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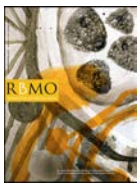

ARTICLE

Fertility preservation in patients undergoing gonadotoxic treatments: a Canadian Fertility and Andrology Society clinical practice guideline

BIOGRAPHY

Dr. Roberts is a clinical professor at University of British Columbia. He completed a fellowship in reproductive endocrinology and infertility through Weill Cornell Medical College. He has a special interest in fertility preservation, that he pursues through his clinical activities and charitable work as president of Fertile Future.

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KEY MESSAGE

Advances in the provision of fertility preservation technologies to individuals undergoing sterilizing medical treatments can improve the likelihood of having children in the future. The delivery of these options requires a multidisciplinary approach and coordination with oncology professionals.

ABSTRACT

The management of young patients with cancer presents several unique challenges. In general, these patients are ill prepared for the diagnosis and the impact on their fertility. With the improved survival for all tumour types and stages, the need for adequate fertility counselling and a multidisciplinary approach in the reproductive care of these patients is paramount. Recent advances in cryopreservation techniques allow for the banking of spermatozoa, oocytes, embryos and ovarian tissue without compromising survival. This Canadian Fertility and Andrology Society (CFAS) guideline outlines the current understanding of social and medical issues associated with oncofertility, and the medical and surgical technologies available to optimize future fertility.

INTRODUCTION

In Canada, 200,000 people are diagnosed with cancer annually. Long-term survival rates for many cancers are continually improving, with 5-year survival rates of over 80% for children and adolescents, and over 70% for adults between 20 and 49 years of age (*Canadian Cancer Society, 2021*). Survival often comes with a loss of reproductive function from gonadal toxicity. High-dose alkylating agents and ionizing radiation are particularly damaging, inducing sterility in a high proportion of patients.

It is estimated that breast cancer affected more than 27,000 Canadians in 2021 (*Canadian Cancer Society, 2021*). Fifteen per cent of these individuals were of reproductive age, making it the most common malignancy in this age group and representing the bulk of referrals to assisted reproductive technology (ART) facilities for fertility preservation (Canadian Cancer Society, 2013). Other common cancers seen in young Canadians include haematological (lymphoma and leukaemia), colorectal, thyroid and testicular cancers, and melanoma. Uncommonly, patients with autoimmune disorders such as systemic lupus erythematosus (SLE) and haematological conditions require gonadotoxic agents for medical management. Fortunately, cancer in young individuals represents a small

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This Clinical Practice Guideline has been prepared with and approved by the Canadian Fertility and Andrology Society (CFAS) Clinical Practice Guideline Committee†. It has also been reviewed and approved by the CFAS membership.
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KEY WORDS

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percentage of cases: 0.7% in children (0–14 years), while adolescents and young adults (15–29 years) account for 1.5% (*Canadian Cancer Society, 2021*). It is estimated that 1 out of 700 adults is a long-term childhood cancer survivor (*Public Health Agency of Canadian Cancer Society, 2018*; *Skinner et al., 2006*). Fertility preservation in children and adolescents merits special considerations that will be addressed separately in this guideline.

One fact is very clear – the majority of young cancer patients want children of their own in the future (*Schover et al., 1999*; *Schover et al., 2002*). The vast majority of these patients survive their disease, so it is critical that they receive the necessary fertility counselling and multidisciplinary care required to address the complex clinical and psychological challenges that they face (*Jemal et al., 2008*).

This guideline was developed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach (Guyatt et al., 2011) when possible. The following electronic bibliographic databases were searched up to March 2022: (i) Ovid MEDLINE, (ii) Ovid EMBASE, and (iii) Cochrane Database of Systematic Reviews. Search terms included: "fertility preservation", "controlled ovarian hyperstimulation", "chemotherapy", "gonadotoxic", "childhood", "adolescent", "survivor", "radiation", "consultation", "gonadotropin-releasing hormone agonist", "oocyte/egg cryopreservation", "embryo cryopreservation", "ovarian tissue cryopreservation", "ovarian tissue transplantation" and "sperm cryopreservation".

FERTILITY PRESERVATION IN PATIENTS WITH OVARIES

All reproductive-aged patients with ovaries who are diagnosed with cancer can benefit from a discussion of fertility preservation. Until recently, most evidence for the impact of cancer treatments came from the Childhood Cancer Survivor Studies (CCSS), which surveyed over 20,000 patients at least 5 years out from treatment. The rate of premature ovarian failure among survivors was 13-fold higher than that of their siblings (*Green et al., 2009*). A recent large cohort study analysed 23,201 cancer patients between 1981 and 2012, who were aged 39 years or less at diagnosis (*Anderson et al., 2018*). Compared with age-matched controls from the general population, survivors were 38% less likely to conceive (standardized incidence ratio 0.62, 95% confidence interval [CI] 0.60–0.63), an effect that was seen across all cancer types. No difference was seen in the risk of spontaneous abortion or stillbirth or the incidence of therapeutic abortion. A similar reduction of fertility is seen in multiple childhood cancer survivor studies (*van Dorp et al., 2018*).

Chemotherapy

The gonadotoxicity of combination chemotherapeutic treatments varies according to the type of cancer, specific agents used, cumulative doses, protocol and reproductive potential of the patient at the time of treatment (*Arnon et al., 2001*; *Goodwin et al., 1999*). Cyclophosphamide and other alkylating agents are the most toxic to the ovary, causing a dose-dependent exponential decline in primordial follicle density (*Meirow et al., 1999*; *Walshe et al., 2006*). Compared with other regimens, cyclophosphamide-containing protocols are four times more likely to result in ovarian failure, with almost 80% of cases occurring within the first year (*Goodwin et al., 1999*). Damage to the follicle may be by a combination of direct cytotoxic effects on the granulosa and oocyte itself by cell cycle-independent agents like alkylating agents, and an accelerated recruitment through a loss of anti-Müllerian hormone (AMH) production from the antral follicles (burnout theory) (*Meirow et al., 2010*; *Rosendahl et al., 2010*). Chemotherapeutic protocols can be classified into a low, intermediate or high risk of inducing ovarian failure, with the incidence of menopause ranging from less than 20% to over 80% (*Hickey et al., 2009*; *Lee et al., 2006*).

Quantifying the gonadotoxic effects of each chemotherapeutic regimen is difficult and poorly studied to date. Most existing clinical trials and population studies for chemotherapeutic agents report the incidence of premature ovarian failure and ovulatory dysfunction as the measures of fertility. Infertility and diminished ovarian reserve are typically associated with eumenorrhoea and ovulatory cycles (*Letourneau et al., 2012*). Destruction of pre-ovulatory follicles commonly causes a temporary arrest of menstruation for up to 6 months. However, long-term ovarian function can be maintained by as little as 10% of the ovary, so clinical measures of menstrual function are a poor assessment of the true ovarian damage (*Wo and Viswanathan, 2009*). In the absence of a long-term follow-up of fertility and pregnancy outcomes, the effects of cancer treatment on future reproductive function will be underestimated.

As expected, the incidence of acute ovarian failure, infertility and early menopause in chemotherapy patients correlates with age (*Letourneau et al., 2012*). Regardless of the type of chemotherapeutic agents administered, at least a fraction of ovarian reserve will be lost, even if this is not immediately apparent with clinical and laboratory evaluation. Most objective measures of ovarian reserve are altered by chemotherapy (*Anderson et al., 2006*). Low-risk treatments such as ABVD (adriamycin, bleomycin, vinblastine and dacarbazine) for Hodgkin lymphoma appear to have short-term reversible effects on AMH concentrations in patients aged under 30 years; however, clear effects are seen in both menstrual function and ovarian reserve testing in older patients (*Behringer et al., 2013*; *Decanter et al., 2010*). Even if a patient is deemed to be at 'low risk' of premature menopause, a shorter reproductive life can be expected even if regular menstrual cycles resume (*Overbeek et al., 2017*; *Partridge et al., 2007*; Sklar et al., 2005).

Protocols utilized for breast cancer have a clear irreversible effect on the ovary, as demonstrated by a number of recent studies performing serial AMH concentrations following the completion of chemotherapy (*Anderson et al., 2013*; *Dezellus et al., 2017*; *Perdrix et al., 2017*). A large prospective trial that randomized patients to no, low-intensity or high-intensity chemotherapy found that the more aggressive protocol resulted in more temporary amenorrhoea (odds ratio [OR] 1.96, $P < 0.0001$) and premature ovarian failure (OR 2.03, $P < 0.0001$), with assessments occurring at the 5- and 10-year marks (*Partridge et al., 2007*).

Anecdotal experience would suggest that cancer survivors with a history of chemotherapy have poor outcomes with medical fertility treatments. Youth is certainly a protective factor, but the long-term follow-up of childhood cancer patients demonstrates clear effects on ovarian reserve and reproductive potential

later in life (*Barton et al., 2013*; *Bath et al., 2003*; *Filippi et al., 2021*; Johnston et al., 2009; *Larsen et al., 2003*a; *Larsen et al., 2003*b; *Reulen et al., 2009*; *Thomas-Teinturier et al., 2013*). Childhood exposure to alkylating agents was a significant risk for acute ovarian failure in the CCSS (*Green et al., 2009*). Premature menopause occurred in 8% of these survivors, compared with 0.8% of siblings (OR 13.2, 95% CI 3.26–53.51, $P = 0001$). In the CCSS cohort, a cumulative cyclophosphamide equivalent dose of alkylators as low as 4 g/m^2 is associated with a risk of premature menopause in female survivors, and a reduced rate of pregnancy in the partners of male survivors, with an incremental effect as doses increase (*Green et al., 2014*).

A large national Dutch nested-cohort study (DCOG LATER) has provided some of the best data to date on fertility in childhood survivors (*van den Berg et al., 2018*). Abnormal ovarian reserve testing is seen after exposure to a number of chemotherapeutic agents. Fortunately, they do not appear to impact the genetic competency of the surviving oocytes or the future pregnancies themselves. However, extrapolating from murine data, there may be short-term effects that merit delaying pregnancy for 6–12 months after exposure (*Meirow et al., 2001*).

Radiation therapy

Radiation causes widespread DNA damage through free radical production, leading to necrosis, apoptosis, mutation and carcinogenesis (*Sanders et al., 1996*; *Wallace et al., 1989*). As with chemotherapeutic agents, the impact of ionizing radiation on the uterus and ovaries relates to the age at exposure and the effective dose (fractionation schedule) (*Ash, 1980*; *Meirow et al., 2010*). Pelvic irradiation can lead to high rates of premature ovarian failure. The effective sterilizing dose to the ovary is age-dependent 20.3 Gy at birth, 18.4 Gy at age 10, 16.5 Gy at age 20, and 14.3 Gy at age 30 (*Wallace et al., 2005*). By comparison, typical doses for gynaecological malignancies reach 50 Gy, and for total-body irradiation for haematopoietic bone marrow transplant, 10–12 Gy. Some studies have demonstrated sterilizing doses of less than 2 Gy (*Sklar et al., 2006*; *Wallace et al., 2003*). The DCOG LATER study showed a reduced ovarian reserve in childhood survivors receiving spinal radiotherapy and total-body irradiation, with a dose-dependent effect of abdominal/pelvic radiotherapy (*van den Berg et al., 2018*). Other risk factors for premature ovarian failure include concurrent alkylating agent administration, high-dose pelvic radiation and a diagnosis of Hodgkin lymphoma (*Sklar et al., 2006*).

In addition to the impact on the ovaries, uterine exposure to radiation is associated with poor obstetric outcomes, including first- and second-trimester loss, preterm birth and low birthweight (*Critchley and Wallace, 2005*). The pathophysiology appears to involve vascular, endometrial and myometrial damage (*Reulen et al., 2009*; *Signorello et al., 2006*). The CCSS found a dose-dependent increase in the risk of preterm birth from a baseline of 20% in survivors who were not exposed to radiation (*Signorello et al., 2006*). With a uterine dose of 50–250 cGy, the risk was 26% (OR 1.8, 95% CI 1.1–3.0), being 40% with 250–500 cGy (OR 2.3, 95% CI 1.0–5.1) and 50% with >500 cGy (OR 3.5,95% CI 1.5– to 8.0). The association is stronger after prepubertal exposure compared with that after menarche (for >250 cGy, OR 4.9, 95% CI 1.7–13.9). Prepubertal exposure appears to impair normal uterine development, resulting in an adult uterus that is small and refractory to oestrogen stimulation. Compared with the 8% risk of low birth weight in controls, the risk in survivors exposed to 250–500 cGy was 26% (OR 4.3, 95% CI 1.4–12.8), and was 36% for those who received >500 cGy (OR 6.8, 95% CI 2.1–22.2). An increased incidence of poor obstetric outcomes was also seen in the DCOG LATER study: survivors had a high risk of preterm delivery (OR 9.74, 95% CI 1.49–63.60) and low birthweight babies (OR 15.66, 95% CI 1.43–171.4) (*van de Loo et al., 2019*).

Abdominal radiotherapy is also associated with other risks in pregnancy, including hypertension, gestational diabetes and anaemia (*Reulen et al., 2017*). Given the implications for pregnancy, patients with a history of abdominal radiation therapy should be offered preconception counselling and should be followed by an obstetrician-gynaecologist during pregnancy. Fortunately, most cancer treatment regimens do not appear to impact the uterus and endometrial receptivity, as survivors have similar outcomes with egg-donation treatments compared with other patients with ovarian failure (Munoz et al., 2015).

Summary statement:

1. Cancer treatments lower the likelihood of future pregnancy.

Fertility preservation consultation

Future fertility potential is a priority for patients (*Gupta et al., 2013*; *Zebrack et al., 2013*). In 2013, the American Society of Clinical Oncology (ASCO) set out to provide guidance to oncologists regarding fertility preservation and concluded that the process of informed consent requires a discussion of future fertility issues and options for fertility preservation (*Loren et al., 2013*). As highlighted, early referral to a fertility specialist after the diagnosis of cancer is critical for the timely delivery of fertility preservation. Many barriers have been identified, including a lack of knowledge of fertility preservation options and available local resources, and the perception that ART is cost prohibitive and of limited efficacy (*Blumenfeld et al., 1999*; *Goodwin et al., 2007*; *Korkidakis et al., 2019*; *Lewin et al., 2017*; *Partridge et al., 2004*; *Quinn et al., 2007*; *Quinn et al., 2008*; *Woodruff, 2010*).

Korkidakis et al. analysed 4452 patients aged 15–39 years with newly diagnosed breast cancer in Ontario from 2000 to 2017, identified using the Ontario Cancer Registry. Of these patients, 178 (4.0%) were referred to a gynaecologist with a billing code of infertility between the cancer diagnosis and initiation of chemotherapy. These referral rates are surprising low, but have increased over time, from 0.4% in 2000 to 11% in 2016 (*Korkidakis et al., 2019*). Given the size of Canada, it is imperative to address any regional disparities in referral patterns and access to care, which in many cases may stem from inadequate professional education on these technologies and a lack of provincial funding. Efforts are required to establish referral networks that allow patients to receive counselling on fertility preservation across the nation.

The constraints of time and concerns for cancer treatment delay are often cited as a barrier for referral (*Schover et al., 1999*; *Vadaparampil et al., 2008*). However, available data demonstrate that the provision of fertility preservation treatments does not cause a delay in the delivery of cancer treatments (*Baynosa et al., 2009*; *Jenninga et al., 2012*; *Lee et al., 2010*). Collaborative efforts between fertility specialists and oncology care providers are critical for addressing the impact on fertility and for the provision of an individualized fertility preservation plan

(*Noyes et al., 2011*). This requires early referral and timely consultation.

Summary statement:

2. A collaborative multidisciplinary approach is important for the timely delivery of both oncological and fertility preservation care.

Recommendation:

1. An urgent fertility preservation consultation should be offered to reproductive-age patients after the diagnosis of cancer or other medical conditions requiring potentially sterilizing treatments.

Fertility assessment

In addition to an assessment of patients' medical fitness to undergo fertility preservation treatments, a fertility assessment is indicated. Age is the most important factor in predicting the outcome with egg and embryo cryopreservation. Beyond the age of 40 years, the likelihood of future pregnancy resulting from fertility preservation treatments is limited (Canadian Assisted Reproductive Technologies Registry, 2022).

A complete transvaginal pelvic ultrasound scan with antral follicle count provides data about the patient's ovarian reserve, pelvic pathology and adnexal anatomy in preparation for oocyte retrieval (*Chang et al., 1998*; *Scheffer et al., 2003*; *Wallace and Kelsey, 2004*). Day 3 FSH concentration was historically the standard evaluation of ovarian reserve, but it is not practical awaiting menses in these cases (*Scott et al., 2008*). AMH is proving to be the most predictive parameter for ovarian response to stimulation (*Arce et al., 2013*; *Brodin et al., 2013*; *Riggs et al., 2008*). AMH is detectable at all ages and can be measured at any point in the menstrual cycle. In combination with the patient's age, AMH can also determine the patient's susceptibility to the gonadotoxic effects of chemotherapy (*Anders et al., 2008*; Anderson et al., 2011; *Anderson et al., 2013*; *Brougham et al., 2012*; *Freeman et al., 2012*; de Vet et al., 2022). The fertility assessment should be repeated no earlier than 6 months after completion of the cancer treatments, to allow for the reproductive axis and ovarian function to stabilize.

Gonadotrophin-releasing hormone agonists

Reports of reduced ovarian failure rates in young patients using adjuvant gonadotrophin-releasing hormone (GnRH) agonists prompted the investigation of their chemoprotective properties in the ovary. Proposed mechanisms of action include hypogonadotrophism-induced ovarian quiescence, reduction of ovarian blood flow and agonistic effects on ovarian GnRH receptors. A recent meta-analysis of the existing randomized trials on the use of GnRH agonists for ovarian protection in breast cancer patients demonstrated a higher rate of recovery of regular menses after a 12-month period of follow-up (OR 1.85, 95% CI 1.02–3.26, $P = 0.04$) (*Munhoz et al., 2016*). As previously stated, a regular menstrual cycle does not necessarily equate to normal fertility; however, the limited data collected on pregnancy outcomes do suggest improved outcomes (*Moore et al., 2015*).

Protective effects for ovarian function have not been demonstrated during the treatment of lymphomas. A randomized trial of premenopausal Hodgkin and non-Hodgkin lymphoma patients showed a similar incidence of ovarian failure with or without the administration of a GnRH agonist (19% versus 25%; *Demeestere et al., 2016*). Menstrual suppression is an additional benefit to GnRH agonist treatment, and should be a consideration for patients experiencing heavy menstrual bleeding secondary to thrombocytopenia (*Kirkham et al., 2019*). There are limited data for a protective effect with salvage chemotherapies for stem cell transplantation (*Blumenfeld et al., 2012*; *Salooja et al., 2001*).

Summary statement:

3. Giving GnRH agonists during the administration of chemotherapy is a highly accessible method for emergency fertility preservation that appears to reduce the risk of acute ovarian failure in the case of breast cancer, with limited data suggesting benefit in other cancers or that fertility itself is preserved.

Recommendation:

2. GnRH agonists should be considered as gonadal cytoprotection prior to combination chemotherapy for the treatment of breast cancer.

Oocyte cryopreservation

Oocyte cryopreservation is one of the most common fertility preservation options in the post-pubertal patient population. Age and oocyte yield are predictive factors for success (*Cobo et al., 2016*; *Doyle et al., 2016*; *Goldman et al., 2017*). Several cohort studies have examined ovarian stimulation responses in oncological populations (*Almog et al., 2012*; *Cardozo et al., 2015*; *Dolinko et al., 2018*; *Friedler et al., 2012*; *Garcia-Velasco et al., 2013*; *Lefebvre et al., 2018*; *Quinn et al., 2017*; *von Wolff et al., 2018*). Ovarian stimulation cycles in oncological patients seem to produce similar results compared with the general ART population, and outcomes do not appear to vary among the different types of malignancy. These studies demonstrate similar oocyte yields from cancer patients compared with the general IVF population.

Limited data exist on pregnancy outcomes from oocyte cryopreservation (vitrification and slow freezing) for cancer; however, oocyte cryopreservation is a safe and effective method of fertility preservation in the general population (*Cobo et al., 2021*; *Specchia et al., 2019*). The largest case series to date analysed 1073 patients, with a mean age of 32.3 ± 0.9 years at the time of egg retrieval. In a total of 80 patients who returned to use their oocytes, 25 healthy babies were born (*Cobo et al. 2018*). Importantly, oocyte cryopreservation provides patients with future reproductive autonomy. In contrast, embryos require the consent of both partners for future use and storage.

Summary statement:

4. Oocyte cryopreservation is a recommended method of fertility preservation.

Embryo cryopreservation

As a method of fertility preservation, embryo cryopreservation has been available to cancer patients for many years. Foremost is the need for a sperm source. The patient's chance of a successful future pregnancy depends on the number of high-quality embryos obtained. In 2015, the live birth rates for frozen embryo transfer among the Canadian IVF facilities in Canada was 31% for patients under the age of 35, with 84% of those using a single embryo (Canadian Fertility and Andrology Society CARTR/BORN Registry. https://cfas.ca/cgi/page.cgi/cartr-annual-reports.html). Small case studies suggest that

outcomes using embryos from cancer survivors are comparable to those in the general infertility population (Lee et al., 2012). Most Canadians have access to embryo cryopreservation as a means of fertility preservation if they have a partner with spermatozoa, or wish to utilize donor spermatozoa.

Summary statement:

5. Embryo cryopreservation is a recommended method of fertility preservation.

Ovarian stimulation of the cancer patients

By employing modern IVF protocols and appropriate doses of gonadotrophins, oocyte and embryo yield, and ultimately the number of future attempts for pregnancy, can be maximized. The timeline for the start of the oncology treatments typically mandates the prompt delivery of fertility preservation shortly after consultation, often on an emergency basis.

Most ovarian stimulation protocols are appropriate in the setting of oncofertility, but GnRH antagonist-based protocols are most widely employed. GnRH antagonist treatments are shorter, require less gonadotrophin, and reduce the risk of ovarian hyperstimulation syndrome (OHSS) (*Al-Inany et al., 2011*; *Depalo et al., 2012*; *Fatemi et al., 2012*; *Pu et al., 2011*). Gonadotrophins are commonly started during the early follicular phase with a spontaneous menses, but depending on the level of urgency, they can be started after truncation of the menstrual cycle with the administration of GnRH antagonists (*von Wolff et al., 2009*), or randomly at any point in the cycle (*Bedoschi et al., 2010*; *Buendgen et al., 2013*; *Cakmak et al., 2013*; *Nayak and Wakim, 2011*; *Sonmezer et al., 2011*). Follicle recruitment appears possible at any stage of the menstrual cycle (*Baerwald et al., 2003*a; *Baerwald et al., 2003*b). On this basis, 'random start' stimulation protocols have been created for cancer patients who require urgent treatment (*Buendgen et al., 2013*; *Kuang et al., 2014*; *Qin et al., 2016*).

Short-term safety of ovarian stimulation in cancer patients

The procedural risks associated with transvaginal ultrasound-guided aspiration of ovarian follicles are small (less than 1%). Beyond the expected symptomatic enlargement of the ovaries, the most common acute complication of gonadotrophin stimulation is OHSS. The condition is associated with the stimulation of high numbers of follicles or eggs and exposure to human chorionic gonadotrophin (HCG). Severe OHSS complicates fewer than 5% of IVF stimulations (*Papanikolaou et al., 2006*). To minimize the risk of OHSS the dose of gonadotrophins should be carefully selected according to the patient's age and ovarian reserve.

Traditionally, HCG has been used to mimic the physiological mid-cycle LH surge, to trigger final oocyte maturation in preparation for oocyte retrieval. Multiple studies have evaluated using lower doses of HCG to reduce the risk of developing OHSS; however, this strategy does not appear to mitigate this risk based on the published randomized controlled trials (*Lin et al., 2011*; *Tsoumpou et al., 2009*). GnRH antagonist protocols have been shown to result in a lower rate of OHSS when compared with traditional GnRH agonist protocols (*Al-Inany et al., 2016*; *Lambalk et al., 2017*; *Toftager et al., 2016*). GnRH antagonist protocols also allow for the triggering of final oocyte maturation with GnRH agonists instead of HCG. A recent Cochrane review involving 17 randomized controlled trials showed a reduction in OHSS incidence in the GnRH agonist trigger group compared with the HCG trigger group (OR 0.05, 95% CI 0.01–0.28) (*Youssef et al., 2014*). The successful use of GnRH agonist in triggering final oocyte maturation and reducing the risk of OHSS has also been demonstrated specifically in fertility preservation cycles (*Oktay et al., 2010*; *Reddy et al., 2014*). However, a GnRH agonist trigger does not eliminate OHSS in all patients and, as such, great caution has to be exercised in cancer patients (*Fatemi et al., 2014*).

Long-term safety of ovarian stimulation in cancer patients

Many breast cancer tumour cells are oestrogen receptor positive, and accordingly are susceptible to environments with oestrogen excess (*Allred et al., 2001*; *Deli et al., 2020*; Ouifki et al., 2022; *Prest et al., 2002*). Even tumours that are classified as receptor negative will contain a small percentage of receptor-positive cells (*Babayan et al., 2013*; *Gonazalez-Angulo et al., 2007*). Serum oestradiol concentrations reach supraphysiological concentrations during ovarian stimulation, typically 5000 pmol/ml (peak natural cycle concentrations 750–1300 pmol/ml) and not uncommonly exceeding 10,000 pmol/ml. Observational data support the safety of these technologies in terms of the recurrence of breast cancer and contralateral disease, although follow-up periods are limited (*Azim et al., 2008*; *Kim et al., 2016*; *Rodgers et al., 2017*; *Wang et al., 2022*). Follow-up data suggest that the incidence of recurrence in breast cancer patients is not elevated; however, high concentrations of oestrogens can in theory stimulate subclinical disseminated disease (*Henderson et al., 1990*), so any therapy that antagonizes this effect is reasonable (*Howell et al., 2005*; *Love et al., 2008*; *Miller, 2006*).

Two strategies are commonly employed to minimize this oestrogen exposure: recovering oocytes from an unstimulated IVF cycle, or administering cytoprotective agents in combination with gonadotrophin stimulation. Aromatase inhibitors have proven efficacious as an adjuvant therapy for the management of micrometastatic disease (*Fisher et al., 1989*; *Goss et al., 2003*; *Howell and Locker, 2005*; *Miller, 2006*). More importantly for breast cancer patients, they suppress oestradiol production during IVF stimulation.

Letrozole is the most potent of the aromatase inhibitors, suppressing greater than 96% of its activity. With the concurrent use of aromatase inhibitors, gonadotrophin doses can be optimized to maximize oocyte yield, while maintaining oestradiol production closer to physiological concentrations (Checa et al., 2012; *Oktay et al., 2003*). Several retrospective reviews of clinics' experiences with the addition of letrozole for breast cancer patients have supported this, although they find mixed results in terms of total FSH requirements and oocyte yield (*Ben-Haroush et al., 2018*; Checa et al., 2012; *Goldrat et al., 2015*; *Oktay et al., 2006*; *Pu et al., 2011*; *Revelli et al., 2013*). Letrozole has also found widespread use in reproductive medicine as an ovulation induction agent and adjunct in IVF protocols (*Schoolcraft et al., 2008*). Since the ovary remains active beyond retrieval of the oocytes, the sustained use of letrozole for at least 1 week beyond egg retrieval seems reasonable, when ovarian sex hormone production related to the treatment subsides.

Recommendations:

3. Efforts should be made to mitigate the risks of ovarian stimulation in cancer patients.

4. To minimize the risk of OHSS, GnRH antagonist protocols and triggering of final maturation with a GnRH agonist should be considered.

5. Random-start protocols should be considered to minimize delaying the start of treatment.

6. Aromatase inhibitors can be considered to minimize oestrogen concentrations in patients with oestrogen-sensitive tumours.

Ovarian tissue cryopreservation and transplantation

Ovarian tissue cryopreservation (OTC) is a fertility preservation option in which a part of or a whole ovary is removed and cryopreserved. The ovarian tissue is later transplanted back into the patient if infertility from ovarian insufficiency is confirmed and pregnancy desired.

OTC should be considered for patients needing gonadotoxic therapy or who need a removal of ovarian tissue for a benign underlying cause. This technique should generally be reserved for pre-pubertal patients with a significant risk of infertility from their treatment but can also be used when there is insufficient time to perform ovarian stimulation, or when the patient declines to undergo egg retrieval. In December 2019, the American Society for Reproductive Medicine released a committee opinion stating: 'Given the current body of literature, OTC should be considered an established medical procedure with limited effectiveness that should be offered to carefully selected patients', page 1025 (*Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion, 2019)*. In 2020, CFAS removed its experimental label for OTC. Like any technique, OTC should ideally be performed prior to cancer treatments; however, it can also be done between rounds of treatment assuming that there is a potential for fertility (*CFAS Position Statement on Ovarian Tissue Cryopreservation, 2020*). Contraindications to OTC include patients with a high risk of complications with general anaesthesia or abdominal surgery, or a lack of resources or expertise using this technology.

The OTC process involves an initial surgical procedure to perform a laparoscopic unilateral partial or complete oophorectomy. This is generally associated with minimal risk related to the surgery itself and anaesthesia. This surgical procedure should ideally be combined with other necessary procedures associated with the patient's treatment. The ovarian cortex is cut into small strips and cryopreserved using slow-freezing or vitrification techniques. Subsequent ovarian tissue transplantation can be performed orthotopically to the native ovary, within the vacant ovarian fossa, or heterotopically within the pelvis or other subcutaneous tissue. These grafts typically become hormonally active as quickly as 3 months after transplantation and remain functional for on average 5 years, but function up to 10 years has been documented (*Andersen et al., 2012*).

To prevent the reintroduction of cancer cells, ovarian biopsy should be performed at the time of oophorectomy, and the risk of ovarian metastasis evaluated based on cancer type and location. Techniques for the in-vitro maturation of oocytes at the time of oophorectomy and later from cryopreserved ovarian tissue are being researched and will hopefully provide an alternative to transplantation and a means of avoiding the possibility of reintroducing tumour cells (*Abir et al., 2016*).

To date, over 160 live births have been reported in humans with this technique, with documented OTC from a premenarchal girl. Spontaneous pregnancy, ovarian stimulation and IVF have all been reported as outcomes with ovarian tissue transplantation (*Demeestere et al., 2007*; *Shea et al., 2014*). A live birth rate of 25–33% has been reported by the few groups that are proficient in this technique (*Jadoul et al., 2017*; *Jensen et al., 2015*; *Van der Ven et al., 2016*).

Summary statement:

6. Ovarian tissue cryopreservation and transplantation is no longer considered an experimental method of fertility preservation: it can be an option in cases with insufficient time for ovarian stimulation and/or when abdominal surgery is required.

Recommendation:

7. Ovarian tissue cryopreservation and future ovarian tissue transplantation can be considered in select cases of emergency fertility preservation when local expertise is available, particularly when abdominal surgery is already planned.

Pregnancy after cancer

There is no consensus on the best time to conceive after cancer treatments, and most data pertain to breast cancer survivors. Since most breast cancer recurrences occur in the first 2 years, patients are normally advised to avoid pregnancy during this period of surveillance. However, some studies suggest that early conception does not negatively impact survival (*Blakely et al., 2004*; *Ives et al., 2007*). A recent large meta-analysis that included 112,840 breast cancer patients, of whom 7505 had a pregnancy after diagnosis, actually showed a higher disease-free survival in these patients (*Lambertini et al., 2021*). Ultimately, the decision on the timing of pregnancy should be determined in consultation with a cancer specialist (*Gelber et al., 2001*; *Helewa et al., 2002*).

Fertility-sparing surgical options

The harmful effects of radiation on the ovaries can be minimized by ovarian transposition. The ovaries are surgically transposed to a location outside the radiation field (*Han et al., 2011*). This may also be combined with gonadal shielding to further reduce the dose effect (*Mazonakis et al., 2006*). Using this technique, reports on the preservation of menstrual function have ranged from 65% to over 88% (*Al-Badawi et al., 2010*; *Bisharah and Tulandi, 2003*; *Pahisa et al., 2008*). The risks associated with the procedure include ovarian cysts, adhesions, pelvic pain, ovarian migration, premature ovarian failure and tubal injury (*Morice et al., 2000*; Wo et al., 2009). A small risk of disease metastasizing to the ovary exists in some malignancies, so transposition could facilitate the spread of disease (*Nguyen et al., 1998*; *Picone et al., 2003*). Any benefits of transposition may be lost when adjuvant chemotherapy is employed (*Morris and Ryley, 2011*; *Williams et al., 1999*). Other fertility-sparing surgical options include cervical conization or trachelectomy for select early-stage cervical cancer patients and unilateral oophorectomy or cystectomy in select ovarian neoplasms (*Ronn and Holzer, 2013*).

Recommendation:

8. Fertility-sparing surgery should be considered when possible if it does not compromise survival.

FERTILITY PRESERVATION IN PATIENTS WITH TESTICLES

The management of fertility preservation needs for patients producing spermatozoa may seem very straightforward, but there are several important considerations. Commonly, patients present with abnormal sperm parameters such as oligozoospermia, an effect that may directly relate to the illness itself (*Karavani et al., 2020*; *Paoli et al., 2016*; *Sieniawski et al., 2008*; *van der Kaaij et al., 2009*). A high percentage of patients exposed to combination chemotherapy develop testicular dysfunction (70–98%) (*Bramswig et al., 1990*; *Green et al., 2010*; *Heikens et al., 1996*; *Meistrich et al., 1992*; *Paoli et al., 2016*; *Rivkees and Crawford, 1988*; *Sieniawski et al., 2008*). A reduced concentration appears related to an epithelial effect, and the less common sequelae of hypogonadism to a loss of Leydig cell function (*Mustieles et al., 1995*; *Zaletel et al., 2010*).

In haematological cancer survivors, the recovery of spermatogenic capacity can take years, so it is important to continue testing to capture cases with latent recovery (*Buchanan et al., 1975*). Sibling studies of childhood cancer survivors demonstrate a 50% higher risk of infertility, but over 60% should achieve parenthood without the need for ART (*Thomson et al., 2002*). Due to a high sperm aneuploidy frequency for up to 2 years after exposure to chemotherapy, pregnancy should be avoided during that time (*Bujan et al., 2014*; *Martinez et al., 2017*; *Rives et al., 2017*; *Tempest et al., 2008*). Exposure to chemotherapy can generate permanent epimutations within the germline, with potential epigenetic transgenerational transmission (*Shnorhavorian et al., 2017*). Fetal malformation rates have been reported as higher in the children conceived with spermatozoa from cancer survivors, but this appears to be related to the diagnosis itself, not exposure to the treatments (*Al-Jebari et al., 2018*; *Stahl et al., 2011*).

The clear recommendation is the cryopreservation of spermatozoa. In cases when patients are unable to produce an ejaculated sample, surgical sperm retrieval procedures can be performed (*Shankara-Narayana et al., 2019*). Several variables may help determine the number of samples to cryopreserve and their future use, including sperm parameters, reproductive needs and the time frame for the medical treatments. ASCO recommends the banking of three ejaculates (*Loren et al., 2013*). However, most patients are restricted by time and many only produce a single sample. Between the quality and amount of spermatozoa banked, many of these samples are only suitable for IVF with intracytoplasmic sperm injection.

Recommendation:

9. Prior to starting gonadotoxic treatments, sperm cryopreservation should be offered.

SPECIAL CONSIDERATIONS FOR CHILDREN AND ADOLESCENTS

The relative 5-year survival rate for all childhood cancers combined exceeds 80% (*Cronin et al., 2018*). With the improved overall survival rate of children affected by childhood cancer, there is now a growing population of survivors of childhood cancer who want children in the future. For patients with ovaries, the retention of oestrogen production is important for cardiac, bone, brain and urogenital health.

ASCO offers clear guidelines for fertility preservation in children, adolescents and young adults (*Oktay et al., 2018*). Recognizing the risks associated with gonadotoxic therapy, ASCO has recommended that oncology healthcare practitioners work in partnership with centres who have expertise in fertility preservation since 2012. These multidisciplinary teams can facilitate fertility preservation (oocytes or OTC) for post-pubertal children, and can help counsel patients and families on the assessment and management of reproductive concerns. Reassuringly, if natural conception occurs from childhood cancer survivors, there is no increased incidence of congenital malformations, chromosomal anomalies or cancers, compared with sibling controls and general population data (*Mueller et al., 2009*; *Seppanen et al., 2016*; *Winther et al., 2012*).

Fertility preservation options in pubertal children/adolescents are the same as in adults, beyond the requirement for general anaesthesia and abdominal ultrasonography in the majority of cases. For pre-pubertal children, the majority of proposed treatment modalities have limited published data attesting to efficacy, with the exception of gonadal shielding or transposition of the gonads to outside the field of radiation. While 60% of patients maintain ovarian function, the pregnancy rate of those desiring conception was only 15% (*Aubard et al., 2001*).

Complex ethical considerations may arise when counselling families about fertility preservation options. The difficulty in decision making is often compounded by the frequently limited time available to make decisions prior to gonadotoxic treatment, as well as navigating consent for patients who cannot provide assent. The majority of post-pubertal patients will be eligible for oocyte cryopreservation; however, for pre-pubertal and some post-pubertal adolescents, OTC may be the only practical option. Although there has been at least one published case report of a live birth after an auto-transplantation of cryopreserved ovarian tissue from a 9-year-old pre-pubertal girl (*Matthews et al., 2018*), patients and their families should be counselled on the relative novelty of the technique and lack of long-term outcomes. For this reason, OTC should be offered under an institutional review board (IRB) approved protocol in the paediatric population. An additional consideration is determination of the capacity of the minor to consent/provide assent.

For prepubertal males the only option is testicular biopsy and testicular tissue cryopreservation. No pregnancies have been documented in humans with this technique, but live birth has been achieved in the primate model (*Faymomi et al., 2019*). For post-pubertal males who are unwilling or unable to provide a sample by masturbation, testicular sperm extraction is an option.

Ethicists are key members of the multidisciplinary oncofertility team and should be involved early on when non-standard therapies are considered. Wallace and colleagues have recommended a framework for patient selection focusing on patients with the highest risk of premature ovarian insufficiency (*Wallace et al., 2016*).

Many families and competent childhood cancer patients may ultimately decline fertility preservation techniques.

Nevertheless, these patients require long-term follow-up once they are in remission and stable. The reasons for follow-up may include ongoing psychosocial support, ensuring pubertal development with early referral for pubertal delay, menstrual cycle monitoring, contraception and healthy sexuality, monitoring for reproductive side effects of treatment (e.g. graft-versus-host disease) and revisiting fertility preservation options, if available. Overall, premature ovarian insufficiency is uncommon (less than 10%) in childhood cancer survivors; however, many survivors can subsequently have diminished ovarian reserve impacting on future fertility (*Klipstein et al., 2020*; *Levine et al., 2018*).

Although there is no marker for fertility, AMH is commonly used to monitor ovarian reserve (*George et al., 2019*). Overall, survivors of childhood cancer often have lower AMH concentrations compared with a control group, increasing the risk of infertility, reduced outcomes with ART and early menopause (*Lunsford et al., 2014*). While the risk of premature ovarian insufficiency and infertility is present, cancer survivors may have less awareness regarding contraceptive options, and those between the ages of 15 and 30 years were more likely to terminate a pregnancy than their age-matched control subjects (*Green et al., 2002*; *Winther et al., 2009*), highlighting the need for complete reproductive care including contraception and safe sexual practices. Of note, some fertility preservation techniques can be offered to children undergoing gonadotoxic therapies for the treatment of medical conditions like juvenile idiopathic arthritis, SLE and conditions with reduced ovarian reserve (galactosaemia and Turner syndrome).

Summary statement:

7. Gonadal shielding and transposition is the only established modality of fertility preservation in the pre-pubertal population.

Recommendations:

10. Consideration of the options for fertility preservation in the pre-pubertal population should be undertaken as part of a multidisciplinary team, including ethicists.

11. All children and adolescents undergoing gonadotoxic therapy should have a discussion of the fertility implications of therapy and be offered referral to a specialist infertility preservation.

12. All children and adolescents undergoing fertility preservation should have the option to provide assent for their care in addition to parental/guardian consent.

13. Post-pubertal patients should be offered oocyte cryopreservation prior to gonadotoxic therapy.

14. OTC in the paediatric population should be undertaken as part of an IRB-approved protocol.

15. Childhood survivors of cancer should be monitored in a long-term follow-up clinic and periodically re-reviewed regarding their options for ongoing fertility preservation.

CONCLUSION

Management of cancer and certain medical conditions present a variety of risks to fertility and pregnancy. Effective fertility preservation options are available. A multidisciplinary approach is key for the appropriate and efficient delivery of these services, including a timely referral for a fertility preservation consultation and assessment.

DATA AVAILABILITY

No data was used for the research described in the article.

REFERENCES

Abir, R., Ben-Aharon, I., Garor, R., Yaniv, I., Ash, S., Stemmer, S.M., Ben-Haroush, A., Freud, E., Dravarusic, D., Sapir, O., Fisch, B., 2016. Cryopreservation of in vitro matured oocytes in addition to ovarian tissue freezing for fertility preservation in paediatric female cancer patients before and after cancer therapy. Hum Reprod 31 (4), 750–762.

Al-Badawi, I.A., Al-Aker, M., AlSubhi, J., Salem, H., Abduljabbar, A., Balaraj, K., Munkarah, A., 2010. Laparoscopic ovarian transposition before pelvic irradiation: a Saudi tertiary center experience. Int J Gynecol Cancer 20 (6), 1082–1086.

Al-Inany, H.G., Youssef, M.A., Aboulghar, M., Broekmans, F., Sterrenburg, M., Smit, J., Abou-Setta, A.M., 2011. Gonadotrophin-releasing hormone antagonists for assisted reproductive technology. Cochrane Database Syst Rev (5), CD001750.

Al-Inany, H.G., Youssef, M.A., Ayeleke, R.O., Brown, J., Lam, W.S., Broekmans, F.J., 2016. Gonadotrophin-releasing hormone antagonists for assisted reproductive technology. Cochrane Database Syst Rev 4, CD001750.

Al-Jebari, Y., Rylander, L., Stahl, O., Giwercman, A., 2018. Risk of Congenital Malformations in Children Born Before Paternal Cancer. JNCI Cancer Spectr 2 (2) pky027.

Allred, C.D., Ju, Y.H., Allred, K.F., Chang, J., Helferich, W.G., 2001. Dietary genistin stimulates growth of estrogen-dependent breast cancer tumors similar to that observed with genistein. Carcinogenesis 22 (10), 1667–1673.

Almog, B., Azem, F., Gordon, D., et al., 2012. Effects of cancer on ovarian response in controlled ovarian stimulation for fertility preservation. Fertil Steril 98 (4), 957–960.

Anders, C., Marcom, P.K., Peterson, B., Gu, L., Unruhe, S., Welch, R., Lyons, P., Behera, M., Copland, S., Kimmick, G., Shaw, H., Snyder, S., Antenos, M., Woodruff, T., Blackwell, K., 2008. A pilot study of predictive markers of chemotherapy-related amenorrhea among premenopausal women with early stage breast cancer. Cancer Invest 26 (3), 286–295.

Andersen, C.Y., Silber, S.J., Bergholdt, S.H., Jorgensen, J.S., Ernst, E., 2012. Long-term duration of function of ovarian tissue transplants: case reports. Reprod Biomed Online 25 (2), 128–132.

Anderson, R.A., Brewster, D.H., Wood, R., Nowell, S., Fischbacher, C., Kelsey, T.W., Wallace, W.H., 2018. The impact of cancer on subsequent chance of pregnancy: a population-based analysis. Hum Reprod 33 (7), 1281–1290.

Anderson, R.A., Rosendahl, M., Kelsey, T.W., Cameron, D.A., 2013. Pretreatment anti-Mullerian hormone predicts for loss of ovarian function after chemotherapy for early breast cancer. Eur J Cancer 49 (16), 3404–3411.

Anderson, R.A., Themmen, A.P., Al-Qahtani, A., Groome, N.P., Cameron, D.A., 2006. The effects of chemotherapy and long-term gonadotrophin suppression on the ovarian reserve in premenopausal women with breast cancer. Hum Reprod 21 (10), 2583–2592.

Arce, J.C., La Marca, A., Mirner Klein, B., Nyboe Andersen, A., Fleming, R., 2013. Antimullerian hormone in gonadotropin releasing-hormone antagonist cycles: prediction of ovarian response and cumulative treatment

outcome in good-prognosis patients. Fertil Steril 99 (6), 1644–1653.
Arnon, J., Meirow, D., Lewis-Roness, H., Ornoy, A., 2001. Genetic and teratogenic effects of cancer treatments on gametes and embryos. Hum Reprod Update 7 (4), 394–403.
Ash, P., 1980. The influence of radiation on fertility in man. Br J Radiol 53 (628), 271–278.
Aubard, Y., Piver, P., Pech, J.C., Galinat, S., Teissier, M.P., 2001. Ovarian tissue cryopreservation and gynecologic oncology: a review. Eu J Obstet Gynecol Reprod Biol 97 (1), 5–14.
Azim, A.A., Costantini-Ferrando, M., Oktay, K., 2008. Safety of fertility preservation by ovarian stimulation with letrozole and gonadotropins in patients with breast cancer: a prospective controlled study. J Clin Oncol 26 (16), 2630–2635.
Babayan, A., Hannemann, J., Spotter, J., Muller, V., Pantel, K., Joosse, S.A., 2013. Heterogeneity of estrogen receptor expression in circulating tumor cells from metastatic breast cancer patients. PloS One 8 (9), e75038.
Baerwald, A.R., Adams, G.P., Pierson, R.A., 2003. A new model for ovarian follicular development during the human menstrual cycle. Fertil Steril 80 (1), 116–122.
Barton, S.E., Najita, J.S., Ginsburg, E.S., Leisenring, W.M., Stovall, M., Weathers, R.E., Sklar, C.A., Robison, L.L., Diller, L., 2013. Infertility, infertility treatment, and achievement of pregnancy in female survivors of childhood cancer: a report from the Childhood Cancer Survivor Study cohort. Lancet Oncol 14 (9), 873–881.
Bath, L.E., Wallace, W.H., Shaw, M.P., Fitzpatrick, C., Anderson, R.A., 2003. Depletion of ovarian reserve in young women after treatment for cancer in childhood: detection by anti-Mu hormone, inhibin B and ovarian ultrasound. Hum Reprod 18 (11), 2368–2374.
Baynosa, J., Westphal, L.M., Madrigrano, A., Wapnir, I., 2009. Timing of breast cancer treatments with oocyte retrieval and embryo cryopreservation. J Am Coll Surg 209 (5), 603–607.
Bedoschi, G.M., de Albuquerque, F.O., Ferriani, R.A., Navarro, P.A., 2010. Ovarian stimulation during the luteal phase for fertility preservation of cancer patients: case reports and review of the literature. J Assist Reprod Genet 27 (8), 491–494.
Behringer, K., Mueller, H., Goergen, H., Thielen, I., Eibl, A.D., Stumpf, V., Wessels, C., Wiehlputz, M., Rosenbrock, J., Halbsguth, T., Reiners, K.S., Schober, T., Renno, J.H., von Wolff, M., van der Ven, K., Kuehr, M., Fuchs, M., Diehl, V., Engert, A., Borchmann, P., 2013. Gonadal function and fertility in survivors after Hodgkin lymphoma treatment within the German Hodgkin Study Group HD13 to HD15 trials. J Clin Oncol 31 (2), 231–239.
Ben-Haroush, A., Wertheimer, A., Klochendler, E., Sapir, O., Shufaro, Y., Oron, G., 2018. Effect of letrozole added to gonadotropins in controlled ovarian stimulation protocols on the yield and maturity of retrieved oocytes. Gynecol Endocrinol 1–4.
Bisharah, M., Tulandi, T., 2003. Laparoscopic preservation of ovarian function: an underused procedure. Am J Obstet Gynecol 188 (2), 367–370.
Blakely, L.J., Buzdar, A.U., Lozada, J.A., Shullaih, S.A., Hoy, E., Smith, T.L., Hortobagyi, G.N., 2004. Effects of pregnancy after treatment for breast carcinoma on survival and risk of recurrence. Cancer 100 (3), 465–469.
Blumenfeld, Z., Avivi, I., Ritter, M., Rowe, J.M., 1999. Preservation of fertility and ovarian function and minimizing chemotherapy-induced gonadotoxicity in young women. J Soc Gynecol Investig 6 (5), 229–239.
Blumenfeld, Z., Patel, B., Leiba, R., Zuckerman, T., 2012. Gonadotropin-releasing hormone agonist may minimize premature ovarian failure in young women undergoing autologous stem cell transplantation. Fertil Steril 98 (5), 1266-70 e1.
Bramswig, J.H., Heimes, U., Heiermann, E., Schlegel, W., Nieschlag, E., Schellong, G., 1990. The effects of different cumulative doses of chemotherapy on testicular function. Results in 75 patients treated for Hodgkin's disease during childhood or adolescence. Cancer 65 (6), 1298–1302.
Brodin, T., Hadziosmanovic, N., Berglund, L., Olovsson, M., Holte, J., 2013. Antimullerian hormone levels are strongly associated with live-birth rates after assisted reproduction. J Clin Endocrinol Metab 98 (3), 1107–1114.
Brougham, M.F., Crofton, P.M., Johnson, E.J., Evans, N., Anderson, R.A., Wallace, W.H., 2012. Anti-Mullerian hormone is a marker of gonadotoxicity in pre- and postpubertal girls treated for cancer: a prospective study. J Clin Endocrinol Metab 97 (6), 2059–2067.
Buchanan, J.D., Fairley, K.F., Barrie, J.U., 1975. Return of spermatogenesis after stopping cyclophosphamide therapy. Lancet 2 (7926), 156–157.
Buendgen, N.K., Schultze-Mosgau, A., Cordes, T., Diedrich, K., Griesinger, G., 2013. Initiation of ovarian stimulation independent of the menstrual cycle: a case-control study. Arch Gynecol Obstet 288 (4), 901–904.
Bujan, L., Walschaerts, M., Brugnon, F., Daudin, M., Berthaut, I., Auger, J., Saias, J., Szerman, E., Moinard, N., Rives, N., Hennebicq, S., 2014. Impact of lymphoma treatments on spermatogenesis and sperm deoxyribonucleic acid: a multicenter prospective study from the CECOS network. Fertil Steril 102 (3), 667-74 e3.
Cakmak, H., Katz, A., Cedars, M.I., Rosen, M.P., 2013. Effective method for emergency fertility preservation: random-start controlled ovarian stimulation. Fertil Steril.
Candian Cancer Society. Canadian Cancer Statistics 2021. Toronto, ON; 2021. cancer.ca/Canadian-Cancer-Statistics-2021-EN. 2021.
Cardozo, E.R., Thomson, A.P., Karmon, A.E., Dickinson, K.A., Wright, D.L., Sabatini, M.E., 2015. Ovarian stimulation and in-vitro fertilization outcomes of cancer patients undergoing fertility preservation compared to age matched controls: a 17-year experience. J Assist Reprod Genet 32 (4), 587–596.
CFAS Position Statement on Ovarian Tissue Cryopreservation. https://cfasca/_Library/2020positionstatements/CFAS-Position-Statement-Ovarian-Cryo-Formattedpdf 2020.
Chang, M.Y., Chiang, C.H., Hsieh, T.T., Soong, Y.K., Hsu, K.H., 1998. Use of the antral follicle count to predict the outcome of assisted reproductive technologies. Fertil Steril 69 (3), 505–510.
Cobo, A., Garcia-Velasco, J., Coello, A., Domingo, J., Pellicer, A., Remohi, J., 2016. Oocyte vitrification as an efficient option for elective fertility preservation. Fertil Steril 105, 755–764.
Cobo, A., Garcia-Velasco, J., Domingo, J., Pellicer, A., 2018. Elective and Onco-fertility preservation: factors related to IVF outcomes. Hum Reprod 33, 2222–2231.
Cobo, A., Garcia-Velasco, J., Remohi, J., Pellicer, A., 2021. Oocyte vitrification for fertility preservation for both medical and nonmedical reasons. Fertil Steril 115 (5), 1091–1101.
Critchley, H.O., Wallace, W.H., 2005. Impact of cancer treatment on uterine function. J Natl Cancer Inst Monographs (34), 64–68.
Cronin, K.A., Lake, A.J., Scott, S., Firth, A.U., Sung, H., Henley, S.J., Sherman, R.L., Siegel, R.L., Anderson, R.N., Kohler, B.A., Benard, V.B., Negoita, S., Wiggins, C., Cance, W.G., Jemal, A., 2018. Annual Report to the Nation on the Status of Cancer, part I: National cancer statistics. Cancer 124 (13), 2785–2800.
Decanter, C., Morschhauser, F., Pigny, P., Lefebvre, C., Gallo, C., Dewailly, D., 2010. Anti-Mullerian hormone follow-up in young women treated by chemotherapy for lymphoma: preliminary results. Reprod Biomed Online 20 (2), 280–285.
Deli, T., Orosz, M., Jakab, A., 2020. Hormone replacement therapy in cancer survivors – Review of the literature. Path Oncol Res 26, 63–78.
Demeestere, I., Brice, P., Peccatori, F.A., Kentos, A., Dupuis, J., Zachee, P., Casasnovas, O., Van Den Neste, E., Dechene, J., De Maertelaer, V., Bron, D., Englert, Y., 2016. No Evidence for the Benefit of Gonadotropin-Releasing Hormone Agonist in Preserving Ovarian Function and Fertility in Lymphoma Survivors Treated With Chemotherapy: Final Long-Term Report of a Prospective Randomized Trial. J Clin Oncol 34 (22), 2568–2574.
Demeestere, I., Simon, P., Emiliani, S., Delbaere, A., Englert, Y., 2007. Fertility preservation: successful transplantation of cryopreserved ovarian tissue in a young patient previously treated for Hodgkin's disease. Oncologist 12 (12), 1437–1442.
Depalo, R., Jayakrishan, K., Garruti, G., et al., 2012. GnRH agonist versus GnRH antagonist in in vitro fertilization and embryo transfer (IVF/ET). Reprod Biol Endocrinol: RB&E 10, 26.
Dezellus, A., Barriere, P., Campone, M., Lemanski, C., Vanlemmens, L., Mignot, L., Delozier, T., Levy, C., Bendavid, C., Debled, M., Bachelot, T., Jouannaud, C., Loustalot, C., Mouret-Reynier, M.A., Gallais-Umbert, A., Masson, D., Freour, T., 2017. Prospective evaluation of serum anti-Mullerian hormone dynamics in 250 women of reproductive age treated with chemotherapy for breast cancer. Eur J Cancer 79, 72–80.
Dolinko, A.V., Farland, L.V., Missmer, S.A., Srouji, S.S., Racowsky, C., Ginsburg, E.S., 2018. Responses to fertility treatment among patients with cancer: a retrospective cohort study. Fertil Res Pract 4, 3.
Doyle, J.O., Richter, K.S., Lim, J., Stillman, R.J., Graham, J.R., Tucker, M., 2016. Successful elective and medically indicated oocyte vitrification and warming for autologous in vitro fertilization, with predicted birth probabilities for fertility preservation according to number of cryopreserved oocytes and age at retrieval. Fertil Steril 105, 459–466.
Fatemi, H.M.P.-T.B., Humaidan, P., Kol, S., Banker, M., Devroey, P., García-Velasco, J.A., 2014. Severe ovarian hyperstimulation syndrome after gonadotropin-releasing hormone (GnRH)

agonist trigger and "freeze-all" approach in GnRH antagonist protocol. Fertil Steril 101 (4), 1008–1011 Apr.
Fatemi, H.M., Blockeel, C., Devroey, P., 2012. Ovarian stimulation: today and tomorrow. Curr Pharm Biotechnol 13 (3), 392–397.
Faymomi, A.P., Peters, K., Sukhwani, M., Valli-Pulaski, H., Shetty, G., Meistrich, M.L., Houser, L., Robertson, N., Roberts, V., Ramsey, C., Hanna, C., Hennebold, J.D., Dobrinski, I., Orwig, K.E., 2019. Autologous grafting of cryopreserved prepubertal rhesus testis produces sperm and offspring. Science 363 (6433), 1314–1319.
Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion. Fertil Steril 2019; 112(6): 1022-33.
Filippi, F., Meazza, C., Somigliana, E., Podda, M., Dallagiovanna, C., Massimino, M., Raspagliesi, F., Terenziani, M., 2021. Fertility preservation in childhood and adolescent female tumor survivors. Fertil Steril 116, 1087–1095.
Fisher, B., Costantino, J., Redmond, C., Poisson, R., Bowman, D., Couture, J., Dimitrov, N.V., Wolmark, N., Wickerham, D.L., Fisher, E.R., 1989. A randomized clinical trial evaluating tamoxifen in the treatment of patients with node-negative breast cancer who have estrogen-receptor-positive tumors. N Engl J Med 320 (8), 479–484.
Freeman, E.W., Sammel, M.D., Lin, H., Gracia, C.R., 2012. Anti-mullerian hormone as a predictor of time to menopause in late reproductive age women. J Clin Endocrinol Metab 97 (5), 1673–1680.
Friedler, S., Koc, O., Gidoni, Y., Raziel, A., Ron-El, R., 2012. Ovarian response to stimulation for fertility preservation in women with malignant disease: a systematic review and meta-analysis. Fertil Steril 97 (1), 125–133.
Garcia-Velasco, J.A., Domingo, J., Cobo, A., Martinez, M., Carmona, L., Pellicer, A., 2013. Five years' experience using oocyte vitrification to preserve fertility for medical and nonmedical indications. Fertil Steril 99 (7), 1994–1999.
Gelber, S., Coates, A.S., Goldhirsch, A., Castiglione-Gertsch, M., Marini, G., Lindtner, J., Edelmann, D.Z., Gudgeon, A., Harvey, V., Gelber, R.D., 2001. Effect of pregnancy on overall survival after the diagnosis of early-stage breast cancer. J Clin Oncol 19 (6), 1671–1675.
George, S.A., Williamson Lewis, R., Schirmer, D.A., Effinger, K.E., Spencer, J.B., Mertens, A.C., Meacham, L.R., 2019. Early Detection of Ovarian Dysfunction by Anti-Mullerian Hormone in Adolescent and Young Adult-Aged Survivors of Childhood Cancer. J Adolesc Young Adult Oncol 8 (1), 18–25.
Goldman, R.H., Racowsky, C., Farland, L.V., Munne, S., Ribustello, L., Fox, J.H., 2017. Predicting the likelihood of live birth for elective oocyte cryopreservation: a counseling tool for physicians and patients. Hum Reprod 32 (4), 853–859.
Goldrat, O., Gervy, C., Englert, Y., Delbaere, A., Demeestere, I., 2015. Progesterone levels in letrozole associated controlled ovarian stimulation for fertility preservation in breast cancer patients. Hum Reprod 30 (9), 2184–2189.
Gonzalez-Angulo, A.M., Morales-Vasquez, F., Hortobagyi, G.N., 2007. Overview of resistance to systemic therapy in patients with breast cancer. Adv Exp Med Biol 608, 1–22.
Goodwin, P.J., Ennis, M., Pritchard, K.I., Trudeau, M., Hood, N., 1999. Risk of menopause during the first year after breast cancer diagnosis. J Clin Oncol 17 (8), 2365–2370.
Goodwin, T., Elizabeth Oosterhuis, B., Kiernan, M., Hudson, M.M., Dahl, G.V., 2007. Attitudes and practices of pediatric oncology providers regarding fertility issues. Pediatr Blood Cancer 48 (1), 80–85.
Goss, P.E., Ingle, J.N., Martino, S., Robert, N.J., Muss, H.B., Piccart, M.J., Castiglione, M., Tu, D., Shepherd, L.E., Pritchard, K.I., Livingston, R.B., Davidson, N.E., Norton, L., Perez, E.A., Abrams, J.S., Therasse, P., Palmer, M.J., Pater, J.L., 2003. A randomized trial of letrozole in postmenopausal women after five years of tamoxifen therapy for early-stage breast cancer. N Engl J Med 349 (19), 1793–1802.
Green, D.M., Kawashima, T., Stovall, M., Leisenring, W., Sklar, C.A., Mertens, A.C., Donaldson, S.S., Byrne, J., Robison, L.L., 2010. Fertility of male survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. J Clin Oncol 28 (2), 332–339.
Green, D.M., Nolan, V.G., Goodman, P.J., Whitton, J.A., Srivastava, D., Leisenring, W.M., Neglia, J.P., Sklar, C.A., Kaste, S.C., Hudson, M.M., Diller, L.R., Stovall, M., Donldson, S.S., Robison, L.L., 2014. The cyclophosphamide equivalent dose as an approach for quantifying alkylating agent exposure: a report from the Childhood Cancer Survivor Study. Pediatr Blood Cancer 61 (1), 53–67.
Green, D.M., Sklar, C.A., Boice, Jr, J.D., Mulvihill, J.J., Whitton, J.A., Stovall, M., Yasui, Y., 2009. Ovarian failure and reproductive outcomes after childhood cancer treatment: results from the Childhood Cancer Survivor Study. J Clin Oncol 27 (14), 2374–2381.
Green, D.M., Whitton, J.A., Stovall, M., et al., 2002. Pregnancy outcome of female survivors of childhood cancer: a report from the Childhood Cancer Survivor Study. Am J Obstet Gynecol 187 (4), 1070–1080.
Gupta, A.A., Edelstein, K., Albert-Green, A., D'Agostino, N., 2013. Assessing information and service needs of young adults with cancer at a single institution: the importance of information on cancer diagnosis, fertility preservation, diet, and exercise. Support Care Cancer 21 (9), 2477–2484.
Han, S.S., Kim, Y.H., Lee, S.H., Kim, G.J., Kim, H.J., Kim, J.W., Park, N.H., Song, Y.S., Kang, S.B., 2011. Underuse of ovarian transposition in reproductive-aged cancer patients treated by primary or adjuvant pelvic irradiation. J Obstet Gynaecol Res 37 (7), 825–829.
Heikens, J., Behrendt, H., Adriaanse, R., Berghout, A., 1996. Irreversible gonadal damage in male survivors of pediatric Hodgkin's disease. Cancer 78 (9), 2020–2024.
Helewa, M., Levesque, P., Provencher, D., Lea, R.H., Rosolowich, V., Shapiro, H.M., 2002. Breast cancer, pregnancy, and breastfeeding. J Obstet Gynaecol Can 24 (2), 164–180.
Henderson, I.C., Garber, J.E., Breitmeyer, J.B., Hayes, D.F., Harris, J.R., 1990. Comprehensive management of disseminated breast cancer. Cancer 66 (6 Suppl), 1439–1448.
Hickey, M., Peate, M., Saunders, C.M., Friedlander, M., 2009. Breast cancer in young women and its impact on reproductive function. Hum Reprod Update 15 (3), 323–339.
Howell, A., Locker, G.Y., 2005. Defining the roles of aromatase inhibitors in the adjuvant treatment of early-stage breast cancer. Clin Breast Cancer 6 (4), 302–309.
Howell, A., Sims, A.H., Ong, K.R., Harvie, M.N., Evans, D.G., Clarke, R.B., 2005. Mechanisms of Disease: prediction and prevention of breast cancer—cellular and molecular interactions. Nature clinical practice Oncology 2 (12), 635–646.
Ives, A., Saunders, C., Bulsara, M., Semmens, J., 2007. Pregnancy after breast cancer: population based study. BMJ 334 (7586), 194.
Jadoul, P., Guilmain, A., Squifflet, J., Luyckx, M., Votino, R., Wyns, C., Dolmans, M.M., 2017. Efficacy of ovarian tissue cryopreservation for fertility preservation: lessons learned from 545 cases. Hum Reprod 32 (5), 1046–1054.
Jemal, A., Thun, M.J., Ries, L.A., Howe, H.L., Weir, H.K., Center, M.M., Ward, E., Wu, X., Eheman, C., Anderson, R., Ajani, U.A., Kohler, B., Edwards, B.K., 2008. Annual report to the nation on the status of cancer, 1975-2005, featuring trends in lung cancer, tobacco use, and tobacco control. J Natl Cancer Inst 100 (23), 1672–1694.
Jenninga, E., Louwe, L.A., Peters, A.A., Nortier, J.W., Hilders, C.G., 2012. Timing of fertility preservation procedures in a cohort of female patients with cancer. Eur J Obstet Gynecol Reprod Biol 160 (2), 170–173.
Jensen, A.K., Kristensen, S.G., Macklon, K.T., Jeppesen, J.V., Fedder, J., Ernst, E., Andersen, C.Y., 2015. Outcomes of transplantations of cryopreserved ovarian tissue to 41 women in Denmark. Hum Reprod 30 (12), 2838–2845.
Karavani, G., Feigin, N., Tachover, T., Bdolah-Abram, T., Lavie, D., Ben-Yehuda, D., Ben-Meir, A., 2020. Parameters associated with sperm quality prior to chemotherapy in lymphoma patients. Andrologia 52 (10), e13794.
Kim, J., Turan, V., Oktay, K., 2016. Long-Term Safety of Letrozole and Gonadotropin Stimulation for Fertility Preservation in Women With Breast Cancer. J Clin Endocrinol Metab 101 (4), 1364–1371.
Kirkham, Y.A., Ornstein, M.P., Aggarwal, A., McQuillan, S., 2019. No. 313-Menstrual Suppression in Special Circumstances. J Obstet Gynaecol Can 41 (2), e7–e17.
Klipstein, S., Fallat, M.E., Savelli, S., Committee On Bioethics; Section on Hematology/Oncology; Section on Surgery, 2020. Fertility Preservation for Pediatric and Adolescent Patients With Cancer: Medical and Ethical Considerations. Pediatrics 145 (3).
Korkidakis, A., Lajkosz, K., Green, M., Strobino, D., Velez, M.P., 2019. Patterns of Referral for Fertility Preservation Among Female Adolescents and Young Adults with Breast Cancer: A Population-Based Study. J Adolesc Young Adult Oncol 8 (2), 197–204.
Kuang, Y., Hong, Q., Chen, Q., Chen, Q., Lyu, Q., Ai, A., Fu, Y., Shoham, Z., 2014. Luteal-phase ovarian stimulation is feasible for producing competent oocytes in women undergoing in vitro fertilization/intracytoplasmic sperm injection treatment, with optimal pregnancy outcomes in frozen-thawed embryo transfer cycles. Fertil Steril 101 (1), 105–111.
Lambalk, C.B.B.F., Huirne, J.A., Toftager, M., Pinborg, A., Homburg, R., van der Veen, F., van Wely, M., 2017. GnRH antagonist versus long agonist protocols in IVF: a systematic review and meta-analysis accounting for patient type. Hum Reprod Update 23 (5), 560–579 Sep 1.

Lambertini, M., Blondeaux, E., Bruzzone, M., Perachino, M., Anderson, R., de Azambuja, E., Poorvu, P., Kim, H.J., Villarreal-Garza, C., Pistilli, B., Vz-Luis, I., Saura, C., Ruddy, K., Franzoi, M.A., Sertoli, C., Ceppi, M., Azim, H.A., Amant, F., Demeestere, I., Del Mastro, L., Partridge, A.H., Pagani, O., Peccatori, F.A., 2021. Pregnancy after breast cancer: A systematic review and meta-analysis. J Clin Oncol 39, 3293–3305.

Larsen, E.C., Muller, J., Rechnitzer, C., Schmiegelow, K., Andersen, A.N., 2003a. Diminished ovarian reserve in female childhood cancer survivors with regular menstrual cycles and basal FSH <10 IU/l. Hum Reprod 18 (2), 417–422.

Larsen, E.C., Muller, J., Schmiegelow, K., Rechnitzer, C., Andersen, A.N., 2003b. Reduced ovarian function in long-term survivors of radiation- and chemotherapy-treated childhood cancer. J Clin Endocrinol Metab 88 (11), 5307–5314.

Lee, S., Ozkavukcu, S., Heytens, E., Moy, F., Oktay, K., 2010. Value of early referral to fertility preservation in young women with breast cancer. J Clin Oncol 28 (31), 4683–4686.

Lee, S.J., Schover, L.R., Partridge, A.H., Patrizio, P., Wallace, W.H., Hagerty, K., Beck, L.N., Brennan, L.V., Oktay, K., 2006. American Society of Clinical Oncology recommendations on fertility preservation in cancer patients. J Clin Oncol 24 (18), 2917–2931.

Lefebvre, T., Mirallie, S., Leperlier, F., Reignier, A., Barriere, P., Freour, T., 2018. Ovarian reserve and response to stimulation in women undergoing fertility preservation according to malignancy type. RMBO 37, 201–207.

Letourneau, J.M., Ebbel, E.E., Katz, P.P., Oktay, K.H., McCulloch, C.E., Ai, W.Z., Chien, A.J., Melisko, M.E., Cedars, M.I., Rosen, M.P., 2012. Acute ovarian failure underestimates age-specific reproductive impairment for young women undergoing chemotherapy for cancer. Cancer 118 (7), 1933–1939.

Levine, J.M., Whitton, J.A., Ginsberg, J.P., Green, D.M., Leisenring, W.M., Stovall, M., Robison, L.L., Armstrong, G.T., Sklar, C.A., 2018. Nonsurgical premature menopause and reproductive implications in survivors of childhood cancer: A report from the Childhood Cancer Survivor Study. Cancer 124 (5), 1044–1052.

Lewin, J., Ma, J.M.Z., Mitchell, L., Tam, S., Puri, N., Stephens, D., Srikanthan, A., Bedard, P., Razak, A., Crump, M., Warr, D., Giuliani, M., Gupta, A., 2017. The positive effect of a dedicated adolescent and young adult fertility program on the rates of documentation of therapy-associated infertility risk and fertility preservation options. Support Care Cancer 25 (6), 1915–1922.

Lin, H.W.W., Li, Y., Chen, X., Yang, D., Zhang, Q., 2011. Triggering final oocyte maturation with reduced doses of hCG in IVF/ICSI: a prospective, randomized and controlled study. Eur J Obstet Gynecol Reprod Biol 159 (1), 43–47.

Loren, A.W., Mangu, P.B., Beck, L.N., Brennan, L., Magdalinski, A.J., Partridge, A.H., Quinn, G., Wallace, W.H., Oktay, K., 2013. Fertility preservation for patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 31 (19), 2500–2510.

Love, R.R., Van Dinh, N., Quy, T.T., Linh, N.D., Tung, N.D., Shen, T., Hade, E.M., Young, G.S., Jarjoura, D., 2008. Survival after adjuvant oophorectomy and tamoxifen in operable breast cancer in premenopausal women. J Clin Oncol 26 (2), 253–257.

Lunsford, A.J., Whelan, K., McCormick, K., McLaren, J.F., 2014. Antimullerian hormone as a measure of reproductive function in female childhood cancer survivors. Fertil Steril 101 (1), 227–231.

Martinez, G., Walschaerts, M., Le Mitouard, M., Borye, R., Thomas, C., Auger, J., Berthaut, I., Brugnon, F., Daudin, M., Moinard, N., Ravel, C., Saias, J., Szerman, E., Rives, N., Nennebicq, S., Bujan, L., 2017. Impact of Hodgkin or non-Hodgkin lymphoma and their treatments on sperm aneuploidy: a prospective study by the French CECOS network. Fertil Steril 107 (2), 341-50 e5.

Matthews, S.J., Picton, H., Ernst, E., Andersen, C.Y., 2018. Successful pregnancy in a woman previously suffering from beta-thalassemia following transplantation of ovarian tissue cryopreserved before puberty. Minerva Ginecol 70 (4), 432–435.

Mazonakis, M., Damilakis, J., Varveris, H., Gourtsoyiannis, N., 2006. Radiation dose to laterally transposed ovaries during external beam radiotherapy for cervical cancer. Acta Oncol 45 (6), 702–707.

Meirow, D., Biederman, H., Anderson, R.A., Wallace, W.H., 2010. Toxicity of chemotherapy and radiation on female reproduction. Clin Obstet Gynecol 53 (4), 727–739.

Meirow, D., Epstein, M., Lewis, H., Nugent, D., Gosden, R.G., 2001. Administration of cyclophosphamide at different stages of follicular maturation in mice: effects on reproductive performance and fetal malformations. Hum Reprod 16 (4), 632–637.

Meirow, D., Lewis, H., Nugent, D., Epstein, M., 1999. Subclinical depletion of primordial follicular reserve in mice treated with cyclophosphamide: clinical importance and proposed accurate investigative tool. Hum Reprod 14 (7), 1903–1907.

Meistrich, M.L., Wilson, G., Brown, B.W., da Cunha, M.F., Lipshultz, L.I., 1992. Impact of cyclophosphamide on long-term reduction in sperm count in men treated with combination chemotherapy for Ewing and soft tissue sarcomas. Cancer 70 (11), 2703–2712.

Miller, W.R., 2006. Aromatase and the breast: regulation and clinical aspects. Maturitas 54 (4), 335–341.

Moore, H.C., Unger, J.M., Phillips, K.A., Boyle, E.H., Porter, D., Francis, P.A., Goldstein, L.J., Gomez, H.L., Vallejos, C.S., Partridge, A.H., Dakhil, S.R., Garcia, A.A., Gralow, J., Lonbard, J.M., Forbes, J.F., Martino, S., Barlow, W.E., Fabian, C.J., Minasian, L., Meyskens, Jr, F.L., Gelber, R.D., Hortobagyi, G.N., Albain, K.S., 2015. Goserelin for ovarian protection during breast-cancer adjuvant chemotherapy. N Engl J Med 372 (10), 923–932.

Morice, P., Juncker, L., Rey, A., El-Hassan, J., Haie-Meder, C., Castaigne, D., 2000. Ovarian transposition for patients with cervical carcinoma treated by radiosurgical combination. Fertil Steril 74 (4), 743–748.

Morris, S.N., Ryley, D., 2011. Fertility preservation: nonsurgical and surgical options. Semin Reprod Med 29 (2), 147–154.

Mueller, B.A., Chow, E.J., Kamineni, A., Daling, J.R., Fraser, A., Wiggins, C.L., Mineau, G.P., Hamre, M.R., Severson, R.K., Drews-Botsch, 2009. Pregnancy outcomes in female childhood and adolescent cancer survivors: a linked cancer-birth registry analysis. Arch Pediatr Adolesc Med 163 (10), 879–886.

Munhoz, R.R., Pereira, A.A., Sasse, A.D., et al., 2016. Gonadotropin-Releasing Hormone Agonists for Ovarian Function Preservation in Premenopausal Women Undergoing Chemotherapy for Early-Stage Breast Cancer: A Systematic Review and Meta-analysis. JAMA Oncol 2 (1), 65–73.

Mustieles, C., Munoz, A., Alonso, M., Ros, P., Yturriaga, R., Maldonado, S., Otheo, E., Barrio, R., 1995. Male Gonadal function after chemotherapy in survivors of childhood malignancy. Med Pediatr Oncol 24 (6), 347–351.

Nayak, S.R., Wakim, A.N., 2011. Random-start gonadotropin-releasing hormone (GnRH) antagonist-treated cycles with GnRH agonist trigger for fertility preservation. Fertil Steril 96 (1), e51–e54.

Nguyen, L., Brewer, C.A., DiSaia, P.J., 1998. Ovarian metastasis of stage IB1 squamous cell cancer of the cervix after radical parametrectomy and oophoropexy. Gynecol Oncol 68 (2), 198–200.

Noyes, N., Knopman, J.M., Melzer, K., Fino, M.E., Friedman, B., Westphal, L.M., 2011. Oocyte cryopreservation as a fertility preservation measure for cancer patients. Reprod Biomed Online 23 (3), 323–333.

Oktay, K., Buyuk, E., Davis, O., Yermakova, I., Veeck, L., Rosenwaks, Z., 2003. Fertility preservation in breast cancer patients: IVF and embryo cryopreservation after ovarian stimulation with tamoxifen. Hum Reprod 18 (1), 90–95.

Oktay, K., Harvey, B.E., Partridge, A.H., Quinn, G.P., Reinecke, J., Taylor, H.S., Wallace, W.H., Wang, E.T., Loren, A.W., 2018. Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update. J Clin Oncol 36 (19), 1994–2001.

Oktay, K., Hourvitz, A., Sahin, G., Oktem, O., Safro, B., Cil, A., Bang, H., 2006. Letrozole reduces estrogen and gonadotropin exposure in women with breast cancer undergoing ovarian stimulation before chemotherapy. J Clin Endocrinol Metab 91 (10), 3885–3890.

Oktay, K., Turkcuoglu, I., Rodriguez-Wallberg, K.A., 2010. GnRH agonist trigger for women with breast cancer undergoing fertility preservation by aromatase inhibitor/FSH stimulation. Reprod Biomed Online 20 (6), 783–788.

Overbeek, A., van den Berg, M.H., van Leeuwen, F.E., Kaspers, G.J., Lambalk, C.B., van Dulmen-den Broeder, E., 2017. Chemotherapy-related late adverse effects on ovarian function in female survivors of childhood and young adult cancer: A systematic review. Cancer Treat Rev 53, 10–24.

Pahisa, J., Martinez-Roman, S., Martinez-Zamora, M.A., Torne, A., Caparros, X., Sanjuan, A., Lejarcegui, J.A., 2008. Laparoscopic ovarian transposition in patients with early cervical cancer. Int J Gynecol Cancer 18 (3), 584–589.

Paoli, D., Rizzo, F., Fiore, G., Pallotti, F., Pulsoni, A., Annechiniet al, 2016. Spermatogenesis in Hodgkin's lymphoma patients: a retrospective study of semen quality before and after different chemotherapy regimens. Hum Reprod 31 (2), 263–272.

Papanikolaou, E.G.P.C., Kolibianakis, E.M., Camus, M., Tournaye, H., Fatemi, H.M., Van Steirteghem, A., Devroey, P., 2006. Incidence and prediction of ovarian

hyperstimulation syndrome in women undergoing gonadotropin-releasing hormone antagonist in vitro fertilization cycles. Fertil Steril 85, 112–120.
Partridge, A., Gelber, S., Gelber, R.D., Castiglione-Gertsch, M., Goldhirsch, A., Winer, E., 2007. Age of menopause among women who remain premenopausal following treatment for early breast cancer: long-term results from International Breast Cancer Study Group Trials V and VI. Eur J Cancer 43 (11), 1646–1653.
Partridge, A.H., Gelber, S., Peppercorn, J., Sampson, E., Knudsen, K., Laufer, M., Rosenberg, R., Przypyszny, M., Rein, A., Winer, E., 2004. Web-based survey of fertility issues in young women with breast cancer. J Clin Oncol 22 (20), 4174–4183.
Perdrix, A., Saint-Ghislain, M., Degremont, M., David, M., Khaznadar, Z., Loeb, A., Leheurteur, M., Di Fiore, F., Clatot, F., 2017. Influence of adjuvant chemotherapy on anti-Mullerian hormone in women below 35 years treated for early breast cancer. Reprod Biomed Online 35 (4), 468–474.
Picone, O., Aucouturier, J.S., Louboutin, A., Coscas, Y., Camus, E., 2003. Abdominal wall metastasis of a cervical adenocarcinoma at the laparoscopic trocar insertion site after ovarian transposition: case report and review of the literature. Gynecol Oncol 90 (2), 446–449.
Prest, S.J., May, F.E., Westley, B.R., 2002. The estrogen-regulated protein, TFF1, stimulates migration of human breast cancer cells. FASEB J 16 (6), 592–594.
Pu, D., Wu, J., Liu, J., 2011. Comparisons of GnRH antagonist versus GnRH agonist protocol in poor ovarian responders undergoing IVF. Hum Reprod 26 (10), 2742–2749.
Public Health Agency of Canadian Cancer Society. Release notice - Canadian Cancer Statistics. Health promotion and chronic disease prevention in Canada: research, policy and practice 2018; 38(7-8): 306.
Qin, N., Chen, Q., Hong, Q., Cai, R., Gao, H., Wang, Y., Sun, L., Zhang, S., Guo, H., Fu, Y., Ai, A., Tian, H., Lyu, Q., Daya, S., Kuang, Y., 2016. Flexibility in starting ovarian stimulation at different phases of the menstrual cycle for treatment of infertile women with the use of in vitro fertilization or intracytoplasmic sperm injection. Fertil Steril 106 (2), 334-41 e1.
Quinn, G.P., Vadaparampil, S.T., Bell-Ellison, B.A., Gwede, C.K., Albrecht, T.L., 2008. Patient-physician communication barriers regarding fertility preservation among newly diagnosed cancer patients. Soc Sci Med 66 (3), 784–789.
Quinn, G.P., Vadaparampil, S.T., Gwede, C.K., Miree, C., King, L.M., Clayton, H.B., Wilson, C., Munster, P., 2007. Discussion of fertility preservation with newly diagnosed patients: oncologists' views. J Cancer Surviv 1 (2), 146–155.
Quinn, M.M., Cakmak, H., Letourneau, J.M., Cedars, M.I., Rosen, M.P., 2017. Response to ovarian stimulation is not impacted by a breast cancer diagnosis. Hum Reprod 32 (3), 568–574.
Reddy, J., Turan, V., Bedoschi, G., Moy, F., Oktay, K., 2014. Triggering final oocyte maturation with gonadotropin-releasing hormone agonist (GnRHa) versus human chorionic gonadotropin (hCG) in breast cancer patients undergoing fertility preservation: an extended experience. J Assist Reprod Genet 31 (7), 927–932.
Reulen, R.C., Bright, C.J., Winter, D.L., Fidler, M.M., Wong, K., Guha, J., Kelly, J.S., Frobisher, C., Edgar, A.B., Skinner, R., Wallace, W.H.B., Hawkins, M.M., 2017. Pregnancy and Labor Complications in Female Survivors of Childhood Cancer: The British Childhood Cancer Survivor Study. J Natl Cancer Inst 109 (11).
Reulen, R.C., Zeegers, M.P., Wallace, W.H., Frobisher, C., Taylor, A.J., Lancashire, E.R., Winter, D.L., Hawkins, M.M., 2009. Pregnancy outcomes among adult survivors of childhood cancer in the British Childhood Cancer Survivor Study. Cancer Epidemiol Biomakers Prev 18 (8), 2239–2247.
Revelli, A., Porcu, E., Levi Setti, P.E., Delle Piane, L., Merlo, D.F., Anserini, P., 2013. Is letrozole needed for controlled ovarian stimulation in patients with estrogen receptor-positive breast cancer? Gynecol Endocrinol 29 (11), 993–996.
Riggs, R.M., Duran, E.H., Baker, M.W., Kimble, T.D., Hobeika, E., Yin, L., Matos-Bodden, L., Leader, B., Stadtmauer, L., 2008. Assessment of ovarian reserve with anti-Mullerian hormone: a comparison of the predictive value of anti-Mullerian hormone, follicle-stimulating hormone, inhibin B, and age. Am J Obstet Gynecol 199 (2), 202 e1-8.
Rives, N., Walschaerts, M., Setif, V., Hennebicq, S., Saias, J., Brugnon, F., Auger, J., Berthaut, I., Szerman, E., Daudin, M., Bujan, L., 2017. Sperm aneuploidy after testicular cancer treatment: data from a prospective multicenter study performed within the French Centre d'Etude et de Conservation des Oeufs et du Sperme network. Fertil Steril 107 (3), 580-8 e1.
Rivkees, S.A., Crawford, J.D., 1988. The relationship of gonadal activity and chemotherapy-induced gonadal damage. JAMA 259 (14), 2123–2125.
Rodgers, R.J., Reid, G.D., Koch, J., Deans, R., Ledger, W.L., Friedlander, M., Gilchrist, R.B., Walters, K.A., Abbot, J.A., 2017. The safety and efficacy of controlled ovarian hyperstimulation for fertility preservation in women with early breast cancer: a systemic review. Hum Reprod 32 (5), 1033–1045.
Ronn, R., Holzer, H.E., 2013. Oncofertility in Canada: an overview of Canadian practice and suggested action plan. Curr Oncol 20 (5), e465–e474.
Rosendahl, M., Andersen, C.Y., la Cour Freiesleben, N., Juul, A., Lossl, K., Andersen, A.N., 2010. Dynamics and mechanisms of chemotherapy-induced ovarian follicular depletion in women of fertile age. Fertil Steril 94 (1), 156–166.
Salooja, N., Szydlo, R.M., Socie, G., Rio, B., Chatterjee, R., Lungman, P., Van Lint, M.T., Powles, R., Jackson, G., Hinterberger-Fischer, M., Kolb, H.J., Apperley, J.F., 2001. Pregnancy outcomes after peripheral blood or bone marrow transplantation: a retrospective survey. Lancet 358 (9278), 271–276.
Sanders, J.E., Hawley, J., Levy, W., Gooley, T., Buckner, C.D., Deeg, H.J., Doney, K., Storb, R., Sullivan, K., Witherspoon, R., Appelbaum, F.R., 1996. Pregnancies following high-dose cyclophosphamide with or without high-dose busulfan or total-body irradiation and bone marrow transplantation. Blood 87 (7), 3045–3052.
Scheffer, G.J., Broekmans, F.J., Looman, C.W., Blankenstein, M., Fauser, B., teJon, F.H., teVelde, E.R., 2003. The number of antral follicles in normal women with proven fertility is the best reflection of reproductive age. Hum Reprod 18 (4), 700–706.
Schoolcraft, W.B., Surrey, E.S., Minjarez, D.A., Stevens, J.M., Gardner, D.K., 2008. Management of poor responders: can outcomes be improved with a novel gonadotropin-releasing hormone antagonist/letrozole protocol? Fertil Steril 89 (1), 151–156.
Schover, L.R., Brey, K., Lichtin, A., Lipshultz, L.I., Jeha, S., 2002. Oncologists' attitudes and practices regarding banking sperm before cancer treatment. J Clin Oncol 20 (7), 1890–1897.
Schover, L.R., Rybicki, L.A., Martin, B.A., Bringelsen, K.A., 1999. Having children after cancer. A pilot survey of survivors' attitudes and experiences. Cancer 86 (4), 697–709.
Scott, Jr., R.T., Elkind-Hirsch, K.E., Styne-Gross, A., Miller, K.A., Frattarelli, J.L., 2008. The predictive value for in vitro fertility delivery rates is greatly impacted by the method used to select the threshold between normal and elevated basal follicle-stimulating hormone. Fertil Steril 89 (4), 868–878.
Seppanen, V.I., Artama, M.S., Malila, N.K., Pitkaniemi, J.M., Rantanen, M.E., Ritvanen, A.K., Madanat-Harjuoja, L., 2016. Risk for congenital anomalies in offspring of childhood, adolescent and young adult cancer survivors. Int J Cancer 139 (8), 1721–1730.
Shankara-Narayana, N., Di Pierro, I., Fennell, C., Ly, L.P., Bacha, F., Vrga, L., Savkovic, S., Turner, L., Jayadev, V., Conway, A.J., Handelsman, D.J., 2019. Sperm cryopreservation prior to gonadotoxic treatment: experience of a single academic centre over 4 decades. Hum Reprod 34 (5), 795–803.
Shea, L.D., Woodruff, T.K., Shikanov, A., 2014. Bioengineering the ovarian follicle microenvironment. Annu Rev Biomed Eng 16, 29–52.
Shnorhavorian, M., Schwartz, S.M., Stansfeld, B., Sadler-Riggleman, I., Beck, D., Skinner, M.K., 2017. Differential DNA Methylation Regions in Adult Human Sperm following Adolescent Chemotherapy: Potential for Epigenetic Inheritance. PloS One 12 (2), e0170085.
Sieniawski, M., Reineke, T., Josting, A., Nogova, L., Behringer, K., Halbsguth, T., Fuchs, M., Diehl, V., Engert, A., 2008. Assessment of male fertility in patients with Hodgkin's lymphoma treated in the German Hodgkin Study Group (GHSG) clinical trials. Ann Oncol 19 (10), 1795–1801.
Signorello, L.B., Cohen, S.S., Bosetti, C., Stovall, M., Kasper, C.E., Weathers, R.E., Whitton, J.A., Green, D.M., Donaldson, S.S., Mertens, A.C., Robison, L.L., Boice, Jr, J.D., 2006. Female survivors of childhood cancer: preterm birth and low birth weight among their children. J Natl Cancer Inst 98 (20), 1453–1461.
Skinner, R., Wallace, W.H., Levitt, G.A., UKCsCSGLE, G., 2006. Long-term follow-up of people who have survived cancer during childhood. Lancet Oncol 7 (6), 489–498.
Sklar, C.A., Mertens, A.C., Mitby, P., Whitton, J., Stovall, M., Kasper, C., Mulder, J., Green, D., Nicholson, H.S., Yasui, Y., Robison, L.L., 2006. Premature menopause in survivors of childhood cancer: a report from the childhood cancer survivor study. J Natl Cancer Inst 98 (13), 890–896.
Sonmezer, M., Turkcuoglu, I., Coskun, U., Oktay, K., 2011. Random-start controlled ovarian hyperstimulation for emergency fertility preservation in letrozole cycles. Fertil Steril 95 (6), 2125 e9-11.

Specchia, C., Baggiani, A., Immediata, V., Ronchetti, C., Cesana, A., Smeraldi, A., Scaravelli, G., Levi-Setti, P.E., 2019. Oocyte cryopreservation in oncological patients: Eighteen years experience of a tertiary care referral center. Front Endocrinol (Laursanne) 10, 600.

Stahl, O., Boyd, H.A., Giwercman, A., Lindholm, M., Jensen, A., Kjaer, S.K., Anderson, H., Cavallin-Stahl, E., Rylander, L., 2011. Risk of birth abnormalities in the offspring of men with a history of cancer: a cohort study using Danish and Swedish national registries. J Natl Cancer Inst 103 (5), 398–406.

Tempest, H.G., Ko, E., Chan, P., Robaire, B., Rademaker, A., Martin, R.H., 2008. Sperm aneuploidy frequencies analysed before and after chemotherapy in testicular cancer and Hodgkin's lymphoma patients. Hum Reprod 23 (2), 251–258.

Thomas-Teinturier, C., El Fayech, C., Oberlin, O., Pacquement, H., Haddy, N., Labbe, M., Veres, C., Guibout, C., Diallo, I., De Vathaire, F., 2013. Age at menopause and its influencing factors in a cohort of survivors of childhood cancer: earlier but rarely premature. Hum Reprod 28 (2), 488–495.

Thomson, A.B., Campbell, A.J., Irvine, D.C., Anderson, R.A., Kelnar, C.J., Wallace, W.H., 2002. Semen quality and spermatozoal DNA integrity in survivors of childhood cancer: a case-control study. Lancet 360 (9330), 361–367.

Toftager, M., Bogstad, J., Bryndorf, T., Lossl, K., Roskaer, J., Holland, T., Praetorius, Z.A., Nilas, L., Pinborg, A., 2016. Risk of severe ovarian hyperstimulation syndrome in GnRH antagonist versus GnRH agonist protocol: RCT including 1050 first IVF/ICSI cycles. Hum Reprod 31 (6), 1253–1264.

Tsoumpou, I.M.J., Gelbaya, T.A., Nardo, L.G., 2009. Symposium: Update on prediction and management of OHSS. Optimal dose of HCG for final oocyte maturation in IVF cycles: absence of evidence? Reprod Biomed Online 19 (1), 52–58 Jul.

Vadaparampil, S., Quinn, G., King, L., Wilson, C., Nieder, M., 2008. Barriers to fertility preservation among pediatric oncologists. Patient Educ Couns 72 (3), 402–410.

van de Loo, L., van den Berg, M.H., Overbeek, A., van Dijk, M., Damen, L., Lambalk, C.B., Ronckers, C.M., van den Heuvel-Eibrink, M.M., Kremer, L.C.M., van der Pal, H., Laven, J.S.E., Tissing, W.J.E., Loonen, J.J., Versluys, B., Bresters, D., Kaspers, G.J.L., van Leeuwen, F.E., van Dulmen-den Broeder, E., 2019. Uterine function, pregnancy complications, and pregnancy outcomes among female childhood cancer survivors. Fertil Steril 111 (2), 372–380.

van den Berg, M.H., Overbeek, A., Lambalk, C.B., Kaspers, G.J.L., Bresters, D., van den Heuvel-Eibrink, M.M., Kremer, L.C., Loonen, J.J., van der Pal, H.J., Ronckers, C.M., Tissing, W.J.E., Versluys, A.B., van der Heiden-van der Loo, M., Heijboer, A.C., Hauptmann, M., Twisk, J.W.R., Laven, J.S.E., Beerendonk, C.C.M., van Leeuwen, F.E., van Dulmen-den Broeder, E., 2018. Long-term effects of childhood cancer treatment on hormonal and ultrasound markers of ovarian reserve. Hum Reprod.

van der Kaaij, M.A., Heutte, N., van Echten-Arends, J., Raemaekers, J.M.M., Carde, P., Noordijk, E.V., Ferme, C., Thomas, J., Eghbali, H., Brice, P., Bonmati, C., Henry-Amar, M., Kluin-Nelemans, H.C., 2009. Sperm quality before treatment in patients with early stage Hodgkin's lymphoma enrolled in EORTC-GELA Lymphoma Group trials. Haematologica 94 (12), 1691–1697.

Van der Ven, H., Liebenthron, J., Beckmann, M., Toth, B., Korell, M., Krussel, J., Frambach, T., Kupka, M., Hohl, M.K., Winkler-Crepaz, K., Seitz, S., Dogan, A., Griesinger, G., Haberlin, F., Henes, M., Schwab, R., Sutterlin, M., von Wolff, M., Dittrich, R., 2016. Ninety-five orthotopic transplantations in 74 women of ovarian tissue after cytotoxic treatment in a fertility preservation network: tissue activity, pregnancy and delivery rates. Hum Reprod 31 (9), 2031–2041.

van Dorp, W., Haupt, R., Anderson, R.A., Mulder, R.L., van den Heuvel-Eibrink, M.M., van Dulmen-den Broeder, E., Su, H.I., Winther, J.F., Hudson, M.M., Levine, J.M., Wallace, W.H., 2018. Reproductive Function and Outcomes in Female Survivors of Childhood, Adolescent, and Young Adult Cancer: A Review. J Clin Oncol 36 (21), 2169–2180.

von Wolff, M., Bruckner, T., Strowitzki, T., Germeyer, A., 2018. Fertility preservation: ovarian response to freeze oocytes is not affected by different malignant diseases-an analysis of 992 stimulations. J Assist Reprod Genet 35 (9), 1713–1719.

von Wolff, M., Thaler, C.J., Frambach, T., Zeeb, C., Lawrenz, B., Popovici, R.M., Strowitzki, T., 2009. Ovarian stimulation to cryopreserve fertilized oocytes in cancer patients can be started in the luteal phase. Fertil Steril 92 (4), 1360–1365.

Wallace, W.H., Kelsey, T.W., Anderson, R.A., 2016. Fertility preservation in pre-pubertal girls with cancer: the role of ovarian tissue cryopreservation. Fertil Steril 105 (1), 6–12.

Wallace, W.H., Kelsey, T.W., 2004. Ovarian reserve and reproductive age may be determined from measurement of ovarian volume by transvaginal sonography. Hum Reprod 19 (7), 1612–1617.

Wallace, W.H., Shalet, S.M., Crowne, E.C., Morris-Jones, P.H., Gattamaneni, H.R., 1989. Ovarian failure following abdominal irradiation in childhood: natural history and prognosis. Clin Oncol 1 (2), 75–79.

Wallace, W.H., Thomson, A.B., Kelsey, T.W., 2003. The radiosensitivity of the human oocyte. Hum Reprod 18 (1), 117–121.

Wallace, W.H., Thomson, A.B., Saran, F., Kelsey, T.W., 2005. Predicting age of ovarian failure after radiation to a field that includes the ovaries. Int J Radiat Oncol Biol Phys 62 (3), 738–744.

Walshe, J.M., Denduluri, N., Swain, S.M., 2006. Amenorrhea in premenopausal women after adjuvant chemotherapy for breast cancer. J Clin Oncol 24 (36), 5769–5779.

Wang, Y., Tesch, M.E., Lim, C., Xu, Y.H., Lee, S., Perdizet, K., Yokom, D., Warner, E., Roberts, J., Lohrisch, 2022. Risk of recurrence and pregnancy outcomes in young women with breast cancer who do and do not undergo fertility preservation. Breast Cancer Res Treat 195, 201–208.

Williams, R.S., Littell, R.D., Mendenhall, N.P., 1999. Laparoscopic oophoropexy and ovarian function in the treatment of Hodgkin disease. Cancer 86 (10), 2138–2142.

Winther, J.F., Boice, Jr, J.D., Svendsen, A.L., Frederiksen, K., Olsen, J.H., 2009. Induced abortions in Danish cancer survivors: a population-based cohort study. J Natl Cancer Inst 101 (9), 687–689.

Winther, J.F., Olsen, J.H., Wu, H., Shyr, Y., Mulvihill, J.J., Stovall, M., Nielsen, A., Schmiegelow, M., Boice, Jr, J.D., 2012. Genetic disease in the children of Danish survivors of childhood and adolescent cancer. J Clin Oncol 30 (1), 27–33.

Wo, J.Y., Viswanathan, A.N., 2009. Impact of radiotherapy on fertility, pregnancy, and neonatal outcomes in female cancer patients. Int J Radiat Oncol Biol Phys 73 (5), 1304–1312.

Woodruff, T.K., 2010. The Oncofertility Consortium—addressing fertility in young people with cancer. Nat Rev Clin Oncol 7 (8), 466–475.

Youssef, M.A., Van der Veen, F., Al-Inany, H.G., Mochtar, M.H., Griesinger, G., Mohesen, M.N., Aboulfoutouh, I., van Wely, M., 2014. Gonadotropin-releasing hormone agonist versus HCG for oocyte triggering in antagonist-assisted reproductive technology. Cochrane Database Syst Rev(10), CD008046.

Zaletel, L.Z., Bratanic, N., Jereb, B., 2010. Gonadal function in patients treated for Hodgkin's disease in childhood. Radiol Oncol 44 (3), 187–193.

Zebrack, B.J., Block, R., Hayes-Lattin, B., Embry, L., Aguilar, C., Meeske, K., Li, Y., Butler, M., Cole, S., 2013. Psychosocial service use and unmet need among recently diagnosed adolescent and young adult cancer patients. Cancer 119 (1), 201–214.

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