AYA CANCER NETWORK AOTEAROA
ADVANCING CANCER CARE FOR 12-24 YEAR OLDS

Fertility Preservation for People with Cancer in Aotearoa

Clinical Practice Guideline
March 2023

Whakatauākī - Hastings Tipa

He mahi kai hōaka, he mahi kai tāngata

Everything worthwhile takes considerable effort

TABLE OF CONTENTS

INTRODUCTION

This guideline has been developed for health professionals involved in the care of people with cancer. The purpose of the guideline is to provide recommendations regarding best practice, and a description of currently available options for fertility preservation for children, adolescents, and adults up to 40 years of age in New Zealand. This is one piece of a wider project being undertaken by the AYA cancer network. The second important piece is the exploration of barriers to accessibility and acceptability of fertility preservation options and services for cancer patients in New Zealand. To date inequitable access and barriers to fertility preservation has been identified for populations based on age, ethnicity, socio-economic status, sexual orientation, gender identity, geographical location, religious affiliation and stage in the cancer care continuum. The Network is overseeing the development of a fertility preservation implementation plan to try and address these barriers. The implementation plan will be guided by the recommendations of the sector, cultural experts and consumers/whānau. Specific equity tools will be utilised to examine the potential for inclusive and responsive initiatives/interventions that honour Te Tiriti o Waitangi principles and meet the diverse needs of cancer patients in Aotearoa.

This is an update to the original guideline, published in 2014. The update was under the banner of the Adolescent and Young Adult (AYA) Cancer Network Aotearoa, with endorsement from Te Aho o Te Kahu. The development group comprised a diverse team of health professionals from throughout New Zealand including paediatric and adult haematology and oncology, radiation oncology, surgery, breast cancer, fertility, endocrinology, and nursing. Three consumer representatives were key contributors to the group.

Many cancers can be successfully treated but unfortunately, cancer treatments may result in damage to fertility in the short and/or long term. Research indicates that people with cancer are concerned about the effect of their diagnosis and treatment on fertility and want information about fertility and fertility preservation options at an early stage [1-11]. **It is therefore important that health professionals involved in the care of those with cancer consider and discuss fertility preservation *before* recommending fertility-damaging treatments.**

This guideline includes current evidence (where available) and international expert opinion regarding the fertility risks associated with cancer treatments, and available or emerging fertility preservation options. As technological advances in fertility preservation become known, and evidence for their safety and efficacy increases, fertility preservation becomes an increasingly important consideration for those with cancer and their health care teams, and those charged with making decisions about funding and access to such technologies. This is particularly so for those whose fertility preservation options are limited by age, availability and/or cost. Where cost is an influencing factor in an individual's decision about whether to pursue an option, equitable access becomes an important ethical and moral consideration.

Definitions

Sex/Gender	Female	Male
	People with ovaries	People with testes

Age	Child	Adolescent/ Young Adult (AYA)	Adult
	0 – 11 years	12 – 24 years	25 years and over

Stage of development	Pre-pubertal	Pubertal	Post- Pubertal
	Tanner Stage 1	Tanner Stage 2 – 5 (Spermbanking should be discussed for males at Tanner Stage 3+)	Tanner Stage 5

Funding for Fertility Preservation for People with Cancer in New Zealand

The Specialist Medical and Surgical Services – Assisted Reproductive Technology Services Tier Two Service Specification describes the minimum services that are required to be publicly funded in New Zealand for eligible people [12]. This service specification includes some services for people whose fertility will be permanently impaired by cancer treatment, as listed below. Those eligible for these services are currently post-pubertal people about to undergo cancer treatment that may permanently impair their fertility, and who are likely to survive that treatment, and do not already have a child.

Publicly funded fertility preservation services include:

- First fertility specialist assessment
- Relevant required investigations
- Retrieval, freezing, and storage of gametes (eggs and sperm) up to 10 years
- In vitro fertilization (IVF) cycle according to relevant clinical priority assessment criteria (CPAC; fertility funding eligibility) tool, embryo freezing, and storage up to10 years
- A second cycle of in vitro fertilization can be funded to those eligible under the CPAC tool if the first is unsuccessful

After cancer therapy, the use of stored reproductive tissue is funded according to the general Service Specifications for those with *non-cancer treatment related* infertility. Disposal of stored tissue adheres to cultural safety practices that are independently determined by the patient, whānau and fertility provider.

Fertility preservation for pre-pubertal children is not currently publicly funded. Funding for ovarian tissue cryopreservation for eligible females up to 18 years of age is via an ethics-approved national protocol, from a philanthropic source. Fertility preservation for pre-pubertal males is not currently available in New Zealand.

Grading of Recommendations

The recommendations in this version of the guideline have been updated according to the international Grading of Recommendations Assessment, Development and Evaluation (GRADE) Evidence to Decision (EtD) framework [13-16], in line with the recently published *Fertility Preservation in Childhood, Adolescent, and Young Adult Cancer* series from the PanCareLIFE Consortium and the International Late Effects of Childhood Cancer Guideline Harmonization Group [7-9].

This framework allows incorporation of a wider range of relevant considerations in addition to the strength or quality of evidence, acknowledging that high level evidence is often not available.

The GRADE criteria for **evidence** are as follows:

Strength of Evidence	Grade of Evidence
Further research is very unlikely to change our confidence in the estimate of effect	High quality
Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate	Moderate quality
Further research is *very* likely to have an important impact on our confidence in the estimate of effect and may change the estimate	Low quality
Any estimate of effect is uncertain	Very low quality

The recommendations in the guideline reflect consideration of grade of evidence according to the table above, expert clinical judgement, cultural and ethical implications, cost, and local context.

FERTILITY DISCUSSION AND INFORMATION PROVISION

Research and expert opinion suggest that issues related to fertility and sexuality are of a high level of concern for many people diagnosed with cancer. This translates into a need for timely, accessible, appropriate and current information [1, 2, 4, 5, 9, 10, 17-20]. Children (and their parents/guardians), AYA and potentially fertile adults who require treatment that poses a risk to future fertility must be given the opportunity to discuss this risk and the available options to protect or preserve their/their child's fertility.

Initial discussions must take place as early as possible in the cancer diagnosis and treatment planning stage, and should be led in a culturally sensitive manner by the most appropriate member of the treating team (oncologist/haematologist, surgeon, nurse specialist, fertility provider, onco-fertility navigator) [7-9, 19, 21-23].

In many cases, urgent referral to a fertility specialist may be required to allow fertility preservation to be undertaken before the commencement of cancer treatment [9, 11, 24, 25]. These discussions should include partners and whānau as appropriate.More than one discussion may be needed to facilitate informed decision-making [26].

Considerations

Cultural Considerations

Cultural concerns, beliefs and practices may have a significant impact on decision-making regarding fertility and fertility preservation for some. This may be of particular concern for Māori, as some iwi disagree with storage of tissue citing whakapapa. Due to the limited published research addressing Māori perspective and uptake of fertility preservation or assisted reproductive technologies in New Zealand, no comment can currently be made regarding the impact of these beliefs and concerns on decisions regarding fertility preservation [27-30]. Nevertheless, engagement with Māori communities is vital, however, to ensure culturally appropriate policies, procedures and practices are established [31]. The He Tangata Kei Tua Guidelines for Biobanking with Māori highlights several transferable principles that should be considered. Human tissue collected for fertility preservation is a connection to one's whakapapa, therefore is deemed a taonga. The concept of taonga is applied to a valued or significant object that must be cared for in an appropriate manner to maintain integrity and respect. Tapu refers to the special or sacred nature of an object that implies it must be actively protected [31]. For Māori female, their reproductive bodies represent the continuation of whakapapa, survival of whānau, hapu and iwi. Hence, it is important that health professionals involved in fertility discussions and fertility care are aware of such beliefs and concerns, and that appropriate support be available to assist with discussions and decision-making regarding fertility issues [27-30]. Furthermore, the principles of kawa and tikanga should be incorporated into the development of fertility preservation processes/policies to ensure Māori core values and ethics are maintained [31].

Ethical Considerations

There are several ethical considerations associated with discussing fertility issues and options with people with cancer and their partners and whānau, including:

- Difficulties associated with encouraging people with a new cancer diagnosis to make decisions about future fertility while they are still coming to terms with their diagnosis and the often urgent need to commence treatment
- Consideration of the extent to which a child or young person can participate in decision-making and provide consent or assent. This will depend on their age, level of development, understanding of their particular situation, and the degree to which they are physically unwell. For younger children, decisions will be made substantially or completely by a parent/guardian; for older children/ younger adolescent, decision-making is a joint process involving both consent (parent/guardian) and assent (young person). AYA aged 16 years and over provide their own consent unless formally assessed to not be competent to do so.
- Decisions regarding delaying the start of cancer treatment to allow for fertility preservation, particularly if the only available fertility preservation option is investigational
- Consideration of the importance of prognosis

Personal Considerations

- Delivery of information must be age-appropriate, particularly in the paediatric and AYA setting. Involvement of a Paediatric or AYA Nurse Specialist/Key worker or another appropriate team member should be considered [32]
- Factors such as ethnicity, sexual orientation, gender identity, personal/sexual history, relationship status and religious or cultural beliefs about reproduction, masturbation and/or assisted reproductive technologies should be considered and attended to with sensitivity in any discussions around fertility

- The person may or may not want their partner and/or whānau, or in the case of children and AYA, their parent/caregiver, to be present for and contribute to discussions regarding fertility risk and options
- Discussions need to take place in a private and safe place. This will enable sensitive conversations that allow the young person to share their thoughts and feelings openly, free of pressure from others
- It is important to respect some young people may need time to make their decision about these matters
- Where language may be a barrier to full communication and understanding, the assistance of an interpreter should be sought with consideration given to the gender of both parties
- For younger people, having children may not be something they have previously considered
- Peoples' feelings about future parenthood may change over time so it is important that the long-term consequences of fertility decisions made prior to treatment are emphasised [21, 33]
- Decisions about fertility need to be made in the patient's best interest and not influenced or diminished by the healthcare provider's own interest or that of parents/guardians/partners [9]
- Trans and nonbinary people, especially if experiencing gender dysphoria, may have added challenges when considering and navigating fertility preservation. It is important for clinicians to be respectful and affirming of gender, using correct names, pronouns and to be aware of potential additional needs. Language used when discussing fertility information may be distressing so it is important to clarify and document where preferred terms for body parts differ from anatomical names.

There are many reasons why people with cancer may decline available fertility preservation options, including [4, 17, 18, 21, 24, 25, 32-35]

- Believing that the risk of fertility damage from their treatment is low
- Not understanding or absorbing information about fertility risks due to feeling overwhelmed by their diagnosis, receiving too much information in a short timeframe, or a lack of emphasis placed on fertility risks by health professionals
- Placing future fertility/parenthood at a lower priority considering the diagnosis of a life-threatening illness
- Being unwilling to delay the start of cancer treatment due to pursue fertility preservation
- Feeling overwhelmed at the need for additional procedures related to fertility preservation
- Concerns regarding the initial and ongoing costs associated with fertility preservation
- Religious, cultural, or ethical concerns about fertility preservation methods
- Being unable to provide a semen sample due to being too unwell or for other reasons (e.g. the embarrassment associated with discussing fertility and/or providing a sample)

Recommendations – Discussion and Information	Strength of Recommendation	Grade of Evidence
Timing: The 'reasonable suspicion' of a cancer likely to require fertility-impairing treatment should prompt discussion of fertility and of options for fertility preservation. Delaying discussion until the diagnosis is confirmed and treatment plan made may limit access to some fertility preservation options. Consideration should also be given to the risk of relapse and/or the need for more gonadotoxic therapy in the future even if the current proposed treatment plan does notpose a major risk to fertility. A patient will be eligible for funded fertility preservation inthe event of disease relapse requiring gonadotoxic treatment.	**Strong**	**Very Low to Moderate**
Healthcare Team Roles: Healthcare providers should remain up to date with the current New Zealand guidelines and local referral practices regarding infertility risk and fertility preservation procedures to ensure their ability to provide **initial** guidance to and appropriate referrals for patients/whānau. **There may be cultural considerations associated with the collection, storage, and possible future disposal of reproductive tissues in terms of peoples' understanding and beliefs about the sacred nature of tissue, and where and when a life begins. Appropriate cultural support should be available and offered where indicated, for assistance in decision making. Acknowledgement and inclusion of tikanga practices and kawa principles by healthcare professionals for Māori patients should be incorporated into fertility preservation discussions.** Information should be clear, age-appropriate, and comprehensive either via written and/or online educational resources in appropriate languages and health literacy levels. This should be implemented in an empathetic and neutral manner. Emotional support for patients and their families about treatment-related infertility and fertility preservation should be readily available. Prompt and appropriate psychosocial specialist referrals are to be offered (e.g., psychologists and social workers). Initiation of counselling should occur as early as possible after diagnosis and if a change in disease status requiring treatment intensification with gonadal toxic agents/modalities arises. Treating centres are to establish referral pathways for accessing fertility specialists andcentres. This can also assist in overcoming barriers related to perceived discomfort surrounding the fertility topic and high-volume workloads.	**Strong**	**Very Low to Moderate**

Discussion Points: Fertility risks and appropriate options for fertility preservation should be discussed with patients (and parents/guardians for young patients) regardless of the person's age, prognosis, treatment plan, perceived level of risk to fertility, sexualorientation, gender identity or relationship status. Patients' options for fertility preservation may be influenced by age, co-morbidities, and previous treatments. Fertility preservation discussions should be undertaken by a member of the treating teamas soon as possible after the suspected diagnosis and *likely* treatment plan is determined. Urgent referral to a fertility specialist team may be required. Healthcare providers need to assist patients and their families in the decision-making process through fostering autonomy and encouraging consideration of personal ideals around parenthood. This should occur prior to decisions being made about fertility preservation. Importantly the treating team need to determine whether the consenting person, particularly where young, is psychologically, mentally, and emotionally competentto consent or assent. *Treating team* discussion with person with cancer/ whānau should include: • the degree of risk to fertility posed by the treatment plan – short and long term • relevant options for fertility preservation that may be available, **to enable initial discussions about possible referral** • the potential impact (if any) of pursuing fertility preservation options on cancer treatment and outcome (e.g., delay to commencement of cancer therapy) • the option of choosing not to pursue fertility preservation • the need for contraception for those who are sexually active as absolute fertility status is difficult to ascertain, particularly during chemotherapy and radiation to the pelvis, and in the early post-treatment phase • the risk of premature menopause even where fertility may not be immediately at risk • the provision of appropriate written and/or digital information • the referral process to specialist team for further discussion including financial implications *Specialist fertility team* discussion with person with cancer/ whānau should include: • reiteration of the points discussed by the referring treating team, as described above • the potential cultural, moral, ethical, and legal issues associated with some fertility preservation options. For example, ownership of embryos or reproductive tissue inthe event of death or incapacity • information about success rates, risks, and complications, published evidence and costs to patient (if relevant) for all options that are under discussion. Long-term coststo patient should be highlighted to avoid future conflict • information regarding storage and disposal of gametes, and the importance of maintaining contact with the fertility centre until such time as gametes are used or disposed of • it is important that people undergoing fertility preservation measures are informed ofthe outcome of the preservation processes and the options available to them regarding the use of their stored material. There is no obligation to use preserved gamete tissue in the future.	**Strong**	**Very Low to Moderate**

MANAGING THE FERTILITY PRESERVATION PROCESS –

MULTI-DISCIPLINARY TEAM

Successful management of the risks to fertility associated with cancer treatment requires a co-ordinated multi-disciplinary approach using appropriate region-specific providers and well-established referral pathways. It is particularly important that the surgery, oncology and specialist fertility teams have established and standardised patterns of referral and communication [4, 9, 23, 33] Key team members may include the person's partner and whānau, Clinical Nurse Specialists or AYA Keyworkers and support staff, local treating teams, cultural support advisors, staff at the appropriate tissue storage facility/fertility clinic, members of the research team for investigational procedures, reproductive endocrinology laboratory staff and providers of psychosocial support

Cancer centres would strongly benefit from the development of specialist roles focused on fertility and sexuality care. This role can maintain responsibility for co-ordination and promotion of fertility preservation discussion, information and referral, and be the central contact for those with needs related to fertility and sexuality [21, 35-37]

Considerations

Psychological Distress

Discussion of fertility issues, decision-making around fertility preservation, and the pursuit of fertility preservation options can lead to psychological distress [11, 38-40] Distress may occur at the time that discussions and interventions take place or at any future stage. It is important that both general psychological support and ongoing information and discussion are provided by members of the haematology/oncology/surgical/gynaecology and fertility teams. Specialist psychological and cultural support should be available and referred to as appropriate.

Local Context

Local written protocols must be developed to clearly outline the service/region-specific implementation of these guideline recommendations [17, 24, 25, 33] Within this, the roles of the key team members involved in fertility preservation should be clearly stated, with appropriate region-specific information highlighted. Clear communication pathways between services should be developed and maintained within each region to facilitate information sharing and best outcomes:

- where a referral to specialist fertility services is made, a detailed referral should be provided, including:
    - cancer diagnosis, including stage and grade of disease (as appropriate) and prognosis, if known
    - anticipated/proposed treatment plan and treatment intent
    - assessment of degree of risk to fertility posed by the anticipated/proposed treatment plan
    - time available until start of treatment, and indication of urgency of treatment commencement
    - relationship/family status, presence of existing children
    - relevant medical, mental health and/or substance abuse history
    - prior treatment for cancer
    - dates of other booked treatments/procedures
    - cultural considerations, i.e. specific tikanga practices
    - if the patient identifies as trans or non-binary, provide clear information on name, gender, pronouns and guidance for preferred language when discussing anatomy in the context of fertility preservation
- after assessment, a detailed description of any fertility preservation plan should be provided by the specialist fertility team to the referring team
- after completion of fertility preservation processes, a detailed description of fertility preservation outcomes should be provided by the specialist fertility team to the referring team and patient, including:
    - fertility preservation processes undertaken and their outcome
    - the likely use of any stored gametes for medical record purposes
    - any further recommendations for management or collection of tissue for fertility preservation
    - any peri-operative complications or other relevant clinical information

Recommendations – Managing the Fertility Preservation Process - Multi-disciplinary Team	Strength of Recommendation	Grade of evidence
Cancer and relevant surgical services have a responsibility to ensure that they establish and maintain a co-ordinated and accessible multi-disciplinary approach to fertility preservation including, but not limited to: • treating clinician and applicable nursing team • fertility specialist and associated nursing, laboratory, and storage facilities • local surgical, gynaecology, medicine, urology teams and radiation oncology teams • AYA key workers and other clinical nurse specialists • cultural support advisors • providers of psycho-social support Cancer services should nominate key team members and/or a specialist role to co-ordinate and promote this multi-disciplinary approach Fertility services should maintain clear communication and co-ordination pathways with which referring services and patients can easily engage.	**Strong**	**Very Low to Moderate**
People with a cancer diagnosis who indicate an interest in pursuing fertility preservation should be urgently referred per agreed local pathways for fertility assessment and/or fertility preservation. An urgent referral is of particular importance where cancer treatment commencement cannot be delayed e.g. acute leukaemia	**Strong**	**Very Low to High**

OPTIONS FOR FERTILITY PRESERVATION

There is currently a limited range of options to preserve or protect the fertility of people diagnosed with cancer. The options available to an individual depend on many factors including sex, age, current relationship status, type of cancer, type/intensity/duration of treatment and co-morbidities. It is recommended that fertility preservation be undertaken prior to the commencement of chemotherapy or radiation therapy that poses a risk to fertility, due to the risk of DNA damage to sperm and oocytes [41-45]. It must be noted that little is known to date regarding the fertility risks associated with immunotherapies and targeted therapies, so an individualised approach must be taken.

Preservation of reproductive tissue whilst receiving chemotherapy/radiation therapy or within 12 months of the end of therapy is not recommended due to the possibility of DNA damage to the stored tissue.

The use of fertility preservation measures must be individualised and personalised in consultation with the person with cancer, their whānau and the multidisciplinary treatment team.

If the efficacy of a particular method of fertility preservation is not established, then this needs to be clearly stated in discussions and consent procedures. Such investigational procedures should be undertaken in the context of a protocol approved by the relevant national Ethics Committee (Ethics Committee on Assisted Reproductive Technology ECART or a general Health and Disability Ethics Committee) particularly in the paediatric and AYA population.

Discussion about fertility preservation options should include an explanation of the processes involved, success rates, risks and side effects, and costs, including:

- The potential for increased risk of birth defects associated with assisted reproduction, particularly intracytoplasmic sperm injection (ICSI)
- Advice that the risk of birth defects associated with oocyte and ovarian tissue cryopreservation is not known

Females

Females

Many cancer treatments have the potential to affect fertility. The major effect of cancer treatment on female reproductive potential is through damage to the ovary and the oocytes, with accelerated oocyte depletion. Due to the limited number, irreplaceable nature and decreasing quality of oocytes over time, rates of successful conception and pregnancy diminish quickly from the age of 30 even without cancer treatments [46]. Cytotoxic agents may accelerate this natural age-related decline by approximately 10 years resulting in premature ovarian insufficiency (POI) [11].

Considerations

- An individual's risk of ovarian damage or failure is influenced by their age, pre-existing fertility status and the type, intensity, and duration of the treatment
- While menstruation may continue throughout gonadotoxic treatment or resume post completion of treatment, it is possible that damage to the ovarian reserve will result in premature menopause. Those who have had cancer treatment at any age should be counselled that they may have a shortened reproductive life span with an earlier menopause [47,48]
- Radiation to the uterus can cause irreversible damage via disruption to uterine vasculature and a decrease in uterine weight and length. This can lead to problems with implantation and uterine growth during pregnancy [4]
- Surgery involving reproductive or other pelvic organs can affect fertility through anatomic or vascular changes.
- Hormone changes resulting from cranial irradiation may negatively impact on female fertility [4]
- Prior treatment with chemotherapy has been shown to significantly reduce the efficacy of assisted reproductive technologies undertaken after the end of cancer treatment [11, 49-51]

Research suggests that children born to cancer survivors are not at increased risk of birth defects, genetic disorders, or chromosomal abnormalities [51-56]. There is, however, a known increased risk of birth defects associated with assisted reproductive technologies in the general population [57-61]. This risk may not be significant for IVF when rates of defects are adjusted for parental factors, but there are risks associated with ICSI [62-64].

Pregnancy following cancer should be considered 'high risk' and be managed by a multidisciplinary team. Studies indicate live births to cancer survivors aged 15-39 years may have an increased risk of preterm birth and low birth weight [65]. Higher incidences of adverse pregnancy outcomes have also been reported in females who received prior pelvic radiation [65].

Those who have been treated for hormone-sensitive cancers such as breast cancer do not appear to be at increased risk of relapse during pregnancies subsequent to cancer therapy [64, 66-68].

Oocyte and Embryo Cryopreservation

Embryo cryopreservation is an established procedure and is highly successful with ≥ 90% of good quality embryos expected to survive the thawing process [41, 61, 70]. The success of this process is dependent on the patient's age at the time that in vitro fertilisation and cryopreservation took place. Current fertility providers in New Zealand report the chance of a live birth per replaced thawed embryo is approximately 50% if the oocytes were collected when the female was aged 30, and approximately 25% if the female was aged 40 at time of collection (M.B., personal communication, 2021).

Oocyte cryopreservation is an established procedure with survival rates of thawed oocytes of approximately 90%. Two or three embryos may be expected from every 10 good quality oocytes obtained at the retrieval procedure, with implantation rates similar to those from frozen embryos. The process of vitrification is used for the freezing of oocytes and embryos [70, 71-76]. New Zealand fertility providers report a live birth rate of approximately 50% can be achieved from 10 oocytes collected from a female aged 36 years at time of collection, and from 16 oocytes in a woman aged 39 at time of collection (M.B., personal communication, 2021).

In-vitro Maturation (IVM)

In-vitro maturation of oocytes (IVM**)** is an emerging but still investigational technique. This involves collection of immature oocytes from small follicles early in the menstrual cycle, with limited or no ovarian stimulation. Current research is limited, however recent studies indicate promising results with the first live births being reported [77, 78]. IVM may be of particular benefit for younger females, particularly those with limited time prior to the commencement of chemotherapy, or those with an oestrogen-sensitive tumour [69, 77, 79, 80]. IVM may be available at some fertility clinics in New Zealand.

Risks and Considerations:

- Neither embryo nor oocyte cryopreservation provide a guarantee of future fertility
- The process of ovarian stimulation and oocyte retrieval requires 10 to 14 days before the start of chemotherapy or pelvic radiotherapy
- In those with a low ovarian reserve and without urgent need to commence treatment, double stimulation could be considered. This requires approximately four weeks of fertility treatment but can increase the number of oocytes retrieved by 50% [22]. The second stimulation cycle is not funded in New Zealand.
- Theoretical concerns exist regarding the use of ovarian stimulation in those with oestrogen-receptor positive breast cancers. In many reports use of an aromatase inhibitor as an ovarian stimulator has been described as a safer alternative [81, 82]. There is no evidence that ovarian stimulation for fertility preservation has an adverse effect on survival in this patient group [22]
- Medically unwell patients may face increased risks related to anaesthetic and oocyte collection processes
- Oocyte retrieval may not be appropriate for patients who have not been sexually active and/or may have a history of trauma, gender dysphoria or other considerations, as this usually involves trans-vaginal procedures that can be painful or uncomfortable [84, 85]
- Embryo cryopreservation carries the risk' that the couple may separate, and one of the former partners may no longer consent to the use of the stored embryos. An option for patients is to have stored half of those collected as oocytes and the other half as embryos. A reasonable number of oocytes (e.g., ≥ 20) is required to make this feasible.
- The consent process for cryopreservation includes what can and cannot happen to embryos after death. Partners of the deceased patient can apply through the ethics committee to gain access to stored embryos if permission has been given prior.
- It is possible that children born by assisted reproductive technologies may have an increased risk of congenital abnormalities compared to naturally conceived children [61]
- New Zealand legislation limits storage of sperm, oocytes, embryos and ovarian or testicular tissue to a maximum of ten years. After this time, an application to ECART must be made by the owner requesting ongoing storage [85]. Approval for ongoing storage does *not* include approval for ongoing funding of the storage.

Ovarian Tissue Cryopreservation

Globally ovarian tissue cryopreservation (OTC) is an established procedure, particularly in post-pubertal females. At centres worldwide OTC is approved in the pre-pubertal age group but is sometimes still offered within an ethics-approved protocol in this age group. In New Zealand it is an approved procedure for pre-pubertal females and those for whom embryo or oocyte cryopreservation is not possible [4, 69, 86-88]. Currently there is a philanthropically funded national ethics-approved paediatric protocol for OTC for eligible females aged 0-18 years, but no publicly funded option.

There is no current international consensus on the lower and upper ages at which ovarian tissue cryopreservation should be performed [22]. The likelihood of achieving pregnancy and live birth after reimplantation of ovarian tissue is partly dependent on the age of the person at the time the tissue was retrieved. Accordingly, upper age limits of 30-35 years [22, 69] or 40 years [4, 91] have been proposed internationally. At present only, a few pregnancies have been reported in people over 36 years [23].

The process requires a laparoscopic procedure to remove part of an ovary or a whole ovary. Retrieval of ovarian tissue usually takes place during another planned surgical procedure. No pre-treatment is required, and cancer therapies could be started the following day if required [23, 24]. The cryopreserved tissue can subsequently be re-implanted either on or very close to the remaining ovary or outside the pelvic cavity with the aim of restoring ovarian function for at least a period of time. Natural conception can occur after re-implantation of ovarian tissue on or close to the remaining ovary where the fallopian tubes are intact, but IVF is often required to obtain oocytes which can be fertilised in vitro [92]. Worldwide over 300 females have undergone reimplantation [22]. Ovarian function has been restored in 95% of cases within 4- 9 months. More than 180 babies have been born through ovarian tissue cryopreservation, of these approximately 85% were cancer survivors. Upwards of 40% were natural conceptions, thus avoiding the need for further medical intervention [22]. Nonetheless it can be difficult to determine the true pregnancy and live birth rate as it is unclear how many people have had ovarian tissue replaced without reporting pregnancy and/or live birth, and in some cases pregnancies may have arisen from the residual un-transplanted ovary [87, 90-92].

At the time of this guideline development New Zealand legislation permits the harvest and cryopreservation/storage or ovarian tissue in children and adults as an established procedure. Reimplantation (auto-transplantation) of ovarian tissue harvested when the patient was post-pubertal [93-95], is also considered an established procedure. There is currently limited evidence for birth outcomes from tissue stored pre-pubertally and some international guidelines recommend that reimplantation of tissue stored pre-pubertally be undertaken within an ethics approved protocol [4, 8, 23, 87, 89, 91, 96, 97]. Such a protocol is under consideration in New Zealand and may be designed to include all ovarian tissue reimplantation regardless of age. This is in line with the associated need for rigorous information and consent procedures for the protection of patients, caregivers, health professionals and health services [8, 74, 88, 98].

The recommendation of this guideline is that ovarian tissue cryopreservation/storage should be available to pre-pubertal patients and those for whom embryo or oocyte cryopreservation is not possible or appropriate. The guideline also recommends that initial approved and funded length of storage time for tissue stored when the patient is ≤10 years of age should be 20 years.

Risks and Considerations:

- There are surgical risks associated with the retrieval of ovarian tissue, similar to those associated with standard laparoscopic or mini-laparotomy surgery. These risks are considered low but include anaesthetic risks and complications such as bleeding and infection; in many cases, ovarian tissue retrieval may take place at the same time as another surgical procedure
- Removal of some ovarian tissue for storage may compromise remaining ovarian function
- Adhesion formation may reduce the chances of spontaneous conception
- Ovarian tissue cryopreservation does not provide a guarantee of future fertility
- Medically unwell patients may face increased risks related to anaesthetic and tissue collection processes
- It is possible that children born as a result of IVF have a minimally increased risk of congenital abnormalities compared to naturally conceived children
- New Zealand legislation limits storage of sperm, oocytes, embryos and ovarian or testicular tissue to a maximum of ten years. After this time, an application to ECART must be made by the owner requesting ongoing storage [85]. Approval for ongoing storage does not include approval for ongoing funding of the storage.
- There may be a delay of initiation of cancer treatment to allow for surgery and recovery, although this is likely to be minimal.
- Very limited data exists on obstetric complications in pregnancies achieved after ovarian tissue cryopreservation and reimplantation. Other than early miscarriage, no pregnancy complications have been reported. There is currently no published data on longer term outcomes for children born as a result of this process [87]

There is a risk of tumour cell transmission in the grafted tissue. A recent review categorised leukaemia, neuroblastoma and Burkitt lymphoma as high risk for ovarian metastasis; at moderate risk are some breast cancers, colon cancer, adenocarcinoma of cervix, non-Hodgkin lymphoma and Ewing Sarcoma; at low risk are some breast cancers, squamous cell carcinoma of cervix, Hodgkin lymphoma, osteogenic carcinoma, rhabdomyosarcoma (non-genital) and Wilms tumour [89, 99]. The risk may be minimised by undertaking a comprehensive assessment of slices of the tissue using techniques most appropriate for each particular tumour type (e.g. immunohistochemistry or molecular testing), looking for the presence of cancer cells or markers, both at the time of tissue excision and prior to reimplantation [87, 91, 100-102]. In New Zealand a portion of all ovarian tissue retrieved for the purposes of cryopreservation is reviewed by an anatomic pathologist for evidence of cancer cells. A report is returned to the requesting service. If cancer cells are found the tissue will continue to be stored but could only be used if a safe process is available to retrieve oocytes from the tissue rather than re-implanting the tissue as a whole. Due to this risk, currently in New Zealand, females with leukaemia are not currently eligible for ovarian tissue cryopreservation within the national protocol [69, 88].

Oophoropexy/Ovarian Transposition

Protection of the ovaries from radiation may be achieved through ovarian transposition (oophoropexy) prior to therapy and may be considered. This technique has a complex role in oocyte preservation and is often used as an attempt to preserve an ovary's hormonal function. Nonetheless it can be indicated in those ≤ 40 years who are scheduled to receive pelvic irradiation or radiation with a reasonable risk of ovarian scatter [22]. The procedure involves relocation of the ovaries out of the radiation field to minimise exposure, thereby protecting future fertility. One ovary can be relocated, however better results have been seen with a bilateral procedure [22, 103]. Often this is feasible prior to pelvic radiotherapy but requires prompt multi-disciplinary discussions involving radiation oncologists and relevant surgical team. Retained ovarian function is approximately 60-65% [22, 104]. Failure has been attributed to necrosis due to vascular impairment and migration post insufficient fixation. There is limited data available for pregnancy rates ranging from 0% to 50%, depending on the organ irradiated. Overall evidence supporting this method of preserving ovarian function is deemed of very low quality. This is due to studies limited by population and short follow-up [22, 103, 104]. Despite this, international recommendations suggest potential benefits probably overweigh potential harms and moderately recommend offering oophoropexy prior to pelvic radiotherapy [8].

Risks/considerations:

- The surgical risk of ovarian transposition is similar to other gynaecological procedures (e.g., vessel or bowel damage, general anaesthesia and laparotomic or laparoscopic approach)
- Despite oophropexy the ovary/ovaries may still receive enough radiation to cause ovarian failure
- Ovarian transposition should be taken into consideration at the time of planning radiation treatment

Ovarian Suppression with GnRH Analogues During Chemotherapy

The administration of gonadotrophin-releasing hormone (GnRH) analogues during chemotherapy suppresses menstruation and may reduce the gonadotoxic effects of chemotherapy on ovarian function. Clinical trials examining ovarian function after chemotherapy with or without GnRH analogues have reported conflicting outcomes [22, 105-112] A meta-analysis published in 2018 which incorporated a longer follow-up window than prior reports concluded that particularly in the population of younger females with breast cancer, GnRH analogue use was both effective and safe at reducing the likelihood of chemotherapy-induced primary ovarian failure [68, 113].

While the routine use of GnRH analogues to preserve ovarian function is not currently recommended in populations other than younger females with breast cancer, a low risk profile means that this is often used alone where fertility risk is not high, or in addition to other fertility preservation procedures where available for those at higher risk. [8] Some suggest that GnRH analogues may be offered within a research setting, in addition to proven options but not as a replacement [8].

The most commonly used GnRH analogue in New Zealand is a depot preparation injected monthly or 3-monthly. When used for durations longer than six months, additional low-dose oestrogen replacement should be considered to reduce the consequences of protracted hypo-oestrogenism (unless the woman has an oestrogen-sensitive tumour).

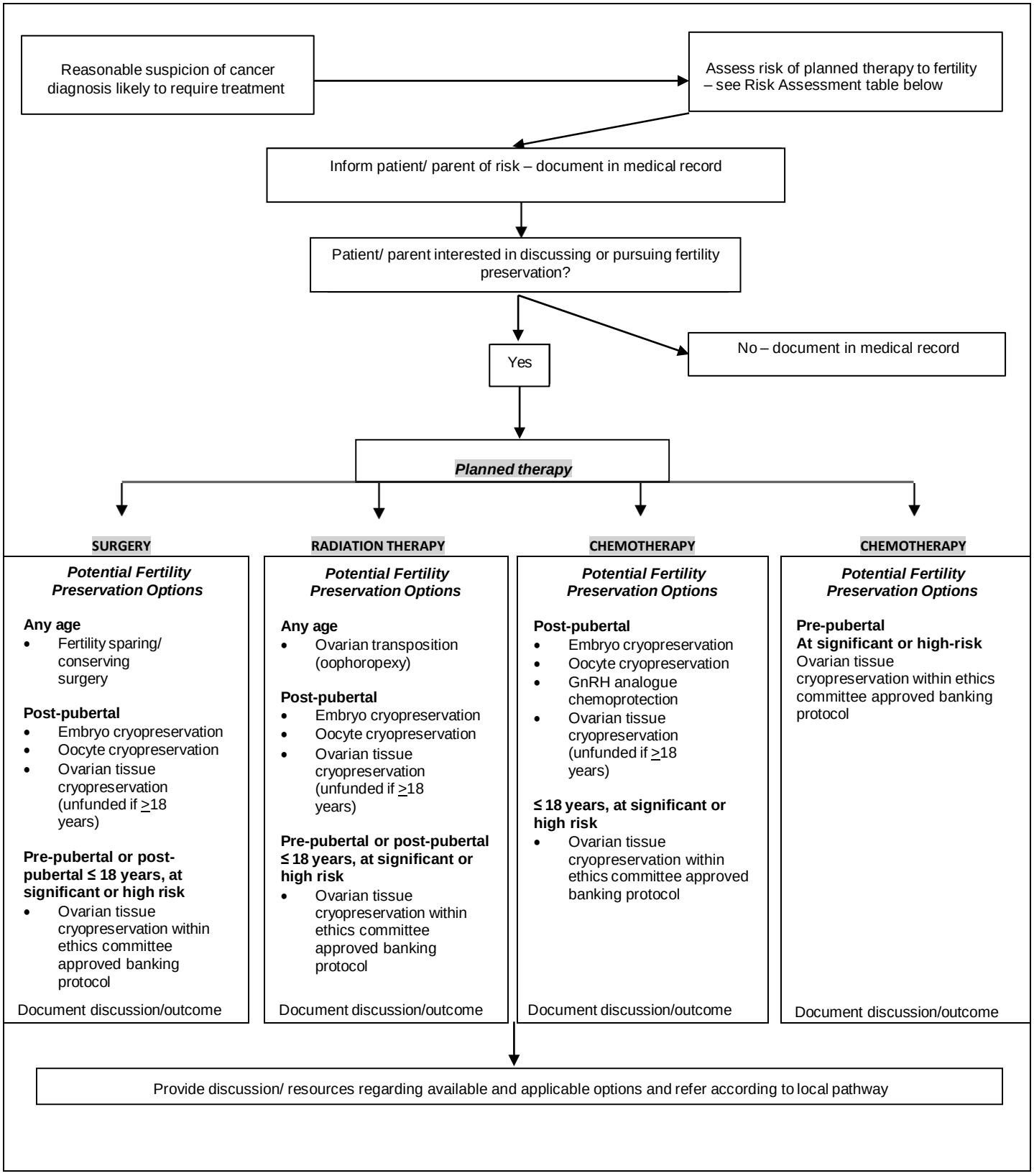
GnRH analogues can be utilised but should not be the primary modality of fertility preservation if superior options are available.

Risks and Considerations:

- The hypo-oestrogenic state induced by GnRH analogue use may cause hot flushes and reduction in vaginal secretions
- There is a risk of bone depletion when GnRH analogues are used for prolonged periods (i.e., > 6 months) without low-dose oestrogen treatment
- GnRH analogues may usefully suppress menstruation during chemotherapies anticipated to cause severe thrombocytopenia. For example, in treatment of acute leukaemia.
- If used to preserve ovarian function, GnRH analogues are best used within a clinical trial *where available* [4, 74]

Female Fertility Preservation Algorithm

Consideration of the potential impact of cancer treatment on fertility and options for fertility preservation should be included in diagnosis and treatment planning for people with cancer or a reasonable suspicion of cancer. Any level of risk to fertility must be disclosed to the person (and/or parents/guardians for children and younger AYA) and their degree of interest in fertility preservation determined and addressed accordingly.



Assessment of Female Fertility Risk

Assessment of the potential for non-surgical cancer treatments to affect fertility involves a combination of the potential risk posed by the planned therapy, the age of the patient, and their current fertility status and genetic fertile lifespan. Measures of fertility status are being investigated for their use as markers of ovarian reserve, but there are currently no fertility risk assessment tools outside of research [114, 115].

Until validated assessment tools are available, the following table offers a means to loosely assess for ***significant to high risk to fertility*** from planned therapy on an individual basis.

The therapies that pose the highest risk to female fertility are alkylating agents and radiation therapy. It must be noted that there is currently minimal evidence regarding the risks associated with immunotherapy or targeted therapy agents.

The table below describes therapies that pose <u>at least significant and possibly high risk</u> to fertility:

<table>
<tr><th>Significant to High Risk Therapy</th><th>High Risk Dose</th></tr>
<tr><td><u>Radiation therapy</u>
Radiation treatment that poses any risk to an individual's fertility should be formally discussed at an MDM meeting and prompt a referral to fertility specialists.

Modern technology and techniques such as intensity modulated radiation therapy (IMRT) brachytherapy, volumetric modulated arc therapy (VMAT) and proton therapy allow for avoidance of reproductive and endocrine structures. Utilisation of these modalities should be incorporated into the patient's individualised treatment plans where possible [116, 117].</td><td>Any radiation to the following areas:
• Ovaries and pelvis
• Cranial (hypothalamus)
• Cranio-spinal irradiation with ovaries in field
• Total body irradiation (TBI) for HSCT

*dose ranges are not used as evidence is conflicting; patient and clinical considerations, and overall treatment plan should form part of the risk assessment</td></tr>
<tr><td><u>Chemotherapy cumulative doses:</u>
Alkylators (particularly if radiation also in treatment plan)

*ranges are used as evidence is conflicting; patient and clinical considerations, and overall treatment plan should form part of the risk assessment

Cisplatin (Heavy metals)</td><td>Cyclophosphamide Equivalent Dose (CED):
Pre-pubertal: ≥6-8 g/m2*
Post-pubertal: ≥6-8 g/m2*
Adult aged 30-40 years: ≥ 5 g/m2

Cyclophosphamide Equivalent Doses:
<table><tr><th>Agent</th><th>Correction Factor</th></tr><tr><td>Cyclophosphamide</td><td>1.0</td></tr><tr><td>Ifosfamide</td><td>0.244</td></tr><tr><td>Procarbazine</td><td>0.857</td></tr><tr><td>Chlorambucil</td><td>14.286</td></tr><tr><td>BCNU (carmustine)</td><td>15</td></tr><tr><td>CCNU (lomustine)</td><td>16</td></tr><tr><td>Melphalan</td><td>40</td></tr><tr><td>Thiotepa</td><td>50</td></tr><tr><td>Nitrogen mustard</td><td>100</td></tr><tr><td>Busulphan</td><td>8.823</td></tr></table>Green Pediatr Blood Ca 2014:61; 53-37 [69]

AND/OR:
Cisplatin:
Child / AYA: >500 mg/m2
Adult: >400 mg/m2</td></tr>
<tr><td>Immunotherapy / Targeted therapy agent with high fertility risk warning</td><td>Per agent</td></tr>
</table>

There are also risks to fertility associated with pelvic surgery. Fertility sparing/conserving surgery should be strongly considered wherever possible [115, 117].

Recommendations – Fertility Preservation for Females	Strength of Recommendation	Grade of Evidence
Damage to fertility due to cancer or its treatment may lead to emotional distress, as can the processes and procedures associated with fertility preservation and treatment • Availability of and referral for cultural and psycho-social support is recommended	**Moderate**	**Very Low to Moderate**

Embryo and oocyte cryopreservation are established procedures that:
• should be discussed, as appropriate, from menarche to menopause prior to therapy that may affect fertility
• should also be discussed with those whose initial planned therapy may not be of significant risk, but who have a reasonable risk of recurrence
• may be suitable for post-pubertal female AYA and adults who:
  ○ are medically fit for the procedure
  ○ are expected to be able to tolerate the treatment regimen
  ○ have sufficient time (10-14 days) before the commencement of their cancer treatment
  ○ are informed of the potential risks of hormonal treatment including the risks of cancer progression
	Strong
	
	Moderate
		Very Low to Moderate

Ovarian tissue cryopreservation is an established procedure that:
• should be discussed with patients (and parents/guardians for younger patients) *prior to significant or high-risk therapy*
• may be suitable for those who:
  ○ are pre-pubertal and/or
  ○ do not have the option of embryo/oocyte cryopreservation
• females aged ≤ 18 years may be eligible for funded ovarian tissue cryopreservation through the national ethics approved protocol. Reimplantation of stored ovarian tissue is not currently funded in New Zealand.
• ovarian tissue must be tested for the presence of cancer calls or markers prior to storage and prior to transplantation
• females aged >18 years may consider ovarian tissue cryopreservation where they do not have the option of embryo/oocyte cryopreservation
	Moderate
	
	Weak
		Very Low
		
		Low to Moderate

In vitro maturation of oocytes (IVM) is an emerging technology and may be an option, but current success rates remain inferior to standard IVF	**Weak**	**Very Low**
The efficacy of GnRH analogues for ovarian protection has been established in pre-menopausal females with breast cancer, but not in other populations • *Pre-menopausal females with breast cancer* should be offered GnRH analogues concurrently with chemotherapy to reduce the risk of primary ovarian insufficiency • In populations other than premenopausal females with breast cancer, GnRH analogues may be used if no other options are available, or in addition to proven options but not as a replacement; discussion of the lack of evidence for the efficacy of this approach should be part of the consenting process	**Strong** **Weak**	**Moderate** **Very Low**
Fertility conserving/sparing surgery should be considered and offered wherever possible when pelvic/gynaecologic surgery is indicated	**Moderate**	**Very Low**

Males

Males

Most cancer treatments have the potential to affect fertility. The major effect of cancer treatment on male reproductive potential is via chemotherapy- or radiation-induced damage to sperm or sperm production, although cranial radiation can impact on the hypothalamic-pituitary axis, and surgery to reproductive or pelvic organs can also affect fertility. An individual's fertility outcome is influenced by the type and extent of disease and the treatment given [7, 22, 118].

Research suggests that children born to male cancer survivors are not more likely to have birth defects, genetic disorders, or chromosomal abnormalities [53-56]. However, higher rates of sperm aneuploidy (incorrect number of chromosomes) have been reported for up to 18 months after chemotherapy and radiotherapy for Hodgkin's Lymphoma and testicular cancer, suggesting that there may be risks associated with having children or providing sperm for banking during this time [45]. The timeframe considered safe to conceive a child or bank sperm is twelve months post completion of treatment [119]. There is an increased risk of birth defects associated with assisted reproductive technologies [57-61, 63, 120,121]. Recent research suggests this risk may not be significant for IVF when rates of birth defects are adjusted for parental factors, but there are risks associated with as intracytoplasmic sperm injection (ICSI) [62,64].

It is recommended patients should have their fertility status evaluated approximately 1-year post therapy to assess for return of natural fertility. Culturally appropriate consideration should be given to the disposal or return of the banked sperm [23].

Cryopreservation of Semen

Semen cryopreservation (sperm banking) before treatment starts is the only well-established method to preserve fertility potential in pubertal and post-pubertal males. Internationally, it is strongly recommended that those in this patient group who are at *any* risk of post-treatment infertility should be offered the opportunity to bank sperm [7, 22, 23]. This is most commonly achieved using ejaculated sperm via masturbation, and the chances of a future pregnancy are increased when more than one sample is provided. Assisted reproductive technology will be to achieve pregnancy with cryopreserved semen. Success using cryopreserved sperm has an aggregate rate for parenthood of 49% [22]. Cases of pregnancies using sperm stored for up to 28 years have been reported [122, 123].

Prior to the commencement of treatment, the quality of sperm in patients with cancer is often decreased [124]. However, moderate-quality evidence indicates sperm condition and yield is sufficient for cryopreservation where the sample is obtained via masturbation [7]. Poor sperm quality has been reported in patients with Hodgkin Disease and testicular cancer [125, 126]. This may mean assisted reproductive technologies such as intra-cytoplasmic sperm injection may be necessary to achieve a pregnancy. Patients should not, however, be discouraged from banking sperm even when sperm quality is reduced.

Where ejaculation by masturbation is not possible penile vibration or electro-ejaculation may be used. In New Zealand these are generally only used in males with a spinal cord injury for whom this would be the only non-surgical option.

Cryopreservation of Epididymal or Testicular Extracted Sperm, and Testicular Biopsy

For others, if semen collection by ejaculation is not possible or successful, evidence strongly recommends offering extraction of sperm by direct testicular or epididymal aspiration, or testicular biopsy. This is particularly relevant for high risk pubertal and post pubertal patients [7, 127]. It is of moderate recommendation in patients who are at high risk of disease recurrence that may require future gonadotoxic treatment. However, extraction of sperm by direct testicular or epididymal aspiration, or testicular biopsy remains secondary to sperm cryopreservation via ejaculation in all groups. For those undergoing orchidectomy for testicular cancer, sperm suitable for use in as ICSI may be extracted from the testis during surgery [128]. Epididymal or testicular sperm extraction is offered in some centres in New Zealand, according to availability of embryologists to attend the procedure to assess the quality of the sample in real time. Testicular biopsy is most often used in younger males and whilst undergoing general anaesthetic for another procedure (e.g. placement of a central line).

Risks and Considerations:

- Sperm banking should be performed prior to commencement of chemotherapy (including intra-thecal chemotherapy) or pelvic radiation therapy to avoid increased sperm aneuploidy rates and increased sperm DNA damage related to chemotherapy exposure.
- Discussion regarding sperm banking must be undertaken with sensitivity in younger AYA and it is preferable that much of the discussion take place without a parent or parents present unless the young person requests otherwise
- Sensitivity is also required for discussion around sperm banking for trans and non-binary people. Consideration of language used and the impact of gender dysphoria on producing a sample is important.
- More than one attempt may be needed to obtain a suitable semen sample for banking
- The collection of more than one semen sample over a period of days is preferable for maximising future fertility potential, however newer techniques such as ICSI allow for successful cryopreservation and future use of small numbers of sperm.
- Trans-females often have lower quality sperm samples (i.e. count and motility) prior to any hormone therapy and may require intra-cytoplasmic sperm injection (ICSI) in order to fertilise and oocyte [129, 130]
- Semen must be transported to the fertility centre laboratory at room temperature and received at the laboratory within 60-90 minutes of collection
- Sperm quality has been found to be poor, including aneuploidy and increased rates of DNA damage in association with testicular cancer, Hodgkin lymphoma and other cancers even prior to treatment and this risk should be made clear
- There are risks such as pain, bleeding, swelling and infection when epididymal/testicular extraction of sperm is used
- Sperm motility is decreased after thawing or cryopreservation [7]
- New Zealand legislation limits storage of sperm, oocytes, embryos and ovarian or testicular tissue to a maximum of ten years. After this time, an application to ECART must be made by the owner requesting ongoing storage [85]. Approval for ongoing storage does not include approval for ongoing funding of the storage.

Cryopreservation of Testicular Tissue Before Puberty

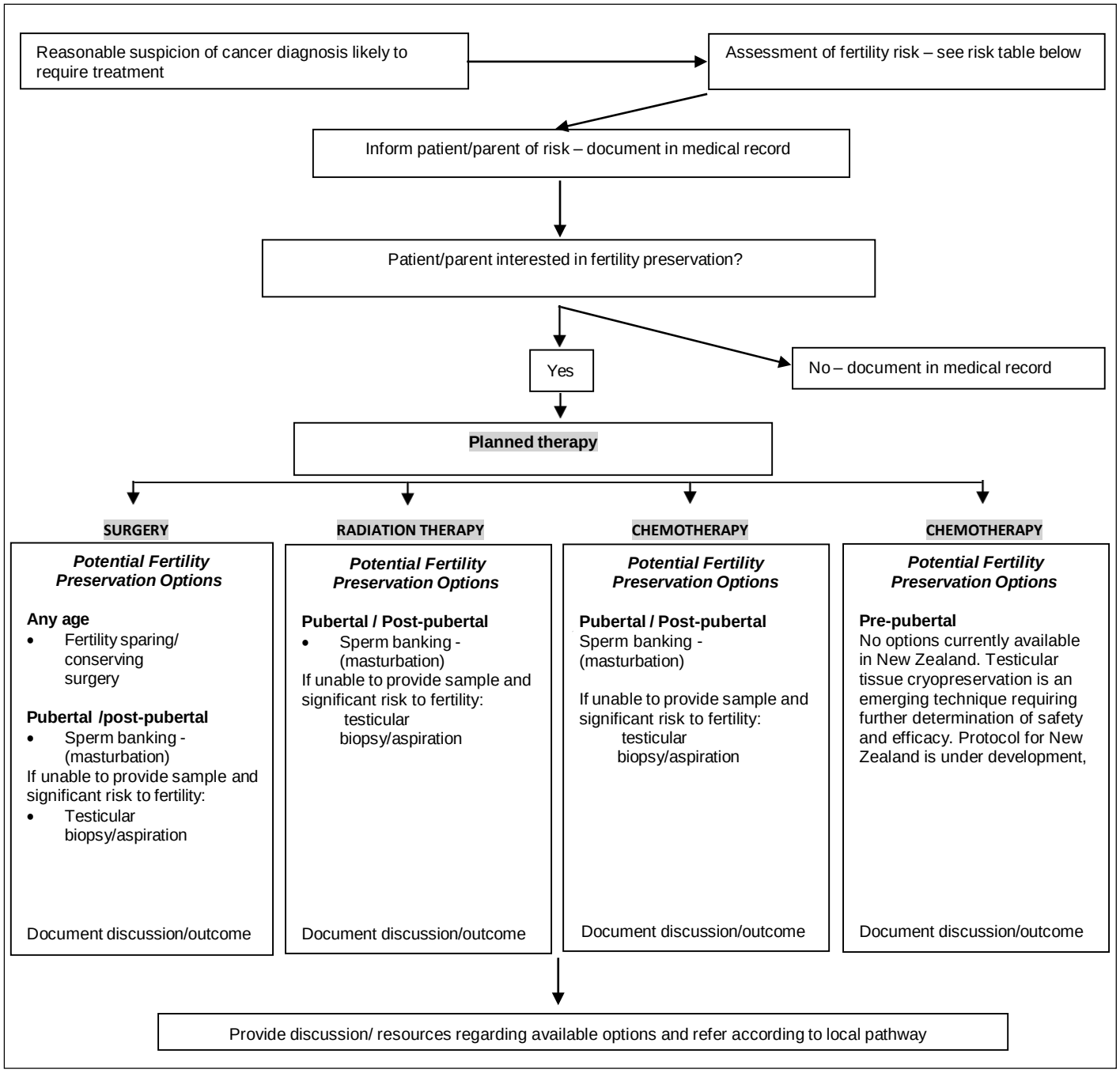
Testicular tissue from prepubertal patients has been cryopreserved in some international centres in the expectation of successful future use [4, 131]. This is an area of active global research and not currently available in New Zealand. International recommendations suggest testicular tissue cryopreservation can be offered to high-risk pre- pubertal and pubertal patients [7]. This should be within an ethics-approved protocol with clear informed consent processes. Such a protocol is under development in New Zealand and once open will be offered via the two children's cancer centres (Starship and Christchurch Hospitals).

Hormone suppression for Males

There is no evidence to support the effectiveness of hormone suppression in pubertal and post-pubertal males. Despite feasibility, low costs and ease of implementation, international standards do not recommend this line of therapy [7, 22, 23]

Male Fertility Preservation Algorithm

Consideration of the potential impact of cancer treatment on fertility and options for fertility preservation should be included in diagnosis and treatment planning for people of any age with cancer or a reasonable suspicion of cancer. Any level of risk to fertility must be disclosed to the person (and/or parents/guardians for children and adolescents) and their degree of interest in fertility preservation determined and addressed accordingly:



Assessment of Male Fertility Risk

Assessment of the potential impact of cancer treatments on male fertility is based on the risk of azoospermia post-treatment and the length of time until sperm production resumes. **Tools such as the following risk table offer a means to loosely assess for *significant* risk to fertility from planned therapy on an individual basis.** The therapies that pose the highest risk to fertility are alkylating agents, heavy metals, and radiation therapy. It must be noted that there is currently minimal evidence regarding the risks associated with immunotherapy or targeted therapy agents.

The table below describes therapies that pose at least significant, and possibly high, risk to fertility:

<table>
<tr><th>Significant Risk Therapy</th><th>Significant Risk Dose</th></tr>
<tr><td><u>Radiation therapy</u>

Radiation treatment that poses any risk to an individual's fertility should be formally discussed at an MDM meeting and prompt a referral to fertility specialists.

Modern technology and techniques such IMRT brachytherapy, VMAT and proton therapy allow for avoidance of reproductive and endocrine structures. Utilisation of these modalities should be incorporated into the patient's individualised treatment plans where possible [116, 132].</td><td>Any radiation to the following areas:
Testes and pelvis
Cranial (hypothalamus)
Total body irradiation (TBI) for HSCT
*doses ranges are not used, as evidence is conflicting; patient and clinical considerations, and overall treatment plan should form part of the risk assessment</td></tr>
<tr><td><u>Chemotherapy cumulative doses:</u>

Alkylators (particularly if radiation also in treatment plan)

Heavy metal (cisplatin)</td><td>Cyclophosphamide Equivalent Dose (CED):
Pre-pubertal: ≥4 g/m2
Post-pubertal / AYA: ≥4 g/m2
Adult: ≥ 7.5 g/m2

Cyclophosphamide Equivalent Doses:<table><tr><th>Agent</th><th>Correction Factor</th></tr><tr><td>Cyclophosphamide</td><td>1.0</td></tr><tr><td>Ifosfamide</td><td>0.244</td></tr><tr><td>Procarbazine</td><td>0.857</td></tr><tr><td>Chlorambucil</td><td>14.286</td></tr><tr><td>BCNU (carmustine)</td><td>15</td></tr><tr><td>CCNU (lomustine)</td><td>16</td></tr><tr><td>Melphalan</td><td>40</td></tr><tr><td>Thiotepa</td><td>50</td></tr><tr><td>Nitrogen mustard</td><td>100</td></tr><tr><td>Busulphan</td><td>8.823</td></tr></table>Green Pediatr Blood Ca 2014:61; 53-37 [69]

AND/ OR:

Cisplatin:
Child / AYA: >500 mg/m2
Adult: >400 mg/m2</td></tr>
<tr><td>Immunotherapy / Targeted therapy agent with high fertility risk warning</td><td>Per agent</td></tr>
</table>

There are also risks to fertility associated with pelvic surgery. Fertility sparing/conserving surgery should be strongly consideredwherever possible [118].

Recommendations – Fertility Preservation for Males	Strength of Recommendation	Grade of Evidence
Damage to fertility due to cancer or its treatment may lead to emotional distress, as can the processes and procedures associated with fertility preservation and treatment • Availability of and referral for psycho-social support is recommended	**Moderate**	**Very Low to Moderate**
Sperm cryopreservation is the only well-established method of preserving fertility in post-pubertal males. • It should be offered to **all** pubertal (Tanner Stage 3) and post-pubertal males prior to chemotherapy, radiotherapy or surgery that may damage the testes or reproductive function	**Strong**	**Very Low to Moderate**
Epididymal or testicular aspiration or biopsy should be offered to pubertal (Tanner stage 2-4) and post-pubertal males at significant risk of infertility, and those of high-risk of disease recurrence who are unableto ejaculate. May be considered for patients with azoospermia.	**Strong**	**Very Low**
Pre-pubertal testicular tissue cryopreservation is an experimental procedure that is not currently available in New Zealand. • It should be offered only within an appropriately ethics-approved protocol (under development in New Zealand)	**Moderate**	**Very Low**
Fertility conserving surgery should be employed wherever possible when pelvic/testicular surgery is indicated	**Weak**	**Very Low**

Long Term Follow up

LONG TERM FOLLOW UP

Current evidence suggests that the impact of cancer and its treatment on fertility is an important consideration for many cancer survivors [4, 5, 18, 20, 74, 131-141]. There is limited high level evidence on which to base recommendations for long term follow-up after cancer treatment, particularly for those treated for cancer as adults. The type of post-treatment follow- up indicated for cancer survivors in relation to fertility should be determined according to sex, diagnosis, type of cancer treatment received, age at diagnosis and treatment, and other patient-specific factors. There are differences in long term follow-up recommendations for paediatric/AYA cancer survivors versus adult survivors related to clinical indication and the pragmatics of resource and service provision. Long term follow-up may also be undertaken within a primary care environment.

For paediatric and AYA cancer survivors an initial clinical review of reproductive health should be undertaken approximately six months after the end of treatment [4, 74, 133]. A plan for follow up should then be drawn up as appropriate with an emphasis on good communication between paediatric (if appropriate) and adult services, the patient's General Practitioner and other relevant health care providers, as well as cultural support. A comprehensive follow-up service for those with a higher degree of need would involve a multidisciplinary team comprised of oncology, psychology, nursing, specialist fertility and endocrinology services, with access to social work, and peer/cultural support. Involvement of whānau and kaupapa support should also be included for Māori patients, along with incorporation of tikanga practices and kawa principles. While it may not be possible to have all members available at one site, clearly defined referral and communication paths must be established between team members. Follow-up services should be able to accommodate the changing needs of survivors over time.

Psycho-Social Assessment

Cancer survivors (their partners and whānau) may experience psychological distress related to the effects of cancer treatment on their reproductive and sexual function and intimate relationships. Pursuing or choosing not to pursue fertility preservation pre- treatment and/or fertility interventions post-treatment may both result in distress, as may the belief that these options were not adequately addressed at diagnosis. Assessment of the psychological health and needs of cancer survivors, particularly relating tothe reproductive sequelae of cancer and its treatment should therefore be a key part of long term follow-up, and provision should be made for specialist psychological input where indicated [3, 17, 18, 40, 74, 137-140, 142-151]. Cultural factors can also heavily impact psychological wellbeing. For instance, Te Whare Tapa Wha (Māori health model) should be included as part of the assessment process for Māori and non-Māori patients.

Pre-treatment discussions regarding fertility, fertility preservation, and the effect of cancer and its treatment on fertility are often undertaken at a time of great stress [32]. Care should be taken to assess the level of understanding of the patient and their whānau regarding the information they were given during their diagnosis and treatment, and to update them on any further developments in the field [152].

Recommendations – Long Term Follow Up	Strength of Recommendation	Grade of Evidence
People treated for cancer as children or adolescents and young adults should have access to systematic long term follow up of their reproductive health via the Late Effects Assessment Programme (LEAP) or other means. Adult cancer survivors should have access to follow-up for reproductive health as appropriate for their age and the treatments received This should include the opportunity, if indicated, to meet with a fertility specialist after treatment completion to review, and where appropriate, assess their reproductive health and plan for future care or intervention.	**Moderate**	**Very Low**
Some cancer survivors have psychological health needs related to the impact of the cancer and its treatment on their reproductive and sexual function. Referral for psychological support should be available.	**Moderate**	**Moderate**
Depending on the treatments received, pregnancy after cancer treatment may be considered 'high risk' due to the potential impact of some cancer treatments on the health of both mother and baby	**Moderate**	**Low**

Females

Females who have undergone cancer treatment may be at increased risk of infertility, premature ovarian failure, sexual dysfunction and associated emotional distress. The degree of risk to fertility and sexual function is influenced by the cancer diagnosis, the type, intensity and duration of treatment, the age at which the diagnosis and treatment occurred, and their pre-existing fertility status and functioning. For childhood and AYA cancer survivors reproductive and sexual health should be checked, as appropriate, as part of overall treatment follow-up. For adult cancer survivors, reproductive and sexual health should be assessed as clinically indicated or requested.

Early referral for specialist fertility review is recommended for those who are at increased risk of premature ovarian failure due to the cancer treatments they have received, and who express a desire to have children in the future, regardless of whether or not they undertook fertility preservation prior to commencing cancer treatment [49, 50].

Childhood cancer survivors should be assessed for overall growth and development during and after cancer treatment and referred for early endocrine review where there are concerns regarding growth velocity or delayed/precocious puberty [127, 129]. Due to the increased risk of premature ovarian failure after cancer treatment it is recommended that early referral for specialist fertility and/or endocrine assessment be discussed to support optimal reproductive and sexual health. Hormone replacement may be a safe therapy for survivors of non-hormone dependent cancers to alleviate symptoms of oestrogen deficiency and maintain bone health. Hormone replacement is contra-indicated in those who have been treated for breast and hormone-dependent gynaecological cancers [74, 153-155].

The return of and/or presence of menstruation is often used as a surrogate marker of fertility but does not provide an accurate indication of ovarian reserve and future fertility. Antimullerian hormone (AMH) is currently considered the most useful marker of ovarian reserve for post-pubertal females. Other markers include early follicular phase (FSH). Ultrasound scan assessment of ovarian volume of antral follicle count may also be used [31, 49, 160, 161].

It is important to discuss contraception with sexually active cancer survivors, even where fertility is impaired, and document discussion in medical record.

Pregnancy after Treatment for Cancer

Current evidence suggests that pregnancy after treatment for cancer is generally safe for both parent and baby, although it is often recommended that pregnancy in cancer survivors be considered 'high risk' and managed through a tertiary obstetric centre if possible [158]. The risks associated with pregnancy in cancer survivors are reflective of the cancer treatments given and therefore it is important that the obstetric team have access to treatment information. Those who have received pelvic radiation therapy are at increased risk of miscarriage, pre-term birth and low birth weight infants due to damage to the uterine wall and vasculature. The long-termimpact of cancer therapies on cardiac, renal, respiratory, and immune function should be considered in terms of pregnancy risk [74, 131, 132].

It is generally recommended that pregnancy be avoided by those treated for cancers *other than breast cancer* for 12 months after the completion of cancer therapy to minimise risks to both mother and baby [157, 159].

In those treated for early breast cancer pregnancy occurring at least 10 months from the time of diagnosis may not have a negative impact on prognosis [66]. However, it is generally recommended that pregnancy be avoided for at least 2 years after a diagnosis of breast cancer in order to minimise the risk to both mother and baby associated with early relapse and allow some endocrine therapy where appropriate [159-161].

Children born to cancer survivors are not at increased risk of birth defects, genetic disorders, or chromosomal abnormalities [53-55].

Other Options

- Adoption processes in New Zealand are overseen by Oranga Tamariki: http://www.orangatamariki.govt.nz/adoption/
- Whāngai adoption through whānau networks
- Use of donor eggs or sperm and options for surrogacy are best discussed with a fertility provider

Female Long-Term Follow-up Clinical Guidance

Prepubertal/Pubertal	
Initial assessment after completion of therapy	• Risk of impaired fertility based on treatment received • Pubertal development (Tanner staging) and history • Height • Serum FSH, LH, oestradiol baseline levels (at age 13 years)
Ongoing assessment	• Pubertal development and history (6 monthly until sexually mature) • Height (6-12 monthly until normal pubertal growth spurt established) • Menstrual history – onset, frequency (6 monthly) • Serum FSH, LH • Oestradiol baseline levels (at age 13 years and then annually or asclinically indicated *) *Clinical indications: as appropriate for stage of developmente.g., Delayed puberty
In the event of: • Poor growth • Delayed puberty • High risk of hypogonadism based on treatment received	Refer to endocrinologist for assessment and treatment if indicated

Post-Pubertal Adolescents and Young Adults	
Initial assessment after completion of therapy *AMH may not be funded in all regions	• Risk of impaired fertility based on treatment received and age at treatment • Menstrual/pregnancy history • Serum FSH, LH, oestradiol, AMH* baseline levels • Sexual health and function • Presence of menopausal symptoms • Use of contraception and/or hormone replacement • Knowledge and concerns regarding sexual health, fertility and contraception including need to avoid pregnancy for 6-12 months post treatment completion • Presence of psychological distress and/or relationship concerns • Use of medications that may impact on sexual function
Ongoing assessment *AMH levels may not be funded in all regions	• Menstrual/pregnancy history (annually) • Serum FSH, LH, oestradiol, AMH* levels (annually or as clinically indicated **) • Sexual health and function (annually or sooner if indicated) • Presence of menopausal symptoms (annually or sooner if indicated) • Use of contraception and/or hormone replacement (annually) • Knowledge and concerns regarding sexual health, fertility, and contraception (annually) • Presence of psychological distress and/or relationship concerns (annually or sooner if indicated) ** Clinical Indications: Irregular menstruation, primary or secondary amenorrhea,signs of oestrogen deficiency

In the event of: • Reduced ovarian function • Received highly gonadotoxic therapy • Increased risk of premature menopause • Pelvic radiation with an intact uterus • Other impediment to natural conception/pregnancy • Evidence of oligo-or anovulation • Gonadotrophins above referenceranges	Offer referral for specialist assessment/management by health professional most appropriate: • Fertility specialist • Reproductive endocrinologist • Obstetrician

Adults	
In the event of: • High or intermediate risk of impaired fertility or ovarian failure • Pelvic radiation with an intact uterus • Other impediment to natural conception or pregnancy • Patient concern about fertility • Clinical indications of reduced ovarian function	Offer referral for assessment/management by healthprofessional most appropriate: • Medical oncologist (for those with breast cancer/hormone-sensitive gynaecologicalcancers) • Haematologist • Gynaecologist • Obstetrician • Reproductive endocrinologist • Women's health specialist

Males

Males who have undergone cancer treatment may be at increased risk of infertility, sexual dysfunction and associated emotional distress. The degree of risk to fertility and sexual function is influenced by the cancer diagnosis, the type, intensity and duration of treatment, the age at which the diagnosis and treatment occurred, and pre-existing fertility status and functioning. For childhood and AYA cancer survivors reproductive and sexual health should be checked, as appropriate, as part of overall treatment follow-up. For adult cancer survivors, reproductive and sexual health should be assessed, as appropriate, after treatment completion. Cancer survivors who undertook fertility preservation prior to commencing cancer treatment should be referred for early specialist fertility review after treatment completion.

Children should be assessed for overall growth and development during and after cancer treatment and referred for early endocrine review where there are concerns regarding growth velocity or delayed/precocious puberty. Testicular volume and serum FSH, LH, testosterone, and inhibin B (if available) provide useful indicators of gonadal damage [132, 134, 161,162]. Semen analysis should be offered to AYA and adults 12 months after treatment completion [74]. Those whose fertility is shown to be unaffected or restored and who have sperm banked from pre-treatment, should be encouraged to arrange for banked sperm to be discarded [162].

It is important to discuss contraception with sexually active cancer survivors, even where fertility is impaired and document the discussion in the medical record.

Children born to cancer survivors are not at increased risk of birth defects, genetic disorders, or chromosomal abnormalities [53-55].

Other Options

- Adoption processes in New Zealand are overseen by Oranga Tamariki: http://www.orangatamariki.govt.nz/adoption/
- Whāngai adoption through whānau networks
- Use of donor eggs or sperm and options for surrogacy are best discussed with a fertility provider

Male Long-Term Follow-up Clinical Guidance

Prepubertal/Pubertal	
Initial assessment after completion of therapy	Risk of impaired fertility based on treatment received • Pubertal development (Tanner Staging) and history • Testicular volume using Prader orchidometer • Height • Serum FSH, LH, testosterone, inhibin B (if available)
Ongoing assessment	• Pubertal development and history (12 monthly) • Testicular volume using Prader orchidometer (12 monthly) • Height (6-12 monthly until normal pubertal growth spurt established) • Serum FSH, LH, testosterone, inhibin B baseline levels (at age 14 years and then annually or as clinically indicated *) *Clinical Indications – as appropriate for stage of development: E.g., Delayed puberty and/or clinical signs of testosterone deficiency
In event of: • Poor growth • Delayed puberty • High risk of hypogonadism based on treatment received	Refer to endocrinologist for assessment and treatment if indicated.

Post-Pubertal Adolescents and Young Adults	
Initial assessment after completion of therapy	• Risk of impaired fertility based on treatment received • Serum FSH, LH, testosterone, inhibin B (if available) • Semen analysis as appropriate 12 months after treatment completion • Sexual health and function • Presence of symptoms of hypogonadism • Use of contraception • Knowledge and concerns regarding sexual health, fertility, and contraception, avoid conceiving a child for 12 months post treatment • Presence of psychological distress and/or relationship concerns
Ongoing assessment	• Use of medications that may impact on sexual function • Serum FSH, LH, testosterone, inhibin B (6-12 monthly if indicated by suggestion of testosterone deficiency) • Semen analysis (as indicated) - If analysis suggests fertility unaffected/restored and patient has sperm banked from pre-treatment fertility preservation, inform sperm bank so that sperm can be discarded. • Sexual health and function (annually or sooner if indicated) • Use of contraception (annually) • Knowledge and concerns regarding sexual health, fertility, and contraception (annually) • Presence of psychological distress and/or relationship concerns (annually or sooner if indicated)
In event of: • Impaired fertility • Patient received highly gonadotoxic therapy • Other impediment to natural reproduction Serum testosterone below reference range	• Offer referral for specialist fertility assessment/ consultation and/or referral for endocrinology review

Adults	
In the event of: • High or intermediate risk of impaired fertility • Patient concerned about fertility	Offer referral for specialist fertility assessment/ consultation
In the event of: • High or intermediate risk of gonadal failure • Signs or symptoms of hypogonadism • Patient not concerned about fertility	Offer referral for endocrinology review

It is acknowledged that there will be variations in the availability of multi-disciplinary team input for long term follow-up.

DEVELOPMENT AND REVIEW OF THE GUIDELINE

This guideline update was performed by the National Fertility Preservation Working Group under the Adolescent and Young Adult (AYA) Cancer Network Aotearoa and endorsed by Te Aho o Te Kahu. The group was comprised of a multidisciplinary team of health professionals from throughout New Zealand with expert knowledge of oncology and fertility, and patient representatives with personal experiences of infertility related to cancer treatment. Additionalconsultation with expert practitioners and cultural representatives was undertaken, along with review of the guidelines by relevant stakeholder groups prior to being finalised.

The primary sources for this update were current peer-reviewed and agreed international guidelines, relevant literature, expert recommendations, and New Zealand legislation. Particular attention was paid to the recently published *Fertility Preservation in Childhood, Adolescent, and Young Adult Cancer* series of the PanCareLIFE Consortium and the International Late Effects of Childhood Cancer Guideline Harmonization Group, and the *Fertility Preservation for AYAs Diagnosed with Cancer: Guidance for Health Professionals* online resource of the Clinical Oncological Society of Australia [7-9, 98]. The recommendations made in these source documents and the basis on which they were made were appraised and considered in light of New Zealand's unique cultural, health and social environment.

This guideline should be used alongside local protocols that specify assessment/referral procedures and key expert practitioners in various aspects of oncology and fertility to facilitate patient access in a timely manner and optimise the outcome of any fertility preservation measures undertaken.

This document is current as of December 2022.

Guideline Development Group Membership

Dr Mary Birdsall		Fertility Specialist, Group Medical Director, Fertility Associates
Talia Cooper		Consumer Representative - Breast Cancer Foundation New Zealand
Mr Steve Evans		Clinical Director Paediatric Surgery, Starship Children's Hospital
Dr Kate Gardner		Medical Oncologist, Canterbury District Health Board
Dr Devashana Gupta		Fertility Specialist/Gynaecologist, Repromed
Ashleigh Guy	Project Manager	Clinical Nurse Specialist Haematology, Canterbury District Health Board
Dr Sarah Hunter	Chair	Research Manager, Starship Blood and Cancer Centre, Starship Children's Hospital
Dr Simon Kelly		Fertility Specialist, Medical Director, Fertility Associates Auckland
Jeanette Mackenzie		Scientific Director, Fertility Plus
Christine Martin		Charge Nurse Manager, Fertility Plus
Paul Mulivai		Consumer Representative – AYA Cancer Network Consumer Advisory Group
Dr Tristan Pettit		Paediatric/AYA Oncologist, Canterbury District Health Board
Heidi Watson	Clinical Lead	Clinical Leader, Adolescent and Young Adult Cancer Network Aotearoa
Tanwen Ward		Consumer Representative – AYA Cancer Network Consumer Advisory Group
Val Waugh		AYA Keyworker- Clinical Nurse Specialist, Southern District Health Board
Paula Whitfield		Clinical Nurse Specialist Breast Cancer, Auckland District Health Board

Expert Contributors

Danielle Duff	Radiation Therapist, Canterbury District Health Board, Project Manager, AYA Cancer Network Aotearoa
Dr Benjamin Hindson	Radiation Oncologist, Canterbury District Health Board
Dr Rachel Johnson	Youth Health Specialist, Paediatrician, Kidz First Centre for Youth Health
Dr Catherine Neal	Haematologist, Canterbury District Health Board
Ellyn Proffit	Clinical Nurse Specialist AYA Adult Cancer Service- Midland, Waikato District Health Board
Dr Humphrey Pullon	Haematologist, Waikato District Health Board
Nadine Riwai	Senior Portfolio Manager National Cervical Screening Programme, Health New Zealand
Dr Myra Ruka	Clinical Haematologist, Clinical Equity Lead – Te Aho o Te Kahu
Dr Frank Saran	Radiation Oncologist, Auckland District Health Board
Dr Ai Ling Tan	Gynaecological Oncologist, Auckland District Health Board

GLOSSARY OF TERMS

- **AMH:** Anti-Mullerian hormone
- **ART:** Assisted reproductive technology
- **Azoospermia:** Complete absence of sperm from semen
- **CPAC:** Clinical priority assessment criteria (fertility funding eligibility tool)
- **ECART:** Ethics committee on assisted reproductive technology
- **FSH**: Follicle stimulating hormone
- **Gamete**: Mature female or male germ cell e.g. egg or sperm
- **Gender dysphoria:** a sense of unease that a person may have because of a mismatch between their biological sex and their gender identity
- **Gonadotoxic therapy:** Chemotherapy, radiation and surgical resection that can compromise future fertility
- **GnRH:** Gonadotropin releasing hormone
- **GRADE:** Grading of recommendations assessment, development and evaluation
- **ICSI:** Intracytoplasmic sperm injection
- **IMRT:** Intensity modulated radiation technology, thin beams of radiation are delivered of varying intensity and angles
- **Inhibin B:** a peptide hormone that is produced primarily by growing antral follicles that are responsive to FSH
- **IVF:** In vitro fertilisation
- **IVM:** In vitro maturation
- **Kaupapa:** principles, ideas and values that form a base or foundation for behaviours and actions.
- **LH:** Luteinizing hormone
- **Oestradiol:** a steroid hormone secreted mainly by the ovary, small amounts are produced by the testis and adrenals
- **Orchidectomy:** Surgical removal of the testes, predominantly indicated in prostate cancer.
- **OTC:** Ovarian tissue cryopreservation
- **POI:** Premature ovarian insufficiency
- **Tanner staging:** also known as sexual maturity rating (SMR), is an objective classification system used to document and track the development and sequence of secondary sex characteristics of children during puberty
- **VMAT:** Volumetric modulated arc therapy, delivers the radiation dose continuously as the treatment machine rotates
- **Whakapapa:** or genealogy, proclaims Māori identity through placing oneself in a wider context with links to land, iwi and mana

REFERENCES

1. Davies, N.J., et al., *Information satisfaction in breast and prostate cancer patients: Implications for quality of life.* Psycho-Oncology, 2008. 17: p. 1048-1052.
2. Jenkins, V., L. Fallowfield, and J. Saul, *Information needs of patients with cancer: Results from a large study in UK cancer centres.* British Journal of Cancer, 2001. 84(1): p. 48-51.
3. Thewes, B., et al., *The fertility and menopause-related information needs of younger women with a diagnosis of breast cancer: A qualitative study.* Psycho-Oncology, 2003. 12: p. 500-511.
4. Lee, S.J., et al., *American Society of Clinical Oncology recommendations on fertility preservation in cancer patients.* Journal of Clinical Oncology, 2006. 24: p. 2917-2931.
5. Beckjord, E.B., et al., *Health related information needs in a large and diverse sample of adult cancer survivors: Implications for cancer care.* Journal of Cancer Survivorship, 2008. 2: p. 179-189.
6. Font-Gonzalez, A., et al., *Fertility preservation in children, adolescents, and young adults with cancer: Quality of clinical practice guidelines and variations in recommendations.* Cancer, 2016. 122(14): p. 2216-23.
7. Mulder, R.L., et al., *Fertility preservation for male patients with childhood, adolescent, and young adult cancer: recommendations from the PanCareLIFE Consortium and the International Late Effects of Childhood Cancer Guideline Harmonization Group.* Lancet Oncol, 2021. 22(2): p. e57-e67.
8. Mulder, R.L., et al., *Fertility preservation for female patients with childhood, adolescent, and young adult cancer: recommendations from the PanCareLIFE Consortium and the International Late Effects of Childhood Cancer Guideline Harmonization Group.* Lancet Oncol, 2021. 22(2): p. e45-e56.
9. Mulder, R.L., et al., *Communication and ethical considerations for fertility preservation for patients with childhood, adolescent, and young adult cancer: recommendations from the PanCareLIFE Consortium and the International Late Effects of Childhood Cancer Guideline Harmonization Group.* Lancet Oncol, 2021. 22(2): p. e68-e80.
10. Suzuki, N., *Clinical Practice Guidelines for Fertility Preservation in Pediatric, Adolescent, and Young Adults with Cancer.* Int J Clin Oncol, 2019. 24(1): p. 20-27.
11. Dolmans, M.M., et al., *EUropean Recommendations for female Fertility preservation (EU-REFER): A joint collaboration between oncologists and fertility specialists.* Crit Rev Oncol Hematol, 2019. 138: p. 233-240.
12. Ministry of Health. *Specialist Medical and Surgical Services – Assisted Reproductive Technology Services (ART) Tier Two Service Specification.* 2018. Wellington, New Zealand.
13. Alonso-Coello, P., et al., *GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 2: Clinical practice guidelines.* BMJ, 2016. 353: p. i2089.
14. Alonso-Coello, P., et al., *GRADE Evidence to Decision (EtD) frameworks: a systematic and transparent approach to making well informed healthcare choices. 1: Introduction.* BMJ, 2016. 353: p. i2016.
15. Andrews, J., et al., *GRADE guidelines: 14. Going from evidence to recommendations: the significance and presentation of recommendations.* J Clin Epidemiol, 2013. 66(7): p. 719-25.
16. Andrews, J.C., et al., *GRADE guidelines: 15. Going from evidence to recommendation-determinants of a recommendation's direction and strength.* J Clin Epidemiol, 2013. 66(7): p. 726-35.
17. Peate, M., et al., *The fertility-related concerns, needs and preferences of young women with cancer: A systematic review.* Breast Cancer Research and Treatment, 2009. 116: p. 215-223.
18. Tschudin S and Bitzer J, *Psychological aspects of fertility preservation in men and women affected by cancer and other life-threatening diseases.* Human Reproduction Update, 2009. 15(5): p. 587-597.
19. Loren AW, et al. *Fertility preservation for patients with cancer: American Society of Clinical Oncology Clinical Practice Guideline update*. Journal of Clinical Oncology, 2013. DOI: 10.1200/JCO.2013.49.2678.
20. Thames Valley Cancer Network, *TVCN Adult Haematology Long Term Follow Up Guideline - Fertility*. 2013, Thames Valley Cancer Network: Oxford.
21. Nagel K and Neal M, *Discussions regarding sperm banking with adolescent and young adult males who have cancer.* Journal of Pediatric Oncology Nursing, 2008. 25(2): p. 102-106.
22. Lambertini, M., et al., *Fertility preservation and post-treatment pregnancies in post-pubertal cancer patients: ESMO Clinical Practice Guidelines(dagger).* Ann Oncol, 2020. 31(12): p. 1664-1678.
23. Oktay, K., et al., *Fertility Preservation in Patients with Cancer: ASCO Clinical Practice Guideline Update.* J Clin Oncol, 2018. 36(19): p. 1994-2001.
24. Achille M A, et al., *Facilitators and obstacles to sperm banking in young men receiving gonadotoxic chemotherapy for cancer: the perspective of survivors and health care professionals.* Human Reproduction, 2006. 21(12): p. 206-3216.
25. Crawshaw M A, et al., *Male and female experiences of having fertility matters raised alongside a cancer diagnosis during the teenage and young adult years.* European Journal of Cancer Care, 2009. 18(4): p. 381-390.
26. Balthazar U, et al., *The current fertility preservation consultation model: are we adequately informing cancer patients of their options?* Human Reproduction, 2012. 27(8): p. 2413-2419.
27. Murphy, N. *Te Awa Atua: Menstruation in the pre-colonial Maori world*. 2013. He Puna Manawa Limited.
28. Walker, T., et al., *The road we travel: Maori experience of cancer.* New Zealand Medical Journal, 2008. 121(1279): p. 27-35.
29. Reynolds Paul and Smith Cherryl, *The gift of children: Maori and infertility*. 2012, Wellington: Huia Publishers.
30. Fitzgerald, R.P., et al., *Excluding indigenous bioethical concerns when regulating frozen embryo storage: An Aotearoa New Zealand case study.* Reprod Biomed Soc Online, 2019. 8: p. 10-22.
31. Hudson M., et al. He Tangata Kei Tua, Guidelines for Biobanking with Māori. 2016. Te Mata Hautū Taketake – Māori & Indigenous Governance Centre University of Waikato, Hamilton, New Zealand.

32. Levine J, Canada A, and Stern C J, *Fertility preservation in adolescents and young adults with cancer.* Journal of Clinical Oncology, 2010. 28(32): p. 4831-41.
33. Edge B, Holmes D, and Makin G, *Sperm banking in adolescent cancer patients.* Archives of Disease in Childhood, 2006. 91(2): p. 149-152.
34. Multidisciplinary Working Group convened by the British Fertility Society, *A strategy for fertility services for survivors of childhood cancer.* Human Fertility, 2003. 6(2): p. A1-A39.
35. Anderson R A, et al., *Do doctors discuss fertility issues before they treat young patients with cancer?* Human Reproduction, 2008. 23(10): p. 2246-2251.
36. Canada, A.L. and L.R. Schover, *Research promoting better patient education on reproductive health after cancer.* Journal of the National Cancer Institute Monographs, 2005. 34: p. 98-100.
37. Foy, S.M. *Provision of a fertility service for women with cancer: Evaluating the educational needs of specialist cancer nurses*. in *15th International Conference on Cancer Nursing*. 2008. Singapore.
38. Alesi, R., *Infertility and its treatment: An emotional rollercoaster.* Australian Family Physician, 2005. 34(3): p. 135-139.
39. Cousineau, T.M. and A.D. Domar, *Psychological impact of infertility.* Best Practice and Research: Clinical Obstetrics and Gynaecology, 2007. 21(2): p. 293-308.
40. Johansson, M. and M. Berg, *Women's experiences of childlessness 2 years after the end of in vitro fertilization treatment.* Scandinavian Journal of Caring Science, 2005. 19: p. 58-63.
41. Bedoschi G and Oktay K, *Current approach to fertility preservation by embryo cryopreservation.* Fertility and Sterility, 2013. 99(6): p. 1496-1502.
42. Chung K, et al., *Emergency IVF versus ovarian tissue cryopreservation: decision making in fertility preservation for female cancer patients.* Fertility and Sterility, 2013. 99(6): p. 1534-1542.
43. Morris ID, *Sperm DNA damage and cancer treatment.* International Journal of Andrology, 2002. 25: p. 255-261.
44. O'Donovan M, *An evaluation of chromatin condensation and DNA integrity in the spermatozoa of men with cancer before and after therapy.* Andrologia, 2005. 37: p. 83-90.
45. Tempest H G, et al., *Sperm aneuploidy frequencies analysed before and after chemotherapy in testicular cancer and Hodgkin's lymphoma patients.* Human Reproduction, 2008. 23(2): p. 251-258.
46. Simon, B., et al., *Preserving fertility after cancer.* CA - A Cancer Journal for Clinicians, 2005. 55(4): p. 211-228.
47. Partridge, A.H., et al., *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.* European Journal of Cancer, 2007. 43: p. 1646-1653.
48. Stroud, J.S., et al., *Effects of cancer treatment on ovarian function.* Fertility and Sterility, 2009. 92(2): p. 417-428.
49. Das M., et al., *Ovarian reserve and response to IVF and in vitro maturation treatment following chemotherapy.* Human Reproduction, 2012. 27(8): p. 2509-2514.
50. Barton SE, et al., *Female cancer survivors are low responders and have reduced success compared with other patients undergoing assisted reproductive technologies.* Fertility and Sterility, 2012. 97(2): p. 381-386.
51. van der Kooi, A.L.F., et al., *Perinatal risks in female cancer survivors: A population-based analysis.* PLoS One, 2018. 13(8): p. e0202805.
52. Mahajan, N., *Fertility preservation in female cancer patients: An overview.* J Hum Reprod Sci, 2015. 8(1): p. 3-13.
53. Blatt J, *Pregnancy outcome in long-term survivors of childhood cancer.* Medical and Pediatric Oncology, 1999. 33(1): p. 29-33.
54. Fossa, S.D., et al., *Parenthood in survivors after adult cancer and perinatal health in their offspring: A preliminary report.* Journal of the National Cancer Institute Monographs, 2005. 34: p. 77-82.
55. Winther J. F., et al., *Chromosomal abnormalities among offspring of childhood-cancer survivors in Denmark: a population-basedstudy.* American Journal of Human Genetics, 2004. 74(6): p. 1282-1285.
56. Green, D.M., et al., *Pregnancy outcome of partners of male survivors of childhood cancer: a report from the Childhood Cancer Survivor Study.* J Clin Oncol, 2003. 21(4): p. 716-21.
57. Hansen M, et al., *Assisted reproductive technologies and the risk of birth defects: a systematic review.* Human Reproduction, 2005. 20(2): p. 328-338.
58. Bonduelle M, et al., *A multi-centre cohort study of the physical health of 5-year old children conceived after intracytoplasmic sperm injection, in vitro fertilisation and natural conception.* Human Reproduction, 2005. 20(2): p. 413-419.
59. Buckett W M, et al., *Obstetric outcomes and congenital abnormalities after in vitro maturation, in vitro fertilization, and intracytoplasmic sperm injection.* Obstetrics and Gynecology, 2007. 110: p. 885-891.
60. Halliday J L, et al., *Increased risk of blastogenesis birth defects, arising in the first 4 weeks of pregnancy, after assisted reproductive technologies.* Human Reproduction, 2010. 25(1): p. 59-65.
61. Wennerholm U B, et al., *Children born after cryopreservation of embryos or oocytes: a systematic review of outcome data.* Human Reproduction, 2009. 24: p. 2158-2172.
62. Davies MJ, et al., *Reproductive technologies and risk of birth defects.* New England Journal of Medicine, 2012. 366: p. 1803-1813.
63. Luke, B., et al., *The risk of birth defects with conception by ART.* Hum Reprod, 2021. 36(1): p. 116-129.
64. Azim, H.A., Jr., et al., *Prognostic impact of pregnancy after breast cancer according to estrogen receptor status: a multicentre retrospective study.* J Clin Oncol, 2013. 31(1): p. 73-9.
65. Anderson, C., et al., *Birth Outcomes Among Adolescent and Young Adult Cancer Survivors.* JAMA Oncol, 2017. 3(8): p. 1078-1084.
66. Valachis A, et al., *Safety of pregnancy after primary breast cancer in young women: A meta-analysis to overcome bias of healthy mother effect studies.* Obstetrical and Gynaecological Survey, 2010. 65(12): p. 786-793.
67. Iqbal, J., et al., *Association of the Timing of Pregnancy with Survival in Women with Breast Cancer.* JAMA Oncol, 2017. 3(5):

p.659-665.
68. Lambertini, M., et al., *Long-term Safety of Pregnancy Following Breast Cancer According to Estrogen Receptor Status.* J Natl Cancer Inst, 2018. 110(4): p. 426-429.
69. Anderson RA, *Report on the current status of the use of cryopreserved ovarian tissue for the Advisory Committee on Assisted Reproductive Technology (ACART) of New Zealand*. 2010, University of Edinburgh: Edinburgh.
70. Birdsall, M. *Personal communication*. Fertility Associates. 2021.
71. Wang Y A, Chambers G M, and Sullivan E A *Assisted reproductive technology in Australia and New Zealand 2008. Assisted reproduction technology series. No. 14. Cat No. PER49*, in *Assisted Reproductive Technology Series*. 2010, AIHW: Canberra.
72. Smith G D, et al., *Prospective randomised comparison of human oocyte cryopreservation with slow-rate freezing or vitrification.* Fertility and Sterility, 2010. 94(6): p. 2088-2095.
73. Rienzi L, et al., *Consistent and predictable delivery rates after oocyte vitrification: an observational longitudinal cohort multicentric study.* Human Reproduction, 2012. 27(6): p. 1606-1612.
74. Clinical Oncological Society of Australia. *Fertility preservation for AYAs diagnosed with cancer: guidance for health professionals*. [cited 2012 7th October 2012]; Available from: http://wiki.cancer.org.au/australia/COSA:AYA_cancer_fertility_preservation.
75. Leader A, et al., *Fertility considerations and preservation in haemato-oncology patients undergoing treatment.* British Journal of Haematology, 2011. 153(3): p. 291-308.
76. Cobo A, et al., *Is vitrification of oocytes useful for fertility preservation of age-related fertility decline and in cancer patients?* Fertility and Sterility, 2013. 99(6): p. 1485-1496.
77. Son, W.Y., et al., *Immature Oocyte for Fertility Preservation.* Front Endocrinol (Lausanne), 2019. 10(1): p. 464.
78. Segers, I., et al., *Live births following fertility preservation using in-vitro maturation of ovarian tissue oocytes.* Hum Reprod, 2020. 35(9): p. 2026-2036.
79. Shalom-Paz E, et al., *Fertility preservation for breast cancer patients using IVM followed by oocyte or embryo vitrification.* Reproductive Biomedicine Online, 2010. 21(4): p. 566-571.
80. Oktay K, B.E., Rodriguez-Wallberg KA, Sahin G, *In vitro maturation improves oocyte or embryo cryopreservation outcome in breast cancer patients undergoing ovarian stimulation for fertility preservation.* Reprod Biomed Online, 2010. 20(5): p. 634-637.
81. Oktay K, et al., *Fertility preservation in breast cancer patients: IVF and cryopreservation after ovarian stimulation with tamoxifen.* Human Reproduction, 2003. 18(1): p. 90-95.
82. Cakmak H and Rosen MP, *Ovarian stimulation in cancer patients.* Fertility and Sterility, 2013. 99(6): p. 1476-1484.
83. Hart R, *Preservation of fertility in adults and children diagnosed with cancer.* British Medical Journal, 2008. 27(337).
84. Oktem O and Oktay K, *Fertility preservation for breast cancer patients.* Seminars in Reproductive Medicine, 2009. 27: p. 486-492.
85. Ministry of Justice, *Human Assisted Reproductive Technology (Storage) Amendment Act*. 2010: New Zealand.
86. Jadoul P, Dolmans M, and Donnez J, *Fertility preservation in girls during childhood: is it feasible, efficient and safe and to whom should it be proposed?* Human Reproduction Update, 2010. 16(6): p. 617-630.
87. Michaeli J, et al., *Fertility preservation in girls.* Obstetrics and Gynaecology International, 2012. 2012.
88. Hunter S, Winstanley M, Birdsall M, Peek J, Pettit T *Ovarian Tissue Cryopreservation/banking protocol for New Zealand paediatric haematology/oncology services* 2020. p. 1-9.
89. The Practice Committee of the American Society for Reproductive Medicine and Practice Committee of the Society for Assisted Reproductive Technology, *Ovarian tissue and oocyte cryopreservation.* Fertility and Sterility, 2008. 90: p. S241-246.
90. Donnez J, et al., *Restoration of ovarian activity and pregnancy after transplantation of cryopreserved ovarian tissue: a review of 60 cases of reimplantation.* fertility and Sterility, 2013. 99(6): p. 1503-1513.
91. Rodriguez-Wallberg KA and Oktay K, *Recent advances in oocyte and ovarian tissue cryopreservation and transplantation.* Best Practice and Research: Clinical Obstetrics and Gynaecology, 2012. 26: p. 391-405.
92. Donnez J, et al., *Children born after auto transplantation of cryopreserved ovarian tissue. A review of 13 live births.* Annals of Medicine, 2011(43): p. 437-450.
93. Ministry of Justice, *Human Assisted Reproductive Technology Act*. 2004: New Zealand.
94. Ministry of Justice, *Human Assisted Reproductive Technology Order* 2005: New Zealand.
95. Ministry of Justice, *Human Assisted Reproductive Technology Amendment Order*. 2021, Ministry of Health New Zealand p. 3.
96. The Practice Committee of the American Society for Reproductive Medicine and Practice Committee of the Society for Assisted Reproductive Technology, *Ovarian tissue and oocyte cryopreservation: Recently reviewed practice committee report.* Fertility and Sterility, 2006. 86(5 Supplement 1): p. S142-S147.
97. Wallace W H B and Barr R D, *Fertility preservation in girls and young women with cancer: what are the remaining challenges?* Human Reproduction Update, 2010. 16(6): p. 614-616.
98. Clinical Oncological Society of Australia. *AYA cancer fertility preservation guidance working group. Fertility preservation for AYAs diagnosed with cancer: Guidance for health professionals.* 2021 Aug 3; Available from: https://wiki.cancer.org.au/australiawiki/index.php?oldid=215312,.
99. Dolmans M, et al., *Risk of transferring malignant cells with transplanted frozen-thawed ovarian tissue.* Fertility and Sterility, 2013. 99(6): p. 1514-1522.
100. Meirow D, et al., *Ovarian tissue banking in patients with Hodgkin's disease: is it safe?* Fertility and Sterility, 1998. 69(6): p. 996-998.
101. Kim S S., et al., *Ovarian tissue harvested from lymphoma patients to preserve fertility may be safe for auto transplantation.* Human Reproduction, 2001. 16(10): p. 2056-2060.
102. Bittinger S E, et al., *Detection of Hodgkin lymphoma within ovarian tissue.* Fertility and Sterility, 2011. 95(2): p. 803-806.
103. Rowell, E.E., et al., *Laparoscopic unilateral oophorectomy for ovarian tissue cryopreservation in children.* J Pediatr Surg, 2019. 54(3): p. 543-549.
104. Hoekman, E.J., et al., *Ovarian survival after pelvic radiation: transposition until the age of 35 years.* Arch Gynecol Obstet, 2018.

298(5): p. 1001-1007.
105. Bedaiwy M A, et al., *Gonadotropin-releasing hormone analog cotreatment for preservation of ovarian function during gonadotoxic chemotherapy: a systematic review and meta-analysis.* Fertility and Sterility, 2011. 95(3): p. 906-914.
106. Ben-Aharon I, et al., *Pharmacological interventions for fertility preservation during chemotherapy: a systematic review and meta-analysis.* Breast Cancer Research and Treatment, 2010. 122(3): p. 803-811.
107. Clowse ME, et al., *Ovarian preservation by GnRH agonists during chemotherapy: a meta-analysis.* Journal of Women's Health, 2009. 18(3): p. 311-319.
108. Beck-Fruchter R, Weiss A, and S. E, *GnRh agonist therapy as ovarian protectants in female patients undergoing chemotherapy: a review of the clinical data.* Human Reproduction Update, 2008. 14(6): p. 553-561.
109. Badawy A, et al., *Gonadotropin-releasing hormone agonists for prevention of chemotherapy-induced ovarian damage: prospective randomised study.* Fertility and Sterility, 2009. 91(3): p. 694-697.
110. Partridge AH, *Ovarian suppression for prevention of premature menopause and infertility: empty promise or effective therapy?* Journal of Clinical Oncology, 2012. 30(5): p. 479-481.
111. Munster PN, et al., *Randomised trial using gonadotropin-releasing hormone agonist triptorelin for the preservation of ovarian function during (neo) adjuvant chemotherapy for breast cancer.* Journal of Clinical Oncology, 2012. 30(5): p. 533-538.
112. Corkum, K.S., et al., *Fertility and hormone preservation and restoration for female children and adolescents receiving gonadotoxic cancer treatments: A systematic review.* J Pediatr Surg, 2019. 54(11): p. 2200-2209.
113. Blumenfeld, Z. *Fertility preservation by endocrine suppression of ovarian function using gonadotropin-releasing hormone agonists: the end of the controversy? .* J Clin Oncol, 2018. 36(19): p. 1895-1897.
114. Usta T and Oral E, *Is the measurement of anti-Mullerian hormone essential?* Current Opinion in Obstetrics and Gynaecology, 2012. 24: p. 151-157.
115. La Marca A, et al., *Possibilities and limits of ovarian reserve testing in ART.* Current Pharmaceutical Biotechnology, 2012. 13: p. 398-408.
116. Santaballa, A, et al. *Multidisciplinary consensus on the criteria for fertility preservation in cancer patients.* Clin Trans Oncol, 2022. 24:227-243.
117. Ghadjar P, Budach V, Kohler C, Jantke A, Marnitz S. *Modern radiation therapy and potential fertility preservation strategies in patients with cervical cancer undergoing chemoradiation.* Rad Onc, 2015. 10(5): 222-229
118. Practice Committee of the American Society for Reproductive Medicine. *Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: committee opinion.* 2019. 112(6): p.1022-1033.
119. Rodriguez-Wallberg K A & Oktay K. *Fertility preservation during cancer treatment: clinical guidelines.* Cancer management and research. 2014. 6(3): p 105-117.
120. Meistrich M L, Vassilopoulou-Sellin R, and Lipschultz L I, *Gonadal Dysfunction*, in *Cancer: Principles and Practice of Oncology*, DeVita V T, Hellman S, and Rosenberg S A, Editors. 2005, Lippincott, Williams and Wilkins: Philadelphia. p. 2560-2574.
121. AYA Cancer Network, *Cancer and fertility; before, during and after treatment* 2019, AYA Cancer Services: Wellington; New Zealand
122. Jensen, E.T., *Higher proportion of birth defects with assisted reproductive technology may not be attributable to advanced maternal age.* BJOG, 2017. 124(10): p. 1545.
123. Feldschuh J, et al., *Successful sperm storage for 28 years.* Fertility and Sterility, 2005. 84(4).
124. Agarwal A and Allamaneni S S, *Disruption of spermatogenesis by the cancer disease process.* Journal of the National Cancer Institute Monographs, 2005. 34: p. 9-12.
125. O'Flaherty C, et al., *Characterization of sperm chromatin quality in testicular cancer and Hodgkin's lymphoma patients prior to chemotherapy.* Human Reproduction, 2008. 23(5): p. 1044-1052.
126. Skakkebaek N E, Rajpert-De Meyts E, and Main K M, *Testicular dysgenesis syndrome: an increasingly common developmental disorder with environmental aspects.* Human Reproduction, 2001. 16(5): p. 972-978.
127. Shin D, Lo K C, and Lipschultz L I, *Treatment options for the infertile male with cancer.* Journal of the National Cancer Institute Monographs, 2005. 34: p. 48-50.
128. Carmignani L, et al., *Testicular sperm extraction in cancerous testicles in patients with azoospermia: a case report.* Human Reproduction, 2007. 22(4): p. 1068-1072.
129. Rodriguez-Wallberg K.A., Häljestig J., Arver S., Johansson A.L.V, Lundberg F. E. *Sperm quality in transgender women before or after gender affirming hormone therapy-A prospective cohort study.* Andrology. 2021. 9(6):1773-1780.
130. I de Nie., et al. *Impaired semen quality in trans women: prevalence and determinant.* Human Reproduction. 2020. 35(7): p1529–1536.
131. Wyns C, et al., *Options for fertility preservation in prepubertal boys.* Human Reproduction Update, 2010. 16(3): p. 312-328.
132. Duman E, Bilek Y, Ceyran G. *A comparison of radiotherapy treatment planning techniques in patients with rectal cancers by analysing testes doses*. 2021. 17(1); 56-61.
133. United Kingdom Children's Cancer Study Group Late Effects Group, *Practice Statement: Therapy Based Long Term Follow Up*. 2005.
134. Children's Oncology Group, *Long-term follow-up guidelines for survivors of childhood, adolescent and young adult cancers*. 2008, Children's Oncology Group: Arcadia, CA.
135. Scottish Intercollegiate Guidelines Network, *Long term follow up of survivors of childhood cancer: A national clinical guideline*. 2004, Scottish Intercollegiate Guidelines Network: Edinburgh.
136. Absolom, K., et al., *Ovarian failure following cancer treatment: Current management and quality of life.* Human Reproduction, 2008. 23(11): p. 2506-2512.
137. Hammond, C.T.C., et al., *Non-Hodgkin's lymphoma survivors' fertility and sexual function-related information needs.* Fertility and Sterility, 2008. 90(4): p. 1258-1260.
138. Hordern, A.J. and A.F. Street, *Constructions of sexuality and intimacy after cancer: Patient and health professional perspectives.*

Social Science and Medicine, 2007a. 64: p. 1704-1718.
139. Hordern, A.J. and A.F. Street, *Communicating about patient sexuality and intimacy after cancer: Mismatched expectations and unmet needs.* Medical Journal of Australia, 2007b. 186(5): p. 224-227.
140. Walton, L.M., et al., *Gynaecologic cancer patients' needs and experiences of supportive health services in New Zealand.* Psycho-Oncology, 2009. 19(2): p. 201-208.
141. Wenzel, L., et al., *Defining and measuring reproductive concerns of female cancer survivors.* Journal of the National Cancer Institute Monographs, 2005. 34: p. 94-98.
142. Zebrack, B.J., J. Mills, and T.S. Weitzman, *Health and supportive care needs of young adult cancer patients and survivors.* Journal of Cancer Survivorship, 2007. 1: p. 137-145.
143. Rosen, A., K.A. Rodriguez-Wallberg, and L. Rosenzweig, *Psycho-social distress in young cancer survivors.* Seminars in Oncology Nursing, 2009. 25(4): p. 268-277.
144. Bloom, J.R., et al., *Then and now: Quality of life of young breast cancer survivors.* Psycho-Oncology, 2004. 13: p. 147-160.
145. Partridge, A.H., et al., *Web-based survey of fertility issues in young women with breast cancer.* Journal of Clinical Oncology, 2004. 22: p. 4174-4183.
146. Carter, J., et al., *Cancer-related infertility in survivorship.* International Journal of Gynaecological Cancer, 2010. 20(1): p. 2-8.
147. Carter, J., et al., *Gynaecologic cancer treatment and the impact of cancer-related infertility.* Gynecologic Oncology, 2005. 97: p. 90-95.
148. Nakayama, K., et al., *Receiving information on fertility- and menopause-related treatment effects among women who undergo hematopoietic stem cell transplantation: Changes in perceived importance over time.* Biology of Blood and Marrow Transplantation, 2009. 15(11): p. 1465-1474.
149. Cancer Control Council of New Zealand, *The voice of experience: Part one*. 2009, Cancer Control Council: Wellington, New Zealand.
150. Allan, H., *Experiences of infertility: Liminality and the role of the fertility clinic.* Nursing Inquiry, 2007. 14(2): p. 132-139.
151. Andrykowski, M.A., E. Lykins, and A. Floyd, *Psychological health in cancer survivors.* Seminars in Oncology Nursing, 2008. 24(3): p. 193-201.
152. Halkett, G.K.B., et al., *The phenomenon of making decisions during the experience of early breast cancer.* European Journal of Cancer Care, 2007. 16: p. 322-330.
153. Schover L R, et al., *Knowledge and experience regarding cancer, infertility and sperm banking in younger male survivors.* Journal of Clinical Oncology, 2002. 20(7): p. 1880-1889.
154. Rees M, *Gynaecological oncology perspective on management of the menopause.* European Journal of Surgical Oncology, 2006. 32(8): p. 892-897.
155. Hickey M, et al., *Practical clinical guidelines for assessing and managing menopausal symptoms after breast cancer.* Annals of Oncology, 2008. 19(10): p. 1669-1680.
156. Kendall A, et al., *Caution: Vaginal estradiol appears to be contraindicated in postmenopausal women on adjuvant aromatase inhibitors.* Annals of Oncology, 2006. 17(4): p. 584-587.
157. Brougham MFH, et al., *Anti-Mullerian Hormone is a Marker of Gonadotoxicity in Pre-and Postpubertal Girls Treated for Cancer: A Prospective Study.* Journal of Clinical Endocrinology and Metabolism, 2012. 97(6): p. 2059-2067.
158. Kelsey TW, et al., *Data driven assessment of the human ovarian reserve.* Molecular Human Reproduction, 2012. 18(2): p. 79-87.
159. Matthews ML, et al., *Cancer, Fertility Preservation and Future Pregnancy: A Comprehensive Review.* Obstetrics and Gynaecology International, 2012. 2012: p. 1-11.
160. De Bree E, et al., *Pregnancy after breast cancer: A comprehensive review.* Journal of Surgical Oncology, 2010. 101(6): p. 534-542.
161. Azim AA, et al., *Safety of pregnancy following breast cancer diagnosis: a meta-analysis of 14 studies.* European Journal of Cancer, 2011. 47: p. 74-83.
162. Skinner R, Mulder RL, Kremer LC, Hudson MM, Constine LS, Bardi E, Boekhout A, Borgmann-Staudt A, Brown MC, Cohn R et al. *Recommendations for gonadotoxicity surveillance in male childhood, adolescent, and young adult cancer survivors: a report from the International Late Effects of Childhood Cancer Guideline Harmonization Group in collaboration with the PanCareSurFup*