

California Health Benefits Review Program

Analysis of Senate Bill 799: Colorectal Cancer: Genetic Testing and Screening

A Report to the 2013-2014 California Legislature

June 7, 2013





The California Health Benefits Review Program (CHBRP) responds to requests from the State Legislature to provide independent analyses of the medical, financial, and public health impacts of proposed health insurance benefit mandates and proposed repeals of health insurance benefit mandates. CHBRP was established in 2002 to respond to requests from the California Legislature to provide independent analysis of the medical, financial, and public health impacts of proposed health insurance benefit mandates and repeals per its authorizing statute.¹ The program was reauthorized in 2006 and again in 2009. CHBRP's authorizing statute defines legislation proposing to mandate or proposing to repeal an existing health insurance benefit as a proposal that would mandate or repeal a requirement that a health care service plan or health insurer: (1) permit covered individuals to obtain health care treatment or services from a particular type of health care provider; (2) offer or provide coverage for the screening, diagnosis, or treatment of a particular disease or condition; (3) offer or provide coverage of a particular type of health care treatment or service, or of medical equipment, medical supplies, or drugs used in connection with a health care treatment or service; and/or (4) specify terms (limits, timeframes, copayments, deductibles, coinsurance, etc.) for any of the other categories.

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

¹ Available at: www.chbrp.org/documents/authorizing_statute.pdf.

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PREFACE

This report provides an analysis of the medical, financial, and public health impacts of Senate Bill 799. In response to a request from the California Senate Committee on Health on April 9, 2013, the California Health Benefits Review Program (CHBRP) undertook this analysis pursuant to the program's authorizing statute.

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

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EXECUTIVE SUMMARY

California Health Benefits Review Program Analysis of Senate Bill 799

The California Senate Committee on Health requested on April 9, 2013, that the California Health Benefits Review Program (CHBRP) conduct an evidence-based assessment of the medical, financial, and public health impacts of Senate Bill (SB) 799: Colorectal Cancer: Genetic Testing and Screening. In response to this request, CHBRP undertook this analysis pursuant to the provisions of the program's authorizing statute.²

In 2014, CHBRP estimates that approximately 25.9 million Californians (67%) will have health insurance that may be subject to a health benefit mandate law passed at the state level.³ Of the rest of the state's population, a portion will be uninsured (and so will have no health insurance subject to any benefit mandate), and another portion will have health insurance subject to other state laws or only to federal laws.

Uniquely, California has a bifurcated system of regulation for health insurance subject to state benefit mandates. The California Department of Managed Health Care (DMHC)⁴ regulates health care service plans, which offer benefit coverage to their enrollees through health plan contracts. The California Department of Insurance (CDI) regulates health insurers,⁵ which offer benefit coverage to their enrollees through health insurance policies.

All DMHC-regulated plans and CDI-regulated policies would be subject to SB 799. Therefore, the mandate would affect the health insurance of approximately 25.9 million enrollees (67% of all Californians).

Developing Estimates for 2014 and the Effects of the Affordable Care Act

The Affordable Care Act (ACA)⁶ is expected to dramatically affect health insurance and its regulatory environment in California, with many changes becoming effective in 2014. It is important to note that CHBRP's analysis of proposed benefit mandate bills typically address the marginal effects of the proposed bills—specifically, how the proposed mandate would impact benefit coverage, utilization, costs, and public health, holding all other factors constant. CHBRP's estimates of these marginal effects are presented in this report. Because expanded enrollment will not occur until January 2014, CHBRP relies on projections from the California

² Available at: www.chbrp.org/docs/authorizing_statute.pdf.

³ CHBRP's estimates are available at: www.chbrp.org/other_publications/index.php.

⁴ The California Department of Managed Care (DMHC) was established in 2000 to enforce the Knox-Keene Health Care Service Plan of 1975; see Health and Safety Code (H&SC) Section 1340.

⁵ The California Department of Insurance (CDI) licenses "disability insurers." Disability insurers may offer forms of insurance that are not health insurance. This report considers only the impact of the benefit mandate on health insurance policies, as defined in Insurance Code (IC) Section 106(b) or subdivision (a) of Section 10198.6.

⁶ The federal "Patient Protection and Affordable Care Act" (P.L. 111-148) and the "Health Care and Education Reconciliation Act" (P.L. 111-152) were enacted in March 2010. Together, these laws are referred to as the Affordable Care Act (ACA).

Simulation of Insurance Markets (CalSIM) model⁷ to help estimate baseline enrollment for 2014. From this projected baseline, CHBRP estimates the marginal impact of benefit mandates proposed that could be in effect after January 2014.

Bill-Specific Analysis of SB 799

SB 799 addresses “genetic testing for hereditary nonpolyposis colorectal cancer (HNPCC).” Based on reviews of the clinical literature and content expert consultation, this analysis uses the term Lynch syndrome (LS) in place of HNPCC. In 2004, the Mallorca Group, a meeting of hereditary cancer experts, determined that LS was a more appropriate term than HNPCC. Although much of the clinical literature had switched from LS to HNPCC, much of the newer clinical literature again refers to LS. Therefore, CHBRP uses LS when referring to the mismatch repair gene mutations that contribute to the increased risk for hereditary cancers, including but not limited to colorectal cancer (CRC).

LS is the most common known cause of hereditary CRC. About 3% of CRCs are caused by LS. LS is defined as a gene mutation occurring in mismatch repair genes MLH1, MSH2, MSH6, or PMS2, which means that first-degree relatives (including children and siblings) have a 50% chance of inheriting the condition from the parent who carries the gene mutation, thereby becoming carriers themselves. When adjusted for stage of disease, the CRC mortality rate associated with LS is lower than the rate for sporadic (non-hereditary) CRC. Scientists have yet to explain the LS paradox of an increased risk for cancer with lower associated mortality rates.

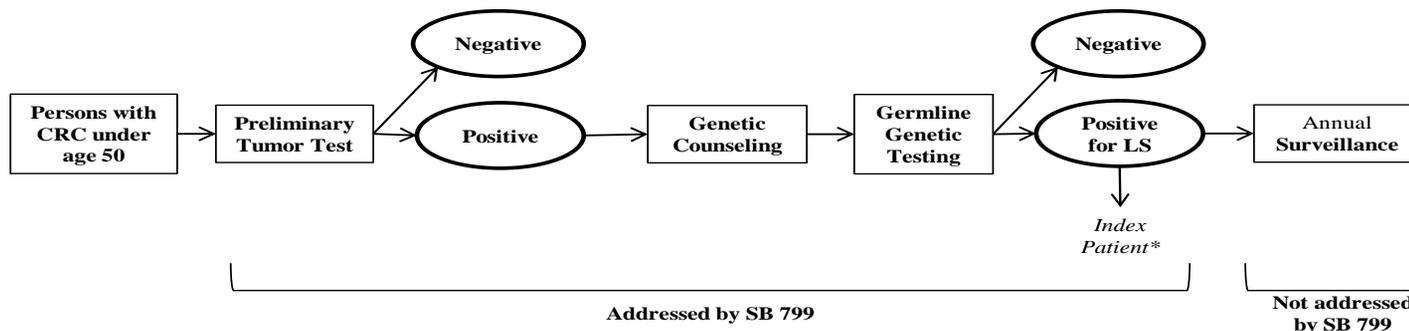
For ease of reading, this report refers to persons diagnosed with colorectal cancer as “persons with CRC” and will refer to persons who have tested positive for Lynch syndrome as “LS+.” For this report, in order to align with SB 799, an “index patient” is a person with CRC who is also LS+.

SB 799 would place requirements on DMHC-regulated plans and CDI-regulated policies. SB 799 would require plans and policies to cover genetic testing for LS for two populations: (1) enrollees younger than 50 years with CRC; and (2) any enrollee who is the child or sibling of an index patient (person with CRC and LS+). SB 799 would also require plans and policies to cover annual CRC screenings, including colonoscopies, for a third population: (3) Any LS+ enrollee who is the child or sibling of an index patient. As described in Figure 1, SB 799’s requirements address particular steps (for particular populations) in the diagnosis and management of LS, as well as CRC-related screening.

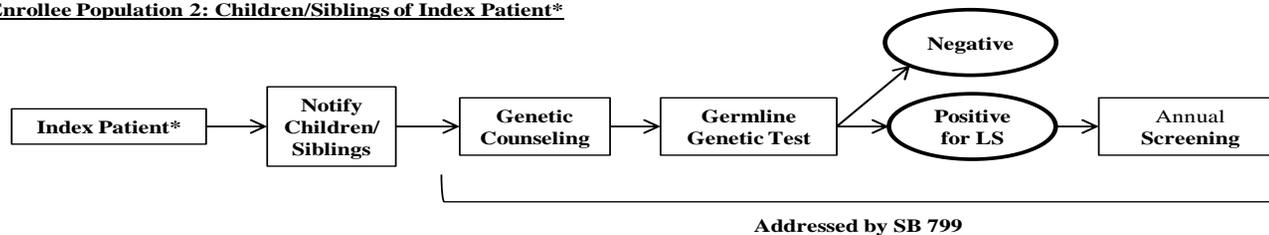
⁷ CalSIM was developed jointly and is operated by the University of California, Los Angeles, Center for Health Policy Research and the University of California, Berkeley, Center for Labor Research. The model estimates the impact of provisions in the ACA on employer decisions to offer, and individual decisions to obtain, health insurance.

Figure 1. SB 799 and the Diagnosis and Management of Lynch Syndrome

Enrollee Population 1: Persons with CRC



Enrollee Population 2: Children/Siblings of Index Patient*



Source: California Health Benefits Review Program, 2013.

Notes: (*) “Index Patient” is defined as an individual with colorectal cancer (CRC) who has Lynch syndrome (LS). The index patients in “Enrollee Population 2” are inclusive of index patients identified in Population 1 and other possible index patients (e.g., patients living out of state or with insurance not subject to SB 799).

Key: CRC=colorectal cancer; LS=Lynch syndrome.

CHBRP's reviews of the clinical literature, clinical guidelines, and content expert consultation indicated that genetic testing generally includes genetic counseling. For this reason, CHBRP has assumed that SB 799's reference to covering "genetic testing" includes genetic counseling.

Because CRC-related screening (testing for persons at risk but not diagnosed) does not include CRC-related surveillance (testing for reoccurrence of cancer in persons with CRC), CHBRP has assumed that SB 799 does not address surveillance.

Interaction with other California requirements

California law⁸ requires DMHC-regulated plans and CDI-regulated policies to cover medically accepted cancer screening tests. Although this benefit mandate requires coverage for CRC screening, at this time it is unclear whether genetic testing for LS or annual CRC screening for any enrollee who is LS+ and whose parent or sibling is both LS+ and diagnosed with CRC are considered "medically accepted cancer screening tests." Therefore, for the purposes of this analysis CHBRP has assumed that the provisions in SB 799 are not already provided for under current California law.

Medical Effectiveness

The use of genetic testing to detect LS among patients with CRC and their family members has been identified as a strategy to improve the clinical management of LS. National organizations and expert groups have developed guidelines that recommend genetic testing begin with testing the CRC patient's tumor with less expensive preliminary genetic tests, such as microsatellite instability (MSI) and immunohistochemistry (IHC) tests. CRC patients who test positive on these preliminary tumor tests move onto the more expensive germline genetic tests, such as DNA sequencing, which can confirm the diagnosis of LS. Once a CRC patient has been diagnosed with LS, their relatives could be notified and offered genetic counseling and genetic testing. Relatives who test LS+ could then be screened for CRC using colonoscopies. Screening for CRC with colonoscopy can reduce mortality and morbidity because lesions can be detected at a precancerous stage and removed before they become cancerous. The medical effectiveness review for SB 799 examined the evidence for this chain-of-event strategy by addressing the following questions:

- What is the effectiveness of genetic testing to identify LS (e.g., clinical validity)?
- What is the take-up rate⁹ of genetic counseling and genetic testing for family members of persons with LS?
- What is the effectiveness of frequent colonoscopy screening among LS+ family members on CRC morbidity and CRC-related mortality?
- What is the take-up rate for frequent colonoscopy screening among children and siblings of persons diagnosed with LS?
- What are harms associated with genetic testing and colonoscopy screening?

⁸ California Health & Safety Code (1367.665) and California Insurance Code (10123.20)

⁹ Take-up rate refers to the proportion of persons who receive a treatment among those who were eligible to receive such treatment.

Methodological Considerations

In the majority of studies reviewed on the impact of colonoscopy screening on CRC morbidity and mortality, persons were recruited from LS surveillance programs where study participants received a type of active reminder to receive ongoing colonoscopies (e.g., clinicians received reminders to contact patients when colonoscopies were due). The findings from these studies may differ from population-based estimates of LS+ persons who are not enrolled in a surveillance registry with reminder notifications.

Over the years, there have been rapid changes in knowledge about genetics and genetic testing technology. Findings from older studies on the clinical validity of the preliminary tumor test may vary from newer studies due in part to variations in tests available at that time.

The criteria used for the identification of LS has also changed over the years. Across current national guidelines and expert groups, LS refers to persons (CRC patients and family members) who have a genetic predisposition to CRC due to germline mismatch repair gene mutations; genetic tests are currently used for identifying LS. Prior to the advent of genetic testing, LS was identified by clinical personal information and a family history of cancer. Given this change in the clinical definition of LS, CHBRP Medical Effectiveness focuses on the most current literature that clinically defines LS as a germline mismatch repair gene mutation.

CHBRP terminology for grading evidence of medical effectiveness

CHBRP uses the following terms to characterize the strength of the evidence it identifies regarding the medical effectiveness of a treatment for which a bill would mandate coverage.

- Clear and convincing evidence
- Preponderance of evidence
- Ambiguous/conflicting evidence
- 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 *ambiguous/conflicting 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.

Study Findings

- The **preponderance of evidence** from systematic reviews on the clinical validity of preliminary genetic tests, MSI, IHC, and BRAF¹⁰ suggests that these preliminary tumor tests can accurately identify most persons with CRC who would benefit from germline genetic testing.
- The **preponderance of evidence** indicates that approximately half of family members of patients with CRC and LS who are offered genetic counseling obtain counseling, and the take-up rate for genetic testing following genetic testing ranged from 79% in a single retrospective study to 95% for a systematic review of six studies.
- There was **insufficient evidence** to assess the effectiveness of annual colonoscopy screening among LS+ family members on CRC morbidity among LS+ family members. The evidence from one nonrandomized controlled study indicates colorectal screening at 3-year intervals leads to a 56% reduction in CRC among LS+ persons.
- There was **insufficient evidence** to assess the effectiveness of annual colonoscopy screening on CRC-related mortality among LS+ family members. The **preponderance of evidence** indicates that colonoscopy screening at 2- to 3-year intervals reduce CRC-related mortality. Evidence from two studies that compared CRC mortality rates among persons who received frequent colonoscopies to persons who did not receive them found that screening at 2- and 3-year intervals is associated with a reduction in CRC mortality rates of 65% to 81%.
- The **preponderance of evidence** indicates that the take-up rate for colonoscopies within 2 to 3 years of diagnosis of LS is approximately 70% to 100%.
- The **preponderance of evidence** suggests that colonoscopies are associated with small increases in risk for bleeding and perforation of the colon. Findings from studies of the impact of frequent colonoscopies on mental health found no harmful emotional impact after receiving colonoscopies.
- The **preponderance of evidence** suggests that genetic counseling reduces anxiety about genetic testing and that there is no long-term difference in psychological distress between persons who are tested and found to have LS and those who are found not to have LS.

Benefit Coverage, Utilization, and Cost Impacts

SB 799 would require DMHC-regulated plans and CDI-regulated policies to cover genetic testing for LS for two populations: (1) enrollees younger than 50 years with CRC and (2) any enrollee who is the child or sibling of an index patient (a person with CRC and LS+). Utilization of genetic testing for LS in this section takes into account expected use of these tests by both populations. In this analysis, CHBRP assumes that counseling would precede testing.

SB 799 would also require plans and policies to cover annual CRC screening, including colonoscopy for a third population: (3) LS+ enrollees who are the children or siblings of an index patient. For this analysis, CHBRP has focused on utilization of colonoscopy because it is the CRC screening test recommended for LS+ persons.

¹⁰ MSI refers to the microsatellite instability test, IHC refers to the immunohistochemistry test, and BRAF refers to testing for the BRAF gene.

The benefit coverage, utilization, and cost impacts expected for SB 799 are presented in Table 1.

Coverage impacts

- Although 96.0% of enrollees in DMHC-regulated plans and CDI-regulated policies have coverage for genetic counseling and testing for LS, only 57.1% have benefit coverage compliant with SB 799. The other 42.9% of enrollees are in plans or policies without the relevant benefit coverage or with utilization management criteria not compliant with SB 799. For example, the enrollee might have to be related to two index patients. SB 799 would require counseling/testing to be covered for enrollees related to only one index patient. Postmandate, all enrollees would have SB 799-compliant benefit coverage.
- Although 100% of enrollees in DMHC-regulated plans and CDI-regulated policies have coverage for CRC screening, including colonoscopy, only 79.9% have benefit coverage compliant with SB 799. The other 20.1% of enrollees are in plans or policies with utilization management criteria not compliant with SB 799. For example, LS+ enrollees might be covered for biennial (alternate year) but not annual colonoscopy. SB 799 would require that LS+ enrollees who are the children or siblings of an index patient be covered for annual colonoscopy. Postmandate, all enrollees would have SB 799-compliant benefit coverage.

Utilization impacts

- Because reviewed utilization management criteria regarding LS-related genetic counseling testing for enrollees younger than 50 years with CRC is compliant with SB 799, CHBRP estimates no postmandate increase in genetic counseling or testing for this population.
- Because, in order to become compliant with SB 799, some reviewed utilization management criteria would have to change in regard to LS-related genetic counseling and testing for enrollees who are the children or siblings of an index patient, CHBRP expects a postmandate increase in utilization among this population. Reviewed examples of noncompliant utilization management criteria are broad; premandate, CHBRP estimates that four of five of the enrollees described by SB 799 would have been covered for LS-related genetic counseling and testing. Postmandate, CHBRP estimates that an additional 420 sessions of genetic counseling and an additional 692 genetic tests among adult enrollees would be covered. Because sequential enrollee expenses have a greater effect on the last step of a multi-step process, decreased enrollee expenses have a greater effect on utilization of the last step (testing) than on the first step (counseling).
- Because, in order to become compliant with SB 799, some reviewed utilization management criteria would have to change in regard to annual colonoscopy for LS+ enrollees who are the children or siblings of an index patient, CHBRP expects a postmandate increase in utilization among this population. Reviewed examples of noncompliant utilization management criteria are broad, covering biennial (alternate year) colonoscopy; premandate, CHBRP estimates that four of five of the enrollees described by SB 799 would have been covered for colonoscopy. Postmandate, CHBRP estimates that an additional 75 colonoscopies among adult enrollees would be covered. In later years, the number of additional screening colonoscopies may increase further,

since SB 799 would mandate coverage for annual screening, and some plans previously only covered biennial (alternate year) colonoscopy screening for this population.

Cost impacts

- SB 799 would increase total net annual expenditures by \$637,000, or 0.0004%, for the insured population. This is due to a \$774,000 total increase in health insurance premiums and a \$95,000 increase in enrollee out-of-pocket expenses for covered benefits (copayments, etc), partially offset by a reduction in enrollee expenses for noncovered benefits (\$232,000).
- Increases in insurance premiums if SB 799 were enacted have some variation by market segment. The increases range from 0.0000% for California Public Employees' Retirement System Health Maintenance Organizations (CalPERS HMOs) to 0.0034% for the plans enrolling beneficiaries of the former Healthy Families Program.

Public Health Impacts

CHBRP estimates that, in the year following enactment of SB 799, about 700 additional enrollees would use genetic testing for LS and about 75 additional enrollees would undergo a screening colonoscopy.

- *Overall public health impact:* CHBRP projects that SB 799 would increase the use of genetic counseling and testing for LS and annual colonoscopies; however, CHBRP projects no measurable public health impact (at the population level) in the first year, postmandate, due to the small number of additional enrollees who would use mandate-relevant services.
 - At the individual-level, SB 799 would likely yield health and quality-of-life improvements for the additional enrollees who would use mandate-relevant services. Genetic testing for relatives of LS+ persons has many benefits, including reliably differentiating between family members who are LS mutation carriers and LS noncarriers, who would not require frequent colorectal screening. Additionally, for LS+ persons, screening colonoscopy at recommended intervals can be expected to reduce mortality and morbidity over time (because lesions can be detected at a precancerous stage and removed before they become cancerous).
- *Premature death:* Although mortality may be decreased for LS+ enrollees through frequent colonoscopy screening, CHBRP is unable to quantify a reduction in mortality due to a lack of relevant literature. However, CHBRP concludes that increased screening colonoscopy among these enrollees would likely contribute to a reduction in CRC deaths in California beyond the first year, postmandate.
- *Potential harms:* The risk of psychological harm from genetic testing or physical harms from colonoscopy are small compared to the health advantages conferred through early identification of LS status and subsequent CRC screening to identify precancerous lesions or early-stage cancer.

- *Financial burden:* CHBRP estimates that SB 799 would reduce the net financial burden (enrollee expenses for uncovered services) by \$137,000 in the first year, postmandate, for the enrollees who use genetic testing and enrollees who use colonoscopy.
- *Gender disparities:* It is unknown whether there are gender disparities in the prevalence of LS-related CRC. CHBRP found no evidence indicating differential use of genetic counseling or testing for LS by males or females, or difference in adherence to screening colonoscopy by gender among LS carriers. CHBRP estimates that, despite SB 799 increasing use of these services and possible gender disparities in LS prevalence, the bill would have no public health impact in the first year postmandate on gender disparities due to no known gender differences in uptake of services and the small additional utilization that would result from SB 799.
- *Racial/ethnic disparities:* There are racial/ethnic disparities in the prevalence of CRC, but it is unknown whether the disparities extend to the LS-related CRCs in California. Although CHBRP estimates a small increase in uptake of genetic counseling and testing and screening colonoscopy for LS+ relatives, CHBRP is unable to estimate how these changes in the utilization might vary by race or ethnicity. In addition, any potential statewide racial/ethnic disparities in LS-related CRC morbidity and mortality are unlikely to be measurably affected, due to the small increase in utilization that would result from SB 799.
- *Economic loss:* Increased utilization of screening colonoscopy related to SB 799 among LS+ enrollees is unlikely to measurably alter the overall societal economic loss due to lost wages and lost productivity attributable to CRC.
- *Long-term impacts:* The preponderance of evidence shows that screening for LS and screening colonoscopies for LS+ persons at recommended levels are considered to be cost-effective over the long-term, resulting in increases in life-years and commonly acceptable quality-adjusted-life-year cost-effectiveness ratios. SB 799 would mandate coverage for annual colonoscopies for an increasing number of LS+ enrollees, thus reducing their risk for cancer, premature death, and associated lost productivity, but at an increased cost.

Interaction With the Federal Affordable Care Act

Below is a discussion of how SB 799 may interact with the ACA's requirement for certain health insurance to cover "essential health benefits"¹¹ (EHBs), as well as other ACA requirements that may interact with this proposed benefit mandate.

- Although medically accepted cancer screenings are part of EHBs, it is unclear whether genetic testing for LS or annual CRC screening for any enrollee who is LS+ and whose parent or sibling is both LS+ and diagnosed with CRC are considered "medically accepted cancer screening tests." Therefore, it is unclear whether SB 799 would exceed EHBs.

¹¹ Resources on EHBs and other ACA impacts are available on the CHBRP website: www.chbrp.org/other_publications/index.php.

- Although colonoscopy for average-risk persons is required to be covered without cost-sharing, neither coverage for genetic testing for LS nor annual CRC screening for any enrollee who is LS+ (and so at higher risk for CRC) and whose parent or sibling is both LS+ and diagnosed with CRC is required by the ACA's preventive services benefit mandate. Therefore, SB 799 appears to address screening not addressed by the ACA's preventive services benefit mandate.

Table 1. SB 799 Impacts on Benefit Coverage, Utilization, and Cost, 2014

	Before Mandate	After Mandate	Increase/ Decrease	Change After Mandate
Benefit coverage				
Total enrollees with health insurance subject to state-level benefit mandates (a)	25,899,000	25,899,000	0	0%
Total enrollees with health insurance subject to SB 799	25,899,000	25,899,000	0	0%
Percentage of enrollees with coverage for the mandated benefit				
Coverage for genetic testing for LS	96.0%	100.0%	4.0%	4.1%
Coverage for genetic testing for LS, compliant with SB 799	57.1%	100.0%	42.9%	75.1%
Coverage for CRC screening	100.0%	100.0%	0%	0%
Coverage for CRC screening, compliant with SB 799	79.9%	100.0%	20.1%	25.2%
Number of enrollees with coverage for the mandated benefit				
Coverage for genetic testing for LS	24,874,000	25,899,000	1,025,000	4.1%
Coverage for genetic testing for LS, compliant with SB 799	14,788,000	25,899,000	11,111,000	75.1%
Coverage for CRC screening	25,899,000	25,899,000	0	0%
Coverage for CRC screening, compliant with SB 799	20,682,000	25,899,000	5,217,000	25.2%
Utilization and cost				
Annual number of procedures				
Genetic counseling due to CRC diagnosis (b)	34	34	0	0%
Germline testing due to CRC diagnosis	34	34	0	0%
Genetic counseling due to relative w/CRC and LS+ (b)	6,627	7,047	420	6.3%
Germline testing due to relative w/CRC and LS+ (c)	6,003	6,695	692	11.5%
Colonoscopy due to LS+ (no CRC) (d)	2,025	2,100	75	3.7%
Average charge per procedure				
Genetic counseling due to CRC diagnosis (b)	\$156.77	\$156.77	\$0.00	0%
Germline testing due to CRC diagnosis	\$549.48	\$549.48	\$0.00	0%
Genetic counseling due to relative w/CRC and LS+ (b)	\$156.77	\$156.77	\$0.00	0%
Germline testing due to relative w/CRC and LS+	\$549.48	\$549.48	\$0.00	0%
Colonoscopy due to LS+ (no CRC) (d)	\$1,386.01	\$1,386.01	\$0.00	0%
Expenditures				
Premium expenditures by private employers for group insurance	\$78,385,161,000	\$78,385,496,000	\$335,000	0.0004%
Premium expenditures for individually purchased insurance	\$13,639,719,000	\$13,639,825,000	\$106,000	0.0008%

	Before Mandate	After Mandate	Increase/ Decrease	Change After Mandate
Premium expenditures by persons with group insurance, CalPERS HMOs, and Covered California (e)	\$21,272,946,000	\$21,273,043,000	\$97,000	0.0005%
CalPERS HMO employer expenditures (f)	\$4,016,233,000	\$4,016,233,000	\$0	0.0000%
Medi-Cal Managed Care Plan expenditures	\$12,480,492,000	\$12,480,705,000	\$213,000	0.0017%
Healthy Families Plan expenditures	\$667,300,000	\$667,323,000	\$23,000	0.0034%
Enrollee out-of-pocket expenses for covered benefits (deductibles, copayments, etc.)	\$14,462,198,000	\$14,462,293,000	\$95,000	0.0007%
Enrollee expenses for noncovered benefits (g)	\$232,000	\$0	-\$232,000	-100%
Total expenditures	\$144,924,281,000	\$144,924,918,000	\$637,000	0.0004%

Source: California Health Benefits Review Program, 2013.

Notes: (a) This population includes persons with privately funded (including Covered California, the state's health insurance exchange) and publicly funded (e.g., CalPERS HMOs, Medi-Cal Managed Care Plans) health insurance products regulated by DMHC or CDI. Population includes enrollees aged 0 to 64 years and enrollees 65 years or older covered by employer-sponsored health insurance.

(b) Utilization for genetic counseling is not explicitly included in SB 799, but is a guideline-recommended precursor to obtaining genetic testing. CHBRP assumes that 66.8% of enrollees have SB 799-compliant benefit coverage for genetic counseling, the same rate as for genetic testing. Utilization presented is only for persons younger than 50 years with CRC or for persons with a parent or sibling with CRC who is LS+.

(c) Sequential enrollee expenses have a greater effect on the last step of a multi-step process and so decreased enrollee expenses have a greater effect on utilization of the last step (testing) than on the first step (counseling).

(d) CHBRP estimates utilization of colonoscopy only, as that is the guideline-recommended procedure for CRC screening among nonsymptomatic persons identified as LS+. Utilization for CRC screenings only includes nonsymptomatic for CRC but LS+ children or siblings of a person who has been both diagnosed with LS and has CRC, as per the population specified in SB 799.

(e) Premium expenditures by enrollees include employee contributions to employer-sponsored health insurance, health insurance purchased through Covered California, and enrollee contributions for Medi-Cal Managed Care.

(f) Of the increase in CalPERS employer expenditures, about 58%, or \$50,000, would be state expenditures for CalPERS members who are state employees, state retirees, or their dependents. This percentage reflects the share of enrollees in CalPERS HMOs as of September 30, 2012. CHBRP assumes the same ratio in 2014.

(g) Includes only those expenses that are paid directly by enrollees or other sources to providers for services related to the mandated benefit that are not currently covered by insurance. This only includes those expenses that would be newly covered, postmandate. Other components of expenditures in this table include all health care services covered by insurance.

Key: CalPERS HMOs=California Public Employees' Retirement System Health Maintenance Organizations; CDI=California Department of Insurance; CRC=colorectal cancer; DMHC=Department of Managed Health Care; LS=Lynch syndrome.

INTRODUCTION

The California Senate Committee on Health requested on April 9, 2013, that the California Health Benefits Review Program (CHBRP) conduct an evidence-based assessment of the medical, financial, and public health impacts of Senate Bill (SB) 799: Colorectal Cancer: Genetic Testing and Screening. In response to this request, CHBRP undertook this analysis pursuant to the provisions of the program's authorizing statute.¹²

In 2014, CHBRP estimates that approximately 25.9 million Californians (67%) will have health insurance that may be subject to a health benefit mandate law passed at the state level.¹³ Of the rest of the state's population, a portion will be uninsured (and so will have no health insurance subject to any benefit mandate), and another portion will have health insurance subject to other state laws or only to federal laws.

Uniquely, California has a bifurcated system of regulation for health insurance subject to state benefit mandates. The California Department of Managed Health Care (DMHC)¹⁴ regulates health care service plans, which offer benefit coverage to their enrollees through health plan contracts. The California Department of Insurance (CDI) regulates health insurers,¹⁵ which offer benefit coverage to their enrollees through health insurance policies.

All DMHC-regulated plans and CDI-regulated policies would be subject to SB 799. Therefore, the mandate would affect the health insurance of approximately 25.9 million enrollees (67% of all Californians).

Developing Estimates for 2014 and the Effects of the Affordable Care Act

The Affordable Care Act (ACA)¹⁶ is expected to dramatically affect health insurance and its regulatory environment in California, with many changes becoming effective in 2014. Beginning in 2014, an expansion of the Medicaid program to cover people up to 133% of the federal poverty level (FPL)¹⁷ and the availability of subsidized and unsubsidized health insurance coverage purchased through newly established state health insurance exchanges are expected to significantly increase the number of people with health insurance in the United States.

¹² Available at: www.chbrp.org/docs/authorizing_statute.pdf.

¹³ CHBRP's estimates are available at: www.chbrp.org/other_publications/index.php.

¹⁴ The California Department of Managed Care (DMHC) was established in 2000 to enforce the Knox-Keene Health Care Service Plan of 1975; see Health and Safety Code (H&SC) Section 1340.

¹⁵ The California Department of Insurance (CDI) licenses "disability insurers." Disability insurers may offer forms of insurance that are not health insurance. This report considers only the impact of the benefit mandate on health insurance policies, as defined in Insurance Code (IC) Section 106(b) or subdivision (a) of Section 10198.6.

¹⁶ The federal "Patient Protection and Affordable Care Act" (P.L. 111-148) and the "Health Care and Education Reconciliation Act" (P.L. 111-152) were enacted in March 2010. Together, these laws are referred to as the Affordable Care Act (ACA).

¹⁷ The Medicaid expansion, which California will pursue, is to 133% of the federal poverty level (FPL)—138% with a 5% income disregard.

State exchanges will sell health insurance in the small-group and individual market¹⁸ through qualified health plans (QHPs), which will be certified by and sold in a state's exchange. QHPs sold through California's state exchange, Covered California,¹⁹ will be DMHC-regulated plans or CDI-regulated policies, and as such will be subject to California state benefit mandates.

It is important to note that CHBRP's analysis of proposed benefit mandate bills typically address the marginal effects of the proposed bills—specifically, how the proposed mandate would impact benefit coverage, utilization, costs, and public health, holding all other factors constant. CHBRP's estimates of these marginal effects are presented in this report. Because expanded enrollment will not occur until January 2014, CHBRP relies on projections from the California Simulation of Insurance Markets (CalSIM) model²⁰ to help estimate baseline enrollment for 2014. From this projected baseline, CHBRP estimates the marginal impact of proposed benefit mandates that could be in effect after January 2014. CHBRP's methods for estimating baseline 2014 enrollment from CalSIM projections are provided in further detail in Appendix D.

Bill-Specific Analysis of SB 799

The full text of SB 799 can be found in Appendix A.

SB 799 addresses “genetic testing for hereditary nonpolyposis colorectal cancer (HNPCC).” Based on reviews of the clinical literature and content expert consultation, this analysis uses the term Lynch syndrome (LS) in place of HNPCC. In 2004, the Mallorca Group, a meeting of hereditary cancer experts, determined that LS was a more appropriate term than HNPCC. Although much of the clinical literature had switched from LS to HNPCC, much of the newer clinical literature again refers to LS. Therefore, CHBRP uses LS when referring to the mismatch repair gene mutations that contribute to the increased risk for hereditary cancers, including but not limited to colorectal cancer (CRC). (See *Background* section for further explanation).

As further described in the *Background* section, LS is the most common known cause of hereditary CRC. About 3% of CRCs are caused by LS. LS is defined as a gene mutation occurring in mismatch repair genes MLH1, MSH2, MSH6, or PMS2. First-degree relatives (including children and siblings) have a 50% chance of inheriting the condition from the parent who carries the gene mutation, thereby becoming carriers themselves. When adjusted for stage of disease, the CRC mortality rate associated with LS is lower than the rate for sporadic (non-hereditary) CRC. Scientists have yet to explain the LS paradox of an increased risk for cancer with lower associated mortality rates.

¹⁸ Effective 2017, states may allow large-group purchasing through the exchange, which may make some large-group plans and policies subject to EHB requirements [ACA Section 1312(f)(2)(B)].

¹⁹ The California Health Benefits Exchange Authorizing Statute is available here:

<http://www.healthexchange.ca.gov/Documents/California%20Codes%20Governing%20the%20Health%20Benefit%20Exchange.pdf>.

²⁰ CalSIM was developed jointly and is operated by the University of California, Los Angeles, Center for Health Policy Research and the University of California, Berkeley, Center for Labor Research. The model estimates the impact of provisions in the ACA on employer decisions to offer, and individual decisions to obtain, health insurance.

For ease of reading, this report refers to persons diagnosed with colorectal cancer as “with CRC” and will refer to persons who have tested positive for Lynch syndrome as “LS+.” For this report, in order to align with SB 799, an “index patient” is a person with CRC who is also LS+.

SB 799 would place requirements on DMHC-regulated plans and CDI-regulated policies. SB 799 would require plans and policies to cover genetic testing for LS for two populations: (1) enrollees younger than 50 years with CRC; and (2) any enrollee who is the child or sibling of an index patient (person with CRC and LS+). SB 799 would also require plans and policies to cover annual CRC screenings, including colonoscopies, for a third population: (3) Any LS+ enrollee who is the child or sibling of an index patient.

As described in Figure 1 (in the *Executive Summary*), SB 799’s requirements address particular steps (for particular populations) in the diagnosis and management of LS. CHBRP’s reviews of the clinical literature, clinical guidelines, and content expert consultation indicated that genetic testing generally includes genetic counseling. For this reason, CHBRP has assumed that SB 799’s reference to covering “genetic testing” includes of genetic counseling. Because CRC-related screening (testing for persons at risk but not diagnosed) does not include CRC-related surveillance (testing for reoccurrence of cancer in persons with CRC), CHBRP has assumed that SB 799 does not address surveillance.

As further discussed in the *Medical Effectiveness* section, colonoscopy, as opposed to other forms of CRC screening, is the recommended CRC screening test for persons who are LS+. For this reason, this analysis has focused on colonoscopy.

Interaction with Other California Requirements

California law²¹ requires DMHC-regulated plans and CDI-regulated policies to cover medically accepted cancer screening tests. Although this benefit mandate requires coverage for CRC screening, at this time it is unclear whether genetic testing for LS or annual CRC screening for any enrollee who is LS+ and whose parent or sibling is both LS+ and diagnosed with CRC are considered “medically accepted cancer screening tests.” Therefore, for the purposes of this analysis CHBRP has assumed that the provisions in SB 799 are not already provided for under current California law.

Requirements in Other States

Although the majority of other states require coverage for CRC screening (BCBSA, 2012), CHBRP is unaware of another state requiring coverage for genetic testing for LS or requiring annual CRC screening for any enrollee who is LS+ and whose parent or sibling is both LS+ and diagnosed with CRC (as would be required by SB 799).

²¹ California Health & Safety Code (1367.665) and California Insurance Code (10123.20)

Interaction With the Affordable Care Act

A number of ACA provisions have the potential to or do interact with state benefit mandates. Below is an analysis of how this proposed benefit mandate may interact with requirements in the ACA, including the requirement for certain health insurance to cover “essential health benefits” (EHBs).²²

Essential Health Benefits

Effective 2014, the ACA requires nongrandfathered small-group and individual market health insurance—including but not limited to QHPs that will be sold in Covered California—to cover 10 specified categories of EHBs.²³ 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.²⁴ California has selected the Kaiser Foundation Health Plan Small Group Health Maintenance Organization (HMO) 30 plan as its benchmark plan.²⁵

The ACA allows a state to “require that a qualified health plan offered in [an exchange] offer benefits in addition to the essential health benefits.”²⁶ If the state does so, the state must make payments to defray the cost of those additionally mandated benefits, either by paying the purchaser directly or by paying the QHP. However, as laid out in the Final Rule on EHBs HHS released in February 2013,²⁷ state benefit mandates enacted on or before December 31, 2011, would be included in the a state’s EHBs for 2014 and 2015 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. State benefit mandates that could exceed EHBs would “be specific to the care, treatment, and services that a state requires issuers to offer to its enrollees,” whereas “state rules related to provider types, cost-sharing, or reimbursement methods” would not meet the definition of state benefit mandates that could exceed EHBs. A

²² Resources on EHBs and other ACA impacts are available on the CHBRP website:

www.chbrp.org/other_publications/index.php.

²³ The 10 specified categories of essential health benefits (EHBs) are ambulatory patient services; emergency services; hospitalization; maternity and newborn care; mental health and substance use disorder services, including behavioral health treatment; prescription drugs; rehabilitative and habilitative services and devices; laboratory services; preventive and wellness services and chronic disease management; and pediatric services, including oral and vision care. [ACA Section 1302(b)].

²⁴ CCIIO, Essential Health Benefits Bulletin. Available at:

http://cciio.cms.gov/resources/files/Files2/12162011/essential_health_benefits_bulletin.pdf. Accessed December 16, 2011.

²⁵ H&SC Section 1367.005; IC Section 10112.27.

²⁶ ACA Section 1311(d)(3).

²⁷ Department of Health and Human Services. 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. 12843. Available at: www.gpo.gov/fdsys/pkg/FR-2013-02-25/pdf/2013-04084.pdf.

state's exchange would be responsible for determining when a state benefit mandate exceeds EHBs, and QHP issuers would be responsible for calculating the cost that must be defrayed.²⁸

For a state benefit mandate to exceed the definition of EHBs in California, triggering the requirement that the state defray the costs, the following must be true:

- The state benefit mandate is not covered in the Kaiser Small Group HMO 30 plan that defines the EHB benchmark package in California in 2014 and 2015;
- The state benefit mandate is not covered under basic health care services (BHCS), as required by the Knox-Keene Health Care Service Plan Act of 1975; and
- The state benefit mandate meets the definition of a benefit mandate that could exceed EHBs as established by federal regulations on EHBs (e.g., it is specific to care, treatment, and/or services).²⁹

SB 799 and essential health benefits

SB 799 would require DMHC-regulated plans and CDI-regulated policies to provide benefit coverage for genetic counseling and testing for LS and CRC screening, including colonoscopy. As more fully described in the *Benefit Coverage, Cost, and Utilization* section, SB 799 would prohibit some forms of utilization management but allow others.

Although the Kaiser Small Group HMO 30 plan provides coverage for genetic counseling and testing for LS, as well as CRC screening (including colonoscopy), the evidence of coverage (EOC) document does not clarify that utilization management criteria comply with what SB 799 would require.

Although BHCS requires coverage for “medically necessary” health care services, it is unclear whether BHCS requires coverage for genetic counseling and testing for LS and it is not clear that BHCS would prohibit utilization management criteria related to LS testing or CRC testing in the same ways that SB 799 would.

Although the terms of benefit coverage that SB 799 would require relate to treatment and services, and therefore may meet the federal definition of a state benefit mandate that could exceed EHBs,³⁰ the lack of clarity regarding the Kaiser Small Group HMO 30 plan and BHCS makes it unclear whether SB 799 would exceed EHBs in California.

For the reasons outlined above, it is unclear whether SB 799 would exceed EHBs in California.

Cost of exceeding EHBs. The state is required to defray the additional cost incurred by enrollees in QHPs³¹ for any state benefit mandate that exceeds EHBs. The *Benefit Coverage, Utilization,*

²⁸ Essential Health Benefits. Final Rule.

²⁹ Essential Health Benefits. Final Rule. 12843.

³⁰ Essential Health Benefits. Final Rule. 12843.

³¹ In California, QHPs are nongrandfathered small-group and individual market DMHC-regulated plans and CDI-regulated policies sold in Covered California, the state's exchange.

and Cost Impacts section of this report discusses the impact of SB 799 on the per member per month (PMPM) premiums in 2014 in the small-group and individual markets, which are the market segments affected by the EHB coverage requirement and for which the state would have to defray costs for enrollees in QHPs, should SB 799 exceed EHBs.

This report presents an evidence-based analysis to provide decision-makers with a more comprehensive understanding of the impacts of SB 799—not only potential costs, such as the cost to defray should SB 799 exceed EHBs, but also reviews of the medical effectiveness evidence and estimates of the proposed mandate’s public health impacts for Californians.

Preventive Services

Some benefit mandates could interact with the federal preventive services benefit mandate, but it appears that SB 799 does not.

The ACA requires that nongrandfathered group and individual health insurance plans and policies 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:³²

- The United States Preventive Services Task Force (USPSTF) A and B recommendations.³³
- The Health Resources and Services Administration (HRSA)-supported health plan coverage guidelines for women’s preventive services.³⁴
- The HRSA-supported comprehensive guidelines for infants, children, and adolescents, which include:
 - The Bright Futures Recommendations for Pediatric Preventive Health Care,³⁵ and
 - The recommendations of the Secretary’s Advisory Committee on Heritable Disorders in Newborns and Children.³⁶
- The Advisory Committee on Immunization Practices (ACIP) recommendations that have been adopted by the Director of the Centers for Disease Control and Prevention (CDC).³⁷

The USPSTF CRC screening recommendation addresses only those at average risk for CRC (screening every 10 years); it does not address the LS+ population addressed in SB 799, who are

³² A resources on this ACA requirement is available on the CHBRP website: www.chbrp.org/other_publications/index.php.

³³ USPSTF created a concise document summarizing its A and B recommendations (last updated in August 2010), available at: www.uspreventiveservicestaskforce.org/uspstf/uspabrecs.htm. However, for this resource CHBRP consulted USPSTF’s A-Z Topic Guide because up-to-date summaries of recommendations are available through links on that webpage: www.uspreventiveservicestaskforce.org/uspsttopics.htm.

³⁴ Available at: www.healthcare.gov/law/resources/regulations/womensprevention.html.

³⁵ Available at: brightfutures.aap.org/pdfs/AAP%20Bright%20Futures%20Periodicity%20Sched%20101107.pdf.

³⁶ Available at: www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/recommendedpanel/uniformscreeningpanel.pdf

³⁷ “Recommended immunization schedules for persons aged 0 through 6—United States, 2012” available at: www.cdc.gov/vaccines/schedules/downloads/child/0-6yrs-schedule-pr.pdf.

recommended to have earlier and more frequent screening (every 1 to 2 years). Therefore, SB 799 would not interact with the federal preventive services mandate.

BACKGROUND ON LYNCH SYNDROME AND CANCER

This *Background* section provides context for understanding the scope and impact of LS (referred to as HNPCC in SB 799) and LS-related colorectal cancer on the California population; therefore, the following population statistics include enrollees with insurance subject to SB 799 as well as the uninsured or persons who have health insurance not subject to SB 799, unless otherwise stated.

What Is Lynch Syndrome?

The terminology for LS, the most common known cause of hereditary CRC, has shifted over time. Vasen et al. (2007) describe the etiology of the contemporary clinical definition of the mismatch repair gene mutations for LS:

“Various names for Lynch syndrome have been used in the past century. A workshop in Amsterdam in 1989 agreed upon the name “HNPCC”, because at that time the syndrome was unknown to most doctors. This name clarified that the syndrome described an inherited form of CRC. The appropriateness of the name was discussed again at an international meeting in Bethesda in 2004...[where] most participants considered the term HNPCC to be inappropriate, since the syndrome is also associated with many other tumours. It was [agreed] that the name “Lynch syndrome” should be reintroduced, and that this name should be reserved for families with strong evidence of MMR deficiency—for example, by the presence of an MMR defect or by the presence of MSI in tumours.”

This definition was agreed upon through expert opinion at the Mallorca meeting in 2004. Since that time, much of the research literature uses the terms HNPCC and Lynch syndrome synonymously. **However, CHBRP uses Lynch syndrome in place of HNPCC based on the rationale quoted above, more recent literature, and because SB 799 addresses asymptomatic relatives of index patients.**

Until the advent of genetic testing for LS (mid 1990s), risk assessment for possible syndrome carriers was based exclusively on family cancer history (Colas et al., 2012). Two tools, the Bethesda and the Amsterdam criteria, were designed to identify family members at risk for LS. These criteria have been adapted over the years to improve their predictive ability (sensitivity and specificity), but more recently have been superseded by genetic testing for the gene mutation (Grover and Syngal, 2010). Current guidelines recommend universal testing for LS for persons diagnosed with CRC (EGAPP, 2009; NCCN, 2012; Weissman et al., 2012). See the *Medical Effectiveness* section for further detail about types of testing and guidelines.

LS, as currently defined, accounts for about 3% of all CRCs diagnosed, and occurs more commonly in persons younger than 50 years (Burt, 2012; Stoffel et al., 2010). Specifically, it is an autosomal dominant gene mutation in the following mismatch repair (MMR) genes: MLH1, MSH2, MSH6, and PMS2 (Jang and Chung, 2010). This means that offspring and siblings have a 50% chance of inheriting the condition from a parent who carries the gene mutation(s), thereby

becoming carriers themselves. In addition to CRC, LS also increases the risk of cancer of the endometrium and ovary (Table 3) and, more rarely, cancers of the stomach, urinary tract, biliary tract, pancreas, small bowel, brain, and skin (Colas et al., 2012).

LS-related CRC typically exhibits few to no polyps or lesions as compared with other hereditary or sporadic (cancer occurring in persons with no family history) colon cancers. Approximately 70% of LS-related CRCs are located in the right (proximal) colon making colonoscopy the preferred screening method for LS+ persons (Grover et al., 2010; Jang and Chung, 2010). LS-related CRCs usually have an early onset of disease (younger than 50 years) that presents as a benign tumor (adenoma); it progresses to cancer (carcinoma) over 2 to 3 years rather than 8 to 10 years, which is common for sporadic cancer.

Prevalence of Lynch Syndrome in California

The literature presents a wide variation in estimates of the prevalence of LS+ persons in the *general population*, ranging from 1:440 (Chen et al., 2006) to 1:500 (Burt, 2012) to 1:660-1:2,000 (de la Chapelle, 2005) and 1:3,139 (Dunlop et al., 2000). Researchers acknowledge serious methodological limitations to these general population estimates due to the sampling process used to find the pool of LS carriers. Known as ascertainment bias, the reliance on index patients (LS+ person with CRC) with known family cancer histories as the starting point for genetic testing may distort the estimates of the actual cancer risk since the selection criteria favors an overrepresentation of higher risk families than the general population (Stoffel et al., 2009).

Estimates of the prevalence of LS in the *population diagnosed with CRC* may be more reliable and typically attribute 3% of all CRCs to LS (with a range of 2% to 7%) (Colas et al., 2012; EGAPP, 2009; Hampel et al., 2008; Ladabaum et al., 2011). Others estimate that 0.8% to 2.0% of endometrial cancers are attributable to LS (Chadwick et al., 2001; Kowalski et al., 1997; Yurgelun et al., 2012).

Burden of Lynch Syndrome and Lynch-Related Cancer in California

Colorectal Cancer

To understand the burden of LS-related CRC in California, baseline data on the incidence of CRC in the general population must be presented first. Of the approximate 144,000 cancers diagnosed in California in 2012, about 14,000 cases among all ages are CRC, making it the third most common cancer among men and women (CDPH, 2009). The California Department of Public Health (CDPH) reports that, in the general population, men have a greater incidence of CRC than women. Additionally, African Americans have the highest risk for CRC, followed by non-Hispanic whites and Asians. Hispanics have the lowest risk (Table 2). However, it is unknown if these rates are relevant to those carriers of LS. Almost all racial/ethnic categories have experienced a drop in CRC incidence and mortality over the last 10 years (CDPH, 2013).

Table 2 includes Californians aged 0 to 64 years, regardless of insurance status, diagnosed with CRC in 2009. CHBRP estimates that fewer than 200 persons with CRC would be LS carriers. California-specific data from the Centers for Disease Control and Prevention indicate that the CRC incidence for this same population over a 10-year period (1999-2009) is about 58,000 Californians with CRC and, of those about 1,700 are estimated to be LS carriers (USDHHS, 2011).

Table 2. Incidence of Colorectal Cancer for Californians Aged 0 to 64 Years, 2009

Demographic	Number	Age-adjusted rate of CRC/100,000 - 95% CI -	Estimated Number with LS (a)
Total CRC (b)	6,089	17.0 (16.6-17.5)	183
Gender			
Female	2,709	15.0 (14.4-15.6)	81
Male	3,380	19.2 (18.6-19.9)	101
Age			
15-19 yrs	-	-	-
20-24 yrs	24	-	1
25-29 yrs	48	-	1
30-34 yrs	100	-	3
35-39 yrs	181	-	5
40-44 yrs	414	-	12
45-49 yrs	761	-	23
50-54 yrs	1,419	-	43
55-59 yrs	1,460	-	44
60-64 yrs	1,675	-	50
Race/Ethnicity(a)			
American Indian/Alaska Native	23	10.9 (6.8-16.1)	1
Asian or Pacific Islander	895	17.2 (16.1-18.5)	27
Black or African American	567	24.9 (22.9-27.1)	17
White	3,175	17.1 (16.5-17.9)	95
Other/Unknown	82	-	2
Hispanic	1,347	14.6 (13.8-15.4)	40

Source: California Health Benefits Review Program, 2013 (based on CDC Online WONDER database).

Note: (a) Estimated number with LS assumes 3% of CRCs are attributable to LS, per literature. Also assumes this rate across all races. (b) Total case counts among the demographic categories may differ slightly, due to rounding.

Key: CI=confidence interval; CRC=colorectal cancer; LS=Lynch syndrome.

Lynch syndrome and Lifetime Risk³⁸ for Cancers

Estimates for lifetime risk of CRC for LS+ persons ranges from 25% to 80% with the literature most commonly citing a range of 60% to 80% lifetime risk (Asgeirsson et al., 2011; Grover et al., 2010; Watkins et al., 2011). However, some analysts argue that ascertainment bias may inflate these higher estimates and that the rates may be closer to 45% for men and 35% for women (Palomaki et al., 2009; Schneider et al., 2010).

³⁸ Lifetime risk is defined as the probability of developing (or dying from) a condition (cancer, in this case) during the course of a lifetime.

Table 3 presents the ranges of estimated lifetime risks of developing certain cancers for those who are LS+ as compared to the general population. Of the LS-related cancers, endometrial cancer presents the second greatest risk to female LS carriers—about equal to that of CRC (Yurgelun et al., 2012).

Table 3. Range of Estimated Lifetime Risk of Cancers for Persons with Lynch Syndrome Compared to the General Population

Cancer Type	LS Carriers (a)		General Population	
	Lifetime Risk	Median Age at Diagnosis	Lifetime Risk (a)	Median Age at Diagnosis (b)
CRC				
Females (c)	35-52%	61	5%	72
Males (c)	45-69%	61	5.5%	68
Endometrial	25-71%	46-62	2%	61
Ovarian	3-14%	40-47	1%	63
Gastric	2-19%	47-56	<1%	70
Small Bowel	1-7%	39-53	<1%	66
Pancreatic/biliary	2-18%	43-66	1%	71
Urinary tract	1-12%	49-60	Rare	69
Brain	1-4%	33-52	<1%	57

Source: California Health Benefits Review Program, 2013.

Note: (a) Estimates for Lynch syndrome carriers from a review by Jang and Chung, 2010. (b) from NCI SEER 2009. (c) from ACS 2008.

Key: CRC=colorectal cancer; LS=Lynch syndrome.

Lynch syndrome-Associated Mortality

Drescher et al. described survival among LS patients with CRC as a “paradox”—patients with LS and CRC have characteristics that are traditionally associated with poor prognosis (early onset, increased risk of developing extracolonic cancers, poorly differentiated, etc.), yet these patients often have enhanced survival compared to those who are diagnosed with sporadic CRC when adjusted for stage at diagnosis (Drescher et al., 2010; Grover et al., 2010; Järvinen et al., 2009). Stigliano et al. (2008) found that among LS patients, the 5-year cumulative disease survival rate following CRC was 94% as compared with 75% in sporadic CRC. Many hypotheses have been put forth to describe these survival advantages, including strong lymphocytic infiltration, fewer distant metastases at diagnosis, and improved immune response (Lynch et al., 2008; Lynch and Lanspa, 2010).

Additionally, LS patients with CRC who undergo frequent colonoscopy experience lower rates of morbidity and mortality than those who do not obtain frequent colonoscopies (Stuckless et al., 2012). For example, one study compared the impact of CRC screening on CRC patients with and without LS to determine the impact of screening on cancer incidence and survival. They found the overall cancer risk among LS+ patients was nearly six times that of patients without the mutation, yet there was no significant difference in the cancer mortality or overall mortality rate between the two groups (Järvenin et al., 2000). (See the *Medical Effectiveness* and *Public Health* sections for more discussion about morbidity and mortality).

Lynch Syndrome and Special Populations

CHBRP found no literature identifying disparities by gender or race/ethnicity regarding the prevalence of LS, or the diagnosis or treatment of LS-related cancers. The literature indicated the likelihood that males may have a higher risk for CRC than females, but the estimated risk difference ranged widely (5 to 40 percentage points) (EGAPP, 2009; Jang and Chung, 2010; Scheuner et al., 2010).

Despite the possible higher lifetime risk for CRC in LS+ males, LS+ females may have a higher cumulative lifetime risk when CRC and endometrial cancer risks are combined. The literature indicated that LS+ females have a 25% to 71% lifetime risk for endometrial cancer compared to 2% lifetime risk in the general population (Hampel et al., 2005; Quehenberger et al., 2005). This is similar to the female lifetime risk of CRC. Stoffel et al. estimate that LS+ females have a 73% cumulative lifetime risk of CRC or endometrial cancer (Stoffel et al., 2009). Additionally, the lifetime risk for ovarian cancer among women with LS ranges from 3% to 14%, compared to 1% in the general population (Jang and Chung, 2010). SB 799 does not address this difference in cumulative lifetime cancer risk between males and females, as the bill does not require coverage of the MMR genetic testing for the children and siblings of LS+ females who have been diagnosed with endometrial or ovarian cancers. Many guidelines continue to recommend cancer screening tests for LS-related endometrial or ovarian cancers despite the lack of evidence regarding the efficacy of such screening methods (e.g., endometrial biopsies and transvaginal ultrasound); other guidelines recommend prophylactic surgery as a preventive option (Bellcross et al, 2012; Palomaki et al., 2009; Yurgelun et al., 2012).

MEDICAL EFFECTIVENESS

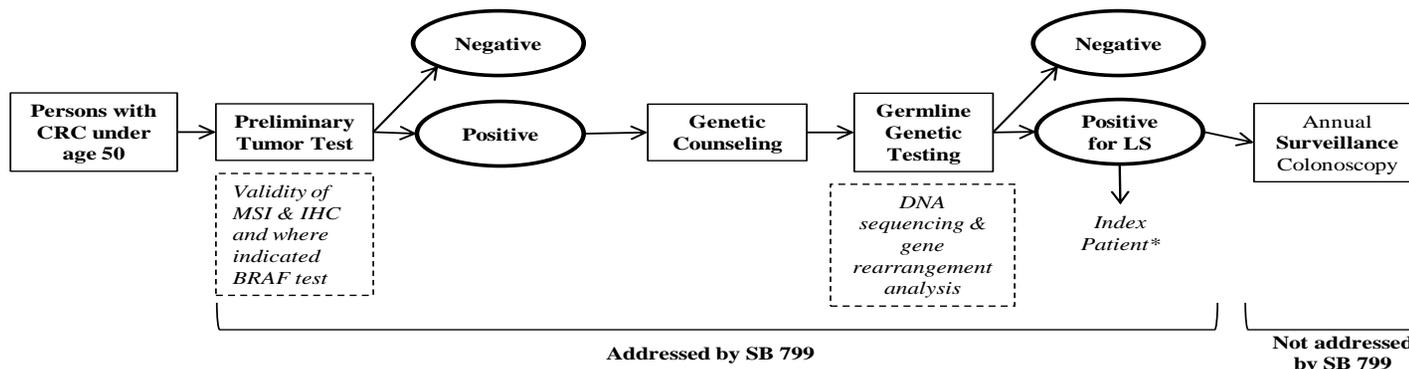
As discussed in the *Introduction*, SB 799 would mandate coverage for genetic testing for LS to enrollees younger than 50 years who have been diagnosed with CRC, and enrollees who are the children and siblings of a person diagnosed with CRC who has been found to have the genetic mutation for LS (relatives). SB 799 would also require coverage for annual colorectal screenings, such as colonoscopies, for LS+ enrollees who are children or siblings of LS+ persons diagnosed with CRC (index patients).

SB 799 does not define the term “genetic testing” or “screenings.” CHBRP assumes that “genetic testing” encompasses both preliminary tumor tests and germline genetic tests, which are recommended by national evidence-based guidelines on testing for LS. CHBRP assumes that “screenings, including colonoscopies” refers only to the colonoscopy examinations as recommended by national evidence-based guidelines on colorectal screening for LS. Although SB 799 does not address genetic counseling, CHBRP included this topic in its review because guidelines for LS testing recommend that persons at risk for LS receive genetic counseling before obtaining germline genetic testing (EGAPP, 2009).

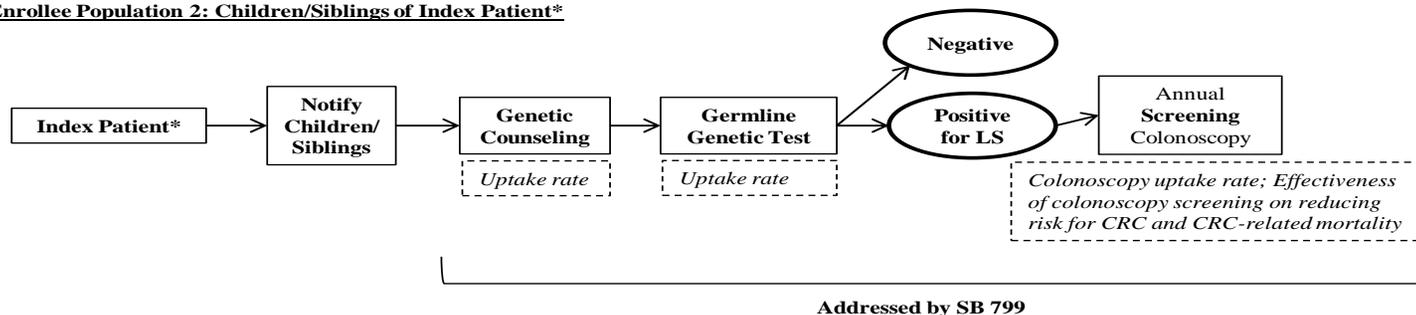
SB 799 requires analysis of two distinct populations: CRC patients, who would be eligible for genetic tumor testing and if indicated would receive germline genetic testing; and, relatives who would be eligible for germline genetic testing and, if found positive, annual colonoscopies. Figure 2 provides an overview of the process for identifying LS and follow-up care.

Figure 2. Process for identifying Lynch Syndrome Carriers and Recommended Surveillance or Screening Colonoscopy

Enrollee Population 1: Persons with CRC



Enrollee Population 2: Children/Siblings of Index Patient*



Source: California Health Benefits Review Program, 2013.

Notes: (*) “Index Patient” is defined as an individual with colorectal cancer (CRC) who has Lynch syndrome (LS). The index patients in “Enrollee Population 2” are inclusive of index patients identified in Population 1 and other possible index patients (e.g., patients living out of state or with insurance not subject to SB 799).

Key: CRC=colorectal cancer; LS=Lynch syndrome.

Evidence-based Guidelines on Genetic Testing for Lynch Syndrome and Colorectal Cancer Screening

Preliminary Tests for CRC Patient

National organizations and expert groups have developed guidelines on the use of genetic testing to detect LS among patients with CRC and their family members. The use of genetic testing to detect LS has been proposed as a strategy to improve the clinical management of LS, which may reduce CRC-related morbidity and mortality (EGAPP, 2009; NCCN, 2009; Weissmen et al., 2012). Guidelines recommend that genetic testing begin with testing the CRC patient's tumor with less expensive preliminary genetic tests, such as microsatellite instability (MSI) and immunohistochemistry (IHC) tests.

Germline Tests for Index Patients and Relatives of LS+ Index Patients

CRC patients who test positive on these preliminary tumor tests move onto the more expensive germline genetic tests, such as DNA sequencing, which can confirm the diagnosis of LS. If a CRC patient is diagnosed with LS, two guidelines recommend that their family members be contacted and offered genetic counseling and germline genetic tests to determine whether they have LS (EGAPP, 2009; NCCN, 2009).

Recommended Colonoscopy for LS Carriers

Among CRC patients and family members who are diagnosed with LS, colonoscopies are recommended every 1 to 2 years as a way to reduce CRC-related morbidity and mortality (ACS, 2013; EGAPP, 2009; NCCN, 2009). Screening at recommended intervals for CRC with colonoscopy can reduce mortality and morbidity because lesions can be detected at a precancerous stage and removed before they become cancerous.

Index patients have a 16% risk of developing a second primary CRC (de Vos tot Nederveen Cappel et al., 2002). In view of this heightened risk, some guidelines recommend discussing with patients with LS and CRC the option of subtotal colectomy as an appropriate surgical treatment (Lindor et al., 2006; Lynch et al., 2009; Palomaki et al., 2009; Vasen et al., 2013). The CHBRP Medical Effectiveness review does not examine the effectiveness of subtotal colectomy as a treatment option because SB799 does not directly require coverage for this procedure.

Research Approach and Methods

The medical effectiveness review for SB 799 addresses the following questions:

- What is the effectiveness of genetic testing to identify LS (e.g., clinical validity)?

- What is the take-up rate³⁹ of genetic counseling and genetic testing for family members of persons with LS?
- What is the effectiveness of frequent colonoscopy screening among LS+ family members on CRC morbidity and CRC-related mortality?
- What is the take-up rate for frequent colonoscopy screening among children and siblings of persons diagnosed with LS?
- What are harms associated with genetic testing and colonoscopy screening?

The medical effectiveness review discusses take-up rates for genetic counseling, genetic testing, and frequent CRC screening because the effectiveness of these interventions on a population level depends on their utilization. It is important to know both whether there is evidence that these interventions can accurately identify persons with LS and reduce CRC morbidity and CRC-related mortality and the extent to which they are utilized by persons who may benefit from them.

Studies of the effectiveness of genetic testing, take-up rates of genetic testing, effectiveness of frequent colonoscopy screening on morbidity and mortality, and take-up rates for frequent colonoscopy screening were identified through searches of PubMed, the Cochrane Library, and Web of Science. Websites maintained by the following organizations were also searched: National Cancer Institute PDQ, American Cancer Society, American Gastroenterological Association, National Guideline Clearinghouse, and U.S. Preventive Services Task Force. The search was limited to abstracts of studies published in English. The search was also limited to studies published from 2006 to the present because CHBRP previously retrieved the Agency for Healthcare Research and Quality's (AHRQ) Evidence Report/Technology Assessment, Hereditary Nonpolyposis Colorectal Cancer: Diagnostic Strategies and Their Implications (Bonis et al., 2007) that is a comprehensive systematic review of the literature up until 2006. The search was limited to studies published from 2006 to present. Of the 382 articles found in the literature review, 57 were reviewed for potential inclusion in this report on SB 799, and a total of 30 studies were included in the medical effectiveness review for this report. The other articles were eliminated because they did not focus on LS patients, were included in subsequent systematic reviews, or were otherwise not applicable. A more thorough description of the methods used to conduct the medical effectiveness review and the process used to grade the evidence for each outcome measure is presented in Appendix B: Literature Review Methods. Appendix C includes a table describing the studies that CHBRP reviewed (Table C-1) and a table summarizing evidence of effectiveness (Table C-2).

Methodological Considerations

Recently there have been rapid changes in knowledge about genetics and genetic testing technology. The optimal study design to test the clinical validity of the preliminary tumor test would be to administer the preliminary tumor test among an LS+ population. Findings from older studies may vary from newer studies due in part to variations in tests available at that time.

³⁹ Take-up rate refers to the proportion of persons who receive a treatment among those who were eligible to receive such treatment.

Of two systematic reviews that CHBRP found on clinical validity of the preliminary tests, one (Palomaki et al., 2009) limited the review to publications from 2003 forward with the intent to include studies based on the same technology of genetic testing. The second (Bonis et al., 2007) systematic review includes studies published from 1979 to 2006.

Most guidelines are in agreement that preliminary tumor testing for LS be performed on all persons with new diagnosis of CRC. Recent studies have found that universal preliminary tumor testing is a cost-effective approach in the identification of LS in all persons with CRC (Moreira et al., 2012; Mvundura et al., 2010). This represents a departure from previous guidelines that recommended preliminary tumor testing for a subset of CRC persons considered to be at higher risk for LS. Over time it has also become more commonplace for institutions to perform IHC or MSI preliminary tumor tests at the time of biopsy. Beamer et al. (2012) found that in 2009, 42% of cancer programs performed IHC and/or MSI testing on CRC tumors and that 16% of programs had future plans for such testing. Positive IHC and/or MSI test results indicate that a person may be at high risk for LS. Knowledge of such risk may influence one's decision to receive germline genetic screening. These recent changes in guidelines and in practice patterns may increase the numbers and rates of uptake of preliminary tumor tests and germline genetic tests over time. Findings from more recent studies on the uptake of testing may vary from older studies due to these changes.

In the majority of studies reviewed on the impact of colonoscopy screening on CRC morbidity and mortality, persons were recruited from an LS surveillance program where study participants received active reminders to receive ongoing colonoscopies. De Jong et al. (2006) and Vasen et al. (2010) recruited LS families enrolled in a Dutch Lynch syndrome registry. These studies state that the registry sent reminders to the clinicians to call their patients about follow-up colonoscopy. In Järvinen et al. (2000) at-risk family members who elected to participate in a screening program were then recruited for repeated colonoscopic examinations. The active recruitments and/or notifications to receive ongoing colonoscopy in these studies may have resulted in an increased compliance with such screening that may affect the rates of detection of CRC and CRC-related mortality. The findings from these studies may differ from other studies that do not enroll family members from LS surveillance registries with reminder notifications.

Study Findings

What Is the Evidence of the Effectiveness of Genetic Testing to Identify Lynch Syndrome (e.g., Clinical Validity)?

Utilization of clinically valid genetic tests to diagnose LS is an important initial step in the clinical management of LS. Clinical validity refers to the accuracy with which a test can predict the presence or absence of a disease. The medical effectiveness review examined the clinical validity of the recommended genetic tests for the identification of LS (see Table 4).

Table 4. Guidelines for Preliminary Tumor Testing for Lynch Syndrome Among Persons with CRC

Guideline	Citation	Recommended Preliminary Tumor Test Prior to Germline Genetic Testing	Population
Mallorca group	Vasen et al., 2013	IHC or MSI (with or without BRAF testing)	Persons with CRC <70 years
EGAPP	EGAPP, 2009	IHC or MSI (with or without BRAF testing)	All persons with a new diagnosis of CRC
NSGC/CGA-ICC	Weissmen et al., 2012	IHC (with or without BRAF testing)	Persons with a diagnosis of CRC
NCCN	NCCN, 2012	IHC or MSI (with or without BRAF testing)	Persons with a diagnosis of CRC

Notes: MSI refers to microsatellite instability, IHC refers to immunohistochemistry, BRAF refers to testing for the BRAF gene.

The Evaluation of Genomic Applications in Practice and Prevention Working Group (EGAPP, 2009), the National Society of Genetic Counselors and Collaborative group of the Americas on Inherited Colorectal Cancer (NSGC/CGA-ICC), the Mallorca Group, and the National Comprehensive Cancer Network (NCCN) have published guidelines on the use of preliminary tumor testing and germline genetic testing as a strategy to identify persons at risk for LS. Most guidelines recommend that preliminary tumor testing should be performed on all persons with a new diagnosis of CRC. The Mallorca group, a group of European experts, recommended preliminary tumor testing among persons with CRC who are younger than 70 years.

While SB 799 would mandate coverage for genetic testing for LS to persons younger than 50 years who have been diagnosed with CRC, the medical effective review found no studies on the clinical validity of genetic tests solely among CRC patients aged 50 years or younger. One study that examined the impact of imposing an age cutoff found that when performing genetic tests among CRC patients aged 50 years or younger, 50% fewer LS+ cases would be detected when compared to testing patients of all ages with CRC (Gudgeon et al., 2012).

The recommended genetic tests for the identification of LS may be divided into two major categories:

- Preliminary tumor tests (MSI, IHC, with or without BRAF gene test)
- Germline genetic testing (DNA sequencing and gene rearrangement analysis)

Preliminary tumor tests are recommended as a first-line testing strategy for persons who are being evaluated for LS. These preliminary tumor tests determine whether a person is at risk to have LS; they are not expected to predict LS with 100% accuracy. Guidelines recommend the use of immunohistochemistry (IHC) or microsatellite instability (MSI) with or without the follow-up BRAF test (BRAF tests for the BRAF gene is indicated by IHC or MSI findings) as the recommended preliminary tumor test. While performing MSI and IHC analyses together can

best predict the risk for LS, the approach of testing with MSI or IHC analysis alone has been shown to be a cost-effective approach (Ladabaum et al., 2011) for a population. The EGAPP review (EGAPP, 2009) did not find evidence to recommend one test over the other (IHC or MSI). A study by Mvundura et al. (2010), however, did find that the use of the IHC test to be the more cost-effective approach to identifying risk for LS (Mvundura et al., 2010). The results of these tests determine whether persons should receive germline genetic tests, which are more expensive. Germline genetic tests are considered the gold standard for identifying LS. Therefore, assessing the clinical validity of such tests does not apply.

The medical effectiveness of the clinical validity of preliminary tumor tests was assessed using the following outcomes:

- Clinical sensitivity: Refers to the likelihood that test results will be positive when LS is present.
- Clinical specificity: Refers to the likelihood that test results will be negative when LS is absent.
- False-positive rate: Refers to the likelihood that test results will be positive when LS is absent.

The medical effectiveness literature review revealed two systematic reviews related to the clinical validity of IHC, MSI, and BRAF tests. Palomaki et al. (2009) limited their review to publications from 2003 forward because technology of genetic testing is rapidly changing. The AHRQ systematic review (Bonis et al., 2007) includes studies published from 1979 to 2006. Approximately 30% of the studies included in the Palomaki et al. (2009) review were also included in the earlier AHRQ review (Bonis et al., 2007).

MSI testing among patients with CRC

LS is caused by a mutation in any of four DNA mismatch repair (MMR) genes: MLH1, MSH2, MSH6, and PMS2 (Vasen and Boland, 2005). This MMR defect results in instability in microsatellites of the tumor DNA, which is called microsatellite instability (MSI). A panel of 5 microsatellite instability markers has been validated and is recommended for MSI testing (Boland et al., 1998). MSI tests the combination of microsatellites to assess whether there is high instability, low instability, or no instability in a tumor. When MSI is high, then germline genetic testing of the MMR genes is warranted.

Palomaki et al. (2009) pooled findings from 11 studies of CRC patients at high risk for LS to examine the clinical sensitivity and specificity of the MSI test. The definition of high risk varied across studies and used criteria such as family history of CRC or early age of CRC among an LS+ family member. The results show the clinical sensitivities of MSI testing to identify microsatellite instability in MLH1, MLH2, and MSH6 genes. There was insufficient evidence to evaluate the clinical validity of MSI testing on the microsatellite instability of PMS2. Eleven studies were pooled across 81 LS+ persons with mutations in MLH1. Results from a random effects model found the sensitivity of MSI testing on microsatellite instability in the MLH1 gene to be 85% (95% CI: 75%-92%). Pooled estimates from the same 11 studies examined MSI testing on identification of high instability in the MLH2 gene; the resulting sensitivity was 85%

(95% CI: 73%-93%). In a subset of 6 studies, the sensitivity of MSI testing on microsatellite instability in the MSH6 gene was 69% (95% CI: 50%-92%). These same authors examined the clinical specificity of MSI testing from six large studies from general populations of newly diagnosed CRC patients. Tumors were tested with MSI and MMR gene mutation (to confirm LS) in 3842 patients; 356 MSI-high tests results were found. Results from a random effects model showed the clinical specificity of MSI testing was 90% (95% CI: 88%-93%) and a false-positive rate of 9.8% (95% CI: 7.3%-13.0%). The authors concluded that there was adequate evidence on the clinical validity of MSI.

A systematic review (Bonis et al., 2007) examined results from 16 studies, of which six were rated as low-quality studies. All studies performed both MSI testing and genetic testing as the reference. Overall, there was a large range for sensitivity (56% to 100%) and for specificity (17% and 93%).

In summary, the MSI test can adequately identify most CRC patients who are at risk for LS and would therefore benefit from germline genetic testing.

IHC testing among patients with CRC

IHC testing differs from MSI testing in that it directly examines the four mismatch genes known to be mutated in LS: MLH1, MSH2, MSH6, or PMS2 (Vasen and Boland, 2005). The IHC analysis tests the mismatch repair proteins in the nucleus of the tumor sample for a loss of protein expression. A normal test means that all four mismatch repair proteins are normally expressed. An abnormal test means that at least one of the proteins is not expressed, which may be due to an inherited mutation in the related gene. When IHC identifies a loss of protein expression, then germline genetic testing of that related gene is warranted. The IHC provides additional information over MSI in that it allows for a single gene to be identified for DNA analysis.

Palomaki et al. (2009) pooled findings from nine studies of various high-risk groups for LS to examine the sensitivity of IHC to detect MLH1, MSH2, and MSH6, separately. Seven studies of patients with identified MHL1 mutation and LS were pooled to test the sensitivity of IHC on MLH1; they found the sensitivity of the IHC to be 78% (95% CI: 65%-88%). Pooled estimates from these same seven studies found the sensitivity of IHC on LS patients with mismatch repair mutations on the MSH2 gene to be 80% (95% CI: 62%-90%). The sensitivity of IHC to detect mutations in the MSH6 gene among LS patients with MSH6 mutations was 74% (95% CI: 57%-86%). The sensitivity of IHC on PMS2 was not tested because of limited data. The clinical specificity of IHC was tested by pooling persons from 3 population-based cohorts of CRC patients. Results from a random effects model showed the clinical specificity is 88.8% (95% CI: 67.6%-94.8%) and a false-positive rate of 11.2% (95% CI: 5.2%-22.4%). The authors concluded that there was adequate evidence on the clinical validity of IHC.

One 2007 review (Bonis et al., 2007) pooled results from six fair to good quality studies that assessed the clinical validity of IHC of patients with available CRC tumor tissue. The summary sensitivity of the IHC test was 74% (95% CI: 54%-87%) and specificity was 77% (95% CI: 61%-88%).

In summary, the IHC test can adequately identify most persons with CRC who are at risk for LS and would benefit from germline genetic testing.

IHC and MSI testing among patients with CRC

An AHRQ (Bonis et al., 2007) review also reported findings from a single study of persons with tumors with high MSI and found the sensitivity of IHC was 94% (95% CI: 71%-100%) and the specificity was 13% (95% CI: 4%-30%).

BRAF testing among patients with CRC

When the IHC tests reveal the absence of protein expression in the MLHI gene, the tumor tissue may also be tested for the BRAF gene. BRAF tests determine whether absence of protein expression in the MLHI gene is due to somatic mutations, which is found in sporadic types⁴⁰ of CRC, but virtually never in LS-related CRC (which is based on germline mutations) (Palomaki et al., 2009). When the BRAF test indicates these somatic events, then no further germline genetic testing on the MLH1 is warranted.

Palomaki et al. (2009) pooled findings from 4 studies of CRC patients with an absence of MLH1 expression who had either LS (germline mutation in MMR gene) or sporadic cancer (somatic hypermethylation of the MLHI gene). Sensitivity was defined as the proportion of sporadic cancers associated with the BRAF mutation; specificity was defined as the proportion of LS patients without the BRAF mutation. The results indicate the sensitivity for BRAF test to be 69% (95% CI: 57%-79%) and a specificity of 100% (95% CI: 93%-100%).

Summary of findings regarding clinical validity of preliminary genetic tests. Overall, the preponderance of evidence from systematic reviews on the clinical validity of MSI, IHC, and BRAF suggests that these preliminary tumor tests can accurately identify most CRC patients who would benefit from germline genetic testing.

Germline genetic testing among persons with CRC

Germline genetic testing is considered the gold standard to detect LS and refers to both DNA sequencing that detects most mismatch repair gene mutations, and gene rearrangement analysis that screens for point mutations, deletion, duplication, and insertions within the MLH1, MSH2, MSH6, PMS2, and EPCAM genes (Bonis et al., 2007; EGAPP, 2009). Across guidelines, germline genetic testing is recommended for CRC patients with preliminary tumor testing suggestive of mismatch repair gene mutations (EGAPP, 2009; Weissman et al., 2012). Once germline genetic testing has confirmed LS, guidelines recommend family members be notified, and offered genetic counseling and germline genetic testing (EGAPP, 2009; Lynch and de la Chapelle, 2003).

⁴⁰ Sporadic cancer refers to a non-hereditary cancer that presents in persons with no family history of colon cancer.

Germline genetic testing among relatives of an index patient

Germline testing is recommended for relatives of an index patient. Since relatives do not have a CRC tumor, no preliminary tumor tests are necessary; they proceed directly to germline testing (see Figure 2). Evaluation of Genomic Applications in Practice and Prevention Working Group (EGAPP, 2009) recommends first- and second-degree relatives be offered genetic counseling prior to germline genetic testing and the National Comprehensive Cancer Network recommends that first-degree relatives be offered genetic counseling and genetic testing (NCCN, 2009). The purpose of genetic counseling is to educate family members about genetic testing for LS and to help them make an informed decision about obtaining testing.

What Is the Take-up Rate of Genetic Counseling and Genetic Testing for Family Member of Persons with LS?

Obtaining the genetic tests to diagnose LS is an important initial step in the clinical management of LS. Practice guidelines recommend that persons at risk for LS must first be identified, counseled, and given the choice to receive these tests. For studies on the take-up rate of genetic counseling among children and siblings of persons with LS, CHBRP assessed the outcome of take-up rate of genetic counseling as the proportion of persons who received genetic counseling among those who were eligible to receive genetic counseling. Similarly, CHBRP assessed the outcome of take-up rate of genetic testing as the proportion of persons who received genetic testing among those who were eligible to receive genetic testing.

The medical effectiveness literature review revealed one systematic review of studies that examined the uptake of genetic counseling and the uptake of genetic testing among family members of persons with LS. Palomaki et al. (2009) summarized finding from six studies of 1,866 relatives of 234 LS+ persons. Methods of delivering counseling varied across the studies. Persons in some studies had to drive to receive counseling while in other studies genetic counselors arranged to meet persons in their communities. Of the 1,866 relatives, 52% (95% CI: 37%-66%) received genetic counseling and of those, 95% (95% CI: 93%-97%) received genetic testing.

One prospective cohort study (Burton-Chase et al., 2013) examined take-up rates of genetic counseling and testing. In a parent study, index patients were invited to refer family members to the current study. The family members were mailed information and asked to participate in a study (Burton-Chase et al., 2013) that offered genetic counseling and the option of genetic testing at no cost. Letters were mailed to 231 family members and 110 (48%) replied, and 97 (42%) received genetic counseling. Of the 97 who received genetic counseling, 91 (94%) received genetic testing, and 89 (92%) received counseling after genetic testing.

One retrospective study (Esposito et al., 2010) reported on the take-up rates of genetic testing among 73 at-risk LS family members who were enrolled in an LS surveillance program in Italy. Persons received genetic counseling, including meeting with a physician and a psychologist and receiving written materials. After receiving genetic counseling, 58 (79%) persons consented and underwent genetic testing.

Sturgeon et al. (2013) examined the take-up rates of genetic testing pre- and post-establishment of a hereditary CRC registry in 2007 in a large medical center in the United States. In 2006, the year prior to the development of the registry, among 115 CRC patients treated in the medical center clinic, 4 patients (3.5%) received additional assessment, and 1 received genetic testing. About four years after registry implementation, 255 CRC patients had consented to participate in the registry. Of the 255 patients, 174 were deemed at risk for LS based on family history and had MSI preliminary tumor testing done at the time of CRC tumor removal; 27 patients had MSI test results indicative of LS. Genetic germline counseling and testing was offered during a follow-up clinic visit to these 27 patients and 20 patients (74%) underwent germline genetic testing.

Summary of findings regarding the take up of genetic counseling. Overall, the preponderance of evidence indicates that approximately half of family members of persons with LS who are offered genetic counseling obtain counseling.

Summary of findings regarding the take up of genetic testing after receiving genetic counseling. Overall, the preponderance of evidence indicates that the take-up rate for genetic testing following genetic counseling is high among family members of persons with LS. Estimates ranged from 79% to 95%. In a single case series study of CRC patients, 74% underwent genetic testing post-genetic counseling.

What Is the Evidence of Frequent Colonoscopy Screening Among Family Members with LS on CRC Morbidity and CRC-Related Mortality?

Persons who have been tested and diagnosed with LS have an increased risk of developing CRC and are recommended to receive earlier and more frequent colonoscopies than persons at average risk for CRC. The lifetime risk of developing CRC among LS+ relatives is estimated at 45% for men and 35% for women by age 70 (Palomaki et al., 2009). The risk of developing a second primary CRC among index patients is 16% (de Vos et al., 2002). Most CRC lesions in LS+ patients arise from adenomas, a small and/or flat lesion that progresses to a cancerous state at a faster rate than adenomas in patients with sporadic cancer (non-hereditary cancer). Evidence suggests that these small and or flat adenomas may also be more difficult to detect than larger non-LS CRC lesions when using conventional colonoscopies (Stoffel et al., 2008). For these reasons, current guidelines recommend for screening LS + persons with colonoscopies every 1 to 2 years (see Table 5). Screening at recommended intervals for CRC with colonoscopy can reduce mortality and morbidity because lesions can be detected at a precancerous stage and removed before they become cancerous.

Table 5. Guidelines for Screening Among LS+ Persons

Guideline	Citation(s)	Colonoscopic test recommended	Frequency of testing for LS+ Persons
Mallorca group	Vasen et al., 2013	Colonoscopy	Every 1 to 2 years
American Cancer Society	ACS, 2013	Colonoscopy	Every 1 to 2 years starting at age 20-25, or 10 years before youngest case in immediate family
EGAPP	EGAPP, 2009	Colonoscopy	Every 1 to 2 years beginning at 20-25
NCCN	NCCN, 2012	Colonoscopy	Every 1 to 2 years at age 20-25 or 2 to 5 years prior to the earliest colon cancer if diagnosed before age 25

Across most guidelines, the recommended standard of care for persons with LS with and without CRC includes colonoscopy every 1 to 2 years beginning at age 20 to 25 (or 2 to 10 years before the youngest case of CRC diagnosis in the family). While SB 799 would mandate coverage of annual colonoscopies, medical effectiveness found limited literature on the effectiveness of annual colonoscopies; therefore medical effectiveness includes findings from studies that examined colorectal screenings at annual to biannual, biannual, and 3-year interval.

The medical effectiveness of frequent colonoscopy screening among LS+ family members on CRC morbidity and CRC-related mortality was assessed using the following outcomes:

- Relative risk for CRC morbidity: This refers to a ratio of the probability of developing CRC when receiving frequent colonoscopy screening compared to the probability of not receiving frequent colonoscopy screening.
- Relative risk for CRC-related mortality: This refers to a ratio of the probability of death from CRC when receiving frequent colonoscopy screening compared to the probability of not receiving frequent colonoscopy screening.

Morbidity

CHBRP did not identify any studies that assessed the impact of colorectal screening at a 1-year interval on CRC morbidity among LS+ persons nor did it identify any studies that compared the effects of screening at different intervals on morbidity.

Finnish nonrandomized controlled 15-year trial examined the efficacy of colorectal screening at 3-year intervals on the incidence of CRC in two cohorts of 252 family members who had a 50% risk *a priori* of being LS mutation carriers (Järvinen et al., 2000). The study group received ongoing colorectal screening, including colonoscopy, while those in the comparison group opted not to receive screening. After 14.5 years, 8 of the 133 (6%) persons in the study group developed CRC compared to 19 of 199 (16%) in the control group. The relative risk of CRC was significantly lower (RR = 0.38 [95% CI: 0.17-0.83]) among those who received screenings compared to those who had opted not to receive screening, representing a 62% reduction (95% CI: 17%-83%) of CRC due to screening. Genetic testing became available later into the trial. A

sub-analysis among LS+ persons found a significant reduction in the relative risk of CRC, with 18% of persons in the study group developing CRC compared to 41% in the control group (RR = 0.44 [95% CI: 0.22-0.90]). This represents a 56% (95% CI: 10%-79%) reduction in CRC due to colorectal screening.

Summary of findings regarding the effectiveness of frequent colonoscopy on reducing CRC morbidity. There was insufficient evidence to assess the effectiveness of annual colonoscopy on CRC morbidity. The evidence from one nonrandomized controlled study indicates colorectal screening at 3-year intervals leads to a 56% reduction in CRC among LS+ persons.

Mortality

CHBRP did not identify any studies that compared persons who received annual colonoscopies to persons who did not receive them on CRC-related mortality among LS+ persons.

One cohort study (de Jong et al., 2006) examined the effects of a large surveillance program of 146 Lynch families on CRC-related mortality. Clinicians of registered families received reminder notification of a planned annual or biannual colonoscopy. Standardized mortality ratios (SMR) were computed by comparing the CRC-related mortality in the registered families to the general population at pre- and post-surveillance program implementation. The SMR significantly decreased from 32.3 to 10.1 over time ($p < .001$).

Järvinen et al. (2000) examined the effects of ongoing colorectal screenings at 3-year intervals on colorectal-related mortality in 252 family members who had a 50% risk *a priori* of having LS. The relative risk of mortality was significantly lower (RR = 0.34 [95% CI: 0.17-0.68]) among those who received screenings compared to those who had opted not to receive screening, representing a 66% (95% CI: 32% - 83%) reduction in death due to CRC. In a sub-analysis among LS+ persons, the relative risk of death due to CRC was also lower (RR = 0.35 [95% CI: 0.12-0.99]) among persons who received screening, representing a 65% reduction in deaths due to CRC in this subgroup.

One cohort study (Stuckless et al., 2012) examined the effects of biannual colonoscopy screening among LS+ persons with the MSH2 mutations who were recruited from a hospital-based genetics program and invited to enroll in a colonoscopy screening program. Of the 322 eligible persons, 152 (47%) entered the colonoscopy screening program and 170 (53%) did not. Among men enrolled in the screening program who had at least two colonoscopies over the study period, the median age to CRC was 58 years and the median survival was 66 years. When compared to the expected median values of men not screened, screened men had lower risk for CRC (RR = 0.29 [95% CI: 0.16-0.53]) and a marginal reduction in deaths (RR = 0.38 [95% CI: 0.13-1.0]). These patterns were similar for women who had at least two colonoscopies over the study period. The risk for CRC was lower among screened women (RR = 0.29 [95% CI: 0.16-0.53]), and screened woman had reduction in deaths (RR = 0.19 [95% CI: 0.09-0.44]).

Summary of findings regarding the effectiveness of colonoscopy on reducing CRC mortality. There was insufficient evidence to assess the effectiveness of annual colonoscopy on reducing CRC mortality. The preponderance of evidence indicates that colonoscopies every 1 to 3 years reduce the CRC-related mortality for LS+ persons. Evidence from the two studies that compared CRC mortality rates among persons who received colonoscopies to persons who did not receive them found that screening at 2 and 3 year intervals is associated with a reduction in death of 65% to 81%.

What Is the Take-Up Rate for Frequent CRC Screening Among Adult Children and Siblings of Persons Diagnosed with LS?

For studies on the take-up rate of frequent CRC screening among children and siblings of LS+ persons, CHBRP assessed the outcome of take-up rate of colonoscopies as the proportion of persons who received colonoscopies among those who were eligible to receive colonoscopies.

One systematic review (Palomaki et al., 2009) summarized findings from seven studies on the effect of genetic testing on the uptake of colonoscopy among LS+ family members. Uptake of colonoscopy was defined as receiving a colonoscopy within 2 years of receiving genetic tests in five studies. Two studies reported uptake of colonoscopy at any time since the receipt of test results. The uptake rates ranged from 53% to 100% across the studies. Summarizing findings across studies resulted in an average uptake rate of 79% (95% CI: 67%-87%) among 135 relatives.

One retrospective study (Esposito et al., 2010) of 40 LS+ family members enrolled in an LS surveillance program found 28 (70%) persons received scheduled ongoing colonoscopies on an average of every two years.

Stoffel et al. (2010) examined the rate of colonoscopy compliance among 181 family members who tested LS+ who were recruited from U.S. cancer genetics clinics. Of the 181 persons, 132 (73%) had colonoscopies at least every 2 years.

Collins et al. (2007) examined the rates of colonoscopy screening at 3 years post-genetic testing. Of the 73 persons, 54 did not have LS and 19 were LS+. Of the 19 LS+ persons, all 19 reported having a colonoscopy 1 to 3 years after receipt of test results.

A Canadian prospective cohort study (Stuckless et al., 2012) recruited patients with confirmed MSH2 mutation and family members at risk for LS from a hospital-based genetics program to participate in an ongoing screening program. Among family members who had at least two colonoscopies over a 10 years study period, 44% of males and 41% of females who were MSH2 mutation carriers received colonoscopies every 1 to 2 years.

Summary of findings regarding the take up of colonoscopies. Overall, the preponderance of evidence indicates that the take-up rate for colonoscopies around 2 to 3 years of diagnosis of LS is approximately 70% to 100%.

Harms

Psychosocial harms related to genetic counseling and testing

A prospective study (Keller et al., 2008) examined the effects of a multidisciplinary counseling program on psychosocial outcomes among 233 family members at risk for LS and among other cancer patients. The counseling program consisted of a consultation by a medical geneticist, including clinical counseling that explained the need for early detection, and psychosocial counseling to elicit perceptions, fears and expectations of genetic testing for LS. Following receipt of genetic counseling, there was a significant reduction in general anxiety, distress, and general cancer worry.

A 2009 systematic review (Palomaki et al., 2010) summarized findings from eight studies on the psychosocial outcome of genetic counseling and genetic testing. Among non-carriers of LS, genetic counseling and testing was associated with psychosocial benefits including a reduction in colon cancer worry, general anxiety, depression, assurance that their children would not inherit the mutation, and perceived discrimination. Among LS+ persons, the effects of counseling and testing were associated with short-term distress.

Aktan-Collan et al. (2013) examined long-term psychosocial outcomes of genetic testing. Among 208 persons at risk for LS, measures of anxiety, fear, satisfaction with life, and perceptions of risk, were measured before testing, at 1 month, 1 year, and at 7 years after genetic testing. Follow-up at 7 years showed no change in the psychosocial variables for both LS+ and non-LS persons. LS+ persons underestimated their CRC risk but worried more about cancer risk than those without LS.

Summary of findings regarding harms of genetic counseling and genetic testing for LS.

The preponderance of evidence suggests that genetic counseling reduces anxiety about genetic testing and that there is no long-term difference in psychological distress between persons who are tested and found to be LS+ and those who are found not to have LS.

Adverse events related to colonoscopies

CHBRP found one systematic review that evaluated the adverse events related to colonoscopies from 12 studies (Palomaki et al., 2009) of general clinic populations. The number of colonoscopy procedures reported across the studies ranged from 1,196 (in a university hospital population) to 116,000 (45 endoscopic surgery center population). The total number of procedures pooled across the 12 studies was 381,066. The most common adverse events reported were perforation, occurring in 1.1 (95% CI: 0.8-1.4) per 1,000 procedures and bleeding occurring in 3.3 (95% CI: 2.3-4.6) per 1,000 procedures.

Psychosocial harms related to colonoscopies

One systematic review (Gopie et al., 2012) summarized the literature on the psychological burden of colonoscopy surveillance in LS families. Two cross-sectional studies on LS families enrolled in a surveillance program with 1 to 3 year colonoscopy screening protocols reported no difference in depression or anxiety compared with a reference population. Another study of 271 LS+ family members found no harmful emotional impact after one year colonoscopic screening.

Summary of findings regarding harms of colonoscopy among persons with LS. The preponderance of evidence suggests that colonoscopies are associated with small increases in risk for bleeding and perforation of the colon. Findings from studies of the impact of frequent colonoscopies on mental health found no harmful emotional impact after receiving colonoscopies.

BENEFIT COVERAGE, UTILIZATION, AND COST IMPACTS

SB 799 would require DMHC-regulated plans and CDI-regulated policies to cover genetic testing for LS for two populations: (1) enrollees younger than 50 years with CRC and (2) any enrollee who is the child or sibling of an index patient (a person with CRC and LS+). Utilization of genetic testing for LS in this section takes into account expected use of these tests by both populations. As noted in the *Medical Effectiveness* section, guidelines recommend tumor testing for persons with CRC and genetic counseling (informing the patient of what genetic testing entails) for all persons precede germline genetic testing. In this analysis, CHBRP assumes that counseling would precede germline testing. Because coverage for preliminary tumor testing for persons with CRC is not expected to be altered by SB 799, discussion of the genetic testing utilization is focused on germline testing. In addition, because counseling and testing are recommended for adults, discussion of utilization is focused on adult enrollees (including the adult children of index patients).

SB 799 would also require plans and policies to cover annual CRC screening, including colonoscopy, for a third population: (3) LS+ enrollees who are the children or siblings of an index patient. As noted in the *Medical Effectiveness* section, guidelines recommend colonoscopy as the screening test for LS+ persons. For this reason, discussion of screening utilization focuses on colonoscopy, and not on other screening tests for CRC that may be used by average-risk enrollees (such as fecal occult blood testing). In addition, because colonoscopy is recommended for adults, discussion of utilization is focused on adult enrollees (including the adult children of index patients).

SB 799 does not address surveillance colonoscopy (which is recommended for persons with CRC), so neither benefit coverage nor utilization of surveillance colonoscopy are addressed in this analysis.

This section will present, first, the current (baseline) benefit coverage, utilization, and costs related to: (1) genetic testing for persons younger than 50 years with CRC, (2) genetic testing and for the children and siblings of the index patient, and (3) annual colonoscopy for the LS+ children and siblings of the index patient. It will then provide estimates of the marginal impacts on benefit coverage, utilization, and cost if SB 799 is enacted. For further details on the underlying data sources and methods, please see Appendix D.

Current (Baseline) Benefit Coverage, Utilization, and Cost

Current Coverage of the Mandated Benefit

Coverage of genetic testing for LS of enrollees with CRC younger than 50 years and enrollees who are the children or siblings of an index patient, as well as annual CRC screening for LS+ enrollees who are children or siblings of the index patient, was determined by a survey of the seven largest providers of health insurance in California. Responses to this survey represented 77.2% of the privately funded, CDI-regulated market and 89.9% of the privately funded,

DMHC-regulated market. Combined, responses to this survey represent 86.8% of the privately funded market subject to state mandates. CHBRP also queried the California Department of Health Care Services and a number of plans enrolling Medi-Cal beneficiaries regarding benefit coverage for Medi-Cal beneficiaries enrolled in Medi-Cal Managed Care, as well as CalPERS regarding benefit coverage for CalPERS' enrollees.

In addition to requiring benefit coverage to be present, SB 799 would require that benefit coverage be compliant with specified terms. Examples of impacts on terms could be as follows:

- SB 799 would require plans and policies to cover genetic testing for LS for enrollees younger than 50 years with CRC. Even where benefit coverage is present, SB 799 could alter it, for example, by prohibiting utilization management criteria from requiring that the enrollee with CRC be less than a younger age, such as 45, for the test to be covered.
- SB 799 would require plans and policies to cover genetic testing for LS for any enrollee with a parent or sibling with CRC and LS+ (the index patient). Even where benefit coverage is present, SB 799 could alter it, for example, by prohibiting utilization management criteria from requiring that an enrollee be related to two or more index patients for the test to be covered.
- SB 799 would require plans and policies to cover annual CRC screening, including colonoscopy, for any LS+ enrollee who is the child or sibling of an index patient. Even where benefit coverage is present, SB 799 could alter it, for example, by prohibiting utilization management criteria from limiting covered colonoscopy for LS+ enrollees to a biennial (alternate year) schedule.

See Appendix D for a full discussion of utilization management changes that SB 799 would require.

Although 96.0% of enrollees in DMHC-regulated plans and CDI-regulated policies have coverage for genetic counseling and testing for LS, only 57.1% have benefit coverage compliant with SB 799 (see Table 1 in *Executive Summary*). The other 42.9% of enrollees are in plans or policies without the relevant benefit coverage or with utilization management criteria not compliant with SB 799.

Although 100% of enrollees in DMHC-regulated plans and CDI-regulated policies have coverage for CRC screening, including colonoscopy, only 79.9% have benefit coverage compliant with SB 799 (see Table 1 in *Executive Summary*). The other 20.1% of enrollees are in plans or policies with utilization management criteria not compliant with SB 799.

Current Utilization Levels

Among enrollees younger than 50 years with CRC, based on studies in the research literature (Sturgeon et al., 2013), CHBRP assumes that 75% of the 5% with LS+ predictive tumor tests proceed to genetic counseling and germline genetic testing (see Figure 3). This 5% figure is derived from the overall prevalence of LS+ predictive tumor tests for all ages, and it is unknown whether the percentage is higher among CRC patients younger than 50 years. Reviewed examples of relevant utilization management criteria were all compliant with SB 799 for this

population. Therefore, CHBRP estimates 34 covered LS-related genetic counseling sessions and 34 covered germline genetic tests among this population (see Table 1 in *Executive Summary*).

To calculate the number of enrollees who are the children or siblings of an index patient, CHBRP applied, based the literature, an average of three close relatives for each index patient (Hampel et al., 2005; Hampel et al., 2008).

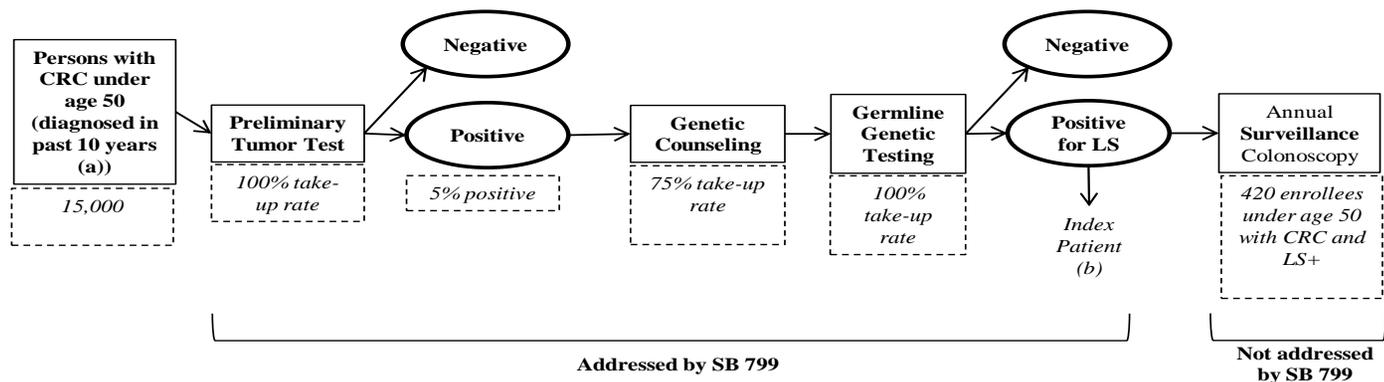
Among enrollees who are children and siblings of an index patient, based on studies in the research literature (Burton-Chase et al., 201; Sturgeon et al., 2013), CHBRP assumes that 50% undergo genetic counseling (see Figure 3). Reviewed examples of relevant utilization management criteria for this population found that even noncompliant utilization management criteria are broad and so, premandate, CHBRP estimates that four of five of the enrollees described by SB 799 would have been covered for LS-related genetic counseling and testing. Among those whose testing would not have been covered, CHBRP has assumed that utilization rates would be half those with mandate-compliant benefit coverage. CHBRP assumes the rate would be less due to increased cost sharing, although no literature could be identified that delineated a price elasticity for this population. Therefore, CHBRP estimates that 6,627 genetic counseling sessions and 6,003 genetic tests among this population (see Table 1). Counseling is slightly more common than testing because sequential enrollee expenses have a greater effect on the last step of a multi-step process, decreased enrollee expenses have a greater effect on utilization of the last step (testing) than on the first step (counseling).

Among enrollees who are the LS+ children or siblings of an index patient, based on the literature (Esposito et al., 2010; Stoffel et al., 2010), CHBRP assumes a 70% take-up rate of screening colonoscopy. Reviewed examples of noncompliant utilization management criteria are broad, covering biennial (alternate year) colonoscopy and so, premandate, CHBRP estimates that four of five of the enrollees described by SB 799 would have been covered for annual colonoscopy. CHBRP has assumed that utilization rates would be half those with mandate-compliant benefit coverage. CHBRP assumes the rate would be less due to increased cost sharing, although no literature could be identified that delineated a price elasticity for this population. Therefore, CHBRP estimates 2,025 screening colonoscopies among this population (Table 1).

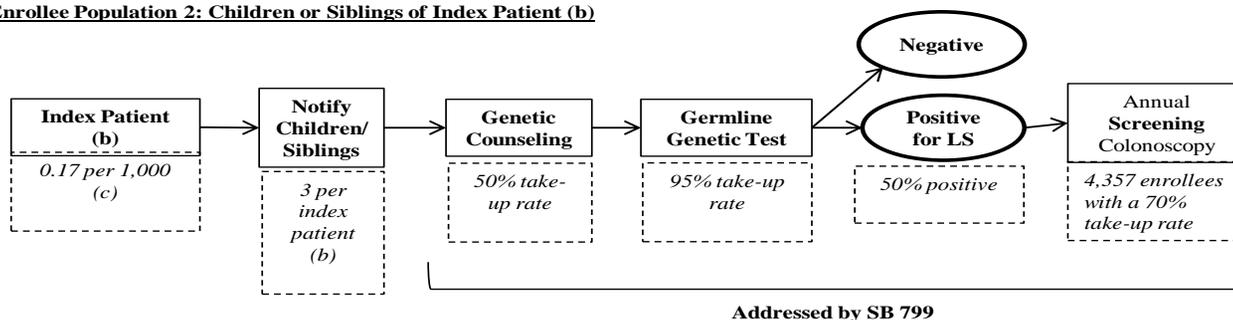
See Appendix D for a full description of utilization assumptions.

Figure 3. SB 799 and the Diagnosis and Management of Lynch Syndrome: Take-up Rates and Population Sizes

Enrollee Population 1: Persons with CRC



Enrollee Population 2: Children or Siblings of Index Patient (b)



Source: California Health Benefits Review Program, 2013.

Notes: (a) CDC, Wonder Database (b) “Index Patient” is defined as an individual with colorectal cancer (CRC) who has Lynch syndrome (LS). The index patients in “Enrollee Population 2” are inclusive of index patients identified in Population 1 and other possible index patients (e.g., patients older than 50 years of age or living out of state). (c) SEER Cancer data

Key: CRC=colorectal cancer; LS=Lynch syndrome.

Current Average Cost of Genetic Counseling, Genetic Testing, and Colonoscopies

The unit cost for genetic counseling is estimated to be \$156.77, for genetic testing \$549.48, and for a colonoscopy \$1,386.01. These unit costs reflect insurer information and may not reflect the charges a person may face if paying for noncovered benefits.

Current (Baseline) Premiums and Expenditures

Table 6 (at the end of this section) presents per member per month (PMPM) premandate estimates for premiums and expenditures by market segment. Prior to the mandate, total expenditures PMPM are \$549.37 in large-group DMHC-regulated plans, \$530.15 in small-group plans, and \$656.26 in individual plans. Total expenditures PMPM are \$705.72 in large-group CDI-regulated policies, \$821.91 in small-group policies, and \$468.82 in individual policies. The final column in Table 6 gives the total annual expenditures for all DMHC-regulated plans and CDI-regulated policies.

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

CHBRP estimated no shift in costs among private or public payers as a result of current benefit coverage. In the long term, to the extent that increased genetic counseling and testing for LS may lead to higher rates of screening colonoscopies that detect colon cancer, more treatment for colon cancer may occur for enrollees in both private and public plans and policies. Alternatively, the increased screening colonoscopies may identify colon cancer at earlier stages, thereby decreasing costs of treatments over the long term (Engel et al., 2010). These potential savings or costs were not estimated in the current analysis, because the CHBRP cost model examines the short-term impact of the proposed benefit coverage mandate. However, CHBRP examines the relevant literature and anticipated long-term cost impact of SB 799 later in this section, under *Impact on Long-Term Costs*.

Public Demand for Benefit Coverage

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 so not subject to state-level mandates) with the benefits that are provided by plans or policies that would be subject to the mandate.

On the basis of conversations with the largest collective bargaining agents in California, CHBRP concluded that unions *currently* do not include CRC-related genetic testing or screening in their health insurance negotiations. 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.

Given the lack of specificity in labor-negotiated benefits and the general match between health insurance that would be subject to the mandate and self-insured health insurance (not subject to state-level mandates), CHBRP concludes that public demand for coverage is essentially satisfied by the current state of the market.

Impacts of Mandated Benefit Coverage

How Would Changes in Benefit Coverage Related to the Mandate Affect the Availability of the Newly Covered Treatment/Service, the Health Benefit of the Newly Covered Treatment/Service, and the Per-Unit Cost?

Impact on access and health treatment/service availability

CHBRP found no anticipated impacts on the availability of genetic testing for LS or colonoscopies for the enrollees for which SB 799 would require increased benefit coverage. The utilization increase is small, as discussed below, and is not expected to alter existing capacity.

Impact on per-unit cost

As there is no evidence in the literature that increasing coverage for genetic testing or colonoscopies increases the prices of those treatments, CHBRP assumes that the unit cost of services that would be required under SB 799 would remain the same postmandate.

How Would Utilization Change As a Result of the Mandate?

Utilization is expected to increase as a result of an increase in mandate-compliant benefit coverage. CHBRP estimated the postmandate utilization rates of genetic counseling, genetic testing, and colonoscopies contingent on the same take-up rates for the relevant populations that would be covered under SB 799 as were presented in the *Current Utilization* section above.

Because premandate utilization management criteria regarding LS-related genetic counseling testing for enrollees younger than 50 years with CRC is compliant with SB 799, CHBRP estimates no postmandate increase in genetic counseling or testing for this population.

Because utilization management criteria regarding LS-related genetic counseling and testing for enrollees who are the children or siblings of an index patient would change, CHBRP expects a postmandate increase in utilization among this population. Reviewed examples of noncompliant utilization management criteria are broad; premandate, CHBRP estimates that four of five of the enrollees described by SB 799 would have been covered for LS-related genetic counseling and testing. Postmandate, CHBRP estimates that an additional 420 sessions of genetic counseling and 692 genetic tests among adult enrollees would be covered. Because sequential enrollee expenses

have a greater effect on the last step of a multi-step process, decreased enrollee expenses have a greater effect on utilization of the last step (testing) than on the first step (counseling). Please see Appendix D for a full explanation.

Because utilization management criteria regarding annual colonoscopy for LS+ enrollees who are the children or siblings of an index patient would change postmandate, CHBRP expects a postmandate increase in utilization among the population. Reviewed examples of noncompliant utilization management criteria are broad, covering biennial (alternate year) colonoscopy; premandate, CHBRP estimates that four of five of the enrollees described by SB 799 would have been covered for colonoscopy. Postmandate, CHBRP estimates that an additional 75 colonoscopies among adult enrollees would be covered (see Table 1). In later years, the number of additional screening colonoscopies may increase further, since SB 799 would mandate coverage for annual screening, and some plans previously only covered biennial (alternate year) colonoscopy screening for this population.

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

CHBRP assumes that if health care costs increase as a result of increased utilization or changes in unit costs, there is a corresponding proportional increase in administrative costs. CHBRP assumes that the administrative cost portion of premiums is unchanged. All health plans and insurers include a component for administration and profit in their premiums. CHBRP estimates that the increase in administrative costs of DMHC-regulated plans and CDI-regulated policies would remain proportional to the increase in premiums reported in Table 7.

Impact of the Mandate on Total Health Care Costs

SB 799 would increase total net annual expenditures by \$637,000, or 0.0004%, for the insured population (see Table 1 in *Executive Summary*). This is due to a \$774,000 total increase in health insurance premiums and a \$95,000 increase in enrollee expenses for covered benefits (copayment, etc), partially offset by a reduction in enrollee expenses for noncovered benefits (\$232,000).

Potential cost offsets or savings in the first 12 months after enactment (January 1 to December 31, 2014)

In some cases, an increase in cost due to an expansion in benefit coverage is accompanied by a decrease in the cost for other health care services, known as a “cost offset.” There is not sufficiently strong evidence to support health cost savings within the 1-year timeframe of this cost analysis. Therefore, CHBRP does not estimate a cost offset in the first year following implementation.

Impact on costs beyond the initial 12 months (post-December 31, 2014)

Costs in the long-term are likely to increase due to the additional expenses of tests and treatments. However, the literature finds that these health care services, when targeted towards CRC patients or immediate family members of CRC patients with LS, are highly cost-effective (Engel et al., 2010; Gudgeon et al., 2011; Mvundura et al., 2010; Wang et al., 2012). Mvundura et al. (2010), found that targeted genetic testing for LS similar to that in SB 799 have cost-

effectiveness ratios ranging from \leq \$25,000 per additional life-year to \leq \$75,000 per additional life-year. The targeted population approach provided increased life-years to those patients with LS in the range of what would be considered a cost-effective threshold (Grosse, 2008).

Engel et al. (2010) found that annual colonoscopies among those diagnosed with LS considerably reduced the stage at diagnosis of any CRC activity found in the annual screenings (only 2 out of 43 tumors found were of advanced stage). They compared multiple groups of patients with LS and determined some benefits to annual screenings for all, although that might be more limited among family members with no symptoms and no microsatellite instability.

Wang et al. (2012) determined that screening for LS costs roughly \$59,000 per “quality-adjusted life year” gained (QALY), which is in the range of the commonly accepted \$50,000 per QALY threshold (Grosse, 2008). Finally, Gudegeon et al. (2011) implemented and evaluated an LS screening intervention among CRC patients in their U.S. integrated healthcare delivery system. At \$25,000 per life-year saved, they determined that LS screening can potentially reduce mortality at a cost-effective rate.

In summary, the research literature agrees that screening for LS and annual colonoscopies of those diagnosed with LS is considered to be cost-effective over the long-term, resulting in increases in life-years and QALYs at acceptable cost effectiveness ratios.

Impacts for Each Category of Payer Resulting from the Benefit Mandate

Changes in expenditures and PMPM amounts by payer category

Increases in insurance premiums in SB 799 were enacted have some variation by market segment (Table 7). The increases range from 0.0000% for CalPERS HMOs to 0.0034% for the plans enrolling beneficiaries of the former Healthy Families Program. In dollar terms, while there are some aggregate total estimated cost increases, the increases round to \$0.00 for all market segments in terms of per member per month premium increases. In terms of total expenses, cost increases range from 0.0000% to 0.0032% across market segments.

Impacts on the Uninsured and Public Programs As a Result of the Cost Impacts of the Mandate

Changes in the number of uninsured persons as a result of premium increases

CHBRP estimates premium increases ranging from 0.0000% to 0.0034% for each market segment, and therefore CHBRP does not anticipate loss of health insurance, changes in availability of the benefit beyond those subject to the mandate, changes in offer rates of health insurance, changes in employer contribution rates, changes in take-up of health insurance by employees, or purchase of individual market policies, due to the small size of the increase in premiums after the mandate. This premium increase would not have a measurable impact on the number of persons who are uninsured.

Impact on public programs as a result of premium increases

CHBRP estimates that the mandate would produce no measurable impact on enrollment in publicly funded insurance programs or on utilization of covered benefits in the publicly funded insurance market.

Table 6. Baseline (Premandate) Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2014

	DMHC-Regulated							CDI-Regulated			Total
	Privately Funded Plans (by Market) (a)			CalPERS HMOs (b)	Medi-Cal Managed Care Plans			Privately Funded Policies (by Market) (a)			
	Large Group	Small Group	Individual		65 and Over (c)	Under 65	Medi-Cal/ Formerly Healthy Families Program (d)	Large Group	Small Group	Individual	
Total enrollees in plans/policies subject to state mandates (e)	11,289,000	2,479,000	1,029,000	854,000	688,000	5,203,000	626,000	539,000	1,315,000	1,877,000	25,899,000
Total enrollees in plans/policies subject to SB 799	11,289,000	2,479,000	1,029,000	854,000	688,000	5,203,000	626,000	539,000	1,315,000	1,877,000	25,899,000
Average portion of premium paid by employer	\$437.53	\$313.63	\$0.00	\$391.90	\$279.00	\$163.00	\$88.83	\$483.35	\$421.89	\$0.00	\$95,549,186,000
Average portion of premium paid by employee	\$83.30	\$169.52	\$546.88	\$97.98	\$0.00	\$0.00	\$8.79	\$135.14	\$190.22	\$305.75	\$34,912,666,000
Total premium	\$520.83	\$483.15	\$546.88	\$489.88	\$279.00	\$163.00	\$97.62	\$618.49	\$612.11	\$305.75	\$130,461,851,000
Enrollee expenses for covered benefits (deductibles, copays, etc.)	\$28.54	\$46.99	\$109.38	\$25.99	\$0.00	\$0.00	\$4.51	\$87.22	\$209.80	\$163.07	\$14,462,198,000
Enrollee expenses for benefits not covered (f)	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$232,000
Total expenditures	\$549.37	\$530.15	\$656.26	\$515.87	\$279.00	\$163.00	\$102.13	\$705.72	\$821.91	\$468.82	\$144,924,282,000

Source: California Health Benefits Review Program, 2013.

Note: (a) Includes enrollees with grandfathered and nongrandfathered health insurance, inside and outside the exchange.

(b) As of September 30, 2012, 57.5%, or 469,000, CalPERS members were state retirees, state employees, or their dependents. CHBRP assumes the same ratio for 2014.

(c) Medi-Cal Managed Care Plan expenditures for members over 65 include those who also have Medicare coverage.

(d) Children in Healthy Families, California's Children's Health Insurance Program, will be moved into Medi-Cal Managed Care by January 1, 2014, as part of the 2012–2013 budget.

(e) This population includes both persons who obtain health insurance using private funds (group and individual) and through public funds (e.g., CalPERS HMOs, Medi-Cal Managed Care Plans). Only those enrolled in health plans or policies regulated by the DMHC or CDI are included. Population includes all enrollees in state-regulated plans or policies aged 0 to 64 years, and enrollees 65 years or older covered by employer-sponsored health insurance.

(f) Includes only those expenses that are paid directly by enrollees or other sources to providers for services related to the mandated benefit that are not currently covered by insurance. This only includes those expenses that will be newly covered, postmandate. Other components of expenditures in this table include all health care services covered by insurance. Expenses per member per month at the market level round to zero, but the total overall does not.

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

Table 7. Impacts of the Mandate on Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2014

	DMHC-Regulated							CDI-Regulated			Total
	Privately Funded Plans (by Market) (a)			CalPERS HMOs (b)	Medi-Cal Managed Care Plans			Privately Funded Policies (by Market) (a)			
	Large Group	Small Group	Individual		65 and Over (c)	Under 65	Medi- Cal/Formerly Healthy Families Program (d)	Large Group	Small Group	Individual	
Total enrollees in plans/policies subject to state mandates (e)	11,289,000	2,479,000	1,029,000	854,000	688,000	5,203,000	626,000	539,000	1,315,000	1,877,000	25,899,000
Total enrollees in plans/policies subject to SB 799	11,289,000	2,479,000	1,029,000	854,000	688,000	5,203,000	626,000	539,000	1,315,000	1,877,000	25,899,000
Average portion of premium paid by employer (f)	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$572,000
Average portion of premium paid by employee (f)	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$202,000
Total premium (f)	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$774,000
Enrollee expenses for covered benefits (deductibles, copays, etc.) (f)	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$95,000
Enrollee expenses for benefits not covered (f)(g)	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	-\$232,000
Total expenditures (f)	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$0.00	\$636,000
Percentage impact of mandate											
Insured premiums	0.0004%	0.0006%	0.0003%	0.0000%	0.0000%	0.0021%	0.0034%	0.0006%	0.0005%	0.0012%	0.0006%
Total expenditures	0.0003%	0.0004%	0.0002%	0.0000%	0.0000%	0.0020%	0.0032%	0.0004%	0.0003%	0.0006%	0.0004%

Source: California Health Benefits Review Program, 2013.

Note: (a) Includes enrollees with grandfathered and nongrandfathered health insurance, inside and outside the exchange.

(b) As of September 30, 2012, 57.5%, or 469,000, of CalPERS members were state retirees, state employees, or their dependents. CHBRP assumes the same ratio for 2014.

(c) Medi-Cal Managed Care Plan expenditures for members over 65 include those who also have Medicare coverage.

(d) Children in Healthy Families, California's Children's Health Insurance Program, will be moved into Medi-Cal Managed Care by January 1, 2014, as part of the 2012–2013 budget.

(e) This population includes both persons who obtain health insurance using private funds (group and individual) and through public funds (e.g., CalPERS HMOs, Medi-Cal Managed Care Plans). Only those enrolled in health plans or policies regulated by the DMHC or CDI are included. Population includes all enrollees in state-regulated plans or policies aged 0 to 64 years, and enrollees 65 years or older covered by employer-sponsored health insurance.

(f) Expenses per member per month at the market level round to zero, but the total overall does not.

(g) Includes only those expenses that are paid directly by enrollees or other sources to providers for services related to the mandated benefit that are not currently covered by insurance. This only includes those expenses that will be newly covered, postmandate. Other components of expenditures in this table include all health care services covered by insurance.

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

PUBLIC HEALTH IMPACTS

As discussed in the *Introduction*, SB 799 would mandate coverage for genetic testing for LS in enrollees younger than 50 years who have been diagnosed with CRC, and for enrollees who are the children or siblings (relatives) of a person diagnosed with CRC who is LS+ (an index patient). SB 799 would require coverage for annual CRC screenings, such as colonoscopies, for LS+ enrollees who are relatives of an index patient (see Table 2).

This section presents the overall public health impact of SB 799, followed by an analysis estimating the bill's impact on gender and racial/ethnic disparities, premature death, societal economic losses, and long-term outcomes. Because CHBRP estimates that almost all enrollees diagnosed with CRC already have mandate-compliant coverage for LS genetic testing, the public health analysis focuses on the marginal impacts for those enrollees who are the relatives of index patients.

Estimated Public Health Outcomes

As presented in the *Medical Effectiveness* section, guidelines recommend that family members of persons diagnosed with CRC and LS be notified, receive genetic counseling, and undergo germline genetic testing. *Medical Effectiveness* found a preponderance of evidence that, among family members of LS+ CRC patients who are offered genetic counseling, approximately 50% obtain counseling, and 79% to 95% of those who obtain counseling will undergo genetic testing. Additionally, guidelines recommend colonoscopy for LS carriers every 1 to 2 years to reduce CRC-related morbidity and mortality.

Furthermore, CHBRP found that colonoscopy screening at the recommended intervals in LS+ persons can reduce mortality and morbidity because lesions can be detected at a precancerous stage and removed before they become cancerous. *Medical Effectiveness* found that LS+ persons who opt to receive recommended CRC screening experience a significant reduction in the risk of developing CRC compared with those who opt not to do so. A decision analysis by Syngal et al. (1998) estimated the colonoscopy screening among LS+ persons would result in approximately 14 quality-adjusted life years per individual screened compared to LS+ persons who did not receive screening. Screening for LS and frequent colonoscopies of those diagnosed with LS is considered to be cost-effective over the long-term, resulting in increases in life-years and quality-adjusted life years (QALYs) (see *Benefit Coverage, Utilization, and Cost Impacts* section).

As presented in the *Benefit Coverage, Utilization, and Cost Impacts* section, CHBRP estimates that about 700 additional enrollees would use genetic counseling and testing for LS and about 75 additional enrollees would undergo screening colonoscopies in the first year postmandate.

CHBRP projects that SB 799 would increase the use of genetic counseling and testing for LS and screening colonoscopies for LS+ relatives; however, CHBRP projects no measurable public health impact (at the population level) on the rates of CRC-LS mortality and morbidity in the first year, postmandate, due to the small number of additional enrollees who would use mandate-relevant services.

Although CHBRP finds SB 799 provides no overall public health impact at the population level in California, *the proposed mandate would likely yield health and quality of life improvements at the individual level for enrollees using additional mandate-relevant services.* Genetic testing for relatives of LS+ persons has many benefits, including reliably differentiating between family members who are LS mutation carriers and LS noncarriers, who would not require frequent colorectal screening (Ahnen et al., 2012).

Potential Harms from Genetic Testing and Colonoscopy

When data are available, CHBRP estimates the marginal change in harms associated with services affected by the proposed mandate. In the case of SB 799, potential harms exist with genetic testing and colonoscopies.

Genetic testing

As discussed in the *Medical Effectiveness* section, the preponderance of evidence suggests that genetic counseling reduces anxiety about genetic testing and that there is no long-term difference in psychological distress between persons who are tested and found to have LS and those who are found to not have LS. Therefore, CHBRP does not estimate any additional harm to the additional enrollees who would use genetic counseling and testing due to SB 799.

Colonoscopy

As noted in the *Medical Effectiveness* section, the preponderance of evidence suggests that colonoscopies are associated with a small increase in potential harms associated with the procedure, including perforation, bleeding, and death. The *Benefit Coverage, Utilization, and Cost Impacts* section estimates that about 75 additional screening colonoscopies would occur in the first postmandate year among LS+ enrollees. Given that one systematic review estimated that for every 1,000 colonoscopies performed there were 1.1 bowel perforations, 3.3 episodes of bleeding, and 0.08 deaths within 30 days of the colonoscopy (Palomaki et al., 2009), CHBRP does not estimate any significant harms occurring in this population of about 75 additional enrollees.

Based on a review of the literature on potential harms, CHBRP concludes that the risk of possible psychological harms from genetic testing or physical harms from colonoscopy are small compared to the advantages conferred through early identification of LS status and subsequent CRC screening to identify precancerous lesions or early-stage CRC.

Estimated Impact on Financial Burden for Enrollees

SB 799 would decrease the financial burden (enrollee expenses for uncovered services) for enrollees who use genetic testing, and the enrollees who use colonoscopy postmandate. The *Benefit Coverage, Utilization, and Cost Impacts* section estimates an *increase* in enrollee out-of-pocket expenses for covered benefits (+\$95,000) and a *decrease* in expenditures for noncovered benefits postmandate (-\$232,000). Therefore, the additional enrollees with uncovered expenses premandate would receive a \$137,000 net reduction in their financial burden associated with genetic testing and colonoscopy postmandate.

CHBRP estimates that SB 799 would modify coverage and reduce the net financial burden by \$137,000 in the first year, postmandate, for enrollees who would be mandate-eligible for genetic testing and colonoscopy.

CHBRP notes that the cost savings to these additional enrollees (associated with newly covered genetic tests and colonoscopies) reflect the negotiated prices achieved by insurance carriers, but may not translate to the retail market. Estimates of retail prices for genetic tests range from \$800 to \$1300 per gene test while CHBRP claims data reflect a \$344 unit cost for gene tests; therefore, the savings to these enrollees may be greater than CHBRP estimates (EGAPP, 2009; Ladabaum et al., 2011; Mvundura et al., 2010).

Impact on Gender and Racial Disparities

Several competing definitions of “health disparities” exist. CHBRP relies on the following definition:

A health disparity/inequality is a particular type of difference in health or in the most important influences of health that could potentially be shaped by policies; it is a difference in which disadvantaged social groups (such as the poor, racial/ethnic minorities, women or other groups that have persistently experienced social disadvantage or discrimination) systematically experience worse health or great health risks than more advantaged groups (Braveman, 2006).

Impact on Gender Disparities

As presented in the *Background* section, the lifetime risk for CRC among males and females in the general population is approximately 5%. In 2009, the age-adjusted CRC-incidence rate among males was 19.2 cases per 100,000 and 15.0 cases per 100,000 among females. The lifetime risk for CRC is significantly higher among persons with LS. By gender, the lifetime risk for LS+ males is higher than that of LS+ females (45% vs. 35%). However, CHBRP found no literature on whether the prevalence of LS differed by gender. Assuming the prevalence of LS is equal among males and females, using 2009 CRC incidence data, CHBRP estimates there are approximately 101 LS+ males with CRC and approximately 81 LS+ females with CRC (see Table 2). Several studies analyzing factors associated with use of genetic counseling and testing

for LS and adherence to screening colonoscopy among LS+ family members found that gender was not associated with counseling, testing, or screening uptake (Hadley et al., 2008; Halbert et al., 2004; Stoffel et al., 2010).

It is unknown whether there are gender disparities in the prevalence of LS-related CRC. CHBRP found no evidence indicating differential use of genetic counseling or testing for LS by males or females, or difference in adherence to screening colonoscopy by gender among LS carriers. CHBRP estimates that, despite SB 799 increasing use of these services and possible gender disparities in LS prevalence, the bill would have no public health impact in the first year postmandate on gender disparities due to no gender differences in uptake of services and the small number of additional enrollees benefiting from SB 799.

Impact on Racial/Ethnic Disparities

Evaluating the impact on racial and ethnic health disparities is particularly important because racial and ethnic minorities report having poorer health status and worse health indicators (KFF, 2007). One important contributor to racial and ethnic health disparities is differences in the prevalence of insurance, where minorities are more likely than whites to be uninsured. However, coverage disparities still exist within the insured population and may contribute to gaps in access and/or utilization among those covered (Kirby et al., 2006; Lille-Blanton and Hoffman, 2005; Rosenthal et al., 2008). To the extent that racial/ethnic groups are disproportionately distributed among policies with more or less coverage, a mandate bringing all policies to parity may impact an existing disparity.

CHBRP analyses are limited to the insured population (because the uninsured would not be affected by a health benefit mandate). Therefore, to assess a mandate's possible effects on health disparities (assuming the covered intervention is medically effective), CHBRP must answer two questions:

- (1) Are there known racial/ethnic disparities in the prevalence or incidence of LS; and
- (2) Are there known racial/ethnic disparities in premandate benefit coverage and/or utilization?

As presented in the *Background* section, in California in 2009, black or African Americans had the highest age-adjusted CRC rate (24.9 per 100,000), followed by Asian or Pacific Islanders (17.2 per 100,000) and whites (17.1 per 100,000). During the same year, a similar trend is seen in age-adjusted mortality rates—black or African Americans had the highest rate (7.4 per 100,000), followed by whites (4.4 per 100,000) and Asian or Pacific Islanders (3.8 per 100,000). However, when applying the estimated 3% prevalence of LS across the number of CRCs diagnosed, whites have the highest number of LS-attributable CRC cases (95 cases), followed by Hispanics (40 cases), Asian or Pacific Islanders (27 cases), and black or African Americans (17) (USDHHS, 2011).

CHBRP found no literature addressing racial/ethnic differences in the utilization of genetic counseling or testing for LS, adherence to screening colonoscopy among LS+ relatives, or reductions in LS-attributable CRC mortality. Although studies report that among average risk

persons, Hispanics and African Americans are less likely to adhere to current colorectal guidelines (Ata et al., 2006; James et al., 2006). CHBRP is unable to determine whether adherence would be different after a diagnosis of LS.

There are racial/ethnic disparities in the prevalence of CRC, but it is unknown whether the disparities extend to the LS-related CRCs in California. Although CHBRP estimates a small increase in uptake of genetic counseling and testing and screening colonoscopy, CHBRP is unable to estimate how these changes in the utilization might vary by race or ethnicity. In addition, any potential statewide racial/ethnic disparities in LS-related CRC morbidity and mortality are unlikely to be measurably affected, due to the small increase in use utilization that would result from SB 799.

Impacts on Premature Death and Economic Loss

Premature death is often defined as death before the age of 75 years (Cox, 2006). The overall impact of premature death due to a particular disease can be measured in years of potential life lost prior to age 75 and summed for the population (generally referred to as “YPLL”) (Cox, 2006; Gardner and Sanborn, 1990). In California, it is estimated that there are nearly 102,000 premature deaths each year, accounting for more than two million YPLL (CDPH, 2013; Cox, 2006). In order to measure the impact of premature mortality across the population impacted by a proposed mandate, CHBRP first collects baseline mortality rates. Next, the literature is examined to determine whether the proposed mandated benefit impacts mortality and whether YPLL have been established for the given condition. Some diseases and conditions do not result in death, and therefore a mortality outcome is not relevant.

Economic loss associated with disease is generally presented in the literature as an estimation of the value of the YPLL in dollar amounts (i.e., valuation of a population’s lost years of work over a lifetime). For CHBRP analyses, a literature review is conducted to determine whether lost productivity has been established in the literature. In addition, morbidity associated with the disease or condition of interest can also result in lost productivity by causing the worker to miss days of work either due to their illness or due to their role as a caregiver for someone else who is ill.

Premature Death

Colonoscopy impacts on Lynch Syndrome-related CRC mortality

As discussed in the *Medical Effectiveness* section, there is a preponderance of evidence that frequent colonoscopies among LS+ family members reduce CRC-related mortality. Evidence from two studies comparing CRC-related mortality rates among LS+ relatives receiving colonoscopies to those who did not found that screening is associated with a 62% to 81% reduction in death from CRC (Jarvinen et al., 2000; Stuckless et al., 2012). Stupart et al. (2009) compared survival among a prospective cohort of persons with LS who chose to either receive or decline screening colonoscopy. Among those receiving screenings, median survival from birth was 78 years and median CRC-free survival from birth was 73 years, compared to median survival of 55 years and 47 years of CRC-free survival among those who did not receive

screenings. CHRBP was unable to find any literature on the number of deaths averted among LS+ family members due to screening colonoscopy.

Although mortality may be decreased for LS+ enrollees by 62% to 81% through frequent colonoscopy screening, CHRBP is unable to quantify a reduction in mortality due to a lack of relevant literature. However, CHRBP concludes that increased screening colonoscopy among LS+ enrollees would likely contribute to a reduction in CRC deaths in California beyond the first year, postmandate.

Economic Loss

In 2010, the National Cancer Institute (NCI) estimated the average annual cost of CRC was \$14 billion, and by 2020, the cost is estimated to reach nearly \$17.5 billion (NCI, 2013). A study by The Lewin Group for the American Gastroenterological Association estimated that in 1998, working-age CRC patients were hospitalized for approximately 2.3 million days, which is the equivalent of nearly \$71 million in lost wages (in 1998 dollars) (AGA, 2001). In 2005, Bradley et al. (2011) estimated lost productivity costs due to CRC to be \$21 billion. However, CHRBP was unable to find any literature specific to economic loss related to CRC caused by LS or related to screening among LS+ family members.

The SB 799-related increase in those diagnosed with LS who undergo screening colonoscopy is unlikely to measurably alter the overall societal economic loss due to lost wages and lost productivity attributable to CRC.

Long-Term Public Health Impacts

In the long term, the number of Californians enrolled in DMHC-regulated plans or CDI-regulated policies who become eligible for genetic testing and subsequent annual colonoscopy due to SB 799 would likely compound annually (due to notification and testing of relatives of index patients). For example, Bellcross et al. (2012) estimated that if LS genetic screening were performed routinely on CRC patients in the U.S., about 4,200 CRC patients would be diagnosed with LS annually. In turn, the newly diagnosed index patient would be able to notify an average of four first-degree relatives, who have a 50% chance of being LS+, thus increasing the number to about 8,000 newly diagnosed LS+ persons annually. About half of them (~4,000) would be expected to develop CRC over a lifetime, and for those who had colonoscopies at the recommended 1-3 year interval, CRC would be prevented in about half of those cases. CHRBP would expect a proportionately similar increase in the number of LS+ persons receiving screening colonoscopies postmandate.

The long-term impacts of SB 799 also have the potential to increase the quality of life for patients diagnosed with either LS or LS-related CRC through the increased genetic counseling, testing, and screening colonoscopies. As described in the *Cost* section, two studies found that LS screening of CRC patients fell into a commonly accepted cost-effectiveness ratio range of \$59,000 to \$25,000 per quality-adjusted life year gained (QALY), which is in the range of the commonly accepted \$50,000 per QALY threshold (Grosse, 2008; Gudegeon et al., 2011).

In summary, the preponderance of evidence shows that screening for LS and screening colonoscopies for LS+ persons at recommended levels are considered to be cost-effective over the long-term, resulting in increases in life-years and commonly acceptable quality-adjusted-life-year cost-effectiveness ratios.

SB 799 would mandate coverage for annual colonoscopies for an increasing number of LS+ enrollees, thus reducing their risk for cancer, premature death, and associated lost productivity, but at an increased cost.

APPENDICES

Appendix A: Text of Bill Analyzed

On April 9, 2013, the Senate Committee on Health requested that CHBRP analyze SB 799.

Below is the bill language, as it was amended on April 1, 2013. The Bill Author has indicated to CHBRP that the bill will be amended again to define “frequent screenings” as “annual screenings.” CHBRP, with agreement from the requesting Health Committee, has analyzed the text as it will be amended. In the text below, [annual] has been inserted to indicate the intended amendments.

BILL NUMBER: SB 799 AMENDED
BILL TEXT

AMENDED IN SENATE APRIL 1, 2013

INTRODUCED BY Senator Calderon

FEBRUARY 22, 2013

An act to ~~amend Section 127405 of~~ add
Section 1367.667 to, and to add Article 4 (commencing with Section
104201) to Chapter 2 of Part 1 of Division 103 of, the Health
and Safety Code, and to add Section 10123.22 to the
Insurance Code, relating to ~~hospitals~~
health care coverage .

LEGISLATIVE COUNSEL'S DIGEST

SB 799, as amended, Calderon. ~~Hospitals: fair pricing.~~
Health care coverage: colorectal cancer: genetic
testing and screening.

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 the act a crime. Existing law also provides for the regulation of health insurers by the Department of Insurance. Existing law requires individual and group health care service plan contracts and health insurance policies to provide coverage for all generally medically accepted cancer screening tests and requires those contracts and policies to also provide coverage for the treatment of breast cancer. Existing law requires an individual or small group health care service plan contract or insurance policy issued, amended, or renewed on or after January 1, 2014, to, at a minimum, include coverage for essential health benefits, which includes preventive services, pursuant to the federal Patient Protection and Affordable Care Act.

This bill would require a health care service plan contract or a health insurance policy, except as specified, that is issued, amended, or renewed on or after January 1, 2014, to provide coverage

for genetic testing for hereditary nonpolyposis colorectal cancer (HNPCC) and screening for colorectal cancer under specified circumstances. Because a willful violation of the bill's requirements relative to health care service plans would be a crime, the bill would impose a state-mandated local program.

This bill would also require a physician and surgeon who makes a diagnosis that a patient has colorectal cancer to provide the patient with specified information.

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.

~~Existing law requires each hospital to maintain an understandable written policy regarding discount payments for financially qualified patients as well as an understandable written charity care policy. Uninsured patients or patients with high medical costs who are at or below 350% of the federal poverty level, as defined, are eligible to apply for participation under a hospital's charity care policy or discount payment policy.~~

~~This bill would make a technical, nonsubstantive change to that provision.~~

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

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

SECTION 1. Section 1367.667 is added to the Health and Safety Code , to read:

1367.667. Every health care service plan contract, except a specialized health care service plan contract, that is issued, amended, or renewed on or after January 1, 2014, shall provide coverage for all of the following:

(a) Genetic testing for hereditary nonpolyposis colorectal cancer (HNPCC) for an enrollee who is under 50 years of age and has been diagnosed with colorectal cancer.

(b) Genetic testing for HNPCC for an enrollee who is the child or sibling of an individual who has been diagnosed with colorectal cancer and has tested positive for the gene mutation for HNPCC.

(c) Frequent [annual] screenings, including colonoscopies, for an enrollee who has tested positive for the gene mutation for HNPCC, and is the child or sibling of an individual who has been diagnosed with colorectal cancer and has tested positive for the gene mutation for HNPCC.

SEC. 2. Article 4 (commencing with Section 104201) is added to Chapter 2 of Part 1 of Division 103 of the Health and Safety Code , to read:

Article 4. Colorectal Cancer

104201. If a physician and surgeon makes a diagnosis that a patient has colorectal cancer, the physician and surgeon shall recommend that the patient be tested for the genetic mutation for

hereditary nonpolyposis colorectal cancer (HNPCC). The physician and surgeon shall also inform the patient that genetic testing for HNPCC may be covered by the patient's health care coverage, and that genetic testing and screening for his or her children or siblings may be covered by the children's or siblings' health care coverage if the patient tests positive for the HNPCC gene mutation.

SEC. 3. Section 10123.22 is added to the Insurance Code , to read:

10123.22. Every health insurance policy, except a specialized health insurance policy, that is issued, amended, or renewed on or after January 1, 2014, shall provide coverage for all of the following:

(a) Genetic testing for hereditary nonpolyposis colorectal cancer (HNPCC) for an insured who is under 50 years of age and has been diagnosed with colorectal cancer.

(b) Genetic testing for HNPCC for an insured who is the child or sibling of an individual who has been diagnosed with colorectal cancer and has tested positive for the gene mutation for HNPCC.

(c) Frequent [annual] screenings, including colonoscopies, for an insured who has tested positive for the gene mutation for HNPCC, and is the child or sibling of an individual who has been diagnosed with colorectal cancer and has tested positive for the gene mutation for HNPCC.

SEC. 4. No reimbursement is required by this act pursuant to Section 6 of Article XIII B of the California Constitution because the only costs that may be incurred by a local agency or school district will be incurred because this act creates a new crime or infraction, eliminates a crime or infraction, or changes the penalty for a crime or infraction, within the meaning of Section 17556 of the Government Code, or changes the definition of a crime within the meaning of Section 6 of Article XIII B of the California Constitution.

~~SECTION 1. Section 127405 of the Health and Safety Code is amended to read:~~

~~127405. (a) (1) (A) Each hospital shall maintain an understandable written policy regarding discount payments for financially qualified patients as well as an understandable written charity care policy. Uninsured patients or patients with high medical costs who are at or below 350 percent of the federal poverty level, as defined in subdivision (b) of Section 127400, shall be eligible to apply for participation under a hospital's charity care policy or discount payment policy. Notwithstanding any other provision of this article, a hospital may choose to grant eligibility for its discount payment policy or charity care policies to patients with incomes over 350 percent of the federal poverty level. Both the charity care policy and the discount payment policy shall state the process the hospital uses to determine whether a patient is eligible for charity care or discounted payment. In the event of a dispute, a patient may seek review from the business manager, chief financial officer, or other appropriate manager as designated in the charity care policy and the discount payment policy.~~

~~(B) The written policy regarding discount payments shall also include a statement that an emergency physician, as defined in Section 127450, who provides emergency medical services in a hospital that provides emergency care is also required by law to provide discounts to uninsured patients or patients with high medical costs who are at or below 350 percent of the federal poverty level. This~~

~~statement shall not be construed to impose any additional responsibilities upon the hospital.~~

~~— (2) Rural hospitals, as defined in Section 124840, may establish eligibility levels for financial assistance and charity care at less than 350 percent of the federal poverty level as appropriate to maintain their financial and operational integrity.~~

~~— (b) A hospital's discount payment policy shall clearly state eligibility criteria based upon income consistent with the application of the federal poverty level. The discount payment policy shall also include an extended payment plan to allow payment of the discounted price over time. The policy shall provide that the hospital and the patient may negotiate the terms of the payment plan.~~

~~— (c) The charity care policy shall state clearly the eligibility criteria for charity care. In determining eligibility under its charity care policy, a hospital may consider income and monetary assets of the patient. For purposes of this determination, monetary assets shall not include retirement or deferred compensation plans qualified under the Internal Revenue Code, or nonqualified deferred compensation plans. Furthermore, the first ten thousand dollars (\$10,000) of a patient's monetary assets shall not be counted in determining eligibility, nor shall 50 percent of a patient's monetary assets over the first ten thousand dollars (\$10,000) be counted in determining eligibility.~~

~~— (d) A hospital shall limit expected payment for services it provides to a patient at or below 350 percent of the federal poverty level, as defined in subdivision (b) of Section 127400, eligible under its discount payment policy to the amount of payment the hospital would expect, in good faith, to receive for providing services from Medicare, Medi-Cal, the Healthy Families Program, or another government sponsored health program of health benefits in which the hospital participates, whichever is greater. If the hospital provides a service for which there is no established payment by Medicare or any other government-sponsored program of health benefits in which the hospital participates, the hospital shall establish an appropriate discounted payment.~~

~~— (e) A patient, or patient's legal representative, who requests a discounted payment, charity care, or other assistance in meeting his or her financial obligation to the hospital shall make every reasonable effort to provide the hospital with documentation of income and health benefits coverage. If the person requests charity care or a discounted payment and fails to provide information that is reasonable and necessary for the hospital to make a determination, the hospital may consider that failure in making its determination.~~

~~— (1) For purposes of determining eligibility for discounted payment, documentation of income shall be limited to recent pay stubs or income tax returns.~~

~~— (2) For purposes of determining eligibility for charity care, documentation of assets may include information on all monetary assets, but shall not include statements on retirement or deferred compensation plans qualified under the Internal Revenue Code, or nonqualified deferred compensation plans. A hospital may require waivers or releases from the patient or the patient's family, authorizing the hospital to obtain account information from financial or commercial institutions, or other entities that hold or maintain the monetary assets, to verify their value.~~

~~— (3) Information obtained pursuant to paragraph (1) or (2) shall~~

~~not be used for collections activities. This paragraph does not prohibit the use of information obtained by the hospital, collection agency, or assignee independently of the eligibility process for charity care or discounted payment.~~

~~— (4) Eligibility for discounted payments or charity care may be determined at any time the hospital is in receipt of information specified in paragraph (1) or (2), respectively.~~

Appendix B: Literature Review Methods

Appendix B describes methods used in the medical effectiveness literature review conducted for SB 799. A discussion of CHBRP's system for grading evidence, as well as lists of MeSH Terms, Publication Types, and Keywords, follows.

The literature search included studies published in English from 2006 to the present. The search was limited to abstracts of studies published in English. The search was also limited to studies published from 2006 to the present because CHBRP previously retrieved the AHRQ Evidence Report/Technology Assessment, Hereditary Nonpolyposis Colorectal Cancer: Diagnostic Strategies and Their Implications (AHRQ, 2007) that is a comprehensive systematic review of the literature up until 2006. The following databases of peer-reviewed literature were searched: MEDLINE (PubMed), the Cochrane Library, and the Web of Science. In addition, Web sites maintained by the following organizations that index or publish systematic reviews and evidence-based guidelines were searched: National Cancer Institute PDQ, American Cancer Society, American Gastroenterological Association, National Guideline Clearinghouse, and U.S. Preventative Services Task Force.

Two 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. Abstracts for 382 articles were found in the literature review, 57 were reviewed for potential inclusion in this report, and a total of 30 studies were added to the medical effectiveness review for SB 799.

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*.⁴¹ 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.

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:

⁴¹ Available at: www.chbrp.org/analysis_methodology/docs/medeffect_methods_detail.pdf.

- Clear and convincing evidence;
- Preponderance of evidence;
- Ambiguous/conflicting 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. This can be further subdivided into preponderance of evidence from high-quality studies and preponderance of evidence from low-quality studies.

A grade of *ambiguous/conflicting 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

The search terms used to locate studies relevant to SB 799 were as follows:

MeSH Terms Used to Search PubMed

- Anxiety/psychology
- Colectomy
- Colonic Neoplasms/diagnosis/genetics
- Colonoscopy
- Colorectal Neoplasms, Hereditary Nonpolyposis/diagnosis/epidemiology/genetics/psychology/surgery
- Cost and Benefit Analysis
- Cost of Illness
- DNA Methylation/genetics
- DNA Mutational Analysis
- Gender disparities
- Genetic Counseling/psychology/utilization
- Genetic Testing/economics/psychology/utilization
- Genetic Predisposition to Disease
- Germ-Line Mutation/genetics
- Follow-up Studies
- Guideline Adherence
- Health Knowledge, Attitudes, Practice
- Human

- Immunohistochemistry
- Insurance Coverage
- Mass Screening/ methods
- Microsatellite Instability
- Morbidity
- Mortality
- MutS Homolog 2 Protein/genetics
- Neoplasms, Second Primary
- Patient Acceptance of Health Care/psychology
- Population Surveillance
- Practice Guidelines as Topic
- Predictive Value of Tests
- Prevalence
- Proto-Oncogene Proteins B-raf/genetics
- Quality-Adjusted Life Years
- Quality of Life
- Racial disparities
- Risk Assessment
- Sensitivity and Specificity
- Stress, Psychological

Keywords used to search PubMed, Cochrane Library, and Web of Science

- Anxiety
- Benefit coverage
- BRAF testing
- Colectomy
- Colonoscopic surveillance
- Colonoscopy
- Cost effectiveness
- DNA mutation
- Economic burden/loss
- Effective
- Efficacy
- Financial burden
- Genetic counseling
- Genetic testing
- Germline genetic testing
- Harm
- Health-adjusted life expectancy
- Hereditary non-polyposis
- HMSH1
- HMSH2
- HMSH6
- HNPCC
- HPMS1
- HPMS2
- Immunohistochemistry
- Insurance coverage
- Lynch syndrome
- Metachronous cancer
- Microsatellite instability
- MLH1
- MMR
- Morbidity
- Mortality
- MSH2
- MSH6
- Out of pocket
- Practice guideline
- Premature death

- Prevalence
- Psychosocial
- Quality of life
- Quality adjusted life expectancy
- Screening
- Sensitivity and specificity
- Stress
- Subtotal surgery
- Take up
- Unmet demand
- Validity

Publication Types

- Clinical Trial
- Comparative Study
- Controlled Clinical Trial
- Meta-Analysis
- Practice Guideline
- Systematic Reviews
- Randomized Control Trial

Appendix C: Summary Findings on Medical Effectiveness

Appendix C describes the meta-analyses, systematic reviews, and individual studies on screening tests for LS that were analyzed by the medical effectiveness team. Table C-1 describes the type of research design, the populations studied, and the intervention and comparison groups. Tables C-2 through C-7 summarize the findings from the studies included in the medical effectiveness review.

Table C-1. Characteristics of Studies That Examined the Effectiveness of Genetic Testing for Lynch Syndrome and Colorectal Screening

Type of Intervention	Citation	Type of Trial	Intervention versus Comparison Group	Population Studied	Location
Lynch syndrome (LS)					
<i>Studies</i>					
HNPCC diagnostic strategies	Bonis et al., 2007	Evidence report / Systematic review	A review of over 100 studies examining a range of diagnostic strategies and their implications for those suspected of having HNPCC. The main objectives were to assess the sensitivity, specificity, and reliability of tumor and genetic tests, to summarize the accuracy of these tests, and to describe the ratio of benefits to harms for patients with a CRC diagnosis and their family members needing screening.	The populations included in these studies are those diagnosed with CRC as well as high risk family members of those found to have LS.	Global
Genetic counseling and genetic testing followed by surveillance colonoscopy	Burton-Chase et al., 2013	Longitudinal Screening study	All study members underwent counseling before genetic testing. Phone questionnaires were conducted at 6 months and twelve months after test results. The study was divided into two groups; those who tested positive for LS, and those who tested negative. Surveillance colonoscopy data uses the negative vs. positive groups as comparisons.	Study members were relatives of CRC patients who had tested positive for LS who were referred to the study.	Texas, USA

Table C-1. Characteristics of Studies That Examined the Effectiveness of Genetic Testing for Lynch Syndrome and Colorectal Screening (Cont'd)

Type of Intervention	Citation	Type of Trial	Intervention versus Comparison Group	Population Studied	Location
Psychological measures and surveillance colonoscopy after genetic screening	Collins et al., 2007	Cohort study	Questionnaires were sent to all persons before testing, then follow-up questionnaires were sent at 2 weeks, 4 months, 12 months, and 3 years after receiving testing results. Groups were divided into those with HNPCC positive test vs. those with a negative test.	Study included persons undergoing predictive genetic testing for HNPCC. Only those with no history of CRC, or other HNPCC related cancers were included in this study.	Australia
Decrease in mortality due to colonoscopy surveillance	de Jong et al., 2006	Cohort study	Cancer mortality in the LS cohort was compared to cancer mortality in the general Dutch population, using computation of standardized mortality ratio (SMR).	Participants were family members in a registry. Cohort members were eligible if they had one family member with a germline mutation in one of the MMR genes. Only subjects alive at or after 1960 were included due to availability of mortality rates. Only those with a 50% probability of being a carrier were selected for this study.	Netherlands
Surveillance colonoscopy 3-5 year intervals	Järvinen et al., 2000	Controlled cohort study	15-year study that had two arms; selection to the intervention versus control group was free choice, and not randomized. The study group received colonoscopies at 3-year intervals during most of the study, but at the start of the study, 5-year screening intervals were used. The control subjects underwent no screening. Genetic testing was only offered to those from families who had a known mutation.	Registry subjects were asymptomatic family members from 22 HNPCC families that had a 50% risk of being mutation carriers, aged 20-66 years old. The control subjects were not actively contacted after 1986, unless they requested screening.	Helsinki, Finland

Table C-1. Characteristics of Studies That Examined the Effectiveness of Genetic Testing for Lynch Syndrome and Colorectal Screening (Cont'd)

Type of Intervention	Citation	Type of Trial	Intervention versus Comparison Group	Population Studied	Location
DNA testing aimed at reducing morbidity and mortality	Palomaki et al., 2009	Evidence review	This review reports on several aspects of DNA testing around LS and analyzes not only the clinical validity, but also looks at psychosocial benefits and harms, as well as evidence for colonoscopy surveillance for those identified with LS. This review also provides a section on definitions used for this genetic disease and provides justification for the chosen language.	The populations of the included studies are newly diagnosed cases of CRC. Included studies were found using a nonsystematic review of the literature with a specific literature search completed for each questions addressed in the review. Literature included was ranked from 1-4, with 1 being the highest quality.	Global
Genetic screening uptake and appropriateness of surveillance colonoscopies every 1-2 years	Stoffel et al., 2010	Cross-sectional surveillance study	Cross-sectional questionnaire study. Subjects were offered questionnaire or in-person study visits. Subjects were enrolled if they underwent genetic evaluation, which included counseling and testing at a high-risk clinic and/or provided genetic test results. Colonoscopy surveillance compared carriers to noncarriers and unknowns, measuring the level of appropriateness.	Subjects 18 years old and older were from families who either met the Amsterdam criteria for LS and/or had a mutation of an MMR gene.	USA
Colonoscopy surveillance	Stuckless et al., 2012	Screening study	This study compares a group of LS+ patients undergoing 1-2 year colonoscopy surveillance compared to those not undergoing surveillance. This is the first study to separately exam colonoscopy outcomes in males compared to females.	The study subjects consisted of those with either a confirmed LS diagnosis with an MSH2 gene mutation, in the line of descent and having offspring with this proven mutation, or in the line of descent and diagnosed with LS+ CRC and the age of 50.	Canada

Table C-2. Summary of Findings from Studies of the Clinical Validity of Preliminary Tumor Test for Lynch Syndrome (LS)

Table C2-a. Clinical Validity of Immunohistochemistry (IHC) Preliminary Tumor Test

Guideline	Citation (s)	Sensitivity	Specificity	Conclusion
EGAPP	Palomaki et al., 2009	MLH1 = 78% MSH2 = 80% MSH6 = 74%	88.8%	IHC tests can accurately identify most persons with colorectal cancer (CRC) who would benefit from germline genetic testing.
AHRQ review	2007	74%	77%	
		94% (after positive Microsatellite Instability [MSI] test)	13% (after positive MSI test)	

Table C2-b. Clinical Validity of Microsatellite Instability (MSI) Preliminary Tumor Test

Guideline	Citation (s)	Sensitivity	Specificity	Conclusion
EGAPP	Palomaki et al., 2009	85 % (MLH1) 85% (MSH2) 69% (MSH6)	90.2%	IHC tests can accurately identify most persons with CRC who would benefit from germline genetic testing.
AHRQ review	2007	56-100%	17-93%	

Table C2-c. Clinical Validity of BRAF Preliminary Tumor Test

Guideline	Citation (s)	Sensitivity	Specificity	Conclusion
EGAPP	Palomaki et al., 2009	69%	100%	BRAF tests in addition to IHC tests can accurately identify most persons with CRC who would benefit from germline genetic testing.

Table C-3. Studies on the Uptake of Genetic Counseling for LS Among Family Members of Persons with LS

Outcome	Citation (s)	Research Design	Statistical Significance	Direction of Effect	Size of Effect	Conclusion
Uptake of counseling	Palomaki et al., 2009 Burton-Chase et al., 2013	Evidence review Level IV 1 of 2	Does not apply	Does not apply	Palomaki: Of 1,866, 52% underwent genetic counseling. Burton-Chase: Of 231 eligible family members, 97 (42%) underwent genetic counseling.	Preponderance of evidence indicates that approximately half of family members of persons with LS who are offered genetic counseling receive genetic counseling.

Table C-4. Studies on the Uptake of Genetic Testing for LS Among Family Members of Persons with LS

Outcome	Citation (s)	Research Design	Statistical Significance	Direction of Effect	Size of Effect	Conclusion
Uptake of genetic testing	Palomaki et al., 2009 Burton-Chase et al., 2013 Esposito et al., 2010	Evidence review Level IV 1 of 4 Longitudinal screening study Level IV 1 of 4 Retrospective surveillance study Level IV 1 of 4	Does not apply	Does not apply	Palomaki: Among those who received genetic counseling, 95% underwent genetic testing. Burton-Chase: Among 97 who received genetic counseling, 91 (95%) underwent genetic testing. Esposito: Post-genetic counseling, 79% underwent genetic testing.	Preponderance of evidence indicates that take-up rate for genetic testing post-genetic counseling ranges from 79% to 95%.

Table C-5. Effect on Colonoscopy Screening on the Reduction of Colorectal Cancer Morbidity

Outcome	Citation (s)	Research Design	Statistical Significance	Direction of Effect	Size of Effect	Conclusion
CRC diagnosis through colonoscopy	Järvinen et al., 2000	Controlled nonrandomized study Level IV 1 of 1	Statistically significant 1 of 1 studies	Better	Jarvinen: 56% reduction in CRC due to ongoing colorectal screening.	Evidence indicates screening leads to a 56% reduction in CRC.

Table C-6. Effect on Colonoscopy Screening on the Reduction of Colorectal Cancer-Related Mortality

Outcome	Citation (s)	Research Design	Statistical Significance	Direction of Effect	Size of Effect	Conclusion
Mortality	Järvinen et al., 2000 Stuckless et al., 2012 de Jung et al., 2006	Controlled nonrandomized trial Level IV study 1 of 3 Surveillance trial Level IV study 2 of 3	Statistically significant 3 of 3	Better	Jarvinen: 65% reduction in death due to ongoing colorectal screening. Stuckless: Males in screening program had lower risk of death (RR = 0.38; 95% CI: 0.13-1.0); females in screening program had lower risk of death RR = 0.19; 95% CI: 0.09-0.44). de Jung: Standardized mortality ratio (SMR) pre- and post-surveillance program implementation , SMR = 32.3, SMR 10.1, respectively	Evidence indicates screening leads to reduction in CRC-related mortality.

Table C-7. Take-Up Rates of Colonoscopy Screening

Outcome	Citation (s)	Research Design	Statistical Significance	Direction of Effect	Size of Effect	Conclusion
Adherence to surveillance colonoscopies	Palomaki et al., 2009 Esposito et al., 2010 Stuckless et al., 2012 Stoffel et al., 2010 Collins et al., 2007	Evidence Review Level IV 1 of 5 studies Retrospective surveillance study Level IV 2 of 5 studies Longitudinal screening study Level IV 1 of 5 studies Cohort study 1 Level IV study	Does not apply	Does not apply	Palomaki: 79% completed colonoscopy since receiving genetic test results. Esposito: 70% received colonoscopies on average every 2 years. Stuckless: 44% of males and 41% of females received colonoscopies every 1-2 years over a 10-year period. Stoffel: Of 181, 132 (73%) had colonoscopies at least every 2 years. Collins: All carriers (n = 19) had colonoscopies 1-2 years after receipt of test results compared to only 7% (n= 4) of noncarriers.	The preponderance of evidence indicates that the take-up rate for colonoscopies within 2 years of diagnosis of LS is approximately 70% to 100%

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

This appendix describes data sources, estimation methodology, as well as general and mandate-specific caveats and assumptions used in conducting the cost impact analysis. For additional information on the cost model and underlying methodology, please refer to the CHBRP website at www.chbrp.org/analysis_methodology/cost_impact_analysis.php.

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, San Diego, the University of California, Los Angeles, the University of California, Davis, and University of California, Berkeley, as well as the contracted actuarial firm, Milliman, Inc. (Milliman).⁴²

Data Sources

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

Baseline model

1. The California Simulation of Insurance Markets (CalSIM) is used to project health insurance status of Californians aged 64 and under in 2014. CalSIM is a microsimulation model that projects the effects of the Affordable Care Act on firms and individuals.⁴³ CalSIM relies on national Medical Expenditure Panel Survey (MEPS) Household Component and Person Round Plan, California Health Interview Survey (CHIS) 2009, and California Employer Health Benefits Survey data.
2. California Health Interview Survey (2011) data is used to estimate the number of Californians aged 65 and older, and the number of Californians dually eligible for both Medi-Cal and Medicare coverage. CHIS 2011 is also used to determine the number of Californians with incomes below 400% of the federal poverty level. CHIS is a continuous survey that provides detailed information on demographics, health insurance coverage, health status, and access to care. CHIS 2011 surveyed approximately 23,000 households and is conducted in multiple languages by the UCLA Center for Health Policy Research. More information on CHIS is available at www.chis.ucla.edu.
3. The latest (2012) California Employer Health Benefits Survey is used to estimate:
 - a. Size of firm
 - b. Percentage of firms that are purchased/underwritten (versus self-insured)
 - c. Premiums for health care service plans regulated by the Department of Managed Health Care (DMHC) (primarily health maintenance organizations [HMOs] and point of service [POS] plans)

⁴² CHBRP's authorizing legislation requires that CHBRP use a certified actuary or "other person with relevant knowledge and expertise" to determine financial impact (www.chbrp.org/docs/authorizing_statute.pdf).

⁴³ UC Berkeley Center for Labor Research and Education and UC Los Angeles Center for Health Policy Research. *Methodology & Assumptions, California Simulation of Insurance Markets (CalSIM) Version 1.7*, June 2012. Available at www.healthpolicy.ucla.edu/pubs/files/calsim_methods.pdf. Accessed October 19, 2012.

- d. Premiums for health insurance policies regulated by the California Department of Insurance (CDI) (primarily preferred provider organizations [PPOs] and fee-for-service [FFS] plans)

This annual survey is currently released by the California Health Care Foundation/National Opinion Research Center (CHCF/NORC) and is similar to the national employer survey released annually by the Kaiser Family Foundation and the Health Research and Educational Trust. Information on the CHCF/NORC data is available at: www.chcf.org/publications/2010/12/california-employer-health-benefits-survey.

4. Milliman data sources are relied on to estimate the premium impact of mandates. Milliman's projections derive from the Milliman Health Cost Guidelines (HCGs). The HCGs are a health care pricing tool used by many of the major health plans in the United States. See www.milliman.com/expertise/healthcare/products-tools/milliman-care-guidelines/index.php. Most of the data sources underlying the HCGs are claims databases from commercial health insurance plans. The data are supplied by health insurance companies, HMOs, self-funded employers, and private data vendors. The data are mostly from loosely managed health care plans, generally those characterized as preferred provider organization (PPO) plans. The HCGs currently include claims drawn from plans covering 37 million members. In addition to the Milliman HCGs, CHBRP's utilization and cost estimates draw on other data, including the following:
 - a. The MarketScan databases, which reflects the healthcare claims experience of employees and dependents covered by the health benefit programs of large employers. These claims data are collected from approximately 100 different insurance companies, Blue Cross Blue Shield plans, and third-party administrators. These data represent the medical experience of insured employees and their dependents for active employees, early retirees, individuals with COBRA continuation coverage, and Medicare-eligible retirees with employer-provided Medicare Supplemental plans. No Medicaid or Workers Compensation data are included.
 - b. An annual survey of HMO and PPO pricing and claim experience. The most recent survey (2010 Group Health Insurance Survey) contains data from seven major California health plans regarding their 2010 experience.
 - c. Ingenix MDR Charge Payment System, which includes information about professional fees paid for healthcare services, based upon approximately 800 million claims from commercial insurance companies, HMOs, and self-insured health plans.
 - d. These data are reviewed for applicability by an extended group of experts within Milliman but are not audited internally.
5. Premiums and enrollment in DMHC-regulated health plans and CDI-regulated policies by self-insured status and firm size are obtained annually from CalPERS for active state and local government public employees and their dependents who receive their benefits through CalPERS. Enrollment information is provided for DMHC-regulated health care service plans covering non-Medicare beneficiaries—about 74% of CalPERS total

enrollment. CalPERS self-funded plans—approximately 26% of enrollment—are not subject to state mandates. In addition, CHBRP obtains information on current scope of benefits from evidence of coverage (EOC) documents publicly available at www.calpers.ca.gov. For the 2013 model, CHBRP assumes CalPERS’s enrollment in 2014 will not be affected by the ACA.

6. Enrollment in Medi-Cal Managed Care (beneficiaries enrolled in Two-Plan Model, Geographic Managed Care, and County Operated Health System plans) is estimated based on data maintained by the Department of Health Care Services (DHCS). CHBRP assesses enrollment information online at: www.dhcs.ca.gov/dataandstats/statistics/Pages/RASB_Medi-Cal_Enrollment_Trends.aspx. Starting with the 2013 model, the most recent Medi-Cal enrollment data from DHCS is projected to 2014 based on CalSIM’s estimate of the impact of the Medi-Cal expansion in 2014.

Estimate of premium impact of mandates

7. CHBRP’s Annual Enrollment and Premium Survey collects information from the seven largest providers of health insurance in California (Aetna, Anthem Blue Cross of California, Blue Shield of California, CIGNA, Health Net, Kaiser Foundation Health Plan, and United Healthcare/PacifiCare) to obtain estimates of baseline enrollment by purchaser (i.e., large and small group and individual), type of plan (i.e., DMHC-regulated or CDI-regulated), grandfathered and nongrandfathered status, and average premiums. Enrollment in plans or policies offered by these seven insurers represents an estimated 97.5% of the persons with health insurance subject to state mandates. This figure represents an estimated 97.9% of enrollees in full-service (nonspecialty) DMHC-regulated health plans and an estimated 96.1% of enrollees in full-service (nonspecialty) CDI-regulated policies.

For CHBRP reports analyzing specific benefit mandates, CHBRP surveys the seven major carriers on current coverage relevant to the benefit mandate. CHBRP reports the share of enrollees—statewide and by market segment—reflected in CHBRP’s bill-specific coverage survey responses. The proportions are derived from data provided by CDI and DMHC. CDI provides data by market segment (large, small, and individual) based on “CDI Licenses With HMSR Covered Lives Greater Than 100,000” as part of the Accident and Health Covered Lives Data Call September 30, 2011, by the California Department of Insurance, Statistical Analysis Division. The Department of Managed Health Care’s interactive website “Health Plan Financial Summary Report,” July–September 2012, provides data on DMHC-regulated plans by segment.⁴⁴

The following table describes the data sources mentioned above, and the data items that they inform.

⁴⁴ CHBRP assumes DMHC-regulated PPO group enrollees and POS enrollees are in the large-group segment. <http://wpsso.dmhc.ca.gov/flash/>.

Table D-1. Population and Cost Model Data Sources and Data Items

Data Source	Items
California Simulation of Insurance Markets (CalSIM)	Uninsured, age: 0–17; 18–64 Medi-Cal (non-Medicare) (a), age: 0–17; 18–64 Other public (b), age: 0–64 Individual market, age: 0–17; 18–64 Small group, age: 0–17; 18–64 Large group, age: 0–17; 18–64
California Health Interview Survey, 2011 (CHIS 2011)	Uninsured, age: 65+ Medi-Cal (non-Medicare), age: 65+ Other public, age: 65+ Employer-sponsored insurance, age: 65+
CalPERS data, annually, enrollment as of September 30	CalPERS HMO and PPO enrollment • Age: 0–17; 18–64; 65+ HMO premiums
California Employer Survey, conducted annually by NORC and funded by CHCF	Enrollment by HMO/POS, PPO/indemnity self-insured, fully insured, Premiums (not self-insured) by: • Size of firm (3–25 as small group and 25+ as large group) • Family vs. single • HMO/POS vs. PPO/indemnity vs. HDHP employer vs. employer premium share
DHCS administrative data for the Medi-Cal program, annually, 11-month lag from the end of November	Distribution of enrollees by managed care or FFS distribution by age: 0–17; 18–64; 65+ Medi-Cal Managed Care premiums
CMS administrative data for the Medicare program, annually (if available) as of end of September	HMO vs. FFS distribution for those 65+ (noninstitutionalized)
CHBRP enrollment survey of the seven largest health plans in California, annually as of end of September	Enrollment by: • Size of firm (2–50 as small group and 51+ as large group), • DHMC vs. CDI regulated • Grandfathered vs. nongrandfathered Premiums for individual policies by: • DMHC vs. CDI regulated • Grandfathered vs. nongrandfathered
Department of Finance population projections, for intermediate CHIS years	Projected civilian, noninstitutionalized CA population by age: 0–17; 18–64; 65+
Medical trend influencing annual premium increases	Milliman estimate

Notes: (a) Includes children previously enrolled in Healthy Families, California’s Children’s Health Insurance Program. By January 1, 2014, children enrolled in Healthy Families will be transitioned into Medi-Cal as required in the 2012–2013 state budget agreement.

(b) Includes individuals dually eligible for Medi-Cal and Medicare.

Key: CDI=California Department of Insurance; CHCF=California HealthCare Foundation; CHIS= California Health Interview Survey; CMS=Centers for Medicare & Medicaid Services; DHCS=Department of Health Care Services; DMHC=Department of Managed Health Care; FFS=fee-for-service; HMO=health maintenance organization; NORC=National Opinion Research Center; PPO=preferred provider organization.

Projecting the Effects of the Affordable Care Act in 2014

This subsection discusses adjustments made to CHBRP's Cost and Coverage Model to account for the potential impacts of the ACA effective January 2014. It is important to emphasize that CHBRP's analysis of specific mandate bills typically addresses the marginal effects of the mandate bill—specifically, how the proposed mandate would impact benefit coverage, utilization, costs, and public health, *holding all other factors constant*. CHBRP's estimates of these marginal effects are presented in the *Benefit Coverage, Utilization, and Cost Impacts* section of this report.

Baseline premium rate development methodology—2014 post-ACA

Mandate bills introduced during 2013 would, if passed, become effective in 2014. Many significant provisions of the Affordable Care Act also become effective in 2014. In many cases, provisions required in the ACA would become effective on the same date as a mandate proposed to California law.

CHBRP's analyses of mandates effective in 2014 assume that carriers implement the new ACA provisions first. The baseline premiums reflect the estimated 2014 premium levels costs *after* carriers have implemented the 2014 ACA provisions. The estimated cost impact of a proposed mandate is then calculated relative to this post-ACA baseline.

The key components of the baseline model for utilization and expenditures are estimates of the per member per month (PMPM) values for each of the following:

- Insurance premiums PMPM;
- Gross claims costs PMPM;
- Member cost sharing PMPM; and
- Health care costs paid by the health plan.

For each plan type, CHBRP first obtained an estimate of the insurance premium PMPM by taking the 2012 reported premium from the above-mentioned data sources and trending that value to 2014. CHBRP uses trend rates published in the Milliman Health Cost Guidelines to estimate the health care costs for each plan segment in 2014.

In 2014, four plan segments in the previous CHBRP model⁴⁵ were split into 12 segments. Each of the two small-group segments (CDI-regulated and DMHC-regulated), and individual segments (CDI-regulated and DMHC-regulated) were split into: grandfathered non-exchange, nongrandfathered non-exchange, and exchange groups in order to separately calculate the impact of ACA and specific mandates that may apply differently to these three subgroups. The premium rate information received from NORC did not split the premiums based on grandfathered or

⁴⁵ In the past, CHBRP's model has reflected large-group, small-group, and individual market segments. These market segments were further subdivided by regulator: DMHC-regulated and CDI-regulated. The four plan segments refer to the small and individual market subdivisions by regulator.

exchange status. The 2012 CHBRP Annual Enrollment and Premium Survey asked the seven largest insurance carriers in California to provide their average premium rates separately for grandfathered and nongrandfathered plans. The ratios from the carrier survey data are then applied to the NORC aggregate premium rates, to estimate premium rates for grandfathered and nongrandfathered plans that were consistent with the NORC results.

The marginal impact of ACA on 2014 premiums was established as follows:

- For nongrandfathered small-group and individual market segments, a 3% increase in medical costs is applied to reflect the total cost of requiring each plan to cover the essential health benefits.
- For nongrandfathered small-group plans, a 5% increase in medical costs is applied to reflect the other additional costs of ACA (e.g., age rating, health status, increased premium taxes and fees, change in actuarial value, etc.).
- For DMHC-regulated individual plans and CDI-regulated individual policies, an increase of 20% and 31%, respectively, in medical costs is applied to reflect the other additional costs of ACA.

The remaining three values were then estimated by the following formulas:

- Health care costs paid by the health plan = insurance premiums PMPM \times (1 – profit/administration load).
- Gross claims costs PMPM = health care costs paid by the health plan \div percentage paid by health plan
- Member cost sharing PMPM = gross claims costs \times (1 – percentage paid by health plan)

In the above formulas, the quantity “profit/administration load” is the assumed percentage of a typical premium that is allocated to the health plan’s administration and profit. These values vary by insurance category, and under the ACA, are limited by the minimum medical loss ratio requirement. CHBRP estimated these values based on Milliman’s knowledge of the health care market.

In the above formulas, the quantity “percentage paid by health plan” is the assumed percentage of gross health care costs that are paid by the health plan, as opposed to the amount paid by member cost sharing (deductibles, copays, etc.). In ACA terminology, this quantity is known as the plan’s “actuarial value.” These values vary by insurance category. For each insurance category, Milliman estimated the member cost sharing for the average or typical plan in that category. Milliman then priced these plans using the Milliman Health Cost Guidelines to estimate the percentage of gross healthcare costs that are paid by the carrier.

Medi-Cal Managed Care

Given that:

- California has not yet decided on Medi-Cal's EHBs for Californians newly eligible for Medi-Cal Managed Care; and,
- The ACA does not require coverage of EHBs for individuals currently eligible for Medicaid,

CHBRP has estimated that the PMPM cost for Medi-Cal's newly eligible population—in the absence of further guidance on EHBs for the newly eligible population—will equal the projected cost of Medi-Cal's currently eligible family population, excluding maternity costs.

General Caveats and Assumptions

The projected cost estimates are estimates of the costs that would result if a certain set of assumptions were exactly realized. Actual costs will differ from these estimates for a wide variety of reasons, including:

- Prevalence of mandated benefits before and after the mandate may be different from CHBRP assumptions.
- Utilization of mandated benefits (and, therefore, the services covered by the benefit) before and after the mandate may be different from CHBRP assumptions.
- Random fluctuations in the utilization and cost of health care services may occur.
- The impact of ACA on the mandated benefit cost may be different from CHBRP assumptions.

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

- Cost impacts are shown only for plans and policies subject to state benefit mandate laws.
- Cost impacts are only for the first year after enactment of the proposed mandate.
- Employers and employees will share proportionately (on a percentage basis) in premium rate increases resulting from the mandate. In other words, the distribution of the premium paid by the subscriber (or employee) and the employer will be unaffected by the mandate.
- For state-sponsored programs for the uninsured, the state share will continue to be equal to the absolute dollar amount of funds dedicated to the program.
- When cost savings are estimated, they reflect savings realized for 1 year. Potential long-term cost savings or impacts are estimated if existing data and literature sources are available and provide adequate detail for estimating long-term impacts. For more information on CHBRP's criteria for estimating long-term impacts, please see: http://chbrp.org/documents/longterm_impacts08.pdf.
- Several studies have examined the effect of private insurance premium increases on the number of uninsured (Chernew et al., 2005; Glied and Jack, 2003; Hadley, 2006).

Chernew et al. (2005) estimate that a 10% increase in private premiums results in a 0.74 to 0.92 percentage point decrease in the number of insured, whereas Hadley (2006) and Glied and Jack (2003) estimate that a 10% increase in private premiums produces a 0.88 and a 0.84 percentage point decrease in the number of insured, respectively. Because each of these studies reported results for the large-group, small-group, and individual insurance markets combined, CHBRP employs the simplifying assumption that the elasticity is the same across different types of markets. For more information on CHBRP's criteria for estimating impacts on the uninsured, please see: http://chbrp.org/documents/uninsured_010109.pdf.

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

- Population shifts by type of health insurance: If a mandate increases health insurance costs, some employer groups and individuals may elect to drop their health insurance. Employers may also switch to self-funding to avoid having to comply with the mandate.
- Changes in benefit plans: To help offset the premium increase resulting from a mandate, subscribers/policyholders may elect to increase their overall plan deductibles or copayments. Such changes would have a direct impact on the distribution of costs between the health plan and policies and enrollees, and may also result in utilization reductions (i.e., high levels of patient cost sharing result in lower utilization of health care services). CHBRP did not include the effects of such potential benefit changes in its analysis.
- Adverse selection: Theoretically, individuals or employer groups who had previously foregone health insurance may now elect to enroll in a health plan or policy, postmandate, because they perceive that it is to their economic benefit to do so.
- Medical management: Health plans and insurers may react to the mandate by tightening medical management of the mandated benefit. This would tend to dampen the CHBRP cost estimates. The dampening would be more pronounced on the plan types that previously had the least effective medical management (i.e., PPO plans).
- Geographic and delivery systems variation: Variation in existing utilization and costs, and in the impact of the mandate, by geographic area and delivery system models: Even within the health insurance types CHBRP modeled (HMO—including HMO and POS plans—and non-HMO—including PPO and FFS policies), there are likely variations in utilization and costs by type. Utilization also differs within California due to differences in the health status of the local population, provider practice patterns, and the level of managed care available in each community. The average cost per service would also vary due to different underlying cost levels experienced by providers throughout California and the market dynamic in negotiations between providers and health plans or insurers. Both the baseline costs prior to the mandate and the estimated cost impact of the mandate could vary within the state due to geographic and delivery system differences. For purposes of this analysis, however, CHBRP has estimated the impact on a statewide level.

- Compliance with the mandate: For estimating the postmandate coverage levels, CHBRP typically assumes that plans and policies subject to the mandate will be in compliance with the coverage requirements of the bill. Therefore, the typical postmandate coverage rates for populations subject to the mandate are assumed to be 100%.

Bill Analysis–Specific Caveats and Assumptions

Utilization Management Criteria

SB 799 would alter the terms of current coverage for some enrollees, prohibiting some forms of utilization management. SB 799 would require that genetic testing be considered medically necessary if the following criteria are met: an enrollee is the child or sibling of a person who has both been diagnosed with CRC and has tested positive for LS (the “index patient”). CHBRP has reviewed utilization management criteria used by DMHC-regulated plans and CDI-regulated policies to make coverage determination regarding genetic testing for enrollees with a family history of LS-related cancers. As the comparison between an example and SB 799’s requirement indicates (see Table D-2), benefit coverage may be SB 799 noncompliant yet cover testing for many enrollees. In fact, the example would cover testing when SB 799 would not require it; the example indicates that testing is covered for an enrollee with a relative with two or more LS-related tumors regardless of the relative’s LS status, where SB 799 only requires testing to be covered when the relative has both been diagnosed with CRC and is known to be LS+. However, SB 799 would require coverage of testing when the example would not; the example stipulates circumstances in which the relative must have been diagnosed prior to age 50 or age 40, where SB 799 would require coverage regardless of the age at which the relative was diagnosed, so long as the relative was also LS+.

Table D-2. Comparison of Utilization Management Criteria and SB 799 Requirements

Example	SB 799 Requirement
<p>For enrollees with a <i>family history</i> of potentially LS-related cancer, genetic testing for LS is considered medically necessary when ANY of the following criteria are met:</p> <ol style="list-style-type: none"> 1. The enrollee has a first- or second-degree relative with 2 or more LS-related tumors (colorectal, endometrial, biliary tract, pancreas, ureter or renal pelvis, ovarian, brain, gastric, or small intestinal cancers, or sebaceous gland adenomas or keratoacanthomas), including synchronous and metachronous tumors; <p style="text-align: center;">OR</p> 2. The enrollee has a first- or second-degree relative with a history of CRC and a first-degree relative with CRC diagnosed prior to age 50; <p style="text-align: center;">OR</p> 3. The enrollee has a first- or second-degree relative with a history of CRC and a first-degree relative with an LS-related cancer diagnosed prior to age 50; <p style="text-align: center;">OR</p> 4. The enrollee has a first- or second-degree relative with a history of CRC and a first-degree relative with colorectal adenoma diagnosed prior to age 40; <p style="text-align: center;">OR</p> 5. The enrollee has a first- or second-degree relative with CRC or endometrial cancer diagnosed prior to age 50; <p style="text-align: center;">OR</p> 6. The enrollee has a first- or second-degree relative with a right-sided CRC with an undifferentiated pattern on histopathology diagnosed prior to age 45. 	<p>Coverage shall be provided for genetic testing for LS for when:</p> <ol style="list-style-type: none"> 1. an enrollee is the child or sibling of a person who has been diagnosed with CRC and who has tested positive for the gene mutation for LS.

Source: California Health Benefits Review Program, 2013

Key: LS=Lynch syndrome, CRC=colorectal cancer

The interaction between the new requirement and noncompliant benefit coverage (such as benefit coverage with utilization management criteria similar to the example in Table D-2) is complex; too complex for CHBRP to estimate precisely how many enrollees could expect change due to changed utilization management criteria. CHBRP has made the simplifying assumption that, premandate, 80% of enrollees with a family history of LS-related CRC with SB 799 noncompliant benefit coverage would have been covered for genetic testing. Postmandate, the figure would be expected to increase to 100%.

Enrollee Population Estimates

In order to estimate the number of enrollees with CRC younger than 50 years of age (eligible for LS-related genetic testing), CHBRP relied upon the assumptions and sources described in Table D-3.

Table D-3. Colorectal Cancer Incidence Rate for Enrollees⁴⁶ Younger Than 50 Years of Age

Description	Assumption	Source
A. CRC diagnoses in California, all age groups, 2012	14,000	CDPH, 2009
B. CRC diagnoses in California, aged < 50, 1999-2009	15,195	CDC Online WONDER Database, 2013
C. Average CRC diagnoses in California per year, age < 50	1,381	= B / 11 ⁴⁷
D. % of CRC in California diagnosed prior to age 50	10.0%	= C / A
E. Enrollees age < 50, 2014	73.6%	CHBRP Cost and Coverage Model
F. Estimated CRC diagnoses, Enrollees age < 50, 2014	1,030	= A * D * E
G. Enrollees, 2014	25,899,000	CHBRP Cost and Coverage Model
H. Incidence rate of CRC among Enrollees age < 50, per 1,000, 2014	0.040	= F / G

Source: California Health Benefits Review Program, 2013

Key: CRC=colorectal cancer; CDPH = California Department of Public Health; CDC=Centers for Disease Control; CHBRP=California Health Benefits Review Program; DMHC=Department of Managed Health Care; CDI=California Department of Insurance

CHBRP further assumes that tumor testing will indicate a possible diagnosis of LS and so promote germline genetic testing in 5% of all CRC cases occurring in enrollees younger than 50 years. Given benefit coverage fully compliant with SB 799, CHBRP expects that 75% of these patients will subsequently receive both genetic counseling and genetic testing (Sturgeon et al., 2013). These take-up rates have been supported by interventions focused on genetic testing for LS. Patients who themselves have CRC have a great deal of personal investment in discovering their related health conditions in order to maximize the success of their cancer treatments. In order to determine the number of enrollees who are the children or siblings of a person with CRC and LS+, CHBRP relied upon the assumptions and sources described in Table D-4.

⁴⁶ Enrollees in DMHC-regulated plans and CDI-regulated policies.

⁴⁷ The period between 1999-2009 includes 11 years, so the prior figure is divided by 11 to provide an annual average.

Table D-4. Colorectal Cancer and Lynch Syndrome Prevalence Rate

Description	Assumption	Source
A. California population, 2014	38,744,000	CHBRP Cost and Coverage Model
B. CRC prevalence per 1,000, all ages	3.75	NCI SEER, 2013
C. CRC prevalence in California	145,225	= A * B / 1,000
D. % of CRC attributable to LS	3.0%	EGAPP, 2009; NCNN, 2009; Weissmen et al., 2012
E. Estimated prevalence of CRC and LS+ in California	4,357	= D * C
F. Untested first-degree relatives per index patient	3	Hampel et al., 2005; Hampel et al., 2008
G. Enrollees in DMHC-regulated plans and CDI-regulated policies	25,899,000	CHBRP Cost and Coverage Model
H. Untested first-degree relatives among enrollees in DMHC-regulated plans and CDI-regulated policies	8,737	= E * F * (G / A)

Source: California Health Benefits Review Program, 2013

Key: LS=Lynch syndrome, CRC=colorectal cancer; DMHC=Department of Managed Health Care; CDI=California Department of Insurance; CHBRP=California Health Benefits Review Program

Given benefit coverage fully compliant with SB 799, CHBRP assumes that 50% of untested first-degree relatives would seek genetic counseling and that 95% of those receiving genetic counseling would receive genetic testing. One half of those members are expected to test positive for LS, and of those, 70% would be expected to receive annual colonoscopies.

Unit Costs

Unit costs for tests were calculated using average allowed charges from the 2011 Marketscan Commercial Claims database using the following procedure:

- Only California claims were included.
- Claims identified by CPT or HCPCS code and assigned to a category: Genetic Counseling, Genetic Screening, Colonoscopy.
- All claims with an allowed amount of \$0.00 were discarded.
- Average allowed charge was calculated from remaining claims.
- All reimbursed related procedures received at a single visit were combined for purposes of estimating the average unit charge.
- Annual trend rate of 5% applied to charges to put them on a 2014 basis.
- No distinction was made for genetic tests on the basis of an accompanying diagnosis of CRC or lack thereof.
- Patients receiving multiple genetic tests on distinct dates were not identified.

Enrollee Expenses and Utilization

Postmandate, CHBRP expects a larger increase in utilization of genetic testing than of genetic counseling in the population of first-degree relatives. This counterintuitive result is a result of the genetic counseling and testing process being made up of multiple decision nodes (see Figure 3 in *Benefit, Utilization and Cost Impacts* section). Multiple nodes offer more opportunities for enrollees to decline a next step, as some will do when faced with additional enrollee expenses. A simple example, using round numbers, clarifies this point (see Table D-5).

Table D-5. Simplified Example, Impact of Enrollee Expenses on Multiple Node Decision Process

Description	With Enrollee Expenses	No Enrollee Expenses	Change
Enrollee pool of first-degree relatives	100	100	0
Subgroup choosing to receive genetic counseling	50	100	50
Subgroup choosing (after genetic counseling) to undergo genetic testing	25	100	75

Source: California Health Benefits Review Program, 2013

In the simplified example, with 100 first-degree relatives, 50 agree to enrollee expenses and undergo genetic counseling but only 25 agree to additional enrollee expenses and continue on to genetic testing. Without enrollee expenses, all 100 enrollees undergo genetic counseling and genetic testing. Changed enrollee expenses have a greater impact on the last step in a multiple node decision process, even though the initial number of people in the pool is unchanged.

Appendix E: Information Submitted by Outside Parties

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

No information was submitted by interested parties for this analysis.

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

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A group of faculty and staff undertakes most of the analysis that informs reports by the California Health Benefits Review Program (CHBRP). The CHBRP **Faculty Task Force** comprises rotating representatives from six University of California (UC) campuses. In addition to these representatives, there are other ongoing contributors to CHBRP from UC. This larger group provides advice to the CHBRP staff on the overall administration of the program and conducts much of the analysis. The **CHBRP staff** coordinates the efforts of the Faculty Task Force, works with Task Force members in preparing parts of the analysis, and coordinates all external communications, including those with the California Legislature. The level of involvement of members of the CHBRP Faculty Task Force and staff varies on each report, with individual participants more closely involved in the preparation of some reports and less involved in others. As required by CHBRP's authorizing legislation, UC contracts with a certified actuary, Milliman Inc., to assist in assessing the financial impact of each legislative proposal mandating or repealing a health insurance benefit. Milliman also helped with the initial development of CHBRP methods for assessing that impact.

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

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