California Health Benefits Review Program

Analysis of California Senate Bill 600
Fertility Preservation

A Report to the 2019–2020 California State Legislature April 17, 2019

CALIFORNIA
HEALTH BENEFITS REVIEW PROGRAM

Key Findings:

Analysis of California Senate Bill 600 Fertility Preservation

Summary to the 2019–2020 California State Legislature, April 17, 2019

CALIFORNIA HEALTH BENEFITS REVIEW PROGRAM

AT A GLANCE

The version of California Senate Bill (SB) 600 analyzed by CHBRP would require coverage for medically necessary expenses for standard fertility preservation services when a medically necessary treatment may directly or indirectly cause iatrogenic infertility.

1. CHBRP estimates that, in 2020, of the 24.5 million Californians enrolled in state-regulated health insurance, 16.9 million of them will have insurance subject to SB 600.
2. **Benefit coverage.** Some fertility preservation services are provided as part of cancer treatment and CHBRP assumes 100% of enrollees have coverage for these standard services. However, 0.9% of enrollees currently have benefit coverage for sperm, oocyte, and embryo cryopreservation, which are classified as standard fertility preservation services by ACSO and ASRM. Benefit coverage would increase to 100% postmandate. SB 600 is unlikely to exceed the essential health benefits.
3. **Utilization.** The number of enrollees utilizing sperm, oocyte, and embryo cryopreservation services would increase from 1,102 premandate to 1,753 postmandate.
4. **Expenditures.** Total expenditures would increase by $6,773,000 (0.0043%).
    a. This is due to premium increases of $8,263,000 and increases in enrollee out-of-pocket expenses of $3,244,000, offset by a decrease of enrollee expenses for noncovered services of $4,734,000.
5. **Medical effectiveness.** The medical effectiveness review found there is:
    a. Preponderance of evidence that **sperm, oocyte, and embryo** cryopreservation is an effective method of fertility preservation.

AT A GLANCE, Cont.

6. **Public health.** SB 600 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 potentially experiencing iatrogenic infertility.
7. **Long-term impacts.** Use of cryopreservation will lead to some increased utilization of infertility treatments to achieve pregnancy among the affected enrollees. CHBRP estimates utilization of cryopreservation services in 2020 would result in additional 86 live births over a 20-year period.

CONTEXT

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. Approximately 90% of iatrogenic infertility is caused by cancer treatment.[1] Including services specified by the American Society of Clinical Oncology (ASCO) and American Society for Reproductive Medicine (ASRM) guidelines, SB 600 would require coverage of: 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.

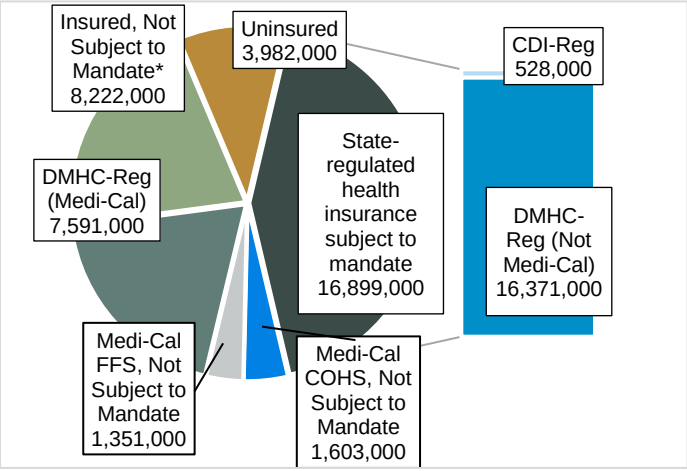
CHBRP assumes that enrollees have coverage for fertility preservation consultation and services that are part of or concurrent with cancer treatment; therefore, this report focuses on the impacts of requiring plans and policies to cover sperm, oocyte, and embryo cryopreservation.

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

BILL SUMMARY

SB 600 would require coverage for medically necessary expenses for standard fertility preservation services when a medically necessary treatment may directly or indirectly cause iatrogenic infertility. SB 600 also provides definitions of iatrogenic infertility, medical treatment that may directly or indirectly cause iatrogenic infertility, standard fertility preservation services, and medical necessity. Figure A notes how many Californians have health insurance that would be subject to SB 600.

Figure A. Health Insurance in CA and SB 600



Source: California Health Benefits Review Program, 2019.
Notes: *Medicare beneficiaries, enrollees in self-insured products, etc.

IMPACTS

Benefit Coverage, Utilization, and Cost

Standard fertility preservation services that do not involve cryopreservation, such as ovarian transposition, are covered by insurance as part of standard cancer treatment. Hence, in this analysis CHBRP focused on examining specifically the coverage of cryopreservation of sperm, mature oocytes, and embryos, including all procedures to harvest the materials and storage for 1 year, among enrollees in DMHC-regulated health plans and CDI-regulated policies in California.

Benefit Coverage

Currently, 0.9% of enrollees with health insurance that would be subject to SB 600 have coverage for cryopreservation services for sperm, mature oocytes, and embryos. Postmandate, the coverage for cryopreservation would increase to 100%.

Utilization

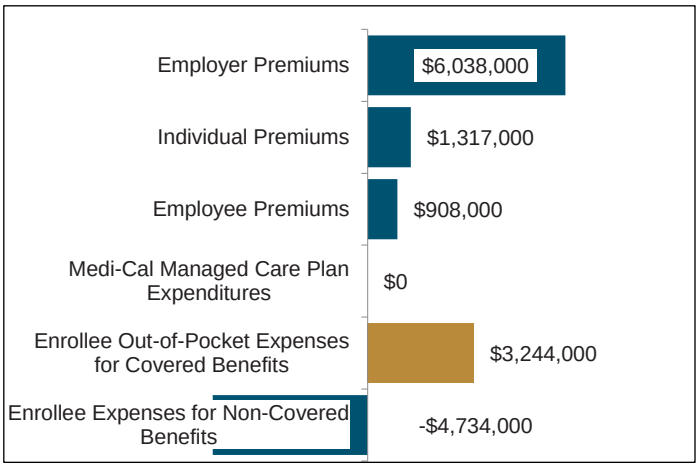
CHBRP estimates that in the first year postmandate, SB 600 would result in 792 male and 961 female enrollees with cancer using cryopreservation services.

Of the 792 male users postmandate, 136 enrollees would be new users of sperm cryopreservation. The estimated 639 male cryopreservation users at baseline using cryopreservation without coverage would experience financial relief postmandate, because coverage would be available to them. Of the 961 female users postmandate, 516 enrollees would be new users (123 new users of embryo cryopreservation and 392 new users of mature oocyte cryopreservation). A total of 428 female enrollees (102 users of embryo cryopreservation and 326 of mature oocyte cryopreservation) would use cryopreservation with coverage postmandate, whereas they were using the services without coverage at baseline.

Expenditures

SB 600 would increase net annual expenditures by total net annual $6,773,000 or total net annual 0.0043% for enrollees with DMHC-regulated plans and CDI-regulated policies. This is due to a $8,263,000 increase in total health insurance premiums paid by employers and enrollees for newly covered benefits, adjusted by a $4,734,000 decrease in enrollee expenses for noncovered benefits.

Figure B. Expenditure Impacts of SB 600



Source: California Health Benefits Review Program, 2019.

Enrollee Out-of-Pocket Spending

About 10% of enrollees in the nongrandfathered large group and 100% of enrollees in the Covered California individual markets with coverage for cryopreservation have the same cost-sharing structure as major medical services. CHBRP assumed the cost-sharing structure for cryopreservation would involve a 50% coinsurance, based, for all other enrollees. Cost-sharing impacts (not including premiums) among enrollees using cryopreservation would range from $184 for CalPERS HMO enrollees to $1,051 for enrollees in small group plans.

Medi-Cal

SB 600 does not apply to Medi-Cal beneficiaries, and therefore, there would be no impact.

CalPERS

Premium employer expenditures would increase by $271,000 (0.0087%) for CalPERS enrollees. Enrollees would also see a corresponding increase in employee premiums and out-of-pocket expenses, but a decrease in enrollee expenses for noncovered benefits.

Number of Uninsured in California

SB 600 would not result in premium increases of more than 1%, and therefore, there would be no measurable impact on the number of uninsured in California.

Medical Effectiveness

Recommendations issued by the ASCO in July 2018 indicate that cryopreservation is considered standard practice for fertility preservation in cancer patients. As discussed above, cryopreservation is not a widely covered form of fertility preservation. Therefore, the *Medical Effectiveness* review examined whether sperm, oocyte, and embryo cryopreservation services used for fertility perseveration resulted in pregnancy and live births, among other outcomes.

- There is a *preponderance of evidence* that **sperm, oocyte, and embryo cryopreservation** are effective methods of preserving fertility.

Other standard fertility preservation services, such as shielding and ovarian transposition, are all covered by insurance as part of standard cancer treatment. Additional fertility preservation services — ovarian suppression with hormones for female breast cancer patients, cryopreservation of ovarian tissue and testicular tissue, testicular suppression with hormones during radiation, and maturation of oocytes outside of the body — are either considered experimental or not broadly recommended.

Public Health

SB 600 would likely improve the quality of life by reducing regret about fertility outcomes, dissatisfaction, and distress for the additional 651 enrollees newly using fertility preservation services to prevent iatrogenic infertility. SB 600 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.

In California, females have twice the rate of cancers with treatments causing iatrogenic infertility as males; furthermore, females pay 23 times more for uncovered fertility preservation services than males. Postmandate, SB 600 would decrease the gender disparity by reducing the financial burden, thereby bringing costs between genders to parity, and reduce the cost consideration from a woman's 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, procedure costs) and insurance cost-sharing structures.

Long-Term Impacts

When the enrollee is ready to use the cryopreserved material at some point in the future, they would incur costs associated with infertility treatments, such as in vitro fertilization. Costs for this treatment incurred by the enrollee would be dependent on whether or not infertility treatment is covered by insurance and the level of coverage. Use of cryopreservation will lead to some increased utilization of infertility services to achieve pregnancy among the affected enrollees. CHBRP estimates utilization of cryopreservation services in 2020 would result in additional 86 live births over a 20-year period.

Essential Health Benefits and the Affordable Care Act

SB 600 is unlikely to exceed EHBs. DMHC confirmed to CHBRP that under existing law, fertility preservation to address potential iatrogenic infertility is a basic health care service within the meaning of Health and Safety Code section 1345(b) when medically necessary for the enrollee.

A Report to the California State Legislature

Analysis of California Senate Bill 600
Fertility Preservation

April 17, 2019

California Health Benefits Review Program
MC 3116; Berkeley, CA 94720-3116
www.chbrp.org

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-related legislation. The state funds CHBRP through an annual assessment on health plans and insurers in California.

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

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

TABLE OF CONTENTS

LIST OF TABLES AND FIGURES

Table 1. SB 600 Impacts on Benefit Coverage, Utilization, and Cost, 2020

	Baseline	Postmandate	Increase/ Decrease	Percentage Change
Benefit coverage				
Total enrollees with health insurance subject to state-level benefit mandates (a)	24,490,000	24,490,000	0	0%
Total enrollees with health insurance subject to SB 600	16,899,000	16,899,000	0	0%
Percentage of enrollees with health insurance subject to SB 600	69%	69%	0	0%
Number of enrollees with fertility preservation coverage fully compliant with SB 600	158,992	16,899,000	16,740,008	10,529%
Percentage of enrollees with fertility preservation coverage fully compliant SB 600	0.94%	100%	99%	10,529%
Utilization and unit cost				
Number of enrollees of child-bearing age with cancer diagnosis where treatment might result in iatrogenic infertility				
Male	2,553	2,553	0	0%
Female	3,799	3,799	0	0%
Total	6,352	6,352	0	0%
Number of enrollees with cancer using cryopreservation covered by insurance				
Embryo	2	227	225	11,955%
Mature oocyte	16	734	718	4,601%
Sperm	17	792	775	4,650%
Number of enrollees with cancer using cryopreservation not covered by insurance				
Embryo	102	0	-102	-100%
Mature oocyte	326	0	-326	-100%
Sperm	639	0	-639	-100%
Average cost per cryopreservation procedure				
Embryo	$11,254	$11,254	0	0%
Mature oocyte	$10,078	$10,078	0	0%
Sperm	$468	$468	0	0%
Expenditures				
Premiums by payer				
Private employers for group insurance	$86,438,375,000	$86,444,142,000	$5,767,000	0.0067%
CalPERS HMO employer expenditures (c) (b)	$3,098,551,000	$3,098,822,000	$271,000	0.0087%
Medi-Cal Managed Care Plan expenditures	$28,492,273,000	$28,492,273,000	$0	0.0000%

Enrollees with individually purchased insurance	$12,045,324,000	$12,046,641,000	$1,317,000	0.0109%
Enrollees with group insurance, CalPERS HMOs, Covered California, and Medi-Cal Managed Care (c)	$14,476,394,000	$14,477,302,000	$908,000	0.0063%
Enrollee expenses				
For covered benefits (deductibles, copayments, etc.)	$14,750,880,000	$14,754,124,000	$3,244,000	0.0220%
Enrollee expenses for noncovered benefits (d)	$4,734,000	0	-$4,734,000	-100%
Total expenditures	$159,306,531,000	$159,313,304,000	$6,773,000	0.0043%

Source: California Health Benefits Review Program, 2019.

Notes: (a) Enrollees in plans and policies regulated by DMHC or CDI aged 0 to 64 years as well as enrollees 65 years or older in employer-sponsored health insurance. This group includes commercial enrollees (including those associated with Covered California or CalPERS) and Medi-Cal beneficiaries enrolled in DMHC-regulated plans.[2]
(b) Approximately 56.17% of CalPERS enrollees in DMHC-regulated plans are state retirees, state employees, or their dependents.

(c) Enrollee premium expenditures include contributions by employees to employer-sponsored health insurance, health insurance purchased through Covered California, and contributions to Medi-Cal Managed Care.

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

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

[2] For more detail, see *Estimates of Sources of Health Insurance in California*, available at http://chbrp.com/analysis_methodology/cost_impact_analysis.php.

POLICY CONTEXT

The California Senate Committee on Health has requested that the California Health Benefits Review Program (CHBRP)[3] conduct an evidence-based assessment of the medical, financial, and public health impacts of SB 600, Fertility Preservation.

Bill-Specific Analysis of SB 600, Fertility Preservation

Bill Language

SB 600 would require individual and group health plans and policies to cover medically necessary expenses for standard fertility preservation services when a medically necessary treatment may directly or indirectly cause iatrogenic infertility. The full text of SB 600 can be found in Appendix A.

SB 600 provides the following definitions:

- "Iatrogenic infertility" means an impairment of fertility caused directly or indirectly by surgery, chemotherapy, radiation, or other medical treatment.
- Medical treatment that "may directly or indirectly cause iatrogenic infertility" means medical treatment with a possible side effect of impaired fertility, as established by the American Society of Clinical Oncology (ASCO) or the American Society for Reproductive Medicine (ASRM), or other reputable professional medical organization.
- "Standard fertility preservation services" means the procedures consistent with the established medical practices and professional guidelines published by ASCO, ASRM, or other reputable professional organizations.
- "Medical necessity" means when a provider states there is a substantial likelihood that treatment may directly or indirectly cause iatrogenic infertility to an enrollee. A plan or policy cannot deny coverage for services based on medical necessity if so declared by the provider.

CHBRP has previously analyzed legislation requiring coverage of Fertility Preservation: AB 428 in 2011, AB 912 in 2013, and SB 172 in 2017. This analysis builds on these previous reports.[4]

Relevant Populations

If enacted, SB 600 would affect the health insurance of approximately 16.9 million enrollees (43% of all Californians). This represents 69% of 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). Medi-Cal beneficiaries would not be subject to SB 600 and are therefore excluded from this analysis.[5]

[3] CHBRP's authorizing statute is available at http://chbrp.org/faqs.php.
[4] CHBRP reports are available at: http://chbrp.com/.
[5] The regulator, DMHC, and the purchaser, the California Department of Health Care Services, have indicated that by referencing "group" plans, SB 600 would not require compliance from plans enrolling Medi-Cal beneficiaries into Medi-Cal Managed Care. C. Robinson, Department of Health Care Services, citing Sec. 2791 of the federal Public Health Service Act, January 2014.

Interaction With Existing Requirements

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

California Policy Landscape

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.[6,7,8] This statute does not require coverage for fertility preservation services. However, AB 767 (Wicks) Infertility, introduced in 2019, would alter this benefit. Please see CHBRP's April 2019 analysis of AB 767 for more information regarding infertility 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 explicitly 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 decision most relevant to SB 600 involved a 33-year old woman who requested embryo cryopreservation following a breast cancer diagnosis.[9] 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.[10] 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 years) whose parents requested oocyte cryopreservation.[11] 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.

Similar requirements in other states

A recent wave of state mandates have expanded what insurers must cover in the area of infertility treatment. Since 2017, 16 states have introduced legislation that would mandate coverage of fertility preservation — which includes the removal and storage of oocytes and sperm — prior to radiation and

[6] H&SC Section 1374.55 and IC Section 10119.6.
[7] 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.
[8] 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
[9] IMR Reference ID EI11-12274.
[10] IMR Reference ID MN15-20864.
[11] IMR Reference ID EI15-20978.

chemotherapy treatment for cancer. Five states — Connecticut, Rhode Island, Maryland, Delaware, and Illinois — have enacted this legislation (Reinecke, 2018). New York recently enacted a budget measure mandating coverage for in vitro fertilization (IVF) and medically necessary egg freezing.

- In July 2017, Rhode Island became the first state to pass legislation mandating fertility preservation coverage prior to medical treatment that could render a patient infertile, setting a new precedent nationwide.
- Taking effect in January 2018, Connecticut's House Bill (HB) 5968 requires health insurance coverage for fertility preservation for insured persons diagnosed with cancer specifically.[12]
- In May 2018, Maryland signed into law legislation that would require coverage for fertility preservation for cancer patients who face infertility from their treatments (SB 271/ HB 908)
- In 2018, Delaware became the fourth state to cover fertility preservation services, with the passage of Senate Bill 139. The bill requires insurers to cover fertility preservation services for anyone who needs medically necessary health care that could cause iatrogenic infertility. Any fertility preservation services that are consistent with ASRM and ASCO guidelines are eligible for coverage.
- In 2018, Illinois became the fifth state to enact fertility preservation coverage with the passage of HB 2617.
- In April 2019, New York enacted a budget measure in the 2020 state budget that mandates certain large-group insurance plans cover IVF, and requires all private insurance companies to cover medically necessary egg freezing.

Federal Policy Landscape

On the federal level, in May 2018, the Access to Infertility Treatment and Care Act (H.R. 5965 and S. 2920), was introduced. Although not enacted, this bill would have required health plans in group and individual markets to cover fertility preservation services for patients undergoing medically-necessary procedures that may result in infertility, as well as treatments for infertility (Reinecke, 2018).

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 600 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).[13]

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

[12] Connecticut House Bill 5968. Available at: https://www.cga.ct.gov/asp/cgabillstatus/cgabillstatus.asp?selBillType=Bill&bill_num=HB05968&which_year=2017.
[13] 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.

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.[14,15]

States may require QHPs to offer benefits that exceed EHBs.[16] 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.[17,18] State rules related to provider types, cost sharing, or reimbursement methods would *not meet* the definition of state benefit mandates that could exceed EHBs.[19]

SB 600 is unlikely to exceed EHBs. DMHC confirmed to CHBRP that under existing law, fertility preservation to address potential iatrogenic infertility is a basic health care service within the meaning of Health and Safety Code section 1345(b) when medically necessary for the enrollee. However, CDI said the current EHB benchmark plan does not include standard fertility preservation services, as defined.[20] CHBRP assumes that DMHC, which also regulates the Kaiser Foundation Health Plan Small Group HMO 30 plan, the state's benchmark plan for federal EHBs, is correct in their interpretation of whether SB 600 would exceed EHBs. DMHC provided a letter to Senator Portantino's office in response to a request for clarification regarding coverage of fertility preservation, in which DMHC confirmed medically necessary fertility preservation services are covered under the Knox-Keene Act's requirement that health plans must cover all basic health care services.[21]

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

[14] 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, Information on Essential Health Benefits Benchmark Plans. Available at: https://www.cms.gov/cciio/resources/data-resources/ehb.html.
[15] H&SC Section 1367.005; IC Section 10112.27.
[16] ACA Section 1311(d)(3).
[17] State benefit mandates enacted on or before December 31, 2011, may be included in a state's EHBs, according to the U.S. Department of Health and Human Services (HHS). Patient Protection and Affordable Care Act: Standards Related to Essential Health Benefits, Actuarial Value, and Accreditation. Final Rule. Federal Register, Vol. 78, No. 37. February 25, 2013. Available at: www.gpo.gov\fdsys\pkg\FR-2013-02-25\pdf\2013-04084.pdf.
[18] 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.
[19] 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.
[20] IC Section 10112.27a-Ai
[21] Letter provided to CHBRP by Senator Portantino's office and bill sponsors, dated 12/21/2018.

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.

Because approximately 90% of iatrogenic infertility is caused by cancer treatment (Lawrenz et al., 2011), for this analysis CHBRP focuses on iatrogenic infertility attributable to cancer treatments. 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.[22] Lastly, 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 biological 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 that 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.[23] 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.

CHBRP's analysis of SB 600 focuses on fertility preservation services in conjunction with a cancer diagnosis and cancer treatment. As specified by ASCO and ASRM, SB 600 would require coverage of: 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.

CHBRP assumes that enrollees have coverage for fertility preservation consultation and services that are part of or concurrent with cancer treatment; therefore, this report focuses on the impacts of requiring plans and policies to cover sperm, oocyte, and embryo cryopreservation. Table 2 in the *Background* section describes the services considered part of the standard of care during cancer treatment and the *Medical Effectiveness* section summarizes all fertility preservation services listed by ACSO and ASRM.

[22] 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…."

[23] https://www.asrm.org/topics/topics-index/infertility/

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. SB 600 would not require coverage of infertility treatment nor would it affect current coverage rates for infertility treatment.

Current California law requires group CDI-regulated policies and most group DMHC-regulated plans to *offer* coverage for infertility treatment.[24] "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 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.

[24] H&SC Section 1374.55 and IC Section 10119.6.

BACKGROUND ON FERTILITY PRESERVATION FOR IATROGENIC INFERTILITY

Fertility preservation services provide patients at risk for iatrogenic infertility with the opportunity to have future fertility 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 600. (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 relationship 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 600 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 sperm, oocytes, 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 600 does not require coverage for the follow-up assisted reproductive technologies (ART) such as artificial insemination, in vitro fertilization, and/or embryo transfer.[25] Additionally, after gonadotoxic therapies many patients will not achieve pregnancy through infertility treatment if they have not taken fertility preservation measures first.

Table 2. Summary of Types of Fertility Preservation and SB 600 Coverage Status

Preservation Service	Definition of Service	FP Service Timing (a)	Other Considerations	Covered by SB 600?
Cryopreservation				
Embryo cryopreservation	Ovarian stimulation via outpatient hormone prescriptions; harvesting oocytes, 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 oocytes	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

[25] For more information about the aforementioned infertility treatments see CHBRP's 2019 analysis of AB 767 at chbrp.org.

Preservation Service	Definition of Service	FP Service Timing (a)	Other Considerations	Covered by SB 600?
Harm reduction (b)				
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
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 (c)	The conservative treatment preserves the uterus and one ovary, in cases where cancer was confined to just one ovary	During cancer surgery		Already covered
Hormone suppression				
Gonadotropin-releasing hormone agonist therapy	The use of a hormone that causes the ovaries to temporarily shut down during chemotherapy, thus potentially reducing damage to the follicles where eggs develop	Occurs in conjunction with chemotherapy	Only recommended for women undergoing treatment for breast cancer	Potentially

Source: California Health Benefits Review Program, 2019. (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) These treatments are already covered and would not be affected by the coverage proposed in SB 600.

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

Key: FP = fertility preservation.

Incidence of Diseases With Treatments Likely to Result in Iatrogenic Infertility

As discussed in the *Policy Context* section, CHBRP relies on rates of cancer among men and women of reproductive age as a proxy of the number of fertility preservation users because cancer treatments are estimated to be the largest contributor to iatrogenic infertility.

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 (2,950 males and 5,701 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 3) (CDC, 2019). The increased risk of iatrogenic infertility for women is due to the high incidence of breast cancer.

Table 3. Incidence of Cancer Using Treatments Likely to Result in Iatrogenic Infertility for Californians Aged 10–44 Years Regardless of Insurance Status, 2015

Cancer Type	Female		Male	
	Count	Rate per 100,000	Count	Rate per 100,000
Breast	2,887	31.2	—	—
Cervix uteri	528	5.7	—	—
Corpus uteri	429	4.6	—	—
Ovarian	357	3.9	—	—
Male genital	—	—	1,035	10.7
Colon and rectum	471	5.1	244	5.3
Hodgkin lymphoma	197	2.1	454	2.5
Non-Hodgkin lymphoma	278	3.0	408	4.7
Leukemia	318	3.4	513	4.2
Brain/CNS	236	2.5	296	3.1
Total	**5,701**	**61.5**	**2,950**	**30.6**

Source: California Health Benefits Review Program, 2019. Based on CDC, 2019.

Note: Cancer incidence estimates are based on data from the CDC WONDER database, which does not indicate treatment type. Not all cancer treatments affect fertility (e.g., surgery and radiation for breast cancer), so this table may present an overestimation of the number of individuals at risk for iatrogenic infertility from cancer treatment.

Key: CNS = central nervous system.

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), whereas 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 age[26] 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 600, CHBRP estimated that 6,352 cancer patients enrolled in health plans subject to SB 600 (2,553 males and 3,799 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 (Oktay et al., 2018a). 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).

Disparities[27] and Social Determinants of Health[28] in Iatrogenic Infertility

Per statute, CHBRP includes discussion of disparities and social determinants of health (SDoH) as it relates to fertility preservation for iatrogenic infertility. Disparities are differences between groups that are modifiable. CHBRP found literature identifying disparities by specify race/ethnicity, sex, age, and gender identity/sexual orientation.

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).

[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.
[27] Several competing definitions of "health disparities" exist. CHBRP relies on the following definition: Health disparity is defined as the differences, whether unjust or not, in health status or outcomes within a population. Wyatt et al., 2016.
[28] CHBRP defines social determinants of health as conditions in which people are born, grow, live, work, learn, and age. These social determinants of health (economic factors, social factors, education, physical environment) are shaped by the distribution of money, power, and resources and impacted by policy (adapted from Healthy People 2020, 2015; CDC, 2014). See CHBRP's SDoH white paper for further information: http://chbrp.com/analysis_methodology/public_health_impact_analysis.php.

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 $1,150 in California for the initial retrieval of sperm, freezing, and short-term storage of up to 1 year. For females, oocyte and embryo cryopreservation are the standard methods of preserving fertility, and they cost, on average, $13,350 and $14,150, respectively, in California for the initial retrieval of the oocyte, sperm retrieval and fertilization (if applicable), freezing, and short-term storage of up to 1 year.

Age

Aside from fertility-conserving surgeries or shielding from radiation, prepubescent cancer patients have no available standard of care fertility preservation options because they have not yet produced mature oocytes or sperm; there are procedures that harvest ovarian or testicular tissue, but these are considered experimental. Although long-term survival following pediatric cancer has increased to more than 80% (Salih et al., 2015), permanent infertility remains an adverse late effect of cancer treatment until prepubescent fertility preservation technology improves. Following puberty, individuals are able to undergo standard of care procedures, including sperm, oocyte, or embryo 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 at those over 35 years (odds ratio [OR][29] = 3.3, 95% confidence interval [CI] = 1.4–7.7).

Gender Identity

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 600. Pooled estimates from the California Health Interview Survey (years 2015 to 2017) indicate that there are approximately 30,000 transgender persons aged 18 to 24 years and 71,000 transgender persons aged 25 to 64 years living in California (0.8% and 0.3% of the California adult population, respectively) (CHIS, 2019; UCLA Center for Health Policy Research, 2019).

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 ASRM, 2015b; Hembree et al., 2009). CHBRP found two small U.S. studies assessing transgender persons' interest in having children. Among a mixed population of transgender patients presenting to a large academic medical center in Missouri, about 10% of all transgender persons expressed a desire for biological children (Schelble et al., 2017). Similarly, about one fourth (25.8%) of transgender adolescents aged 14–17 years expressed an interest in biological parenthood when responding to a 2016 online survey, and 60.9% were interested in learning more about their fertility options in the future (Chen et al., 2018). The proportion of transgender persons in California or the United States undergoing gender confirmation treatment and using fertility preservation is unknown; however, three studies of transgender youth and adolescents indicate that utilization of fertility preservation services at the time of transition is low, ranging from 3% to 5% of transgender persons who attended fertility counseling (Chen et al., 2017; Nahata et al., 2017a; Schelble et al., 2017).

[29] 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.

Societal Impact of Iatrogenic Infertility in California

The presence of iatrogenic infertility in California/the United States creates a societal impact. In dollar terms, the societal impact can be indirect (lost wages, etc.) as well as direct (medical care, etc.). CHBRP is unable to find data that describe the larger societal impact of iatrogenic infertility specifically. The *Benefit Coverage, Utilization, and Cost Impacts* estimates cost impacts on payers, including enrollees. Such figures represent a subset of the total societal impact related to iatrogenic infertility.

MEDICAL EFFECTIVENESS

As discussed in the *Policy Context* section, SB 600 would mandate coverage for standard fertility preservation services when a medically necessary treatment may directly or indirectly cause iatrogenic infertility. The *Medical Effectiveness* review summarizes findings from the literature on the effectiveness of specific fertility preservation services (as described in the *Background on Fertility Preservation* section).

This *Medical Effectiveness* review focuses on three services that would be newly covered under SB 600: sperm cryopreservation, oocyte cryopreservation, and embryo cryopreservation. Recommendations issued by the American Society of Clinical Oncology (ASCO) in July 2018 indicate that cryopreservation is considered standard practice for fertility preservation in cancer patients (Oktay et al., 2018b). Other standard fertility preservation services, such as shielding and ovarian transposition, are all covered by insurance as part of standard cancer treatment. Other fertility preservation services — ovarian suppression with hormones for female breast cancer patients, cryopreservation of ovarian tissue and testicular tissue, testicular suppression with hormones during radiation, and maturation of oocytes outside of the body — are not broadly recommended and are described, but no conclusion as to their overall effectiveness is presented because they would not be covered by the bill. As described in more detail below, the focus of this review is 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: the Agency for Healthcare Research and Quality (AHRQ), the International Network of Agencies for Health Technology Assessment (INAHTA), the National Health Service (NHS) Centre for Reviews and Dissemination, the National Institute for Health and Clinical Excellence (NICE), and the Scottish Intercollegiate Guideline Network.

The search was limited to studies published since 2017 to the present because CHBRP had previously conducted thorough literature searches on these topics in 2011, 2013, and 2017 for Assembly Bill (AB) 428, SB 912, and SB 172, respectively. The search was limited to abstracts of studies published in English. Of the 360 articles found in the literature review, 31 were reviewed for potential inclusion in this report on SB 600, and a total of 4 studies were included in the medical effectiveness review for this report, in addition to those identified as part of previous CHBRP reviews. The other articles were eliminated because they did not focus on patients undergoing fertility preservation due to cancer treatment or reported findings from case reports or case series, which are considered to be low quality in CHBRP's hierarchy of evidence due to their high risk of bias (California Health Benefits Review Program, 2019). The other articles were eliminated because they were not limited to patients undergoing fertility preservation due to cancer treatment or were case reports or case series, which are considered to be low quality in CHBRP's hierarchy of evidence due to their high risk of bias (California Health Benefits Review Program, 2019). 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.

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

Key Questions

1. What is the medical effectiveness of sperm, oocyte, and embryo cryopreservation in preserving fertility following cancer treatment?

2. What are the harms of sperm, oocyte and embryo cryopreservation?

Methodological Considerations

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, the most prevalent types of cancer that impact women of reproductive age have 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; Molodecky et al., 2012; Pons-Estel et al., 2010). Third, although treatments for transgender patients and individuals with differences in sex development have a high likelihood of 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, 2015a). This review summarizes findings from the literature on fertility preservation services used in conjunction with cancer treatment but also includes a discussion of 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 7 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 any birth (live births and stillbirths).

5. Live birth rate: the percentage of attempts that result in a live birth (excludes stillbirths).

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[30]

Embryo, oocyte, and sperm cryopreservation are methods of fertility preservation endorsed by the American Society for Clinical Oncologists (ASCO). CHBRP found evidence that embryo cryopreservation is an effective method of fertility preservation. Meta-analyses have found that the clinical pregnancy rate is higher among frozen embryos compared to fresh transfers, and data shows that the live birth rate is inversely related to patient age. Similarly, CHBRP found evidence that oocyte cryopreservation is an effective method of fertility preservation. Women returning to use cryopreserved oocytes saw successful implantation of the embryos and resulting live pregnancies. Evidence also shows that men returning to use cryopreserved sperm are able to achieve parenthood.

Effectiveness of Embryo Cryopreservation for Female Cancer Patients

There are nearly 14,000 births in the United States every year from embryo cryopreservation (SART, 2016). 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%, whereas implantation rates are between 8% and 42% (Dunn and Fox, 2009; Loren et al., 2013; Seli and Tangir, 2005; Wallberg et al., 2009). According to 2016 data from the Society of Assisted Reproductive Technology (SART), clinical pregnancies (those resulting in a pregnancy confirmed by ultrasound) from frozen embryos ranged from 35% to 55%, and birth rates ranged from 23% to 37%, depending on patient age (with higher rates among women younger than 35 years) (SART, 2016). Two meta-analyses have found that the clinical pregnancy rate is higher among frozen embryo transfers compared to fresh embryo transfers (Roque et al., 2013; Zhang et al., 2018).

Birth rates per embryo transfer using cryopreserved embryos have risen from approximately 28% in 2004 to 35% in 2011 (Dunn and Fox, 2009; SART, 2016). The live birth rate from embryo cryopreservation depends on the age of the patient and the number of embryos available (Lee et al., 2006). SART data from 2015 indicated that the percentages of thawed embryo transfers resulting in live births were inversely related to age: 44.4% in women less than 35 years of age, 40.1% in the 35 to 37 age group, 35.0% in the 38 to 40 age group, 30.1% in the 41 to 42 age group, and 25.4% in the >42 age group (SART, 2015). However, these studies all have small sample sizes and were not limited to patients cryopreserving embryos for fertility preservation.

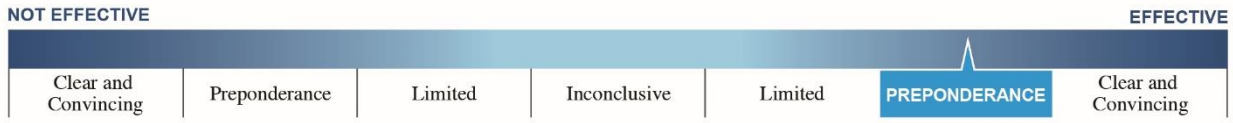
CHBRP identified one cohort study published since 2016 assessing the effectiveness of embryo cryopreservation among female cancer patients. This cohort was composed of 82 women participating in a U.S.-based randomized controlled trial; 34 of these women underwent either oocyte (n = 16) and/or embryo cryopreservation (n = 20), and 48 women did not (control group). The age range of the entire cohort was 24 to 42 years. After 6 years, 30% (n = 6/20) of women returned to use their preserved embryos, resulting in two live births (one patient with a twin pregnancy). The study did not report reproductive outcomes among the control group (Chien et al., 2017).

[30] The following figures in this section summarize CHBRP's findings regarding the strength of the evidence for the effects fertility preservation services addressed by SB 600. For test, treatments, and services for which CHBRP concludes that there is clear and convincing, preponderance, limited, or inconclusive evidence, the placement of the highlighted box indicates the strength of the evidence. If CHBRP concludes that evidence is insufficient, a figure that states "Insufficient Evidence" will be presented.

The previous medical effectiveness review for SB 172 identified two cohort studies (Knopman et al., 2009; Robertson et al., 2011), two case-control studies (Cardozo et al., 2015; Domingo et al., 2012), and two case series (Dolmans et al., 2015; Oktay et al., 2015) reporting on patients cryopreserving embryos for fertility preservation. Three 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). Studies published since 2015 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 effectiveness of embryo cryopreservation: There is a *preponderance of evidence* that embryo cryopreservation is an effective method of fertility preservation.

Figure 1. Effectiveness of Embryo Cryopreservation



Effectiveness of Oocyte (Egg) Cryopreservation for Female Cancer Patients

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 American Society for Reproductive Medicine (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 ASCO in July 2018 indicate that oocyte cryopreservation is considered a standard practice (Oktay et al., 2018b).

CHBRP identified three cohort studies published since 2016 assessing the effectiveness of oocyte cryopreservation among female cancer patients (Chien et al., 2017; Cobo et al., 2018; Diaz-Garcia et al., 2018). Chien and colleagues reported on a cohort comprised of 82 women participating in a U.S.-based randomized controlled trial; 34 of these women underwent either oocyte (n = 16) and/or embryo cryopreservation (n = 20), and 48 women did not (control group). The age range of the entire cohort was 24 to 42 years. After 6 years, none of the women who preserved oocytes had returned to use them (Chien et al., 2017). Cobo and colleagues reported on a cohort of women undergoing oocyte cryopreservation either due to cancer treatment (n = 1,073) or age-related fertility decline (n = 5,289) in Spain. Of those undergoing cryopreservation due to cancer treatment, 7.4% (79 women) returned to use their preserved oocytes after a mean storage time of 4.1 years. Eighty-two percent of oocytes were successfully thawed with an implantation rate of 32.5%, and there were 18 live births among these women (birth rate, 22.8% among women returning to use their preserved oocytes) (Cobo et al., 2018). Diaz-Garcia and colleagues also reported on a cohort of Spanish women undergoing fertility preservation due to cancer treatment; 1,024 women underwent oocyte cryopreservation, and 800 underwent ovarian tissue cryopreservation. Of those undergoing oocyte cryopreservation, 4.8% (n = 49) returned to use their preserved oocytes after a mean storage time of 3.9 years. Seventy-seven percent of oocytes were successfully thawed, and there were 16 patients with 17 live births (birth rate, 34.7%) (Diaz-Garcia et al., 2018).

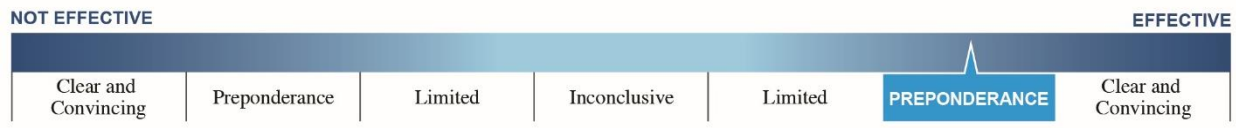
The medical effectiveness review for SB 172 also included two studies reporting relevant outcomes after oocyte cryopreservation in female cancer patients (Druckenmiller et al., 2016; Martinez et al., 2014). Druckenmiller et al. (2016) reported on 176 patients who cryopreserved their oocytes, of which 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. Martinez 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 a birth rate of 36.4% (4 births).

The previous medical effectiveness review summarized four completed randomized controlled trials comparing IVF outcomes using cryopreserved oocytes with outcomes using fresh oocytes (Cobo et al., 2008; Cobo et al., 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 (OR = 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). One cohort study reported that 1,027 babies were born from cryopreserved oocytes in 2014 with no observed increase in congenital abnormalities (Cobo et al., 2014). However, these studies were not limited to patients cryopreserving embryos for fertility preservation.

Summary of findings regarding effectiveness of oocyte cryopreservation: There is a *preponderance of 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.

Figure 2. Effectiveness of Oocyte Cryopreservation



Effectiveness of Sperm Cryopreservation for Male Cancer Patients

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).

CHBRP did not identify any studies published since 2016 reporting on the effectiveness of sperm cryopreservation. One new case series was identified, which reported on 898 men who underwent sperm cryopreservation between 1983 and 2013 at a single institution in the Netherlands. This report found that 96 men (10.7%) returned to use their sperm, and 60 men (62.5%) achieved parenthood (22% via intrauterine insemination, 32% via in vitro fertilization, and 46% via intracytoplasmic sperm injection) (Muller et al., 2016). However, it should be noted that case reports and case series are considered to be low-quality in CHBRP's hierarchy of evidence due to their high risk of bias (California Health Benefits Review Program, 2019).

The previous review for SB 172 identified one systematic review including 30 studies with a combined total of 11,798 patients undergoing sperm cryopreservation. 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). The previous review included two case series which found that sperm cryopreservation is effective in providing male cancer patients a chance at parenthood (Hourvitz et al., 2008; van Casteren et al., 2008).

Summary of findings regarding effectiveness of sperm cryopreservation: There is a *preponderance of evidence* that sperm cryopreservation is an effective method of fertility preservation as measured by pregnancy rates and live births.

Figure 3. Effectiveness of Sperm Cryopreservation

Harms of Fertility Preservation Treatments

Ovarian hyperstimulation syndrome (OHSS) is a harm specific to oocyte and embryo harvesting for cryopreservation. OHSS occurs when the ovaries are hyperstimulated and enlarged to allow oocytes to be harvested for cryopreservation, before or after fertilization (for embryo cryopreservation). Clinical features of OHSS range be mild (e.g., abdominal distention, diarrhea), moderate (same symptoms as mild, along with abdominal fluid buildup visible on ultrasound), severe (e.g., severe abdominal pain, rapid weight gain, syncope), or critical (e.g., acute renal failure, sepsis, thromboembolism). An older systematic review (including literature published between 1990 and 2002) found that the incidence of moderate OHSS ranges from 3% to 6% and severe/critical OHSS ranges from 0.1% to 2%; the incidence of mild OHSS is higher, ranging from 20% to 33% of IVF cycles (Delvigne and Rozenberg, 2002). Other harms of oocyte and embryo cryopreservation include procedure-related complications, such a bleeding and possible infection.

Fertility Preservation Services Already Covered by Standard Cancer Treatment

Ovarian and testicular shielding

Ovarian and testicular shielding during radiation therapy, as well as certain surgeries — ovarian transposition (oophoropexy) and conservative gynecologic surgeries — are services covered as part of standard cancer treatment. 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 92% (Georgescu et al., 2008; Seli and Tangir, 2005; Thibaud et al., 1992). A 2014 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. This review also found that there was no evidence of metastases to the transposed ovary (Gubbala et al., 2014).

In order to protect the ovaries or testes during cancer treatment with radiation, a special external shield can be placed over the organs 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). Research from case series has shown that testicular shielding 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).

Ovarian transposition

The 2018 ASCO recommendations indicate 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 (Oktay et al., 2018b). The two surgeries specified in the recommendations are conservative surgery for cervical cancer (trachelectomy) and conservative surgery for ovarian cancer. 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). The 2018 ASCO recommendations note that this procedure should be restricted to certain stage 1 cervical cancers (Oktay et al., 2018b). The standard treatment for ovarian cancer, including borderline ovarian tumor, is removal of the uterus (hysterectomy) and removal of both ovaries. Conservative surgeries preserve one ovary with or without the uterus. This is only possible in cases where the cancer was confined to only one ovary. The 2018 ASCO recommendations note that ovarian cystectomy, a laparoscopic procedure typically done to remove ovarian cysts, can be performed for early-stage ovarian cancer (Oktay et al., 2018b).

Other Potential Fertility Preservation Services

Ovarian suppression for female breast cancer patients

Gonadotropin-releasing hormone (GnRH) agonist (GnRHa) therapy is the use of a hormone that causes the ovaries to temporarily shut down during chemotherapy, thus potentially reducing damage to the follicles where eggs develop. 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. GnRHa do not protect against radiation effects or from very aggressive forms of chemotherapy (Levine et al., 2010). The 2018 ASCO recommendations conclude that there is conflicting evidence that ovarian suppression using GnRH analogs are effective and that this approach should not be used in place of other proven methods; however, the guidelines also note that this therapy may be offered when other fertility preservation options are not available or for young women with breast cancer to reduce the likelihood of chemotherapy-induced ovarian insufficiency. The 2018 ASCO guidelines identify 5 of 7 medical association guidelines that recommend the use of GnRHa for fertility preservation in certain breast cancer patients (Oktay et al., 2018b).

Experimental fertility preservation services

The 2018 ASCO recommendations note that certain fertility preservation services are considered experimental: ovarian or testicular tissue cryopreservation and transplantation, in vitro follicle maturation (IVM) in females, and hormonal gonadoprotection in males (Oktay et al., 2018b).

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 reimplanted after the patient has finished with her treatment. The first ovarian transplant procedure was performed in 2000, and as of 2017, there had been at least 82 births as a result of this procedure (Jadoul et al., 2017). A 2017 meta-analysis including 8 studies reported a combined live birth and ongoing pregnancy rate of 37.7% per woman undergoing ovarian tissue cryopreservation and transplantation and desiring pregnancy (Pacheco and Oktay, 2017). Based on recent data, the 2018 ASCO recommendations note that although this procedure is still considered experimental, emerging data may prompt reconsideration in the future, especially given the lack of current nonexperimental fertility preservation options for prepubescent females (Oktay et al., 2018b).

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 not yet produced any live births (Lee et al., 2006; Levine et al., 2010; Loren et al., 2013; Onofre et al., 2016).

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 without ovarian stimulation. In this case, immature oocytes are collected and matured outside of the body. There are 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). One retrospective study including women with cancer undergoing either conventional IVF (n = 187 cycles) or IVM (n = 207 cycles) found that only 7% of women in the conventional IVF group (n = 19 cycles) and 10% in the IVM group (n = 14) returned to use the preserved oocytes or embryos. Of women using the preserved oocytes or embryos, the study found no difference in oocyte or embryo survival rates by procedure. However, IVM resulted in a significantly lower implantation rate (3.7% vs. 21.9% for conventional IVF) and fewer live births per embryo transfer (7.1% vs. 31.6% for conventional IVF), and the proportion of miscarriages was higher in the IVM group (50% vs. 16.7%) (Creux et al., 2018).

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 testicular hormonal suppression has only been evaluated in very small studies and is considered experimental (Lee et al., 2006; van der Kaaij et al., 2010). It is not endorsed by the recent ASCO recommendations (Oktay et al., 2018b).

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 changes 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 sperm, oocyte or embryo 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 oocytes 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.

BENEFIT COVERAGE, UTILIZATION, AND COST IMPACTS

As discussed in the *Policy Context* section, SB 600 would require DMHC-regulated health plans and CDI-regulated policies to cover medically necessary expenses for standard fertility preservation services when a medically necessary treatment may directly or indirectly cause iatrogenic infertility.

This section reports the potential incremental impacts of SB 600 on estimated baseline benefit coverage, utilization, and overall cost. CHBRP's approach and key assumptions for this analysis are described below:

- SB 600 states that the coverage of fertility preservation services be consistent with how "standard fertility preservation services" are defined by established medical practices and professional guidelines published by ASCO, ASRM, or other reputable professional organizations. According to ASCO and ASRM, cryopreservation of sperm, mature oocytes, and embryos falls under the definition of standard fertility preservation services.[31] Other standard fertility preservation services that do not involve cryopreservation, such as ovarian transposition, are all covered by insurance as part of standard cancer treatment. Cryopreservation is not generally covered by insurance as part of standard cancer treatment. Hence, in this analysis, CHBRP focused on examining specifically the coverage of cryopreservation of sperm, mature oocytes, and embryos among enrollees in DMHC-regulated health plans and CDI-regulated policies in California.
- Claims data from MarketScan database, could not be used to obtain utilization estimates because there are too few claims for cryopreservation use among enrollees with a cancer diagnosis to make robust estimates of utilization for this population. Thus, CHBRP estimated utilization of cryopreservation, both for baseline and postmandate, using cancer incidence rates grouped by sex, the peer-reviewed literature, and input from CHBRP's content expert. Details regarding these assumptions are presented in Appendix C.
- In its analysis, CHBRP included the top 10 types of cancer whose treatments pose the highest iatrogenic infertility risk. Cryopreservation utilization rates were assumed to be consistent across all types of cancer. Cancer incidence rates for reproductive age Californians were estimated using cancer statistics data from the 2015 Center for Disease Control and Prevention's WONDER Database on males 10 to 49 years of age and females 10 to 44 years of age in California (see the *Background* section).
- CHBRP estimated the unit costs of cryopreservation services for sperm, mature oocytes, and embryos based on 2016 MarketScan and Milliman's proprietary 2016 Consolidated Health Cost Guidelines Sources Database (CHSD). 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.

For further details on the underlying data sources and methods used in this analysis, please see Appendix C.

[31] As noted in the *Medical Effectiveness* section, the 2018 ASCO recommendations conclude that there is conflicting evidence that ovarian suppression using GnRH analogs are effective and that this approach should not be used in place of other proven methods; however, the guidelines also note that this therapy may be offered when other fertility preservation options are not available or for young women with breast cancer to reduce the likelihood of chemotherapy-induced ovarian insufficiency. CHBRP does not include utilization of GnRHa in the cost impact analysis.

Baseline and Postmandate Benefit Coverage

Current coverage of cryopreservation was determined by a survey of the largest (by enrollment) providers of health insurance in California. Responses to this survey represent 53% of enrollees with private market health insurance that can be subject to state mandates. SB 600 does not apply to Medi-Cal Managed Care enrollees.

Currently, 0.9% of enrollees with health insurance that would be subject to SB 600 have coverage for cryopreservation services for sperm, mature oocytes, and embryos. Postmandate, the coverage for cryopreservation would increase to 100% based on the CHBRP assumption that all noncompliant plans and policies at baseline would become compliant postmandate (see estimate in Table 1).

Baseline and Postmandate Utilization

To determine the baseline utilization, CHBRP analyzed incidence rates of the top 10 cancers with treatments that pose the highest iatrogenic infertility risk (see the *Background* section). These incidence rates represent the population with newly diagnosed cancers annually, which CHBRP assumes is the population that would potentially seek and use cryopreservation. Out of the 16.9 million enrollees with coverage subject to the bill, the total number of enrollees of reproductive age with a new cancer diagnosis (2,553 males and 3,799 females) would remain constant from baseline to postmandate.

Among this population, the baseline total proportion using fertility preservation services was derived using the findings from a study of the use of fertility preservation among cancer survivors when they underwent treatment for cancer and at risk of iatrogenic infertility (Bann et al., 2015).[32] CHBRP applied findings from the study by Bann et al. (2015), data from the 2017 Society for Reproductive Technology[33], and content expert input to estimate baseline utilization for enrollees with and without coverage CHBRP estimates postmandate utilization increases to the level of those enrollees who had coverage at baseline plus an additional 10% increase in utilization due to increased awareness, increased provider and enrollee knowledge of coverage, and a corresponding greater willingness to discuss fertility preservation options (Vindrola-Padros et al., 2017) that might occur with the passage SB 600.[34]

Postmandate, no enrollees would use cryopreservation without coverage. CHBRP estimates that in the first year postmandate, SB 600 would result in 792 males and 961 female enrollees with cancer using cryopreservation services postmandate. Of the 792 male users postmandate, 136 enrollees would be new users of sperm cryopreservation. The estimated 639 male cryopreservation users at baseline using cryopreservation without coverage would experience financial relief postmandate as coverage would be available to them. Of the 961 female users postmandate, 516 enrollees would be new users (123 new users of embryo cryopreservation and 392 new users of mature oocyte cryopreservation). A total of 428 female enrollees (102 users of embryo cryopreservation and 326 of mature oocyte cryopreservation) will

[32] In the study by Bann et al (2015), of the 812 survey respondents living in the U.S. with complete data on fertility preservation and gender, 264 reported no interest in having any/any more children, thus approximately 70% of the final sample of participants (550) in the study were interested in having a child. Among the final sample, 49% of male and 22% of female cancer survivors took steps to preserve fertility. CHBRP additionally assumed females would be twice as likely to forgo steps to pursue cryopreservation than males due to the higher cost of oocyte ($10,078) and embryo ($11,254) cryopreservation compared to sperm cryopreservation ($468).
[33] In 2017, 23% of utilization of female cryopreservation was for embryos and 775 for mature oocytes.
[34] Studies of utilization change over time due to the passage of fertility preservation legislation do not exist; the 10% increase is an assumed based on implications of findings in Vindrola-Padros et al (2017) and CHBRP's content expert.

use cryopreservation with coverage postmandate, whereas they were using the services without coverage at baseline.

Baseline and Postmandate Per-Unit Cost

Using claims from the 2016 CHSD and MarketScan, CHBRP estimates that the per-unit cost of fertility preservation services averages $468 for sperm cryopreservation and $11,254 for embryo cryopreservation and $10,078 for mature oocyte cryopreservation. 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 1 year. Female fertility preservation services have a higher average unit cost due to increased costs for harvesting the reproductive oocytes, because 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 sperm from a spouse through the same insurance coverage. CHBRP assumes unit costs for these cryopreservation services/procedures would not change from baseline to postmandate.

Baseline and Postmandate Expenditures

SB 600 would increase net annual expenditures by total net annual $6,773,000 or total net annual 0.0043% for enrollees with DMHC-regulated plans and CDI-regulated policies.

Premiums

Changes in premiums as a result of SB 600 would vary by market segment. Note that such changes are related to the number of enrollees (see Table 1, Table 5, and Table 6), with health insurance that would be subject to SB 600. The largest increases are in the individual markets for CDI-regulated policies (0.008%) and DMHC-regulated plans and products (0.01%); the smallest increases in premiums are in the CDI-regulated large group policies (0.003%). Among publicly funded DMHC-regulated CalPERS HMOs, the premium increase is about 0.009%.

Enrollee Expenses

SB 600–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 with health insurance that would be subject to SB 600 expected to use the relevant fertility preservation services in the first year after enactment. Enrollee expenses for noncovered benefits would decrease by about $0.02 for all plans. The decrease in expenditures for noncovered benefits for CalPERS HMOs is $0.022. An increase in enrollee expenses for covered benefits (i.e., how much enrollees pay for services that would be covered postmandate) would also occur as enrollees gain coverage, ranging from $0.014 for DMHC-regulated large group plans to $0.026 for CDI-regulated small group plans. The increase in expenditures for covered benefits for CalPERS HMOs is $0.004 (see Table 3).

Out-of-Pocket Spending for Covered and Noncovered Expenses

CHBRP estimates that for newly covered enrollees, expenses for noncovered cryopreservation postmandate would be reduced by $4,734,000 overall and an increase in expenses for covered benefits (via co-payments, for example) of $3,244,000 (Table 1).

CHBRP estimates are based on claims data that reflect charges to carriers for cryopreservation services. It may underestimate the costs for enrollees due to carriers' ability to negotiate discounted rates that are unavailable to patients and their families. The rates paid by patients for noncovered services may be as much as 40% greater than the rates reflected in this analysis.

According to CHBRP's carrier survey responses, about 10% of enrollees in the nongrandfathered large group and 100% of enrollees in the Covered California individual markets with coverage for cryopreservation have the same cost structure as major medical services. CHBRP assumes the cost-sharing structure for cryopreservation will involve a 50% coinsurance, based on responses to the carrier surveys, for all other enrollees. Because SB 600 does not specify requirements regarding cost sharing or coinsurance, CHBRP assumes carriers would cover cryopreservation with the same cost-sharing structure as seen at baseline. For enrollees with cancer using treatment that can cause iatrogenic infertility and using cryopreservation, SB 600 would result in varied impacts on out-of-pocket costs for covered cryopreservation. As noted in Table 4 below, cost-sharing impacts (not including premiums) among enrollees using cryopreservation would range from $184 for CalPERS HMO enrollees to $1,051 for enrollees in small group plans.

Table 4. Cost-Sharing Impact of SB 600 Among Enrollees Diagnosed With Cancer That May Result in Iatrogenic Infertility

	Large Group	Small Group	Individual	CalPERS HMO
% of enrollees with cost-sharing impact from SB 600*	0.03%	0.03%	0.03%	0.03%
Average annual cost sharing for cryopreservation services among impacted members*	$611.32	$1,051.21	$575.65	$184.44

Source: California Health Benefits Review Program, 2019.

Notes: *Not including impacts on premiums.

Key: CalPERS HMO = California Public Employees' Retirement System Health Maintenance Organization.

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, because fertility preservation services do not correspond to any reduction in use of infertility services during the first year. As discussed in the *Public Health Impacts* section in greater detail below, studies have suggested potential delays in cancer treatment due to the use of fertility preservation, however no studies reported an increased risk of mortality for the cancer patients (Baynosa et al., 2009; Madrigrano et al., 2007; Waimey et al., 2015).

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 it is unclear whether this bill would exceed essential health benefits (EHBs).

Postmandate Changes in the Number of Uninsured Persons[35]

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 600.

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 600.

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). No other payers have been affected by the lack of benefit coverage.

[35] See also CHBRP's *Uninsured: Criteria and Methods for Estimating the Impact of Mandates on the Number of Individuals Who Become Uninsured in Response to Premium Increases (December 2015)*, available at http://chbrp.com/analysis_methodology/cost_impact_analysis.php.

Table 5. Baseline Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2020

	DMHC-Regulated						CDI-Regulated			
	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*	**Total**
Enrollee counts										
Total enrollees in plans/policies subject to state mandates (d)	10,565,000	3,099,000	2,184,000	523,000	6,796,000	795,000	318,000	108,000	102,000	24,490,000
Total enrollees in plans/policies subject to SB 600	10,565,000	3,099,000	2,184,000	523,000	0	0	318,000	108,000	102,000	16,899,000
Premiums										
Average portion of premium paid by employer	$555.35	$341.99	$0.00	$493.71	$268.13	$694.55	$710.92	$462.84	$0.00	$118,029,198,000
Average portion of premium paid by employee	$39.66	$205.44	$437.39	$94.04	$0.00	$0.00	$250.37	$202.64	$475.67	$26,521,718,000
Total premium	**$595.01**	**$547.43**	**$437.39**	**$587.76**	**$268.13**	**$694.55**	**$961.29**	**$665.48**	**$475.67**	**$144,550,916,000**
Enrollee expenses										
For covered benefits (deductibles, copays, etc.)	$46.18	$121.03	$115.38	$48.33	$0.00	$0.00	$162.44	$186.84	$168.51	$14,750,880,000
For noncovered benefits (e)	$0.02	$0.02	$0.02	$0.02	$0.00	$0.00	$0.02	$0.02	$0.02	$4,734,000
Total expenditures	**$641.22**	**$668.49**	**$552.80**	**$636.10**	**$268.13**	**$694.55**	**$1,123.75**	**$852.34**	**$644.20**	**$159,306,530,000**

Source: California Health Benefits Review Program, 2019.

Notes: (a) Includes enrollees with grandfathered and nongrandfathered health insurance acquired outside or through Covered California (the state's health insurance marketplace).

(b) Approximately 56.17% of CalPERS enrollees in DMHC-regulated plans are state retirees, state employees, or their dependents.

(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) Enrollees in plans and policies regulated by DMHC or CDI aged 0 to 64 years as well as enrollees 65 years or older in employer-sponsored health insurance. This group includes commercial enrollees (including those associated with Covered California or CalPERS) and Medi-Cal beneficiaries enrolled in DMHC-regulated plans.[36]

(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 will be newly covered, postmandate. Other components of expenditures in this table include all health care services covered by insurance.

Key: CalPERS HMOs = California Public Employees' Retirement System Health Maintenance Organizations; CDI = California Department of Insurance; COHS = County Organized Health Systems; DMHC = Department of Managed Health Care; MCMC = Medi-Cal Managed Care.

[36] For more detail, see *Estimates of Sources of Health Insurance in California*, available at http://chbrp.com/analysis_methodology/cost_impact_analysis.php.

Table 6. Postmandate Per Member Per Month Premiums and Total Expenditures by Market Segment, California, 2020

	DMHC-Regulated						CDI-Regulated			
	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*	**Total**
Enrollee counts										
Total enrollees in plans/policies subject to state mandates (d)	10,565,000	3,099,000	2,184,000	523,000	6,796,000	795,000	318,000	108,000	102,000	24,490,000
Total enrollees in plans/policies subject to SB 600	10,565,000	3,099,000	2,184,000	523,000	0	0	318,000	108,000	102,000	16,899,000
Premiums										
Average portion of premium paid by employer	$0.0385	$0.0208	$0.0000	$0.0432	$0.0000	$0.0000	$0.0229	$0.0224	$0.0000	$6,039,000
Average portion of premium paid by employee	$0.0027	$0.0125	$0.0484	$0.0082	$0.0000	$0.0000	$0.0081	$0.0098	$0.0402	$2,225,000
Total premium	$0.0412	$0.0333	$0.0484	$0.0514	$0.0000	$0.0000	$0.0309	$0.0323	$0.0402	**$8,263,000**
Enrollee expenses										
For covered benefits (deductibles, copays, etc.)	$0.0138	$0.0252	$0.0149	$0.0042	$0.0000	$0.0000	$0.0224	$0.0258	$0.0210	$3,244,000
For noncovered benefits (e)	-$0.0228	-$0.0242	-$0.0249	-$0.0224	$0.0000	$0.0000	-$0.0227	-$0.0241	-$0.0247	-$4,734,000
Total expenditures	$0.0322	$0.0342	$0.0384	$0.0333	$0.0000	$0.0000	$0.0306	$0.0339	$0.0365	**$6,773,000**
Percent change										
Premiums	0.0069%	0.0061%	0.0111%	0.0087%	0.0000%	0.0000%	0.0032%	0.0048%	0.0084%	0.0057%
Total expenditures	0.0050%	0.0051%	0.0069%	0.0052%	0.0000%	0.0000%	0.0027%	0.0040%	0.0057%	0.0043%

Source: California Health Benefits Review Program, 2019.

Notes: (a) Includes enrollees with grandfathered and nongrandfathered health insurance acquired outside or through Covered California (the state's health insurance marketplace).

(b) Approximately 56.17% of CalPERS enrollees in DMHC-regulated plans are state retirees, state employees, or their dependents.

(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) Enrollees in plans and policies regulated by DMHC or CDI aged 0 to 64 years as well as enrollees 65 years or older in employer-sponsored health insurance. This group includes commercial enrollees (including those associated with Covered California or CalPERS) and Medi-Cal beneficiaries enrolled in DMHC-regulated plans.[37]

(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 will be newly covered, postmandate. Other components of expenditures in this table include all health care services covered by insurance.

Key: CalPERS HMOs = California Public Employees' Retirement System Health Maintenance Organizations; CDI = California Department of Insurance; COHS = County Organized Health Systems; DMHC = Department of Managed Health Care; MCMC = Medi-Cal Managed Care.

[37] For more detail, see *Estimates of Sources of Health Insurance in California*, available at http://chbrp.com/analysis_methodology/cost_impact_analysis.php.

PUBLIC HEALTH IMPACTS

As discussed in the *Policy Context* section, SB 600 would mandate coverage of medically necessary expenses for standard fertility preservation services when a medically necessary treatment may directly or indirectly cause iatrogenic infertility, and defines iatrogenic infertility, medical treatment that causes iatrogenic infertility, standard fertility preservation services, and medical necessity.

The public health impact analysis estimates the short-term impacts (within 12 months of implementation) of SB 600 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 sperm, oocytes, or embryos obtained through fertility preservation and for discussion of the health of the subsequent children.

Estimated Public Health Outcomes

The section focuses on three services: sperm cryopreservation, oocyte (egg) cryopreservation, and embryo cryopreservation (freezing of embryos). 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 assumes that these services would already be covered by state-regulated plans and policies (see **Error! Reference s ource not found.**for more information).

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

The *Benefit Coverage, Cost, and Utilization Impacts* section estimates that 0.9% of enrollees with health insurance subject to SB 600 have coverage for fertility preservation at baseline with 6,352 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 1,102 enrollees to 1,753 enrollees in the first year postmandate.

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 600 would likely improve the quality of life by reducing regret about fertility outcomes, dissatisfaction, and distress for the additional 651 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. A literature review by Panagiotopoulou et al. (2018) 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 discussions about fertility preservation (Adams et al., 2013; Miller et al., 2014; Nahata et al., 2017b; Panagiotopoulou et al., 2018).

Perhaps most relevant to SB 600 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 600 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[38]

Insurance benefit mandates that bring more state-regulated plans and policies to parity may change an existing disparity.**Error! Bookmark not defined.** As described in the ***Error! Reference source not fo und.*** 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.

[38]. For details about CHBRP's methodological approach to analyzing disparities, see the *Benefit Mandate Structure and Unequal Racial/Ethnic Health Impacts* document here: http://chbrp.com/analysis_methodology/public_health_impact_analysis.php.

Impact on Racial/Ethnic Disparities

As presented in the ***Error! Reference source not found.*** section, several studies report that racial and e thnic disparities may exist with respect to provider discussions regarding infertility risks, 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 600 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 cancer 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 $468. For females, the standard fertility preservation methods average an estimated $10,666, or about 23 times the cost that males incur. CHBRP estimates that, in the first year postmandate, SB 600 would reduce cost-sharing for noncovered services for 428 females by more than $4.4 million in uncovered treatment costs, whereas 639 males would see a reduction of about $300,000 in uncovered costs. However, enrollees would still be responsible for the cost-sharing determined by their insurer, which may be as high as 50% for covered services.

Gender disparities exist in both counselling for and use of fertility preservation services. Evidence in the ***Error! Reference source not found.*** section indicates that males are more likely to be referred for f ertility 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., 2018). 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 (Nahata et al., 2017b; Panagiotopoulou et al., 2018). 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-reported reasons, SB 600 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 23 times more for uncovered fertility preservation services than males. Postmandate, SB 600 would decrease the gender disparity by reducing financial burden thereby bringing costs between genders to parity, 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 ***Error! Reference source not found.*** section, transgender persons undergoing g ender 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 600) (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 600 would provide fertility preservation coverage for an unknown number of newly covered enrollees who will experience iatrogenic infertility due to gender confirmation treatments, thus reducing any potential disparities in access to care.

LONG-TERM IMPACTS

Long-term utilization are expected to remain constant with the findings of year 1 and year 2 projections, 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 Utilization and Cost Impacts

Utilization Impacts

Postmandate, CHBRP estimates that SB 600 would increase utilization of cryopreservation services among enrollees with cancer by an additional people 123 using embryo cryopreservation, 392 using mature oocyte cryopreservation, and 136 using sperm cryopreservation during the first year. This estimate is based on an annual incidence rate of the top 10 cancers, which will likely remain constant per annum over the long term as long as the incidence rates also remain constant. It must be noted, however, that the demand for fertility preservation services is dependent on the wishes of the patient, and those who do not wish to have future children will dampen demand. In the long term, use of cryopreservation will lead to some increased utilization of infertility services to achieve pregnancy among the affected enrollees.

Cost Impacts

Although SB 600 would decrease the financial burden of fertility preservation services for enrollees in the short term, SB 600 would not cover future storage costs or assisted reproductive technology that is required to achieve pregnancy; those who retrieve cryopreserved sperm, oocytes, or embryos would likely pay out of pocket for assisted reproductive technology to become pregnant. The cost of cryopreservation — retrieval and storage— may change over time as technology advances are introduced to this industry. It is possible that technological advances will reduce the cost of cryopreservation in the future, but it is unclear whether these technologies are on the horizon or how they will impact overall expenditures for cryopreservation.

CHBRP estimates that SB 600 would increase health care costs by 0.0043%, based on the utilization of fertility preservation services in year 1. As mentioned above, excluded from the cost estimates were the infertility services that will be needed to implant the frozen embryos, or perform IVF with oocytes or sperm, and enable enrollees with iatrogenic infertility due to cancer to become parents. CHBRP assumes that the use of cryopreserved sperm, oocytes, and embryos is likely to occur in the future after chemotherapy treatment is complete and the enrollee is at a stage of life where they are ready to have a child. When the enrollee is ready to use the cryopreserved material at some point in the future, they would incur costs associated with infertility treatment. Costs for this treatment incurred by the enrollee would be dependent on whether or not infertility is covered by insurance and the level of coverage. Age of final attempt at pregnancy also can influence the long-term cost impacts. One study found oocyte preservation before age 35 years by women planning to defer pregnancy attempts until age 40 would decrease cost per live birth to $39,946 (and increase odds of live birth to 62% by the end of the model), compared to the cost per live birth of $55,060 (and 42% chance of live birth) for women over 40 who did not undergo oocyte preservation (Devine et al., 2015). It is possible, therefore, that the costs for pregnancy among women undergoing fertility preservation would be lower in the long term compared to the general population, due to preserving eggs of better quality when they were younger.

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 600, 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 136 males would use sperm cryopreservation annually as a result of SB 600. 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. Using these retrieval rates, in the case of SB 600, about 13 males undergoing fertility preservation in a given year would eventually retrieve cryopreserved sperm to reproduce. As reported in the ***Error! Reference source not found.*** section, the birth rate using cryopreserved sperm is 49% (Stefania Ferrari et al., 2016). Thus, CHBRP estimates that 6 births would occur in the original cohort of 136 males newly using fertility preservation in a given year. Note that more than one cycle of artificial insemination or IVF may be required to achieve pregnancy followed by live birth.

For each cohort of males seeking fertility preservation for iatrogenic infertility in a given year, CHBRP estimates the long-term marginal impact of SB 600 would yield an estimated 6 more live births to these men and their partners over time.

Females

CHBRP estimates that an additional 515 females would use either embryo or oocyte cryopreservation annually as a result of SB 600. Although CHBRP found one single center study about differential use of oocyte and embryo cryopreservation (9.5% and 90.5%, respectively) (Cardozo 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.

Embryo cryopreservation is considered the most successful fertility preservation approach for females and the standard preservation method for women with a male partner (see ***Error! Reference source not found.*** section), whereas 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% of female cancer survivors retrieved frozen oocytes or embryos, 47% of which resulted in live births. In the case of SB 600, an estimated 170 females of the 515 women newly accessing fertility preservation services in the first year would eventually retrieve the frozen oocytes or embryos. The live birth rate is 47%; thus, about 80 live births from these retrievals would occur in the original cohort of 515 females newly using fertility preservation in the first year. Note that more than one IVF cycle may be required to achieve the live birth.

Note that these are estimates. As stated earlier, success in achieving live births is inversely associated with age, with the highest success rates in women under age 35 years and lowest success in women over age 40 years (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 or higher order multiples. 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.

For each cohort of females seeking fertility preservation for iatrogenic infertility in a given year, CHBRP estimates the long-term marginal impact of SB 600 would yield an estimated 80 more live births among these women over time.

Potential Harms Associated With Cryopreservation and ART

Those who use cryopreservation prior to gonadotoxic treatments and experience ongoing infertility must use assisted reproductive technology (ART) or artificial insemination to become pregnant using the cryopreserved materials. The literature contains 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.

CHBRP reviewed harms of IVF and planned oocyte preservation for the April 2019 analysis AB 767 Infertility. In summary, the preponderance of evidence shows that ART leads to some maternal harms, and to both maternal and offspring harms due to multiple gestation and pre-term delivery. CHBRP also noted, based on American Society of Reproductive Medicine's Ethics Committee opinion on oocyte preservation, that oocyte preservation cannot be seen as a guarantee of future fertility (ASRM, 2018). Please see AB 767 *Medical Effectiveness* and *Long-Term Impacts* sections for full details.

Evidence-based literature indicates that although there may be some risk of negative health outcomes for ART-conceived infants or to women undergoing ART overall, fertility preservation does not pose a higher risk to the health outcomes of children born from cryopreserved sperm, oocytes, or embryos from persons with iatrogenic infertility than those risks associated with assisted reproductive technology used to treat noniatrogenic infertility.

APPENDIX A TEXT OF BILL ANALYZED

On February 25, 2019, the California Senate Committee on Health requested that CHBRP analyze SB 600.

SENATE BILL **No. 600**

Introduced by Senator Portantino

February 22, 2019

An act to add Sections 1374.551 and 1374.552 to the Health and Safety Code, and to add Sections 10119.61 and 10119.62 to the Insurance Code, relating to healthcare coverage.

LEGISLATIVE COUNSEL'S DIGEST

SB 600, as introduced, Portantino. Healthcare 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 issued, amended, or renewed on or after January 1, 2017, to include, at a minimum, coverage for essential health benefits, including medically necessary basic health care services, as defined.

This bill would clarify that an individual or group health care service plan contract or health insurance policy that covers hospital, medical, or surgical expenses includes coverage for standard fertility preservation services when a medically necessary treatment may cause iatrogenic infertility to an enrollee or insured. The bill would state that these provisions are declaratory of existing law.

This bill would also prohibit a health care service plan or health insurer from denying coverage for standard fertility preservation services based on medical necessity when a provider of a treatment of a medical condition authorized by the plan or policy states that the treatment may 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, the bill would impose a state-mandated local program.

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

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

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. (a) An individual or group health care service plan contract that covers hospital, medical, or surgical expenses includes coverage for medically necessary expenses for standard fertility preservation services when a medically necessary treatment may directly or indirectly cause iatrogenic infertility to an enrollee.

(b) For purposes of this section and Section 1374.552, the following definitions apply:

(1) “Iatrogenic infertility” means an impairment of fertility caused directly or indirectly by surgery, chemotherapy, radiation, or other medical treatment.

(2) Medical treatment that “may directly or indirectly cause iatrogenic infertility” means medical treatment with a possible side effect of impaired fertility, as established by the American Society of Clinical Oncology, the American Society for Reproductive Medicine, or other reputable professional association or organization.

(3) “Standard fertility preservation services” means procedures consistent with the established medical practices and professional guidelines published by the American Society of Clinical Oncology, the American Society for Reproductive Medicine, or other reputable professional medical organization.

SEC. 2. Section 1374.552 is added to the Health and Safety Code, to read:

1374.552. (a) Standard fertility preservation services shall be deemed medically necessary when a provider of treatment of a medical condition authorized by a health care service plan states that there is a substantial likelihood that the treatment may directly or indirectly cause iatrogenic infertility to the enrollee.

(b) When a provider states that standard fertility preservation services are medically necessary pursuant to subdivision (a), a health care service plan shall not deny coverage for those services based on medical necessity.

SEC. 3.

Section 10119.61 is added to the Insurance Code, to read:

10119.61. (a) An individual or group health insurance policy that covers hospital, medical, or surgical expenses includes coverage for medically necessary expenses for standard fertility preservation services when a medically necessary treatment may directly or indirectly cause iatrogenic infertility to an insured.

(b) For purposes of this section and Section 10119.62, the following definitions apply:

(1) "Iatrogenic infertility" means an impairment of fertility caused directly or indirectly by surgery, chemotherapy, radiation, or other medical treatment.

(2) Medical treatment that "may directly or indirectly cause iatrogenic infertility" means medical treatment with a possible side effect of impaired fertility, as established by the American Society of Clinical Oncology, the American Society for Reproductive Medicine, or other reputable professional association or organization.

(3) "Standard fertility preservation services" means procedures consistent with the established medical practices and professional guidelines published by the American Society of Clinical Oncology, the American Society for Reproductive Medicine, or other reputable professional medical organization.

SEC. 4.

Section 10119.62 is added to the Insurance Code, to read:

10119.62. (a) Standard fertility preservation services shall be deemed medically necessary when a provider of treatment of a medical condition authorized by a health insurance policy states that there is a substantial likelihood that the treatment may cause iatrogenic infertility to the insured.

(b) When a provider states that standard fertility preservation services are medically necessary pursuant to subdivision (a), an insurer shall not deny coverage for those services based on medical necessity.

SEC. 5.

The addition of Section 1374.551 to the Health and Safety Code and Section 10119.61 to the Insurance Code by this act does not constitute a change in, but is declaratory of, existing law.

SEC. 6.

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

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

Studies of 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: the Agency for Healthcare Research and Quality (AHRQ), the International Network of Agencies for Health Technology Assessment (INAHTA), the National Health Service (NHS) Centre for Reviews and Dissemination, the National Institute for Health and Clinical Excellence (NICE), and the Scottish Intercollegiate Guideline Network.

The search was limited to studies published since 2017 to the present because CHBRP had previously conducted thorough literature searches on these topics in 2011, 2013, and 2017 for Assembly Bill (AB) 428, SB 912, and SB 172, respectively. The search was limited to abstracts of studies published in English. Of the 360 articles found in the literature review, 31 were reviewed for potential inclusion in this report on SB 600, and a total of 4 studies were included in the medical effectiveness review for this report, in addition to those identified as part of previous CHBRP reviews. The other articles were eliminated because they did not focus on patients undergoing fertility preservation due to cancer treatment or reported findings from case reports or case series, which are considered to be low quality in CHBRP's hierarchy of evidence due to their high risk of bias (California Health Benefits Review Program, 2019). The other articles were eliminated because they were not limited to patients undergoing fertility preservation due to cancer treatment or were case reports or case series, which are considered to be low quality in CHBRP's hierarchy of evidence due to their high risk of bias (California Health Benefits Review Program, 2019).

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.*[39] To grade the evidence for each outcome measured, the team uses a grading system that has the following categories:

- Research design;
- Statistical significance;
- Direction of effect;
- Size of effect; and
- Generalizability of findings.

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

[39] Available at: http://chbrp.com/analysis_methodology/medical_effectiveness_analysis.php.

- *Clear and convincing evidence;*
- *Preponderance of evidence;*
- *Limited evidence*
- *Inconclusive evidence; and*
- *Insufficient evidence.*

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

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

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

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

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

Search Terms (* indicates truncation of word stem)

The following Medical Subject Headings (MeSH) were used to search PubMed and Cochrane:

- Age Factors
- Antineoplastic Agents/adverse effects
- Autism Spectrum Disorder
- Autistic Disorder
- Birth Rate
- Cardiovascular Diseases
- Cerebral Palsy
- Cleft Palate
- Cost Benefit Analysis
- Cost of Illness
- Cost Savings
- Counseling
- Cryopreservation
- Depression
- Depressive Disorder
- Developmental Disabilities
- Down Syndrome
- Educational Status
- Ethnic Groups
- Embryo Transfer
- Fallopian Tube diseases
- Fertility Preservation
- Fertilization in Vitro
- Freezing
- Gender Identity
- Gynecologic Surgical Procedures
- Health Care Costs
- Health Impact Assessment
- Health Services Accessibility
- Health Services Needs and Demand
- Health Status Disparities
- Healthcare Disparities
- Homosexuality, Female
- Homosexuality, Male
- Iatrogenic Disease
- Incidence
- Infant, Low Birth Weight
- Infertility/Therapy

- Insemination, Artificial
- Insurance, Health
- Insurance Coverage
- Live Birth
- Menopause premature
- Minority Health
- Neoplasms
- Neoplasms/therapy
- Oocytes
- Organ Sparing Treatments
- Outcome Assessment (Health Care)
- Ovary/surgery
- Pregnancy Complications
- Pregnancy Outcome
- Pregnancy Rate
- Premature Birth
- Prevalence
- Quality of Life
- Race Factors
- Radiation Injuries
- Radiotherapy/adverse effects
- Referral and Consultation
- Reproductive Medicine/Legislation and jurisprudence
- Reproductive Techniques
- Reproductive Techniques, Assisted
- Risk Assessment
- Risk Factors
- Semen
- Sexuality
- Social Determinants of Health
- Sperm Injections, Intracytoplasmic/adverse effects
- Stress, Psychological
- Surrogate Mothers
- Tissue Banks
- Trachelectomy
- Transgendered Persons
- Treatment Outcome

The following keywords were used to search PubMed, Cochrane, Web of Science, EMBASE, Business Source Complete, and web sites:

- Access
- Adverse effect*
- Age
- Anxiet*
- Artificial insemination
- Assisted reproduction
- Assisted reproductive technology
- Assistive reproductive technology
- Autism
- Autistic
- Barrier*
- Behavioral disorder*
- Birth
- Birth outcomes
- Birth rates
- Cancer*
- Cancer therapy
- Cancer treatment*
- Cardiovascular disease*
- Cerebral palsy
- Childhood tumors
- Cleft palate
- Complications
- Conservative gynecologic surgery
- Consultation*
- Cost*
- Cost offset
- Cost savings
- Cost effective*
- Cost utility
- Counsel*
- Cryopreservation
- Death
- Depression
- Demand
- Demographic*
- Developmental disabilit*
- Discrimination*
- Disparit*
- Down’s syndrome
- Economic loss
- Education
- Educational attainment
- Educational status
- Effects of insurance mandates
- Effective*
- Embryo*
- Embryo transfer
- Ethnic*
- Ethnic disparities

- Fertilization in vitro
- Fertility preservation
- Financial burden
- Freezing
- Gonadal shielding
- Gender
- Harms
- Healthy child at birth
- Homosexual*
- Iatrogenic infertility
- Impact*
- In-vitro fertilization
- Income
- infertility
- Infertility insurance mandates
- Infertility therapy
- Infertility treatments
- Insurance coverage
- Insurance mandates
- Intracytoplasmic sperm injection
- Health outcomes
- Lesbian*
- Live birth rates
- Long term impacts
- Malformations
- Market
- Maternal fertility status
- Mature oocyte cryopreservation
- Mental retardation
- Miscarriage
- Morbidity
- Mortality
- Multiple birth rates
- Neoplasms
- Obstetric outcome*
- Oocytes
- Oophoropexy
- Out of pocket
- Outcome*
- Ovarian shielding
- Ovarian suppression
- Ovarian tissue cryopreservation
- Ovarian transposition
- Perinatal outcome*
- Physician referral
- Postnatal growth
- Pregnancy
- Pregnancy completed
- Pregnancy complication*
- Pregnancy outcome*
- Pregnancy rate*
- Premature death
- Premature menopause
- Premature ovarian failure
- Premium*
- Preservation
- Preventive fertility care treatment*
- Price elasticity
- Productivit*
- Psychological
- Quality of life
- Race
- Racial disparities
- Radiation injuries
- Referral
- Religion
- Religious
- Reproductive Medicine
- Reproductive technique*
- Risk*
- Risk factors
- Safety
- Same sex couples
- Sex differences
- Sexual orientation
- Side effect*
- Sperm Banks
- Social determinants
- Stigma
- Stress
- Surrogacy
- Surrogate
- Testicular suppression
- Testicular tissue cryopreservation
- Trachelectomy
- Transgender*
- Treatment outcomes
- Treatment utilization
- Uncovered costs
- Utilisation
- Utilization

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, Milliman, Inc[40]

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.[41]

This appendix describes 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 2015 cancer statistics data from the online Centers for Disease Control and Prevention CDC WONDER database. CHBRP was able to limit the CDC WONDER database to ages 10 to 44 years, which closely aligns with the content expert's recommendations for reproductive age definitions for this analysis of 12 to 44 years for females and 12 to 49 years for males.
- In its analysis, CHBRP included the top 10 types of cancer whose treatments pose the highest iatrogenic infertility risk (see the *Background* 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 applied findings from the study by Bann et al (2015), data from the 2017 Society for Reproductive Technology (SART)[42] and content expert input to estimate baseline utilization for enrollees with and without coverage.
    - In the study by Bann et al (2015), of the 812 survey respondents living in the United States with complete data on fertility preservation and gender, 264 reported no interest in having any/any more children, thus approximately 70% of the final sample of participants (550) in the study were interested in having a child. Among the final sample, 49% of male and 22% of female cancer survivors took steps to preserve fertility. CHBRP additionally assumed females would be twice as likely to forgo steps to pursue cryopreservation than males due to the higher cost of oocyte ($10,078) and embryo ($11,254) cryopreservation compared to sperm cryopreservation ($468).
    - In 2017 SART data, 23% of utilization of female cryopreservation was for embryos and 77% for mature oocytes.

[40] CHBRP's authorizing statute, available at http://chbrp.com/CHBRP%20authorizing%20statute_2018_FINAL.pdf, requires that CHBRP use a certified actuary or "other person with relevant knowledge and expertise" to determine financial impact.
[41] See method documents posted here, http://chbrp.com/analysis_methodology/cost_impact_analysis.php; in particular, see *2019 Cost Analyses: Data Sources, Caveats, and Assumptions*.
[42] https://www.sartcorsonline.com/rptCSR_PublicMultYear.aspx?reportingYear=2017

- CHBRP estimates postmandate utilization increases to the level of those enrollees who had coverage at baseline plus an additional 10% increase in utilization due to increased awareness, increased provider and enrollee knowledge of coverage, and a corresponding greater willingness to discuss fertility preservation options (Vindrola-Padros et al., 2017) that might occur with the passage SB 600. Postmandate, no enrollees would use cryopreservation without coverage. The assumed proportions of enrollees using cryopreservation by coverage at baseline and postmandate is shown in the table here below.

Fertility Preservation Method	Baseline Utilization		Post Mandate Utilization with Coverage
	With Coverage	Without Coverage	
Male – sperm cryopreservation	37.7%	34.2%	41.4%
Female – embryo cryopreservation	7.2%	3.6%	7.9%
Female – mature oocyte cryopreservation	23.2%	11.6%	25.5%

- CHBRP estimated the unit costs for cryopreservation services based on 2016 MarketScan data and 2016 Consolidated Health Cost Guidelines Sources Database (CHSD). Only CHSD data was used for pharmacy claims. The data were limited to California commercial enrollees and further refined to identify only enrollees with a cryopreservation procedure. Medical and surgical services and drugs related to cryopreservation occurring 45 days 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.

- Male cryopreservation case rate includes each of the following Healthcare Common Procedure Coding System (HCPCS) codes: Cryopreservation of sperm (89259) and sperm isolation (89261). The average cost of semen analysis codes 89320 and 89322 was also included in the case rate.

- Female oocyte cryopreservation case rate includes the following HCPCS: follicle puncture for oocyte retrieval (58970), oocyte identification from follicular fluid (89524), and cryopreservation of mature oocytes (89337).

- Female mature embryo cryopreservation case rate includes the following HCPCS: follicle puncture for oocyte retrieval (58970), oocyte identification from follicular fluid (89524), cryopreservation of embryos (89258), sperm isolation (89261), and insemination of oocytes (89268).

- The content expert indicated that 95% of women would receive one cycle. The case rates above were doubled for the women expected to undergo two cycles and weighted at 5%.

- In addition to the case rates listed above, medical services occurring within 45 days prior to the cryopreservation procedure were added to the female cryopreservation case rates. The HCPCS categorized into the office/home visits, office administered drugs, inpatient radiology and pathology/laboratory categories by Milliman's HCG grouper were reviewed by the content expert.

All codes flagged as irrelevant to cryopreservation were excluded from the analysis. The anesthesia codes 00840 and 00940 and imaging HCPCS 74177 were included in the other medical services. The average cost per woman receiving cryopreservation services was added to the case rate. In addition to the medical services above, the average cost of pharmaceuticals per woman were included in the case rate. The pharmaceuticals included in the analysis are presented in Table 7.

Table 7. Pharmaceuticals Included in Average Fertility Preservation Unit Costs

Pharmaceuticals
Cabergoline
Cetrorelix acetate
Cetrotide
Chorionic gonadotropin
Chorionic gonadotropin alfa rec
Clomiphene citrate
Dexamethasone
Etonogestrel
Follistim aq
Follitropin alfa
Follitropin beta
Ganirelix acetate
Gonal F
Gonal F RFF
Letrozole
Menopur
Metformin hcl
Metformin hydrochloride
Norethindrone
Norethindrone acetate
Novarel
Ovidrel
Pregnyl w diluent benzyl
Progesterone
Progesterone micronized

Source: CHBRP analysis of MarketScan data, 2019.

- The average unit costs based on 2016 data were trended to the 2020 projection period using the CPI-Medical rate of 2% on medical services and the Milliman HCG pharmacy rate of 7.5% on the pharmacy component.

- CHBRP estimates are based on allowed claims data and may underestimate the costs of services not covered due to carriers' ability to negotiate discounted rates that are unavailable to patients and their families.

- SB 600 does not specify requirements regarding cost sharing or coinsurance, thus CHBRP assumes carriers would cover cryopreservation with the same cost-sharing structure as seen at

baseline. Current coverage was determined using carrier surveys. Of members who currently have coverage, approximately 10% of large group nongrandfathered plan and 100% of individual Covered California plan enrollees have the same cost-sharing structure as other major medical services. CHBRP assumed the cost share is equal to the actuarial value with a maximum payment of atypical out-of-pocket maximums for the line of business. CHBRP assumed that the enrollee does not have any other claims accumulated to their out-of-pocket maximum. CHBRP assumed a 50% coinsurance without an out of pocket maximum for enrollees with a different cost share. This assumption is based on the infertility riders received.

Determining Public Demand for the Proposed Mandate

This subsection discusses public demand for the benefits SB 600 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.

Second Year Impacts on Benefit Coverage, Utilization, and Cost

In order to develop Table 8, CHBRP has considered whether continued implementation during the second year of the benefit coverage requirements of SB 600 would have a substantially different impact on utilization of either the tests, treatments or services for which coverage was directly addressed, the utilization of any indirectly affected utilization, or both. To generate this table, CHBRP reviewed the literature and consulted content experts about the possibility of varied second year impacts and applied what was learned to a projection of a second year of implementation.

Table 8. SB 600 Impacts on Benefit Coverage, Utilization, and Cost, 2021

	Baseline	Postmandate	Increase/ Decrease	Percentage Change
Benefit coverage				
Total enrollees with health insurance subject to state-level benefit mandates (a)	24,490,000	24,490,000	0	0%
Total enrollees with health insurance subject to SB 600	16,899,000	16,899,000	0	0%
Percentage of enrollees with health insurance subject to SB 600	69%	69%	0	0%
Number of enrollees with fertility preservation coverage fully compliant with SB 600	159,216	16,899,000	16,739,784	10514%
Percentage of enrollees with fertility preservation coverage fully compliant SB 600	0.94%	100%	99%	10514%
Utilization and unit cost				
Number of enrollees of child-bearing age with cancer diagnosis where treatment might result in iatrogenic infertility				
Male	2,518	2,518	0	0%
Female	3,741	3,741	0	0%
Total	6,258	6,258	0	0%
Number of enrollees with cancer using cryopreservation covered by insurance				
Embryo	2	225	223	11821%
Mature oocyte	16	725	709	4568%
Sperm	17	784	767	4623%
Number of enrollees with cancer using cryopreservation not covered by insurance				
Embryo	101	0	-101	-100%
Mature oocyte	322	0	-322	-100%
Sperm	633	0	-633	-100%
Average cost per cryopreservation procedure				
Embryo	$11,730	$11,730	0	0%
Mature oocyte	$10,531	$10,531	0	0%
Sperm	$477	$477	0	0%
Expenditures				
Premiums by payer				
Private employers for group insurance	$90,700,422,000	$90,706,476,000	$6,054,000	0.0067%
CalPERS HMO employer expenditures (c) (b)	$3,234,903,000	$3,235,187,000	$284,000	0.0088%
Medi-Cal Managed Care Plan expenditures	$29,186,401,000	$29,186,401,000	$0	0.0000%
Enrollees with individually purchased insurance	$13,111,153,000	$13,112,512,000	$1,359,000	0.0104%
Enrollees with group insurance, CalPERS HMOs, Covered California, and Medi-Cal Managed Care (c)	$15,255,718,000	$15,256,649,000	$931,000	0.0061%
Enrollee expenses				

For covered benefits (deductibles, copayments, etc.)	$15,636,259,000	$15,639,508,000	$3,249,000	0.0208%
For noncovered benefits (d) (e)	$4,877,000	$0	-$4,877,000	-100%
Total expenditures	$167,129,733,000	$167,136,733,000	$7,000,000	0.0042%

Source: California Health Benefits Review Program, 2019.

Notes: (a) Enrollees in plans and policies regulated by DMHC or CDI aged 0 to 64 years as well as enrollees 65 years or older in employer-sponsored health insurance. This group includes commercial enrollees (including those associated with Covered California or CalPERS) and Medi-Cal beneficiaries enrolled in DMHC-regulated plans.[43]
(b) Approximately 56.17% of CalPERS enrollees in DMHC-regulated plans are state retirees, state employees, or their dependents.

(c) Enrollee premium expenditures include contributions by employees to employer-sponsored health insurance, health insurance purchased through Covered California, and contributions to Medi-Cal Managed Care.

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

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

[43] For more detail, see *Estimates of Sources of Health Insurance in California*, available at http://chbrp.com/analysis_methodology/cost_impact_analysis.php.

REFERENCES

Adams E, Hill E, Watson E. Fertility preservation in cancer survivors: a national survey of oncologists' current knowledge, practice and attitudes. *British Journal of Cancer*. 2013;108:1602-1615.

American Society for Reproductive Medicine (ASRM). Access to fertility services by transgender persons: an Ethics Committee opinion. *Fertility and Sterility*. 2015;104:1111-1115.

American Society for Reproductive Medicine (ASRM). Mature oocyte cryopreservation: a guideline. *Fertility and Sterility*. 2013;99:37-43.

American Society of Reproductive Medicine (ASRM). Planned oocyte cryopreservation for women seeking to preserve future reproductive potential: an Ethics Committee opinion. *Fertility and Sterility*. 2018;110:1022-1028.

Bann CM, Treiman K, Squiers L, et al. Cancer survivors' use of fertility preservation. J*ournal of Women's Health (2002)*. 2015;24:1030-1037.

Baynosa J, Westphal LM, Madrigrano A, Wapnir I. Timing of breast cancer treatments with oocyte retrieval and embryo cryopreservation. *Journal of the American College of Surgery*. 2009;209:603-607.

Bermas BL, Sammaritano LR. Fertility and pregnancy in rheumatoid arthritis and systemic lupus erythematosus. *Fertility Research and Practice*. 2015;1:13.

California Health Benefits Review Program. *Medical Effectiveness Analysis and Research Approach*. 2019.Available at: http://chbrp.com/Medical%20Effectiveness%20Approach%2001172019%20FINAL.pdf. Accessed April 1, 2019.

California Health Interview Survey (CHIS). Gender Identity Among Persons Aged 18-64 in California, 2015-2017. 2019. Available at: ask.chis.ucla.edu. Accessed March 30, 2019.

Canada AL, Schover LR. The psychosocial impact of interrupted childbearing in long-term female cancer survivors. *Psychooncology*. 2012;21:134-143.

Cardozo ER, Thomson AP, Karmon AE, Dickinson KA, Wright DL, Sabatini ME. Ovarian stimulation and in-vitro fertilization outcomes of cancer patients undergoing fertility preservation compared to age matched controls: a 17-year experience. *Journal of Assisted Reproduction and Genetics*. 2015;32:587-596.

Centers for Disease Control and Prevention (CDC). United States and Puerto Rico Cancer Statistics, 1999-2015 Incidence Request. WONDER Database. 2019. Available at: http://wonder.cdc.gov/cancer-v2015.html. Accessed March 28, 2019.

Centers for Disease Control and Prevention (CDC). NCHHSTP Social Determinants of Health. Frequently Asked Questions. Page last reviewed: March 10, 2014. Available at: http://www.cdc.gov/nchhstp/socialdeterminants/faq.html. Accessed August 27, 2015.

Chen D, Matson M, Macapagal K, et al. Attitudes toward fertility and reproductive health among transgender and gender-nonconforming adolescents. *Journal of Adolescent Health*. 2018;63:62-68.

Chen D, Simons L, Johnson EK, Lockart BA, Finlayson C. Fertility preservation for transgender adolescents. *Journal of Adolescent Health.* 2017;61:120-123.

Chien AJ, Chambers J, McAuley F, et al. Fertility preservation with ovarian stimulation and time to treatment in women with stage II-III breast cancer receiving neoadjuvant therapy. *Breast Cancer Research and Treatment*. 2017;165:151-159.

Cobo A, Diaz C. Clinical application of oocyte vitrification: a systematic review and meta-analysis of randomized controlled trials. *Fertility and Sterility*. 2011;96:277-285.

Cobo A, Garcia-Velasco J, Domingo J, Pellicer A, Remohi J. Elective and onco-fertility preservation: factors related to IVF outcomes. *Human Reproduction (Oxford, England)*. 2018;33:2222-2231.

Cobo A, Kuwayama M, Perez S, Ruiz A, Pellicer A, Remohi J. Comparison of concomitant outcome achieved with fresh and cryopreserved donor oocytes vitrified by the Cryotop method. *Fertility and Sterility*. 2008;89:1657-1664.

Cobo A, Meseguer M, Remohi J, Pellicer A. Use of cryo-banked oocytes in an ovum donation programme: a prospective, randomized, controlled, clinical trial. *Human Reproduction (Oxford, England)*. 2010;25:2239-2246.

Cobo A, Serra V, Garrido N, Olmo I, Pellicer A, Remohi J. Obstetric and perinatal outcome of babies born from vitrified oocytes. *Fertility and Sterility*. 2014;102:1006-1015.e1004.

Coccia PF, Pappo AS, Altman J, et al. Adolescent and young adult oncology, version 2.2014. *Journal of the National Comprehensive Cancer Network*. 2014;12:21-32; quiz 32.

Creux H, Monnier P, Son WY, Buckett W. Thirteen years' experience in fertility preservation for cancer patients after in vitro fertilization and in vitro maturation treatments. *Journal of Assisted Reproduction and Genetics*. 2018;35:583-592.

Creux H, Monnier P, Son WY, Tulandi T, Buckett W. Immature oocyte retrieval and in vitro oocyte maturation at different phases of the menstrual cycle in women with cancer who require urgent gonadotoxic treatment. *Fertility and Sterility*. 2017;107:198-204.

Delvigne A, Rozenberg S. Epidemiology and prevention of ovarian hyperstimulation syndrome (OHSS): a review. *Human Reproduction Update*. 2002;8:559-577.

Deshpande NA, Braun IM, Meyer FL. Impact of fertility preservation counseling and treatment on psychological outcomes among women with cancer: a systematic review. *Cancer*. 2015;121:3938-3947.

Devine K, Mumford SL, Goldman KN, et al. Baby budgeting: oocyte cryopreservation in women delaying reproduction can reduce cost per live birth. *Fertility and Sterility*. 2015;103:1446-1453.e1-2.

Diaz-Garcia C, Domingo J, Garcia-Velasco JA, et al. Oocyte vitrification versus ovarian cortex transplantation in fertility preservation for adult women undergoing gonadotoxic treatments: a prospective cohort study. *Fertility and Sterility*. 2018;109:478-485.e472.

Dolmans MM, Hollanders de Ouderaen S, Demylle D, Pirard C. Utilization rates and results of long-term embryo cryopreservation before gonadotoxic treatment. *Journal of Assisted Reproduction and Genetics*. 2015;32:1233-1237.

Domingo J, Guillen V, Ayllon Y, et al. Ovarian response to controlled ovarian hyperstimulation in cancer patients is diminished even before oncological treatment. *Fertility and Sterility*. 2012;97:930-934.

Druckenmiller S, Goldman KN, Labella PA, Fino ME, Bazzocchi A, Noyes N. Successful oocyte cryopreservation in reproductive-aged cancer survivors. *Obstetrics and Gynecology*. 2016;127:474-480.

Dunn L, Fox KR. Techniques for fertility preservation in patients with breast cancer. *Current Opinion in Obstetrics & Gynecology*. 2009;21:68-73.

Fawcett SL, Gomez AC, Barter SJ, Ditchfield M, Set P. More harm than good? The anatomy of misguided shielding of the ovaries. *British Journal of Radiology*. 2012;85:e442-447.

Ferrari S, Paffoni A, Filippi F, Busnelli A, Vegetti W, Somigliana E. Sperm cryopreservation and reproductive outcome in male cancer patients: a systematic review. *Reproductive BioMedicine Online*. 2016;33:29-38.

Finlayson C, Johnson EK, Chen D, et al. Proceedings of the Working Group Session on Fertility Preservation for Individuals with Gender and Sex Diversity. *Transgender Health*. 2016;1:99-107.

Forman EJ, Anders CK, Behera MA. A nationwide survey of oncologists regarding treatment-related infertility and fertility preservation in female cancer patients. *Fertility and Sterility*. 2010;94:1652-1656.

Forman EJ, Li X, Ferry KM, Scott K, Treff NR, Scott RT Jr. Oocyte vitrification does not increase the risk of embryonic aneuploidy or diminish the implantation potential of blastocysts created after intracytoplasmic sperm injection: a novel, paired randomized controlled trial using DNA fingerprinting. *Fertility and Sterility*. 2012;98:644-649.

Georgescu ES, Goldberg JM, du Plessis SS, Agarwal A. Present and future fertility preservation strategies for female cancer patients. *Obstetrical & Gynecological Survey*. 2008;63:725-732.

Goodman LR, Balthazar U, Kim J, Mersereau JE. Trends of socioeconomic disparities in referral patterns for fertility preservation consultation. *Human Reproduction (Oxford, England)*. 2012;27:2076-2081.

Gubbala K, Laios A, Gallos I, Pathiraja P, Haldar K, Ind T. Outcomes of ovarian transposition in gynaecological cancers; a systematic review and meta-analysis. *Journal of Ovarian Research*. 2014;7:69.

Hembree WC, Cohen-Kettenis P, Delemarre-van de Waal HA, et al. Endocrine treatment of transsexual persons: an Endocrine Society clinical practice guideline. *Journal of Endocrinology and Metabolism*. 2009;94:3132-3154.

Hourvitz A, Goldschlag DE, Davis OK, Gosden LV, Palermo GD, Rosenwaks Z. Intracytoplasmic sperm injection (ICSI) using cryopreserved sperm from men with malignant neoplasm yields high pregnancy rates. *Fertility and Sterility*. 2008;90:557-563.

Ishiguro H, Yasuda Y, Tomita Y, et al. Gonadal shielding to irradiation is effective in protecting testicular growth and function in long-term survivors of bone marrow transplantation during childhood or adolescence. *Bone Marrow Transplantatio*n. 2007;39:483-490.

Jadoul P, Guilmain A, Squifflet J, et al. Efficacy of ovarian tissue cryopreservation for fertility preservation: Lessons learned from 545 cases. *Human Reproduction (Oxford, England)*. 2017;32:1046-1054.

Johnson MD, Cooper AR, Jungheim ES, Lanzendorf SE, Odem RR, Ratts VS. Sperm banking for fertility preservation: a 20-year experience. *European Journal of Obstet rics, Gynecology, and Reproductive Biology*. 2013;170:177-182.

Kato K. Vitrification of embryos and oocytes for fertility preservation in cancer patients. *Reproductive Medicine and Biology*. 2016;15:227-233.

Knopman JM, Noyes N, Talebian S, Krey LC, Grifo JA, Licciardi F. Women with cancer undergoing ART for fertility preservation: a cohort study of their response to exogenous gonadotropins. *Fertility and Sterility*. 2009;91(4 suppl):1476-1478.

Kohler TS, Kondapalli LA, Shah A, Chan S, Woodruff TK, Brannigan RE. Results from the survey for preservation of adolescent reproduction (SPARE) study: gender disparity in delivery of fertility preservation message to adolescents with cancer. *Journal of Assisted Reproduction and Genetics*. 2011;28:269-277.

Lambertini M, Del Mastro L, Pescio MC, et al. Cancer and fertility preservation: international recommendations from an expert meeting. *BMC Medicine*. 2016;14:1.

Lawrenz B, Jauckus J, Kupka MS, Strowitzki T, von Wolff M. Fertility preservation in >1,000 patients: patient's characteristics, spectrum, efficacy and risks of applied preservation techniques. *Archives of Gynecology and Obstetrics*. 2011;283:651-656.

Lawson AK, Klock SC, Pavone ME, Hirshfeld-Cytron J, Smith KN, Kazer RR. Psychological counseling of female fertility preservation patients. *Journal of Psychosocial Oncolog*y. 2015;33:333-353.

Lee SJ, Schover LR, Partridge AH, et al. American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. *Journal of Clinical Oncology*. 2006;24:2917-2931.

Levine J, Canada A, Stern CJ. Fertility preservation in adolescents and young adults with cancer. *Journal of Clinical Oncology*. 2010;28:4831-4841.

Li L, Zeng D, Li F, Cui D, Zhang Y. Prevalence and risk factors of ejaculation failure on the day of operation among Chinese males undergoing assisted reproductive technique treatments. *Journal of Reproductive Medicine*. 2016;61:385-389.

Livestrong Foundation. Livestrong Fertility Program. Available at: https://www.livestrong.org/what-we-do/program/fertility. Accessed February 17, 2017.

Loren AW, Mangu PB, Beck LN, 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.

Madrigrano A, Westphal L, Wapnir I. Egg retrieval with cryopreservation does not delay breast cancer treatment. *American Journal of Surgery*. 2007;194:477-481.

Martinez M, Rabadan S, Domingo J, Cobo A, Pellicer A, Garcia-Velasco JA. Obstetric outcome after oocyte vitrification and warming for fertility preservation in women with cancer. *Reproductive BioMedicine Online*. 2014;29:722-728.

Miller SD, Li Y, Meyers KE, Caplan A, Miller VA, Ginsberg JP. Fertility preservation in paediatric nephrology: results of a physician survey. *Journal of Renal Care*. 2014;40:257-262.

Molodecky NA, Soon IS, Rabi DM, et al. Increasing incidence and prevalence of the inflammatory bowel diseases with time, based on systematic review. *Gastroenterology*. 2012;142:46-54.e42; quiz e30.

Muller I, Oude Ophuis RJA, Broekmans FJM, Lock TMTW. Semen cryopreservation and usage rate for assisted reproductive technology in 898 men with cancer. *Reproductive BioMedicine Online*. 2016;32:147-153.

Nahata L, Tishelman AC, Caltabellotta NM, Quinn GP. Low fertility preservation utilization among transgender youth. *Journal of Adolescent Health.* 2017a;61 :40-44.

Nahata L, Ziniel SI, Garvey KC, Yu RN, Cohen LE. Fertility and sexual function: a gap in training in pediatric endocrinology. *Journal of Pediatric Endocrinology & Metabolism*. 2017b;30:3-10.

Office of Disease Prevention and Health Promotion. Healthy People 2020: Social Determinants of Health. Available at: http://www.healthypeople.gov/2020/topics-objectives/topic/socialdeterminantshealth/addressing-determinants. Accessed February 16, 2016.

Oktay K, Harvey BE, Loren AW. Fertility preservation in patients with cancer: ASCO clinical practice guideline update summary. *Journal of Oncology Practice*. 2018a;14:381-385.

Oktay K, Harvey BE, Partridge AH, et al. Fertility preservation in patients with cancer: ASCO clinical practice guideline update. *Journal of Clinical Oncology*. 2018b;36:1994-2001.

Oktay K, Oktem O. Ovarian cryopreservation and transplantation for fertility preservation for medical indications: report of an ongoing experience. *Fertility and Sterility.* 2010;93:762-768.

Oktay K, Turan V, Bedoschi G, Pacheco FS, Moy F. Fertility preservation success subsequent to concurrent aromatase inhibitor treatment and ovarian stimulation in women with breast cancer. *Journal of Clinical Oncology*. 2015;33:2424-2429.

Onofre J, Baert Y, Faes K, Goossens E. Cryopreservation of testicular tissue or testicular cell suspensions: a pivotal step in fertility preservation. *Human Reproduction Update*. 2016;22:744-761.

Pacheco F, Oktay K. Current success and efficiency of autologous ovarian transplantation: a meta-analysis. *Reproductive Sciences (Thousand Oaks, Calif.)*. 2017;24:1111-1120.

Panagiotopoulou N, Ghuman N, Sandher R, Herbert M, Stewart JA. Barriers and facilitators towards fertility preservation care for cancer patients: a meta-synthesis. *European Journal of Cancer Care*. 2018;27(1):e12428.

Parmegiani L, Cognigni GE, Bernardi S, et al. Efficiency of aseptic open vitrification and hermetical cryostorage of human oocytes. *Reproductive Biomedicine Online*. 2011;23:505-512.

Partridge AH, Gelber S, Peppercorn J, et al. Web-based survey of fertility issues in young women with breast cancer. *Journal of Clinical Oncology*. 2004;22:4174-4183.

Pons-Estel GJ, Alarcon GS, Scofield L, Reinlib L, Cooper GS. Understanding the epidemiology and progression of systemic lupus erythematosus. *Seminars in Arthritis and Rheumatism*. 2010;39:257-268.

Quinn GP, Block RG, Clayman ML, et al. If you did not document it, it did not happen: rates of documentation of discussion of infertility risk in adolescent and young adult oncology patients' medical records. *Journal of Oncology Practice*. 2015;11:137-144.

Reinecke J. States Add Coverage Mandates to Cover Infertility Treatment Following Cancer Treatments. National Academy for State Health Policy. Page last reviewed: November 20, 2018. Available at: https://nashp.org/states-add-coverage-mandates-to-cover-infertility-treatment-following-cancer-treatments/. Accessed April 3, 2019.

Reinecke JD, Kelvin JF, Arvey SR, et al. Implementing a systematic approach to meeting patients' cancer and fertility needs: a review of the Fertile Hope Centers of Excellence program. *Journal of Oncology Practice.* 2012;8:303-308.

Rienzi L, Romano S, Albricci L, et al. Embryo development of fresh 'versus' vitrified metaphase II oocytes after ICSI: a prospective randomized sibling-oocyte study. *Human Reproduction (Oxford, England)*. 2010;25:66-73.

Robertson AD, Missmer SA, Ginsburg ES. Embryo yield after in vitro fertilization in women undergoing embryo banking for fertility preservation before chemotherapy. *Fertility and Sterility*. 2011;95:588-591.

Roque M, Lattes K, Serra S, et al. Fresh embryo transfer versus frozen embryo transfer in in vitro fertilization cycles: a systematic review and meta-analysis. *Fertility and Sterility*. 2013;99:156-162.

Salih SM, Albayrak S, Seo S, Stewart SL, Bradley K, Kushner DM. Diminished utilization of in vitro fertilization following ovarian transposition in cervical cancer patients. *Journal of Reproductive Medicine*. 2015;60:345-353.

Schelble A, Fisher A, Jungheim E, Lewis C, Omurtag KJF, Fertility preservation (FP) referral and follow-up in male-to-female (MTF) and female-to-male (FTM) transgender patients. *Sterility.* 2017;108:e115-e116.

Seli E, Tangir J. Fertility preservation options for female patients with malignancies. Current Opinion in Obstetrics & Gynecology. 2005;17:299-308.

Shnorhavorian M, Harlan LC, Smith AW, et al. Fertility preservation knowledge, counseling, and actions among adolescent and young adult patients with cancer: a population-based study. *Cancer*. 2015;121:3499-3506.

Society of Assisted Reproductive Technology (SART). National Summary Report: All SART Member Clinics. 2015. Available at: https://www.sartcorsonline.com/Csr/Public?ClinicPKID=0. Accessed April 2, 2019.

Society of Assisted Reproductive Technology (SART). National Summary Report: All SART Member Clinics. 2016; https://www.sartcorsonline.com/rptCSR_PublicMultYear.aspx?reportingYear=2016#patient-cumulative. Accessed April 2, 2019.

Thibaud E, Ramirez M, Brauner R, et al. Preservation of ovarian function by ovarian transposition performed before pelvic irradiation during childhood. *Journal of Pediatrics*. 1992;121:880-884.

Tincani A, Dall'Ara F, Lazzaroni MG, Reggia R, Andreoli L. Pregnancy in patients with autoimmune disease: a reality in 2016. *Autoimmunity Reviews*. 2016;15:975-977.

Tiseo BC, Cocuzza M, Bonfa E, Srougi M, Silva CA. Male fertility potential alteration in rheumatic diseases: a systematic review. *International Braz J Urol*. 2016;42(1):11-21.

van Casteren NJ, van Santbrink EJ, van Inzen W, Romijn JC, Dohle GR. Use rate and assisted reproduction technologies outcome of cryopreserved semen from 629 cancer patients. *Fertility and Sterility*. 2008;90:2245-2250.

van der Kaaij MA, van Echten-Arends J, Simons AH, Kluin-Nelemans HC. Fertility preservation after chemotherapy for Hodgkin lymphoma. *Hematological Oncology*. 2010;28:168-179.

Vindrola-Padros C, Dyer KE, Cyrus J, Lubker IM. Healthcare professionals' views on discussing fertility preservation with young cancer patients: a mixed method systematic review of the literature. *Psychooncology*. 2017;26:4-14.

Waimey KE, Smith BM, Confino R, Jeruss JS, Pavone ME. Understanding fertility in young female cancer patients. *Journal of Women's Health (2002)*. 2015;24:812-818.

Wallace WH, Anderson RA, Irvine DS. Fertility preservation for young patients with cancer: who is at risk and what can be offered? *Lancet Oncology*. 2005;6:209-218.

Wallberg KA, Keros V, Hovatta O. Clinical aspects of fertility preservation in female patients. *Pediatric Blood & Cancer*. 2009;53:254-260.

Wyatt R, Laderman M, Botwinick L, Mate K, Whittington J. *Achieving Health Equity: A Guide for Health Care Organizations*. IHI White Paper. Cambridge, Massachusetts: Institute for Healthcare Improvement; 2016.

Zhang W, Xiao X, Zhang J, et al. Clinical outcomes of frozen embryo versus fresh embryo transfer following in vitro fertilization: a meta-analysis of randomized controlled trials. *Archives of Gynecology and Obstetrics*. 2018;298:259-272.

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 researchers and analysts who are **Task Force Contributors** to CHBRP from UC that conduct much of the analysis. The **CHBRP staff** coordinates the efforts of the Faculty Task Force, works with Task Force members in preparing parts of the analysis, and manages all external communications, including those with the California Legislature. As required by CHBRP's authorizing legislation, UC contracts with a certified actuary, **Milliman**, 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.

Faculty Task Force

Janet Coffman, MA, MPP, PhD, *Vice Chair for Medical Effectiveness*, University of California, San Francisco
Sylvia Guendelman, PhD, LCSW, University of California, Berkeley
Gerald Kominski, PhD, University of California, Los Angeles
Sara McMenamin, PhD, *Vice Chair for Medical Effectiveness and Public Health*, University of California, San Diego
Joy Melnikow, MD, MPH, *Vice Chair for Public Health*, University of California, Davis
Jack Needleman, PhD, University of California, Los Angeles
Ninez Ponce, PhD, University of California, Los Angeles
Nadereh Pourat, PhD, *Vice Chair for Cost*, University of California, Los Angeles
Marilyn Stebbins, PharmD, University of California, San Francisco
Ed Yelin, PhD, Professor Emeritus, University of California, San Francisco

Task Force Contributors

Danielle Casteel, MA, University of California, San Diego
Shana Charles, PhD, MPP, University of California, Los Angeles, and California State University, Fullerton
Shauna Durbin, MPH, University of California, Davis
Margaret Fix, MPH, University of California, San Francisco
Sarah Hiller, MA, University of California, San Diego
Naomi Hillery, MPH, University of California, San Diego
Jeffrey Hoch, PhD, University of California, Davis
Michelle Ko, MD, PhD, University of California, Davis
Kevin Lee, PhD Candidate, University of California, Berkeley
Elizabeth Magnan, MD, PhD, University of California, Davis
Ying-Ying Meng, PhD, University of California, Los Angeles
Jacqueline Miller, University of California, San Francisco
Dominique Ritley, MPH, University of California, Davis

National Advisory Council

CHBRP Staff

Garen Corbett, MS, Director
John Lewis, MPA, Associate Director
Adara Citron, MPH, Principal Policy Analyst
Karen Shore, Contractor*
Karla Wood, Project Analyst
Ana Ashby, Health Policy Graduate Assistant

California Health Benefits Review Program
MC 3116
Berkeley, CA 94720-3116
info@chbrp.org
www.chbrp.org
(510) 664-5306

*Karen Shore is an Independent Contractor with whom CHBRP works to support legislative analyses and other special projects on a contractual basis.

CHBRP is an independent program administered and housed by the University of California, Berkeley, in the Office of the Vice Chancellor for Research.

ACKNOWLEDGMENTS

CHBRP gratefully acknowledges the efforts of the team contributing to this analysis:

Meghan Soulsby Weyrich, MPH, and Elizabeth Magnan, MD, PhD, of the University of California, Davis, prepared the medical effectiveness analysis. Min-Lin Fang of the University of California, San Francisco, conducted the literature search. Shauna Durbin, MPH, and Elizabeth Magnan, MD, PhD, of the University of California, Davis, prepared the public health impact analysis. Riti Shimkhada, PhD, of the University of California, Los Angeles prepared the cost impact analysis. Casey Hammer, FSA, MAAA of Milliman, provided actuarial analysis. Content expert H. Irene Su, MD, MSCE of the University of California, San Diego provided technical assistance with the literature s and expert input on the analytic approach. Adara Citron, MPH, of CHBRP staff prepared the Policy Context and synthesized the individual sections into a single report, assisted by Karla Wood. A subcommittee of CHBRP's National Advisory Council (see final pages of this report) and members of the CHBRP Faculty Task Force, Sylvia Guendelman, PhD, LCSW, of the University of California, Gerald Kominski, PhD, of the University of California, Los Angeles, and Joy Melnikow, MD, MPH, of the University of California, Davis, reviewed the analysis for its accuracy, completeness, clarity, and responsiveness to the Legislature's request.

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.

Garen Corbett, MS
Director

Please direct any questions concerning this document to: California Health Benefits Review Program; MC 3116; Berkeley, CA 94720-3116, info@chbrp.org, or www.chbrp.org