4.02.04	Reproductive Techniques		
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Policy Statement

The following reproductive techniques are considered **medically necessary** for **any** of the following:

- Blastocyst transfer
- Cryopreservation of testicular tissue in adult men with azoospermia as part of an intracytoplasmic sperm injection procedure
- Intracytoplasmic sperm injection for male factor infertility

The following reproductive techniques are considered **investigational** for **any** of the following:

- Assisted hatching
- Co-culture of embryos
- Cryopreservation of ovarian tissue, or oocytes
- Cryopreservation of testicular tissue in prepubertal boys
- Intracytoplasmic sperm injection in the absence of male factor infertility
- Storage and thawing of ovarian tissue, oocytes, or testicular tissue

Policy Guidelines

Coding

The following CPT codes describe procedures that would be routinely performed in all assisted reproductive technology (ART) procedures involving in vitro fertilization (IVF):

- **58970:** Follicle puncture for oocyte retrieval, any method

Either:

- **89250:** Culture of oocyte(s)/embryo(s), less than 4 days
- **89272**: Extended culture of oocyte(s)/embryo(s), 4-7 days

Either:

- **89268**: Insemination of oocytes
- **89280:** Assisted oocyte fertilization, microtechnique; less than or equal to 10 oocytes
- **89281:** Assisted oocyte fertilization, microtechnique; greater than 10 oocytes
- **89260:** Sperm isolation; simple prep (e.g., sperm wash and swim-up) for insemination or diagnosis with semen analysis
- **89261**: Sperm isolation; complex prep (e.g., Percoll gradient, albumin gradient) for insemination or diagnosis with semen analysis
- **89255:** Preparation of embryo for transfer (any method)
- **58974:** Embryo transfer, intrauterine
- **58976:** Gamete, zygote, or embryo intrafallopian transfer, any method

The following CPT codes describe procedures that would *not* be routinely performed in all ART procedures involving IVF:

- **89257:** Sperm identification from aspiration (other than seminal fluid)
- Only performed in patients with oligospermia who have undergone a prior testicular or epididymal aspiration; typically performed as a part of an intracytoplasmic sperm injection procedure (ICSI)
- **89264:** Sperm identification from testis tissue, fresh or cryopreserved. Only performed in patients with oligospermia who have undergone a prior testicular biopsy; typically performed as a part of an ICSI procedure
- **89253:** Assisted embryo hatching, microtechniques (any method). Only performed in women over the age of 40, or in cases in which prior ART attempts resulted in failed implantation
- **89258** Cryopreservation; embryo(s)

- **89259** Cryopreservation; sperm
- **89342**: Storage (per year); embryo(s)
- **89343**: Storage (per year); sperm/semen
- **89344**: Storage (per year); reproductive tissue, testicular/ovarian
- **89346**: Storage (per year); oocyte(s)
- **89352**: Thawing of cryopreserved; embryo(s)
- **89353**: Thawing of cryopreserved; sperm/semen, each aliquot
- **89354**: Thawing of cryopreserved; reproductive tissue, testicular/ovarian
- **89356**: Thawing of cryopreserved; oocytes, each aliquot

The following CPT codes describe procedures that would be routinely performed as part of an intrauterine or intracervical artificial insemination:

- **58321** Artificial insemination; intra-cervical
- **58322** Artificial insemination; intra-uterine
- **58323** Sperm washing for artificial insemination

Note also that "S" codes are available (see Coding section) that describe in vitro fertilization (IVF) globally.

The following codes are available for cryopreservation of oocytes:

- **89337:** Cryopreservation, mature oocyte(s)
- **0357T:** Cryopreservation; immature oocyte(s)

Description

A variety of techniques are available to establish a viable pregnancy for couples who have been diagnosed with infertility and for whom assisted insemination has been unsuccessful.

Related Policies

- Preimplantation Genetic Testing

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

There are no medical devices or diagnostic tests related to assisted reproductive technologies that require U.S. Food and Drug Administration approval or clearance.

Rationale

Background

Infertility

Infertility can be due either to female factors (i.e., pelvic adhesions, ovarian dysfunction, endometriosis, prior tubal ligation), male factors (i.e., abnormalities in sperm production, function, or transport or prior vasectomy), a combination of male and female factors, or unknown causes.

Treatment

Various reproductive techniques are available to establish a viable pregnancy; different techniques are used depending on the reason for infertility. Assisted reproductive technologies (ARTs), as defined by the Centers for Disease Control and Prevention and other organizations, refer to fertility treatments in which both the eggs and sperm are handled. Not included in assisted reproduction is assisted insemination (artificial insemination) using sperm from either a woman's partner or a sperm donor. In most instances, assisted reproduction will involve in vitro fertilization, a procedure in which oocytes harvested from the female are inseminated in vitro with sperm harvested from the male. Following the fertilization procedure, the zygote is cultured and ultimately transferred back into the female's uterus or fallopian tubes. In some instances, the oocyte and sperm are collected, but no in vitro fertilization takes place, and the gametes are reintroduced into the fallopian tubes. Examples of ARTs include, but are not limited to, gamete intrafallopian transfer, transuterine fallopian transfer, natural oocyte retrieval with intravaginal fertilization, pronuclear state tubal transfer, tubal embryo transfer, zygote intrafallopian transfer, gamete and embryo cryopreservation, oocyte and embryo donation, and gestational surrogacy.

The various components of ART and implantation into the uterus can be broadly subdivided into oocyte harvesting procedures, which are performed on the female partner; sperm collection procedures, which are performed on the male partner; and the in vitro component (i.e., the laboratory procedures), which are performed on the collected oocyte and sperm. The final step is the implantation procedure.

Most CPT codes describing the various steps in ART procedures are longstanding. They include codes for oocyte retrieval, sperm isolation, culture and fertilization of the oocyte, and embryo; zygote; or gamete transfer into the uterus or fallopian tubes. Only the relatively new reproductive techniques (i.e., intracytoplasmic sperm injection, assisted hatching, co-culture of embryos) and cryopreservation of reproductive tissue (i.e., testicular, ovarian, oocytes) will be considered within this evidence summary.

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be

adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Assisted Hatching
Implantation of the embryo in the uterus is a key component of success with in vitro fertilization (IVF). Although the exact steps in implantation are poorly understood, normal rupture of the surrounding zona pellucida with escape of the developing embryo (termed hatching) is crucial. Mechanical disruption of the zona pellucida (i.e., assisted hatching) has been proposed as a mechanism to improve implantation rates.

Clinical Context and Therapy Purpose
The purpose of IVF with assisted hatching in patients with infertility is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does IVF with assisted hatching treat infertility and improve the net health outcome?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is patients who are infertile.

Interventions
The therapy being considered is IVF with assisted hatching.

Comparators
The following practice is currently being used to make decisions about infertility: IVF without assisted hatching.

Outcomes
The general outcomes of interest are live birth rates and infant abnormalities.

Timing
Follow-up is measured in weeks to confirm a successful pregnancy and months to confirm a successful birth.

Setting
Patients with infertility are actively managed by gynecologists, endocrinologists, and primary care providers in an outpatient setting.

Systematic Reviews
A Cochrane review and meta-analysis by Carney et al (2012) identified 31 RCTs evaluating assisted hatching (total N=5728 individuals).[1] Twelve studies included women with a poor fertility prognosis, 12 studies included women with a good fertility prognosis, and the remaining 7 studies did not report this factor. Fifteen studies used a laser for assisted hatching, 11 used chemical means, and 5 used mechanical means. Live birth rates were reported in 9 studies (n=1921 women). A pooled analysis of data from the 9 studies did not find a statistically significant difference between the groups receiving assisted hatching and a control condition (odds ratio [OR], 1.03; 95% confidence interval [CI], 0.85 to 1.26). The rate of live birth was 313 (31%) of 995 in the assisted hatching group and 282 (30%) of 926 in the control group. All 31 trials reported clinical pregnancy rates. In a meta-analysis of all trials, assisted hatching improved the pregnancy rate, but the estimate for the odds was marginally statistically significant (OR=1.13; 95% CI, 1.01 to 1.27).

Randomized Controlled Trials

Two RCTs not assessed in the Cochrane review have compared laser-assisted hatching with the standard of care. Shi et al (2016) evaluated 178 patients of advanced maternal age (age range, 35-42 years).[2] There were no statistically significant differences in implantation rates (32.5% in the assisted hatching group vs 39.3% in the control group) or in clinical pregnancy rates (48.8% in the assisted hatching group vs 50.4% in the control group; p values not reported). Kanyo et al (2016) assessed 413 women (mean age, 33 years).[3] In the overall study population, there was no statistically significant difference in the clinical pregnancy rate between the assisted hatching group (33.3%) and the control group (27.4%; p=0.08). However, in the subgroup of patients ages 38 or older, the clinical pregnancy rate was significantly higher in the assisted hatching group (18.4%) than in the control group (11.4%; p=0.03). There was no significant between-group difference in clinical pregnancy rate among women younger than 38 years old. The age groupings (i.e., <38 years vs ≥38 years) were not specifically discussed as a prespecified subgroup analysis. Neither trial reported live birth rates.

Retrospective Studies

Knudtson et al (2017), in a retrospective cohort study, analyzed live birth rates in women who underwent first-cycle, autologous frozen embryo transfer.[4] From data reported between 2004 and 2013 to the Society for Assisted Reproductive Technology Clinic Outcomes Reporting System, 151,533 cycles were identified, 70,738 (46.7%) with assisted hatching and 80,795 (53.3%) without. Assisted hatching had a significantly lower live birth rate (34.2%) than nonassisted hatching (35.4%; p<0.001). Also, older patients (age ≥38 years) who received assisted hatching were associated with lower live birth rates (p≤0.05). The study was limited by the retrospective nature of the database, incomplete data, and the inability due to deidentification to link thawed cycles to original retrieval and insemination techniques.

Kissin et al (2014) retrospectively reviewed data on assisted hatching in the United States from 2000 to 2010.[5] Data were taken from the Centers for Disease Control and Prevention's National Assisted Reproductive Technology Surveillance System. The analysis of outcomes was limited to fresh autologous IVF cycles for which a transfer was performed on day 3 or 5. For the total patient population (N=536,852), rates of implantation, clinical pregnancy, and live births were significantly lower when assisted hatching was used. For example, the live birth rate was 28.3% with assisted hatching and 36.5% without (adjusted odds ratio [AOR], 0.75; 95% CI, 0.70 to 0.81). Moreover, the rate of miscarriage was significantly higher when assisted hatching was used (18.0% vs 13.5%; AOR=1.43; 95% CI, 1.34 to 1.52).

Section Summary: Assisted Hatching

The available literature has generally not found better outcomes with assisted hatching than with standard of care. A 2012 Cochrane review of heterogeneous RCTs found that clinical pregnancy rates but not the live birth rates improved with assisted hatching. In subsequent RCTs, laser-assisted hatching did not improve the clinical pregnancy rate but, in 1 study, there was a higher rate of clinical pregnancy in the subgroup of women 38 years or older. In addition, analysis of a large national database found better outcomes (e.g., clinical pregnancy and live birth rates) when assisted hatching was not used.

Embryo Co-Culture

In routine IVF procedures, the embryo is transferred to the uterus on day 2 or 3 of development, when it has between 4 and 8 cells. Embryo co-culture techniques, used successfully in domestic animals, represent an effort to improve the culture media for embryos such that a greater proportion of embryos will reach the blastocyst-stage, in an attempt to improve implantation and pregnancy rates. In addition, if co-culture results in a higher implantation rate, fewer embryos could be transferred in each cycle, decreasing the incidence of multiple pregnancies. A variety of co-culture techniques have been investigated involving the use of feeder cell layers derived from a range of tissues, including the use of human reproductive tissues (i.e., oviducts) to nonhuman cells (i.e., fetal bovine uterine or oviduct cells) to established cell lines (i.e., Vero cells or bovine kidney cells).

Clinical Context and Therapy Purpose
The purpose of IVF with embryo co-culture in patients with infertility is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does IVF with embryo co-culture to treat infertility improve the net health outcome?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is patients who are infertile.

Interventions
The therapy being considered is IVF with embryo co-culture.

Comparators
The following practice is currently being used to make decisions about infertility: IVF without embryo co-culture.

Outcomes
The general outcomes of interest are live birth rates and infant abnormalities.

Timing
Follow-up is measured in weeks to confirm a successful pregnancy and months to confirm a successful birth.

Setting
Patients with infertility are actively managed by gynecologists, endocrinologists, and primary care providers in an outpatient setting.

Randomized Controlled Trials
Currently, no standardized method of co-culture has emerged, and clinical trials have generally not found that co-culture is associated with an improved implantation or pregnancy rates.[6-11] For example, Wetzels et al (1998) reported on an RCT that assigned IVF treatments to co-culture with human fibroblasts or no culture.[11] Patients in the 2 groups were stratified by age (older or younger than 36 years) and prior IVF attempts (yes vs no). The trialists reported that fibroblast co-culture did not affect the implantation or pregnancy rates. More recently, Ohl et al (2015) reported on a novel co-culture technique involving autologous endometrial cell co-culture.[12] In an interim analysis of 320 patients, the clinical pregnancy rate per embryo transfer was significantly higher in the co-culture group (53.4%) than in the control group (37.3%; p=0.025).

Section Summary: Embryo Co-Culture
There is no standardized method of co-culture, and few clinical trials have evaluated outcomes. Most have not found improved implantation or pregnancy rates after co-culture. A 2015 RCT has reported on a novel co-culture method and an interim analysis of the trial found a higher clinical pregnancy rate with co-culture than with standard practice control group. Additional studies are needed to evaluate this novel co-culture technique. No studies have reported on the impact of co-culture on live birth rates.

Cryopreservation of Ovarian Tissue
Clinical Context and Therapy Purpose
The purpose of cryopreservation of ovarian tissue in patients with cancer who will undergo treatment that could precipitate infertility is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the cryopreservation of ovarian tissue treat infertility and improve the net health outcome?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is cancer patients who undergo treatment that could precipitate infertility.

Interventions
The therapy being considered is cryopreservation of ovarian tissue.

Comparators
The following practice is currently being used to make decisions about infertility: cryopreservation of embryos, but not of ovarian tissue.

Outcomes
The general outcomes of interest are live birth rates and infant abnormalities.

Timing
Follow-up is measured in weeks to confirm a successful pregnancy and months to confirm a successful birth.

Setting
Patients with cancer who will undergo treatment that might lead to infertility are actively managed by an oncologist, gynecologists, endocrinologists, and primary care providers in an outpatient setting.

Case Series
Cryopreservation of ovarian tissue or an entire ovary with subsequent auto- or heterotopic transplant has been investigated as a technique to sustain the reproductive function of women or children who are faced with sterilizing procedures, such as chemotherapy, radiotherapy, or surgery, frequently due to malignant diseases. There are a few case reports assessing the return of ovarian function using this technique.[13,14] There are also case series describing live births using cryopreserved ovarian tissue.[15-17] However, in general, the technique is not standardized and insufficiently studied to determine the success rate.[18,19] Johnson and Patrizio (2011) commented on whole ovary freezing as a fertility preservation technique in women with disease or disease treatment that threaten their reproductive tract function.[20] They concluded: "Although theoretically optimal from the point of view of maximal follicle protection and preservation, the risks and difficulties involved in whole ovary freezing limit this technique to experimental situations."

Section Summary: Cryopreservation of Ovarian Tissue
As a technique, cryopreservation of ovarian tissue has not been standardized, and there are insufficient published data that this reproductive technique is effective and safe.

Cryopreservation of Oocytes
Cryopreservation of oocytes has been examined as a fertility preservation option for reproductive-age women undergoing cancer treatment. The mature oocyte is very fragile due to its large size, high water content, and chromosomal arrangement. For example, the mature oocyte is arrested in meiosis, and as such, the chromosomes are aligned in a meiotic spindle. This spindle is easily damaged in freezing and thawing. Survival after thawing may also be associated with sublethal damage, which may further impact on the quality of the subsequent embryo. Moreover, due to a large amount of water when the oocyte is frozen, ice crystals may form that can damage the integrity of the cell. To reduce or prevent ice crystals, oocytes are dehydrated using cryoprotectants, which replace the water in the cell. There are 2 primary

approaches to cryopreservation: a controlled-rate slow-cooling method and a flash-freezing process known as vitrification. Vitrification, the newer method, is faster and requires a higher concentration of cryoprotectants.

Clinical Context and Therapy Purpose
The purpose of cryopreservation of oocytes in cancer patients who will undergo treatment that might precipitate infertility is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does the cryopreservation of oocytes treat infertility improve and the net health outcome?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is cancer patients who undergo treatment that might precipitate infertility.

Interventions
The therapy being considered is cryopreservation of oocytes.

Comparators
The following practice is currently being used to make decisions about infertility: cryopreservation of embryos, but not of ovarian tissue.

Outcomes
The general outcomes of interest are live birth rates and infant abnormalities.

Timing
Follow-up is measured in weeks to confirm a successful pregnancy and months to confirm a successful birth.

Setting
Patients with cancer who will undergo treatment that may lead to infertility are actively managed by an oncologist, gynecologists, endocrinologists, and primary care providers in an outpatient setting.

Systematic Reviews
The American Society for Reproductive Medicine and Society for Assisted Reproductive Technology (2013) updated their joint guidelines on mature oocyte cryopreservation.[21] A systematic review of the literature, conducted as part of guideline development, identified 4 RCTs comparing outcomes of assisted reproduction with cryopreserved and fresh oocytes. All trials were conducted in Europe and none among patients who desired to preserve fertility after medical treatment (e.g., chemotherapy). In these studies, fertilization rates ranged from 71% to 79%, and the clinical pregnancy rates per transfer ranged from 36% to 61%. The largest RCT (N=600) cited in the guidelines was published by Cobo et al (2010) in Spain.[22] This trial included oocyte recipients between 18 and 49 years of age who had failed fewer than 3 previous IVF attempts. The primary outcome was the ongoing pregnancy rate; this was defined as the presence of at least 1 viable fetus 10 to 11 weeks after embryo transfer. In an intention-to-treat analysis, the ongoing pregnancy rate was 43.7% in the vitrification group and 41.7% in the fresh oocyte group. Vitrification was considered noninferior to fresh oocyte transfer according to a prespecified margin of difference. The guidelines noted that the available data might not be generalizable to the United States, to clinics with less experience with these techniques, or to other populations (e.g., older women, cancer patients). The authors stated that data from the United States are available only from a few clinics and report on young highly select populations. Pregnancy outcomes and rates of congenital anomalies were not discussed.

Observational Studies
After the American Society for Reproductive Medicine and Society for Assisted Reproductive Technology guidelines were released, Levi Setti et al (2013) in Italy published an observational study.[23] This study compared outcomes in pregnancies achieved with fresh or frozen oocytes. The investigators identified 855 patients in an Italian database who had become pregnant using fresh and/or cryopreserved and thawed oocytes. The authors did not state the reasons for a desire for fertility preservation. The 855 patients had a total of 954 clinical pregnancies; 197 were obtained with frozen oocytes and 757 with fresh oocytes. There were 687 pregnancies from fresh cycle oocytes only, 129 pregnancies with frozen oocytes only, and 138 pregnancies from both fresh and frozen oocyte cycles. The live birth rate was 68% (134/197) from frozen and thawed oocytes and 77% (584/757) fresh oocyte cycles. The live birth rate was significantly higher after fresh cycle oocytes (p=0.008).

Section Summary: Cryopreservation of Oocytes
There are insufficient published data on the safety and efficacy of cryopreservation of oocytes; and data are only available from select clinical settings, generally outside of the United States. Moreover, there is a lack of published data on success rates with cryopreserved oocytes in women who froze oocytes because they were undergoing chemotherapy. Data on health outcomes (e.g., clinical pregnancy rate, live birth rate) in the population of interest are needed.

Blastocyst Transfer
The most common days for embryo transfer in the clinical IVF setting are day 3 or day 5. Embryo transfer at the blastocyst-stage on day 5 continues to be less common than cleavage-stage transfer on day 3. First introduced in clinical practice in 2005, use of blastocyst transfer is increasing in clinical practice. The rationale and reported advantages for blastocyst transfer are: higher implantation and clinical pregnancy rates, a more viable option for limiting to single embryo transfer, more appropriate endometrium-embryo synchronicity, optimization of embryo selection due to embryo development progression, and decreased potential for embryo trauma with biopsy obtained for preimplantation genetic testing. Advances in cell culture techniques and embryology assessments have facilitated an increased use of blastocyst transfer and research into the technique. Critics of blastocyst transfer have raised concerns about the limitation on the number of available embryos for transfer once the cleavage-stage is passed; critics also cite concerns due to uncertainties about the effects of the culture microenvironment, as well as early indicators of a higher rate of adverse pregnancy outcomes.

Clinical Context and Therapy Purpose
The purpose of IVF with blastocyst transfer in patients with infertility is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does IVF with blastocyst transfer treat infertility and improve the net health outcome?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is patients who are infertile.

Interventions
The therapy being considered is IVF with blastocyst transfer.

Comparators
The following practice is currently being used to make decisions about infertility: IVF without cleavage-stage transfer.

Outcomes
The general outcomes of interest are live birth rates and infant abnormalities.

Timing
Follow-up is measured in weeks to confirm a successful pregnancy and months to confirm a successful birth.

Setting
Patients with infertility are actively managed by gynecologists, endocrinologists, and primary care providers in an outpatient setting.

Systematic Reviews
Several systematic reviews of studies comparing outcomes associated with blastocyst-stage transfer with those of earlier stage transfer have been published. Only the Cochrane review by Glujovsky et al (2012) included RCTs.[24] They identified 23 RCTs, 12 of which reported on the rates of live births per couple. A pooled analysis of these trials found a significantly higher live birth rate with blastocyst transfer (292/751 [39%]) than with cleavage-stage transfer (237/759 [31%]). The odds for live birth was 1.40 (95% CI, 1.13 to 1.74). There was no significant difference in the rate of multiple pregnancies between the 2 treatment groups (16 RCTs; OR=0.92; 95% CI, 0.71 to 1.19). In addition, there was no significant difference in the miscarriage rate (14 RCTs; OR=1.14; 95% CI, 0.84 to 1.55). Glujovsky et al (2016), in their updated Cochrane review, placed more emphasis on whether blastocyst-stage (day 5-6) embryo transfers improved the live birth rates, and other associated outcomes, compared with cleavage-stage (day 2-3) embryo transfers.[25] Data from 4 new studies, 3 of which were published studies[26-28] and resulted in a total of 27 parallel-design RCTs that included 4031 couples or women. The data from a fourth study was only available in abstract form and reported on outcomes from a multicenter trial comparing blastocyst with day 2-3 transfer in intracytoplasmic sperm injection (ICSI) cycles for male factor infertility. There were no exclusions from the 2012 review. The live birth rate following fresh transfer was higher in the blastocyst transfer group (OR=1.48; 95% CI, 1.20 to 1.82; 13 RCTs, 1630 women, I^2=45%, low-quality evidence). There was no evidence of a difference between groups in rates of cumulative pregnancy per couple following fresh and frozen-thawed transfer after 1 oocyte retrieval (OR=0.89; 95% CI, 0.64 to 1.22; 5 RCTs, 632 women, I^2=71%, very low quality evidence). The clinical pregnancy rate was also higher in the blastocyst transfer group, following fresh transfer (OR=1.30; 95% CI, 1.14 to 1.47; 27 RCTs, 4031 women, I^2=56%, moderate-quality evidence). Embryo freezing rates were lower in the blastocyst transfer group (OR=0.48; 95% CI, 0.40 to 0.57; 14 RCTs, 2292 women, I^2=84%, low-quality evidence). Failure to transfer any embryos was higher in the blastocyst transfer group (OR=2.50; 95% CI, 1.76 to 3.55; 17 RCTs, 2577 women, I^2=36%, moderate-quality evidence). The data for rates of multiple pregnancy and miscarriage were incomplete in 70% of the trials and limit conclusions concerning the following findings. There was no evidence of a difference between the groups in rates of multiple pregnancies (OR=1.05, 95% CI, 0.83 to 1.33; 19 RCTs, 3019 women, I^2=30%, low-quality evidence) or miscarriages (OR=1.15, 95% CI, 0.88 to 1.50; 18 RCTs, 2917 women, I^2=0%, low-quality evidence). Reviewers reported that the main limitation of the RCTs assessed was a high risk of bias, which was associated with failure to describe acceptable methods of randomization and unclear or high risk of attrition bias.

Maheshwari et al (2013) identified 8 observational studies analyzing singleton births following embryo transfer at the blastocyst or cleavage stage and reporting obstetric and/or perinatal outcomes.[29] Meta-analysis of 6 studies found a significantly higher rate of preterm delivery at less than 37 weeks after blastocyst-stage transfer compared with cleavage-stage transfer (relative risk, 1.27; 95% CI, 1.22 to 1.31); the absolute increase in risk was 2% (95% CI, 1% to 4%). Other pooled analyses of 2 to 3 studies each did not find significantly increased rates of low birth weight less than 1500 grams, congenital anomalies, or perinatal mortality following blastocyst-stage vs cleavage-stage embryo transfer.

Observational Studies
A retrospective cohort study by Kallen et al (2010) reported on risks associated with blastocyst transfer.[30] Data were taken from the Swedish Medical Birth Register. There were 1311 infants born after blastocyst transfer and 12,562 born after cleavage-stage transfer. There were no significant differences in the rates of multiple births (10% after blastocyst transfer vs 8.9% after cleavage-

stage transfer). Among singleton births, the rate of preterm birth (<32 weeks) was 1.7% (18/1071) in the blastocyst transfer group and 1.35% (142/10513) in the cleavage-stage transfer group. In a multivariate analysis controlling for year of birth, maternal age, parity, smoking habits, and body mass index, the AOR was 1.44 (95% CI, 0.87 to 2.40). The rate of low birth weight singletons (<1500 g or <2500 g) did not differ significantly between the blastocyst transfer group and the cleavage-stage transfer group. There was a significantly higher rate of relatively severe congenital malformation (e.g., spina bifida, cardiovascular defects, cleft palate) after blastocyst transfer (61/1311 [4.7%]) than after cleavage-stage transfer (509/12,562 [4.1%]; AOR=1.33; 95% CI, 1.01 to 1.75). The groups did not differ significantly in their rates of low Appearance, Pulse, Grimace, Activity and Respiration scores, intracranial hemorrhage rates, respiratory diagnoses, or cardiovascular malformations. Respiratory diagnoses were given to 94 (7.2%) of 1311 infants born after blastocyst transfer and to 774 (6.2%) of 12,562 after cleavage-stage transfer (OR=1.15; 95% CI, 0.90 to 1.47).

Ginström Ernstad et al (2016) published another retrospective registry cohort study using data crosslinked across the Swedish Medical Birth Register, the Register of Birth Defects, and the National Patient Register.[31] All singleton deliveries after blastocyst transfer in Sweden from 2002 through 2013 were compared with deliveries after cleavage-stage transfer and deliveries after spontaneous conception. There were 4819 singletons born after blastocyst transfer, 25,747 after cleavage-stage transfer, and 1,196,394 after spontaneous conception. Singletons born after blastocyst transfer had no increased risk of birth defects compared with singletons born after cleavage-stage transfer (AOR=0.94; 95% CI, 0.79 to 1.13) or spontaneous conception (AOR=1.09; 95% CI, 0.92 to 1.28). Perinatal mortality was higher in the blastocyst group vs the cleavage-stage group (AOR=1.61; 95% CI, 1.14 to 2.29). When comparing singletons born after blastocyst transfer with singletons born after spontaneous conception, a higher risk of preterm birth (<37 weeks) was detected (AOR=1.17; 95% CI, 1.05 to 1.31). Singletons born after blastocyst transfer had a lower rate of low birthweight (AOR=0.83; 95% CI, 0.71 to 0.97) than singletons born after cleavage-stage transfer. The rate of being small for gestational age was also lower in singletons born after blastocyst transfer than after both cleavage-stage conception (AOR=0.71; 95% CI, 0.56 to 0.88) and spontaneous conception (AOR=0.70; 95% CI, 0.57 to 0.87). The risks of placenta previa and placental abruption were higher in pregnancies after blastocyst transfer than in pregnancies after cleavage-stage (AOR=2.08; 95% CI, 1.70 to 2.55; AOR=1.62; 95% CI, 1.15 to 2.29, respectively) and after spontaneous conception (AOR=6.38; 95% CI, 5.31 to 7.66; AOR=2.31; 95% CI, 1.70 to 3.13, respectively).

Section Summary: Blastocyst Transfer
An updated 2016 Cochrane review of 27 RCTs compared the effectiveness of blastocyst transfers with cleavage-stage transfers. The primary outcomes of live birth and cumulative clinical pregnancy rates were higher with fresh blastocyst transfer. There were no differences between groups in multiple pregnancies or early pregnancy loss (miscarriage). The main limitation of the RCTs evaluated in the Cochrane review was a high risk of bias associated with failure to describe acceptable methods of randomization and unclear or high risk of attrition bias. Differences in outcomes with the use of cryopreserved blastocysts and cleavage-stage embryos have been reported, and the mechanisms are not well-understood. There are conflicting reports from retrospective studies on the incidence of pregnancy and neonatal adverse outcomes, including low birth weight and increased congenital anomalies.

ICSI for Male Factor Infertility
ICSI is performed in cases of male factor infertility (MFI) when either insufficient numbers of sperm, abnormal sperm morphology, or poor sperm motility preclude unassisted IVF. Fertilization rates represent an intermediate outcome; the final outcome is the number of pregnancies per initiated cycle or per embryo transfer.

Clinical Context and Therapy Purpose
The purpose of IVF with ICSI in patients with MFI is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does IVF with ICSI treat MFI and improve the net health outcome?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is men with MFI.

Interventions
The therapy being considered is IVF with ICSI.

Comparators
The following practice is currently being used to make decisions about infertility: IVF without ICSI.

Outcomes
The general outcomes of interest are live birth rates and infant abnormalities.

Timing
Follow-up is measured in weeks to confirm a successful pregnancy and months to confirm a successful birth.

Setting
Patients with MFI are actively managed by gynecologists, endocrinologists, and primary care providers in an outpatient setting.

Case Series
The number of pregnancies per cycle and per embryo transfers, reported in relatively large series published in the mid-1990s, ranged between 45% and 50%.[32-36] At the time, those rates were very competitive with those of the standard IVF.

More recently, Borges et al (2017) retrospectively analyzed ICSI outcomes for patients with MFI compared with isolated tubal factor infertility (TFI).[37] Nine hundred twenty-two ICSI cycles (743 for MFI, 179 for TFI) performed between 2010 and 2016 were identified. No significant differences were observed between the groups for rates of implantation (MFI=35.5% vs TFI=32%, p=0.34), pregnancy (MFI=46.9% vs TFI=40.9%, p=0.184), and miscarriage (MFI 10.3% vs TFI 10.6%, p=0.572); rates remained similar even after women were stratified into groups by age (≤35 years: MFI=531 vs TFI=112; >35 years: MFI=212 vs TFI=67). The study was limited by its retrospective design and by the fact that MFI severity could not be determined because patients were not categorized by diagnosis.

Boulet et al (2015) published a large retrospective analysis of the outcomes following ICSI vs standard IVF (data captured from the Centers for Disease Control and Prevention's National Assisted Reproductive Technology Surveillance System from 2008 to 2012).[38] During that time, there were data on 494,907 fresh IVF cycles. A total of 74.6% of cycles used ICSI, with 92.9% of the cycles involving MFI and 64.5% of the cycles not. Among couples with MFI, there was a statistically significantly lower rate of implantation after ICSI (25.5%) than after standard IVF (25.6%; p=0.02); however, this difference between groups was not clinically significant. Rates of clinical intrauterine pregnancy and live birth did not differ significantly between ICSI and standard IVF. In couples without MFI, implantation, clinical pregnancy, and live birth rates were all significantly higher with standard IVF than with ICSI.

Adverse Events
A systematic review and meta-analysis by Massaro et al (2015) examined adverse events related to ICSI and standard IVF without ICSI.[39] Twenty-two observational studies were included; no RCTs were identified. Meta-analysis of 12 studies found a significantly increased odds of congenital genitourinary malformations in children conceived using ICSI vs standard IVF (pooled

OR=1.27; 95% CI, 1.02 to 1.58; p=0.04; I^2=0). Five studies in this analysis were considered at high risk of bias, and a pooled analysis of the 4 studies considered at low risk of bias did not determine whether ICSI was associated with a statistically increased odds of genitourinary malformations.

Section Summary: ICSI for Male Factor Infertility
There is a lack of RCTs comparing ICSI with standard IVF. Observational studies have found similar rates of clinical pregnancy and live births after ICSI and standard IVF, but those observational studies are subject to limitations (e.g., selection bias). A 2015 meta-analysis of observational studies found a significantly higher rate of congenital genitourinary malformations in children born after ICSI vs IVF, but there was no significant difference when only studies with low risk of bias were analyzed. RCTs comparing health outcomes after ICSI for MFI with standard IVF would strengthen the evidence base.

Cryopreservation of Testicular Tissue in Adult Men with Azoospermia
Testicular sperm extraction refers to the collection of sperm from testicular tissue in men with azoospermia. Extraction of testicular sperm may be performed during or subsequent to a diagnostic biopsy, specifically for the collection of spermatozoa. Spermatozoa may be isolated immediately and a portion used for an ICSI procedure during oocyte retrieval from the partner, with the remainder cryopreserved. Alternatively, the entire tissue sample can be cryopreserved with portion thawed and sperm isolation performed at subsequent ICSI cycles.

Clinical Context and Therapy Purpose
The purpose of the cryopreservation of testicular tissue as part of ICSI in patients with azoospermia is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does cryopreservation of testicular tissue as part of ICSI treat azoospermia and improve the net health outcome?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is men who are infertile.

Interventions
The therapy being considered is cryopreservation of testicular tissue as part of ICSI.

Comparators
The following practice is currently being used to make decisions about infertility: IVF without cryopreservation of testicular tissue.

Outcomes
The general outcomes of interest are live birth rates and infant abnormalities.

Timing
Follow-up is measured in weeks to confirm a successful pregnancy and months to confirm a successful birth.

Setting
Patients with azoospermia are actively managed by endocrinologists, primary care providers, and urologists in an outpatient setting.

Case Series
Testicular tissue extraction appears to be a well-established component of the overall ICSI procedure; cryopreservation of either the isolated sperm or the tissue sample eliminates the need for multiple biopsies to obtain fresh tissue in the event of a failed initial ICSI cycle.[40]

However, clinical trials evaluating health outcomes after cryopreservation of testicular tissue in adult men with azoospermia were not identified.

Section Summary: Cryopreservation of Testicular Tissue in Adult Men with Azoospermia
While cryopreservation of testicular tissue in adult men with azoospermia is a well-established component of the ICSI procedure, there is a lack of clinical trials to support this treatment.

Cryopreservation of Testicular Tissue in Prepubertal Boys with Cancer
A potential application of cryopreservation of testicular tissue is its potential to preserve the reproductive capacity in prepubertal boys undergoing cancer chemotherapy; cryopreservation of an ejaculate is not an option in these patients.

Clinical Context and Therapy Purpose
The purpose of the cryopreservation of testicular tissue in prepubertal boys with cancer is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does cryopreservation of testicular tissue from prepubertal boys with cancer improve the net health outcome?

The following PICOTS were used to select literature to inform this review.

Patients
The relevant population of interest is prepubertal boys with cancer.

Interventions
The therapy being considered is the cryopreservation of testicular tissue.

Comparators
The following practice is currently being used to make decisions about infertility: no cryopreservation of testicular tissue.

Outcomes
The general outcomes of interest are live birth rates and infant abnormalities.

Timing
Follow-up is measured in weeks to confirm a successful pregnancy and months to confirm a successful birth.

Setting
Prepubertal boys with cancer are actively managed by endocrinologists, primary care providers, and urologists in an outpatient setting.

Modeling Studies
It has been hypothesized that reimplantation of the frozen-thawed testicular stem cells will reinitiate spermatogenesis or, alternatively, spermatogenesis could be attempted in vitro, using frozen-thaw spermatogonia. While these strategies have been explored in animals, there are inadequate human studies.[41,42]

Section Summary: Cryopreservation of Testicular Tissue in Prepubertal Boys with Cancer
No clinical trials were identified evaluating the safety and efficacy of cryopreservation of testicular tissue in prepubertal boys undergoing cancer therapy.

Potential Adverse Events to Offspring Conceived Via Assisted Reproduction
Systematic Reviews
Several systematic reviews have addressed the risk of birth defects.[43-46] A systematic review by Kettner et al (2015) considered potential adverse events in children of various ages.[43] Reviewers

included controlled studies reporting at least 1 postnatal morbidity outcome in children who were and were not conceived using assisted reproductive. Twenty studies met the eligibility criteria; 30 were cohort studies, and 8 were case-control studies. There were no strong, consistent associations between use of reproductive techniques and childhood disease. For example, no statistically significant differences were found in rates of the following in children conceived spontaneously or with ART: chronic diseases (2 studies), cancer (3 studies), and allergic disease (5 studies). Findings were mixed on the risk of infectious and parasitic diseases. In the 8 studies examining this outcome, the odds varied between 0.37 and 5.7, and most results were not statistically significant. Rates of asthma or obstructive bronchitis were examined in 8 studies; 3 found significantly increased risk in children conceived by ART vs conceived spontaneously. The review with the most data is that by Hansen et al (2013).[45] They examined 45 cohort studies with outcomes in 92,671 infants born following assisted reproduction and 3,870,760 naturally conceived infants. In a pooled analysis, there was a higher risk of birth defects in infants born using reproductive techniques (relative risk, 1.32; 95% CI, 1.24 to 1.42). The risk of birth defects was also elevated when the analysis was limited to the 6 studies conducted in the United States or Canada (relative risk, 1.38; 95% CI, 1.16 to 1.64). Another review, published by Davies et al (2012), included data on 308,974 live births in Australia, 6163 of which used ART.[46] There was a higher rate of birth defects after assisted conception (8.3%) compared with births to fertile women who did not use assisted reproduction (5.8%; unadjusted OR=1.47; 95% CI, 1.33 to 1.62). The risk of birth defects was still significantly elevated but was lower in an analysis that adjusted for other factors that might increase risk (e.g., maternal age, parity, maternal ethnicity, maternal smoking during pregnancy, socioeconomic status; OR=1.28; 95% CI, 1.16 to 1.41).

Registry Studies
A Danish registry study by Bay et al (2013) addressed the risk of childhood and adolescent mental disorders following assisted reproduction.[47] The study included 524 children born after IVF or ICSI and 22,009 children born after spontaneous conception. In an analysis adjusted for potential confounders, compared with spontaneously conceived children, there were no statistically significant increases in mental disabilities, disorders of psychological development (e.g., autism spectrum disorders, speech and language disorders, others), attention-deficit/hyperactivity disorder or conduct, emotional, or social disorders.

Summary of Evidence
For individuals who have infertility who receive IVF with assisted hatching, the evidence includes RCTs, a systematic review, and retrospective studies. Relevant outcomes are health status measures and treatment-related morbidity. RCTs have not shown that assisted hatching improves the live birth rate compared with standard care. Clinical pregnancy rates after assisted hatching have been mixed, but RCTs have generally not found improvements in assisted hatching vs standard care. A large observational study found that assisted hatching was associated with worse outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have infertility who receive IVF with embryo co-culture, the evidence includes RCTs and case series. Relevant outcomes are health status measures and treatment-related morbidity. Most clinical trials have not found improved implantation or pregnancy rates after co-culture, and studies have not reported live birth rates. Moreover, co-culture techniques have not been standardized. One RCT did report a higher clinical pregnancy rate with co-culture than with a standard practice control group, however, the process was novel and not yet fully evaluated. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have cancer who will undergo treatment that may lead to infertility who receive cryopreservation of ovarian tissue, the evidence includes case series that have reported on the technique as well as pregnancy and live birth rates after transplantation. Relevant outcomes are health status measures and treatment-related morbidity. The technique used has not been standardized, and there is a lack of controlled studies on health outcomes following

cryopreservation of ovarian tissue. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have cancer who will undergo treatment that may lead to infertility who receive cryopreservation of oocytes, the evidence includes RCTs and a systematic review assessing the technique in related populations. Relevant outcomes are health status measures and treatment-related morbidity. The systematic review found that fertilization rates ranged from 71% to 79%, and the clinical pregnancy rates per transfer ranged from 36% to 61%. The available studies have been conducted in highly select populations and may not be generalizable to the population of interest, women with cancer. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have infertility who receive IVF with blastocyst transfer, the evidence includes RCTs and meta-analyses. Relevant outcomes are health status measures and treatment-related morbidity. The RCTs and meta-analyses have found that blastocyst transfer is associated with higher live birth rates than cleavage-stage transfer. One retrospective cohort study has reported a significantly higher rate of preterm birth after blastocyst-stage vs cleavage-stage transfer and did not find increased risks of other outcomes such as low birth rate or perinatal mortality. A retrospective registry review of a similar population reported different findings. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have male factor infertility who receive IVF with ICSI, the evidence includes observational studies and a systematic review. Relevant outcomes are health status measures and treatment-related morbidity. No RCTs are available. Observational studies, which are subject to design limitations (e.g., selection bias), have found similar rates of clinical pregnancy and live birth after ICSI and standard IVF, and a meta-analysis of observational studies found a higher rate of genitourinary malformations in children born after ICSI (but only when lower quality studies were included in the analysis). Multiple RCTs are needed to compare health outcomes after ICSI for male factor infertility and standard IVF. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have azoospermia who receive cryopreservation of testicular tissue as part of ICSI, the evidence includes no clinical trials. Relevant outcomes are health status measures and treatment-related morbidity. While cryopreservation of testicular tissue in adult men with azoospermia is a well-established component of the ICSI procedure, there is a lack of clinical trials assessing safety and efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who are prepubertal boys with cancer who receive cryopreservation of testicular tissue, the evidence includes no clinical trials. Relevant outcomes are health status measures and treatment-related morbidity. No clinical trials were identified evaluating the safety and efficacy of cryopreservation of testicular tissue in prepubertal boys undergoing cancer therapy. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information
Clinical Input from Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests from Blue Cross Blue Shield Association, input was received from 4 physician specialty societies and 2 academic medical centers in 2012. There was general agreement that intracytoplasmic sperm injection and cryopreservation of testicular tissue in adult men with azoospermia as part of an intracytoplasmic sperm injection procedure may be

considered medically necessary. Three of 5 reviewers who responded agreed that co-culture of embryos is considered investigational. In addition, 4 of 5 reviewers did not agree that blastocyst transfer is investigational; these reviewers considered blastocyst transfer to be medically necessary to decrease multiple gestations. Three of 6 reviewers agreed that cryopreservation of ovarian tissue or oocytes is investigational. The other three thought that cryopreservation of oocytes, but not ovarian tissue, is medically necessary. Clinical input on other policy statements was more variable.

Practice Guidelines and Position Statements

American Society for Reproductive Medicine and Society for Assisted Reproductive Technology

The American Society for Reproductive Medicine (ASRM) and the Society for Assisted Reproductive Technology (SART) (2014) published joint guidelines on assisted hatching and in vitro fertilization (IVF).[48] The single recommendation in these guidelines stated that assisted hatching should not be used routinely for all patients undergoing IVF.

In 2013, ASRM and SART published joint guidelines on mature oocyte cryopreservation.[21] The guidelines stated: "evidence indicates that oocyte vitrification and warming should no longer be considered experimental" and included the following recommendations:

- "In patients facing infertility due to chemotherapy or other gonadotoxic therapies, oocyte cryopreservation is recommended with appropriate counseling."
- "More widespread clinic-specific data on the safety and efficacy of oocyte cryopreservation in donor populations are needed before universal donor oocyte banking can be recommended."
- "There are not yet sufficient data to recommend oocyte cryopreservation for the sole purpose of circumventing reproductive aging in healthy women."
- "More data are needed before this technology should be used routinely in lieu of embryo cryopreservation."

A 2012 committee opinion from ASRM and SART stated that intracytoplasmic sperm injection (ICSI) is a safe and effective treatment for male factor infertility.[49] The opinion also indicated that ICSI for unexplained fertility, low oocyte yield, and advanced maternal age does not improve clinical outcomes. The opinion included a statement that ICSI may benefit patients undergoing IVF with preimplantation genetic testing, in vitro matured oocytes, and cryopreserved oocytes. ASRM and SART also issued a committee opinion on blastocyst transfer in 2008,[50] which was updated in 2013. The opinion concluded that "evidence supports blastocyst transfer in 'good prognosis' patients."

American College of Obstetricians and Gynecologists

The American College of Obstetricians and Gynecologists (2014) endorsed the 2013 ASRM-SART joint guidelines on mature oocyte cryopreservation.[51] The endorsement was affirmed in 2016.

American Society of Clinical Oncology

The American Society of Clinical Oncology (2018) updated its 2013 guidelines (with no changes to its recommendations) on fertility preservation for patients with cancer.[52,53] The guidelines included the following recommendations for males and females, respectively.

> "Recommendation 2.1. Sperm cryopreservation: Sperm cryopreservation is effective, and health care providers should discuss sperm banking with postpubertal males receiving cancer treatment.
>
> Recommendation 2.2. Hormonal gonadoprotection: Hormonal therapy in men is not successful in preserving fertility. It is not recommended.
>
> Recommendation 2.3. Other methods to preserve male fertility: Other methods, such as testicular tissue cryopreservation and reimplantation or grafting of human testicular tissue, should be performed only as part of clinical trials or approved experimental protocols...."

"Recommendation 3.1. Embryo cryopreservation: Embryo cryopreservation is an established fertility preservation method, and it has routinely been used for storing surplus embryos after in vitro fertilization.

Recommendation 3.2. Cryopreservation of unfertilized oocytes: Cryopreservation of unfertilized oocytes is an option, particularly for patients who do not have a male partner, do not wish to use donor sperm, or have religious or ethical objections to embryo freezing.…"

Agency for Healthcare Research and Quality
Myers et al (2008), in an evidence report conducted for the Agency for Healthcare Research and Quality, evaluated the effectiveness of assisted reproductive technology.[54] They reviewed evidence on the outcomes of interventions used in ovulation induction, superovulation, and IVF for the treatment of infertility. Reviewers concluded that:

"[i]nterventions for which there was sufficient evidence to demonstrate improved pregnancy or live birth rates included: …, a pertinent to this evidence review: (c) ultrasound-guided embryo transfer, and transfer on day 5 post-fertilization, in couples with a good prognosis; and (d) assisted hatching in couples with previous IVF failure. There was insufficient evidence on other interventions.
Infertility itself is associated with most of the adverse longer-term outcomes."

Reviewers concluded that "[d]espite the large emotional and economic burden resulting from infertility, there was relatively little high-quality evidence to support the choice of specific interventions." This conclusion was based primarily on studies that had pregnancy rates as the primary end point, not live births. In addition, studies used multiple assisted hatching techniques.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
Ovarian tissue cryopreservation			
NCT02646384	Ovarian Tissue Freezing For Fertility Preservation In Girls Facing A Fertility Threatening Medical Diagnosis Or Treatment Regimen: A Study By The National Physicians Cooperative of the Oncofertility Consortium At Northwestern University	100	Jan 2020
NCT02900625	Validation of a Method to Search Residual Disease in Auto-cryopreserved Ovarian Tissues	240	May 2020
NCT02846064	Development of Ovarian Tissue Autograft in Order to Restore Ovarian Function	50	Oct 2020
NCT02678910	Ovarian Tissue Freezing For Fertility Preservation In Women Facing A Fertility Threatening Medical Diagnosis/Treatment	24	Jan 2021
NCT01993732	Ovarian Tissue Cryopreservation in Females Undergoing Procedures That Will Potentially Lead To Loss of Ovarian Function	15	Dec 2041
Blastocyst transfer			
NCT02148393	Implantation Enhancement by Elective Cryopreservation of All Viable Embryos	212	Feb 2018
NCT02999958[a]	Adding Antioxidants Into Human Sequential Culture Media System	128	Mar 2018
NCT02746562	A Multicentre Randomized Controlled Trial of a "Freeze-All and Transfer Later" Versus a Conventional "Fresh Embryo Transfer"	424	Feb 2020

NCT No.	Trial Name	Planned Enrollment	Completion Date
	Strategy for Assisted Reproductive Technology (ART) in Women With a Regular Menstrual Cycle		
NCT03173885	An RCT Evaluating the Implantation Potential of Vitrified Embryos Screened by Next Generation Sequencing Following Trophectoderm Biopsy, Versus Vitrified Unscreened Embryos in Good Prognosis Patients Undergoing IVF	276	Jan 2022
Testicular tissue cryopreservation			
NCT02872532	Testicular Tissue Cryopreservation for Fertility Preservation in Males Facing Fertility Threatening Diagnoses or Treatment Regimens	100	Aug 2020
NCT02972801	Testicular Tissue Cryopreservation for Fertility Preservation in Patients Facing Infertility-causing Diseases or Treatment Regimens	250	Jan 2021

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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Documentation for Clinical Review

Please provide the following documentation (if/when requested):

- History and physical and/or consultation notes including:
  - Previous history of fertility/infertility
  - Previous treatment plan and response
  - Previous procedures to address infertility
  - Request for procedure per ongoing treatment plan
- Laboratory report including: specific name and test requested

Post Services

- Operative/procedure notes (if applicable)

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of codes does not constitute or imply member coverage or provider reimbursement.

MN/IE

The following services may be considered medically necessary in certain instances and investigational in others. Services may be considered medically necessary when policy criteria are met. Services may be considered investigational when the policy criteria are not met or when the code describes application of a product in the position statement that is investigational.

Type	Code	Description
CPT®	54500	Biopsy of testis, needle (separate procedure)
	54505	Biopsy of testis, incisional (separate procedure)
	54800	Biopsy of epididymis, needle
	55400	Vasovasostomy, vasovasorrhaphy
	55870	Electroejaculation
	58321	Artificial insemination; intra-cervical
	58322	Artificial insemination; intra-uterine
	58323	Sperm washing for artificial insemination
	58970	Follicle puncture for oocyte retrieval, any method
	58974	Embryo transfer, intrauterine
	58976	Gamete, zygote, or embryo intrafallopian transfer, any method
	89240	Unlisted miscellaneous pathology test
	89250	Culture of oocyte(s)/embryo(s), less than 4 days;
	89251	Culture of oocyte(s)/embryo(s), less than 4 days; with co-culture of oocyte(s)/embryos
	89253	Assisted embryo hatching, microtechniques (any method)

Type	Code	Description
	89254	Oocyte identification from follicular fluid
	89255	Preparation of embryo for transfer (any method)
	89257	Sperm identification from aspiration (other than seminal fluid)
	89258	Cryopreservation; embryo(s)
	89259	Cryopreservation; sperm
	89260	Sperm isolation; simple prep (e.g., sperm wash and swim-up) for insemination or diagnosis with semen analysis
	89261	Sperm isolation; complex prep (e.g., Percoll gradient, albumin gradient) for insemination or diagnosis with semen analysis
	89264	Sperm identification from testis tissue, fresh or cryopreserved
	89268	Insemination of oocytes
	89272	Extended culture of oocyte(s)/embryo(s), 4-7 days
	89280	Assisted oocyte fertilization, microtechnique; less than or equal to 10 oocytes
	89281	Assisted oocyte fertilization, microtechnique; greater than 10 oocytes
	89335	Cryopreservation, reproductive tissue, testicular
	89337	Cryopreservation, mature oocyte(s)
	89342	Storage (per year); embryo(s)
	89343	Storage (per year); sperm/semen
	89344	Storage (per year); reproductive tissue, testicular/ovarian
	89346	Storage (per year); oocyte(s)
	89352	Thawing of cryopreserved; embryo(s)
	89353	Thawing of cryopreserved; sperm/semen, each aliquot
	89354	Thawing of cryopreserved; reproductive tissue, testicular/ovarian
	89356	Thawing of cryopreserved; oocytes, each aliquot
	0058T	Cryopreservation; reproductive tissue, ovarian
	0357T	Cryopreservation; immature oocyte(s)
HCPCS	S4011	In vitro fertilization; including but not limited to identification and incubation of mature oocytes, fertilization with sperm, incubation of embryo(s), and subsequent visualization for determination of development
	S4013	Complete cycle, gamete intrafallopian transfer (GIFT), case rate
	S4014	Complete cycle, zygote intrafallopian transfer (ZIFT), case rate
	S4015	Complete in vitro fertilization cycle, not otherwise specified, case rate
	S4016	Frozen in vitro fertilization cycle, case rate
	S4017	Incomplete cycle, treatment cancelled prior to stimulation, case rate
	S4018	Frozen embryo transfer procedure cancelled before transfer, case rate
	S4020	In vitro fertilization procedure cancelled before aspiration, case rate
	S4021	In vitro fertilization procedure cancelled after aspiration, case rate
	S4022	Assisted oocyte fertilization, case rate
	S4023	Donor egg cycle, incomplete, case rate
	S4025	Donor services for in vitro fertilization (sperm or embryo), case rate
	S4026	Procurement of donor sperm from sperm bank
	S4027	Storage of previously frozen embryos
	S4028	Microsurgical epididymal sperm aspiration (MESA)
	S4030	Sperm procurement and cryopreservation services; initial visit

Type	Code	Description
	S4031	Sperm procurement and cryopreservation services; subsequent visit
	S4035	Stimulated intrauterine insemination (IUI), case rate
	S4037	Cryopreserved embryo transfer, case rate
	S4040	Monitoring and storage of cryopreserved embryos, per 30 days
	S4042	Management of ovulation induction (interpretation of diagnostic tests and studies, nonface-to-face medical management of the patient), per cycle
ICD-10 Procedure	0U804ZZ	Division of Right Ovary, Percutaneous Endoscopic Approach
	0U814ZZ	Division of Left Ovary, Percutaneous Endoscopic Approach
	0U824ZZ	Division of Bilateral Ovaries, Percutaneous Endoscopic Approach
	0V1N07J	Bypass Right Vas Deferens to Right Epididymis with Autologous Tissue Substitute, Open Approach
	0V1N07K	Bypass Right Vas Deferens to Left Epididymis with Autologous Tissue Substitute, Open Approach
	0V1N07N	Bypass Right Vas Deferens to Right Vas Deferens with Autologous Tissue Substitute, Open Approach
	0V1N07P	Bypass Right Vas Deferens to Left Vas Deferens with Autologous Tissue Substitute, Open Approach
	0V1N0JJ	Bypass Right Vas Deferens to Right Epididymis with Synthetic Substitute, Open Approach
	0V1N0JK	Bypass Right Vas Deferens to Left Epididymis with Synthetic Substitute, Open Approach
	0V1N0JN	Bypass Right Vas Deferens to Right Vas Deferens with Synthetic Substitute, Open Approach
	0V1N0JP	Bypass Right Vas Deferens to Left Vas Deferens with Synthetic Substitute, Open Approach
	0V1N0KJ	Bypass Right Vas Deferens to Right Epididymis with Nonautologous Tissue Substitute, Open Approach
	0V1N0KK	Bypass Right Vas Deferens to Left Epididymis with Nonautologous Tissue Substitute, Open Approach
	0V1N0KN	Bypass Right Vas Deferens to Right Vas Deferens with Nonautologous Tissue Substitute, Open Approach
	0V1N0KP	Bypass Right Vas Deferens to Left Vas Deferens with Nonautologous Tissue Substitute, Open Approach
	0V1N0ZJ	Bypass Right Vas Deferens to Right Epididymis, Open Approach
	0V1N0ZK	Bypass Right Vas Deferens to Left Epididymis, Open Approach
	0V1N0ZN	Bypass Right Vas Deferens to Right Vas Deferens, Open Approach
	0V1N0ZP	Bypass Right Vas Deferens to Left Vas Deferens, Open Approach
	0V1N47J	Bypass Right Vas Deferens to Right Epididymis with Autologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1N47K	Bypass Right Vas Deferens to Left Epididymis with Autologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1N47N	Bypass Right Vas Deferens to Right Vas Deferens with Autologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1N47P	Bypass Right Vas Deferens to Left Vas Deferens with Autologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1N4JJ	Bypass Right Vas Deferens to Right Epididymis with Synthetic Substitute, Percutaneous Endoscopic Approach
	0V1N4JK	Bypass Right Vas Deferens to Left Epididymis with Synthetic Substitute, Percutaneous Endoscopic Approach
	0V1N4JN	Bypass Right Vas Deferens to Right Vas Deferens with Synthetic Substitute, Percutaneous Endoscopic Approach

Type	Code	Description
	0V1N4JP	Bypass Right Vas Deferens to Left Vas Deferens with Synthetic Substitute, Percutaneous Endoscopic Approach
	0V1N4KJ	Bypass Right Vas Deferens to Right Epididymis with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1N4KK	Bypass Right Vas Deferens to Left Epididymis with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1N4KN	Bypass Right Vas Deferens to Right Vas Deferens with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1N4KP	Bypass Right Vas Deferens to Left Vas Deferens with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1N4ZJ	Bypass Right Vas Deferens to Right Epididymis, Percutaneous Endoscopic Approach
	0V1N4ZK	Bypass Right Vas Deferens to Left Epididymis, Percutaneous Endoscopic Approach
	0V1N4ZN	Bypass Right Vas Deferens to Right Vas Deferens, Percutaneous Endoscopic Approach
	0V1N4ZP	Bypass Right Vas Deferens to Left Vas Deferens, Percutaneous Endoscopic Approach
	0V1P07J	Bypass Left Vas Deferens to Right Epididymis with Autologous Tissue Substitute, Open Approach
	0V1P07K	Bypass Left Vas Deferens to Left Epididymis with Autologous Tissue Substitute, Open Approach
	0V1P07N	Bypass Left Vas Deferens to Right Vas Deferens with Autologous Tissue Substitute, Open Approach
	0V1P07P	Bypass Left Vas Deferens to Left Vas Deferens with Autologous Tissue Substitute, Open Approach
	0V1P0JJ	Bypass Left Vas Deferens to Right Epididymis with Synthetic Substitute, Open Approach
	0V1P0JK	Bypass Left Vas Deferens to Left Epididymis with Synthetic Substitute, Open Approach
	0V1P0JN	Bypass Left Vas Deferens to Right Vas Deferens with Synthetic Substitute, Open Approach
	0V1P0JP	Bypass Left Vas Deferens to Left Vas Deferens with Synthetic Substitute, Open Approach
	0V1P0KJ	Bypass Left Vas Deferens to Right Epididymis with Nonautologous Tissue Substitute, Open Approach
	0V1P0KK	Bypass Left Vas Deferens to Left Epididymis with Nonautologous Tissue Substitute, Open Approach
	0V1P0KN	Bypass Left Vas Deferens to Right Vas Deferens with Nonautologous Tissue Substitute, Open Approach
	0V1P0KP	Bypass Left Vas Deferens to Left Vas Deferens with Nonautologous Tissue Substitute, Open Approach
	0V1P0ZJ	Bypass Left Vas Deferens to Right Epididymis, Open Approach
	0V1P0ZK	Bypass Left Vas Deferens to Left Epididymis, Open Approach
	0V1P0ZN	Bypass Left Vas Deferens to Right Vas Deferens, Open Approach
	0V1P0ZP	Bypass Left Vas Deferens to Left Vas Deferens, Open Approach
	0V1P47J	Bypass Left Vas Deferens to Right Epididymis with Autologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1P47K	Bypass Left Vas Deferens to Left Epididymis with Autologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1P47N	Bypass Left Vas Deferens to Right Vas Deferens with Autologous Tissue Substitute, Percutaneous Endoscopic Approach

Type	Code	Description
	0V1P47P	Bypass Left Vas Deferens to Left Vas Deferens with Autologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1P4JJ	Bypass Left Vas Deferens to Right Epididymis with Synthetic Substitute, Percutaneous Endoscopic Approach
	0V1P4JK	Bypass Left Vas Deferens to Right Epididymis with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1P4JN	Bypass Left Vas Deferens to Right Vas Deferens with Synthetic Substitute, Percutaneous Endoscopic Approach
	0V1P4JP	Bypass Left Vas Deferens to Left Vas Deferens with Synthetic Substitute, Percutaneous Endoscopic Approach
	0V1P4KJ	Bypass Left Vas Deferens to Right Epididymis with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1P4KK	Bypass Left Vas Deferens to Left Epididymis with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1P4KN	Bypass Left Vas Deferens to Right Vas Deferens with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1P4KP	Bypass Left Vas Deferens to Left Vas Deferens with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1P4ZJ	Bypass Left Vas Deferens to Right Epididymis, Percutaneous Endoscopic Approach
	0V1P4ZK	Bypass Left Vas Deferens to Left Epididymis, Percutaneous Endoscopic Approach
	0V1P4ZN	Bypass Left Vas Deferens to Right Vas Deferens, Percutaneous Endoscopic Approach
	0V1P4ZP	Bypass Left Vas Deferens to Left Vas Deferens, Percutaneous Endoscopic Approach
	0V1Q07J	Bypass Bilateral Vas Deferens to Right Epididymis with Autologous Tissue Substitute, Open Approach
	0V1Q07K	Bypass Bilateral Vas Deferens to Left Epididymis with Autologous Tissue Substitute, Open Approach
	0V1Q07N	Bypass Bilateral Vas Deferens to Right Vas Deferens with Autologous Tissue Substitute, Open Approach
	0V1Q07P	Bypass Bilateral Vas Deferens to Left Vas Deferens with Autologous Tissue Substitute, Open Approach
	0V1Q0JJ	Bypass Bilateral Vas Deferens to Right Epididymis with Synthetic Substitute, Open Approach
	0V1Q0JK	Bypass Bilateral Vas Deferens to Left Epididymis with Synthetic Substitute, Open Approach
	0V1Q0JN	Bypass Bilateral Vas Deferens to Right Vas Deferens with Synthetic Substitute, Open Approach
	0V1Q0JP	Bypass Bilateral Vas Deferens to Left Vas Deferens with Synthetic Substitute, Open Approach
	0V1Q0KJ	Bypass Bilateral Vas Deferens to Right Epididymis with Nonautologous Tissue Substitute, Open Approach
	0V1Q0KK	Bypass Bilateral Vas Deferens to Left Epididymis with Nonautologous Tissue Substitute, Open Approach
	0V1Q0KN	Bypass Bilateral Vas Deferens to Right Vas Deferens with Nonautologous Tissue Substitute, Open Approach
	0V1Q0KP	Bypass Bilateral Vas Deferens to Left Vas Deferens with Nonautologous Tissue Substitute, Open Approach
	0V1Q0ZJ	Bypass Bilateral Vas Deferens to Right Epididymis, Open Approach
	0V1Q0ZK	Bypass Bilateral Vas Deferens to Left Epididymis, Open Approach
	0V1Q0ZN	Bypass Bilateral Vas Deferens to Right Vas Deferens, Open Approach

Type	Code	Description
	0V1Q0ZP	Bypass Bilateral Vas Deferens to Left Vas Deferens, Open Approach
	0V1Q47J	Bypass Bilateral Vas Deferens to Right Epididymis with Autologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1Q47K	Bypass Bilateral Vas Deferens to Left Epididymis with Autologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1Q47N	Bypass Bilateral Vas Deferens to Right Vas Deferens with Autologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1Q47P	Bypass Bilateral Vas Deferens to Left Vas Deferens with Autologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1Q4JJ	Bypass Bilateral Vas Deferens to Right Epididymis with Synthetic Substitute, Percutaneous Endoscopic Approach
	0V1Q4JK	Bypass Bilateral Vas Deferens to Left Epididymis with Synthetic Substitute, Percutaneous Endoscopic Approach
	0V1Q4JN	Bypass Bilateral Vas Deferens to Right Vas Deferens with Synthetic Substitute, Percutaneous Endoscopic Approach
	0V1Q4JP	Bypass Bilateral Vas Deferens to Left Vas Deferens with Synthetic Substitute, Percutaneous Endoscopic Approach
	0V1Q4KJ	Bypass Bilateral Vas Deferens to Right Epididymis with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1Q4KK	Bypass Bilateral Vas Deferens to Left Epididymis with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1Q4KN	Bypass Bilateral Vas Deferens to Right Vas Deferens with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1Q4KP	Bypass Bilateral Vas Deferens to Left Vas Deferens with Nonautologous Tissue Substitute, Percutaneous Endoscopic Approach
	0V1Q4ZJ	Bypass Bilateral Vas Deferens to Right Epididymis, Percutaneous Endoscopic Approach
	0V1Q4ZK	Bypass Bilateral Vas Deferens to Left Epididymis, Percutaneous Endoscopic Approach
	0V1Q4ZN	Bypass Bilateral Vas Deferens to Right Vas Deferens, Percutaneous Endoscopic Approach
	0V1Q4ZP	Bypass Bilateral Vas Deferens to Left Vas Deferens, Percutaneous Endoscopic Approach
	0V993ZX	Drainage of Right Testis, Percutaneous Approach, Diagnostic
	0V993ZZ	Drainage of Right Testis, Percutaneous Approach
	0V994ZX	Drainage of Right Testis with Drainage Device, Percutaneous Endoscopic Approach
	0V9B3ZX	Drainage of Left Testis, Percutaneous Approach, Diagnostic
	0V9B3ZZ	Drainage of Left Testis, Percutaneous Approach
	0V9B4ZX	Drainage of Left Testis, Percutaneous Endoscopic Approach, Diagnostic
	0V9C3ZX	Drainage of Bilateral Testes, Percutaneous Approach, Diagnostic
	0V9C3ZZ	Drainage of Bilateral Testes, Percutaneous Approach
	0V9C4ZX	Drainage of Bilateral Testes, Percutaneous Endoscopic Approach, Diagnostic
	0V9F0ZX	Drainage of Right Spermatic Cord, Open Approach, Diagnostic
	0V9F3ZX	Drainage of Right Spermatic Cord, Percutaneous Approach, Diagnostic
	0V9F4ZX	Drainage of Right Spermatic Cord, Percutaneous Endoscopic Approach, Diagnostic

Type	Code	Description
	0V9G0ZX	Drainage of Left Spermatic Cord, Open Approach, Diagnostic
	0V9G3ZX	Drainage of Left Spermatic Cord, Percutaneous Approach, Diagnostic
	0V9G4ZX	Drainage of Left Spermatic Cord, Percutaneous Endoscopic Approach, Diagnostic
	0V9H0ZX	Drainage of Bilateral Spermatic Cords, Open Approach, Diagnostic
	0V9H3ZX	Drainage of Bilateral Spermatic Cords, Percutaneous Approach, Diagnostic
	0V9H4ZX	Drainage of Bilateral Spermatic Cords, Percutaneous Endoscopic Approach, Diagnostic
	0V9J00Z	Drainage of Right Epididymis with Drainage Device, Open Approach
	0V9J0ZX	Drainage of Right Epididymis, Open Approach, Diagnostic
	0V9J0ZZ	Drainage of Right Epididymis, Open Approach
	0V9J30Z	Drainage of Right Epididymis with Drainage Device, Percutaneous Approach
	0V9J3ZX	Drainage of Right Epididymis, Percutaneous Approach, Diagnostic
	0V9J3ZZ	Drainage of Right Epididymis, Percutaneous Approach
	0V9J40Z	Drainage of Right Epididymis with Drainage Device, Percutaneous Endoscopic Approach
	0V9J4ZX	Drainage of Right Epididymis, Percutaneous Endoscopic Approach, Diagnostic
	0V9J4ZZ	Drainage of Right Epididymis, Percutaneous Endoscopic Approach
	0V9K00Z	Drainage of Left Epididymis with Drainage Device, Open Approach
	0V9K0ZX	Drainage of Left Epididymis, Open Approach, Diagnostic
	0V9K0ZZ	Drainage of Left Epididymis, Open Approach
	0V9K30Z	Drainage of Left Epididymis with Drainage Device, Percutaneous Approach
	0V9K3ZX	Drainage of Left Epididymis, Percutaneous Approach, Diagnostic
	0V9K3ZZ	Drainage of Left Epididymis, Percutaneous Approach
	0V9K40Z	Drainage of Left Epididymis with Drainage Device, Percutaneous Endoscopic Approach
	0V9K4ZX	Drainage of Left Epididymis, Percutaneous Endoscopic Approach, Diagnostic
	0V9K4ZZ	Drainage of Left Epididymis, Percutaneous Endoscopic Approach
	0V9L00Z	Drainage of Bilateral Epididymis with Drainage Device, Open Approach
	0V9L0ZX	Drainage of Bilateral Epididymis, Open Approach, Diagnostic
	0V9L0ZZ	Drainage of Bilateral Epididymis, Open Approach
	0V9L30Z	Drainage of Bilateral Epididymis with Drainage Device, Percutaneous Approach
	0V9L3ZX	Drainage of Bilateral Epididymis, Percutaneous Approach, Diagnostic
	0V9L3ZZ	Drainage of Bilateral Epididymis, Percutaneous Approach
	0V9L40Z	Drainage of Bilateral Epididymis with Drainage Device, Percutaneous Endoscopic Approach
	0V9L4ZX	Drainage of Bilateral Epididymis, Percutaneous Endoscopic Approach, Diagnostic
	0V9L4ZZ	Drainage of Bilateral Epididymis, Percutaneous Endoscopic Approach
	0V9N0ZX	Drainage of Bilateral Epididymis, Percutaneous Endoscopic Approach, Diagnostic

Type	Code	Description
	0V9N3ZX	Drainage of Right Vas Deferens, Percutaneous Approach, Diagnostic
	0V9N4ZX	Drainage of Right Vas Deferens, Percutaneous Endoscopic Approach, Diagnostic
	0V9P0ZX	Drainage of Left Vas Deferens, Open Approach, Diagnostic
	0V9P3ZX	Drainage of Left Vas Deferens, Percutaneous Approach, Diagnostic
	0V9P4ZX	Drainage of Left Vas Deferens, Percutaneous Endoscopic Approach, Diagnostic
	0V9Q0ZX	Drainage of Bilateral Vas Deferens, Open Approach, Diagnostic
	0V9Q3ZX	Drainage of Bilateral Vas Deferens, Percutaneous Approach, Diagnostic
	0V9Q4ZX	Drainage of Bilateral Vas Deferens, Percutaneous Endoscopic Approach, Diagnostic
	0VB93ZX	Excision of Right Testis, Percutaneous Approach, Diagnostic
	0VB94ZX	Excision of Right Testis, Percutaneous Endoscopic Approach, Diagnostic
	0VBB3ZX	Excision of Left Testis, Percutaneous Approach, Diagnostic
	0VBB4ZX	Excision of Left Testis, Percutaneous Endoscopic Approach, Diagnostic
	0VBC3ZX	Excision of Bilateral Testes, Percutaneous Approach, Diagnostic
	0VBC4ZX	Excision of Bilateral Testes, Percutaneous Endoscopic Approach, Diagnostic
	0VBF0ZX	Excision of Right Spermatic Cord, Open Approach, Diagnostic
	0VBF3ZX	Excision of Right Spermatic Cord, Percutaneous Approach, Diagnostic
	0VBF4ZX	Excision of Right Spermatic Cord, Percutaneous Endoscopic Approach, Diagnostic
	0VBG0ZX	Excision of Left Spermatic Cord, Open Approach, Diagnostic
	0VBG3ZX	Excision of Left Spermatic Cord, Percutaneous Approach, Diagnostic
	0VBG4ZX	Excision of Left Spermatic Cord, Percutaneous Endoscopic Approach, Diagnostic
	0VBH0ZX	Excision of Bilateral Spermatic Cords, Open Approach, Diagnostic
	0VBH3ZX	Excision of Bilateral Spermatic Cords, Percutaneous Approach, Diagnostic
	0VBH4ZX	Excision of Bilateral Spermatic Cords, Percutaneous Endoscopic Approach, Diagnostic
	0VBJ0ZX	Excision of Right Epididymis, Open Approach, Diagnostic
	0VBJ3ZX	Excision of Right Epididymis, Percutaneous Approach, Diagnostic
	0VBJ4ZX	Excision of Right Epididymis, Percutaneous Endoscopic Approach, Diagnostic
	0VBK0ZX	Excision of Left Epididymis, Open Approach, Diagnostic
	0VBK3ZX	Excision of Left Epididymis, Percutaneous Approach, Diagnostic
	0VBK4ZX	Excision of Left Epididymis, Percutaneous Endoscopic Approach, Diagnostic
	0VBL0ZX	Excision of Bilateral Epididymis, Open Approach, Diagnostic
	0VBL3ZX	Excision of Bilateral Epididymis, Percutaneous Approach, Diagnostic
	0VBL4ZX	Excision of Bilateral Epididymis, Percutaneous Endoscopic Approach, Diagnostic
	0VBN0ZX	Excision of Right Vas Deferens, Open Approach, Diagnostic
	0VBN3ZX	Excision of Right Vas Deferens, Percutaneous Approach, Diagnostic

Type	Code	Description
	0VBN4ZX	Excision of Right Vas Deferens, Percutaneous Endoscopic Approach, Diagnostic
	0VBP0ZX	Excision of Left Vas Deferens, Open Approach, Diagnostic
	0VBP3ZX	Excision of Left Vas Deferens, Percutaneous Approach, Diagnostic
	0VBP4ZX	Excision of Left Vas Deferens, Percutaneous Endoscopic Approach, Diagnostic
	0VBQ0ZX	Excision of Bilateral Vas Deferens, Open Approach, Diagnostic
	0VBQ3ZX	Excision of Bilateral Vas Deferens, Percutaneous Approach, Diagnostic
	0VBQ4ZX	Excision of Bilateral Vas Deferens, Percutaneous Endoscopic Approach, Diagnostic
	0VCJ0ZZ	Extirpation of Matter from Right Epididymis, Open Approach
	0VCJ3ZZ	Extirpation of Matter from Right Epididymis, Percutaneous Approach
	0VCJ4ZZ	Extirpation of Matter from Right Epididymis, Percutaneous Endoscopic Approach
	0VCK0ZZ	Extirpation of Matter from Left Epididymis, Open Approach
	0VCK3ZZ	Extirpation of Matter from Left Epididymis, Percutaneous Approach
	0VCK4ZZ	Extirpation of Matter from Left Epididymis, Percutaneous Endoscopic Approach
	0VCL0ZZ	Extirpation of Matter from Bilateral Epididymis, Open Approach
	0VCL3ZZ	Extirpation of Matter from Bilateral Epididymis, Percutaneous Approach
	0VCL4ZZ	Extirpation of Matter from Bilateral Epididymis, Percutaneous Endoscopic Approach
	0VJM0ZZ	Inspection of Epididymis and Spermatic Cord, Open Approach
	0VJR0ZZ	Inspection of Vas Deferens, Open Approach
	0VPR0DZ	Removal of Intraluminal Device from Vas Deferens, Open Approach
	0VPR3DZ	Removal of Intraluminal Device from Vas Deferens, Percutaneous Approach
	0VPR4DZ	Removal of Intraluminal Device from Vas Deferens, Percutaneous Endoscopic Approach
	0VPR7DZ	Removal of Intraluminal Device from Vas Deferens, Via Natural or Artificial Opening
	0VPR8DZ	Removal of Intraluminal Device from Vas Deferens, Via Natural or Artificial Opening Endoscopic
	0VQJ0ZZ	Repair Right Epididymis, Open Approach
	0VQJ3ZZ	Repair Right Epididymis, Percutaneous Approach
	0VQJ4ZZ	Repair Right Epididymis, Percutaneous Endoscopic Approach
	0VQK0ZZ	Repair Left Epididymis, Open Approach
	0VQK3ZZ	Repair Left Epididymis, Percutaneous Approach
	0VQK4ZZ	Repair Left Epididymis, Percutaneous Endoscopic Approach
	0VQL0ZZ	Repair Bilateral Epididymis, Open Approach
	0VQL3ZZ	Repair Bilateral Epididymis, Percutaneous Approach
	0VQL4ZZ	Repair Bilateral Epididymis, Percutaneous Endoscopic Approach
	0VQN0ZZ	Repair Right Vas Deferens, Open Approach
	0VQN3ZZ	Repair Right Vas Deferens, Percutaneous Approach
	0VQN4ZZ	Repair Right Vas Deferens, Percutaneous Endoscopic Approach
	0VQP0ZZ	Repair Left Vas Deferens, Open Approach
	0VQP3ZZ	Repair Left Vas Deferens, Percutaneous Approach
	0VQP4ZZ	Repair Left Vas Deferens, Percutaneous Endoscopic Approach

Type	Code	Description
	0VQQ0ZZ	Repair Bilateral Vas Deferens, Open Approach
	0VQQ3ZZ	Repair Bilateral Vas Deferens, Percutaneous Approach
	0VQQ4ZZ	Repair Bilateral Vas Deferens, Percutaneous Endoscopic Approach
	0WQM0ZZ	Repair Male Perineum, Open Approach
	0WQM3ZZ	Repair Male Perineum, Percutaneous Approach
	0WQM4ZZ	Repair Male Perineum, Percutaneous Endoscopic Approach
	0WQMXZZ	Repair Male Perineum, External Approach
	0WQN0ZZ	Repair Female Perineum, Open Approach
	0WQN3ZZ	Repair Female Perineum, Percutaneous Approach
	0WQN4ZZ	Repair Female Perineum, Percutaneous Endoscopic Approach
	0WQNXZZ	Repair Female Perineum, External Approach
	0WWM07Z	Revision of Autologous Tissue Substitute in Male Perineum, Open Approach
	0WWM0KZ	Revision of Nonautologous Tissue Substitute in Male Perineum, Open Approach
	0WWM37Z	Revision of Autologous Tissue Substitute in Male Perineum, Percutaneous Approach
	0WWM3KZ	Revision of Nonautologous Tissue Substitute in Male Perineum, Percutaneous Approach
	0WWM47Z	Revision of Autologous Tissue Substitute in Male Perineum, Percutaneous Endoscopic Approach
	0WWM4KZ	Revision of Nonautologous Tissue Substitute in Male Perineum, Percutaneous Endoscopic Approach
	3E0P3LZ	Introduction of Sperm into Female Reproductive, Percutaneous Approach
	3E0P3Q0	Introduction of Autologous Fertilized Ovum into Female Reproductive, Percutaneous Approach
	3E0P3Q1	Introduction of Nonautologous Fertilized Ovum into Female Reproductive, Percutaneous Approach
	3E0P7LZ	Introduction of Sperm into Female Reproductive, Via Natural or Artificial Opening
	3E0P7Q0	Introduction of Autologous Fertilized Ovum into Female Reproductive, Via Natural or Artificial Opening
	3E0P7Q1	Introduction of Nonautologous Fertilized Ovum into Female Reproductive, Via Natural or Artificial Opening
	8E0VX63	Sperm Collection

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action	Reason
08/31/2015	BCBSA Medical Policy adoption	Medical Policy Committee
11/01/2016	Policy revision without position change	Medical Policy Committee
10/01/2017	Policy revision without position change	Medical Policy Committee
10/01/2018	Policy revision without position change	Medical Policy Committee

Definitions of Decision Determinations

Medically Necessary: A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not

investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.