

California Health Benefits Review Program

Analysis of California Senate Bill 172 Fertility Preservation

A Report to the 2017-2018 California State Legislature

April 13, 2017



Key Findings:

Analysis of California Senate Bill 172 Fertility Preservation

Summary to the 2017-2018 California State Legislature, April 13, 2017.



AT A GLANCE

As introduced, Senate Bill (SB) 172 would require that individual or group health care service plans or policies shall include coverage for standard fertility preservation services when a necessary medical treatment may cause iatrogenic infertility. As amended (March 7, 2017), the bill would require coverage for evaluation and treatment of iatrogenic infertility including but not limited to standard fertility preservation services. The cost section of this report estimates impacts of both the introduced and amended language. However, the rest of the report reflects only the language as introduced.

1. CHBRP estimates that, in 2018, of the approximately 24 million Californians enrolled in state-regulated health insurance, 16.2 million will have insurance subject to SB 172.
2. **Benefit coverage.** At baseline, 85% of enrollees with health insurance that would be subject to SB 172 have coverage that is mandate compliant (13.7 million). CHBRP assumes this would increase to 100% if the bill becomes law. It is unclear whether SB 172 would or would not exceed the essential health benefits (EHBs).
3. **Utilization.** Utilization of fertility preservations covered by insurance would increase by 30% with 219 more male enrollees and 216 more female enrollees using fertility preservation services covered by insurance.
4. **Expenditures.** Under the language as introduced, CHBRP estimates that SB 172 would increase total net annual expenditures by \$2,197,000 or 0.0015% for enrollees with DMHC-regulated plans and CDI-regulated policies. Under the amended language, SB 172 would increase total net annual expenditures by \$6,001,000 or 0.041% for enrollees with DMHC-regulated plans and CDI-regulated policies.
5. **Medical effectiveness.** CHBRP found limited evidence that embryo, oocyte, and sperm cryopreservation are effective methods of fertility preservation based on successful thawing of eggs, sperm, or embryos, implantation, subsequent pregnancy rates, and live births.
6. **Public health.** Based on the literature, CHBRP finds that SB 172 would likely improve the quality of life by reducing regret about fertility outcomes, dissatisfaction, and distress. CHBRP also anticipates that SB 172 could decrease barriers to access and alleviate the current fertility preservation sex-related disparities for women.
7. **Long-term impacts.** In the long term, CHBRP estimates that utilization will remain similar to utilization in the first year of implementation. These fertility preservation services could lead to a slight increase in utilization of infertility services to achieve pregnancy among the affected enrollees.

CONTEXT

Iatrogenic infertility is medically induced infertility caused by a medical intervention that treats a primary disease or condition.¹ If a patient anticipates a treatment that could increase the risk of iatrogenic infertility, the patient and their provider may pursue fertility preservation services prior to the treatment. The National Cancer Institute defines fertility preservation as a type of procedure used to maintain an individual's ability to have children.

BILL SUMMARY

As introduced (January 23, 2017), Senate Bill (SB) 172 would require that individual or group health care service plans or policies issued, amended, or renewed on and after January 1, 2018, that covers hospital, medical, or surgical expenses, shall include coverage for standard fertility preservation services when a necessary medical treatment may cause iatrogenic infertility. As amended (March 7, 2017), the bill would require coverage for evaluation and treatment of iatrogenic infertility including, but not limited to, standard fertility preservation services. The amended language could be interpreted to require coverage for infertility treatment for iatrogenic infertility. CHBRP received a follow-up request from the Senate Health Committee to also include a cost estimate for the amended language. Thus, the cost section of this report estimates impacts of both the introduced and amended language. However, the rest of the report reflects only the language as introduced. The full text of SB 172 can be found in Appendix A.

Key Assumption and Focus on Cancer-Related Iatrogenic Infertility

Iatrogenic infertility is most commonly caused by cancer treatments including radiation, chemotherapy (gonadotoxic treatments), and surgical removal of reproductive organs. Autoimmune conditions such as systemic lupus erythematosus, rheumatoid arthritis, or Crohn's disease sometimes require gonadotoxic or surgical treatments. However, exposure doses to

¹ Refer to CHBRP's full report for full citations and references.

potentially iatrogenic treatments are lower for autoimmune conditions than for cancer. Also, gonadotoxic treatments are often first-line therapy for patients with cancer, but not for patients with autoimmune diseases. Individuals with who are transgender may also experience gonadotoxic treatments.

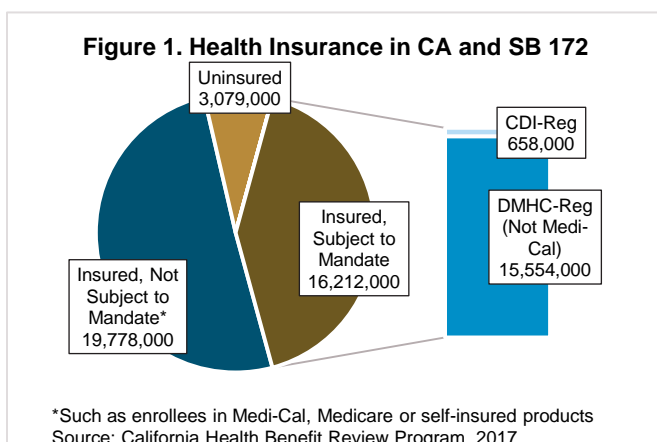
For this analysis, CHBRP focuses on iatrogenic infertility attributable to cancer treatments due to the higher prevalence of cancer (and concordant volume of literature), which outweighs that of the aforementioned conditions.

IMPACTS

Benefit Coverage, Utilization, and Cost

For full impacts for both the language as introduced and the amended bill language, see the full Benefit Coverage, Utilization and Cost section.

To determine the baseline utilization, CHBRP analyzed incidence rates from the most recent CDC data available of the top 10 cancers using treatments that put patients at risk of iatrogenic infertility. These incidence rates represent the population with newly diagnosed cancers, the population CHBRP assumed would potentially seek fertility preservation services prior to gonadotoxic treatment. Utilization was estimated only for females aged 12 to 44 and males aged 12 to 49, as those are the appropriate ages in which the risk of iatrogenic infertility could occur.



Benefit Coverage

CHBRP considered benefit coverage to be mandate compliant if enrollees were covered for at least one fertility

preservation service (see Appendix C for a complete list of services included in the model). Benefit coverage that only included a fertility preservation service for either men or women (but not both) was not considered to be fully mandate compliant.

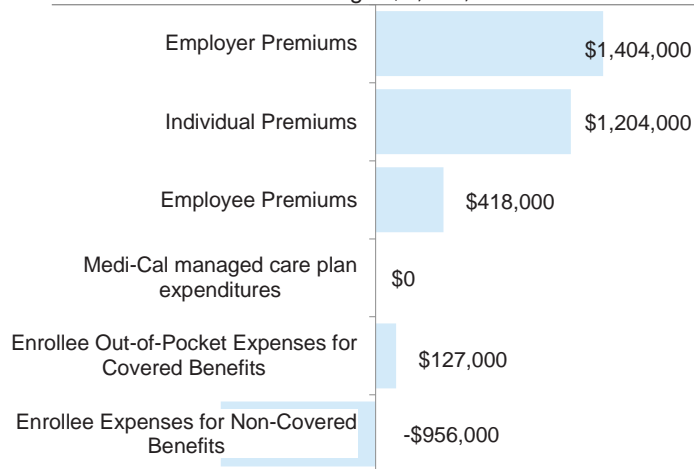
At baseline, 85% of enrollees with health insurance that would be subject to SB 172 have coverage that is mandate compliant for fertility preservation coverage (13.7 million), with at least one fertility preservation service included for enrollees (for each gender). CHBRP assumes that benefit coverage for fertility services among enrollees in DMHC-regulated plans or CDI-regulated policies would increase to 100%.

Utilization

At baseline, CHBRP estimates that 85% of enrollees with health insurance subject to SB 172 have coverage for fertility preservation at baseline with 7,589 cancer patients at risk of iatrogenic infertility. The number of cancer patients remains the same postmandate; however, the number using fertility preservation services would increase from 1,452 enrollees to 1,887 enrollees postmandate in the first year postmandate. These additional 435 cancer patients using fertility preservation (219 males and 216 females) are comprised of the previously uncovered enrollees using services (121 males and 65 females) as well as an assumed 10% increase in service use among previously covered enrollees due to new provider and public awareness of fertility preservation coverage.

Expenditures

Figure 2. Expenditure Impacts of SB 172 (Language As Introduced)
Expenditures by Category Postmandate, SB 172
Net Change: \$2,197,000



Source: California Health Benefits Review Program, 2017.

SB 172 as introduced would increase total net annual expenditures by \$2,197,000 or 0.0015% for enrollees with DMHC-regulated plans and CDI-regulated policies. This is due to a \$3,153,000 increase in total health insurance premiums paid by employers and enrollees for newly covered benefits, adjusted by a \$956,000 decrease in enrollee expenses for covered and/or noncovered benefits.

Under the amended language, SB 172 would increase total net annual expenditures by \$6,001,000 or 0.041% for enrollees with DMHC-regulated plans and CDI-regulated policies. For a corresponding figure of the amended language’s expenditures impacts by category, see the *Benefit Coverage, Utilization and Cost Impacts* section.

Medi-Cal

SB 172 would have no projected impact on Medi-Cal as the bill does not apply to Medi-Cal. Among publicly funded DMHC-regulated health plans, there would be no impact for Medi-Cal managed care plans.

CalPERS

CalPERS managed care plans are estimated to have a \$0.0068 increase in premiums under the bill language as

introduced, and a \$0.0300 increase in premiums under the amended language.²

Number of Uninsured in California

CHBRP would expect no measurable change in the number of uninsured persons due to the enactment of SB 172.

Medical Effectiveness

CHBRP summarized the effectiveness of specific fertility preservation services. Eight of these services are considered standard of care and would be covered under SB 172: embryo cryopreservation, oocyte (egg) cryopreservation, sperm cryopreservation, ovarian transposition (oophoropexy), ovarian shielding during radiation therapy, testicular shielding during radiation therapy, and conservative surgical approaches for gynecologic cancers (conservative ovarian cancer surgery and radical trachelectomy [surgical removal of the uterine cervix]).

Nonexperimental Fertility Preservation for Females

Fertility preservation options in females depend on many factors such as patient age, type of cancer diagnosis, prescribed cancer treatment, the length of time the patient can wait before starting cancer treatment, and whether the cancer has metastasized to the patient’s ovaries. Personal factors such as if the patient has a partner, cultural background, and religious beliefs can also influence fertility preservation decisions.

The review found limited evidence that embryo cryopreservation and oocyte (egg) cryopreservation (freezing) are effective methods of fertility preservation measured by three different outcomes: successful thawing of embryos or oocytes; successful implantation of embryos or oocytes; and resulting live births.

The following services are typically performed in conjunction with or as a part of cancer treatment. CHBRP

² It should be noted, however, that should CalPERS choose to make similar adjustments for consistency to the benefit coverage of enrollees associated with CalPERS’ self-insured products, the fiscal impact on CalPERS could be greater.

found limited evidence that ovarian transposition (surgery to move ovaries out of the field of radiation) is effective in maintaining ovarian function among women undergoing radiation as part of their cancer treatment. There is insufficient evidence that ovarian shielding (decreasing radiation to ovaries) during radiation therapy is an effective method of fertility preservation. A grade of insufficient evidence indicates that there is not enough evidence available to know whether or not a treatment is effective — it does not indicate that a treatment is not effective.

There is limited evidence that trachelectomy (surgical removal of the uterine cervix) and conservative ovarian surgery are effective surgeries in preserving fertility preservation measured by pregnancy rates and live births. There is a preponderance of evidence that trachelectomy and conservative ovarian surgery have no apparent increase in cancer recurrence or mortality for specific cases.

Nonexperimental Fertility Preservation for Males

For males, sperm cryopreservation is the most established technique for maintaining fertility. The review found that there is limited evidence that sperm cryopreservation is an effective method of fertility preservation as measured by pregnancy rates and live births. There is insufficient evidence that testicular shielding is an effective method of fertility preservation in males. A grade of insufficient evidence indicates that there is not enough evidence available to know whether or not a treatment is effective — it does not indicate that a treatment is not effective.

The summary of the literature on fertility preservation described in this report was graded as being of “limited evidence.” A grade of *limited evidence* indicates that the studies had limited generalizability to the population of interest because they were not limited to cancer patients and/or the studies had a flaw in research design or implementation due to being observational in nature.

Public Health

Quality of Life

Loss of fertility can negatively impact the quality of life for cancer survivors of reproductive age, including unresolved grief, depression, and anxiety. A systematic review was identified regarding the psychosocial and quality of life effects on female cancer patients undergoing fertility

preservation. It concluded that those who received counseling and services (for those who chose fertility preservation) experienced reduced regret and dissatisfaction about fertility outcomes.

Based on this and other literature, CHBRP finds that SB 172 would likely improve the quality of life by reducing regret about fertility outcomes, dissatisfaction, and distress for the additional estimated 435 enrollees newly using fertility preservation services in the first year postmandate.

Barriers to Access

SB 172 could potentially increase the rate of physician referrals for fertility counseling and preservation by providing coverage for such services and reducing out-of-pocket costs for patients experiencing iatrogenic infertility. Broader insurance coverage might also remove cost as a provider-perceived barrier.

Impact on Disparities by Sex

In California, females have twice the rate of cancers with treatments causing iatrogenic infertility as males; furthermore, females pay 12 times more for uncovered fertility preservation services than males. Postmandate, SB 172 would decrease the gender disparity by reducing the female financial burden of fertility preservation services. However, CHBRP estimates that some females would still face greater out-of-pocket expense burdens than males, postmandate, due to differences in costs of sex-specific preservation methods.

Long-term Impacts

Utilization and Cost Impacts

Postmandate, CHBRP estimates that SB 172 would increase utilization of fertility preservation services among enrollees with cancer by an additional 435 people during the first year. This estimate is based on an annual incidence rate of the top 10 cancers, and will likely remain constant per annum over the long term as long as the incidence rates also remain constant.

In the long term, these fertility preservation services will lead to some increased utilization of infertility services to achieve pregnancy among the affected enrollees. Research indicates that the percentage of people using

their frozen embryos, oocytes, or sperm is in a range of less than 5% of those who use fertility preservation.

Essential Health Benefits and the Affordable Care Act

It is unclear whether SB 172 (bill language as introduced) would exceed EHBs. In some cases, fertility preservation services may be considered a medically necessary component of a service that falls within the EHBs such as chemotherapy treatment for cancer. Also, fertility preservation services for iatrogenic infertility occur before a patient experiences infertility. Thus, fertility preservation is distinct from infertility treatment, which is not included in the state's benchmark plan.

However, the amended bill language could be interpreted to exceed the EHBs, because the amended language requires coverage of the "evaluation and treatment of iatrogenic infertility." The treatment of iatrogenic infertility could be interpreted to include a larger range of services beyond fertility preservation services, including infertility treatment. Infertility treatment is a coverage exclusion in the state's EHB benchmark plan. Therefore, the amended bill language could be interpreted to exceed the EHBs.

A Report to the California State Legislature

Analysis of California Senate Bill 172 Fertility Preservation

April 13, 2017

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ABOUT CHBRP

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

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

More detailed information on CHBRP's analysis methodology, authorizing statute, as well as all CHBRP reports and other publications are available at www.chbrp.org.

TABLE OF CONTENTS

| | |
|---|-----|
| About CHBRP | vii |
| List of Tables and Figures | ix |
| Policy Context | 1 |
| Bill-Specific Analysis of SB 172, Fertility Preservation | 1 |
| Background on Fertility Preservation | 8 |
| Incidence of Iatrogenic Infertility | 10 |
| Medical Effectiveness | 13 |
| Research Approach and Methods | 13 |
| Methodological Considerations | 13 |
| Outcomes Assessed | 14 |
| Study Findings | 14 |
| Summary of Findings | 21 |
| Benefit Coverage, Utilization, and Cost Impacts | 25 |
| Baseline and Postmandate Benefit Coverage | 26 |
| Baseline and Postmandate Utilization | 26 |
| Baseline and Postmandate Per-Unit Cost | 28 |
| Baseline and Postmandate Expenditures | 28 |
| Other Considerations for Policymakers | 30 |
| Public Health Impacts | 38 |
| Estimated Public Health Outcomes | 38 |
| Impact on Disparities | 40 |
| Estimated Impact on Financial Burden | 41 |
| Long-Term Impacts | 42 |
| Long-Term Utilization and Cost Impacts | 42 |
| Long-Term Public Health Impacts | 42 |
| Appendix A Text of Bill Analyzed | A-1 |
| Appendix B Literature Review Methods | B-1 |
| Appendix C Cost Impact Analysis: Data Sources, Caveats, and Assumptions | C-1 |
| Appendix D Information Submitted by Outside Parties | D-1 |
| References | |
| California Health Benefits Review Program Committees and Staff | |
| Acknowledgements | |

LIST OF TABLES AND FIGURES

| | |
|---|-----|
| Table 1. Scenario 1: SB 172 (as Introduced) Impacts on Benefit Coverage, Utilization, and Cost, 2018 ... | x |
| Table 2. Scenario 2: SB 172 (as Amended 3/7/2017) Impacts on Benefit Coverage, Utilization, and Cost, Total Annual Impact | xii |
| Table 3. Summary of Types of Fertility Preservation and SB 172 Coverage Status..... | 8 |
| Table 4. Incidence of Cancer Using Treatments Likely to Result in Iatrogenic Infertility for Californians Aged 10–44 Years Regardless of Insurance Status, 2013..... | 10 |
| Table 5. Baseline Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2018 | 32 |
| Table 6. Scenario 1: Postmandate (as Introduced) Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2018 | 34 |
| Table 7. Scenario 2: Postmandate (as Amended) Per Member Per Month Premiums and Total Expenditures by Market Segment, California, Total Annual Impact | 36 |
| Table 8. Services Included in Average Fertility Preservation Unit Costs | C-2 |
| | |
| Figure 1. Covered and Uncovered Fertility Preservation Services of SB 172 based on Bill Language as Introduced and Amended Bill Language..... | 3 |
| Figure 2. Embryo Cryopreservation | 21 |
| Figure 3. Oocyte (Egg) Cryopreservation | 22 |
| Figure 4. Ovarian Transposition (Oophoropexy)..... | 22 |
| Figure 5. Ovarian Shielding During Radiation Therapy | 22 |
| Figure 6. Conservative Gynecologic Surgery (Radical Trachelectomy) | 23 |
| Figure 7. Conservative Gynecologic Surgery (for Ovarian Cancer)..... | 23 |
| Figure 8. Sperm Cryopreservation | 23 |
| Figure 9. Testicular Shielding During Radiation Therapy | 24 |
| Figure 10. Enrollees Impacted by SB 172 and Utilization of Fertility Preservation Services at Baseline .. | 27 |
| Figure 11. Scenario 2 (Amended Language) Expenditure Impacts by Category Postmandate, SB 172 .. | 29 |

Table 1. Scenario 1: SB 172 (as Introduced) Impacts on Benefit Coverage, Utilization, and Cost, 2018

| | Baseline | Postmandate | Increase/ Decrease | Change Postmandate |
|---|--------------------------|--------------------------|-----------------------|-----------------------|
| Benefit Coverage | | | | |
| Total enrollees with health insurance subject to state-level benefit mandates (a) | 24,048,000 | 24,048,000 | 0 | 0% |
| Total enrollees with health insurance subject to SB 172 | 16,212,000 | 16,212,000 | 0 | 0% |
| Percentage of enrollees with health insurance subject to SB 172 | 67% | 67% | 0% | 0% |
| Number of enrollees with health insurance fully compliant with SB 172 | 13,721,034 | 16,212,000 | 2,490,966 | 18% |
| Percentage of enrollees with health insurance fully compliant SB 172 | 85% | 100% | 15% | 18% |
| Utilization and Cost | | | | |
| Number of enrollees of child bearing age with cancer diagnosis where treatment might result in iatrogenic infertility | | | | |
| Male | 2,482 | 2,482 | 0 | 0% |
| Female | 5,107 | 5,107 | 0 | 0% |
| Number of these enrollees with cancer using fertility preservation services covered by insurance | | | | |
| Male | 731 | 950 | 219 | 30% |
| Female | 721 | 937 | 216 | 30% |
| Total Fertility Preservation | 1,452 | 1,887 | 435 | 30% |
| Number of these enrollees with cancer using fertility preservation services <u>not</u> covered by insurance | | | | |
| Male | 121 | 0 | -121 | -100% |
| Female | 65 | 0 | -65 | -100% |
| Total Fertility Preservation | 186 | 0 | -186 | -100% |
| Average cost per fertility preservation procedure, including prescription drugs | | | | |
| Male | \$600 | \$600 | \$0 | 0% |
| Female | \$13,500 | \$13,500 | \$0 | 0% |
| Expenditures | | | | |
| Private Employers for group insurance | \$64,820,615,000 | \$64,821,961,000 | \$1,346,000 | 0.0021% |
| CalPERS HMO employer expenditures (c) | \$4,884,262,000 | \$4,884,320,000 | \$58,000 | 0.0012% |
| Medi-Cal Managed Care Plan expenditures (d) | \$27,983,856,000 | \$27,983,856,000 | \$0 | 0.0000% |
| Enrollees for individually purchased insurance | \$14,608,214,000 | \$14,609,418,000 | \$1,204,000 | 0.0082% |
| Individually Purchased – Outside Exchange | \$6,304,061,000 | \$6,304,648,000 | \$587,000 | 0.0093% |
| Individually Purchased – Covered California | \$8,304,153,000 | \$8,304,770,000 | \$617,000 | 0.0074% |
| Enrollees with group insurance, CalPERS HMOs, Covered California, and Medi-Cal Managed Care (a) (b) | \$20,387,090,000 | \$20,387,508,000 | \$418,000 | 0.0021% |
| Enrollee out-of-pocket expenses for covered benefits (deductibles, copayments, etc.) | \$13,565,623,000 | \$13,565,750,000 | \$127,000 | 0.0009% |
| Enrollee expenses for noncovered benefits (e) | \$956,000 | \$0 | -\$956,000 | -100.0000% |
| Total Expenditures | \$146,250,616,000 | \$146,252,813,000 | \$2,197,000 | 0.0015% |

Source: California Health Benefits Review Program, 2017.

Notes: (a) This population includes persons with privately funded 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 employment sponsored insurance.

(b) Premium expenditures by enrollees include employee contributions to employer-sponsored health insurance and enrollee contributions for publicly purchased insurance.

(c) Of the increase in CalPERS employer expenditures, about 56.7% or \$33,000 would be state expenditures for CalPERS members who are state employees or their dependents. It should be noted, however, that should CalPERS choose to make similar adjustments for consistency to the benefit coverage of enrollees associated with CalPERS' self-insured products, the fiscal impact on CalPERS could be greater.

(d) Does not include enrollees in County Operated Health Systems (COHS).

(e) Includes only those expenses that are paid directly by enrollees to providers for services related to the mandated benefit that are not currently covered by insurance. In addition, 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.

Table 2. Scenario 2: SB 172 (as Amended 3/7/2017) Impacts on Benefit Coverage, Utilization, and Cost, Total Annual Impact

| | Baseline | Postmandate | Increase/ Decrease | Change Postmandate |
|---|------------|-------------|-----------------------|-----------------------|
| Benefit Coverage | | | | |
| Total enrollees with health insurance subject to state-level benefit mandates (a) | 24,048,000 | 24,048,000 | 0 | 0% |
| Total enrollees with health insurance subject to SB 172 | 16,212,000 | 16,212,000 | 0 | 0% |
| Percentage of enrollees with health insurance subject to SB 172 | 67% | 67% | 0% | 0% |
| Number of enrollees with fertility preservation coverage that is fully compliant with SB 172 | 13,721,034 | 16,212,000 | 2,490,966 | 18% |
| Percentage of enrollees with fertility preservation coverage that is fully compliant with SB 172 | 85% | 100% | 15% | 18% |
| Number of enrollees with infertility treatment coverage fully compliant with SB 172 | 6,225,320 | 16,212,000 | 9,986,680 | 160% |
| Percentage of enrollees with infertility treatment coverage fully compliant with SB 172 | 38% | 100% | 62% | 160% |
| Utilization and Cost | | | | |
| Number of enrollees of child bearing age with cancer diagnosis where treatment might result in iatrogenic infertility | | | | |
| Male | 2,482 | 2,482 | 0 | 0% |
| Female | 5,107 | 5,107 | 0 | 0% |
| Number of these enrollees with cancer using fertility preservation services covered by insurance | | | | |
| Male | 731 | 950 | 219 | 30% |
| Female | 721 | 937 | 216 | 30% |
| Total Fertility Preservation | 1,452 | 1,887 | 435 | 30% |
| Number of enrollees using infertility treatment services covered by insurance | | | | |
| Male | 31 | 90 | 59 | 186% |
| Female | 108 | 309 | 201 | 186% |
| Total Infertility Treatment | 139 | 399 | 260 | 186% |
| Number of enrollees using infertility treatment services resulting in a delivery covered by insurance | | | | |
| Male | 15 | 44 | 29 | 186% |
| Female | 51 | 145 | 95 | 186% |
| Total Enrollees with Live Births | 66 | 190 | 123 | 186% |
| Number of enrollees using infertility treatment services resulting in a miscarriage covered by insurance | | | | |
| Male | 8 | 22 | 14 | 186% |
| Female | 25 | 73 | 47 | 186% |
| Total Enrollees with Miscarriages | 33 | 95 | 62 | 186% |
| Average cost per fertility preservation procedure, including prescription drugs | | | | |
| Male | \$600 | \$600 | \$0 | 0% |
| Female | \$13,500 | \$13,500 | \$0 | 0% |

| | | | | |
|---|--------------------------|--------------------------|--------------------|----------------|
| Average cost per infertility treatment procedure | | | | |
| Male | \$1,750 | \$1,750 | \$0 | 0% |
| Female | \$9,800 | \$9,800 | \$0 | 0% |
| Average cost per live delivery | | | | |
| Male | \$19,500 | \$19,500 | \$0 | 0% |
| Female | \$19,500 | \$19,500 | \$0 | 0% |
| Average cost per miscarriage | | | | |
| Male | \$4,150 | \$4,150 | \$0 | 0% |
| Female | \$4,150 | \$4,150 | \$0 | 0% |
| Expenditures | | | | |
| Private Employers for group insurance | \$64,820,615,000 | \$64,824,647,000 | \$4,032,000 | 0.0062% |
| CalPERS HMO employer expenditures (c) | \$4,884,262,000 | \$4,884,517,000 | \$255,000 | 0.0052% |
| Medi-Cal Managed Care Plan expenditures (d) | \$27,983,856,000 | \$27,983,856,000 | \$0 | 0.0000% |
| Enrollees for individually purchased insurance | \$14,608,214,000 | \$14,610,194,000 | \$1,980,000 | 0.0136% |
| Individually Purchased – Outside Exchange | \$6,304,061,000 | \$6,305,014,000 | \$953,000 | 0.0151% |
| Individually Purchased – Covered California | \$8,304,153,000 | \$8,305,180,000 | \$1,027,000 | 0.0124% |
| Enrollees with group insurance, CalPERS HMOs, Covered California, and Medi-Cal Managed Care (a) (b) | \$20,387,090,000 | \$20,388,378,000 | \$1,288,000 | 0.0063% |
| Enrollee out-of-pocket expenses for covered benefits (deductibles, copayments, etc.) | \$13,565,623,000 | \$13,565,954,000 | \$331,000 | 0.0024% |
| Enrollee expenses for noncovered benefits (e) | \$1,885,000 | \$0 | -\$1,885,000 | -100.0000% |
| Total Expenditures | \$146,251,545,000 | \$146,257,546,000 | \$6,001,000 | 0.0041% |

Source: California Health Benefits Review Program, 2017.

Notes: (a) This population includes persons with privately funded 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 employment sponsored insurance.

(b) Premium expenditures by enrollees include employee contributions to employer-sponsored health insurance and enrollee contributions for publicly purchased insurance.

(c) Of the increase in CalPERS employer expenditures, about 56.7% or \$144,000 would be state expenditures for CalPERS members who are state employees or their dependents. It should be noted, however, that should CalPERS choose to make similar adjustments for consistency to the benefit coverage of enrollees associated with CalPERS' self-insured products, the fiscal impact on CalPERS could be greater.

(d) Does not include enrollees in County Operated Health Systems (COHS).

(e) Includes only those expenses that are paid directly by enrollees to providers for services related to the mandated benefit that are not currently covered by insurance. In addition, 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.

POLICY CONTEXT

The California Senate Committee on Health requested that the California Health Benefits Review Program (CHBRP)³ conduct an evidence-based assessment of the medical, financial, and public health impacts of Senate Bill (SB) 172 (Portantino), Fertility Preservation, introduced January 23, 2017.

CHBRP received a follow-up request from the Senate Health Committee to also include a cost estimate for the amended language (amended March 7, 2017). Thus, the cost section of this report estimates impacts of both the introduced and amended language. However, the rest of the report reflects only the language as introduced.

If enacted, SB 172 would affect the health insurance of approximately 16,212,000 enrollees (approximately 43 percent of all Californians). This represents 67% of the approximately 24 million Californians who will have health insurance regulated by the state that may be subject to any state health benefit mandate law — health insurance regulated by the California Department of Managed Health Care (DMHC) or the California Department of Insurance (CDI). If enacted, the law would affect the health insurance of enrollees in DMHC-regulated plans and CDI-regulated policies, exempting specialized health care service plans (e.g., vision only, dental only) and Medi-Cal.

Bill-Specific Analysis of SB 172, Fertility Preservation

Bill Language

As introduced (January 23, 2017), SB 172 would require that individual or group health care service plans or policies issued, amended, or renewed on and after January 1, 2018, that cover hospital, medical, surgical, and other iatrogenic expenses for diagnoses with medical interventions that may directly or indirectly cause iatrogenic infertility shall include coverage for evaluation and treatment of iatrogenic infertility, including but not limited to standard fertility preservation services.

As amended (March 7, 2017), the bill would require coverage for evaluation and treatment of iatrogenic infertility including, but not limited to, standard fertility preservation services. The full text of SB 172 can be found in Appendix A.

Analytic Approach and Key Assumptions

Iatrogenic infertility

Iatrogenic infertility is medically induced infertility caused by a medical intervention used to treat a primary disease or condition. Iatrogenic infertility is typically caused by cancer treatments, such as radiation and chemotherapy (gonadotoxic treatments) or surgical removal of reproductive organs. Less frequently, fertility is compromised by treatments for autoimmune disorders such as systemic lupus erythematosus or rheumatoid arthritis or Crohn's disease (Bermas and Sammaritano, 2015; Lawrenz et al., 2011). Autoimmune conditions sometimes require gonadotoxic or surgical treatments (Bermas and Sammaritano 2015); individuals with gender and sex diversity such as individuals who are transgender may also undergo gonadotoxic treatments.

³ CHBRP's authorizing statute is available at <http://chbrp.org/faqs.php>.

For this analysis, CHBRP focuses on iatrogenic infertility attributable to cancer treatments due to the higher prevalence of cancer (and concordant volume of literature), which outweighs that of the aforementioned conditions. The fertility preservation studies identified by the CHBRP literature search were almost exclusively focused on the cancer population (see the *Medical Effectiveness* section.). In addition, there are no evidence-based recommendations for fertility preservation for patients outside of cancer patients, and thus the research on fertility preservation has focused almost exclusively on this group.⁴ Lastly, it is estimated that approximately 90% of iatrogenic infertility is caused by cancer treatment (Lawrenz et al., 2011). This approach was confirmed by a clinical content expert with expertise in reproductive medicine.

Fertility preservation

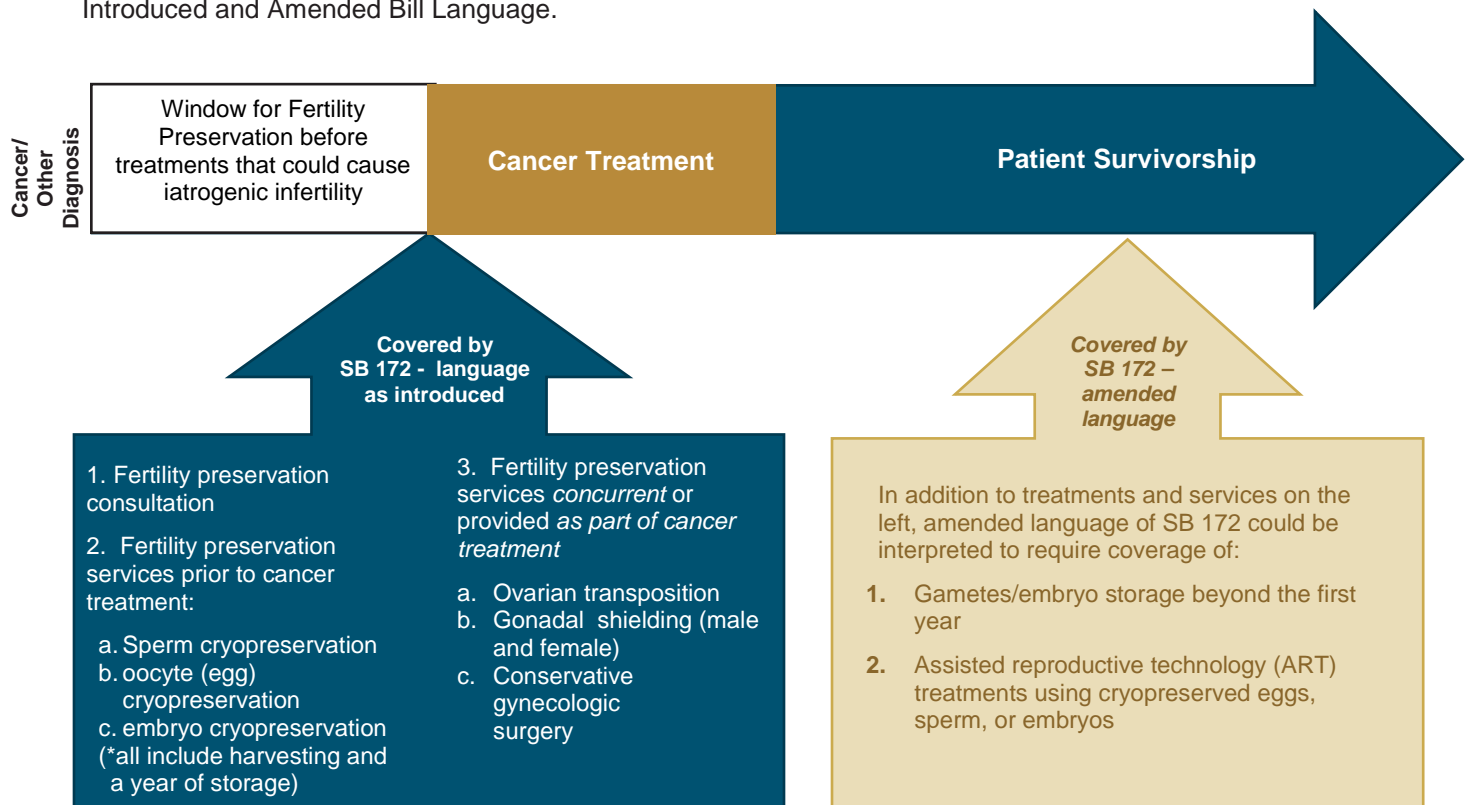
The National Cancer Institute defines fertility preservation as a type of procedure used to maintain an individual's ability to have children. If a patient is expected to undergo a treatment that could increase the risk of iatrogenic infertility, the patient and their provider may pursue fertility preservation services prior to the treatment. For example, a cancer patient who is currently not experiencing infertility may choose to undergo fertility preservation services before beginning a gonadotoxic treatment which may cause iatrogenic infertility.

Patients at risk for iatrogenic infertility differ from patients being treated for infertility in that they need to take steps to preserve their fertility prior to undergoing treatment that may put them at risk of infertility. Most cancer patients will not know beforehand if their treatment will lead to infertility. Fertility preservation services are also distinct from infertility treatment. Infertility is defined as the inability to conceive after 12 months of unprotected intercourse.⁵ Infertility treatments occur while a patient is already experiencing infertility. Conversely, fertility preservation services occur before a patient experiences infertility or may be at risk for infertility.

⁴ In 2015, the American Society of Reproductive Medicine published a statement that transgender patients should be informed of and offered fertility preservation services before gender confirmation treatment. The statement also notes: "There are currently no practice guidelines for physicians providing fertility preservation and reproductive care to transgender patients....However, further research is needed to provide evidence-based and patient-centered care...."

⁵ https://www.asrm.org/Booklet_Infertility_An_Overview/

Figure 1. Covered and Uncovered Fertility Preservation Services of SB 172 based on Bill Language as Introduced and Amended Bill Language.



Source: California Health Benefits Review Program, 2017.

Figure 1 provides an overview of fertility preservation services in conjunction with a cancer diagnosis and cancer treatment. The SB 172 language as introduced (Scenario 1) only covers fertility preservation consultation; sperm, oocyte, and embryo cryopreservation; and services as part of or concurrent with cancer treatment for persons likely to experience *iatrogenic infertility*. However, the amended language of SB 172 (Scenario 2) could be interpreted to cover both the services covered by the language as introduced *and* infertility treatment for iatrogenic infertility, including assisted reproductive technology (ART) treatments. The *Benefit Coverage, Utilization, and Cost Impacts* section of the report estimates costs for both the language as introduced (Scenario 1) and the amended language (Scenario 2). However, the other main sections of the report (Background, Medical Effectiveness, and Public Health) only address the language as introduced.

Coverage for fertility preservation services versus coverage for infertility treatment

An enrollee may have coverage for *infertility treatment* but may not have coverage for *fertility preservation services*, and vice versa. The SB 172 bill language as introduced would not require coverage of infertility treatment nor would it affect current coverage rates for infertility treatment. The amended language could be interpreted to require coverage for infertility treatment for iatrogenic infertility.

Current California law requires group CDI-regulated policies and most group DMHC-regulated plans to *offer coverage* for infertility treatment.⁶ “Mandate to offer” means all health care service plans and health insurers selling health insurance subject to the mandate are required to offer coverage for the benefit for

⁶ H&SC Section 1374.55 and IC Section 10119.6.

purchase. The health plan or insurer may comply with the mandate either (1) by including the benefit as standard in its health insurance products, or (2) by offering coverage for the benefit separately at an additional cost (e.g., a rider). “Mandate to cover” means that all health insurance subject to the law must cover the benefit.

Interaction with Existing Requirements

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

State Requirements

California law and regulations

Current California law requires group CDI-regulated policies and most group DMHC-regulated plans to offer coverage for infertility treatment, except in vitro fertilization.^{7,8,9} This statute does not require coverage for fertility preservation services.

Other existing California state benefit mandates require coverage for various aspects of the screening, diagnosis, and treatment of cancer. However, these existing state benefit mandates do not require coverage for fertility preservation services as part of cancer treatment.

CHBRP reviewed the state’s Independent Medical Review (IMR) determinations and found three determinations related to fertility preservation. The most relevant decision to SB 172 involved a 33-year old woman who requested embryo cryopreservation following a breast cancer diagnosis.¹⁰ The decision noted that embryo cryopreservation is the best established method of fertility preservation. The IMR decision ruled that this was an appropriate therapy, and the enrollee’s only option to preserve fertility; the health plan’s decision was overturned.

Another decision involved an enrollee request for a fertility specialist consultation and potential egg retrieval and use of a surrogate.¹¹ Partially due to the patient’s age, the IMR deemed that the patient’s request was medically necessary and the health plan decision was overturned. The third decision involved an enrollee undergoing gender transition (aged 11–20) whose parent requested oocyte cryopreservation.¹² The reviewers noted it was not clear whether the patient had expressed a desire to preserve his fertility, and thus, the reviewers deemed that the service was not medically necessary for the enrollees’ treatment. The IMR decision upheld the health plan’s decision.

⁷ H&SC Section 1374.55 and IC Section 10119.6.

⁸ California code defines (1) the presence of a demonstrated condition recognized by a licensed physician and surgeon as a cause of infertility, or (2) the inability to conceive a pregnancy or to carry a pregnancy to a live birth after a year or more of regular sexual relations without contraception. “Treatment for infertility” means procedures consistent with established medical practices in the treatment of infertility by licensed physicians and surgeons including but not limited to diagnosis, diagnostic tests, medication, surgery, and gamete intrafallopian transfer. “In vitro fertilization” means the laboratory medical procedures involving the actual in vitro fertilization process.

⁹ While California does not require plans or policies to offer coverage for in vitro fertilization, the state does require that plans offer coverage for gamete intrafallopian transfer (GIFT). <http://www.asrm.org/insurance.aspx>

¹⁰ IMR Reference ID EI11-12274.

¹¹ IMR Reference ID MN15-20864.

¹² IMR Reference ID EI15-20978.

Similar requirements in other states

At the time of this report's publication, no state has a law requiring coverage for fertility preservation services in the event of iatrogenic infertility. Currently and over the past year, some states have introduced bills to require coverage of fertility preservation services related to iatrogenic infertility. Some states have introduced standalone bills focused on fertility preservation alone, while others have introduced bills mandating coverage for in vitro fertilization and fertility preservation in the event of iatrogenic infertility.

Some states have introduced fertility preservation bills in 2017:

- In January 2017, Senate Bill S3148 was introduced in New York. It would require coverage for in vitro fertilization and other fertility preservation treatments when necessary medical treatment may directly or indirectly cause iatrogenic infertility.¹³
- In January 2017, House Bill (HB) 5968 was introduced in Connecticut. HB 5968 would require health insurance coverage for fertility preservation for insureds diagnosed with cancer specifically.¹⁴
- In February 2017, SB 918 was introduced in Maryland. SB 918 would require certain insurers, nonprofit health service plans and HMOs to provide coverage for certain fertility preservation services. SB 918 defines "standard fertility preservation procedures" as procedures to preserve fertility that are consistent with established medical practices and professional guidelines published by the American Society for Reproductive Medicine, the American College of Obstetricians and Gynecologists, or the American Society of Clinical Oncology.¹⁵
- Also in February 2017, HB 1562 was introduced in Hawaii. HB 1562 would require Hawaii insurance companies to include as a covered benefit embryo, oocyte, and sperm cryopreservation procedures for "adult females of reproductive potential" and adult males who are diagnosed with cancer and have not started cancer treatment.¹⁶

In the previous legislative season (2015-2016), both Connecticut and Hawaii introduced bills related to fertility preservation that were not enacted into law. Connecticut's bill (House Bill No. 5968) would have required coverage for fertility preservation for insureds diagnosed with cancer.¹⁷ Hawaii's SB 781 would have required coverage for embryo, oocyte, and sperm cryopreservation, including in vitro fertilization procedures, for insureds and covered dependents if several requirements are met. Those requirements include: the patient must be an adult female of reproductive potential or an adult male; the patient has been diagnosed with cancer but has not yet started treatment; and the procedures conform to guidelines of the American College of Obstetricians and Gynecologists for in vitro fertilization or the minimum standards of the American Society of Reproductive Medicine for in vitro fertilization.¹⁸

Distinct from fertility preservation services, 15 states require health insurers to cover (13) or offer coverage (2) for infertility diagnosis and treatment, including: Arkansas, California, Connecticut, Hawaii, Illinois, Louisiana, Maryland, Massachusetts, Montana, New Jersey, New York, Ohio, Rhode Island, Texas and West Virginia (NCSL, 2014). Laws in California and Texas require insurers to offer coverage

¹³ New York Senate Bill S3148. Available at: <https://www.nysenate.gov/legislation/bills/2017/S3148>.

¹⁴ Connecticut House Bill 5968. Available at: https://www.cga.ct.gov/asp/cgabillstatus/cgabillstatus.asp?selBillType=Bill&bill_num=HB05968&which_year=2017.

¹⁵ Maryland Senate Bill 918. Available at: <http://mgaleg.maryland.gov/2017RS/bills/sb/sb0918F.pdf>.

¹⁶ Hawaii House Bill 1562. Available at: <https://legiscan.com/HI/text/HB1562/id/1481519>.

¹⁷ Proposed HB No. 5968. Connecticut General Assembly. Available at: https://www.cga.ct.gov/asp/cgabillstatus/cgabillstatus.asp?selBillType=Bill&bill_num=HB05968&which_year=2017.

¹⁸ Hawaii SB 781. Available at: http://www.capitol.hawaii.gov/session2016/bills/SB781_.PDF.

for infertility treatment (Resolve: The National Infertility Association, 2017). As in California, state laws in Louisiana and New York also specifically exclude coverage for in vitro fertilization (NCSL, 2014).

Federal requirements

Affordable Care Act

A number of Affordable Care Act (ACA) provisions have the potential to or do interact with state benefit mandates. Below is an analysis of how SB 172 may interact with requirements of the ACA as presently exists in federal law, including the requirement for certain health insurance to cover essential health benefits (EHBs).¹⁹

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

Essential Health Benefits

State health insurance marketplaces, such as Covered California, are responsible for certifying and selling qualified health plans (QHPs) in the small-group and individual markets. QHPs are required to meet a minimum standard of benefits as defined by the ACA as essential health benefits (EHBs). In California, EHBs are related to the benefit coverage available in the Kaiser Foundation Health Plan Small Group Health Maintenance Organization (HMO) 30 plan, the state's benchmark plan for federal EHBs.^{20,21}

States may require QHPs to offer benefits that exceed EHBs.²² However, a state that chooses to do so must make payments to defray the cost of those additionally mandated benefits, either by paying the purchaser directly or by paying the QHP.^{23,24} State rules related to provider types, cost-sharing, or reimbursement methods would *not meet* the definition of state benefit mandates that could exceed EHBs.²⁵

Based on the language as introduced, it is unclear whether SB 172 would exceed EHBs. In some cases, fertility preservation services may be considered a medically necessary component of a service that falls

¹⁹ The ACA requires nongrandfathered small-group and individual market health insurance — including but not limited to QHPs sold in Covered California — to cover 10 specified categories of EHBs. Resources on EHBs and other ACA impacts are available on the CHBRP website: http://www.chbrp.org/other_publications/index.php.

²⁰ 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. CCIIO, Essential Health Benefits Bulletin. Available at: cciio.cms.gov/resources/files/Files2/12162011/essential_health_benefits_bulletin.pdf.

²¹ H&SC Section 1367.005; IC Section 10112.27.

²² ACA Section 1311(d)(3).

²³ State benefit mandates enacted on or before December 31, 2011, may be included in a state's EHBs, according to the U.S. Department of Health and Human Services (HHS). Patient Protection and Affordable Care Act: Standards Related to Essential Health Benefits, Actuarial Value, and Accreditation. Final Rule. Federal Register, Vol. 78, No. 37. February 25, 2013. Available at: www.gpo.gov/vfdsys/pkg/FR-2013-02-25/pdf/2013-04084.pdf.

²⁴ However, as laid out in the Final Rule on EHBs HHS released in February 2013, state benefit mandates enacted on or before December 31, 2011, would be included in the state's EHBs and there would be no requirement that the state defray the costs of those state mandated benefits. For state benefit mandates enacted after December 31, 2011, that are identified as exceeding EHBs, the state would be required to defray the cost.

²⁵ Essential Health Benefits. Final Rule. A state's health insurance marketplace 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.

within the EHBs (e.g., chemotherapy treatment for cancer). Also, fertility preservation services for iatrogenic infertility occur before a patient becomes infertile; thus, fertility preservation is distinct from infertility treatment, which is not included in the state's benchmark plan (CMS, 2017).

However, the amended bill language could be interpreted to exceed the EHBs, because the amended language requires coverage of the "evaluation and treatment of iatrogenic infertility." The treatment of iatrogenic infertility could be interpreted to include a larger range of services beyond fertility preservation services, including infertility treatment. Infertility treatment is a coverage exclusion in the state's EHB benchmark plan (CMS, 2017). Therefore, the amended bill language could be interpreted to exceed the EHBs.

BACKGROUND ON FERTILITY PRESERVATION

Fertility preservation services provide patients at risk for iatrogenic infertility with the ability to conceive children following gonadotoxic treatments (e.g., radiation, chemotherapy, prolonged endocrine therapy, gonadotoxic medications, surgery). In order to preserve reproductive capabilities, fertility preservation services are obtained prior to primary disease treatment. Table 2 describes the standard (nonexperimental) types of fertility preservation services, and whether they are subject to SB 172. (Note that CHBRP assumes harm reduction procedures and conservative gynecologic surgery are covered by an enrollee’s medical benefit for cancer treatment.)

The selection of an appropriate fertility preservation service for patients at risk for iatrogenic infertility varies by the age and gender of the patient, the patient’s marital status, cultural and religious beliefs, and the type of cancer treatment the patient is undergoing. For example, a female adolescent may be more likely to choose oocyte cryopreservation over embryo cryopreservation, compared to an older woman with a partner.

SB 172 language as introduced addresses the first stage of fertility care: fertility preservation services. However, at some point, cancer survivors may choose to have a child and retrieve cryopreserved eggs, sperm, or embryos to use for artificial insemination or in vitro fertilization; the timeframe for retrieval has been documented to range from 1 to 10 years later (Oktay and Oktem, 2010). Note that SB 172 as introduced does not require coverage for the follow-up assisted reproductive technologies (ART) such as artificial insemination, in vitro fertilization, and/or embryo transfer.

Table 3. Summary of Types of Fertility Preservation and SB 172 Coverage Status

| Preservation Service | Definition of Service | FP Service Timing ^(a) | Other Considerations | Covered by SB 172? |
|--|---|---|--|--------------------|
| CRYOPRESERVATION | | | | |
| Embryo cryopreservation | Ovarian stimulation via outpatient hormone prescriptions; harvesting eggs, IVF, and freezing of embryos | Occurs before or during cancer treatment Outpatient process takes 10–15 days | Need partner or donor sperm | Yes |
| Oocyte cryopreservation | Ovarian stimulation; harvesting and freezing of unfertilized eggs | Occurs before or during cancer treatment Outpatient process takes 10–15 days | | Yes |
| Sperm cryopreservation | Collection and freezing of sperm | Occurs before cancer treatment Outpatient process takes 1–2 days | | Yes |
| HARM REDUCTION | | | | |
| Ovarian shielding during radiation therapy (radiation shielding) | Use of shielding to reduce scatter radiation to the ovaries | Occurs in conjunction with radiation treatments | Does not protect against effects of chemotherapy | Already covered* |

| Preservation Service | Definition of Service | FP Service Timing ^(a) | Other Considerations | Covered by SB 172? |
|---|--|---|--|--------------------|
| Testicular shielding during radiation therapy (radiation shielding) | Using shielding to reduce the dose of radiation delivered to the testicles during cancer treatment | Occurs in conjunction with radiation treatments | Does not protect against effects of chemotherapy | Already covered* |
| Ovarian transposition (oophoropexy) | Surgical repositioning of ovaries out of radiation field | Occurs before treatment. Outpatient procedure (1 week of recovery time) | | Already covered* |

CONSERVATIVE GYNECOLOGIC SURGERY

| | | | | |
|--|---|------------------------------|--|------------------|
| Radical trachelectomy | Surgical removal of the cervix with preservation of the uterus | Inpatient surgical procedure | Limited to early stage cervical cancer | Already covered* |
| Conservative ovarian cancer surgery ^(b) | The conservative treatment preserves the uterus and one ovary, in cases where cancer was confined to just one ovary | During cancer surgery | | Already covered* |

Source: California Health Benefits Review Program, 2017. (Adapted from a table by Save My Fertility, an initiative of the Oncofertility Consortium at Northwestern University and the Endocrine Society with input from content expert, Dr. H. Irene Su, Associate Professor of Reproductive Medicine at the University of California, San Diego.)

Notes: (a) “During” treatment is defined as preservation services occurring after surgery and before chemotherapy, radiation, or other gonadotoxic medication administration.

(b) The standard treatment for ovarian cancer is the removal of the uterus (hysterectomy) and removal of both ovaries.

Incidence of Diseases with Treatments Likely to Result in Iatrogenic Infertility

As no estimates of the incidence of all-cause iatrogenic infertility exist, and treatments for autoimmune illnesses less commonly lead to iatrogenic infertility, CHBRP relies on rates of cancer among men and women of reproductive age as a proxy of number of fertility preservation users (see *Policy Context* for further details).

The definition of reproductive age for purposes of iatrogenic infertility due to cancer treatment is typically under 45 years old, including children aged 0 to 15 years whose cancer treatment could impact their future fertility (Reinecke et al., 2012). According to data from the California Cancer Registry, more than 8,000 Californians of reproductive age (2,711 males and 5,364 females aged 10 to 44 years), regardless of insurance status, are diagnosed annually with a cancer whose treatments are likely to result in iatrogenic infertility (see Table 4) (CDC, 2017). The increased risk of iatrogenic infertility for women is due to the high incidence of breast cancer.

Table 4. Incidence of Cancer Using Treatments Likely to Result in Iatrogenic Infertility for Californians Aged 10–44 Years Regardless of Insurance Status, 2013

| Cancer Type | Female | | Male | |
|----------------------|--------------|------------------|--------------|------------------|
| | Count | Rate per 100,000 | Count | Rate per 100,000 |
| Breast | 2806 | 30.3 | -- | -- |
| Cervix uteri | 504 | 5.4 | -- | -- |
| Corpus uteri | 384 | 4.1 | -- | -- |
| Ovarian | 267 | 2.9 | -- | -- |
| Male genital | -- | -- | 1033 | 10.7 |
| Colon and rectum | 398 | 4.3 | 243 | 2.5 |
| Hodgkin lymphoma | 223 | 2.4 | 265 | 2.7 |
| Non-Hodgkin lymphoma | 301 | 3.2 | 443 | 4.6 |
| Leukemia | 269 | 2.9 | 438 | 4.5 |
| Brain/CNS | 212 | 2.3 | 289 | 3.0 |
| Total | 5,364 | | 2,711 | |

Source: California Health Benefits Review Program, 2017. Based on CDC, 2017.

Incidence of Iatrogenic Infertility

The extent to which patients will become infertile after undergoing cancer treatment varies by sex, age, type of cancer, and type and duration of treatment (Coccia et al., 2014; Lambertini et al., 2016). For example, rates of ovarian failure due to chemotherapy averages 38% regardless of age; however, dose-related risk for premature menopause due to lymphoma treatment ranges from 15% (low-dose procarbazine) to 64% (cumulative high-dose procarbazine) (Coccia et al., 2014). Men also experience varying rates of iatrogenic infertility depending on treatment and dose. For example, more than 90% of men receiving procarbazine therapy experience azoospermia (sperm absent from semen) while other chemotherapies permit fertility to return soon after treatment concludes (Coccia et al., 2014). The Livestrong Foundation developed a fertility risk tool that shows risk estimates for different types of cancers and treatments for males and females ranging from low-no risk for thyroid cancer to 80% amenorrhea (cessation of menses) for ovarian cancer (Livestrong, 2017). Because it is unknown who will experience permanent iatrogenic infertility, it is recommended that anyone undergoing gonadotoxic treatments be offered fertility preservation services (Loren et al., 2013). Note that some cases of iatrogenic infertility can be temporary, and not all patients receiving gonadotoxic treatments become permanently infertile.

Using probabilities of developing cancer by age²⁶ and gender for the top 10 cancers with treatments most likely to lead to iatrogenic infertility (Appendix C), and adjusting for the population subject to SB 172,

²⁶ Based on content expert input, this analysis is restricted to those of reproductive age, which is defined as ages 12 to 44 years for females and ages 12 to 49 years for males.

CHBRP estimated that 7,589 cancer patients enrolled in health plans subject to SB 172 (2,482 males and 5,107 females, see Table 1) would be at risk for infertility due to cancer treatments each year.

Fertility Preservation: Physician Referral and Counseling

The fertility preservation guidelines issued by the American Society of Clinical Oncology (ASCO) indicate that all patients of childbearing age and prepubescent children should be counseled about their fertility preservation options prior to starting treatment that could impair their future fertility (Loren et al., 2013). One survey reported that although 95% of oncologists discussed fertility risk, 61% rarely or never referred patients for fertility preservation (Forman et al., 2010). A 2011 survey showed that less than 50% of pediatric oncologists referred patients for fertility preservation overall, and 12% referred female patients prior to treatment (Kohler et al., 2011).

Health Disparities²⁷ in Iatrogenic Infertility and Fertility Preservation

“‘Health disparity’ denotes differences, whether unjust or not. ‘Health inequity’ on the other hand, denotes differences in health [status or] outcomes that are systematic, avoidable, and unjust.” (Wyatt et al., 2016). There is a paucity of literature regarding disparities in fertility preservation. This section includes discussion about differences in physician fertility preservation referral rates, and fertility preservation cost differentials, when possible.

Race/Ethnicity

Although the incidence of various cancers is known to disproportionately affect certain minority groups, CHBRP found no evidence that evaluated the extent to which iatrogenic infertility varied by race/ethnicity. There is a paucity of literature comparing fertility preservation referral and counseling among cancer patients of reproductive age by race or ethnicity. Of the three studies CHBRP found, all had small sample sizes and statistically insignificant findings showing that whites were more likely to have fertility preservation discussions and referrals than minorities (Goodman et al., 2012; Quinn et al., 2015; Shnorhavorian et al., 2015).

Sex

Some studies reported inequity in physician referrals for fertility preservation by sex, with males more likely to be referred than females. One reason for differential referral rates is physician perception that male fertility preservation is less invasive and more affordable than female fertility preservation methods. (Bann et al., 2015; Kohler et al., 2011; Quinn et al., 2015; Shnorhavorian et al., 2015). Costs are lower for male fertility preservation methods compared to methods used for females. For males, sperm cryopreservation is the standard method of preserving fertility, costing approximately \$600 in California. For females, oocyte and embryo cryopreservation are the standard methods of preserving fertility and cost, on average, \$13,500 in California.

²⁷ Several competing definitions of “health disparities” exist. CHBRP relies on the following definition: Health disparity is defined as the difference in health outcomes between groups within a population. While the terms may seem interchangeable, “health disparity” is different from “health inequity.” “Health disparity” denotes differences, whether unjust or not. “Health inequity,” on the other hand, denotes differences in health [status or] outcomes that are systematic, avoidable, and unjust.” Wyatt et al., 2016.

Age

Aside from fertility conserving surgeries or shielding from radiation, prepubescent cancer patients have no available standard of care fertility preservation options; there are procedures that harvest ovarian or testicular tissue, but these are experimental. Although long-term survival following pediatric cancer has increased to more than 80 percent (Salih et al., 2015), permanent infertility remains an adverse late effect of cancer treatment until fertility preservation technology improves. Following puberty, individuals are able to undergo standard of care procedures including oocyte, embryo, or sperm cryopreservation; and children as well as adults may undergo fertility conserving surgeries and procedures. Goodman et al. (2012) found that female adults younger than 35 years received fertility preservation counseling three times as often as those over 35 years (OR 3.3, 95% CI 1.4-7.7).

Gender Identity/Sexual Orientation

People who identify as transgender and choose gender confirmation surgery or hormonal therapy could become infertile; thus, they would be eligible for coverage under SB 172. Flores et al. (2016) estimate that in 2014 in California, there were 33,450 transgender persons aged 18 to 24 years and 154,750 transgender persons aged 25 to 64 years (0.84% and 0.77% of the California adult population, respectively).

Both the American Society of Reproductive Medicine and the Endocrine Society published separate statements that patients should be informed about and offered fertility preservation services before gender confirmation treatment (American Society for Reproductive Medicine, 2015; Hembree et al., 2009). CHBRP found two small international studies assessing transgender persons' interest in having children. More than half of 50 transgender men reported a desire for children (Wierckx et al., 2012), and 51% of 121 transgender women would have thought seriously about or cryopreserved sperm if the service had been available (De Sutter et al., 2002). The proportion of transgender persons in California or the United States undergoing gender confirmation treatment and using fertility preservation is unknown.

MEDICAL EFFECTIVENESS

As discussed in the *Policy Context*, SB 172 as introduced would require coverage of “medically necessary expenses for standard fertility preservation services when a necessary medical treatment may directly or indirectly cause iatrogenic infertility.” This review summarizes findings from the literature on the effectiveness of specific fertility preservation services (as described in Table 3 in the *Background on Fertility Preservation* section). Eight of these services are considered standard of care: embryo cryopreservation, oocyte (egg) cryopreservation, sperm cryopreservation, ovarian transposition (oophoropexy), ovarian shielding during radiation therapy, testicular shielding during radiation therapy, conservative surgical approaches for gynecologic cancers (conservative ovarian cancer surgery and radical trachelectomy), and the focus of the *Medical Effectiveness* section is on these procedures. The other five services not subject to SB 172 — cryopreservation (ovarian tissue and testicular tissue), suppression with hormones during radiation (ovarian and testicular), and maturation of oocytes outside of the body — are considered experimental and are described, but no conclusion as to their overall effectiveness is presented because they would not be included in the bill. As described in more detail below, the focus of this review will be fertility preservation in cancer patients.

Research Approach and Methods

Studies of the effects of fertility preservation services for patients at risk for iatrogenic infertility were identified through searches of PubMed, the Cochrane Library, and Web of Science. Websites maintained by the following organizations that produce and/or index meta-analyses and systematic reviews were also searched: Agency for Healthcare Research and Quality; American Cancer Society; American College of Obstetricians and Gynecologists; Fertile Hope Program; Institute for Clinical Systems Improvement; International Network of Agencies for Health Technology Assessment; National Comprehensive Cancer Network, Inc.; National Guideline Clearinghouse; National Institute for Clinical Excellence; National Institutes of Health; National Health Service Centre for Reviews and Dissemination; Oncofertility Consortium; Scottish Intercollegiate Guideline Network; and World Health Organization.

The search was limited to abstracts of studies published in English. The search was also limited to studies published from 2013 to present because CHBRP had previously conducted thorough literature searches on these topics in 2011 and 2013 for Assembly Bill (AB) 428 and SB 912, respectively. Of the 859 articles found in the literature review, 76 were reviewed for potential inclusion in this report on SB 172, and a total of 20 studies published since 2012 were added to the literature in the medical effectiveness review for this report. The other articles were eliminated because they were individual studies that were included in a selected systematic review, did not focus on cancer patients, were of poor quality, or did not report findings from clinical research studies. A more thorough description of the methods used to conduct the medical effectiveness review and the process used to grade the evidence for each outcome measure is presented in Appendix B: Literature Review Methods.

Methodological Considerations

Many of the studies included in the meta-analyses and systematic reviews that CHBRP assessed are of low quality. There are very few RCTs across all the fertility preservation options, and most of them have very small sample sizes. It is widely acknowledged among researchers and clinicians in the field that larger randomized studies are necessary. In previous analyses (CHBRP, 2011; CHBRP, 2013a) the majority of the findings were categorized as “preponderance of evidence.” In 2017, CHBRP introduced a new grading scale, which includes a new category, “limited” to designate evidence which should be downgraded from preponderance of evidence due to a lack of studies (less than 3), evidence that is not

generalizable for the population subject to the bill, or evidence with methodological flaws. For SB 172, since the evidence is mainly on patients with infertility, not patients with cancer, the evidence was re-categorized as “limited.”

Iatrogenic infertility is most commonly caused by cancer treatments such as radiation and chemotherapy (gonadotoxic treatments) or surgical removal of reproductive organs. Less frequently, fertility is compromised by treatments for autoimmune disorders such as systemic lupus erythematosus, rheumatoid arthritis, or Crohn’s disease, or for individuals with gender and sex diversity such as individuals who are transgender or those with differences of sex development. The decision was made to focus the medical effectiveness review on fertility preservation in cancer patients for three reasons. First, with the help of a content expert, we identified the most prevalent types of cancer that impact women of reproductive age and that had treatments with a high likelihood of resulting in iatrogenic infertility. It is estimated that approximately 90% of iatrogenic infertility is caused by cancer treatment (Lawrenz et al., 2011). Second, although it is possible for treatment for autoimmune disorders to impact fertility, gonadotoxic treatments are not the first-line treatments for these conditions and are less frequently found among people of reproductive age (Bermas and Sammaritano, 2015; Pons-Estel et al., 2010; Molodecky et al., 2012). Third, although treatments for transgender patients and individuals with differences in sex development have a high likelihood in resulting in iatrogenic infertility, there are no current guidelines for providing fertility preservation in this population; therefore, there is limited literature addressing this topic (ASRM, 2015). Therefore, this review will summarize findings from the literature on fertility preservation services used in conjunction with cancer treatment, but will also include a discussion of the relevant issues for other populations of patients.

Outcomes Assessed

The medical effectiveness of fertility preservation services was assessed using the following outcomes:

1. **Clinical pregnancy rate:** The percentage of attempts that lead to a pregnancy as confirmed by ultrasound early in pregnancy, usually around seven weeks.
2. **Pregnancy rate:** The percentage of attempts that lead to any pregnancy.
3. **Cumulative pregnancy rate:** Pregnancy rate across multiple attempts.
4. **Birth rate:** The percentage of attempts that result in a birth.
5. **Live birth rate:** The percentage of attempts that result in a live birth (excludes still birth).
6. **Cumulative birth rate:** Birth rate across multiple attempts.

Intermediate outcomes were also assessed such as post-thaw survival rate of embryos, oocytes, or sperm; fertilization rate (how many oocytes become fertilized by sperm); and implantation rate (the percentage of embryos that become successfully implanted). Adverse outcomes associated with fertility preservation services as measured in the literature were cancer-recurrence rates, preterm delivery rates, miscarriage rates, and rates of chromosomal abnormalities.

Study Findings

This review started with the list of fertility preservation services reviewed in the American Society of Clinical Oncology (ASCO) Recommendations on Fertility Preservation in Cancer Patients (Lee et al.,

2006; Loren et al., 2013). The findings are broken out by gender and by status (standard or experimental) according to the American Society of Reproductive Medicine (ASRM) and ASCO. These are the leading national organizations of physicians specializing in evidence-based guidelines for cancer care and reproduction care in the United States. Literature regarding standard fertility preservation services was reviewed by CHBRP, and conclusions regarding the medical effectiveness of these services are presented below. This review does not draw conclusions as to the state of the evidence of the medical effectiveness for fertility preservation services that are considered experimental because there is insufficient evidence to evaluate their medical effectiveness.

Fertility Preservation for Individuals with Autoimmune Rheumatic Disorders

A systematic review of males with rheumatic diseases such as systemic lupus erythematosus and rheumatoid arthritis was conducted in 2016 by Tiseo and colleagues. A total of 19 articles were identified that addressed impaired fertility among males undergoing treatments for rheumatic diseases. The authors concluded that although these treatments had the potential to reduce fertility, permanent infertility was rare (Tiseo et al., 2016). Similarly, research among women undergoing treatments for autoimmune rheumatic disorders has found that newer medications that are safe to use during pregnancy can be utilized instead of fertility impairing medications to improve chances of pregnancy without harm (Tincani et al., 2016).

Fertility Preservation for Transgender Individuals and Individuals with Differences in Sex Development

A national working group on fertility preservation for individuals with gender and sex diversity was convened in November of 2015 (Finlayson et al., 2016). This discussion centered around two groups: individuals whose gender identity is incongruent with their birth-assigned sex (i.e., transgender) and individuals who have differences in sex development (DSD) where the reproductive organs do not develop as expected given their male or female chromosomes. For those who are postpubertal, standard options for maintaining fertility include embryo, oocyte, or sperm cryopreservation. Transgender and DSD individuals who are prepubescent only have fertility preservation options available to them that are considered experimental. Transgender individuals face challenges in preserving their fertility in that the optimal time period for harvesting of oocyte or sperm for cryopreservation is prior to initiation of hormone therapy but after reaching sexual maturity. This generally requires the patient to delay gender-affirming hormone treatment.

Standard Fertility Preservation Treatments for Female Cancer Patients

Fertility preservation options in females depend on many factors such as patient age, type of cancer diagnosis, prescribed cancer treatment, the amount of time the patient can wait before starting cancer treatment, and whether the cancer has metastasized to the patient's ovaries (Oktem and Urman, 2010). Personal factors such as if the patient has a partner, cultural background, and religious beliefs can also influence fertility preservation decisions. This review presents evidence as to the effectiveness of five standard fertility preservation services for females: embryo cryopreservation; oocyte cryopreservation; ovarian shielding during radiation therapy; ovarian transposition; and conservative gynecologic surgery (ASRM, 2013; Lee et al., 2006; Levine et al., 2010, Loren et al., 2013).²⁸

²⁸ Levine et al. (2010) list four other standard parenthood options (donor embryos, donor eggs, gestational surrogacy, adoption) that were not considered in this report because they would not be covered under SB 172 as they are not considered "fertility preservation" services.

Embryo cryopreservation

There are nearly 10,000 births in the United States every year from embryo cryopreservation (SART, 2014). Embryo cryopreservation involves harvesting the patient's eggs, using in vitro fertilization (IVF) to fertilize the eggs, and freezing any resulting embryos for later implantation. This fertility preservation service is available to females who have gone through puberty. The post-thaw survival rate of embryos ranges between 35% to 90%, while implantation rates are between 8% and 42% (Dunn and Fox, 2009; Loren et al., 2013; Rodriguez-Macias Wallberg et al., 2009; Seli and Tangir, 2005). Pregnancy rates per transferred embryo are reported at 19% while cumulative pregnancy rates (pregnancy rate across multiple attempts) can be more than 60% (Ata et al., 2010; Rodriguez-Macias Wallberg et al., 2009; Seli and Tangir, 2005). A recent meta-analysis of three clinical trials found that the clinical pregnancy rate was higher among frozen embryo transfers compared to fresh embryo transfers (relative risk²⁹ = 1.31, 95% confidence interval [CI] = 1.10–1.56) (Roque et al., 2013).

Birth rates per embryo transfer using cryopreserved embryos have risen from approximately 28% in 2004 to 35% in 2011 (Dunn and Fox, 2009; SART, 2014). The live birth rate from embryo cryopreservation depends on the age of the patient and the number of embryos available (Lee et al., 2006). The Society for Assisted Reproductive Technology/Centers for Disease Control data from 2014 indicated that the percentages of thawed embryo transfers resulting in live births were inversely related to age: 42.7% in women less than 35 years of age, 39.6% in the 35 to 37 age group, 33.7% in the 38 to 40 age group, 27.3% in the 41 to 42 age group, and 19.6% in the >42 age group (SART, 2014).

The studies mentioned previously all have small sample sizes and were not limited to patients cryopreserving embryos for fertility preservation. Three out of four studies comparing infertility procedures between women undergoing gonadotoxic treatments and women seeking IVF for male-factor infertility found no difference in outcomes (Cardozo et al., 2015; Domingo et al., 2012; Knopman et al., 2009; Robertson et al., 2011). More recent studies among cancer patients found a 37% to 66% pregnancy rate and a 30% to 45% live birth rate per embryo transfer (Cardozo et al., 2015; Dolmans et al., 2015; Oktay et al., 2015).

Summary of findings regarding embryo cryopreservation. There is limited³⁰ evidence that embryo cryopreservation is an effective method of fertility preservation measured by three different outcomes: successful thawing of embryos; successful implantation of embryos; and resulting live births. A grade of *limited evidence* was assigned due to the low quality of the studies and the limited generalizability.

Oocyte (egg) cryopreservation

For postpubertal women who do not have a partner, who do not wish to use a sperm donor, or have objections to freezing embryos, the standard option for preserving fertility is oocyte cryopreservation. Due to an advance in technology, the viability of oocytes after thawing has greatly improved, leading the ASRM to issue new recommendations in January of 2013 that oocyte cryopreservation should be offered to patients facing chemotherapy or other gonadotoxic therapies (ASRM, 2013). Recommendations issued by the American Society of Clinical Oncology in July 2013 indicate that oocyte cryopreservation is considered a standard practice (Loren et al., 2013).

²⁹ The risk ratio (or relative risk) is the ratio of the risk of an event in the two groups.

³⁰ In previous analyses (CHBRP, 2011; CHBRP, 2013) the majority of the findings were categorized as "preponderance of evidence." In 2017, CHBRP introduced a new grading scale, which includes a category for evidence that is not generalizable for the population subject to the mandate. For SB 172, since the evidence is mainly on patients with infertility, not patients with cancer, the evidence was recategorized as "limited."

There have been four randomized controlled trials comparing IVF outcomes using cryopreserved oocytes with outcomes using fresh oocytes (Cobo et al., 2008, 2010; Parmegiani et al., 2011; Rienzi et al., 2010). Across the four studies identified, the oocyte post-thaw survival rate ranged from 90% to 97%, the fertilization rate ranged from 71% to 79%, the implantation rate ranged from 17% to 41%, the clinical pregnancy rate per embryo transfer ranged from 36% to 61%, and the clinical pregnancy rate per thawed oocyte ranged from 4.5% to 12%. These rates compared favorably with fresh oocytes (ASRM, 2013; Kato, 2016). A meta-analysis of three of the four above articles reported no significant difference in fertilization rates of thawed oocytes (using the vitrification freezing method) versus fresh oocytes (odds ratio³¹ = 1.02, 95% CI = 0.91–1.13) (Cobo and Diaz, 2011). Later research also found no differences between fresh and vitrified warmed oocytes (Forman et al., 2012; Parmegiani et al., 2011). Cobo et al. (2014) reported that 1,027 babies were born from cryopreserved oocytes in 2014 with no observed increase in congenital abnormalities.

Among studies examining oocyte cryopreservation solely among women with a cancer diagnosis, there is limited evidence regarding the effectiveness of this method of fertility preservation due to small sample sizes. For example, Druckenmiller et al. (2016) reported on 176 patients who cryopreserved their oocytes, of which 10 returned to retrieve their eggs for 11 cycles of thawing. Among these, there was an 86% oocyte survival rate with 9 of 11 cycles leading to an embryo suitable for transfer with a 44% live birth rate per embryo transfer. Martinex et al. (2014) reported on 357 patients who cryopreserved oocytes, with 11 returning for egg retrieval. Among this group there was an oocyte survival rate of 92.3%, a fertilization rate of 76.6%, and four pregnancies and four deliveries.

Summary of findings regarding oocyte (egg) cryopreservation. There is limited evidence that oocyte cryopreservation is an effective method of fertility preservation measured by three different outcomes: successful thawing of oocytes; successful implantation of embryos; and resulting live births. A grade of *limited evidence* was assigned due to the low quality of the studies and the limited generalizability.

Ovarian transposition (oophoropexy)

For women undergoing radiation of the pelvis, ovarian transposition (oophoropexy) is used to minimize the damage to the ovaries caused by pelvic radiation (Levine et al., 2010). This surgery involves repositioning the ovaries higher up in the abdomen and away from the radiation field. Rates of successful preservation of ovarian function after oophoropexy vary greatly, with a reported range of 16% to 90% (Georgescu et al., 2008; Seli and Tangir, 2005; Thibaud et al., 1992). A more recent systematic review and meta-analysis of 24 articles representing 892 patients undergoing ovarian transposition found that ovarian function was preserved in 90% of the cases (Gubbala et al., 2014). In addition, this review found that there was no evidence of metastases to the transposed ovary (Gubbala et al., 2014).

Adverse outcomes related to this procedure include: the destruction of all or part of the fallopian tube; chronic ovarian pain; ovarian cyst formation; and migration of the ovaries back to their original position (Lee et al., 2006; Oktem and Urman, 2010). In addition, the ovaries may need to be moved back to the pelvic region before an IVF procedure can be performed (Lee et al., 2006).

Of the articles reviewed in the three review articles referenced above, none were randomized controlled trials or large cohort studies. Most were case series of 20 or fewer patients, which are considered to be of low quality in the hierarchy of evidence described in Appendix B.

³¹ The odds ratio is the ratio of the chance of an event occurring in one group compared to the chance of it occurring in another group.

Summary of findings regarding ovarian transposition. There is limited evidence that ovarian transposition is effective in maintaining ovarian function among women undergoing radiation as part of their cancer treatment. A grade of *limited evidence* was assigned due to the low quality of the available studies.

Ovarian shielding during radiation therapy

In order to protect the ovaries during cancer treatment with radiation, a special external shield can be placed over the ovaries to minimize the damage caused by radiation. Ovarian shielding is generally used for cervical or vaginal cancer patients undergoing radiation therapy to treat their cancer. Expertise in ovarian shielding is needed to ensure that it is done properly (Levine et al., 2010). In addition, questions remain regarding the correct positioning of the shield, given that not all ovaries are in the exact same location (Fawcett et al., 2012). Although four review articles recommended the use of ovarian shielding during radiation therapy, no research to support these recommendations were cited (Gurgan et al., 2008; Lee et al., 2006; Levine et al., 2010; Rodriguez-Macias Wallberg and Oktay, 2012). In addition, CHBRP's review of the literature found two articles reporting on a combined nine patients that found that ovarian function was protected by ovarian shielding (Kanda et al., 2014; Shibashi et al., 2015).

Summary of findings regarding ovarian shielding. There is insufficient evidence that ovarian shielding during radiation therapy is an effective method of fertility preservation. A grade of insufficient evidence indicates that there is not enough evidence available to know whether or not a treatment is effective — it does not indicate that a treatment is not effective. Despite this, it stands to reason that under specific circumstances, females undergoing pelvic radiation where there is a high risk of ovarian failure may want to consider ovarian shielding during radiation therapy.

Conservative gynecologic surgery

The recommendations released by ASCO indicated that conservative gynecologic surgery should be considered for certain kinds of gynecologic cancers if fertility preservation is desired and conservative surgery is appropriate given the stage of cancer (Lee et al., 2006). The two surgeries specified in the recommendations are conservative surgery for cervical cancer (trachelectomy) and conservative surgery for ovarian cancer (Lee et al., 2006; Loren et al., 2013).

A trachelectomy is a surgical procedure to remove the cervix while preserving the uterus. This procedure is used in place of a hysterectomy (removal of the uterus) as part of cancer treatment for patients wanting to preserve their fertility. This procedure is recommended for early-stage cervical cancer where the cancer has not spread beyond the cervix. It is estimated that half of women of reproductive age diagnosed with cervical cancer are eligible for the procedure (Lee et al., 2006). Pregnancy rates following trachelectomy procedures range between 41% and 79% (Beiner and Covens, 2007; Dursun et al., 2007). Among pregnant women, the live birth rate was calculated across 10 studies as 64%, ranging from 50% to 100% (Eskander et al., 2011). More recent data reported by Bentivegna et al. (2016) found that of 2,777 patients who underwent conservative surgery for cervical cancer, 55% became pregnant and 70% of those had live births. The most common complications from the trachelectomy procedure are higher rates of second trimester miscarriages and preterm deliveries (Beiner and Covens, 2007). Preterm delivery rates (before 37 weeks) were reported in 20% of pregnancies and 10% of women had a second trimester miscarriage (Eskander et al., 2011). Tumor recurrence rates ranged from 3.9% to 5% while the observed mortality rate ranged from 2% to 3% (Beiner and Covens, 2007; Dursun et al., 2007; Eskander et al., 2011; Seli and Tangir, 2005). These rates are comparable to rates observed in women with a hysterectomy to treat cervical cancer. Therefore, the authors concluded that there are no increased risks of cancer recurrence or mortality to women undergoing trachelectomy for early stage cervical cancer

(Beiner and Covens, 2007; Dursun et al., 2007; Eskander et al., 2011; Lee et al., 2006; Seli and Tangir, 2005).

The standard treatment for ovarian cancer, including borderline ovarian tumor, is removal of the uterus (hysterectomy) and removal of both ovaries. The conservative treatment preserves one ovary with or without the uterus. This is only possible in cases where the cancer was confined to only one ovary. A meta-analysis of 10 studies with a total of 626 patients with borderline ovarian tumors reported 185 pregnancies and 107 live births. Among pregnant women, the live birth rate was calculated across nine studies as 75%, ranging from 59% to 100% (Eskander et al., 2011). A more recent meta-analysis of 10 studies representing 793 women found a 74% successful conception rate (range 63–100%) (Zapardiel et al., 2014). Tumor recurrence rates ranged from 5% to 32% while only one death was observed across all 10 studies (0.2%) (Eskander et al., 2011; Zapardiel et al., 2014). Therefore, the authors concluded that conservative surgery should be considered in young women desiring to preserve their fertility in the appropriate stage of disease and where the tumor can be completely removed (Eskander et al., 2011).

Summary of findings regarding conservative gynecologic surgery. There is limited evidence that trachelectomy and conservative ovarian surgery are effective conservative gynecologic surgeries in preserving fertility preservation measured by pregnancy rates and live births. There is limited evidence that trachelectomy and conservative ovarian surgery have no apparent increase in cancer recurrence or mortality for specific cases. A grade of *limited evidence* was assigned due to the low quality of the available studies.

Experimental Fertility Preservation Options for Female Cancer Patients (Not Covered Under SB 172)

There are three fertility preservation options for females that are classified as experimental and thus not covered under SB 172: ovarian tissue cryopreservation and transplantation, in vitro follicle maturation, and ovarian suppression with GnRH analogs. Ovarian tissue cryopreservation is the only option available for fertility preservation in prepubescent girls undergoing chemotherapy. In this experimental surgical procedure, ovarian tissue is removed and frozen. This allows for the ovarian tissue to be thawed and re-implanted after the patient has finished with her treatment. The first ovarian transplant procedure was performed in 2000, and as of 2015, there had been at least 42 births as a result of this procedure (Dittrich et al., 2012; Lee et al., 2006; Levine et al., 2010; Salamai et al., 2015). In vitro follicle maturation (IVM) is used when fertility-threatening treatment is needed immediately, and it is not possible to delay treatment in order to collect mature oocytes. In this case, immature oocytes are collected and matured outside of the body. There is preliminary data to suggest that IVM may be a feasible alternative for women, but as of 2017 only a few live births had been reported as a result of this procedure (Creux et al., 2017).

Gonadotropin-releasing hormone (GnRH) analog is an experimental hormonal therapy that causes the ovaries to temporarily shut down during chemotherapy, thus potentially reducing damage to the follicles where eggs develop (Ben-Aharon and Gafter-Gvili, 2010). This service is available to women who have completed puberty and is used in conjunction with chemotherapy, starting a week prior to chemotherapy and continuing for the course of chemotherapy treatment. GnRH analogs do not protect against radiation effects or from very aggressive forms of chemotherapy (Levine et al., 2010). Overall, the literature does not support the routine use of GnRH analogs for fertility preservation (Ben-Aharon and Gafter-Gvili, 2010; Loren et al., 2013). In addition, there is some concern that the use of GnRH analogs is not appropriate for women undergoing treatment for breast cancer because the hormone treatment may reduce the tumor sensitivity to chemotherapy (de Ziegler et al., 2010; Loren et al., 2013).

Standard Fertility Preservation Treatments for Male Cancer Patients

This review presents evidence as to the effectiveness of two standard fertility preservation treatments for males: sperm cryopreservation (sperm banking) and testicular shielding during radiation therapy.

Sperm cryopreservation

Sperm cryopreservation is the most established technique for maintaining fertility in men. In this technique, sperm is collected prior to the initiation of cancer treatment and then frozen. Males start producing sperm after puberty, around 13 to 14 years of age; therefore, this treatment is not appropriate for prepubescent males (Levine et al., 2010). Research has indicated that long-term cryopreservation of sperm is possible with reported pregnancies using sperm stored between 10 and 28 years (Levine et al., 2010).

Studies of the effectiveness of sperm cryopreservation in cancer patients found that this fertility preservation method is effective in providing male cancer patients a chance at parenthood (Ferrari et al., 2016; Hourvitz et al., 2008; van Casteren et al., 2008; van der Kaaij et al., 2010). A recent review by Ferrari et al. (2016) combined results from 30 studies for a combined total of 11,798 patients. They found that 8% of those who cryopreserved their sperm prior to cancer treatment returned to use this sperm with 49% achieving parenthood (Ferrari et al., 2016).

Summary of findings regarding sperm cryopreservation. There is limited evidence that sperm cryopreservation is an effective method of fertility preservation as measured by pregnancy rates and live births. A grade of *limited evidence* was assigned due to the low quality of the available studies.

Testicular shielding during radiation therapy

To protect the testes during radiation treatment, a shield can be placed over the testicles to reduce the amount of radiation they are exposed to (Lee et al., 2006). Research from case series has shown that this treatment is effective in reducing the damage to the testicles, but that it is only possible with selected radiation fields and anatomy (Ishiguro et al., 2007; Lee et al., 2006). In addition, expertise is required to make sure that the shielding does not increase the amount of radiation delivered to the reproductive organs (Lee et al., 2006).

Summary of findings regarding testicular shielding. There is insufficient evidence that testicular shielding is an effective method of fertility preservation in males. A grade of insufficient evidence indicates that there is not enough evidence available to know whether or not a treatment is effective — it does not indicate that a treatment is not effective. Despite this, it stands to reason that under specific circumstances, males undergoing pelvic radiation where there is a high risk of testicular failure may want to consider testicular shielding during radiation therapy.

Experimental Fertility Preservation Treatments for Male Cancer Patients (Not Covered by SB 172)

There are two fertility preservation treatments for males that are considered experimental: testicular tissue cryopreservation and testicular suppression with GnRH analogs or antagonists. Testicular tissue

cryopreservation is an outpatient surgical procedure where tissue is surgically removed and frozen. It is available for males either before or after puberty, but it is the main option for prepubescent males. This method has produced no live births and is considered experimental (Lee et al., 2006; Levine et al., 2010; Loren et al., 2013). GnRH analogs or antagonists are an experimental hormonal therapy that causes the testicles to temporarily shut down during chemotherapy, thus potentially causing a reduction in the damage to the sperm. The efficacy of this method has only been evaluated in very small studies and is considered experimental (Lee et al., 2006; van der Kaaij et al., 2010).

Summary of Findings

The charts in this section summarize CHBRP’s findings regarding the strength of the evidence for the effects of specific fertility preservation services addressed by SB 172. Separate charts are presented for each fertility preservation treatment. The title of the chart indicates the treatment for which evidence is summarized. The statement under the heading “Conclusion” presents CHBRP’s conclusion regarding the strength of evidence about the effect of a particular fertility preservation treatment and the number of studies on which CHBRP’s conclusion is based. For treatments for which CHBRP concludes that there is clear and convincing, preponderance, limited, or conflicting evidence, the placement of the vertical bar indicates the strength of the evidence. If CHBRP concludes that evidence is insufficient, a graph that states “Insufficient Evidence” will be presented.

The majority of the studies reviewed here were of observational nature and not methodologically rigorous. It is widely acknowledged among researchers and clinicians in the field that larger randomized studies are necessary. In addition, many of the studies reviewed were conducted on people undergoing general infertility procedures and were not limited to those undergoing treatments leading to iatrogenic infertility. Therefore, of the eight treatments reviewed, 6 of them were classified as having limited evidence of effectiveness, with the other 2 having insufficient evidence to evaluate their effectiveness. In addition, this review found relatively low rates of utilization of cryopreserved eggs, sperm, or embryos. The low oocyte and sperm retrieval rate is due, in part, to the inability to determine which patients will suffer from iatrogenic infertility post treatment. Therefore it is recommended that all patients undergo fertility preservation even though a small proportion of the patients will need to retrieve their cryopreserved eggs, sperm, or embryos to conceive.

Figure 2. Embryo Cryopreservation

Conclusion

There is limited evidence that embryo cryopreservation is effective in preserving fertility among women undergoing cancer treatment from two cohort studies and one retrospective study of 248 women of which 63 retrieved cryopreserved embryos.

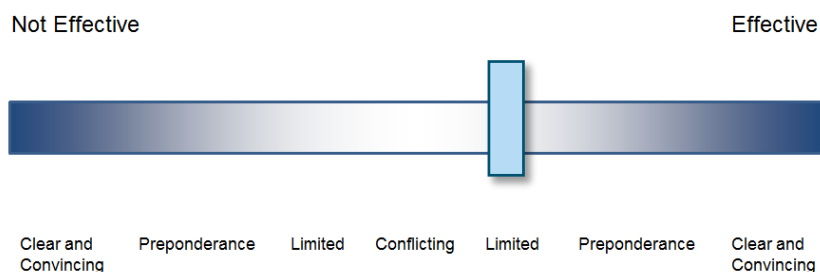


Figure 3. Oocyte (Egg) Cryopreservation

Conclusion

There is limited evidence that oocyte (egg) cryopreservation is effective in preserving fertility among women undergoing cancer treatment from two cohort studies of 533 women of which 21 retrieved cryopreserved oocytes.

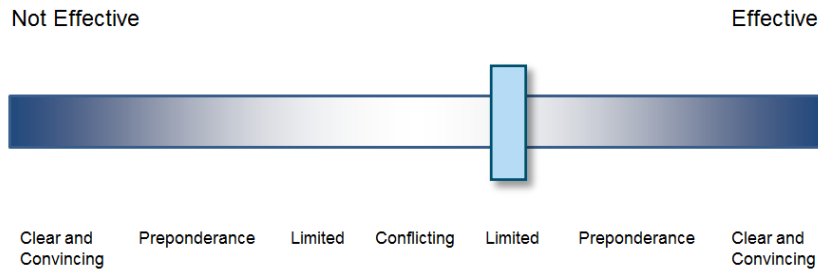


Figure 4. Ovarian Transposition (Oophoropexy)

Conclusion

There is limited evidence that ovarian transposition (oophoropexy) is effective in maintaining ovarian function based on 24 small cohort studies representing a total of 892 patients.

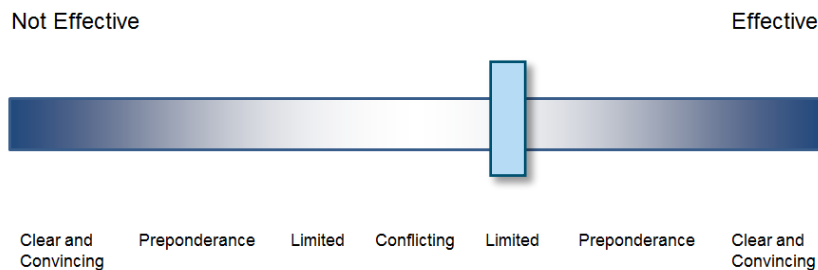


Figure 5. Ovarian Shielding During Radiation Therapy

Conclusion

There is insufficient evidence that ovarian shielding during radiation therapy is effective.

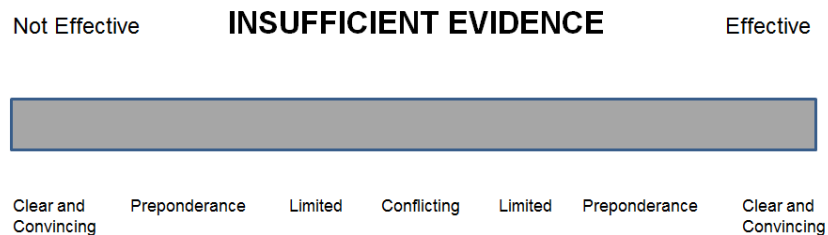


Figure 6. Conservative Gynecologic Surgery (Radical Trachelectomy)

Conclusion

There is limited evidence that conservative gynecologic surgery (radical trachelectomy) is effective based on 11 cohort studies representing 2,777 women.

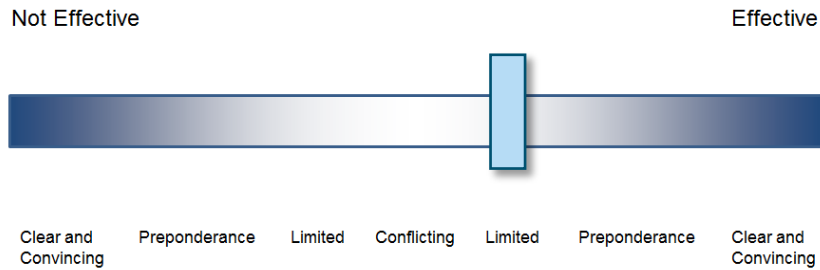


Figure 7. Conservative Gynecologic Surgery (for Ovarian Cancer)

Conclusion

There is limited evidence that conservative gynecologic surgery (for ovarian cancer) is effective based on 10 cohort studies of 793 women.

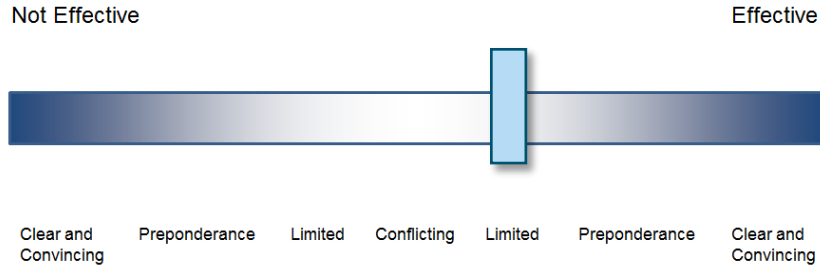


Figure 8. Sperm Cryopreservation

Conclusion

There is limited evidence that sperm cryopreservation is effective based on a systematic review of 30 cohort studies representing 11,798 cancer patients and 943 retrieving their cryopreserved sperm.

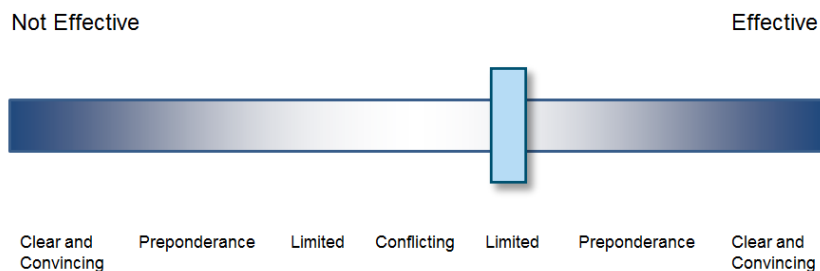
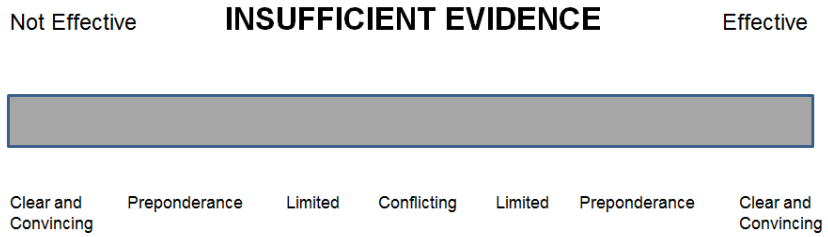


Figure 9. Testicular Shielding During Radiation Therapy

Conclusion

There is insufficient evidence that testicular shielding during radiation therapy is effective.



BENEFIT COVERAGE, UTILIZATION, AND COST IMPACTS

For the projected cost impacts of SB 172, CHBRP only models utilization, both baseline and postmandate, among enrollees with the top 10 cancer diagnoses (see the *Background on Fertility Preservation* section for prevalence rates), and the utilization estimates presented in this section should be considered conservative.

CHBRP considers two scenarios in this report: Scenario 1 is based on the bill language as originally introduced, which covers only fertility preservation services. Scenario 2 includes fertility preservation services as well as the cost and utilization of infertility treatment that some patients with iatrogenic fertility would seek following recovery from their primary condition (e.g., cancer) (see Figure 1 in the *Policy Context* section).

- **Scenario 1 (bill language as introduced):** Estimates coverage, costs, and utilization of fertility preservation services for cryopreservation of sperm, eggs, and embryos, for the first year postmandate (see Appendix C for full details), including:
 - associated pharmaceutical;
 - procedural; and
 - storage costs.
- **Scenario 2 (amended bill language):** Includes cost and utilization of Scenario 1 and also estimates utilization and costs of infertility treatment for the cohort using fertility preservation services under Scenario 1, including:
 - assisted reproductive technology (ART), artificial insemination, or IVF; and
 - successful pregnancies and their associated live births or miscarriages.

Some enrollees who receive fertility preservation services are likely to eventually receive infertility treatment services sometime in the near or distant future. Scenario 2 represents a steady state wherein some enrollees that faced iatrogenic infertility in the past would utilize their cryopreserved embryos, oocytes, or sperm, and achieved live births in the 12 months following SB 172.

In both scenarios, CHBRP considered benefit coverage to be mandate compliant for fertility preservation if enrollees were covered for at least one fertility preservation service (see *Background on Fertility Preservation* for complete list of possible services, and Appendix C for a complete list of services included in the model). Benefit coverage that only included a fertility preservation service for either men or women (but not both) was not considered to be fully mandate compliant. Although conservative gynecological surgery, radiation shielding, and ovarian transposition are also considered standard fertility preservation services, these are considered to be included in standard cancer treatment, and therefore are not included in the Cost and Coverage Model estimates (see Figure 1 in the *Policy Context* section).

This section reports the potential incremental impact of SB 172 on estimated baseline benefit coverage, utilization, and overall cost. For further details on the underlying data sources and methods, please see Appendix C.

Baseline and Postmandate Benefit Coverage

Current coverage of fertility preservation services for enrollees with cancer who are at risk for iatrogenic infertility was determined by a survey of the largest (by enrollment) providers of health insurance in California. Responses to this survey represent 69% of enrollees with private market health insurance that can be subject to state mandates.

SB 172 does not apply to Medi-Cal Managed Care enrollees. In the Cost and Coverage Model, the impact of SB 172 was therefore only assessed for enrollees in the other insurance plans or policies. In total, 67% of enrollees in DMHC-regulated plans or CDI-regulated policies are subject to SB 172 (see Table 1).

At baseline **for both Scenarios 1 and 2**, 85% of enrollees with health insurance that would be subject to SB 172 have coverage that is mandate compliant (13.7 million), with at least one cryopreservation service included for enrollees who are undergoing cancer treatment that may cause iatrogenic infertility (see Table 1). Under **Scenario 2**, CHBRP assumed that the benefit coverage rates from a legislative analysis of infertility treatment in 2013 (AB 460) still apply (CHBRP, 2013b). CHBRP estimates that 38% of enrollees have current coverage for infertility treatment.

Under **both Scenarios 1 and 2**, benefit coverage for relevant fertility services among enrollees in DMHC-regulated plans or CDI-regulated policies would increase to 100% based on the CHBRP assumption that all noncompliant plans and policies at baseline would become compliant postmandate.

Baseline and Postmandate Utilization

To determine the baseline utilization, CHBRP analyzed incidence rates from the 2013 CDC Wonder dataset (the most recent data available) of the top 10 cancers using treatments that place California patients at risk of iatrogenic infertility (see Table 3 in *Background* section). These incidence rates represent the population with newly diagnosed cancers, which CHBRP assumes is the population that would potentially seek fertility preservation services. Utilization was estimated for females aged 12 to 44 years and males ages 12 to 49 years, as those are the reproductive ages in which the risk of iatrogenic infertility is more likely to occur.³² Out of the 16 million enrollees with coverage subject to the bill, the total number of enrollees with a new cancer diagnosis (2,482 males and 5,107 females, or 0.02% and 0.03%; see Figure 10) in these age ranges would remain constant from baseline to postmandate.

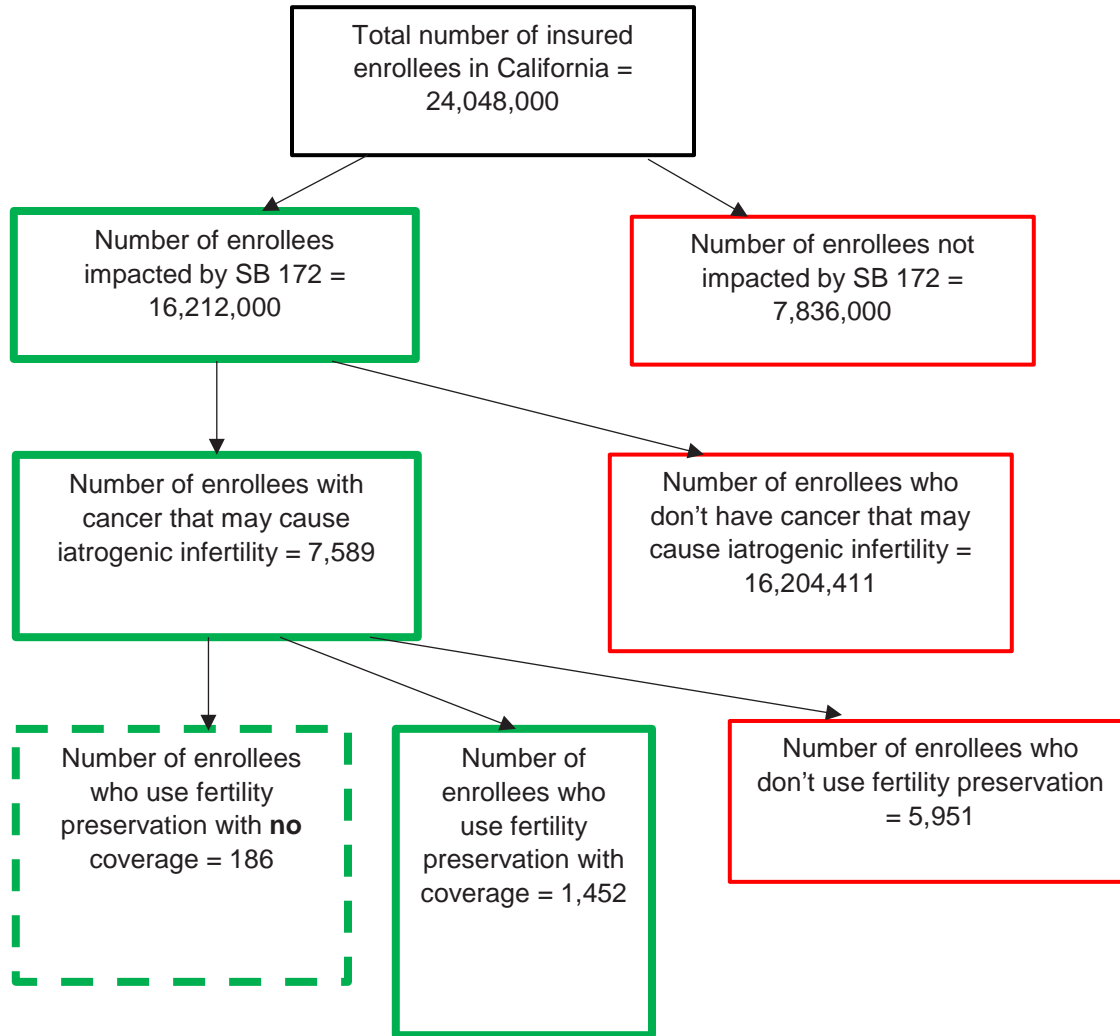
Among this population, the baseline total proportion using fertility preservation services **for both Scenarios 1 and 2** was derived using the findings from a study of propensity to undergo cryopreservation when facing iatrogenic infertility (Bann et al., 2015), for those enrollees in DMHC-regulated plans or CDI-regulated policies without benefit coverage. CHBRP applied the findings from this study, that among enrollees without coverage, 31.6% of child-bearing age males with cancer and 8.3% of child-bearing age females with cancer choose to undergo fertility preservation services, to enrollees in DMHC-regulated plans and CDI-regulated policies in California. This results in 121 males and 65 females (or 4.9% and 1.3% of the total enrollees of reproductive age with top 10 cancers) who currently undergo fertility preservation and lack coverage for these services (see Figure 10).

Additionally, CHBRP applied Bann et al. (2015) rates of use of fertility preservation services among enrollees who currently have coverage; 34.8% for males and 16.7% for females. CHBRP estimates that

³² Dr. Irene Su, content expert consultation on February 9, 2017.

731 males and 721 females with cancer (or 29.4% and 14.2% of the total enrollees with cancer; see Figure 10) currently with coverage use fertility preservation services.

Figure 10. Enrollees Impacted by SB 172 and Utilization of Fertility Preservation Services at Baseline



Postmandate, the utilization of enrollees of fertility preservation services would increase. Overall, enrollees with new benefit coverage would increase their utilization to the level of those enrollees who had coverage previously. Additionally, CHBRP estimates that there would be a 10% increase in overall utilization due to the increased provider knowledge of coverage, and corresponding greater willingness to discuss fertility preservation options with their patients (Vindrola-Padros et al., 2017). No enrollees would be using fertility preservation services without benefit coverage postmandate. CHBRP estimates that this would result in an additional 219 males and 216 female enrollees with cancer using fertility preservation services newly covered by their insurance plans or policies (see Table 1, Scenario 1).

Scenario 2 includes assessment of infertility utilization at baseline and postmandate. Currently, literature indicates that among populations with insurance coverage for infertility treatment, 9.5% of males and 33% of females who had used fertility preservation services because of the risk of iatrogenic infertility, return later for infertility treatment using their preserved oocytes, sperm, or embryos (Cardozo et al., 2015;

Johnson et al., 2013). Applying these rates to enrollees in California in DMHC-regulated plans and CDI-regulated policies subject to SB 172, CHBRP estimates that 31 males and 108 females currently use their previously cryopreserved embryos, oocytes or sperm (Table 2) using their benefit coverage. Two-thirds of these attempts will result in pregnancies (Dolmans et al., 2015), and of those pregnancies, 47% will result in a live birth (Ferrari et al., 2016), for an estimated 66 live births and 33 miscarriages, at baseline.

Postmandate, under Scenario 2, CHBRP estimates that the increase in benefit coverage would lead to an increase in utilization of infertility treatment in 59 males and 201 females. This would lead to an additional 123 live births and 62 miscarriages among those who achieved pregnancy (Table 2).

Baseline and Postmandate Per-Unit Cost

Using claims data, CHBRP estimates that the per-unit cost of fertility preservation services would not change from baseline to postmandate, with male services costing an average of \$600 and female services costing an average of \$13,500 (Table 1 and Table 2; both **Scenarios 1 and 2**). These unit costs include medical, surgical, and drug costs related to retrieving and preserving sperm, oocytes, and embryos, culturing of oocytes and embryos, and storage for one year. Female fertility preservation services have a higher average unit cost due to increased costs for harvesting the reproductive oocytes, as it is a surgical procedure for females and a nonsurgical procedure for males. The higher average unit cost for females also includes the common procedure, when applicable, of harvesting of sperm from a spouse through the same insurance coverage, and the storage of the resulting embryos for the first year.

Under **Scenario 2** (Table 2), costs for infertility treatment are included in the model, with an average of \$1,750 per procedure for males and \$9,800 for females. Both estimates include thawing of the preserved materials, but the costs for males only includes artificial insemination, as the female partner of a male with iatrogenic infertility is assumed to not have iatrogenic infertility. The average costs for females include ART or IVF procedures to implant the embryos, as well as prescription costs to increase a female's likelihood of becoming pregnant. After pregnancy has been achieved, the average cost for a miscarriage is \$4,150 and the average cost of a live delivery is \$19,500. These would also remain constant from baseline to postmandate.

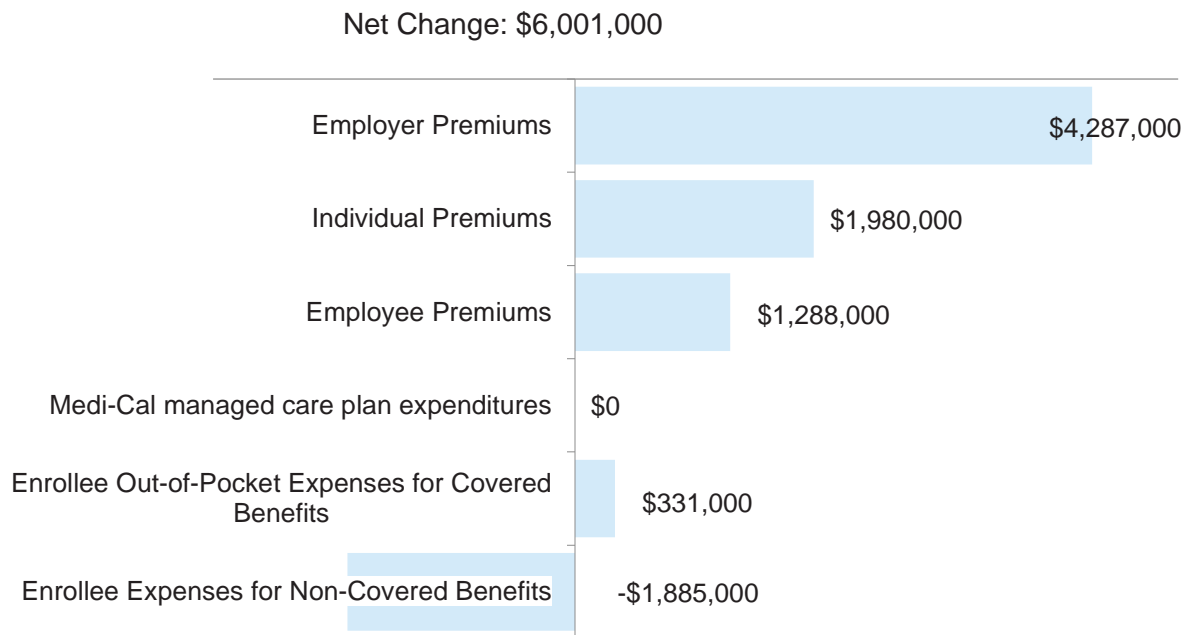
Baseline and Postmandate Expenditures

Table 5, Table 6, and Table 7 present baseline and postmandate expenditures (for Scenarios 1 and 2 respectively) by market segment for DMHC-regulated plans and CDI-regulated policies. The tables present per member per month (PMPM) premiums, enrollee expenses for both covered and noncovered benefits, and total expenditures (premiums as well as enrollee expenses).

Under **Scenario 1**, SB 172 would increase total net annual expenditures by \$2,197,000 or 0.0015% for enrollees with DMHC-regulated plans and CDI-regulated policies (Table 5). This is due to a \$3,153,000 increase in total health insurance premiums paid by employers and enrollees for newly covered benefits, adjusted by a \$956,000 decrease in enrollee expenses for covered and/or noncovered benefits. Under **Scenario 2** with the added expenses of infertility treatment, CHBRP estimates that SB 172 would increase total net annual expenditures by \$6,001,000 or 0.0041% for enrollees with DMHC-regulated plans and CDI-regulated policies (Table 7). This is due to a \$7,886,000 increase in total health insurance premiums paid by employers and enrollees for newly covered benefits, adjusted by a \$1,885,000 decrease in enrollee expenses for covered and/or noncovered benefits.

An overview of the expenditures impacts of Scenario 2 is included in Figure 11. A corresponding figure for Scenario 1 is included in the Key Findings of this report.

Figure 11. Scenario 2 (Amended Language) Expenditure Impacts by Category Postmandate, SB 172



Source: California Health Benefits Review Program, 2017.

Premiums

Changes in premiums as a result of SB 172 would vary by market segment. Note that such changes are related to the number of enrollees (see Table 5, Table 6, and Table 7), with health insurance that would be subject to SB 172. Under **Scenario 1**, increases in PMPM premiums in the private market range from a high of \$0.0644 in the CDI-regulated individual market to a low of \$0.0092 for the DMHC-regulated small-group market. Under **Scenario 2**, increases in premiums in the private market range from a high of \$0.1015 in the CDI-regulated individual market to a low of \$0.0327 for the DMHC-regulated large-group market.

Among publicly funded DMHC-regulated health plans, there would be no impact for Medi-Cal managed care plans. CalPERS managed care plans are estimated to have a \$0.0068 increase in premiums under Scenario 1, and a \$0.0300 increase in premiums under Scenario 2.

Enrollee Expenses

SB 172-related changes in enrollee expenses for covered benefits (deductibles, copays, etc.) and enrollee expenses for noncovered benefits would vary by market segment. Note that such changes are related to the number of enrollees (see Table 5, Table 6, and Table 7) with health insurance that would be subject to SB 172 expected to use the relevant fertility preservation services in the first year after enactment.

Under **Scenario 1**, enrollee expenses for noncovered benefits would decrease by a range of \$0.0017 for DMHC-regulated small-group plans to \$0.0283 for CDI-regulated large-group plans. A smaller increase in enrollee expenses for covered benefits would also occur as enrollees gain coverage, ranging from

\$0.0005 to \$0.0020 for DMHC-regulated plans and CDI-regulated policies (see Table 6). Under **Scenario 2**, enrollee expenses for noncovered benefits would decrease by a range of \$0.0064 for DMHC-regulated large-group plans to \$0.0356 for CDI-regulated individual plans. A smaller offsetting increase in enrollee expenses for covered benefits would also occur, ranging from \$0.0015 to \$0.0035 for DMHC-plans and CDI-policies (see Table 7).

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

CHBRP does not anticipate any cost offsets or savings in the first year postmandate, as fertility preservation services do not correspond to any reduction in use of infertility services during the first year.

Postmandate Administrative Expenses and Other Expenses

CHBRP estimates that the increase in administrative costs of DMHC-regulated plans and/or CDI-regulated policies would remain proportional to the increase in premiums. 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, which are passed on to consumers in the form of increased premiums. CHBRP assumes that the administrative cost proportion of premiums is unchanged. All health plans and insurers include a component for administration and profit in their premiums.

Other Considerations for Policymakers

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

Potential Cost of Exceeding Essential Health Benefits

As explained in the *Policy Context* section, based on the **Scenario 1** bill language as introduced, it is unclear whether this bill would exceed essential health benefits (EHBs). However, based on the **Scenario 2** amended bill language, the bill could be interpreted to exceed EHBs. The state is required to defray the additional cost incurred by enrollees in qualified health plans (QHPs) for any state benefit mandate that exceeds the state's definition of EHBs. However, this report does not provide an estimate for the state's responsibility for exceeding EHBs for this particular bill, because due to time constraints related to the amended language (**Scenario 2**), CHBRP did not request current health insurer responses for infertility treatment. CHBRP assumed that the benefit coverage rates from a legislative analysis of infertility treatment in 2013 (AB 460) would still apply.

Postmandate Changes in the number of uninsured persons³³

As the change in average premiums does not exceed 1% for any market segment (see Table 6), CHBRP would expect no measurable change in the number of uninsured persons due to the enactment of SB 172.

³³ See also CHBRP's *Criteria and Methods for Estimating the Impact of Mandates on the Number of Uninsured*, available at www.chbrp.org/analysis_methodology/cost_impact_analysis.php.

Changes in public program enrollment

CHBRP estimates that the mandate would produce no measurable impact on enrollment in publicly funded insurance programs due to the enactment of SB 172.

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

Foundation support (particularly the Livestrong Foundation) has assisted in reducing the cost of fertility preservation services for either: (1) enrollees who do not have benefit coverage in cases of potential iatrogenic infertility due to cancer treatment, or (2) people who are completely uninsured. In general, a subsidy reduces costs for women to \$3,000, which is then paid for out-of-pocket by the enrollee (Livestrong, 2017). Livestrong also has some support for infertility treatment, as well. No other payers have been affected by the lack of benefit coverage.

Table 5. Baseline Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2018

| | DMHC-Regulated | | | | | | CDI-Regulated | | | Total |
|--|--|-----------------|-----------------|--------------------------------|--------------------------------------|------------------------------|--|-----------------|-----------------|--------------------------|
| | Privately Funded Plans (by Market) ^(a) | | | Publicly Funded Plans | | | Privately Funded Plans (by Market) ^(a) | | | |
| | Large Group | Small Group | Individual | CalPERS HMOs ^(b) | MCMC (Under 65) ^(c) | MCMC (65+) ^(c) | Large Group | Small Group | Individual | |
| Enrollee counts | | | | | | | | | | |
| Total enrollees in plans/policies subject to state mandates ^(d) | 9,128,000 | 3,163,000 | 2,379,000 | 884,000 | 7,192,000 | 644,000 | 276,000 | 145,000 | 237,000 | 24,048,000 |
| Total enrollees in plans/policies subject to SB 172 | 9,128,000 | 3,163,000 | 2,379,000 | 884,000 | 0 | 0 | 276,000 | 145,000 | 237,000 | 16,212,000 |
| Premiums | | | | | | | | | | |
| Average portion of premium paid by employer | \$456.42 | \$324.76 | \$0.00 | \$460.43 | \$257.00 | \$751.00 | \$527.06 | \$433.40 | \$0.00 | \$97,688,732,000 |
| Average portion of premium paid by employee | \$115.59 | \$149.62 | \$469.56 | \$115.11 | \$0.00 | \$0.00 | \$166.32 | \$157.88 | \$423.05 | \$34,995,304,000 |
| Total premium | \$572.01 | \$474.38 | \$469.56 | \$575.54 | \$257.00 | \$751.00 | \$693.38 | \$591.28 | \$423.05 | \$132,684,037,000 |
| Enrollee expenses | | | | | | | | | | |
| for covered benefits (deductibles, copays, etc.) | \$44.11 | \$103.11 | \$126.07 | \$31.49 | \$0.00 | \$0.00 | \$115.39 | \$166.25 | \$75.74 | \$13,565,623,000 |
| Enrollee expenses for noncovered benefits ^(e) | \$0.01 | \$0.01 | \$0.02 | \$0.00 | \$0.00 | \$0.00 | \$0.04 | \$0.02 | \$0.04 | \$1,885,000 |
| Total expenditures | \$616.13 | \$577.49 | \$595.66 | \$607.04 | \$257.00 | \$751.00 | \$808.80 | \$757.55 | \$498.83 | \$146,251,545,000 |

Source: California Health Benefits Review Program, 2017.

Notes: (a) Includes enrollees with grandfathered and nongrandfathered health insurance, both on Covered California and outside the health insurance marketplace.

(b) As of June 1, 2016, 58.82% of CalPERS members were state retirees, state employees, or their dependents. CHBRP assumes the same ratio for 2018.

(c) Medi-Cal Managed Care Plan expenditures for members over 65 include those who are also Medicare beneficiaries. This population does not include enrollees in COHS.

(d) 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.

(e) 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; DMHC = Department of Managed Health Care; COHS = County Organized Health Systems; MCMC = Medi-Cal Managed Care.

Table 6. Scenario 1: Postmandate (as Introduced) Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2018

| | DMHC-Regulated | | | | | | CDI-Regulated | | | Total |
|--|--|----------------|------------|--------------------------------|--------------------------------------|------------------------------|--|----------------|------------|-------------|
| | Privately Funded Plans (by Market) ^(a) | | | Publicly Funded Plans | | | Privately Funded Plans (by Market) ^(a) | | | |
| | Large Group | Small Group | Individual | CalPERS HMOs ^(b) | MCMC (Under 65) ^(c) | MCMC (65+) ^(c) | Large Group | Small Group | Individual | |
| Enrollee counts | | | | | | | | | | |
| Total enrollees in plans/policies subject to state mandates ^(d) | 9,128,000 | 3,163,000 | 2,379,000 | 884,000 | 7,192,000 | 644,000 | 276,000 | 145,000 | 237,000 | 24,048,000 |
| Total enrollees in plans/policies subject to SB 172 | 9,128,000 | 3,163,000 | 2,379,000 | 884,000 | 0 | 0 | 276,000 | 145,000 | 237,000 | 16,212,000 |
| Premiums | | | | | | | | | | |
| Average portion of premium paid by employer | \$0.0084 | \$0.0063 | \$0.0000 | \$0.0055 | \$0.0000 | \$0.0000 | \$0.0456 | \$0.0183 | \$0.0000 | \$1,404,000 |
| Average portion of premium paid by employee | \$0.0021 | \$0.0029 | \$0.0357 | \$0.0014 | \$0.0000 | \$0.0000 | \$0.0144 | \$0.0067 | \$0.0644 | \$1,621,000 |
| Total premium | \$0.0106 | \$0.0092 | \$0.0357 | \$0.0068 | \$0.0000 | \$0.0000 | \$0.0599 | \$0.0250 | \$0.0644 | \$3,025,000 |
| Enrollee expenses | | | | | | | | | | |
| for covered benefits (deductibles, copays, etc.) | \$0.0005 | \$0.0005 | \$0.0013 | \$0.0004 | \$0.0000 | \$0.0000 | \$0.0020 | \$0.0010 | \$0.0019 | \$172,000 |
| for noncovered benefits ^(e) | -\$0.0020 | -\$0.0017 | -\$0.0168 | \$0.0000 | \$0.0000 | \$0.0000 | -\$0.0283 | -\$0.0109 | -\$0.0278 | -\$956,000 |
| Total expenditures | \$0.0090 | \$0.0080 | \$0.0203 | \$0.0072 | \$0.0000 | \$0.0000 | \$0.0336 | \$0.0151 | \$0.0386 | \$2,197,000 |
| Percent Change | | | | | | | | | | |
| Premiums | 0.0018% | 0.0019% | 0.0076% | 0.0012% | 0.0000% | 0.0000% | 0.0086% | 0.0042% | 0.0152% | 0.0023% |
| Total expenditures | 0.0015% | 0.0014% | 0.0034% | 0.0012% | 0.0000% | 0.0000% | 0.0042% | 0.0020% | 0.0077% | 0.0015% |

Source: California Health Benefits Review Program, 2017.

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

(b) As of September 2016, 57% of CalPERS members were state retirees, state employees, or their dependents. CHBRP assumes the same ratio for 2018.

(c) Medi-Cal Managed Care Plan expenditures for members over 65 include those who are also Medicare beneficiaries. This population does not include enrollees in COHS.

(d) 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.

(e) 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; DMHC = Department of Managed Health Care; COHS = County Organized Health Systems; MCMC = Medi-Cal Managed Care

Table 7. Scenario 2: Postmandate (as Amended) Per Member Per Month Premiums and Total Expenditures by Market Segment, California, Total Annual Impact

| | DMHC-Regulated | | | | | | CDI-Regulated | | | Total |
|--|--|-----------------|-----------------|--------------------------------|--------------------------------------|------------------------------|--|-----------------|-----------------|--------------------|
| | Privately Funded Plans (by Market) ^(a) | | | Publicly Funded Plans | | | Privately Funded Plans (by Market) ^(a) | | | |
| | Large Group | Small Group | Individual | CalPERS HMOs ^(b) | MCMC (Under 65) ^(c) | MCMC (65+) ^(c) | Large Group | Small Group | Individual | |
| Enrollee counts | | | | | | | | | | |
| Total enrollees in plans/policies subject to state mandates ^(d) | 9,128,000 | 3,163,000 | 2,379,000 | 884,000 | 7,192,000 | 644,000 | 276,000 | 145,000 | 237,000 | 24,048,000 |
| Total enrollees in plans/policies subject to SB 172 | 9,128,000 | 3,163,000 | 2,379,000 | 884,000 | 0 | 0 | 276,000 | 145,000 | 237,000 | 16,212,000 |
| Premiums | | | | | | | | | | |
| Average portion of premium paid by employer | \$0.0261 | \$0.0229 | \$0.0000 | \$0.0240 | \$0.0000 | \$0.0000 | \$0.0689 | \$0.0431 | \$0.0000 | \$4,288,000 |
| Average portion of premium paid by employee | \$0.0066 | \$0.0105 | \$0.0592 | \$0.0060 | \$0.0000 | \$0.0000 | \$0.0217 | \$0.0157 | \$0.1015 | \$3,268,000 |
| Total premium | \$0.0327 | \$0.0334 | \$0.0592 | \$0.0300 | \$0.0000 | \$0.0000 | \$0.0906 | \$0.0587 | \$0.1015 | \$7,555,000 |
| Enrollee expenses | | | | | | | | | | |
| for covered benefits (deductibles, copays, etc.) | \$0.0015 | \$0.0016 | \$0.0024 | \$0.0014 | \$0.0000 | \$0.0000 | \$0.0034 | \$0.0026 | \$0.0035 | \$331,000 |
| for noncovered benefits ^(e) | -\$0.0064 | -\$0.0068 | -\$0.0219 | -\$0.0044 | \$0.0000 | \$0.0000 | -\$0.0350 | -\$0.0187 | -\$0.0356 | -\$1,885,000 |
| Total expenditures | \$0.0278 | \$0.0282 | \$0.0398 | \$0.0270 | \$0.0000 | \$0.0000 | \$0.0589 | \$0.0426 | \$0.0694 | \$6,001,000 |
| Percent Change | | | | | | | | | | |
| Premiums | 0.0057% | 0.0071% | 0.0126% | 0.0052% | 0.0000% | 0.0000% | 0.0131% | 0.0099% | 0.0240% | 0.0057% |
| Total expenditures | 0.0045% | 0.0049% | 0.0067% | 0.0044% | 0.0000% | 0.0000% | 0.0073% | 0.0056% | 0.0139% | 0.0041% |

Source: California Health Benefits Review Program, 2017.

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

(b) As of September 2016, 57% of CalPERS members were state retirees, state employees, or their dependents. CHBRP assumes the same ratio for 2018.

(c) Medi-Cal Managed Care Plan expenditures for members over 65 include those who are also Medicare beneficiaries. This population does not include enrollees in COHS.

(d) 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.

(e) 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; DMHC = Department of Managed Health Care; COHS = County Organized Health Systems; MCMC = Medi-Cal Managed Care

PUBLIC HEALTH IMPACTS

The public health impact analysis estimates the short-term impacts (within 12 months of implementation) of SB 172 (as introduced) on quality of life, potential harms from fertility preservation treatment, financial burden, and the impact on potential disparities by sex, race/ethnicity, and sexual orientation. See the *Long-Term Impacts* section for estimates of birth outcomes for men and women using cryopreserved eggs, sperm, or embryos obtained through fertility preservation and discussion of the health of the subsequent children.

Estimated Public Health Outcomes

The section focuses on three services: embryo cryopreservation (freezing of embryos), oocyte (egg) cryopreservation, and sperm cryopreservation. This section does not address the remaining standard of care fertility preservation services (ovarian transposition, ovarian and testicular shielding during radiation therapy, conservative gynecologic surgery, and radical trachelectomy) because CHBRP estimated that these services would already be covered by state-regulated plans and policies (see Appendix C for more information).

As presented in the *Medical Effectiveness* section, there is limited evidence that embryo, oocyte, and sperm cryopreservation are effective methods of fertility preservation.

The *Benefit Coverage, Utilization, and Cost Impacts* section estimates that 85% of enrollees with health insurance subject to SB 172 have coverage for fertility preservation at baseline with 7,589 cancer patients at risk of iatrogenic infertility. The number of cancer patients remains the same postmandate; however, the number using fertility preservation services would increase from 1,452 enrollees to 1,887 enrollees in the first year postmandate. These additional 435 cancer patients using fertility preservation (219 males and 216 females) are comprised of the previously uncovered enrollees using services (121 males and 65 females) as well as an assumed 10% increase in service use among previously covered enrollees due to new provider and public awareness of fertility preservation coverage (Vindrola-Padros et al., 2017).

Quality of Life

Loss of fertility can negatively impact the quality of life for cancer survivors of reproductive age, including unresolved grief, depression, and anxiety (Lawson et al., 2015; Lee et al., 2006; Wallace et al., 2005). For instance, a survey of breast cancer patients of reproductive age documented that 57% were very or somewhat concerned about their fertility (Partridge et al., 2004). Distress regarding iatrogenic infertility can persist for many years, as demonstrated by one study that contacted women 10 years after they received cancer treatment and found that childless women had a statistically significant increase in distress and more intrusive thoughts about infertility than those who had at least one biological child or adopted or had stepchildren (Canada and Schover, 2012).

A systematic review identified 47 articles focused on the psychosocial and quality of life effects on female cancer patients undergoing fertility preservation. It concluded that those who received counseling and services (for those who chose fertility preservation) experienced reduced regret and dissatisfaction about fertility outcomes (Deshpande et al., 2015). A literature review including 24 articles about fertility-preservation decision-making reported similar conclusions; decisional regret or uncertainty was greatly reduced for those with better fertility knowledge regardless of patient choice to use the service or not (Li et al., 2016).

In the first year postmandate, SB 172 would likely improve the quality of life by reducing regret about fertility outcomes, dissatisfaction, and distress for the additional 435 enrollees newly using fertility preservation services to treat iatrogenic infertility.

Barriers to Fertility Preservation Services

Patients and providers face different barriers to obtaining fertility preservation services. From the patient perspective, a literature review by Panagiotopoulou et al. (2015) reported that, frequently, newly diagnosed patients were overwhelmed with handling their cancer diagnosis and, therefore, were unable to process fertility-related information. Some survivors also reported that fertility issues were not addressed or inadequately addressed by providers, which led to decision regret by survivors. Patients also reported concerns about delays in cancer treatment to preserve fertility, moral dilemmas, and offspring health as barriers to seeking fertility preservation. Another barrier was the absence of health insurance coverage because the out-of-pocket cost of fertility preservation was considered prohibitive by many patients. All these barriers were reported more often by females than males. Gaps in obtaining fertility preservation counseling and services (care coordination) were also problematic for some cancer patients.

The literature review also reported barriers posed or experienced by providers. For example, multiple studies found that providers were less likely to counsel certain patients about fertility preservation based on a patient's age (older), gender (female), relationship status (unmarried), sociocultural background, and perceived lack of willingness to self-fund fertility preservation. Providers also reported language barriers and incomplete knowledge of fertility preservation and referral networks as barriers to fulsome discussions about fertility preservation (Adams et al., 2013; Miller et al., 2014; Nahata et al., 2017; Panagiotopoulou et al., 2015).

Perhaps most relevant to SB 172 are study findings regarding provider perception of cost of fertility preservation. A systematic review about health care professionals' discussions of fertility preservation with cancer patients found five studies concluding that providers did not discuss fertility preservation with young patients if they thought they could not afford treatment costs (Vindrola-Padros et al., 2017).

SB 172 could potentially increase the rate of physician referrals for fertility counseling and preservation by providing coverage for such services and reducing out-of-pocket costs for patients experiencing iatrogenic infertility. Broader insurance coverage might also remove cost as a provider-perceived barrier.

Potential Harms from SB 172

When data are available, CHBRP estimates the marginal change in relevant harms associated with interventions affected by the proposed mandate. In the case of SB 172, CHBRP found no conclusive evidence regarding significant harms associated with fertility preservation. CHBRP found several studies assessing potential delays in cancer treatment due to fertility preservation; no studies reported an increased risk of mortality for the cancer patients (Baynosa et al., 2009; Madrigano et al., 2007; Waimey et al., 2015).

CHBRP found limited evidence that there are no significant harms resulting from fertility preservation procedures. CHBRP found limited evidence that fertility preservation does not lead to an increased risk in cancer patient mortality due to delays in cancer treatment.

Impact on Disparities³⁴

Insurance benefit mandates that bring all state-regulated plans and policies to parity may change an existing disparity.²⁷ As described in the *Background on Fertility Preservation* section, there is limited evidence of differences in fertility preservation counseling and utilization by race/ethnicity, sex, and gender identity; however, the extent to which these differences result from disparities is unknown.

Impact on Racial/Ethnic Disparities

As presented in the *Background on Fertility Preservation* section, several studies report that racial and ethnic disparities may exist with respect to provider discussions regarding infertility risks and fertility preservation options and referrals for fertility preservation services. However, findings from these studies were not statistically significant and were of insufficient quality to conclude whether racial/ethnic minorities were more likely than whites to experience barriers to access or poorer fertility preservation outcomes.

The extent of racial or ethnic disparities in the use of or outcomes related to fertility preservation for iatrogenic infertility is unknown due to a lack of evidence. Therefore, although limited evidence finds fertility preservation for patients with iatrogenic infertility medically effective, the impact of SB 172 on potential racial/ethnic disparities is unknown.

Impact on Disparities by Sex

Gender differences in rates of cancer and the cost of fertility preservation are notable. For instance, there are almost twice as many California females as males of reproductive age who have cancers with treatments likely to produce iatrogenic infertility (due primarily to the high incidence of breast cancer in females). For males, sperm cryopreservation is the standard method of preserving fertility, costing approximately \$600. For females, the standard fertility preservation methods average an estimated \$13,500, or about 12 times the cost that males incur. Assuming these costs in California, CHBRP estimates that, in the first year postmandate, SB 172 would save 65 females almost \$880,000 in uncovered treatment costs, while 121 males would see a reduction of about \$73,000 in uncovered costs.

Gender disparities exist in both counselling for and use of fertility preservation services. Evidence in the *Background on Fertility Preservation* section indicates that males are more likely to be referred for fertility preservation services than females. This may be partially due to physician reluctance to address fertility preservation with certain patients because of provider-perceived prohibitive costs (Panagiotopoulou et al., 2015). Higher fertility preservation utilization by males was reported in another study, which found that 33% of young adult cancer survivors used fertility preservation services, with males more than twice as likely than females to use services (49% and 22%, respectively) (Bann et al., 2015).

The Bann et al. (2015) study also reported on those survivors who did not use fertility preservation services. More women than men (33% and 28%, respectively) reported a lack of information as a key reason (defined as not enough information about their fertility risk; availability of fertility preservation options; and how to obtain those services). This finding is consistent with other studies reporting that more men receive counseling and referral than women (Panagiotopoulou et al., 2015; Nahata et al., 2017). Bann et al. (2015) also cite other reasons for declining fertility preservation including not enough time before cancer treatment (women 39%; men 25%) and cost (women 24%; men 27%). Of these self-

³⁴. For details about CHBRP's methodological approach to analyzing disparities, see http://www.chbrp.org/analysis_methodology/docs/Estimating_Impacts_on_Racial_and_Ethnic_Disparities_FINAL.pdf.

reported reasons, SB 172 could remove or reduce the cost barrier, which could increase utilization for both genders.

In California, females have twice the rate of cancers with treatments causing iatrogenic infertility as males; furthermore, females pay 12 times more for uncovered fertility preservation services than males. Postmandate, SB 172 would decrease the gender disparity by reducing the female financial burden of fertility preservation services, and reduce the cost consideration from her decision-making process regarding iatrogenic infertility risk. However, CHBRP estimates that some females would still face greater out-of-pocket expense burdens than males, postmandate, due to differences in costs of sex-specific preservation methods (e.g., more office visits, prescription drug cost).

Impact on the Transgender Population and Individuals with Differences in Sex Development

As presented in the *Background on Fertility Preservation* section, transgender persons undergoing gender confirmation surgery or hormonal treatment will experience iatrogenic infertility. Furthermore, a portion of those individuals are likely interested in future parenthood, and according to the American Society for Reproductive Medicine, should be informed about and offered fertility preservation services to retain their ability to reproduce following gonadotoxic treatment (and would be eligible for coverage under SB 172) (ASRM, 2015). However, there is insufficient literature to understand whether disparities for this population exist regarding fertility preservation access, utilization, and outcomes as compared with other populations experiencing iatrogenic fertility.

CHBRP projects that SB 172 would provide fertility preservation coverage for an unknown number of newly covered enrollees who will experience iatrogenic infertility due to gender confirmation treatments, thus eliminating any potential disparities in access to care.

Estimated Impact on Financial Burden

When possible, CHBRP estimates the marginal impact of mandates on financial burden, defined as uncovered medical expenses paid by the enrollee as well as out-of-pocket expenses (e.g., deductibles, copayments, and co-insurance). CHBRP estimates that the additional 435 enrollees with noncovered expenses at baseline would receive a \$956,000 reduction in their financial burden associated with fertility preservation services (Table 1). Due to new coverage, CHBRP also estimates that enrollees with existing coverage at baseline and those who are newly covered would see a net increase of \$127,000 in total out-of-pocket expenses for these services. CHBRP estimates are based on claims data and may underestimate the cost savings for enrollees due to carriers' ability to negotiate discounted rates that are unavailable to patients and their families.

In the first year postmandate, CHBRP estimates that SB 172 would eliminate \$956,000 in uncovered expenses for the 435 previously uncovered enrollees, and all 1,887 enrollees who obtain fertility preservation services to prevent iatrogenic infertility would see a net out-of-pocket increase of \$127,000. Based on CHBRP assumptions for SB 172, enrollees would still pay for storage services beyond the first year and future assisted reproductive technology services to become pregnant; these services are outside of the scope of fertility preservation in SB 172.

LONG-TERM IMPACTS

Long-Term Utilization and Cost Impacts

CHBRP estimated two different Scenarios postmandate for SB 172 using the Cost and Coverage Model, with Scenario 2 capturing the increases in utilization and costs associated with a sample year postmandate. The long-term utilization and costs are expected to remain constant with these findings, assuming that the number of enrollees in DMHC-regulated plans or CDI-regulated policies remains constant along with the costs of fertility preservation services and infertility treatments.

Long-Term Public Health Impacts

When possible, CHBRP estimates the long-term effects (beyond 12 months postmandate) to the public's health that would be attributable to the legislation, including impacts on social determinants of health, premature death, and economic loss. In the case of SB 172, enrollees with iatrogenic infertility may choose to conceive once the acute phase of their illness is over (Waimey et al., 2015). CHBRP estimates the number of live births associated with retrieving frozen sperm, oocytes, or embryos obtained during the fertility preservation phase of care.

Long-Term Impacts on Public Health: Deliveries/Births

Males

CHBRP estimates that an additional 219 males would use sperm cryopreservation annually as a result of SB 172. Johnson et al. (2013) reported that over a 20-year period, 9.5% of 378 male cancer survivors retrieved frozen sperm for reproductive purposes. The study's long time period for retrieval is a good representation of the varied timeframe in which males might retrieve sperm, and includes those who may have been adolescents or very young adults when storing sperm originally. In the case of SB 172, about 21 males undergoing fertility preservation in a given year would eventually retrieve cryopreserved sperm to reproduce. As reported in the *Medical Effectiveness* section, the birth rate using cryopreserved sperm is 49% (Ferrari et al., 2016). Thus, CHBRP estimates that 10 births would occur in the original cohort of 219 newly covered males using fertility preservation in a given year. Note that more than one IVF cycle may be required to achieve the delivery.

For each cohort of males seeking fertility preservation for iatrogenic infertility in a given year, CHBRP estimates the long-term marginal impact of SB 172 would yield about 10 more live births to these men and their partners over time.

Females

CHBRP estimates that an additional 216 females would use either embryo or oocyte cryopreservation annually as a result of SB 172. Although CHBRP found one single center study about differential use of oocyte and embryo cryopreservation (9.5% and 90.5%, respectively) (Cardoza et al., 2015), the method chosen by the patient is informed by clinical and personal factors such as type of cancer and treatment, age at cancer diagnosis, relationship status, and moral beliefs and values. The Cardoza study is the only long-term study CHBRP found that estimates live birth outcomes for both oocyte and embryo cryopreservation (Cardoza et al, 2015).

Embryo cryopreservation is considered the most successful fertility preservation approach for females and the standard preservation method for women with a male partner (see *Medical Effectiveness* section), while oocyte cryopreservation may be more appropriate for those females without partners or who have a belief system at odds with storing embryos. CHBRP found one study reporting on live birth outcomes for cancer survivors using cryopreservation. Cardoza et al. (2015) report that over a 17-year period, 33 percent of female cancer survivors retrieved frozen oocytes or embryos, 47 percent of which resulted in live births. In the case of SB 172, an estimated 71 females newly covered for fertility preservation in a given year would eventually retrieve the frozen eggs, sperm, or embryos. The live birth rate is 47%; thus, about 34 live births would occur in the original cohort of 216 newly covered females using fertility preservation. Note that more than one embryo transfer cycle may be required to achieve the live birth.

For each cohort of females seeking fertility preservation for iatrogenic infertility in a given year, CHBRP estimates the long-term marginal impact of SB 172 would yield about 34 more live births among these women over time.

Although SB 172 (as introduced) would decrease the financial burden of fertility preservation services in the short term, SB 172 (as introduced) would not cover future storage costs or assisted reproductive technology that is required to conceive a child; those who retrieve frozen sperm, oocytes, or embryos would likely pay out of pocket for assisted reproductive technology to become pregnant.

Note that these are estimates. As stated earlier, success in achieving live births is inversely associated with age with highest success rates in women under age 35 and lowest success in women over age 40 (SART, 2014). Also, this estimate assumes a minimum of one birth per couple, but some couples may choose to have several children over time or have twins. Finally, the birth estimates do not represent live births per year; they represent deliveries that may occur over many years, depending upon when survivors retrieve cryopreserved sperm, oocytes, or embryos.

Potential Harms Associated with Cryopreservation and ART

Those who use cryopreservation prior to gonadotoxic treatments must use assisted reproductive technology (ART) to become pregnant. The literature contains multiple studies reporting on the health outcomes of children born using ART, but little evidence regarding the long-term outcomes of cryopreservation. Cobo et al. (2014) reported that 1,027 babies were born from cryopreserved oocytes in 2014 with no observed increase in congenital abnormalities.

As a proxy for health outcomes of infants conceived with cryopreserved sperm, oocytes, or embryos from iatrogenic infertile patients, CHBRP researched outcomes for ART-conceived children using frozen eggs, sperm, or embryos (rather than fresh embryos). Two studies and a meta-analysis reported higher risks of poorer outcomes for infants conceived by ART than those conceived spontaneously. Risks included low birthweight (possibly leading to developmental delays or other health problems), preterm birth, cesarean section, small for gestational age, macrosomia, perinatal mortality, neonatal mortality, infant mortality, future hospital admissions, and congenital malformations compared to spontaneously conceived infants (Pandey et al., 2012; Pelkonen et al., 2015; Wennerholm et al., 2013).

However, earlier studies concluded that ART-conceived children are generally healthy and develop similarly to those children conceived spontaneously. Four studies concluded that ART-conceived children are likely to have normal cognitive, motor, behavioral, socioemotional, and language development compared to their spontaneously conceived counterparts (Wagenaar et al., 2009; Wagenaar et al., 2011;

Yeung et al., 2016; Zhan et al., 2013). In addition, three large cohort studies found no overall increased risk of cancer for ART-conceived children compared to spontaneously conceived children and population cancer incidence rates (Reigstad et al., 2016; Sundh et al., 2014; Williams et al., 2013).

Evidence-based literature indicates that although there may be some risk of negative health outcomes to ART-conceived infants overall, fertility preservation poses no higher risk to the health outcomes of children conceived with cryopreserved eggs, sperm, or embryos from persons with iatrogenic infertility than those risks associated with assisted reproductive technology used to treat non-iatrogenic infertility.

APPENDIX A TEXT OF BILL ANALYZED

On January 23, 2017, the California Senate Committee on Health requested that CHBRP analyze SB 172. The bill was amended on March 7, 2017. The text below reflects those amendments.

Introduced by Senator Portantino

An act to add Section 1374.551 to the Health and Safety Code, and to add Section 10119.61 to the Insurance Code, relating to health care coverage.

LEGISLATIVE COUNSEL'S DIGEST

SB 172, as introduced, Portantino. Health care coverage: fertility preservation.

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 every group health care service plan contract and health insurance policy that covers hospital, medical, or surgical expenses to offer coverage for the treatment of infertility, as defined, except in vitro fertilization.

This bill would require an individual or group health care service plan contract or health insurance policy issued, amended, or renewed on and after January 1, 2018, that covers hospital, medical, or surgical expenses to include coverage for medically necessary expenses for standard fertility preservation services when a necessary medical treatment may directly or indirectly cause iatrogenic infertility to an enrollee or insured.

Because a willful violation of these provisions by a health care service plan would be a crime, this bill would impose state-mandated local program.

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

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

DIGEST KEY

Vote: majority Appropriation: no Fiscal Committee: yes Local Program: yes

BILL TEXT

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

SECTION 1. Section 1374.551 is added to the Health and Safety Code, to read:

1374.551. An individual or group health care service plan contract issued, amended, or renewed on and after January 1, 2018, that covers hospital, medical, or surgical expenses shall include coverage for medically necessary expenses for standard fertility preservation services when a necessary medical treatment may directly or indirectly cause iatrogenic infertility to an enrollee.

(a) An individual or group health care service plan contract issued, amended, or renewed on and after January 1, 2018, that covers hospital, medical, surgical, and other iatrogenic expenses for diagnoses with medical interventions that may directly or indirectly cause iatrogenic infertility shall include coverage for evaluation and treatment of iatrogenic infertility including, but not limited to, standard fertility preservation services.

SEC. 2. Section 10119.61 is added to the Insurance Code, to read:

10119.61. An individual or group health insurance policy issued, amended, or renewed on and after January 1, 2018, that covers hospital, medical, or surgical expenses shall include coverage for medically necessary expenses for standard fertility preservation services when a necessary medical treatment may directly or indirectly cause iatrogenic infertility to an enrollee.

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

APPENDIX B LITERATURE REVIEW METHODS

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

Studies of the effects of fertility preservation treatments for patients at risk of iatrogenic infertility were identified through searches of PubMed, the Cochrane Library, and Web of Science. Websites maintained by the following organizations were also searched: Agency for Healthcare Research and Quality; American Cancer Society; American College of Obstetricians and Gynecologists; Fertile Hope Program; Institute for Clinical Systems Improvement; International Network of Agencies for Health Technology Assessment; National Comprehensive Cancer Network, Inc.; National Guideline Clearinghouse; National Institute for Clinical Excellence; National Institutes of Health; National Health Service Centre for Reviews and Dissemination; Oncofertility Consortium; Scottish Intercollegiate Guideline Network; and World Health Organization.

The search was limited to abstracts of studies published in English. The medical effectiveness search was limited to studies published from 2013 to present, because CHBRP had previously reviewed this literature using the same search terms in 2011 and 2013 for the AB 428 and SB 912 analyses, respectively. The literature on the effectiveness of fertility preservation treatments did not include any randomized controlled trials. The majority of the papers returned were case reports or systematic reviews.

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

Abstracts for 859 articles were screened, of which 76 were reviewed for inclusion in this report. A total of 20 new studies since 2012 were included in the medical effectiveness review for SB 172.

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*.³⁵ 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.

³⁵ Available at: http://www.chbrp.org/analysis_methodology/medical_effectiveness_analysis.php.

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

- Clear and convincing evidence;
- Preponderance of evidence;
- Limited evidence
- 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.

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

A grade of *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 (* indicates truncation of word stem)

Search Terms (* indicates truncation of the word stem. [Majr] indicates increased relevance weighting of subject term.

[Subheading] indicates "floating" subheading)

Medical Subject Headings (MeSH) – PubMed

"Antineoplastic Agents/adverse effects"[Majr]

"Continental Population Groups"[Mesh]

"Cost-Benefit Analysis"[Mesh]

"Cost of Illness"[Mesh]

"Cost Sharing"[Mesh]

"Costs and Cost Analysis"[Mesh]

"Counseling"[Mesh]

"Cryopreservation/economics"[Mesh]

"economics"[Subheading]

"epidemiology" [Subheading]

"Ethnic Groups"[Mesh]

"Ethnic Groups"[Mesh]

"Fertility Preservation"[Majr]

"Fertility Preservation"[Mesh]

"Fertility Preservation/adverse effects"[Majr]

"Fertility Preservation/adverse effects"[Mesh]

"Fertility Preservation/economics"[Majr]

"Fertility Preservation/economics"[Mesh]

"Fertility Preservation/epidemiology"[Majr]

"Fertility Preservation/psychology"[Majr]

"Fertility Preservation/psychology"[Mesh]

"Fertility Preservation/statistics and numerical data"[Mesh]

"Gonads/radiation effects"[Majr]

"Health Services Needs and Demand"[Mesh]

"Health Services Needs and

Demand/economics"[Mesh]

"Health Services Needs and

Demand/statistics and numerical data"[Mesh]

"Health Services Needs and

Demand/utilization"[Mesh]

| | |
|---|--|
| "Healthcare Disparities"[Mesh] | "fertility preservation" |
| "Infertility/drug effects"[Mesh] | "fertility sparing" |
| "Infertility/etiology"[Mesh] | "financial burden" |
| "Insurance Coverage"[Mesh] | "financial burdens" |
| "Menopause, Premature"[Mesh] | "iatrogenic infertility" |
| "Minority Health"[Mesh] | "incremental cost effectiveness ratio" |
| "Neoplasms/complications"[Majr] | "long term impact" |
| "Neoplasms/radiotherapy"[Majr] | "long term impacts" |
| "Neoplasms/surgery"[Majr] | "oocyte retrieval" |
| "Oocyte Retrieval"[Mesh] | "out-of-pocket" |
| "Organ Sparing Treatments"[Mesh] | "pregnancy outcome" |
| "Pregnancy Outcome"[Mesh] | "pregnancy outcomes" |
| "Pregnancy Rate"[Mesh] | "premature menopause"[ti] |
| "Pregnancy"[Majr:NoExp] | "premature ovarian failure"[ti] |
| "Prevalence"[Mesh] | "preservation of fertility" |
| "Primary Ovarian Insufficiency"[Mesh] | "price elasticity" |
| "Public Health Surveillance"[Mesh] | "productivity" |
| "Public Health"[Mesh] | "psychological burden" |
| "Quality of Life"[Mesh] | "quality of life"[tiab] |
| "Racism"[mesh] | "reproductive success" |
| "Radiotherapy/adverse effects"[Majr] | "sex differences" |
| "Reproductive Techniques, Assisted"[Mesh] | "sperm extraction" |
| "Semen Preservation"[Mesh] | "sperm retrieval" |
| "Sexism"[Mesh] | "treatment-related infertility" |
| "Social Discrimination"[Mesh] | "treatment cost" |
| "Sperm Banks"[Mesh] | "uncovered cost" |
| "Sperm Retrieval"[Mesh] | "uncovered costs" |
| "statistics and numerical data"[Subheading] | "unit cost" |
| "supply and distribution"[Subheading] | access[ti] |
| "Utilization Review"[Mesh] | accessibil*[ti] |
| "utilization"[Subheading] | barrier*[ti] |
| | barrier*[tiab] |
| | benefit |
| | cancer[ti] |
| | cervicectomy |
| | co-payment |
| | coinsurance |
| | conservative[ti] |
| | copayment |
| | cost[ti] |
| | cost[tiab] |
| | costs[ti] |
| | cryopreservation |
| | deductible |
| | demand[tiab] |
| | disparities[ti] |
| | disparity[ti] |
| | egg |
| | eggs |
| | embryo |
| | embryos |

Keywords & Keyword Phrases – PubMed

"benefit cap"
 "conservative gynecologic surgery"
 "conservative surgery"
 "cost analysis"
 "cost barrier"
 "cost barriers"
 "cost benefit"
 "cost effective"
 "cost effectiveness"
 "cost of treatment"
 "cost offset"
 "cost savings"
 "cost sharing"
 "cost utility"
 "economic loss"
 "economic losses"

benefit
 cancer[ti]
 cervicectomy
 co-payment
 coinsurance
 conservative[ti]
 copayment
 cost[ti]
 cost[tiab]
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 cryopreservation
 deductible
 demand[tiab]
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 egg
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 embryo
 embryos

ethnic
ethnicity
extraction[ti]
fertility[ti]
freeze
freezing
gender[ti]
generosity
gnrh
gnrha
gonad
gonadal
gonadotrophin releasing hormone
gonads
gynecologic[ti]
incidence[ti]
insurance
oncofertility
oocyte
oocyte[ti]
oocytes
out-of-pocket
outcome*[ti]
ovarian
ovarian transposition
pregnancy[ti]
preservation
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racism
radiation
radiotherapies
radiotherapy
retrieval[ti]
semen
sexism[tiab]
shielding
shielding[tiab]
sperm
sperm banking
sperm banks
sperm[ti]
suppression
surgery[ti]
testes
testicular

tier
trachelectomy
treatment[tiab]
utilisation[tiab]
utilization[tiab]

Terms Excluded from Search

Publication Types

Addresses[ptyp]
Autobiography[ptyp]
Biography[ptyp]
Comment[ptyp]
Dictionary[ptyp]
Directory[ptyp]
Editorial[ptyp]
Electronic Supplementary Materials[ptyp]
Festschrift[ptyp]
Historical Article[ptyp]
In Vitro[ptyp]
Interactive Tutorial[ptyp]
Letter[ptyp]
News[ptyp]
Newspaper Article[ptyp]
Patient Education Handout[ptyp]
Periodical Index[ptyp]
Personal Narratives[ptyp]
Portraits[ptyp]
Video-Audio Media[ptyp]
Webcasts[ptyp]

Econlit

Keywords & Keyword Phrases

"benefit cap"
"cost analysis"
"cost benefit"
"cost effective"
"cost effectiveness"
"cost of treatment"
"cost offset"
"cost savings"
"cost sharing"
"cost utility"
"incremental cost effectiveness ratio"
"out-of-pocket"

"price elasticity"
"treatment cost"
"unit cost"
cancer
co-payment
coinsurance
copayment
cost
costs
cryo-preservation
cryopreservation
deductible
economics
egg
eggs
embryo*
fertility
fertility preserv*
fertility preservation
freez*
gonad*
iatrogenic infertility
infertility
insurance
oocyte*
ovarian
pregnancy
premature menopause
premature ovarian failure
preservation
price
prices
semen
semen cryopreservation
sperm
sperm cryopreservation
testicular
testicular tissue cryopreservation
tier

Web of Science

Keywords & Keyword Phrases

TOPIC:
"assisted reproductive techniques"
"benefit cap"
"cost analysis"
"cost benefit"
"cost effectiv*"
"cost effectiveness*"

"cost offset"
"cost savings"
"cost sharing"
"cost utility"
"fertility sparing"
"out-of-pocket"
"premature menopause"
"premature ovarian failure"
"price elasticity"
"primary ovarian insufficiency"
"quality of life"
"uncovered cost*"
"unit cost"
cancer
cancer
carcinoma*
carcinoma*
cervicectomy
chemotherapy
co-payment
coinsurance
conservative NEAR/2 surgery
copayment
cost
cost-benefit
cost NEAR/2 illness
cost NEAR/2 treatment*
costs
cryo-preservation
cryopreservation
cytotoxic
deductible
disparities
disparity
economic NEAR/2 loss*
economics
egg
eggs
embryo*
ethnic
ethnicity
fertility NEAR/2 outcome*
fertility NEAR/4 preserv*
financial NEAR/2 burden*
freez*
gender
gnrh
gnrha
gonad
gonad*
gonadal

gonadotoxicity
gonadotrophin releasing hormone
gonads
iatrogenic NEAR/4 infertility
insurance
long-term NEAR/2 impacts
melanoma
minorities
minority
neoplasms
oncofertility
oocyte*
out-of-pocket
ovarian
ovarian transposition
pregnanc* NEAR/4 outcome*
pregnanc* NEAR/4 rate*
pregnancy NEAR/2 outcome
preservation
price
prices
productivity
psycholog*
psychosocial
qol
racial
racism
radiation
radiotherapy
reproductive NEAR/2 success
semen
sexism
shield*
sperm
suppression
testicular
tier
trachelectomy
treatment-related NEAR/2 infertility
utilis*
utiliz*

TITLE:
access*
cancer
carcinoma*
chemotherapy
counseled
counseling
counselled
counselling

cytotoxic
demand
demand
egg
eggs
embryo*
fertility NEAR/4 preserv*
gonad*
iatrogenic NEAR/4 infertility
incidence
melanoma
neoplasms
oncofertility
oocyte*
ovarian
prevalence
semen
supply
testicular
treatment-related NEAR/2 infertility
tumor*
utilis*
utiliz*

Keywords Excluded from Search

TOPIC:

rat
rats
mice
mouse
bovine
cow
cattle
horse*
equine
monkey
monkeys
canine*
feline*
dogs
cats
hamster*

Cochrane Library

Keywords & Keyword Phrases

"benefit cap"
"cost analysis"

| | |
|--|--|
| "cost benefit" | gonad |
| "cost effective" | gonad* |
| "cost effectiveness" | gonadal |
| "cost of treatment" | gonadotrophin releasing hormone |
| "cost offset" | gonads |
| "cost savings" | incidence |
| "cost sharing" | infertility |
| "cost utility" | insurance |
| "fertility preservation" | minorities |
| "iatrogenic infertility" | neoplasms |
| "incremental cost effectiveness ratio" | oncofertility |
| "out-of-pocket" | oocyte* |
| "preservation of fertility" | ovarian |
| "price elasticity" | ovarian transposition |
| "quality of life" | pregancy |
| "sperm bank**" | pregnancies |
| "sperm retrieval" | pregnancy |
| "treatment-related infertility" | pregnant |
| "treatment cost" | preservation |
| "unit cost" | prevalance |
| access | price |
| accessibil* | prices |
| cancer | qol |
| cervicectomy | racial |
| co-payment | racism |
| coinsurance | radiation |
| conservative surgery | radiotherapy |
| copayment | semen |
| cost | sexism |
| costs | sperm |
| counseling | supply |
| counselling | testes |
| cryopreservation | testicular |
| deductible | tier |
| demand | trachelectomy |
| disparities | utilisation |
| disparity | utilization |
| economic loss | |
| economics | MeSH Terms |
| egg | MeSH descriptor: [Fertility Preservation] |
| eggs | explode all trees |
| embryo* | MeSH descriptor: [Fertility Preservation] with |
| ethnic | qualifier(s) Psychology |
| ethnicity | |
| explode all trees | |
| fertility | |
| financial burden | |
| freez* | |
| gender | |
| gnrh | |
| gnrha | |

APPENDIX C COST IMPACT ANALYSIS: DATA SOURCES, CAVEATS, AND ASSUMPTIONS

The cost analysis in this report was prepared by the members of the cost team, which consists of CHBRP task force members and contributors from the University of California, Los Angeles, and the University of California, Davis, as well as the contracted actuarial firm PricewaterhouseCoopers (PwC).³⁶

Information on the generally used data sources and estimation methods, as well as caveats and assumptions generally applicable to CHBRP's cost impacts analyses are available at CHBRP's website.³⁷

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

Analysis Specific Caveats and Assumptions

CHBRP estimated utilization of fertility preservation services, both for baseline and postmandate, using cancer incidence rates grouped by sex, the peer-reviewed literature, and input from content experts. Cancer incidence rates for reproductive age Californians were estimated using 2013 cancer statistics data from the online Centers for Disease Control and Prevention CDC WONDER Database. CHBRP was able to limit the CDC WONDER to ages 10 to 44, which closely aligns with the content expert's recommendations for reproductive age definitions for this analysis of 12 to 44 for females and 12 to 49 for males.

In its analysis, CHBRP included the top 10 types of cancer whose treatments pose the highest iatrogenic infertility risk (see the *Background on Fertility Preservation* section). The utilization rates, both for baseline and postmandate, were assumed to be consistent across all types of cancer due to the very limited relevant data in the literature or from content expert input. Estimates of those who use fertility preservation services were made using very limited relevant literature and/or from content expert input. The body of literature on this topic is also thin.

CHBRP estimated the unit costs for fertility preservation services based on Truven MarketScan data. The data were limited to California enrollees and further refined to identify only enrollees with a cryopreservation procedure. Medical and surgical services and drugs related to fertility preservation occurring prior to the cryopreservation were included and services after the cryopreservation were excluded. Services related to infertility treatments, such as treatments of fertility problems, intrauterine insemination, implantation, and surrogacy were excluded. The table below provides a summary of the inclusion and exclusion of services in the development of the average unit costs.

³⁶ CHBRP's authorizing statute, available at www.chbrp.org/docs/authorizing_statute.pdf, requires that CHBRP use a certified actuary or "other person with relevant knowledge and expertise" to determine financial impact.

³⁷ See *2017 Cost Impact Analyses: Data Sources, Caveats, and Assumptions*, available at www.chbrp.org/analysis_methodology/cost_impact_analysis.php.

Table 8. Services Included in Average Fertility Preservation Unit Costs

| Included | Excluded |
|-----------------------------------|--|
| Medical/Surgical | Infertility treatments |
| Office visits and consultations | Embryo implantation |
| Fertility counseling | Intrauterine insemination |
| Surgical facility | Surrogacy |
| Surgical retrieval of oocyte | Services received after cryopreservation |
| Anesthesia | |
| Culture of Oocyte/Embryo < 4 Days | |
| Extended Culture of Oocytes | |
| Assisted Oocyte Fertilization | |
| Insemination of Oocytes | |
| Oocyte Identification | |
| Sperm Isolation | |
| Semen Analysis | |
| Cryopreservation | |
| Storage – 1 year | |
| Diagnostic Ultrasound | |
| Laboratory Tests | |
| Specimen Handling | |
| Pharmacy (Drug Classes) | |
| Follitropins & Combinations | |
| Menotropins | |
| Chorionic Gonadotropin | |
| Ganirelix | |
| Progesterone & Combinations | |
| Cetrotide | |

Source: CHBRP analysis of MarketScan data, 2017.

Fertility preservation services were analyzed separately for enrollees with and without a primary cancer diagnosis, and the unit costs were not found to be significantly different. The average unit costs based on 2014 data were trended to the 2018 projection period using the CPI-Medical rate. No utilization trend was applied.

CHBRP estimated the baseline utilization rate of cryopreservation for males to be 31.5% for those without insurance coverage of fertility preservation services and 34.6% for those with coverage, while baseline cryopreservation utilization for females were estimated to be 8.1% without coverage and 16.2% for those with coverage. These estimates were informed by a study which summarized the results of a survey of

reproductive age cancer patients that indicated that 49% of male patients and 22% of female patients, who wanted to eventually have children, took steps to preserve their fertility (Bann et al., 2015). The survey also indicated that approximately one-third of the reproductive age cancer patients did not want children. This study is consistent with other research findings that demonstrate that adolescent males are more likely to be referred to fertility preservation specialists than their female counterparts. Due to the relatively low cost, CHBRP assumed that males without coverage of fertility preservation services would pursue these services at a rate 10% less than the rate for males with coverage of fertility preservation services. Conversely, due to the relatively high cost, CHBRP assumed that females without coverage of fertility preservation services would pursue these services at a rate one-half of the rate for females with coverage of fertility preservation services.

CHBRP estimates 10% additional induced utilization increase for the postmandate scenario compared to baseline utilization assumptions. This is due to the expected impact of increased public and provider awareness with the passage of the mandate and oncologist engagement in recommending fertility preservation procedures to their patients.

From these assumptions, CHBRP estimated that the use of sperm cryopreservation by male cancer patients who are reproductive age and at risk for iatrogenic infertility would rise from a 2018 baseline of 851 to 945 postmandate. Similarly, CHBRP estimated that the use of oocyte and embryo cryopreservation by female cancer patients who are reproductive age and at risk for iatrogenic infertility would rise from a 2018 baseline of 786 to 912 postmandate.

Determining Public Demand for the Proposed Mandate

This subsection discusses public demand for the benefits SB 172 would mandate. Considering the criteria specified by CHBRP's authorizing statute, CHBRP reviews public demand for benefits relevant to a proposed mandate in two ways. CHBRP:

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

On the basis of conversations with the largest collective bargaining agents in California, CHBRP concluded that unions currently do not include cost-sharing arrangements for description treatment or service. In general, unions negotiate for broader contract provisions such as coverage for dependents, premiums, deductibles, and broad coinsurance levels.

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

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

APPENDIX D INFORMATION SUBMITTED BY OUTSIDE PARTIES

In accordance with the California Health Benefits Review Program (CHBRP) policy to analyze information submitted by outside parties during the first 2 weeks of the CHBRP review, the following parties chose to submit information.

The following information was submitted by bill author's office (Portantino) and bill sponsors in February, 2017.

American Medical Association. American Medical Association: Report of Reference Committee. 2013.

Available at: <http://www.allianceforfertilitypreservation.org/pdf/2013AMAMeeting.pdf>.

American Society for Reproductive Medicine (ASRM). Fertility Preservation and Reproduction in Patients Facing Gonadotoxic Therapies. 2013. Available at:

https://www.asrm.org/uploadedFiles/ASRM_Content/News_and_Publications/Practice_Guidelines/Committee_Opinions/Fertility%20preservation%20and%20reproduction%20in%20patients%20facing%20gonadotoxic%20therapies2013.pdf.

Benedict, C., et al. Young Adult Female Cancer Survivors' Unmet Information Needs and Reproductive Concerns Contribute to Decisional Conflict Regarding Posttreatment Fertility Preservation. *Cancer*. 2016;122:2101-2109.

Jensen, J., et al. Fertility Preservation. *Mayo Clinic Proceedings*. 2011; 86(1): 45–49.

Llarena, C., et al. Impact of Fertility Concerns on Tamoxifen Initiation and Persistence. *Journal of the National Cancer Institute*. 2015;107(10): djv202.

Loren, A., et al. Fertility Preservation for Patients With Cancer: American Society of Clinical Oncology Clinical Practice Guideline Update. *Journal of Clinical Oncology*. 2013; 31:2500-2510

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Adolescent and Young Adult (AYA) Oncology. Available at:

https://www.nccn.org/professionals/physician_gls/f_guidelines.asp.

Submitted information is available upon request. 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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CALIFORNIA HEALTH BENEFITS REVIEW PROGRAM COMMITTEES AND STAFF

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

The **National Advisory Council** provides expert reviews of draft analyses and offers general guidance on the program to CHBRP staff and the Faculty Task Force. CHBRP is grateful for the valuable assistance of its National Advisory Council. CHBRP assumes full responsibility for the report and the accuracy of its contents.

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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 multiple 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.

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.

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CHBRP assumes full responsibility for the report and the accuracy of its contents. All CHBRP bill analyses and other publications are available at www.chbrp.org.

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