to present. CHBRP relied on a systematic review published in 2013 for findings from studies published prior to December 2012. Of the 235 articles identified in the current literature search, 43 were reviewed for potential inclusion in this report on AB 2342, and a total of five studies published since 2012 were included in the medical effectiveness review for this report. The other articles were eliminated because they did not focus primarily on asymptomatic women, assessed an intervention deemed out-of-scope (e.g., sophisticated kindred analysis models, psychological harms of direct-to-consumer genetic testing), were of poor quality, or did not report findings from clinical research studies. 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.

To align with the bill language, CHBRP only included studies conducted primarily in women. AB 2342 defines the intended population as women who have not been diagnosed with BRCA-related cancer and do not have signs or symptoms of cancer; as such, we did not include studies of screening, counseling, or testing among women with early-onset breast or ovarian cancer, or whose genetic mutation was identified after a cancer diagnosis. The bill language specifies that a “generally accepted screening tool designed to identify a family history” should be used prior to a referral for genetic counseling. We interpreted those

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<sup>21</sup> Much of the discussion that follows is focused on reviews of available literature. However, as noted in the medical effectiveness approach document (see p.8 in the document posted [here](#)), in the absence of “fully-applicable to the analysis” peer-reviewed literature on well-designed randomized controlled trials (RCTs), CHBRP’s hierarchy of evidence allows for the inclusion of other evidence.

tools to be familial screening risk assessment tools that would be used in primary care settings, and were included in the 2013 USPSTF B recommendation (the Ontario Family History Assessment Tool [FHAT], Manchester scoring system, Referral Screening Tool [RST], Pedigree Assessment Tool [PAT], and the Family History Screen-7 [FHS-7]). Other more sophisticated models for predicting breast cancer risk exist (Myriad, BOADICEA, BRCAPRO), but they are more appropriately used during genetic counseling. General breast cancer risk models (Gail model) that do not fully incorporate family history were found to have lower accuracy in the USPSTF review and were not included in this review. Because the bill language explicitly outlines the clinical pathway to be followed for mandated insurance coverage, we did not include studies of direct-to-consumer genetic testing, which may occur without risk assessment or genetic counseling. As previously mentioned, we reviewed the evidence on risk-reducing interventions that may arise as part of this clinical pathway; however, as these interventions are not mandated by AB 2342, we have limited our discussion of the evidence to summarizing existing systematic reviews of their effectiveness and harms.

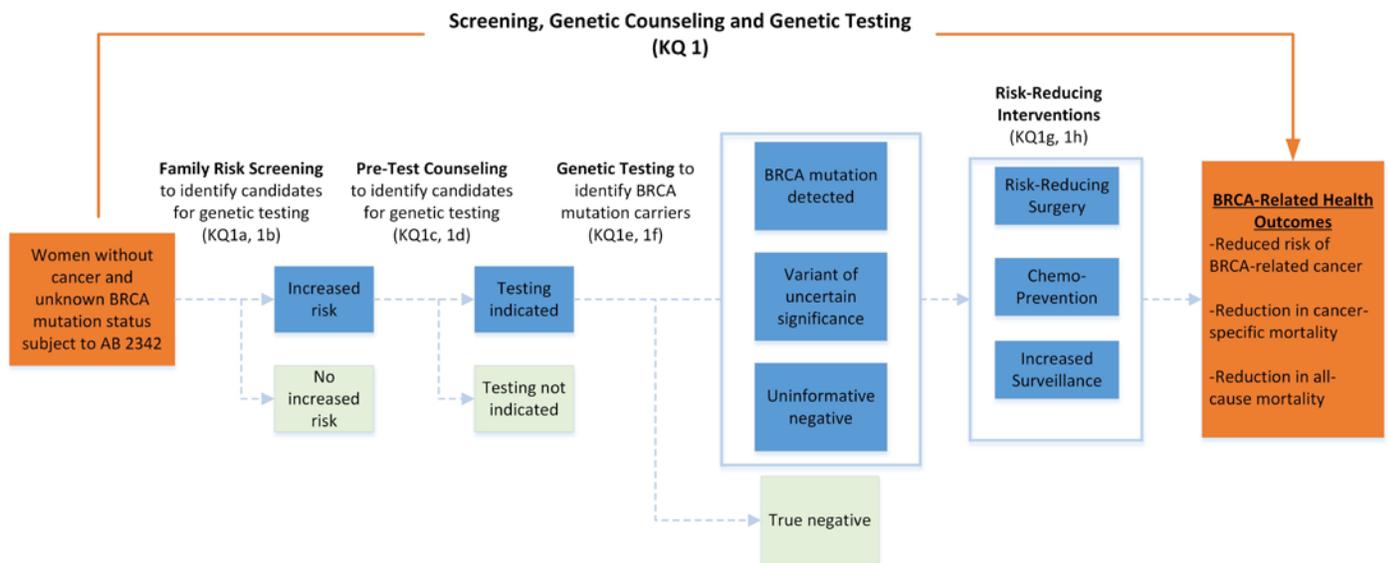
The conclusions below are based on the best available evidence from peer-reviewed and grey literature. Unpublished studies are not reviewed because the results of such studies, if they exist, cannot be obtained within the 60-day timeframe for CHBRP reports.

### Key Questions

To determine the medical effectiveness of the clinical pathway outlined in AB 2342 — screening, genetic counseling, and genetic testing for BRCA mutations — the medical effectiveness review sought to answer the following key question (denoted by the solid line in Figure 3 below):

1. Does screening, genetic counseling, and genetic testing lead to reduced incidence of BRCA-related cancer and reduced BRCA-related cancer-specific and all-cause mortality?

**Figure 3.** Analytic Framework of Medical Effectiveness Review



In the absence of direct evidence establishing the impact of the clinical pathway on long-term BRCA-related health outcomes, the medical effectiveness review reviewed the indirect evidence of the short-term benefits and harms of each component of the clinical pathway (familial risk screening, genetic

counseling and genetic testing), as well as the benefits and harms of risk-reducing interventions for BRCA mutation carriers. These questions are outlined below, and are denoted by the dotted lines in Figure 3.

- 1a. What is the diagnostic accuracy of “generally accepted screening tools” used for familial risk assessment for BRCA-related cancer?
- 1b. What are the harms of screening for familial risk assessment?
- 1c. What are the benefits and harms of genetic counseling in determining eligibility for genetic testing?
- 1d. What are the harms of genetic counseling in determining eligibility for genetic testing?
- 1e. Among women with increased risk for BRCA-related cancer, does genetic testing for BRCA mutations accurately predict risk of future breast or ovarian cancer?
- 1f. What are the harms of genetic testing for BRCA-related cancer?
- 1g. Among women with increased risk for BRCA-related cancer due to BRCA mutation, do risk-reducing interventions (i.e., intensive screening, risk-reducing medications, and risk-reducing surgeries) lead to reduced incidence of BRCA-related cancer and reduced BRCA-related cancer-specific and all-cause mortality?
- 1h. Among women with increased risk for BRCA-related cancer due to BRCA mutation, what are the harms of risk-reducing interventions for BRCA-related cancers?

If the evidence shows that familial risk screening and genetic counseling can accurately identify women at increased risk for BRCA mutations, and that a positive genetic test accurately predicts future cancer risk, and that risk-reducing interventions for mutation carriers can mitigate that risk, then it is possible to conclude that the clinical pathway is effective in reducing BRCA-related cancer incidence and mortality.

## Outcomes Assessed

To assess the benefits of screening, genetic counseling, and genetic testing for *BRCA1* and *BRCA2* mutations, as well as the beneficial outcomes of risk-reducing interventions, we included studies reporting the incidence of BRCA-related cancer, disease-specific mortality, or all-cause mortality. To assess the test performance (accuracy) of familial risk assessment tools, we included studies reporting the sensitivity, specificity, positive predictive value, or negative predictive value against a clearly defined reference standard. To assess the benefits and harms of genetic counseling, we included studies reporting changes in patient knowledge, risk perception, and other psychological outcomes. To assess the accuracy of genetic tests for BRCA mutations, we included studies reporting the clinical validity and utility of genetic testing (assessed using prevalence and penetrance). To assess the harms of screening, counseling and genetic testing, we included studies reporting on the rates of inappropriate testing, false-positive and false-negative test results, adverse effects on social relationships, and impacts on worry, anxiety, and depression. To assess the harms of risk-reducing interventions, we included studies reporting the harms of rescreening, harms of medications, or the harms of risk-reducing surgeries.

## Study Findings

As previously mentioned, in addition to the five recently published studies, the medical effectiveness review relied on a 2013 systematic review conducted to inform the USPSTF on the benefits and harms of

screening genetic counseling and genetic testing for BRCA-related cancer in women (Nelson et al., 2013; 2014). The USPSTF systematic review searched the literature on the benefits and harms of screening, genetic counseling, genetic testing, and risk-reducing interventions from January 2002 through December 2012. Of 5,268 unique citations, the USPSTF review included 140 fair- or good-quality full-text articles. As described in the *Policy Context* section, the USPSTF recommends with a grade “B” that “women whose family history is associated with an increased risk for deleterious mutations in the *BRCA1* or *BRCA2* genes be referred for genetic counseling and evaluation for BRCA testing (Moyer, 2014).

The following figures summarize CHBRP’s findings regarding the strength of the evidence for the effects of screening, genetic counseling, and genetic testing addressed by AB 2342. Separate figures are presented for each service for which the bill would mandate coverage and for each outcome for which evidence of the effectiveness of a treatment is available. The title of the figure indicates the test, treatment, or service for which evidence is summarized. The statement under the title presents CHBRP’s conclusion regarding the strength of evidence about the effect of a particular test, treatment, or service on a specific relevant outcome and the number of studies on which CHBRP’s conclusion is based. For test, treatments, and services for which CHBRP concludes that there is *clear and convincing*, *preponderance*, *limited*, or *inconclusive evidence*, the placement of the highlighted box indicates the strength of the evidence. If CHBRP concludes that evidence is insufficient, a figure that states “Insufficient Evidence” will be presented.

### Effectiveness of Familial Risk Screening, Genetic Counseling, and Genetic Testing for BRCA Gene Mutations on BRCA-Related Cancer Incidence or Mortality

Neither the 2013 USPSTF review nor this medical effectiveness review identified any studies that addressed whether screening, counseling and testing for BRCA gene mutations among asymptomatic women with a family history leads to reduced incidence of BRCA-related cancer or reduced cancer-specific or all-cause mortality (Nelson et al., 2013; 2014). In order to see cancer incidence or mortality effects at a population level, studies need to follow patients who tested positive for a mutation and who would then undergo risk-reducing interventions, compared to patients with similar risk who were not tested, until cancer develops or death occurs. Cancer incidence and mortality outcomes at a population-level would not occur for several decades and women have been undergoing *BRCA1* mutation testing only since the gene was discovered in 1994 (*BRCA2* in 1996) (Memorial Sloan Kettering Cancer Center, 2014), with testing becoming more widely available after a 2013 Supreme Court decision (Peshkin and Isaacs, 2017).

**Summary of findings regarding the effectiveness of familial risk screening, genetic counseling and genetic testing for BRCA mutations:** CHBRP finds insufficient evidence to conclude whether screening, counseling, and testing for BRCA gene mutations leads to reduced incidence of BRCA-related cancer or reduced mortality due to the lack of studies addressing this question.

**Figure 4.** Effectiveness of Screening, Counseling and Testing for BRCA Gene Mutations on BRCA-Related Cancer Incidence or Mortality

NOT EFFECTIVE		INSUFFICIENT EVIDENCE				EFFECTIVE	
Clear and Convincing	Preponderance	Limited	Inconclusive	Limited	Preponderance	Clear and Convincing	

In the absence of evidence addressing the effectiveness of familial risk screening, genetic counseling and genetic testing on health outcomes, CHBRP reviewed the evidence of benefits and harms for each intermediate step of the clinical pathway, as well as risk-reducing interventions for mutation carriers.

## Effectiveness of Familial Risk Screening Tools to Identify BRCA Mutation Carriers

The 2013 USPSTF review included ten studies that assessed the performance of five risk-screening tools — the Ontario Family History Assessment Tool (FHAT), Manchester scoring system, Referral Screening Tool (RST), Pedigree Assessment Tool (PAT), and the Family History Screen-7 (FHS-7). These risk-screening tools are described in more detail in *Appendix D*. These diagnostic accuracy studies determined the performance of the screening tool by comparing screening tool scores of mutation carriers to noncarriers or more complex cancer risk prediction models (e.g., the Breast and Ovarian Analysis of Disease Incidence and Cancer Estimation Algorithm [BOADICEA], BCRAPro, or Myriad II). The 2013 USPSTF review found that the sensitivity of these tools (i.e., the tools ability to correctly identify individuals with a BRCA mutation) was generally high, ranging from 81% to 100%. The specificity of these tools (i.e., the tools ability to correctly identify those without the BRCA mutation) was lower, ranging from 33% to 93%. Overall, the USPSTF review concluded that the screening tools had high accuracy (c-statistic >0.80) (Nelson et al., 2013; 2014).

The CHBRP literature review did not identify any studies published since 2012 assessing the accuracy of familial risk screening tools for BRCA mutations. CHBRP did not identify any studies assessing any harms attributable to undergoing familial risk screening.

**Summary of findings regarding the effectiveness of familial risk screening tools to identify BRCA mutation carriers:** There is a preponderance of evidence from a well-conducted systematic review including 10 diagnostic accuracy studies that familial risk screening tools are effective in accurately identifying women at risk for a BRCA mutation.

**Figure 5.** Effectiveness of Familial Risk Screening Tools for BRCA Mutations



## Effectiveness of Pre-Testing Genetic Counseling

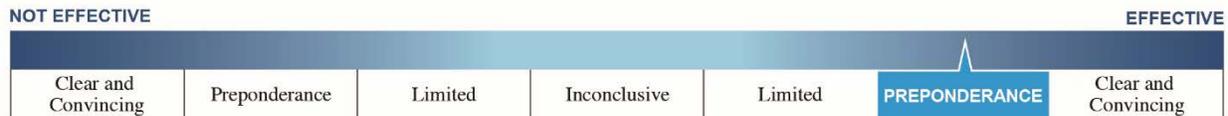
The 2013 USPSTF review included 27 studies of pre-testing genetic counseling that reported on risk perception, testing intention, and distress related to genetic testing (1 systematic review, 15 randomized controlled trials [RCTs], 4 cohort studies, 1 case-control study, and 6 with before-and-after designs).

Eight studies included in the previous USPSTF review (Nelson et al., 2005) found inconclusive evidence on whether counseling prior to genetic testing impacted risk perception, but eight additional studies published between 2005 and 2012 (3 RCTs, 2 cohorts, and 3 with before-and-after designs) consistently found improved accuracy of risk perception after genetic counseling. The 2013 review notes that accuracy of risk perception improved when counseling provided personal risk estimates, information about family history or heredity, and facilitated informed decision making. The review included five RCTs that reported decreased intention to pursue genetic testing after counseling among women who were unlikely to be carriers. The review also found that after genetic counseling, women experienced a decrease in breast cancer-related worry and that anxiety and depression generally decreased or was not affected.

The CHBRP literature review did not identify any studies published since 2012 assessing the effectiveness of genetic counseling before or after BRCA mutation testing.

**Summary of findings regarding the effectiveness of genetic counseling before BRCA mutation genetic testing** There is a preponderance of evidence from a well-conducted systematic review including 27 studies that genetic counseling before testing improves risk perception accuracy, decreases breast cancer–related worry and decreases intention to pursue genetic testing among women unlikely to be carriers.

**Figure 6.** Effectiveness of Genetic Counseling Before BRCA Mutation Testing



### Effectiveness of BRCA Genetic Mutation Testing

To determine the effectiveness of BRCA genetic mutation testing, CHBRP assessed the clinical validity and utility of BRCA mutation testing, an approach consistent with that taken by the 2013 USPSTF systematic review. The review defined the clinical validity and utility of BRCA genetic testing as how well a positive *BRCA1* or *BRCA2* mutation testing result predicts risk for BRCA-related cancer, using measures of prevalence and penetrance. Prevalence is defined as the frequency of BRCA mutations in a population (e.g., unselected women, women with breast or ovarian cancer, women with high-risk families, Ashkenazi Jewish women). Penetrance is defined as the likelihood of developing a BRCA-related cancer in women with a *BRCA1* or *BRCA2* mutation and is age-dependent. The likelihood of developing a BRCA-related cancer after a positive test for a BRCA mutation also depends on whether a single individual or multiple individuals in a family tested positive in the studies.

The clinical validity can also be assessed by determining the cancer incidence rate among women who did not receive a positive test result indicating a *BRCA1* or *BRCA2* mutation; these results may indicate variants of uncertain significance, an uninformative negative result, or a true negative result. A result indicating *variants of uncertain significance* means that the genetic test detected an abnormality of the BRCA gene, but it is unknown if this mutation is associated with an increased risk of cancer. An *uninformative negative* test result occurs when there is no genetic mutation detected in a patient and the mutation status of their relatives is unknown because: (1) other family members haven’t been tested, (2) mutation carried by family is undetected due to testing limitations, (3) the family carries a different high-risk genetic mutation than was tested, or (4) no high-risk mutation is segregating in the family (Nelson et al., 2013). A *true negative* test result occurs when there is a known mutation in a relative with cancer and the patient undergoing testing has a negative genetic test for that mutation.

#### *Positive BRCA1 or BRCA2 mutation test result*

##### Prevalence

The USPSTF performed a meta-analysis of 11 studies of women recruited to genetic testing based on a family history of breast and/or ovarian cancer, and found prevalence of 13.6% for *BRCA1*, 7.9% for *BRCA2*, and 19.8% for both *BRCA1* and *BRCA2* combined. Among Ashkenazi Jews without a family or personal history of breast and/or ovarian cancer, a meta-analysis of 5 studies of *BRCA1*, and 6 studies of *BRCA2* estimates the prevalence of *BRCA1* at 1.2% (95% CI, 0.98 to 1.42), *BRCA2* at 1.17% (95% CI, 0.95 to 1.38), and both *BRCA1* and *BRCA2* combined at 2.08% (95% CI, 1.28 to 2.88) (Nelson et al., 2013).

Penetrance

In addition to the 16 studies included in the 2013 USPSTF review, the CHBRP literature search identified 2 studies published since 2012 that reported penetrance, or cumulative incidence, for breast or ovarian cancer among *BRCA1* or *BRCA2* mutation carriers. For detailed results, please refer to Appendix C.

The USPSTF meta-analysis found that penetrance, or risk of breast or ovarian cancer, among women with *BRCA* gene mutations and high-risk family or medical histories (women with a family history of breast or ovarian cancer, or women with breast or ovarian cancer before age 45 years) was higher across studies in which multiple family members were tested compared to studies in which a single individual was tested. Among these high-risk women, the USPSTF meta-analysis found that the risk for developing breast cancer by age 70 years was 46% to 70% for *BRCA1* mutation carriers and 50% to 71% for *BRCA2* carriers. The meta-analysis estimated the risk for developing ovarian cancer at 41% for *BRCA1* mutation carriers and 17% for *BRCA2* carriers (Nelson et al., 2013).

A 2014 retrospective cohort study conducted in the United Kingdom included 492 female mutation carriers without a previous breast or ovarian cancer diagnosis but with a *BRCA* mutation (254 with *BRCA1* and 238 with *BRCA2*) who underwent familial genetic testing. They found an estimated risk of breast cancer by age 70 years of 54% for both *BRCA1* and *BRCA2* combined, 45% for *BRCA1* and 59% for *BRCA2* (Evans et al., 2014). A 2013 prospective cohort study, the Epidemiological Study of *BRCA1* and *BRCA2* Mutations Carriers (EMBRACE), included 988 female mutation carriers without a previous breast or cancer diagnosis who underwent familial genetic testing. This analysis estimated the risk of breast cancer by age 70 to be 60% (95%CI, 44% to 75%) among *BRCA1* mutation carriers and 55% (95% CI, 41% to 70%) among *BRCA2* carriers, and estimated the risk of ovarian cancer to age 70 to be 59% (95% CI, 43% to 76%) among *BRCA1* carriers and 16.5% among *BRCA2* carriers (Mavaddat et al., 2013).

Among Ashkenazi Jewish women with positive *BRCA* gene mutation testing and without a family history of breast and/or ovarian cancer, the USPSTF meta-analyzed ten studies and estimated breast cancer risk of 33.7% (95% CI, 24.1% to 44.9%) to age 75 years. Their meta-analysis of five studies estimates the ovarian cancer risk at 21.4% (95% CI, 14.9% to 29.7%) to age 75 (Nelson et al., 2013).

As noted in the USPSTF review, studies of penetrance have several limitations. Individuals and their family members selected for testing are more likely to have additional risk factors for breast or ovarian cancer, and studies infrequently report the specific mutation within the *BRCA* gene, both of which can impact penetrance estimates (Nelson et al., 2013).

**Summary of findings regarding the effectiveness of *BRCA1* and *BRCA2* genetic testing for predicting *BRCA*-related cancer risk:** There is a preponderance of evidence from a well-conducted 2013 systematic review including 21 studies, as well as evidence from two new studies published since 2012, that positively detecting a *BRCA1* or *BRCA2* mutation consistently and accurately predicts risk for *BRCA*-related breast or ovarian cancer.

**Figure 7.** Effectiveness of *BRCA* Genetic Testing for Predicting *BRCA*-Related Cancer Risk Among Women With a Positive Test Result



*Variants of uncertain significance*

Neither the 2013 USPSTF review nor this medical effectiveness review identified any studies of determining the risk of developing BRCA-related cancer among women whose genetic testing results indicated variants of uncertain significance (Nelson et al., 2013).

**Summary of findings regarding the effectiveness of a *BRCA1* or *BRCA2* genetic testing result indicating variants of uncertain significance on BRCA-related cancer risk:** CHBRP finds insufficient evidence to conclude whether a genetic testing result indicating variants of uncertain significance can accurately predict risk for BRCA-related breast or ovarian cancer.

**Figure 8.** Effectiveness of BRCA Genetic Testing on BRCA-Related Cancer Risk Among Women With a Result Indicating Variants of Uncertain Significance



*Uninformative negative results*

The 2013 USPSTF review meta-analyzed data from three studies, and estimated the standardized incidence ratio for developing breast cancer among women with uninformative negative results compared to the general population to be 3.81 (95% CI, 3.06 to 4.75; range, 3.25 to 3.32). Study estimates for ovarian cancer varied more widely across the three studies, ranging from 0.85 to 11.6; this heterogeneity was correlated with differing ascertainment criteria for relatives of cases (i.e., one study only included first-degree relatives of breast cancer cases, another included families only with at least two first-degree relatives with ovarian cancer) (Nelson et al., 2013).

The CHBRP literature review did not identify any studies published since 2012 estimating breast or ovarian cancer incidence among women with uninformative negative results.

**Summary of findings regarding the effectiveness of a *BRCA1* or *BRCA2* genetic testing indicating an uninformative negative result on BRCA-related cancer risk:** There is limited evidence from a well-conducted systematic review including three studies that a genetic testing result indicating an uninformative negative result can accurately predict risk for BRCA-related breast or ovarian cancer.

**Figure 9.** Effectiveness of BRCA Genetic Testing on BRCA-Related Cancer Risk Among Women With an Uninformative Negative Test Result



*True negative results*

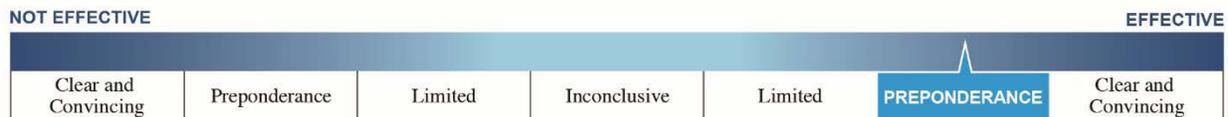
The 2013 USPSTF meta-analyzed data from 10 studies, and estimated the standardized incidence ratio for developing breast cancer among women with true negative results compared to the general population to be 1.13 (95% CI, 0.81 to 1.58). The 2013 USPSTF review only identified two studies of ovarian cancer incidence among true negatives. Standardized incidence ratios ranged from 0.0 in one

study and 4.6 (95% CI, 1.2 to 11.7) in the second. The review concluded that a true negative test does indicate no increased risk of breast cancer; results for ovarian cancer were highly heterogeneous (Nelson et al., 2013).

The CHBRP literature review did not identify any studies published since 2012 estimating breast or ovarian cancer incidence among women with true negative results.

**Summary of findings regarding the effectiveness of *BRCA1* and *BRCA2* genetic testing indicating a true negative result *BRCA*-related breast cancer risk:** There is a preponderance of evidence from a well-conducted systematic review including ten studies that a true negative *BRCA1* or *BRCA2* test result indicates no increase in breast cancer risk compared to the general population (pooled SIR, 1.13; 95% CI, 0.81 to 1.58).

**Figure 10.** Effectiveness of BRCA Genetic Testing on BRCA-Related Breast Cancer Risk Among Women With a True Negative Test Result



**Summary of findings regarding the effectiveness of *BRCA1* and *BRCA2* genetic testing indicating a true negative result *BRCA*-related ovarian cancer risk:** There is inconclusive evidence from a well-conducted systematic review including two studies that a true negative *BRCA1* or *BRCA2* test result indicates no increase in ovarian cancer risk.

**Figure 11.** Effectiveness of BRCA Genetic Testing on BRCA-Related Ovarian Cancer Risk Among Women With a True Negative Test Result



### Harms of BRCA Mutation Testing

In addition to the 2013 USPSTF review, the CHBRP literature search identified two studies published since 2012 reporting harms associated with genetic testing for BRCA.

The 2013 USPSTF review included five studies reporting significant increases in breast cancer-related worry after receiving BRCA testing results among mutation carriers compared with: (a) mutation carriers pre-testing, (b) noncarriers, or (c) untested women. One included study reported a decrease in worry among both carriers and noncarriers. The review found mixed findings on the effects of testing on anxiety. Some studies reported decreased anxiety regardless of mutation status, while others found significantly higher anxiety among carriers (versus noncarriers) and women with family history who were not tested (versus carriers), or no difference in anxiety among any groups. The USPSTF review included four studies that did not find any difference in depression either over time among carriers or among carriers versus noncarriers, and one prospective cohort found higher depression scores among women with a family history who did not receive testing compared to women with positive testing results. Another cohort study found that noncarriers had lower depression scores compared with carriers and untested women (Nelson et al., 2013; 2014).

A 2012 cohort study of 485 women (and 67 men) undergoing BRCA mutation assessed whether testing impacted family relationships. After 3-years of follow-up, the study found that 85% of participants did not report any effects of genetic testing on family relationships. The 3-year incidence of negative effects of testing on family relationships was 3.7% (95% CI, 2.1 to 5.3), compared to 13.2% for positive effects (95% CI, 10.3 to 16.1). A multivariate analysis found that while the test result was not associated with reporting negative family relationship effects, having a low education level, considering or having a prophylactic mastectomy, and dissatisfaction with social support were associated with negative family relationship effects (Lapointe et al., 2012).

A 2017 retrospective cohort study of 91 women (both patients with breast or ovarian cancer initiating counseling and their relatives) undergoing BRCA mutation testing evaluated their emotional state 1 month after testing. Women were significantly more likely to report symptoms of anxiety than depression ( $p < 0.001$ ), and relatives of cancer patients were more likely to report anxious and depressive symptoms than cancer patients (Mella et al., 2017).

**Summary of findings regarding the harms of BRCA1 and BRCA2 genetic testing:** There is limited evidence from a well-conducted systematic review including five studies and two additional cohort studies that breast cancer–related worry and anxiety may increase after a positive test result; results indicating any impact on depression were mixed. One study did not report any impact on BRCA mutation testing on family relationships.

### Effectiveness of Risk-Reducing Interventions for BRCA-Related Cancer

As mentioned previously, we reviewed the evidence on risk-reducing interventions that may arise as part of this clinical pathway; however, because these interventions are not mandated by AB 2342, we have limited our discussion of the evidence to summarizing existing systematic reviews of their effectiveness and harms.

Neither the 2013 USPSTF review, nor other recent systematic reviews (Li et al., 2016), have identified any trials assessing the effect of intensive screening using imaging or lab tests, risk-reducing medications (RRM) or risk-reducing surgeries (RRS) in BRCA mutation carriers on cancer incidence or mortality. The studies described below all enrolled participants at increased risk for breast or ovarian cancer based on family history.

#### Intensive screening

**Breast cancer screening.** The 2013 USPSTF review identified four observational studies (3 prospective) reporting the accuracy of breast cancer screening with MRI compared with mammography in women at increased risk of breast cancer. The review found that the sensitivity of MRI was higher than with mammography (71% vs. 41%); specificity was similar (90% vs. 95%). Across all four studies, there were 189 breast cancers detected; majority of cancers detected were invasive (64% to 83%) and 12% were interval cancers (Nelson et al., 2013).

**Figure 12.** Effectiveness of Breast Cancer Screening for BRCA-Related Breast Cancer Among BRCA Mutation Carriers



**Summary of findings regarding the effectiveness of screening for BRCA-related breast cancer among BRCA mutation carriers:**

There is a preponderance of evidence from a well-conducted systematic review including four observational studies of breast cancer screening among BRCA mutation carriers MRI screening has higher sensitivity than mammography, and that screening mutation carriers can identify a majority invasive breast cancers.

**Ovarian cancer screening.** The 2013 USPSTF review identified two descriptive studies reporting the accuracy of ovarian cancer screening with transvaginal ultrasound (TVUS) and serum CA-125 testing in women at increased risk of ovarian cancer. The first study found that among 1,610 women with family histories of ovarian cancer, 61 (3.8%) women had an abnormal TVUS; of those 61 women, 6 (9.8%) had ovarian cancer. The second descriptive study included 459 women aged 30 to 35 years at increased risk of ovarian cancer undergoing annual TVUS and serum CA-125 testing. The sensitivity of serum CA-125 alone was 71%, 43% for TVUS alone, and 71% for both modalities combined (specificity was 99% for all modalities alone or in combination). Fourteen (3%) of women had an abnormality detected by the screening modalities; seven ovarian cancers were diagnosed. (Nelson et al., 2013).

**Summary of findings regarding the effectiveness of screening for BRCA-related ovarian cancer among BRCA mutation carriers:**

There is limited evidence from a well-conducted systematic review including two descriptive studies of ovarian cancer screening that screening with serum CA-95 alone or with TVUS has the highest sensitivity and specificity. These studies found that screening detects abnormalities in approximately 3% to 4% of women, but only a small portion of women (0.6% overall) ultimately had a cancer diagnosed.

**Figure 13.** Effectiveness of Ovarian Cancer Screening for BRCA-Related Ovarian Cancer Among BRCA Mutation Carriers



*Risk-reducing medications*

CHBRP examined FDA-approved risk reduction medications for use in high-risk women. The USPSTF review did not identify any trials of tamoxifen or raloxifene specifically in women who are BRCA mutation carriers. However, they did identify a meta-analysis of trials of these risk-reducing medications that provided efficacy outcomes for women with a family history of breast cancer. The results of these trials are presented below. No trials were identified which described the impact of risk-reducing medications on ovarian cancer risk.

**Tamoxifen.** Across four trials, the risk of invasive breast cancer was reduced by 27% to 57% with the use of tamoxifen versus placebo. Risk reductions were higher with increased numbers of relatives with breast cancer. The NSABP-1 and Royal-Marsden trials found that women with fewer identified relatives with breast cancer had less of a risk reduction (NSABP-1: 0 relatives, RR, 0.54 [95% CI, 0.34 to 0.83]; Royal-Marsden: 0 to 2 relatives, RR, 0.51 [95% CI, 0.27 to 0.96]) than women with three or more affected relatives (NSABP-1: RR, 0.49 [95% CI, 0.16 to 1.34]; Royal-Marsden: RR, 0.43 [95% CI, 0.19 to 0.95]). Only one trial conducted in Italy reported an increase in risk among tamoxifen users, but the increase was not significant (RR, 1.43; 95% CI, 0.65 to 3.15). In one additional head-to-head trial of tamoxifen versus raloxifene, tamoxifen users experienced a greater risk reduction (Nelson et al., 2013).

**Raloxifene.** In the two trials randomizing women to raloxifene versus placebo, women without a family history of breast cancer experienced a 45% to 47% reduction in breast cancer risk using tamoxifen. The MORE/CORE trial reported a greater risk reduction with one or more affected family members (RR, 0.16; 95% CI, 0.06 to 0.42), but the RUTH trial did not report an effect of family history (RR, 0.89; 95% CI, 0.34 to 2.31).

**Summary of findings regarding the effectiveness of risk-reducing medications for BRCA-related breast cancer among BRCA mutation carriers:** Although there is no direct trial evidence examining the use of tamoxifen or raloxifene in BRCA mutation carriers, there is limited evidence from a well-conducted systematic review reporting outcomes of seven trials of tamoxifen or raloxifene use among women with a family history of breast cancer that this medication can reduce the risk of invasive breast cancer. Risk reductions tended to be greater in women with more affected family members.

**Figure 14.** Effectiveness of Risk-Reducing Medications for BRCA-Related Breast Cancer Among BRCA Mutation Carriers



**Summary of findings regarding the effectiveness of risk-reducing medications for BRCA-related ovarian cancer among BRCA mutation carriers:** CHBRP finds insufficient evidence to conclude whether the use of any risk-reducing medications can reduce the risk of ovarian cancer in BRCA mutation carriers.

**Figure 15.** Effectiveness of Risk-Reducing Medications for BRCA-Related Ovarian Cancer Risk Among BRCA Mutation Carriers



*Risk-reducing surgery*

**Mastectomy.** The 2013 USPSTF review identified four observational studies (three prospective) reporting breast cancer outcomes after risk-reducing bilateral mastectomy. These studies reported a reduction in breast cancer incidence by 85% to 100%. An 81% to 100% reduction in breast cancer-specific mortality was reported after risk-reducing bilateral mastectomy in one study (Nelson et al., 2013). A 2016 meta-analysis by Li et al. included six studies (two of which were included in the USPSTF review) that estimated a pooled 89% reduction in breast cancer incidence (relative risk [RR], 0.11; 95% CI, 0.04 to 0.32). This meta-analysis did not find a significant impact on all-cause mortality (two studies, pooled hazard ratio [HR], 0.23; 95% CI, 0.05 to 1.016); breast cancer-specific mortality estimates were not reported (Li et al., 2016).

**Salpingo-oophorectomy or oophorectomy.** The 2013 USPSTF review identified four observational studies (three prospective) reporting ovarian cancer outcomes after risk-reducing salpingo-oophorectomy (RRSO) or oophorectomy. These studies reported a reduction in ovarian cancer incidence by 69% to 100%. A 55% to 100% reduction in all-cause mortality was reported after RRSO one study included in the

review (Nelson et al., 2013). The 2016 Li et al. meta-analysis included five total studies (one of which was included in the USPSTF review) reporting breast cancer outcomes after RRSO. Among both *BRCA1* and *BRCA2* mutation carriers, RRSO led to a 45% reduction in breast cancer risk (three studies: RR, 0.55; 95% CI, 0.45 to 0.68). When looking at *BRCA1* and 2 carriers separately, the reduction in breast cancer risk was 53% for *BRCA1* (four studies: RR, 0.47; 95% CI, 0.35 to 0.64) and 53% for *BRCA2* (three studies: RR, 0.47; 95% CI, 0.26 to 0.83). This meta-analysis found that RRSO was associated with significantly lower all-cause mortality (pooled HR, 0.35; 95% CI, 0.19 to 0.64); breast cancer-specific mortality estimates were not reported (Li et al., 2016).

**Figure 16.** Effectiveness of Risk-Reducing Surgery for BRCA-Related Cancer Among BRCA Mutation Carriers



**Summary of findings regarding the effectiveness of risk-reducing surgery for BRCA-related breast and ovarian cancer among BRCA mutation carriers:** There is a preponderance of evidence from two well-conducted systematic reviews that risk-reducing mastectomy can reduce the incidence of breast cancer, and may reduce all-cause and breast cancer-specific mortality.

There is a preponderance of evidence from two well-conducted systematic reviews that risk-reducing salpingo-oophorectomy or oophorectomy can reduce the incidence of ovarian cancer reduce all-cause mortality.

## Harms of Risk-Reducing Interventions for BRCA-Related Cancer

### *Intensive screening*

**Breast cancer screening.** The 2013 USPSTF review identified five studies reporting harms associated with breast cancer screening among BRCA mutation carriers. One study reported a significantly higher false-positive rate for screening with MRI versus mammography (14% vs. 5.5%), whereas a second study reported similar false-positive rates for both modalities (MRI, 11% vs. mammography, 15%). One study reported a higher recall rate among women who received MRI compared with mammography (11% vs. 3.9% per woman-year); across both modalities, there were 8.5 recalls per cancer detected. Studies reported discomfort, pain, and anxiety were similar among women undergoing mammography, MRI, or clinical breast examination, but that women who were recalled reported higher anxiety scores compared to those who were not recalled at 4 to 6 weeks post-screening (but these differences were not significant by 6 months) (Nelson et al., 2013).

**Ovarian cancer screening.** The 2013 USPSTF review identified two studies reporting harms associated with ovarian cancer screening among BRCA mutation carriers. These studies reported high rates of unnecessary diagnostic surgery after screening with TVUS and serum CA-125 testing. Following an abnormal serum CA-125 test, ovarian cancer was not detected in 67% of cases (compared with 100% of abnormal TVUS screens). Using TVUS and serum CA-125 testing combined resulted in an unnecessary diagnostic surgery rate of 55%. A second study reported a false-positive rate of 3.4% with TVUS.

**Summary of findings regarding the harms of intensive screening for BRCA-related breast and ovarian cancer among BRCA mutation carriers:** There is inconclusive evidence whether breast or ovarian cancer screening results in higher false-positive rates among mutation carriers, and insufficient evidence from a single study as to whether it increases recall rates. Discomfort and anxiety were not increased for women undergoing intensive screening, but women who were recalled experienced short-term increases in anxiety.

### *Risk-reducing medications*

As described previously, the USPSTF review did not identify any trials of risk-reducing medications in women who are BRCA mutation carriers, but instead summarized effectiveness evidence from trials of women with family histories of breast cancer. However, these trials did not stratify adverse outcomes by family history risk status. Below, we summarize the adverse outcomes reported for the broader high risk patient population.

**Tamoxifen.** Four placebo-controlled trials found that tamoxifen use increased the incidence of thromboembolic events (RR, 1.93; 95% CI, 1.41 to 2.64). Tamoxifen use also caused more cases of endometrial cancer (3 trials; RR, 2.13; 95% CI, 1.36 to 3.32) and was associated with other gynecological conditions, surgical procedures such as hysterectomy, and uterine bleeding. One trial also reported an increase in cataract surgeries for women using tamoxifen compared with placebo (RR, 1.14; 95% CI, 1.01 to 1.29). Other reported harms included vasomotor symptoms, bladder control symptoms, and vaginal discharge, itching, or dryness.

**Raloxifene.** Two placebo-controlled trials found that raloxifene use increased the incidence of thromboembolic events (RR, 1.60; 95% CI, 1.15 to 2.23). Studies did not find an increase in endometrial cancer risk or uterine bleeding with raloxifene use. In one head-to-head trial, women randomized to raloxifene had higher stroke mortality than women randomized to tamoxifen (RR, 1.49; 95% CI, 1.00 to 2.24), but caused fewer cataracts than tamoxifen (RR, 0.80; 95% CI, 0.72 to 0.95). Other reported harms include vasomotor symptoms, leg cramps, musculoskeletal problems, dyspareunia (painful intercourse), and weight gain.

**Summary of findings regarding the harms of risk-reducing medications for BRCA-related breast cancer among BRCA mutation carriers:** There is evidence from one well-conducted systematic review that the use of tamoxifen or raloxifene can increase the incidence of thromboembolic events, and is associated with harms such as vasomotor symptoms, musculoskeletal problems, bladder control and vaginal discharge, itching or dryness. There is also evidence that tamoxifen use can lead to increased risk of endometrial cancer and lead to other gynecological conditions, surgical procedures, and uterine bleeding.

### *Risk-reducing surgery*

**Mastectomy.** The 2013 USPSTF review identified four descriptive studies reporting physical and psychological harms related to risk-reducing mastectomy for BRCA-related breast cancer. Studies reported that 3% to 59% of women experienced a surgical complication. Additionally, 64% to 87% experienced postsurgical symptoms, including (but not limited to) numbness, pain, swelling, infection, or bleeding. Studies reported that women undergoing risk-reducing mastectomy experienced decreased pleasure in sexual activity. One pre-post study of 90 high-risk women undergoing risk-reducing bilateral mastectomy found significant decreases in anxiety scores at 6-months and 1-year post-surgery, compared with pre-surgery anxiety scores.

**Salpingo-oophorectomy or oophorectomy.** The 2013 USPSTF review identified one before-and-after study of 114 BRCA mutation carriers undergoing risk-reducing salpingo-oophorectomy. Most women experienced significant worsening of vasomotor symptoms, as well as decreased sexual functioning, after surgery.

**Summary of findings regarding the harms of risk-reducing surgeries for BRCA-related breast and ovarian cancer among BRCA mutation carriers:** There is limited evidence that risk-reducing mastectomy can lead to physical and psychological harms, such as surgical complications, post-surgical symptoms, and decreased pleasure in sexual activities. There is limited evidence based on a single study that risk-reducing salpingo-oophorectomy can lead to worsening vasomotor symptoms and sexual functioning.

## Conclusion

Although there is no direct evidence that the clinical pathway outlined in AB 2342 — familial risk screening, genetic counseling, and then genetic testing — leads to reductions in the incidence of BRCA-related cancer, cancer-related mortality, or all-cause mortality, there is indirect evidence supporting that each of these activities, as well as risk-reducing interventions for women identified as *BRCA1* or *BRCA2* mutation carriers, are effective. Through CHBRP's review of the 2013 systematic review to inform the USPSTF, as well as studies published since 2012, CHBRP finds evidence that:

- Familial risk screening tools can accurately identify women at risk for BRCA mutations.
- Genetic counseling before genetic testing improves risk perception accuracy and decreases intention to pursue testing among women unlikely to be BRCA carriers.
- Positive BRCA mutation test results accurately predict the risk of developing BRCA-related cancer.
- Risk-reducing interventions (intensive screening, medications, and surgery) can mitigate some BRCA-related cancer risk, particularly for BRCA-related breast cancer, leading to reduced incidence of breast cancer and mortality.

## **BENEFIT COVERAGE, UTILIZATION, AND COST IMPACTS**

As discussed in the *Policy Context* section, AB 2342 would require that DMHC-regulated health plans and CDI-regulated policies provide screening of family history risk for breast cancer susceptibility gene (BRCA) mutations, and if indicated, genetic counseling and genetic testing for women who meet certain criteria.

This section reports the potential incremental impacts of AB 2342 on estimated baseline benefit coverage, utilization, and overall cost. As discussed in the *Policy Context* section, nongrandfathered group and individual health insurance plans and policies are already currently required to cover, without cost sharing, screening, genetic counseling, and genetic testing, if indicated, for women whose family history is associated with an increased risk for BRCA gene mutations. On the basis of a survey of health insurers and Medi-Cal managed care plans, CHRBP has also determined that grandfathered plans and Medi-Cal managed care plans also already provide coverage for these services. Therefore, CHRBP estimates no impact on coverage, utilization or overall costs associated with AB 2342. Additional detail on specific estimated postmandate impacts are discussed below.

### **Baseline and Postmandate Benefit Coverage**

CHBRP estimates 100% of enrollees with health insurance that would be subject to AB 2342 have coverage for screening of family history risk for breast cancer susceptibility genes (BRCA), genetic counseling, and BRCA mutation testing.

Current coverage of BRCA family history screening, genetic counseling, and testing was determined by a survey of the largest (by enrollment) providers of health insurance in California. Responses to this survey represent 78% of enrollees in privately funded health insurance market that can be subject to state mandates, 59% of enrollees with Medi-Cal Managed Care Plan coverage, and 100% with CalPERS benefit coverage. The California Department of Healthcare Services indicates that Medi-Cal covers and provides reimbursement for all USPSTF preventive services assigned a grade of A or B which CHBRP assumes includes BRCA counseling and genetic testing, which received a grade B for women meeting family history risk criteria.<sup>22</sup> CHBRP therefore estimates a postmandate change in benefit coverage of 0% of enrollees due to AB 2342 (see Table 1).

CHBRP recognizes other population subgroups that may potentially experience slight modifications of benefit coverage postmandate (see Appendix D), but does not have available evidence or data to support estimation of impact on benefit coverage.

### **Baseline and Postmandate Utilization**

Because an estimated 100% enrollees have coverage for the benefits outlined in AB 2342, CHBRP estimates no change in utilization following enactment of AB 2342 (Table 1).

Based on MarketScan 2016 data, CHBRP estimates that of all female enrollees ages 18 to 64, 1.1% (20,000) have a documented family history of breast or ovarian cancer at baseline and used genetic counseling or BRCA testing (Table 1). CHBRP is unable to ascertain from MarketScan data the results of family history risk screening or testing, and thus reports only utilization and costs of services of those with a family cancer history and no personal diagnosis of cancer. CHBRP estimates may underestimate

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<sup>22</sup> [http://www.dhcs.ca.gov/services/medi-cal/Documents/prev\\_m01o03.pdf](http://www.dhcs.ca.gov/services/medi-cal/Documents/prev_m01o03.pdf).

population prevalence of family history of cancers due to patient lack of knowledge on family history or failure of providers to document family history as a claims diagnosis. However, because CHBRP identified enrollees with a documented history for *any* family members with breast and ovarian cancers, not only those with listed in AB 2342 (i.e., relatives with breast cancer under age 50 years, bilateral breast cancer) the CHBRP estimate is somewhat more inclusive than the risk group specified in AB 2342.

Because family history risk screening is not identified separately from standard Evaluation and Management claims, CHBRP is unable to estimate utilization or costs associated with a screening procedure specifically for family history risk of BRCA mutations. Thus, only utilization and costs associated with genetic counseling and BRCA testing are presented.

Because AB 2342 does not address cost sharing, CHBRP assumes no change in utilization among enrollees of grandfathered plans with existing coverage subject to cost sharing.

Similarly, as noted above, respondents to the carrier survey indicated applying utilization management practices, specifically pre-authorization for BRCA testing typically based upon National Comprehensive Cancer Network (NCCN) guidelines. A search of DMHC Independent Medical Review reports identified multiple reports of enrollees for whom coverage for BRCA testing was denied and the health plan decision was overturned for lack of compliance with NCCN guidelines. CHBRP is unable to estimate how often these situations occur, but because AB 2342 does not address pre-authorization or application of NCCN guidelines for BRCA testing, CHBRP assumes the incidence of these cases would be unchanged postmandate.

CHBRP recognizes that utilization may increase following enactment of AB 2342 due to greater provider awareness of existing coverage for BRCA genetic counseling and testing. However, CHBRP has no evidence base, literature or data to estimate the impact of AB 2342 on provider behavior. As noted above, CHBRP assumes it is unlikely that AB 2342 would raise awareness beyond the prior effects of publication from passage of the Affordable Care Act and Department of Health and Human Services notification specifically regarding coverage of BRCA screening, genetic counseling and testing (CMS, 2015). Because AB 2342 will not lead to a change in benefits for health plans, CHBRP assumes health plans will not invest in new marketing or documentation changes that may raise provider awareness or education.

## **Baseline and Postmandate Per-Unit Cost**

Due to the negligible impact on coverage and utilization, CHBRP assumes no postmandate change in unit costs for BRCA screening, counseling or genetic testing. Based upon 2016 MarketScan data, CHBRP estimates per-unit costs of \$161 for genetic counseling and \$1,307 for BRCA testing (see Table 1) at baseline and postmandate.

CHBRP notes that family history risk screening is already billed under provider Evaluation and Management codes, and thus assumes per-unit costs under AB 2342 are limited to those associated with genetic counseling and BRCA testing, which are separate billable services.

## **Baseline and Postmandate Expenditures**

Table 1 presents member per month (PMPM) expenditures associated with genetic counseling and BRCA testing at baseline and postmandate.

AB 2342 would result in no change in total net annual expenditures, premiums, or enrollee expenses for covered and/or noncovered benefits.

## **Premiums**

CHBRP anticipates no changes in premiums as a result of AB 2342 for commercial plans. Among publicly funded DMHC-regulated health plans, CHBRP estimates no impact on Medi-Cal Managed Care or CalPERS. Because AB 2342 does not apply to Medi-Cal Fee-for-Service or Medi-Cal County Organized Health Systems, CHBRP estimates no impact on these market segments.

## **Enrollee Expenses**

CHBRP anticipates no changes in enrollee expenses for covered benefits as a result of AB 2342. As noted above, grandfathered plans are not subject to federal preventive services recommendations. Carrier survey respondents indicated grandfathered plan products may have cost-sharing requirements for genetic counseling and BRCA testing; however, because grandfathered plans are estimated to provide 100% benefit coverage at baseline, CHBRP estimates no change in enrollee expenses due to AB 2342 for grandfathered plan enrollees.

## **Out-of-Pocket Spending for Covered and Noncovered Expenses**

When possible, CHBRP estimates the marginal impact of the bill on out-of-pocket spending for covered and noncovered expenses, defined as uncovered medical expenses paid by the enrollee as well as out-of-pocket expenses (e.g., deductibles, copayments, and coinsurance). Because CHBRP estimates no impact on utilization or costs, CHBRP estimates no change in out-of-pocket spending. CHBRP estimates average cost sharing of \$3 per unit for genetic counseling and \$26 for BRCA testing at baseline and postmandate (Table 1). CHBRP estimates are based on claims data and may underestimate the costs for enrollees due to carriers' ability to negotiate discounted rates.

## **Potential Cost Offsets or Savings in the First 12 Months After Enactment**

CHBRP does not project any cost offsets or savings in health care that would result because of the enactment of provisions in AB 2342. CHBRP recognizes that genetic counseling and BRCA testing are associated with utilization and costs of intensive screening and risk mitigation services among enrollees who are identified as BRCA mutation carriers. CHBRP is unable to identify those who test positive for BRCA mutations, but provides an illustration of estimated utilization of services among those with a family history of breast or ovarian cancer who received BRCA tests. These services include (but are not limited to): mammography, breast magnetic resonance imaging (MRI), use of chemoprevention medications (such as tamoxifen, aromatase-inhibitor medications, and oral contraceptives), and surgical procedures, including breast biopsies, bilateral mastectomy and bilateral salpingo-oophorectomy (Table 3). Among those with a family history of breast or ovarian cancer and who receive BRCA testing, CHBRP estimates baseline utilization of these services are 13.3% for mammography, 6.7% for breast MRI, 3.6% for chemoprevention and 0.6% for surgical procedures (Table 3, based on 2016 MarketScan data).

**Table 3.** Utilization of Additional Services Associated With BRCA Genetic Mutation Testing

Service	% of Enrollees With Family History of Cancer and Received BRCA Testing
<b>Screening Procedures</b>	
Mammography (a)	13.3%
Breast MRI	6.7%
<b>Risk Mitigation Procedures</b>	
Chemoprevention (b)	3.6%
Surgical Procedures (c)	0.6%

Source: California Health Benefits Review Program, 2018. Based on an analysis of MarketScan 2016.

Notes: (a) Mammography includes screening and diagnostic mammography using both 2D (standard) and 3D (breast tomosynthesis).

(b) Chemoprevention includes Selective Estrogen Receptor Modulators (SERMS) tamoxifen and raloxifene, and aromatase inhibitors, anastrozole, exemestane, and letrozole.

(c) Surgical procedures include breast biopsies, bilateral mastectomies, and salpingo-oophorectomies.

Key: MRI = magnetic resonance imaging.

## **Postmandate Administrative Expenses and Other Expenses**

CHBRP estimates that no increase in administrative costs, because all market segments report current coverage for the benefits outlined in AB 2342. All health plans and insurers include a component for administration and profit in their premiums.

## **Other Considerations for Policymakers**

In addition to the impacts a bill may have on benefit coverage, utilization, and cost, related considerations for policymakers are discussed below.

## **Postmandate Changes in the Number of Uninsured Persons<sup>23</sup>**

Because there is no change in average premiums due to AB 2342, (see Table 1), CHBRP would expect no measurable change in the number of uninsured persons due to the enactment of AB 2342.

## **Changes in Public Program Enrollment**

CHBRP estimates that the mandate would produce no measurable impact on enrollment in publicly funded insurance programs due to the enactment of AB 2342.

## **How Lack of Benefit Coverage Results in Cost Shifts to Other Payers**

CHBRP recognizes that enrollees may pay for genetic counseling and BRCA testing directly, for several reasons including: 1) privacy concerns, e.g., a reluctance to have genetic risk information linked to medical records, and 2) desire for multigene panel testing that may not be covered by health plans that may include BRCA (even if enrollees were not a priori interested in BRCA mutations). CHBRP has no evidence, literature, or data to estimate the current extent to which lack of benefit coverage shifts costs to other payers. CHBRP was unable to identify a count of enrollees lacking coverage for genetic counseling and BRCA testing, and thus assumes the potential impact of cost-shifting to other payers is small and does not impact premiums for enrollees in plans with existing coverage for genetic counseling and BRCA testing.

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<sup>23</sup> See also CHBRP's *Criteria and Methods for Estimating the Impact of Mandates on the Number of Uninsured*, available at [www.chbrp.org/analysis\\_methodology/cost\\_impact\\_analysis.php](http://www.chbrp.org/analysis_methodology/cost_impact_analysis.php).

## PUBLIC HEALTH IMPACTS

As discussed in the *Policy Context* section, AB 2342, if enacted, would require DMHC-regulated health plans and CDI-regulated policies to cover family history-based risk screening for breast cancer susceptibility gene (BRCA)-related mutations, and if indicated, genetic counseling and genetic testing for women who meet certain risk criteria.

Although the continuum of screening services for BRCA gene mutations — family-history based risk screening, genetic counseling, and genetic testing — is medically effective, **CHBRP concludes that passage of AB 2342 would have no short-term<sup>24</sup> public health impact** on breast or ovarian cancer outcomes or disparities in screening among women in California due to no population level changes in coverage or utilization for BRCA screening services. As discussed in the *Benefit Coverage, Utilization, and Cost Impacts* section, screening and testing services for BRCA gene mutations are currently covered in California private group and individual health insurance plans, with no cost sharing, since they qualify as preventive services under the federal Affordable Care Act (ACA). CHBRP acknowledges that there may be some grandfathered plans in the individual market that are not subject to the ACA's preventive services clause; however, based on surveys to carriers, coverage for these services is also widespread in grandfathered plans.

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<sup>24</sup> CHBRP defines short-term impacts as changes occurring within 12 months of bill implementation.

## LONG-TERM IMPACTS

In this section, CHBRP estimates the long-term impact<sup>25</sup> of AB 2342 which CHBRP defines as impacts occurring beyond the first 12 months after implementation. These estimates are qualitative and based on the existing evidence available in the literature. CHBRP does not provide quantitative estimates of long-term impacts because of unknown improvements in clinical care, changes in prices, implementation of other complementary or conflicting policies, and other unexpected factors.

### Long-Term Utilization and Cost Impacts

#### Utilization Impacts

CHBRP anticipates no long-term increases in utilization of family history risk screening, genetic counseling and BRCA testing after enactment of AB 2342. However, if the Affordable Care Act were to be repealed or altered, AB 2342 would preserve coverage in California for BRCA screening, counseling, and testing.

#### Cost Impacts

CHBRP anticipates no long-term cost impacts as a result of AB 2342. Utilization and costs associated with screening and risk mitigation for those with BRCA mutations may be offset by future reductions in cancer incidence and severity. A 2015 cost-effectiveness analysis of BRCA genetic testing estimated full-population (not family history-based) costs at \$53,000 per quality-adjusted life-years (QALY) gained (Long and Ganz, 2015). However, CHBRP is unable to anticipate long-term cost-effectiveness due to rapid changes in genetic testing technology, clinical practices and markets. Since 2013, the end of the Myriad monopoly on BRCA testing has introduced competition and unit cost has declined from over \$3000 to \$1300 for testing covered by health plans and policies; direct-to-consumer marketed tests charge even lower prices, including \$99 from Color.<sup>26</sup> Also, CHBRP notes the availability of lower-cost tests that only assess three BRCA mutations associated with Ashkenazi Jewish ancestry, including most recently the direct-to-consumer \$159 test from 23andMe;<sup>27</sup> impact of receipt of these tests on utilization of full BRCA susceptibility gene mutations is unknown. At the same time, clinical practice is moving toward multigene panel testing;<sup>28</sup> a recent cost-effectiveness evaluation of multigene versus *BRCA1/2* population testing estimated multigene \$54,770 per QALY, but as noted above, AB 2342 does not differentiate between BRCA vs. multigene panel testing and thus long-term cost impacts are unknown (Manchanda et al., 2018).

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<sup>25</sup> See also CHBRP's *Criteria and Guidelines for the Analysis of Long-Term Impacts on Healthcare Costs and Public Health*, available at [www.chbrp.org/analysis\\_methodology/cost\\_impact\\_analysis.php](http://www.chbrp.org/analysis_methodology/cost_impact_analysis.php).

<sup>26</sup> Color BRCA Test. Available at: [www.color.com/product/brca-genetic-test](http://www.color.com/product/brca-genetic-test).

<sup>27</sup> 23andMe. Available at: <https://www.23andme.com/dna-health-ancestry>

<sup>28</sup> Personal communication, Patricia Ganz, MD, University of California, Los Angeles. March 2, 2018.

## **Appendix A    TEXT OF BILL ANALYZED**

On February 15, 2018, the California Assembly Committee on Health requested that CHBRP analyze AB 2342.

**ASSEMBLY BILL**

**No. 2342**

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**Introduced by Assembly Members Burke and Waldron**

February 13, 2018

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An act to add Sections 1367.615 and 104150.5 to the Health and Safety Code, and to add Section 10123.815 to the Insurance Code, relating to cancer.

### **Legislative Counsel's Digest**

AB 2342, as introduced, Burke. BRCA gene mutations: screening, counseling, and testing.

Existing law, the Knox-Keene Health Care Service 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 its provisions a crime. Existing law provides for the regulation of health insurers by the Department of Insurance. Existing law requires every health care service plan contract and health insurance policy to provide coverage for screening for, diagnosis of, and treatment for, breast cancer, consistent with generally accepted medical practice and scientific evidence, upon the referral of the enrollee's or insured's participating physician.

Existing law requires the State Department of Health Care Services to perform various health functions, including providing breast and cervical cancer screening and treatment for low-income individuals.

This bill would require health care service plans, health insurers, and the State Department of Health Care Services to cover screening, genetic counseling, and testing for BRCA gene mutations in women who have not been diagnosed with BRCA-related cancer and do not have signs or symptoms of the disease, but who may have an increased risk based

on one or more of specified family history risk factors. By creating a new crime with respect to health care service plans, the bill 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:*

1 SECTION 1. Section 1367.615 is added to the Health and  
2 Safety Code, to read:

3 1367.615. (a) In addition to the services described in  
4 subdivision (c) of Section 1367.6, every health care service plan  
5 contract, except a specialized health care service plan contract,  
6 that is issued, amended, delivered, or renewed on or after January  
7 1, 2019, shall provide breast cancer susceptibility gene (BRCA)  
8 screening, genetic counseling, and testing services under the  
9 circumstances described in this section.

10 (b) Screening shall be provided for women who have not been  
11 diagnosed with BRCA-related cancer and do not have signs or  
12 symptoms of the disease, but who may have an increased risk for  
13 potentially harmful mutations in breast or ovarian cancer  
14 susceptibility genes, based on one or more of the following family  
15 history risk factors:

- 16 (1) Breast cancer diagnosis before 50 years of age.  
17 (2) Bilateral breast cancer.  
18 (3) Breast and ovarian cancer.  
19 (4) Presence of breast cancer in at least one male family member.  
20 (5) Multiple cases of breast cancer in the family.  
21 (6) At least one family member with two types of BRCA-related  
22 cancer.

23 (7) Ashkenazi Jewish ancestry.  
24 (c) Screening shall be provided using a generally accepted  
25 screening tool designed to identify a family history that may be  
26 associated with an increased risk for potentially harmful mutations  
27 in breast or ovarian cancer susceptibility genes *BRCA1* or *BRCA2*.

1 (d) Genetic counseling shall be provided for women with  
2 positive screening results. If indicated after counseling, BRCA  
3 testing shall be provided.

4 SEC. 2. Section 104150.5 is added to the Health and Safety  
5 Code, to read:

6 104150.5. (a) In addition to the services described in  
7 subdivision (b) of Section 104150, screening shall be provided for  
8 women who have not been diagnosed with breast cancer  
9 susceptibility gene-(BRCA)-related cancer and do not have signs  
10 or symptoms of the disease, but who may have an increased risk  
11 for potentially harmful mutations in breast or ovarian cancer  
12 susceptibility genes, based on one or more of the following family  
13 history risk factors:

- 14 (1) Breast cancer diagnosis before 50 years of age.
- 15 (2) Bilateral breast cancer.
- 16 (3) Breast and ovarian cancer.
- 17 (4) Presence of breast cancer in at least one male family member.
- 18 (5) Multiple cases of breast cancer in the family.
- 19 (6) At least one family member with two types of BRCA-related  
20 cancer.
- 21 (7) Ashkenazi Jewish ancestry.

22 (b) Screening shall be provided using a generally accepted  
23 screening tool designed to identify a family history that may be  
24 associated with an increased risk for potentially harmful mutations  
25 in breast or ovarian cancer susceptibility genes *BRCA1* or *BRCA2*.

26 (c) Genetic counseling shall be provided for women with  
27 positive screening results. If indicated after counseling, BRCA  
28 testing shall be provided.

29 SEC. 3. Section 10123.815 is added to the Insurance Code, to  
30 read:

31 10123.815. (a) In addition to the services described in  
32 subdivision (c) of Section 10123.8, every policy of disability  
33 insurance that provides coverage for hospital, medical, or surgical  
34 expenses, that is issued, amended, delivered, or renewed on or  
35 after January 1, 2019, shall provide breast cancer susceptibility  
36 gene (BRCA) screening, genetic counseling, and testing services  
37 under the circumstances described in this section.

38 (b) Screening shall be provided for women who have not been  
39 diagnosed with BRCA-related cancer and do not have signs or  
40 symptoms of the disease, but who may have an increased risk for

1 potentially harmful mutations in breast or ovarian cancer  
2 susceptibility genes, based on one or more of the following family  
3 history risk factors:  
4 (1) Breast cancer diagnosis before 50 years of age.  
5 (2) Bilateral breast cancer.  
6 (3) Breast and ovarian cancer.  
7 (4) Presence of breast cancer in at least one male family member.  
8 (5) Multiple cases of breast cancer in the family.  
9 (6) At least one family member with two types of BRCA-related  
10 cancer.  
11 (7) Ashkenazi Jewish ancestry.  
12 (c) Screening shall be provided using a generally accepted  
13 screening tool designed to identify a family history that may be  
14 associated with an increased risk for potentially harmful mutations  
15 in breast or ovarian cancer susceptibility genes *BRCA1* or *BRCA2*.  
16 (d) Genetic counseling shall be provided for women with  
17 positive screening results. If indicated after counseling, BRCA  
18 testing shall be provided.  
19 SEC. 4. No reimbursement is required by this act pursuant to  
20 Section 6 of Article XIII B of the California Constitution because  
21 the only costs that may be incurred by a local agency or school  
22 district will be incurred because this act creates a new crime or  
23 infraction, eliminates a crime or infraction, or changes the penalty  
24 for a crime or infraction, within the meaning of Section 17556 of  
25 the Government Code, or changes the definition of a crime within  
26 the meaning of Section 6 of Article XIII B of the California  
27 Constitution.

## Appendix B LITERATURE REVIEW METHODS

This appendix describes methods used in the medical effectiveness literature review conducted for this report. A discussion of CHBRP's system for grading evidence, as well as lists of MeSH Terms, publication types, and keywords, follows.

Studies of screening, genetic counseling and genetic testing for BRCA gene mutations were identified through searches of PubMed, the Cochrane Library, Web of Science, EconLit, and Business Source Complete, the Cumulative Index of Nursing and Allied Health Literature, and PsycINFO. Websites maintained by the following organizations that produce and/or index meta-analyses and systematic reviews were also searched: the Agency for Healthcare Research and Quality (AHRQ), the International Network of Agencies for Health Technology Assessment (INAHTA), the National Health Service (NHS) Centre for Reviews and Dissemination, the National Institute for Health and Clinical Excellence (NICE), and the Scottish Intercollegiate Guideline Network. The search was limited to abstracts of studies published in English.

Reviewers screened the title and abstract of each citation retrieved by the literature search to determine eligibility for inclusion. The reviewers acquired the full text of articles that were deemed eligible for inclusion in the review and reapplied the initial eligibility criteria.

The medical effectiveness review searched the literature from 2012 to present. CHBRP relied on a systematic review published in 2013 for findings from studies published prior to December 2012. Of the 235 articles identified in the current literature search, 43 were reviewed for potential inclusion in this report on AB 2342 and a total of five studies published since 2012 were included in the medical effectiveness review for this report. The other articles were eliminated because they did not focus primarily on asymptomatic women, assessed an intervention deemed out-of-scope (e.g., sophisticated kindred analysis models, psychological harms of direct-to-consumer genetic testing), were of poor quality, or did not report findings from clinical research studies. 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.

### Evidence Grading System

In making a "call" for each outcome measure, the medical effectiveness lead and the content expert consider the number of studies as well the strength of the evidence. Further information about the criteria CHBRP uses to evaluate evidence of medical effectiveness can be found in CHBRP's *Medical Effectiveness Analysis Research Approach*.<sup>29</sup> 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; and
- Generalizability of findings.

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<sup>29</sup> Available at: [www.chbrp.org/analysis\\_methodology/docs/medeffect\\_methods\\_detail.pdf](http://www.chbrp.org/analysis_methodology/docs/medeffect_methods_detail.pdf).

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;*
- *Limited evidence*
- *Inconclusive evidence; and*
- *Insufficient evidence.*

A grade of *clear and convincing evidence* indicates that there are multiple studies of a treatment and that the large majority of studies are of high quality and consistently find that the treatment is either effective or not effective.

A grade of *preponderance of evidence* indicates that the majority of the studies reviewed are consistent in their findings that treatment is either effective or not effective.

A grade of *limited evidence* indicates that the studies had limited generalizability to the population of interest and/or the studies had a fatal flaw in research design or implementation.

A grade of *inconclusive evidence* indicates that although some studies included in the medical effectiveness review find that a treatment is effective, a similar number of studies of equal quality suggest the treatment is not effective.

A grade of *insufficient evidence* indicates that there is not enough evidence available to know whether or not a treatment is effective, either because there are too few studies of the treatment or because the available studies are not of high quality. It does not indicate that a treatment is not effective.

### **Search Terms (\* indicates truncation of word stem)**

- Incidence
- Mortality
- BRCA screening tools
- Familial risk assessment
- Risk assessment
- Test performance
- Accuracy
- Clinical validity
- Sensitivity
- Specificity
- Positive predictive value
- Negative predictive value
- Positive likelihood ratio
- Negative likelihood ratio
- False-positive results
- False-negative results
- Knowledge
- Satisfaction
- Understanding
- Risk perception
- Risk reduction
- Adverse effects
- Harms
- Psychological harms
- race
- racial disparities
- ethnicity
- gender
- sex differences
- prevalence
- incidence
- premature death
- economic loss
- morbidity
- mortality
- long term impacts
- productivity and cost of illness

## Appendix C MEDICAL EFFECTIVENESS DETAILED RESULTS

**Table C1.** BRCA Gene Mutation Penetrance (Breast and Ovarian Cancer Cumulative Incidence Risk) By Age 70 Years, Among Women with a Positive BRCA Gene Mutation Test and a Family or Personal History of Breast or Ovarian Cancer

Study Type	BRCA Testing Approach	Cumulative Risk (%)	95% CI
<b>Breast cancer</b>			
Meta-analysis of 8 studies (Nelson et al., 2013)	Individual tested — <i>BRCA1</i> mutation	46	40% – 52%
Meta-analysis of 8 studies (Nelson et al., 2013)	Individual tested — <i>BRCA2</i> mutation	50	40% – 60%
Meta-analysis of 8 studies (Nelson et al., 2013)	Family tested — <i>BRCA1</i> mutation	70	61% – 79%
Cohort of 492 <i>BRCA1</i> or 2 mutation carriers (Evans et al., 2014)	Family tested — <i>BRCA1</i> mutation	45	27% – 58%
Cohort of 998 <i>BRCA1</i> or 2 mutation carriers (Mavaddat et al., 2013)	Family tested — <i>BRCA1</i> mutation	60	44% – 75%
Meta-analysis of 8 studies (Nelson et al., 2013)	Family tested — <i>BRCA2</i> mutation	71	59% – 83%
Cohort of 492 <i>BRCA1</i> or 2 mutation carriers (Evans et al., 2014)	Family tested — <i>BRCA2</i> mutation	60	42% – 73%
Cohort of 998 <i>BRCA1</i> or 2 mutation carriers (Mavaddat et al., 2013)	Family tested — <i>BRCA2</i> mutation	55	41% – 70%
Cohort of 492 <i>BRCA1</i> or 2 mutation carriers (Evans et al., 2014)	Family tested — <i>BRCA1</i> or 2 mutation combined	54	40% – 63%
<b>Ovarian cancer</b>			
Meta-analysis of 7 studies (Nelson et al., 2013)	Individual tested — <i>BRCA1</i> mutation	41	32% – 49%
Meta-analysis of 7 studies (Nelson et al., 2013)	Individual tested — <i>BRCA2</i> mutation	17	11% – 24%
Meta-analysis of 6 studies (Nelson et al., 2013)	Family tested — <i>BRCA1</i> mutation	46	35% – 57%
Cohort of 998 <i>BRCA1</i> or 2 mutation carriers (Mavaddat et al., 2013)	Family tested — <i>BRCA1</i> mutation	59	43% – 76%
Meta-analysis of 6 studies (Nelson et al., 2013)	Family tested — <i>BRCA2</i> mutation	23	12% – 34%
Cohort of 998 <i>BRCA1</i> or 2 mutation carriers (Mavaddat et al., 2013)	Family tested — <i>BRCA2</i> mutation	17	8% – 34%

Source: California Health Benefits Review Program, 2018.

## Appendix D COST IMPACT ANALYSIS: DATA SOURCES, CAVEATS, AND ASSUMPTIONS

The cost analysis in this report was prepared by the members of the cost team, which consists of CHBRP task force members and contributors from the University of California, Los Angeles, the University of California, Davis, as well as the contracted actuarial firm, PricewaterhouseCoopers (PwC).<sup>30</sup>

Information on the generally used data sources and estimation methods, as well as caveats and assumptions generally applicable to CHBRP's cost impacts analyses are available at CHBRP's website.

This appendix describes any analysis-specific data sources, estimation methods, caveats and assumptions used in preparing this cost impact analysis.

### Analysis Specific Caveats and Assumptions

CHBRP considers the following subpopulations may experience a change in benefit coverage following enactment of AB 2342:

- *Women of Ashkenazi Jewish ancestry with no family history of cancer.* Current USPSTF guidelines recommend use of a family history risk screening tool for those with a family history of cancer. AB 2342 requires coverage for screening benefits for all women of Ashkenazi Jewish ancestry, irrespective of family history of cancer. However, health plans reporting on the CHBRP carrier survey indicated full coverage for screening without utilization management restrictions, i.e. screening benefits are not limited to the populations specified under USPSTF. Thus, although AB 2342 mandates a slightly more expansive population than USPSTF guidelines, CHBRP assumes based on carrier reporting that this population already has coverage for the screening outlined in AB 2342. CHBRP notes 2 out of 5 USPSTF-evaluated screening tools include Ashkenazi Jewish ancestry (without family history of cancer) as a risk factor that may lead to referral for genetic counseling, but AB 2342 does not mandate use of a specific screening tool, and current utilization of listed screening tools are not known. CHBRP is thus unable to estimate the impact of AB 2342 on benefit coverage for genetic counseling. CHBRP also notes that current NCCN guidelines for BRCA testing do not include women of Ashkenazi Jewish heritage with no family history of cancer. However, because existing USPSTF recommendations are the most relevant to benefit coverage due to ACA preventive services requirements, and because 2 of 5 USPSTF-evaluated screening tools include Ashkenazi Jewish ancestry (without family history of cancer) as a risk factor that may lead to referral for genetic counseling, CHBRP anticipates no change in benefit coverage for this population.
- *Women who receive a recommendation for BRCA testing following genetic counseling but do not meet health plan pre-authorization requirements for testing.* Under AB 2342, BRCA testing shall be covered if recommended following genetic counseling. Five respondents to the CHBRP carrier survey indicated requirement of pre-authorization for coverage of BRCA testing, primarily based upon NCCN guidelines for BRCA testing.<sup>31</sup> AB 2342 does not mandate BRCA testing for assessments based upon NCCN guidelines- AB 2342 only mandates BRCA testing based upon

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<sup>30</sup> CHBRP's authorizing statute, available at [www.chbrp.org/docs/authorizing\\_statute.pdf](http://www.chbrp.org/docs/authorizing_statute.pdf), requires that CHBRP use a certified actuary or "other person with relevant knowledge and expertise" to determine financial impact.

<sup>31</sup> Available at:

<https://static1.squarespace.com/static/5653d3d5e4b096a50bf60d54/t/59d4ff0e8fd4d2bbdfa981c2/1507131155590/10-2017+Br+Ov+NCCN.pdf>

genetic counseling recommendation. Three plans indicated additional coverage for BRCA testing based upon genetic counseling risk assessment even if NCCN guidelines are not met. AB 2342 may increase coverage for women who receive a recommendation for testing following genetic counseling, and do not meet NCCN guidelines. CHBRP has no evidence, literature or data to estimate the percentage of enrollees who do not meet NCCN guidelines but are nevertheless recommended to receive BRCA testing following genetic counseling. Of note, CHBRP identified one preliminary study that suggests that use of genetic counseling increases BRCA testing in compliance with NCCN guidelines (Roberts et al., 2018).

- *Women in plans that did not respond to the carrier survey and without coverage for genetic counseling or BRCA testing.* The CHBRP carrier survey respondents represent 78% of the commercial market and 59% of the Medi-Cal managed care market. CHBRP recognizes that it is possible that carriers with grandfathered plans not responding to the survey may not offer coverage for benefits outlined in AB 2342; however, based on the consistent response across all respondents, CHBRP assumes this is unlikely and furthermore has no evidence or data to estimate the number of women in this category. Because the Department of Healthcare Services has indicated that Medi-Cal enrollees have coverage for genetic counseling and BRCA testing, CHBRP likewise assumes it is unlikely that women covered by Medi-Cal managed care plans not included in the survey lack coverage for the benefits outlined in AB 2342.

## Determining Public Demand for the Proposed Mandate

This subsection discusses public demand for the benefits AB 2342 would mandate. Considering the criteria specified by CHBRP's authorizing statute, CHBRP reviews public demand for benefits relevant to a proposed mandate in two ways. CHBRP:

- Considers the bargaining history of organized labor; and
- Compares the benefits provided by self-insured health plans or policies (which are not regulated by the DMHC or CDI and therefore not subject to state-level mandates) with the benefits that are provided by plans or policies that would be subject to the mandate.

CHBRP concluded that unions currently do not include cost-sharing arrangements for description treatment or service. In general, unions negotiate for broader contract provisions such as coverage for dependents, premiums, deductibles, and broad coinsurance levels.

Among publicly funded self-insured health insurance policies, the preferred provider organization (PPO) plans offered by CalPERS currently have the largest number of enrollees. The CalPERS PPOs currently provide benefit coverage similar to what is available through group health insurance plans and policies that would be subject to the mandate.

To further investigate public demand, CHBRP used the bill-specific coverage survey to ask carriers who act as third-party administrators for (non-CalPERS) self-insured group health insurance programs whether the relevant benefit coverage differed from what is offered in group market plans or policies that would be subject to the mandate. The responses indicated that there were no substantive differences.

## BRCA Screening, Testing and Counseling Services

This subsection discusses the caveats and assumptions specifically relevant to the coverage requirement for BRCA screening, testing and counseling services for asymptomatic women, age 18 to 64 with a family history of susceptibility to breast, ovarian or fallopian tube cancer per AB 2342.

The population subject to the mandated offering includes enrollees in DMHC-regulated plans and CDI-regulated policies for large group, small group, individual marketplace plans, Medi-Cal and CalPERS plans.

Baseline BRCA screening, testing and counseling costs and associated utilization were based on 2016 MarketScan® commercial claims and enrollment data for the state of California. Since the potential impact change of this mandate affects those enrollees who have a family history risk factor for BRCA but are asymptomatic, the analysis was limited to enrollees who do not have a personal history of breast, ovarian or fallopian tube cancer.

- CHBRP expects that any mandate utilization changes from this component of the bill would be based on changes to current BRCA screening, testing and counseling coverage.
- CHBRP expects that the cost per unit of service stays the same between pre and post mandate.
- CHBRP assumes that the mandate would not impact any forms of member cost sharing, such as deductibles, copays, and coinsurance.
- It is also assumed that the bill would not affect plan/insurer methods of utilization management that may impact the coverage of medical treatments between baseline and post mandate periods, such as use of prior authorization requirements and medical review for medical treatments.

The following tables list the diagnosis codes used to identify BRCA risk factor diagnosed enrollees and procedure codes used to identify genetic testing and counseling related to the BRCA risk factor diagnosis.

Genetic testing and counseling for BRCA risk factor diagnosed used Healthcare Common Procedure Coding System (HCPCS) and Current Procedural Terminology (CPT) codes identified with carrier coverage guidelines and reviewed by a content expert.

<b>Diagnosis Codes (ICD-10):</b>	<b>Description</b>
Z1501	Genetic susceptibility to malignant neoplasm of breast
Z1502	Genetic susceptibility to malignant neoplasm of ovary
Z803	Family history of malignant neoplasm of breast
Z8041	Family history of malignant neoplasm of ovary
Z8049	Family history of malignant neoplasm of other genital organs [fallopian tube]
Z8481	Family history of carrier of genetic disease

CPT/HCPCS Codes	Mandated Services Category:
81162, 81211, 81212, 81213, 81214, 81215, 81216, 81217, S3818, S3819, S3820, S3822, S3823	BRCA Specific Genetic Sequencing Test
81292, 81294, 81295, 81297, 81298, 81300, 81317, 81319, 81321, 81403, 81405, 81406, 81408, 81432, 81433, 81479, G0452	Broad Panel Genetic Sequencing Test
96040, S0265	Genetic Counseling Code

CHBRP used the BRCA Risk Factor diagnosis codes to produce a list of individuals in the 2016 MarketScan® Commercial Claims and Encounters Database with BRCA risk factor diagnoses. Based on that list of unique individuals, CHBRP identified all individuals with a BRCA risk factor diagnosis who used genetic testing and counseling services throughout the year and then calculated utilization and baseline cost information for individuals with a BRCA risk factor diagnosis using genetic testing and counseling services.

Although CHBRP could identify the number of women with a BRCA risk factor diagnoses, there were no clear CPT/HCPCS codes for the genetic screening of BRCA risk factors. *BRCA1/BRCA2* genetic screening was likely included in a physician new patient visit code as part of the family history of the patient. Therefore, CHBRP was unable to model the utilization or average cost of genetic risk factor screening.

Baseline unit costs were trended at an annual rate 5.4% per year from 2016 to 2019 based on the “Prof and Clinical” trends published in the National Health Expenditures report. The analysis assume that the unit cost per service does not change postmandate.

BRCA screening, testing and counseling services are considered preventive services under the Affordable Care Act (ACA) and are not subject to member cost sharing. The effective date for coverage of preventive services, some in 2010 and others in 2014, predates the 2016 MarketScan® Commercial Claims and Encounters Database. CHBRP expects the MarketScan® data to represent current compliance with the ACA preventive guidelines. The analysis assumed that utilization rates per 1,000 enrollees would only change postmandate due to increased coverage under grandfathered plans that are not required to cover the preventive services. Baseline utilization rates per 1,000 were developed based on MarketScan® data for women aged 18 to 64 with a BRCA risk factor diagnosis, but no personal history of BRCA related cancers, who received genetic testing and counseling services for the year.

The Medi-Cal and CalPERS populations are included in the affected population. Medi-Cal Managed Care and Commercial Health Plan Carrier responses indicated that there was full coverage for all screening, testing and counseling services for women with a BRCA risk factor diagnosis within their covered populations. Given that insurers indicated that even grandfathered plans included coverage of BRCA preventive services, CHBRP applied a 100% Pre- and Post-Mandate compliance rate for the requirement to cover BRCA screening, testing and counseling services for health insurers subject to AB 2342. As such, there was no impact related with this portion of the mandate.

### Post BRCA Test Preventive Services

To comment on longer term and follow up preventive cost, CHBRP examined several common preventative treatment options for women who have been diagnosed with a BRCA risk factor and were tested positive for the gene mutation. The text of AB 2342 does not mandate coverage of post-testing

preventative actions should a woman be found positive for a *BRCA1/BRCA2* mutation. However, the US Preventive Services Task Force recommends chemo-preventive medications for women deemed high risk. Therefore, risk-reducing medications, such as tamoxifen, must be covered without cost sharing when prescribed to women who are at increased risk for breast cancer.<sup>32</sup>

The following tables list the HCPCS and CPT codes used to identify the post-test preventative professional/outpatient services. Drug preventative treatment of BRCA related cancers used National Drug Codes (NDC) codes identified using the Truven Health Analytics Red Book™ and were reviewed by a content expert.

ICD-10/CPT/HCPCS/NDC Codes	Preventative Services Category:
77057, 77052, G0202, Z1231, Z1239	Screening Mammography
77055, 77056, G0204, G0206, 77051	Diagnostic Mammography
77061, 77062, 77063	Tomosynthesis Testing
77058, 77059	MRI Mammography
See table below	Tamoxifen
See table below	Raloxifene
See table below	Arimidex
See table below	Anastrozole
See table below	Aromasin
See table below	Femara
See table below	Letrozole
19081, 19082, 19083, 19084, 19085, 19086	Breast Biopsy
58720, 58700, 19301, 19302, 19303, 19304, 19305, 19306, 19307	Salpingectomy/Oophorectomy/Mastectomy

CHBRP used the BRCA Risk Factor diagnosis codes to produce a list of individuals in the 2016 MarketScan® Commercial Claims and Encounters Database with BRCA risk factor diagnoses. Based on that list of unique individuals, CHBRP identified all individuals with a BRCA risk factor diagnosis who used genetic testing and counseling services throughout the year. Using only those women aged 18 to 64 who had been diagnosed with a BRCA risk factor and received a genetic test for the gene mutation within the year, CHBRP flagged those claims matching the CPT or NDC codes in the table above to identify those who had also had one of the preventative actions after the genetic test. CHBRP then calculated utilization and baseline cost information for individuals with a BRCA risk factor diagnosis who used genetic testing and preventative services post-test.

Baseline unit costs for professional or OP services were trended at an annual rate 5.4% per year from 2016 to 2019 based on the “Prof and Clinical” trends published in the National Health Expenditures report. Baseline unit costs for the BRCA pharmaceuticals were trended at an annual rate of 0.8% per year

<sup>32</sup> Kaiser Family Foundation, Preventive Services Covered by Private Health Plans under the Affordable Care Act, August 4, 2015. Available at: [www.kff.org/health-reform/fact-sheet/preventive-services-covered-by-private-health-plans/](http://www.kff.org/health-reform/fact-sheet/preventive-services-covered-by-private-health-plans/). KFF references Centers for Medicare and Medicaid Services, FAQs about Affordable Care Act Implementation — Set 26.

from 2016 to 2019 based on the 2017 Express Scripts Drug Report. The analysis assume that the unit cost per service does not change postmandate.

Although BRCA screening, testing and counseling services are considered preventative under the ACA guidelines, the coverage of post-testing preventative services vary by carrier. For women who are found to be BRCA positive in their genetic tests, coverage of preventative or preemptive services could be covered with or without cost sharing. Since there is no presumed increase in testing utilization from AB 2342 this analysis assumed there will be no subsequent increase in post-testing preventative services.

Drug	NDC Codes Used (2016)
Tamoxifen	38779034101, 38779034103, 38779034104, 38779034105, 38779034108, 38779034110, 38779034130, 38779034140, 38779034150, 38779034180, 42254034390, 49452757101, 49452757102, 49452757103, 49452757104, 49452757105, 49452757106, 49452775301, 49452775302, 49452775303, 49452775304, 49452775305, 51552083802, 51862044601, 51862044605, 51862044610, 51862044630, 51862044705, 51862044710, 51862044760, 51862044918, 51862044960, 51862045030, 51862045090, 51927297600, 52372075601, 52372075602, 54569376500, 54569376501, 54569571600, 54569585700, 54569860200, 54868300400, 54868300401, 54868300402, 54868300403, 54868300404, 54868300405, 54868428700, 54868428701, 54868428702, 54868428703, 54868428704, 60346090060, 60429090960, 60429091030, 62991115101, 62991115102, 62991115103, 62991115104, 63307047001, 63307047005, 63370025110, 63370025115, 63370025125, 63370025135, 63739026910, 63739026915, 68084092411, 68084092421, 68084093511, 68084093521, 68258596006, 75840011001, 00054483121, 00054483126, 00054483413, 00054483422, 00054883125, 00054883425, 00093078201, 00093078205, 00093078210, 00093078256, 00093078405, 00093078406, 00093078410, 00093078486, 00172565649, 00172565658, 00172565670, 00172565680, 00172565746, 00172565760, 00172565770, 00172565780, 00310073060, 00310073130, 00378014405, 00378014491, 00378027401, 00378027493, 00555044603, 00555044605, 00555044609, 00555044663, 00555090401, 00555090405, 00555090414, 00591223218, 00591223260, 00591223319, 00591223330, 00591247218, 00591247260, 00591247319, 00591247330
Raloxifene	31722025601, 31722025610, 31722025630, 42291072610, 42291072690, 43598050501, 43598050510, 43598050530, 60687026611, 60687026621, 65162005703, 65162005709, 65162005710, 65162005711, 66993041702, 66993041730, 66993041788, 66993066102, 66993066130, 66993066188, 68084087111, 68084087121, 68462039301, 68462039330, 69097082502, 69097082507, 69097082515, 76282025605, 76282025630, 00093729001, 00093729010, 00093729056, 00591236701, 00591236710, 00591236730
Arimidex	12280034630, 35356027030, 54569573100, 54868500000, 55175550503, 00310020130, 00310020137
Anastrozole	16571042103, 16729003510, 16729003515, 16729003516, 21695099030, 33261095700, 33261095730, 33261095760, 33261095790, 38779227403, 38779227404, 38779227406, 38779255503, 38779255504, 38779255506, 42043018003, 42254016130, 42291010530, 46144020001, 46144020005, 51079032301, 51079032306, 51655063853, 51927443500, 51991062010, 51991062033, 54569619800, 54868613000, 54868613001, 55111064730, 58597808001, 58597808002, 58597808004, 60258086603, 60429028630, 60429028690, 60505298503, 60687011211, 60687011221, 62033037606, 62756025013, 62756025083, 63275993001, 63275993002, 63275993003, 63275993004, 63275993005, 63323012930, 66336053330, 66336053390, 66435041530, 67877017110, 67877017130, 68001015504, 68001015508, 68084044821, 68382020906, 68382020910, 76418001301, 00054016413, 00093753656, 00378603405, 00378603477, 00378603493, 00781535631, 00904619546, 00904622961
Aromasin	49999098630, 54569573200, 54868526100, 63629126201, 00009766304
Femara	35356040930, 54569571400, 54868415100, 00078024915, 00078088150, 00078090961, 00078091661, 00078092361
Letrozole	16729003410, 16729003415, 42254024330, 42291037490, 51991075910, 51991075933, 53217010830, 54868625200, 55111064630, 60505325503, 60505325508, 62756051183, 63323077230, 68084080311, 68084080321, 68258595503, 00054026913, 00093762056, 00378207105, 00378207193, 00603418016

## Appendix E BACKGROUND DETAIL

**Table 4.** Models Estimating Individual Risk for BRCA Mutations to Guide Referrals

Model	Data Collection and Calculation Method	Relatives with Breast or Ovarian Cancer	Additional Risk Factors in Model
FHAT	Clinical scoring tool; referral threshold of 10 is equivalent to a 2-fold increase in risk for breast or ovarian cancer.	First-, second-, and third-degree	Age at diagnosis, bilateral breast cancer, breast and ovarian cancer in the same person, breast cancer in men, colon and prostate cancer
Manchester Scoring System	Clinical scoring tool; referral threshold of 10 for <i>BRCA1</i> - or <i>BRCA2</i> -specific scores or 15 combined. Not intended for Ashkenazi Jewish persons.	First-, second-, and third-degree	Type of cancer (breast, ovarian, pancreatic, or prostate), affected family members, age at diagnosis
RST	Clinical checklist of 13 items; referral threshold of 2 positive responses.	First- and second-degree	Breast cancer in women ≤50 y (self or relatives), ovarian cancer at any age (self or relatives), ≥2 cases of breast cancer in women aged >50 y on the same side of the family; breast cancer in men; Jewish ancestry
PAT	Clinical scoring tool; optimum referral threshold of 8.	First-, second-, and third-degree	Breast cancer in women aged ≤50 y or >50 y, ovarian cancer at any age, breast cancer in men, Ashkenazi Jewish ancestry
FHS-7	Clinical checklist of 7 items; referral threshold of 1 positive response.	First-degree	Any relatives with breast cancer at age ≤50 y, bilateral breast cancer, breast and ovarian cancer in the same person, breast cancer in men, ≥2 relatives with breast and/or ovarian cancer, ≥2 relatives with breast and/or colon cancer

Source: Nelson et al., 2013.

Note: This table a representative sample of available risk stratification tools; it is not a comprehensive list.

Key: BRCA = Breast Cancer 1 and 2, Early Onset; FHAT = Family History Assessment Tool; FHS-7 = Family History Screen-7; PAT = Pedigree Assessment Tool; RST = Referral Screening Tool.

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A group of faculty, researchers, and staff complete the analysis that informs California Health Benefits Review Program (CHBRP) reports. The CHBRP **Faculty Task Force** comprises rotating senior faculty from University of California (UC) campuses. In addition to these representatives, there are other ongoing researchers and analysts who are **Task Force Contributors** to CHBRP from UC that conduct 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 manages all external communications, including those with the California Legislature. As required by CHBRP's authorizing legislation, UC contracts with a certified actuary, **PricewaterhouseCoopers**, to assist in assessing the financial impact of each legislative proposal mandating or repealing a health insurance benefit.

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 of its National Advisory Council. CHBRP assumes full responsibility for the report and the accuracy of its contents.

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