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November 30, 2023

VIA EMAIL

The Honorable Ronald D. Kouchi Senate President 415 South Beretania Street Hawai'i State Capitol, Room 409 Honolulu, Hawai'i 96813

VIA EMAIL

The Honorable Scott K. Saiki Speaker, House of Representatives 415 South Beretania Street Hawai'i State Capitol, Room 431 Honolulu, Hawai'i 96813

Re: <u>Study of Proposed Mandatory Health Insurance Coverage for Standard Fertility</u> <u>Preservation Services, Report No. 23-11</u>

Dear President Kouchi and Speaker Saiki:

Please find attached Report No. 23-11, *Study of Proposed Mandatory Health Insurance Coverage for Standard Fertility Preservation Services*, along with a copy of the Auditor's Summary. This report is being issued pursuant to House Concurrent Resolution No. 96 of the 2023 Legislative Session, which requested the Auditor to assess the social and financial effects of the mandated coverage as proposed in Senate Bill No. 1446, which was also introduced in the 2023 Legislative Session.

The report is accessible through our website at: https://files.hawaii.gov/auditor/Reports/2023/23-11.pdf.

The summary is also accessible through our website at: <u>https://files.hawaii.gov/auditor/Overviews/2023/23-11AuditorSummary.pdf</u>.

If you or other Legislators have any questions about the report or would like a printed version of the report, please let me know.

Very truly yours,

Leslie H. Kondo

State Auditor

LHK:emo

Attachments ec/attach:

Members of the Senate Members of the House of Representatives Carol Taniguchi, Senate Chief Clerk Brian Takeshita, House Chief Clerk

Auditor's Summary Study of Proposed Mandatory Health Insurance Coverage for Standard Fertility Preservation Services

Report No. 23-11



IN THE 2023 LEGISLATIVE SESSION, the Hawai'i State Legislature contemplated mandating insurance coverage for standard fertility preservation services. Senate Bill No. 1446 (SB 1446) requires each individual or group health insurance policy to provide coverage to the policyholder and individuals under 26 years of age covered under the policy for standard fertility preservation services if they undergo a medically necessary treatment that may directly or indirectly cause iatrogenic infertility.¹ In addition, House Concurrent Resolution No. 96 (HCR 96), also adopted in the Regular Session of 2023, requests the Auditor, in accordance with Sections 23-51 and 23-52, Hawai'i Revised Statutes (HRS), to assess the social and financial effects of mandating health insurance coverage for fertility preservation services for certain insured persons who have been diagnosed with cancer and whose cancer or cancer treatment may adversely affect the insured person's fertility.

¹ SB 1446 will also require individual and group hospital or medical service plans issued by a mutual benefit society or health maintenance organization pursuant to Chapter 432 or Chapter 432D, HRS, respectively, to include the identical coverage for standard fertility preservation services. Our discussion regarding the coverage proposed to be mandated for health insurance policies is equally applicable to the coverage proposed under the plans issued by a mutual benefit society or health maintenance organization.

HCR 96 further requests the Auditor to examine "the necessity of extending the mandatory health insurance coverage for fertility preservation procedures for the spouse or partner of an insured person who has been diagnosed with cancer or whose cancer treatment may adversely affect the insured person's fertility, to allow the insured person to have a child in the future, and the social and financial effects of extending the mandatory coverage to such spouses or partners."

In Report No. 23-11, *Study of Proposed Mandatory Health Insurance Coverage for Standard Fertility Preservation Services*, to conduct our assessment of the impacts of the proposed mandatory coverage for standard fertility preservation services as provided in SB 1446, we had to make numerous and significant assumptions about the Legislature's intent in order to resolve certain ambiguities in SB 1446 and HCR 96. Among the assumptions we had to make was that any cancer-related medical treatment with a likely side effect of infertility would be covered under the proposed coverage. We also had to assume that coverage would not include the cost of storing cryopreserved material and that coverage had no maximum age for the policyholder. Additionally, SB 1446 specifically excludes a policyholder's spouse from coverage for standard fertility preservation services as defined by SB 1446 if that spouse is aged 26 years or older.

If the bill is considered during the upcoming legislative session, we suggest the Legislature consider clarifying those parts of the bill to help insurers as well as the public better understand who, when, and what is covered by the mandate.

What is the Relationship Between Cancer and Fertility Preservation?

Cancer treatment can impact a person's fertility. The effects of cancer treatment on fertility depends on a variety of factors, such as the medicine used, the size and location of the radiation field, the dose, dose intensity, or method of administration, or the age, sex, and fertility of the patient before treatment. In males, chemotherapy or radiotherapy can negatively affect sperm number, motility, morphology, and DNA integrity. In females, any treatment that decreases the number of primordial follicles², affects hormonal balance, or interferes with the functioning of the ovaries, fallopian tubes, uterus, or cervix can negatively affect fertility.

Additionally, surgical treatments for cancer can cause fertility problems such as through the removal of all or part of the testicles, penis, ovaries, uterus, or cervix.

Some aggressive forms of cancer such as leukemia require immediate treatment, while treatment for other forms of cancer may be delayed to allow a patient time to preserve their fertility. This is of particular importance for female patients, as they need additional time for stimulation and retrieval of their oocytes.³

² Primordial follicles can transform into pre-ovulatory follicles after puberty which, during ovulation, release mature oocytes.

³ Oocytes are female germ cells that can mature into an egg, which is the cell that can be fertilized to produce an embryo.

Study of Proposed Mandatory Health Insurance Coverage for Standard Fertility Preservation Services

A Report to the Governor and the Legislature of the State of Hawai'i

Report No. 23-11 November 2023





OFFICE OF THE AUDITOR STATE OF HAWAI'I



OFFICE OF THE AUDITOR STATE OF HAWAI'I

Constitutional Mandate

Pursuant to Article VII, Section 10 of the Hawai'i State Constitution, the Office of the Auditor shall conduct post-audits of the transactions, accounts, programs and performance of all departments, offices and agencies of the State and its political subdivisions.

The Auditor's position was established to help eliminate waste and inefficiency in government, provide the Legislature with a check against the powers of the executive branch, and ensure that public funds are expended according to legislative intent.

Hawai'i Revised Statutes, Chapter 23, gives the Auditor broad powers to examine all books, records, files, papers and documents, and financial affairs of every agency. The Auditor also has the authority to summon people to produce records and answer questions under oath.

Our Mission

To improve government through independent and objective analyses.

We provide independent, objective, and meaningful answers to questions about government performance. Our aim is to hold agencies accountable for their policy implementation, program management and expenditure of public funds.

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We report our findings and make recommendations to the Governor and the Legislature to help them make informed decisions.

For more information on the Office of the Auditor, visit our website: <u>https://auditor.hawaii.gov</u>

Foreword

We assessed the social and financial effects of mandating health insurance coverage for standard fertility preservation services proposed in Senate Bill No. 1446, introduced in the Regular Session of 2023, in accordance with Sections 23-51 and 23-52, Hawai'i Revised Statutes. The 2023 Legislature requested this assessment through House Concurrent Resolution No. 96.

House Concurrent Resolution No. 96 also requested that we examine the necessity of extending the mandatory health insurance coverage for fertility preservation services for the spouse or partner of an insured person who has been diagnosed with cancer or whose cancer treatment may adversely affect the insured person's fertility, to allow the insured person to have a child in the future, and the social and financial effects of extending the mandatory coverage to such spouses or partners.

We appreciate the cooperation and assistance of the Association of Clinical Oncology and other organizations and individuals we contacted during this assessment.

Leslie H. Kondo State Auditor

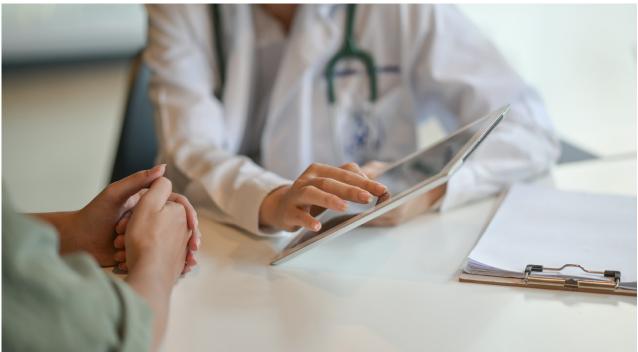
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Study of Proposed Mandatory Health Insurance Coverage for Standard Fertility Preservation Services

Introduction

House Concurrent Resolution No. 96

House Concurrent Resolution No. 96 (HCR 96), adopted in the Regular Session of 2023, requests the Auditor, in accordance with Sections 23-51 and 23-52, Hawai'i Revised Statutes (HRS), to assess the social and financial effects of mandating health insurance coverage for fertility preservation services for certain insured persons who have been diagnosed with cancer and whose cancer or cancer treatment may adversely affect the insured person's fertility, as provided in Senate Bill No. 1446 (SB 1446), introduced in the Regular Session of 2023.

HCR 96 further requests the Auditor to examine "the necessity of extending the mandatory health insurance coverage for fertility preservation procedures [proposed in SB 1446] for the spouse or partner of an insured person who has been diagnosed with cancer or whose cancer treatment may adversely affect the insured person's fertility, to allow the insured person to have a child in the future, and the social and financial effects of extending the mandatory coverage to such spouses or partners."

Senate Bill No. 1446

SB 1446 requires each individual or group health insurance policy to provide coverage to the policyholder and individuals under 26 years of age covered under the policy for standard fertility preservation services if they undergo a medically necessary treatment that may directly or indirectly cause iatrogenic infertility.¹ "Medically necessary treatment that may directly or indirectly cause iatrogenic infertility" is defined in SB 1446 to mean "medical treatment with a likely side effect of infertility as established by the American Society of Clinical Oncology."

SB 1446 defines "standard fertility preservation services" to mean "the procedures to preserve fertility as outlined and established according to the professional guidelines published by the American Society of Clinical Oncology" and "includes the full scope of services or treatments, without any exclusions or limitations, as defined in *the most recent* professional guidelines established by the American Society of Clinical Oncology." (Emphasis added.) They do not include experimental procedures or other procedures which the American Society of Clinical Oncology has not recognized as established medical practice.

The American Society of Clinical Oncology and Fertility Preservation Services

The American Society of Clinical Oncology (ASCO), founded in 1964, describes itself as the world's leading professional organization for physicians and oncology professionals caring for people with cancer. ASCO first published clinical practice guidelines on fertility preservation in 2006, updated its guidelines in 2013, and published its most recent update in 2018. As ASCO states, the goal of the 2018 update "is to provide oncologists, other health care providers, and caregivers with [current] recommendations regarding fertility preservation options for adults, adolescents, and children with cancer."

¹ SB 1446 will also require individual and group hospital or medical service plans issued by a mutual benefit society or health maintenance organization pursuant to Chapter 432 or Chapter 432D, HRS, respectively, to include the identical coverage for standard fertility preservation services. Our discussion regarding the coverage proposed to be mandated for health insurance policies is equally applicable to the coverage proposed under the plans issued by a mutual benefit society or health maintenance organization.

The 2018 update to ASCO's clinical practice guidelines (ASCO Guidelines) was developed by a multidisciplinary panel, which included a patient representative and an ASCO Guidelines staff member with health research methodology expertise. The panel reviewed abstracts of randomized controlled trials, systematic reviews, meta-analyses, and clinical practice guidelines.

SB 1446 references "the most recent" ASCO Guidelines to define "standard fertility preservation services."

What is the relationship between cancer and fertility preservation?

Cancer treatment can impact a person's fertility. The effects of cancer treatment on fertility depends on a variety of factors, such as the medicine used, the size and location of the radiation field, the dose, dose intensity, or method of administration, or the age, sex, and fertility of the patient before treatment.

In males, chemotherapy or radiotherapy can negatively affect sperm number, motility, morphology, and DNA integrity. In females, any treatment that decreases the number of primordial follicles,² affects hormonal balance, or interferes with the functioning of the ovaries, fallopian tubes, uterus, or cervix can negatively affect fertility. Additionally, surgical treatments for cancer can cause fertility problems such as the removal of all or part of the testicles, penis, ovaries, uterus, or cervix.

Some aggressive forms of cancer such as leukemia require immediate treatment, while treatment for other forms of cancer may be delayed to allow a patient time to preserve their fertility. This is of particular importance for female patients, as additional time is needed for stimulation and retrieval of oocytes.³

² Primordial follicles can transform into pre-ovulatory follicles after puberty which, during ovulation, release mature oocytes.

³ Oocytes are female germ cells that can mature into an egg, which is the cell that can be fertilized to produce an embryo.

The ASCO Guidelines include recommendations regarding fertility preservation procedures for adults, adolescents, and children with cancer. The procedures that qualify as "standard fertility preservation services" pursuant to the 2018 ASCO Guidelines are summarized in the chart below. Both adults and postpubertal children are included, as appropriate, under the headings "males" and "females."

Fertility Preservation Procedures Included in 2018 ASCO Guidelines

Males	Sperm cryopreservation
Females	Embryo cryopreservation Oocyte cryopreservation Ovarian transposition

Additional fertility preservation procedures are mentioned in the 2018 ASCO Guidelines, but are not assessed in this report as they do not meet the definition of "standard fertility preservation services" contained in SB 1446 or are already covered as medically necessary cancer treatment. These procedures include:

Procedure	Reason for exclusion
Hormonal gonadoprotection	Not recommended by ASCO
Conservative gynecological surgery	Coverage already exists
Ovarian suppression	Not recommended by ASCO
Ovarian tissue cryopreservation	Experimental
Testicular tissue cryopreservation	Experimental

The ASCO Guidelines, which define the "standard fertility preservation services" covered under the bill, are intended by ASCO to be "practice guidelines" to assist providers in clinical decision making.⁴ Consistent with that purpose, the guidelines' recommendations emphasize communication between health care providers and patients with cancer, such as discussing the possibility of infertility with those patients as early as possible and referring them to reproductive specialists.

⁴ The ASCO Guidelines include an express disclaimer: "The information herein should not be relied upon as being complete or accurate, nor should it be considered as inclusive of all proper treatments or methods of care or as a statement of the standard of care." The disclaimer further notes that, while scientific knowledge develops rapidly, the guidelines are "not continually updated and may not reflect the most recent evidence."

Exhibit 1

Standard Fertility Preservation Services Identified in SB 1446

Descriptions of the fertility preservation services recommended in the 2018 ASCO Guidelines, identified in this exhibit, were obtained from Hawai'i-based reproductive endocrinologists we interviewed during our assessment, as well as from the Hawai'i Medical Service Association and the Alliance for Fertility Preservation.

Females	Males
Embryo Cryopreservation	Sperm Cryopreservation
 After an initial consultation, a timeline is established depending on how long a patient can afford to delay cancer treatment.⁵ 	 Semen collection can be done as soon as the male is ready to provide a sample, and the
 The treatment begins with the female receiving injectable medications to stimulate ovarian follicles that contain egg cells. The typical course of injectable follicle-stimulating hormones is ten days. 	sperm will be cryopreserved immediately. There is no need for an initial consultation or medications required for semen collection.
 Two days after the final injection of follicle- stimulating hormone is administered, the eggs are retrieved. 	 Males may be able to provide semen samples daily and
 Once retrieved, the eggs are grown in a lab for five to six days, after which time they are fertilized with sperm. Embryos can be frozen by "vitrification," or fast freezing, at different stages of embryo development. 	 continue to do so until they begin cancer treatment. There are rare cases where testicular sperm aspiration is required to obtain sperm.
Oocyte Cryopreservation	
• The oocyte retrieval process follows nearly the same procedures as the embryo cryopreservation process described above. However, instead of being matured and fertilized, the unfertilized oocytes are frozen after being retrieved.	
Ovarian Transposition	
 A rare procedure that involves surgically moving the ovaries outside of the pelvic radiation treatment field for the duration of cancer treatment. 	

⁵ Due to the urgency of commencing cancer treatment and the length of time needed to stimulate ovarian follicles and perform the oocyte retrieval, most females diagnosed with cancer only have time to undergo one cycle of oocyte or embryo cryopreservation.

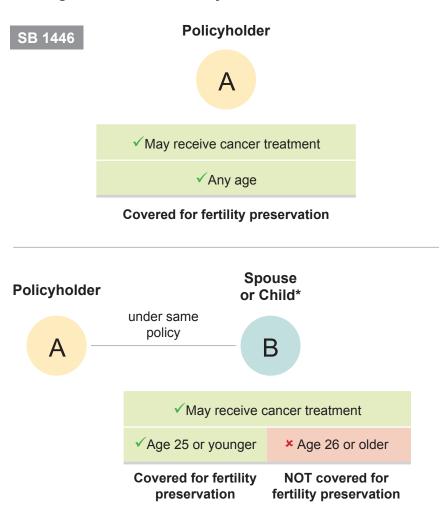


Exhibit 2 Coverage for Standard Fertility Preservation Services

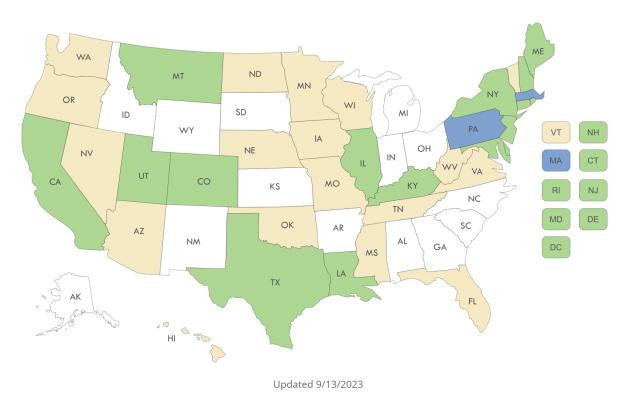
*Children can only remain on their parent's insurance plans over age 26 if they are disabled and fulfill certain limited criteria.

Source: Office of the Auditor

Fertility Preservation Coverage in Other States

According to the Alliance for Fertility Preservation, an organization with a focus on fertility preservation for cancer patients, as of September 2023, 16 states and Washington, D.C., currently have some form of mandated health insurance coverage for "fertility preservation procedures" for cancer patients and others who are facing potential infertility as a result of their medical treatment. Some states have issued studies on the expected effects of mandating health insurance coverage for fertility preservation services as a result of medically necessary medical treatments.

Exhibit 3 State Laws and Legislation



📕 Fertility Preservation Coverage 🛛 🗧 Active Legislation 📄 Inactive Legislation 📄 No coverage/No Legislation

Note: A state with "Active Legislation" is a state where a bill has been introduced for a currently on-going legislative session. A state with "Inactive Legislation" is a state where a bill has been introduced in a past legislative session.

Source: Alliance for Fertility Preservation

In November 2017, an actuarial consulting company issued a report on coverage for fertility preservation to the Maryland Health Care Commission. This report was in response to a Maryland proposal, Senate Bill No. 918 (SB 918), to mandate coverage for sperm and oocyte cryopreservation and evaluations, laboratory assessments, medications, and treatments associated with sperm and oocyte cryopreservation for patients that undergo a medically necessary cancer treatment that may directly or indirectly cause iatrogenic infertility. The proposed mandated coverage would not include the storage of sperm or oocytes. The report estimated that SB 918 would increase insurance premiums per member, per month by 14 to 24 cents depending on the type of plan and the number of patients who pursue fertility preservation. The report did not specify the population of insureds used for its analysis. In February 2019, the New York State Department of Financial Services issued a report on fertility preservation coverage that stated, though data was limited, a medically necessary fertility preservation requirement with storage costs included would have a premium impact of approximately 0.02 percent. The report did not state the population considered for its cost analysis.

In April 2019, the California Health Benefits Review Program (CHBRP) issued a report on California Senate Bill No. 600 (SB 600), which would require coverage for medically necessary expenses for standard fertility preservation services when a medically necessary treatment may directly or indirectly cause iatrogenic infertility, including 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. That report estimated that total healthcare expenditures would increase by \$6,773,000 in the state – an increase of 0.0043 percent. According to the CHBRP, 16.9 million Californians would have insurance expanded by SB 600. There was an estimated price per member, per month cost increase of up to 5 cents.

In October 2019, the New Jersey Mandated Health Benefits Advisory Commission issued a report for New Jersey Senate Bill No. 2133 (1R), which would mandate coverage for "procedures consistent with established medical practices and professional guidelines published by the American Society for Reproductive Medicine, The American Society of Clinical Oncology, or as defined by the New Jersey Department of Health, but does not include the storage of sperm or oocytes." The coverage applied to patients who undergo a medically necessary treatment that may directly or indirectly cause iatrogenic infertility. This report estimated a price per member, per month cost increase of 3 to 6 cents. It was estimated that 1,179,000 people would be affected by this proposed mandate.

In June 2021, a mandated benefit review was reported to the 192nd General Court on Massachusetts House Bill No. 1116 and Senate Bill No. 640, which would require coverage for standard fertility preservation services when diagnosed with a medical or genetic condition that might directly or indirectly cause "impairment of fertility." The bill further stipulated that the coverage must include procurement, cryopreservation, and storage of gametes, embryos, or other reproductive materials. The report stated that fully insured premiums would increase by as much as 0.006 percent or 4 cents per member, per month. The review projected about two million people on fully insured plans in 2023.

In March 2023, the Kentucky Department of Insurance issued a financial impact statement on House Bill No. 170 House Committee

Substitute 1, which would require coverage for evaluation expenses, laboratory assessments, and treatments associated with oocyte and sperm cryopreservation procedures, including first year storage costs, when a medically necessary treatment may directly or indirectly cause iatrogenic infertility. The impact statement stated mandating coverage for these services would not materially increase premiums. The report did not state the population of covered individuals under consideration.

Study Objectives

- Assess the social and financial effects of mandating health insurance coverage for "standard fertility preservation services" as defined in SB 1446, pursuant to Section 23-52, HRS.
- 2) Make recommendations as appropriate.

Scope and Methodology

The assessment was conducted from June 2023 to October 2023. We sent surveys to ten health insurers. The six health insurers that responded were the Hawai'i Medical Service Association (HMSA), Kaiser Permanente Hawai'i (Kaiser Permanente), Department of Human Services Med-QUEST Division (DHS), Hawai'i-Western Management Group (a third-party administrator for Hawai'i Medical Assurance Association), 'Ohana Health Plan, and University Health Alliance. Of the remaining four, three did not provide a substantive response, and one did not respond.

Of the three organizations that did not provide a substantive response, one stated it believed that their responses would not apply to our assessment, one stated that it only processed benefits according to the health plans it worked with, and one stated that it does not participate in the market being surveyed.

The insurers that provided substantive responses, with the exception of DHS, insure a total of 1,182,470 individuals, including policyholders, members, and covered dependents. HMSA and Kaiser Permanente, together, comprise 87 percent of that total. These insurers reported that 133,317 (or 11.27 percent) of their policies, collectively, covered a spouse or partner. DHS reported that they have a membership of 461,789 individuals with 30,190 plans covering a spouse or partner. However, we have elected to exclude them from the above totals as DHS administers most of its health plans through five providers: AlohaCare, HMSA, Kaiser Permanente, 'Ohana Health Plan, and UnitedHealthcare Community Plan.

We sent surveys to three collective bargaining organizations, and received a substantive response from only one organization, the Hawai'i Employee-Union Trust Fund. One organization declined to participate in the survey. We received no response from the third organization. We also attempted to contact two additional collective bargaining organizations but received no response to our inquiries.

We also sent surveys to judgmentally selected Hawai'i-based medical professionals, including two reproductive endocrinologists, five adult oncologists, and two pediatric oncologists.

We interviewed two Hawai'i-based reproductive endocrinologists and one Hawai'i-based gynecologic oncologist. We also interviewed representatives from the Association of Clinical Oncology, an organization established by and affiliated with ASCO, as well as representatives from the Alliance for Fertility Preservation. Additionally, we interviewed representatives from HMSA and Kaiser Permanente.

We reviewed ASCO Guidelines published in 2006, updated ASCO guidelines published in 2013, and the most recent ASCO Guidelines published in 2018.

We reviewed written public testimony regarding HCR 96 and SB 1446. We also reviewed University of Hawai'i Cancer Center publications and studies from other states on the change in cost of healthcare relating to mandating health insurance coverage for similar fertility preservation services. (See "Fertility Preservation Coverage in Other States" above.)

Challenges in Assessing the Social and Financial Impacts and Assumptions

To conduct our assessment of the impacts of the proposed mandatory coverage for standard fertility preservation services as provided in SB 1446, we were required to make numerous and significant assumptions about the Legislature's intent in order to resolve certain ambiguities in SB 1446 and HCR 96. We detail those assumptions below.

Assumption One

We have assumed that "medical treatment with a likely side effect of infertility as established by the American Society of Clinical Oncology" means any cancer-related medical treatment with a likely side effect of infertility. Per this assumption, standard fertility preservation services would be covered for any policyholder and individual under 26 years of age covered under the policy who may undergo any cancer-related medical treatment with a likely side effect of infertility.

SB 1446 defines "[m]edically necessary treatment that may directly or indirectly cause iatrogenic infertility" to mean "medical treatment with a likely side effect of infertility as established by the American Society of Clinical Oncology." The ASCO Guidelines, however, have not published a list of medical treatments that may result in a patient being at risk for infertility since 2006.⁶ In response to questions that we had about the guidelines, ASCO said that there may be treatments in addition to those used in 2006 that pose a risk to a patient's fertility.

Assumption Two

We have assumed the proposed coverage for standard fertility preservation services does not include the cost of storing the cryopreserved material.

Cryopreservation is the process of cooling biological materials to very low temperatures to preserve them, sometimes for an extended period of time. While many of the fertility preservation services recommended by ASCO in its guidelines require cryopreservation of reproductive materials, the ASCO Guidelines do not discuss procedures for the storage of cryopreserved sperm, oocytes, or embryos. SB 1446 also does not discuss the inclusion or exclusion of storage of cryopreserved reproductive materials or the length of time that coverage for storage would exist.

The long-term cost of storing embryos, sperm, or oocytes is about \$1,250 to \$1,500 annually, according to Kaiser Permanente and a Hawai'i-based reproductive endocrinology group practice. If a child is diagnosed with cancer, the need to store their reproductive materials may continue for decades.

According to Hawai'i-based reproductive endocrinologists we interviewed, many cancer patients send their cryopreserved reproductive materials to the U.S. mainland where storage costs are lower, though it was not stated by how much. They also stated that cryopreserved sperm, oocytes, and embryos can remain viable even after two to three decades.

A Hawai'i-based gynecologic oncologist stated any discussion of "cryopreservation" implies storage to some degree because it would be senseless to retrieve and cryopreserve reproductive material if it cannot be stored. However, we note that, for purposes of our assessment of the coverage proposed in SB 1446, the issue under consideration is not whether storage of cryopreserved material is necessary but, rather, whether the cost of storage is required to be covered.

⁶ See Appendix 1 and Appendix 2 for listings of medical treatments that may result in a patient being at risk for infertility published in the 2006 ASCO Guidelines.

Assumption Three

We have assumed that coverage for embryo cryopreservation does not include coverage for sperm retrieval and sperm cryopreservation, regardless of whether the sperm is from a spouse, partner, or donor.

The ASCO Guidelines recommend embryo cryopreservation as a fertility preservation option for "adult women." Embryo cryopreservation involves fertilizing a female patient's matured oocytes with sperm. It is unclear, based on the description of embryo cryopreservation as recommended by the ASCO Guidelines, whether coverage for embryo cryopreservation includes procedures and services for the male spouse, partner, or donor. Moreover, it is possible that the sperm could have been retrieved or donated well before it is used, which means there are associated costs relating to cryopreservation of the sperm.

Assumption Four

We have assumed coverage for standard fertility preservation services, as defined in the bill, has no maximum age for the policyholder. The only age limitation in SB 1446 relates to insureds under the policy who are not the policyholder. An example of these insureds would be the spouse or children of the policyholder, who only qualify for coverage if they are under age 26 years.

The ASCO Guidelines do not define or specify an age range for patients, though all of the current recommended procedures are only applicable to adults and postpubescent children.

Assumption Five

We have assumed that any limitation to coverage for standard fertility preservation services "based on the covered individual's medical history and clinical guidelines adopted by the insurer" pursuant to proposed Section 431:10A-__(c) is not based on any prior diagnosis or prior fertility treatment or on the person's expected length of life, present or predicted disability, degree of medical dependency, perceived quality of life, or other health conditions.

Proposed Section 431:10A-__(b)(1) states that "[n]o policy that provides coverage for standard fertility preservation services as required by subsection (a) shall: (1) Use any prior diagnosis or prior fertility treatment as a basis for excluding, limiting, or otherwise restricting the availability of the required coverage; or (2) Discriminate based on the insured's expected length of life, present or predicted disability, degree of medical dependency, perceived quality of life, or other health conditions." However, the proposed Section 431:10A-__(c) states that "[a]ny limitations imposed by a policy shall be based on the covered individual's medical history and clinical guidelines adopted by the insurer. Any clinical guidelines used by the insurer shall be based on the current guidelines developed by the American Society of Clinical Oncology and shall not deviate from the full scope of the guidelines."

Subsections (b) and (c) include seemingly inconsistent requirements regarding the use of a covered individual's medical history.

Who is Covered Under SB 1446?

SB 1446 provides coverage for standard fertility preservation services to the policyholder and individuals under 26 years of age covered under the policy who may undergo a cancer-related medical treatment with a likely side effect of infertility. These individuals covered under the policy include both a policyholder's spouse who is under 26 years of age as well as children who are under 26 years of age.⁷

We note that the proposed coverage for standard fertility preservation services does not include a policyholder's spouse who may undergo a cancer-related medical treatment with a likely side effect of infertility if the spouse is age 26 or older.

The Additional Request per HCR 96

HCR 96 includes an additional request for the Auditor to "examine the necessity of extending the mandatory health insurance coverage for fertility preservation procedures for the 'spouse or partner' of an 'insured person' who has been diagnosed with cancer or whose cancer treatment may adversely affect the insured person's fertility, to allow the insured person to have a child in the future, and the social and financial effects of extending the mandatory coverage to such spouses or partners."

The request contains a number of undefined and ambiguous terms. "Necessity" is not defined in HCR 96, and we are uncertain whether that term is intended to be based on the social and financial impacts that we are required to assess under Section 23-52, HRS. It also is unclear whether the insured person's spouse or partner must be insured under the same policy. We suspect that, if coverage is extended to the spouse or partner who is not insured under the policy, the impacts are different than those associated with extending proposed coverage only to the spouse or partner who is covered by the policy. Lastly, we note that

⁷ An individual aged 26 or older with disabilities may qualify as an eligible dependent under their parent's health insurance policy under limited circumstances. However, SB 1446 does not include coverage for standard fertility preservation services for insureds aged 26 or older who are not the policyholder.

the request involves coverage that is broader than that proposed in SB 1446. Specifically, SB 1446 will provide coverage for standard fertility preservation services when a patient undergoes a cancerrelated medical treatment with a likely side effect of infertility. HCR 96 expands that proposal to also include coverage when a patient has cancer, but seemingly without a requirement that the person undergo treatment for the cancer.

Because of the described issues, we elected not to separately assess the impacts of coverage for standard fertility preservation services beyond the coverage proposed in SB 1446. That said, as noted below, the insurers did not provide claims data that distinguishes policyholders from others covered under the policy. Our analysis, therefore, includes all insureds, irrespective of the insured's age, which may have been the intent of the requested additional assessment.

Social and Financial Impacts Assessment

Section 23-52, HRS, requires the Auditor to assess the impact of proposed mandated coverage to include, at the minimum and to the extent the information is available, the social and financial impacts listed in that section.

Our analysis can be found under the sections labeled Social Impact and Financial Impact below. Because SB 1446 proposes coverage for standard fertility preservation services for the policyholder and others under age 26 insured under the policy, we have separated our data between age 25 and below and age 26 and above where possible, but we are unable to distinguish policyholders from individuals covered under the policy in the claims or procedure data that insurers provided us. Thus, in our analysis, we have included all insureds, including policyholders, plan members, and policyholders' and plan members' spouses and children, without any age restrictions or limitations.

As noted above, we have made a number of assumptions in order to assess the social and financial impacts per Section 23-52, HRS.

Social Impact

The extent to which the treatment or service is generally utilized by a significant portion of the population. (Section 23-52(1)(A), HRS)

We are unable to determine the extent to which standard fertility preservation services are generally utilized by a significant portion of the population, but it is likely that only a small percentage of the population utilize these services. A Hawai'i-based reproductive endocrinology group practice that responded to our survey stated that, from 2020 to 2022, the group performed the following standard fertility preservation services for patients with cancer:

Standard Fertility Preservation Services Performed for Patients with Cancer

Service	Ages	Number of Services Performed from 2020 to 2022
	25 and below	2
Embryo Cryopreservation	26 and above	4
	25 and below	12
Sperm Cryopreservation	26 and above	70
	25 and below	6
Oocyte Cryopreservation	26 and above	17
Ovarian Transposition	All	0
	25 and below	20
TOTAL	26 and above	91

The reproductive endocrinology group practice further explained that the extent to which fertility preservation services are generally used by a significant portion of the population is difficult to quantify, as "only a small percentage make it to our office for the initial consultation."

Of the insurers surveyed, only HMSA and Kaiser Permanente reported claims being submitted for fertility preservation services in 2020, 2021, and 2022, which are reproduced below:

Service	Ages	Total HMSA and Kaiser Permanente Claims Submitted
	25 and below	0
Embryo Cryopreservation	26 and above	40
	25 and below	5
Sperm Cryopreservation	26 and above	37
	25 and below	2
Oocyte Cryopreservation	26 and above	7
	25 and below	0
Ovarian Transposition	26 and above	10
	25 and below	7
TOTAL	26 and above	94

All claims were denied except one for the embryo cryopreservation and another for sperm cryopreservation, as well as the ten ovarian transposition claims. As stated in the following impact section, HMSA and Kaiser Permanente have optional coverage available for cryopreservation and storage for embryos, oocytes, and sperm as a result of iatrogenic infertility, which may have resulted in the approved claims for embryo and sperm cryopreservation. According to HMSA, ovarian transposition is a covered treatment in various patient circumstances, including for cancer and non-cancer patients. This may have resulted in all ten claims for ovarian transposition being approved.

University Health Alliance (UHA), Hawai'i-Western Management Group (HWMG), 'Ohana Health Plan (OHP), and DHS did not provide information about the utilization of standard fertility preservation services in their survey responses.

The extent to which such insurance coverage is already generally available. (Section 23-52(1)(B), HRS)

Coverage for fertility preservation services is not generally available in Hawai'i as part of standard policies, though ovarian transposition is covered for certain cancer and non-cancer patients. Two of the insurers surveyed, HMSA and Kaiser Permanente, indicated they had optional coverage available for cryopreservation and storage for embryos, oocytes, and sperm as a result of iatrogenic infertility. HMSA stated that, as of the date of its survey responses, eight employers have chosen to include cryopreservation of embryos, oocytes, and sperm for members with iatrogenic infertility as a benefit to their employees, with plans that require a copayment for the services that range from 10 percent to 20 percent through a participating provider. Kaiser Permanente stated that it offers cryopreservation and storage for iatrogenic infertility as an optional rider to large groups only, which have \$0 cost sharing and 20 percent coinsurance. As reflected in the previous section, this may have resulted in the one covered embryo cryopreservation and one covered sperm cryopreservation for 2020, 2021, and 2022. Additionally, coverage exists under various circumstances for ovarian transposition.

If coverage is not generally available, the extent to which the lack of coverage results in persons being unable to obtain necessary health care treatment. (Section 23-52(1)(C), HRS)

We are unable to determine the extent to which the lack of coverage for standard fertility preservation services results in persons being unable to obtain necessary health care treatment, which we construe to mean standard fertility preservation services as defined in SB 1446. None of the insurers we surveyed could state whether the lack of coverage results in persons being unable to obtain necessary health care treatment.

A Hawai'i-based reproductive endocrinology group practice responded that a lack of insurance coverage results in cancer patients not seeking consultations for fertility preservation services due to the perceived costs for the services.

If the coverage is not generally available, the extent to which the lack of coverage results in unreasonable financial hardship on those persons needing treatment. (Section 23-52(1)(D), HRS)

We are unable to determine the extent to which lack of coverage for standard fertility preservation services results in unreasonable financial hardship on those persons who are undergoing cancer-related treatment and want to preserve their ability to have children in the future. None of the insurers surveyed stated whether the lack of coverage results in unreasonable financial hardship on those persons needing fertility preservation services.

Cancer patients may have only a short period of time to undergo fertility preservation services prior to commencing cancer treatment, sometimes as little as two weeks. A Hawai'i-based reproductive endocrinology group practice noted that some cancer patients who have an initial consultation on fertility preservation do not move forward with fertility preservation services due to the cost of the procedures, as they are often young adults or do not have financial stability at that time. Female patients face significantly higher costs than male patients.

The following range of costs were reported to us by Kaiser Permanente and a Hawai'i-based reproductive endocrinology group practice. They do not include storage or transportation costs.

	Total	\$5,700
	Other	\$500
varian Transposition*	Consultation	\$200
	Medication	\$1,000
	Procedure	\$4,000
	Total	\$13,700 – \$18,400
	Other	\$500 – \$800
Ocyte Cryopreservation	Consultation	\$200 - \$300
	Medication	\$4,000 - \$6,300
	Procedure	\$9,000 - \$11,000
	Total	\$500 - \$6,800
	Other	\$0 - \$500
perm Cryopreservation	Consultation	\$200 – \$300
	Medication	\$0-\$2,000
	Procedure	\$300 - \$4,000
	Total	\$17,700 – \$21,800
	Other	\$500 – \$700
mbryo Cryopreservation	Consultation	\$200 – \$300
	Medication	\$4,000 - \$6,300
	Procedure	\$13,000 - \$14,500

*Numbers for ovarian transposition are estimated numbers provided only by Kaiser Permanente.

The level of public demand for the treatment or service. (Section 23-52(1)(E), HRS)

We are unable to determine the level of public demand for fertility preservation services. None of the insurers surveyed offered comments on the level of public demand for fertility preservation services. Hawai'i Employee-Union Trust Fund indicated low to no level of demand among their members for coverage for fertility preservation services.

Cancer and cancer treatment can impact a person's fertility, so the portion of the population who may be interested in and eligible for fertility preservation services are those who have been diagnosed with cancer and may undergo a cancer-related medical treatment with a likely side effect of infertility. A Hawai'i-based gynecologic oncologist estimated that under 100 people per year would qualify for the proposed coverage.

Not every incident of cancer impacts a patient's fertility. The Alliance for Fertility Preservation provided us with estimates that approximately 60 percent of patients below age 39 are at risk of infertility from their cancer treatments. The Alliance for Fertility Preservation further stated that approximately 54 percent of men and 32 percent of women would preserve their fertility if their cancer treatment put them at risk for fertility problems. Based on the statistics provided by the Alliance for Fertility Preservation, for every 100 males and 100 females below age 39 diagnosed with cancer and whose cancer or cancer treatment may adversely affect their fertility, about 32.4 males and 19.2 females would preserve their fertility.

The University of Hawai'i Cancer Center's "Hawai'i Cancer at a Glance 2014-2018" report stated that, annually, on average there are 7,393 Hawai'i residents diagnosed with an invasive cancer. On average, 2,393 Hawai'i residents die of cancer annually. In 2018, there were over 66,779 Hawai'i residents (28,976 males, 37,803 females) who were living with cancer, including those newly diagnosed and those diagnosed in the past.

The level of public demand for individual or group insurance coverage of the treatment or service. (Section 23-52(1)(F), HRS)

We are unable to determine the level of public demand for individual or group insurance coverage for fertility preservation services. None of the insurers surveyed indicated a level of public demand for such coverage beyond the claims described above. The Hawai'i Employer-Union Trust Fund indicated that demand for coverage among their members was "low to none."

The level of interest of collective bargaining organizations in negotiating privately for inclusion of this coverage in group contracts. (Section 23-52(1)(G), HRS)

Due to the lack of responses from collective bargaining organizations, we are unable to determine their level of interest in negotiating privately for inclusion of fertility preservation services in group contracts; however, the level of interest is likely low. The Hawai'i Employer-Union Trust Fund expressed their organization had no interest in negotiating privately for inclusion of coverage for fertility preservation services.

Kaiser Permanente indicated that the level of interest for fertility preservation services is very low, explaining that it has received no requests or complaints from collective bargaining organizations regarding cancer-related infertility coverage. No other insurer surveyed indicated there was interest from collective bargaining organizations.

The impact of providing coverage for the treatment or service (such as morbidity, mortality, quality of care, change in practice patterns, provider competition, or related items). (Section 23-52(1)(H), HRS)

We are unable to determine an impact on morbidity, mortality, quality of care, change in practice patterns, provider competition, or related items if coverage for standard fertility preservation services is mandated. None of the insurers surveyed, except HMSA, indicated whether there would be an impact on morbidity, mortality, quality of care, change in practice patterns, provider competition, or related items if there was mandated coverage for standard fertility preservation services. HMSA did clarify that, for males, standard fertility preservation services had no significant risk.

A Hawai'i-based reproductive endocrinology group practice anticipated an increase in the demand for the services, but that quality of care would not be impacted. It was further stated that morbidity and mortality would be unchanged as standard fertility preservation services do not generally cause major side effects or complications.

The impact of any other indirect costs upon the costs and benefits of coverage as may be directed by the Legislature or deemed necessary by the Auditor in order to carry out the intent of 23-52(1), HRS. (Section 23-52(1)(I), HRS)

We are unable to determine the impact of any other indirect costs upon the costs and benefits of coverage as may be directed by the Legislature or deemed necessary by the Auditor in order to carry out the intent of Section 23-52(1), HRS. None of the insurers surveyed indicated whether there would be any other indirect costs. A Hawai'i-based reproductive endocrinology group practice indicated that there may be other indirect costs for the patient including travel, such as for air travel between O'ahu and the neighbor islands, as well as costs for using the stored embryos, oocytes, and sperm in the future.⁸

The extent to which insurance coverage of the kind proposed would increase or decrease the cost of the treatment or service. (Section 23-52(2)(A), HRS)

We are unable to determine the extent to which insurance coverage of standard fertility preservation services would increase or decrease the cost of the services. HMSA and UHA stated that the cost of services would increase. HWMG stated that it anticipated providers would increase the cost of the services if coverage is provided. Neither HMSA, nor UHA, nor HWMG provided further explanation as to why they anticipated that the cost of services would increase, what data may have been used to forecast an increase in cost of services, or to what extent the cost of the services would increase. Absent any data supporting a direct relationship between mandating coverage and the costs of these services, we cannot conclude that insurance coverage of this kind would increase the costs of the services based on these survey responses.

None of the other insurers provided information as to whether insurance coverage for standard fertility preservation services would increase or decrease the cost of the services.

The extent to which the proposed coverage might increase the use of the treatment or service. (Section 23-52(2)(B), HRS)

We are unable to determine the extent to which the proposed coverage might increase the use of the services, but we anticipate there would likely be an increase in the use of services if standard fertility preservation services were covered. HMSA and UHA indicated that there would be an increase in the use of the services if coverage is mandated but could not clarify the extent of the anticipated increase. Additionally, a Hawai'i-based reproductive endocrinology group practice indicated that, by making standard fertility preservation services more affordable by mandating insurance coverage, there may be an increase in the utilization of the services.

Kaiser Permanente, DHS, HWMG, and OHP did not indicate whether there would be an increase in the use of the services in their survey responses.

⁸ Per Sections 431:10A-116.5 and 432:1-604, HRS, in vitro fertilization is provided as a one-time mandated benefit. Additionally, per Section 432D-23, HRS, health maintenance organizations are required to provide the same benefits as those described in Section 431:10A-116.5, HRS.

The extent to which the mandated treatment or service might serve as an alternative for more expensive treatment or service. (Section 23-52(2)(C), HRS)

We are unable to determine the extent to which the standard fertility preservation services as defined in SB 1446 might serve as alternatives for more expensive treatments or services. According to the ASCO Guidelines, alternative methods to preserve a cancer patient's fertility exist. These alternative methods include testicular tissue cryopreservation and reimplantation, ovarian tissue cryopreservation and reimplantation, and ovarian suppression. However, ovarian tissue cryopreservation and reimplantation is considered experimental, testicular tissue cryopreservation and reimplantation should be performed only as part of clinical trials or approved experimental protocols, and ovarian suppression should not be considered a proven fertility preservation method.

While we note several alternative fertility preservation procedures above, these procedures were not identified in the survey responses we received. HMSA stated that there are currently no alternative treatments to the standard fertility preservation services as defined in SB 1446. All other insurers surveyed could not state the extent to which the mandated treatment or service might serve as an alternative for more expensive treatment or service.

A Hawai'i-based reproductive endocrinology group practice indicated that whether the mandated standard fertility preservation services defined in SB 1446 might serve as an alternative for more expensive treatments or services depended on the specific coverage provided, the circumstances of the individual or the couple seeking the treatments or services, and the overall pricing of fertility treatments in the area.

The extent to which insurance coverage of the health care service or provider can be reasonably expected to increase or decrease the insurance premium and administrative expenses of policyholders. (Section 23-52(2)(D), HRS)

While we are unable to determine the extent to which insurance coverage for standard fertility preservation services can be reasonably expected to increase or decrease the insurance premium and administrative expenses of policyholders, any increases are likely to be minimal. In other jurisdictions we reviewed, as discussed starting on page 6, we found that there was a range of 0 to 24 cent increases to premium price per member, per month costs if coverage for similar fertility preservation services was mandated. The other states considered, with the exception of Massachusetts⁹, would provide coverage when a patient underwent

⁹ Massachusetts House Bill No. 1116 and Senate Bill No. 640, would require coverage for standard fertility preservation services when diagnosed with a medical or genetic condition that might directly or indirectly cause "impairment of fertility."

a medically necessary treatment that may directly or indirectly cause iatrogenic infertility. This is a slightly broader scope than what SB 1446 proposes as, according to the California Health Benefits Review Program, 90 percent of iatrogenic infertility is caused by cancer treatment.

Kaiser Permanente indicated that legislative mandates for insurance coverage tend to raise the cost of delivering health care, resulting in higher premiums. Kaiser Permanente stated it also operates in California, Colorado, and Maryland, all of which have some form of mandated coverage for fertility preservation services. Kaiser Permanente also stated that it has not conducted a study on whether the plan premiums per member, per month increased or decreased in those states as a result of the new mandated coverage. Additionally, Kaiser Permanente indicated that the level of public demand for covering these services was low. In the absence of more specific data or information from Kaiser Permanente, we are unable to determine what its reasoning is that this mandate would result in higher premiums.

UHA indicated that mandating coverage for standard fertility preservation services can be expected to increase the insurance premiums and administrative costs, but also could not quantify the extent of that increase. HWMG and HMSA indicated that mandating coverage for these services would increase insurance premiums, but that the extent of that increase would be unknown. DHS and OHP did not indicate whether insurance premiums and administrative expenses of policyholders would increase or decrease.

As stated previously beginning on page 15, the utilization of standard fertility preservation services is likely low. A Hawai'i-based gynecologic oncologist estimated less than 100 people per year would qualify for coverage. Additionally, as stated on page 15, over three years, a Hawai'i-based reproductive endocrinology group practice performed a total of 111 standard fertility preservation services for patients with cancer. With such a limited number of people who would qualify for coverage for these services, we believe it is unlikely that premiums would increase beyond a minimal amount.

The impact of this coverage on the total cost of health care. (Section 23-52(2)(E), HRS)

We are unable to determine the impact of coverage for standard fertility preservation services on the total cost of health care. UHA stated that mandating this coverage can be expected to increase the total cost of healthcare but did not clarify the extent of such an increase. Kaiser Permanente, HMSA, HWMG, OHP, and DHS did not provide survey responses regarding the impact of mandating coverage for standard fertility preservation services as defined in SB 1446 on the total cost of health care. In California, the California Health Benefits Review Program estimated that total healthcare expenditures would increase by \$6,773,000 in the state – an increase of 0.0043 percent – as a result of mandating coverage for similar fertility preservation services. According to the California Health Benefits Review Program, 16.9 million Californians would have their insurance expanded, with an estimated price per member, per month cost increase of up to 5 cents.

A Hawai'i-based reproductive endocrinology group practice indicated that the total added cost of healthcare for mandated health insurance coverage for standard fertility preservation services as defined in SB 1446 would be minimal.

Impact of the Patient Protection and Affordable Care Act on SB 1446

The Patient Protection and Affordable Care Act (ACA) provides that states may require that qualified health plans offer benefits in addition to those defined as essential health benefits under the ACA. If a state requires plans sold in the ACA marketplace to cover benefits beyond those defined as essential health benefits under the ACA, the state may be required to defray the costs of those additional benefits.

According to testimony submitted by the Hawai'i Insurance Commissioner on SB 1446, it is unclear whether SB 1446, which would mandate coverage for standard fertility preservation services, would be construed as "in addition to the essential health benefits" under the ACA or be subject to defrayment.

Kaiser Permanente and HMSA both stated that they are unaware of any other insurance mandates passed by the Legislature for which the State is defraying such costs.

Conclusion

Pursuant to Section 23-52, HRS, we have assessed the social and financial effects of mandating health insurance coverage for fertility preservation procedures for certain insured persons who may undergo a medically necessary cancer treatment that may directly or indirectly cause iatrogenic infertility, as provided in SB 1446.

To do this analysis, we had to make numerous and significant assumptions which we described earlier. Additionally, SB 1446 specifically excludes a policyholder's spouse from coverage for standard fertility preservation services as defined by SB 1446 if that spouse is aged 26 years or older. However, we could not separate out policyholders from insureds who are not a policyholder based on the data that we were provided. As a result, we included all insureds, including policyholders, plan members, and policyholders' and plan members' spouses and children, without any age restrictions or limitations in our analysis. If the bill is considered during the upcoming legislative session, we suggest the Legislature consider clarifying those parts of the bill to help insurers as well as the public better understand who, when, and what is covered by the mandate.

Appendix 1

Table on the effects on sperm production in men, by medication, as it appears in the 2006 ASCO Guidelines.

Effect
Prolonged azoospermia
Azoospermia in adulthood after treatment before puberty
Azoospermia likely, but always given with other highly sterilizing agent
Prolonged azoospermia not often observed at indicated dose
Can be additive with above agents in causing prolonged azoospermia, but cause only temporary reductions in sperm count when not combined with above agents
Only temporary reductions in sperm count at doses used in conventional regioments, but additive effects are possible
Unlikely to affect sperm production
No effects on sperm production
Unknown effects on sperm production

Source: 2006 ASCO Guidelines

Appendix 2

Table of the risks of permanent amenorrhea in women, by medication, as it appears in the 2006 ASCO Guidelines.

Degree of Risk	Cancer Treatment
High risk (> 80%)	Hematopoietic stem cell transplantation with cyclophosphamide/total body irradiation or cyclophosphamide/busulfan
	External beam radiation to a field that includes the ovaries
	CMF, CEF, CAF × 6 cycles in women age 40 and older (adjuvant breast cancer therapy with combinations of cyclophosphamide, methotrexate, fluorouracil, doxorubicin, epirubicin)
Intermediate risk	CMF, CEF, CAF × 6 cycles in women age 30- 39 (adjuvant breast cancer therapy with combinations of cyclophosphamide, methotrexate, fluorouracil, doxorubicin, epirubicin)
	AC × 4 in women age 40 and older (adjuvant breast cancer therapy with doxorubicin/cyclophosphamide)
Lower risk (< 20%)	ABVD
	(doxorubicin/bleomycin/vinblastin/dacarbazine CHOP × 4-6 cycles (cyclophosphamide/doxorubicin/vincristine/ prednisone)
	CVP (cyclophosphamide/vincristine/prednisone) AML therapy (anthracycline/cytarabine)
	ALL therapy (multi-agent)
	CMF, CEF, CAF × 6 cycles in women less than 30 (adjuvant breast cancer therapy with combinations of cyclophosphamide, methotrexate, fluorouracil, doxorubicin, epirubicin)
	AC × 4 in women less than 40 (adjuvant breast cancer therapy with doxorubicin/cyclophosphamide)
Very low or no risk	Vincristine
	Methotrexate
	Fluorouracil
Unknown risk (examples)	Taxanes
	Oxaliplatin
	Irinotecan Monoclonal antibodies (trastuzumab, bevacizumab, cetuximab)
	Tyrosine kinase inhibitors (erlotinib, imatinib)
actors, particularly pre-treat nd age determine individu	nes based on best available literature. Additional ment ovarian reserve, specific treatment regimen, al risk for immediate infertility, or for premature tion of menses. Please see text for details.

Source: 2006 ASCO Guidelines