EAU Guidelines on Male Infertility

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EPIDEMIOLOGY

- **Definition**
- “Infertility is the inability of a sexually active, non-contracepting couple to achieve spontaneous pregnancy in one year” (WHO)
- About 15% of couples do not achieve pregnancy within one year and seek medical treatment for infertility.
- One in eight couples encounter problems when attempting to conceive a first child and one in six when attempting to conceive a subsequent child.

EPIDEMIOLOGY

- In 50% of voluntarily childless couples, a male-infertility-associated factor is found together with abnormal semen parameters.
- A fertile partner may compensate for the fertility problem of the man and thus infertility usually manifests if both partners have reduced fertility

AETIOLOGY

- congenital or acquired urogenital abnormalities
- malignancies
- urogenital tract infections
- increased scrotal temperature (e.g. as a consequence of varicocele)
- endocrine disturbances
- genetic abnormalities
- immunological factors

PROGNOSTIC FACTORS

- Duration of infertility
- Primary or secondary infertility
- Results of semen analysis
- Age and fertility status of female partner

Diagnostic Evaluations

- **Initial evaluation of the male for fertility should include a reproductive history. (Clinical Principle)**

- **Initial evaluation of the male should also include one or more semen analyses (Strong Recommendation; Evidence Level: Grade B)**

Semen Parameter	One-Sided Lower Reference Limit (Fifth Centiles With 95% Confidence Intervals)
Semen Volume	1.5 mL (1.4-1.7)
Total Sperm Number	39 million per ejaculate (33-46)
Sperm Concentration	15 million/mL (12-16 million/mL)
Vitality	58% Live (55-63%)
Progressive Motility	32% (31-34%)
Total Motility (Progressive + Non-Progressive)	40% (38-42%)
Morphologically Normal Forms	4.0% (3.0-4.0)

***Semen samples from 4500 men (men with proven fertile, with unknown fertility status and other men who were normozoospermic) from 14 countries and 4 continents were analyzed. Men described above were all fertile (Partners' time-to-pregnancy < or = 12 months) and their parameters were selected to calculate the values shown below.[17,28]**

Lower reference limits (5th centiles and their 95% CIs) for semen characteristics

Other consensus threshold values	
pH	> 7.2
Peroxidase-positive leukocytes (10^6/mL)	< 1.0
Optional investigations	
MAR test (motile spermatozoa with bound particles, %)	< 50
Immunobead test (motile spermatozoa with bound beads, %)	< 50
Seminal zinc (µmol/ejaculate)	≥ 2.4
Seminal fructose (µmol/ejaculate)	≥ 13
Seminal neutral glucosidase (mU/ejaculate)	≤ 20

Frequency of semen analysis

- If the results of semen analysis are normal according to WHO criteria, one test is sufficient
- If the results are abnormal in at least two tests, further andrological investigation is indicated
- **In couples with failed ART cycles or recurrent pregnancy losses (RPL) (two or more losses), evaluation of the male should be considered. (Expert Opinion)**

Comorbidities

- 1-6% of men have undiagnosed medical diseases at the time of an infertility evaluation
- men with abnormal SAs have higher rates of medical comorbidities

Possible Medical Comorbidities Associated with Male Infertility			
Condition	MULTIPLE studies indicate increased risk	SINGLE study indicates increased risk	Evidence is UNCLEAR or CONFLICTING
Abnormal semen parameters	Testicular cancer Mortality CCI	Diabetes Multiple sclerosis Chronic epididymitis	Prostate cancer Melanoma Other cancers Sexually transmitted infections Thyroid disorders

Infertile men with specific, identifiable causes of male infertility should be informed of relevant, associated health conditions (Moderate Recommendation; Evidence Level Grade: B)

Condition	MULTIPLE studies indicate increased risk	SINGLE study indicates increased risk	Evidence is UNCLEAR or CONFLICTING
Klinefelter syndrome	• Testosterone deficiency	• All-cause mortality • Specific-cause mortality (perinatal disorders, congenital anomalies and genetic disorders, respiratory diseases, cardiovascular diseases, endocrine diseases, and malignant neoplasms)	• Other specific-cause mortality (infections, nervous system diseases, digestive diseases, musculoskeletal diseases, trauma, other causes) • Metabolic syndrome
Cystic fibrosis	• Tooth enamel defects of permanent teeth • Pulmonary • Pancreatic		• Dental caries • Plaque • Gingival bleeding • Dental calculus
Hypospadias			• Urinary anomalies
Cryptorchidism	• Testicular cancer		
Testosterone Deficiency	• Diabetes • Metabolic syndrome • CVD • Hypertension • All-cause mortality • CVD mortality • CVD morbidity • Alzheimer's disease	• Peripheral artery disease • Intima-media thickness • Rapid bone loss • Lung cancer • Testicular cancer	• Charlson Comorbidity Index • Periodontal disease • Ischemic heart disease • Prostate cancer • Colorectal cancer

Male age factor

- **Clinicians should advise couples with advanced paternal age (≥40) that there is an increased risk of adverse health outcomes for their offspring. (Expert Opinion)**

Parameters of reproductive function	Effect of male age	Specific effects with increasing age
Reproductive hormones	Yes	FSH level: increasing; testosterone level: decreasing
Sexual function	Yes	Sexual activity: decreasing; male sexual dysfunction: increasing
Testicular morphology	Yes	Sertoli cells: number (n) decreasing; Leydig cells: n decreasing; germ cells: n decreasing; thickness of basal membrane of seminiferous tubules: increasing; testicular size: unchanged (until the eighth decade)
Semen parameters: sperm	Yes	Concentration: unchanged; motility: decreasing; morphology: normal; forms: decreasing
Semen parameters: semen	Yes	Volume: decreasing; fructose level: decreasing; α-glucosidase level: decreasing; zinc level: decreasing; PSA level: decreasing
Infections of the accessory glands	Yes	Prevalence: increasing
Vascular disease	Yes	Vascularization of testicular parenchyma: decreasing
Genetics: sperm aneuploidies	Yes	Chromosomes 3,6,7,8,10,11,12,13,14,17: unchanged; 1,19,18,21, X,Y: conflicting results
Genetics: aneuploidies in offspring	Yes	Trisomy 21: increasing; trisomy 13: decreasing; trisomy 18: unchanged; other trisomies: unchanged; sex chromosomes: unchanged
Genetics: Sperm DNA integrity	Yes	DNA damage: increasing
Genetics: telomeres (TL)	Yes	TL length in spermatozoa: increasing; TL in peripheral leucocytes: decreasing
Genetics: epigenetics	Yes	Methylations in somatic cells: increasing; methylations in germ cells: suggested
Fertility	Yes	Fertility: decreasing (male age effect in couples with female >35 years)
Miscarriage	Yes	Miscarriage rate: increasing (male age effect in couples with female >35 years)

Abnormal Semen Analysis

- cryptorchidism (uni- or bilateral);
- testicular torsion and trauma;
- genitourinary infection;
- exposure to environmental toxins;
- gonadotoxic medication (anabolic drugs, SSRIs, etc);
- exposure to radiation or cytotoxic agents;
- testicular cancer;
- absence of testes;
- abnormal secondary sexual characteristics;
- gynaecomastia;
- abnormal testicular volume and/or consistency;
- varicocele

k factor	Methodology conclusion
mographic	
e	Older men have slightly reduced fertility
esity	Obese men have moderately reduced fertility
estyle	
et	Poor diet results in reduced fertility
ffeine	Not a risk factor, except for sperm aneuploidy
cohol	Drinkers have slightly lower semen volume and slightly poorer sperm morphology, but drinking does not adversely affect sperm concentration or sperm motility
noking	Smokers have slightly reduced fertility
abolic steroid use	Anabolic steroid use is associated with reduced fertility
ress	Stress is associated with reduced sperm progressive motility, but has no association with semen volume; data were inconclusive for sperm concentration and sperm morphology
llphones	Not a risk factor
dical treatment	
ti-rheumatic medications	Evidence inconclusive
iopurines	Evidence inconclusive

mic dermatologic medications: otrexate	Not a risk factor
mic dermatologic medications: cor-eroids	Evidence inconclusive
nal hernia repair: Open repair with-esh	Evidence inconclusive
nal hernia repair: Open repair with	Evidence inconclusive
nal hernia repair: Laparoscopic re-vith mesh	Evidence inconclusive
g testicular cancer	Those with testicular cancer have reduced fertility
onmental	
ophenone	Evidence inconclusive
ethylhexyl phthalate (DEHP)	DEHP exposure is associated with lower sperm quality (sperm concentration, sperm motility, sperm DNA damage)
chemicals in consumer products	Evidence inconclusive
crine disruptors	Evidence inconclusive
cides	Associations between exposure to certain pesticides (pyrethroids, organophos-phates, and abamectin) and poorer semen parameters; evidence inconclusive on organochlorines, mancozeb, and other pesticides
d natural gas extraction	Occupational exposure reduces semen volume and sperm motility
oor air pollution	Evidence inconclusive
zinc, copper	Lead levels are higher in infertile men than fertile men; zinc levels are lower in infertile men than fertile men; evidence inconclusive on copper levels in semen
ium	Cadmium levels are higher in infertile men than fertile men

The results from the SA should be used to guide management of the patient. In general, results are of greatest clinical significance when multiple abnormalities are present. (Expert Opinion)

Abnormalities in any one or more of these parameters can compromise a man's ability to naturally impregnate his female partner

except in cases of azoospermia,
some types of teratozoospermia (e.g., complete globozoospermia),
necrozoospermia, or complete asthenozoospermia

hormonal evaluation

- **FSH and testosterone for infertile men with:**
- **impaired libido**
- **erectile dysfunction**
- **oligozoospermia or azoospermia**
- **atrophic testes**
- **evidence of hormonal abnormality on physical evaluation. (Expert Opinion)**

Hormonal determinations

- In men with testicular deficiency, hypergonadotropic hypogonadism is usually present, with high levels of follicle-stimulating hormone (FSH) and luteinising hormone (LH), and with or without low levels of testosterone.
- Generally, the levels of FSH correlate with the number of spermatogonia: when spermatogonia are absent or markedly diminished, FSH values are usually elevated;
- when the number of spermatogonia is normal, but maturation arrest exists at the spermatocyte or spermatid level, FSH values are within the normal range.
- However, for an individual patient, FSH levels do not accurately predict the spermatogenesis status because men with maturation arrest histology could have normal FSH and testis volume and still be azoospermic

	Severely Impaired Spermatogenesis	Obstructive Azoospermia	Hypogonadotropogonadism
	- or Nl	Nl	-
	-	Nl	-
terone	- or Nl	Nl	-

Ultrasonography

- US may be helpful in finding signs of obstruction (e.g., dilatation of rete testis, enlarged epididymis with cystic lesions, or absent vas deferens)
- may demonstrate signs of testicular dysgenesis (e.g., non-homogeneous testicular architecture and microcalcifications)
- Testis tumours
- For patients with a low seminal volume and in whom distal obstruction is suspected, transrectal ultrasound (TRUS) is essential

Testicular biopsy

- Testicular biopsy can be part of intracytoplasmic sperm injection (ICSI) treatment in patients with clinical evidence of NOA. Testicular sperm extraction (TESE) is the technique of choice(genetic consult)

- Spermatogenesis may be focal, which means that in about 50% of men with NOA, spermatozoa can be found and used for ICSI

- no threshold value has been found for FSH, inhibin B, or testicular volume and successful sperm harvesting

- Contraindication complete AZFa and AZFb microdeletions

- Microsurgical TESE> multiple TESE >conventional TESE

Testicular biopsy

- The results of ICSI : NOA < ejaculated semen obstructive azoospermia (OA)

- Birth rates are lower in NOA vs.OA (19% vs 28%) ICSI results in significantly lower fertilisation and implantation rates

- patients with NOA as defined by testicular histopathology, only one out of seven NOA patients embarking for TESE and eventually ICSI will father their genetically-own child

RPL

- **For couples with RPL, men should be evaluated with:**
- **Karyotype (Expert Opinion)**
- **Sperm DNA fragmentation. (ModerateRecommendation; Evidence Level Grade: C)**

- chromosomal defects (translocations, inversions, deletions, duplications)
- numerical
- Sperm aneuploidy testing involves the use of fluorescent molecular probes for chromosomes :13, 18, 21, X, Y

Karyotype and Y-chromosome microdeletion analysis

- **Recommended for men with:**
- **Primary infertility and azoospermia or severe oligozoospermia (<5 million sperm/mL)**
- **Elevated FSH or testicular atrophy**
- **Presumed diagnosis of impaired sperm production as the cause of azoospermia**

(Expert Opinion)

Genetic disorders in infertility

- provide correct advice to couples seeking fertility treatment

- Men with very low sperm counts can be offered a reasonable chance of paternity, using *in IVF, ICSI and* sperm harvesting from the testes in case of azoospermia

- spermatozoa of infertile men show an increased rate of aneuploidy, structural chromosomal abnormalities, and DNA damage, carrying the risk of passing genetic abnormalities to the next generation.

Chromosomal abnormalities

- numerical (e.g. trisomy) or structural (e.g. inversions or translocations).
- In infertile men, the incidence of chromosomal abnormalities was 5.8%
  sex chromosome abnormalities : 4.2%
  autosomal abnormalities :1.5%
- the incidence of abnormalities was 0.38% in newborn male infants
- The frequency of chromosomal abnormalities increases as testicular deficiency becomes more severe.
- Patients with a spermatozoa count < 5 million/mL already show a ten-fold higher incidence (4%) of mainly autosomal structural abnormalities compared with the general population
- Men with NOA are at highest risk, especially for sex chromosomal anomalies.
- Karyotype analysis is indicated in men with azoospermia or oligozoospermia (spermatozoa < 10 million/mL)

Klinefelter's syndrome and variants [47,XXY; 46,XY/47, XXY mosaicism])

- Germ cell presence and sperm production are variable in men with Klinefelter's mosaicism, 46,XY/47,XXY
- increased frequency of sex chromosomal abnormalities and increased incidence of autosomal aneuploidy (disomy for chromosomes 13, 18 and 21), concerns have been raised about the chromosomal normality of the embryos generated through ICSI

- TESE (42%)or micro-TESE (57%) can be proposed as a therapeutic option since spermatozoa can be recovered in about 50% of cases
- higher sperm recovery rates when done at a younger age
- Numerous healthy children have been born using ICSI without pre-implantation genetic diagnosis (PGD) and the conception of one 47,XXY foetus has been reported

Autosomal abnormalities

- Genetic counselling should be offered to all couples seeking fertility treatment (including IVF/ICSI) when the male partner has an autosomal karyotype abnormality.
- The most common autosomal karyotype abnormalities are Robertsonian translocations, reciprocal translocations, paracentric inversions, and marker chromosomes
- It is important to look for these structural chromosomal anomalies because there is an increased associated risk of aneuploidy or unbalanced chromosomal complements in the foetus
- As with Klinefelter's syndrome, sperm FISH analysis provides a more accurate risk estimation of affected offspring
- When IVF/ICSI is carried out for men with translocations, PGD or amniocentesis should be performed

Sperm chromosomal abnormalities

- Sperm can be examined for their chromosomal constitution using multicolour FISH both in men with normal karyotype and with anomalies
- Aneuploidy in sperm, particularly sex chromosome aneuploidy, is associated with severe damage to spermatogenesis
- specific andrology conditions e.g. macrocephalia

Genetic defects

- *Kallmann syndrome*

  (X-linked, autosomal dominant or recessive)

- *Mild androgen insensitivity syndrome*

Y-chromosome and male infertility

- Microdeletions on the Y-chromosome are termed AZFa, AZFb and AZFc

- partially<< completely one or more of the AZF

- severe oligozoospermia & azoospermia

...AZF

- The highest frequency of Y-deletions is found in azoospermic men (8-12%), followed by oligozoospermic (3-7%) men
- AZFc deletions are most common (65-70%)
- AZFb and AZFb+c or AZFa+b+c (25-30%)
- AZFa region deletions are rare (5%).

...AZF

- Complete removal of the AZFa region is associated with severe testicular phenotype (Sertoli cell only syndrome)
- complete removal of the AZFb region is associated with spermatogenic rest
- Complete removal of the AZFc region causes a variable phenotype ranging from azoospermia to oligozoospermia
- any Y-deletions are transmitted obligatorily to the male offspring

Cystic fibrosis mutations and male infertility

- Autosomal-Recessive disorder
- 4% are carriers of gene mutations involving the CF transmembrane conductance regulator (CFTR) gene located on chromosome 7p
- It encodes a membrane protein that functions as an ion channel and influences the formation of the ejaculatory duct, seminal vesicle, vas deferens and distal two-thirds of the epididymis

…CF

- Congenital bilateral absence of the vas deferens (CBAVD) is associated with CFTR gene mutations
- *Unilateral or bilateral absence/abnormality of the vas and renal anomalies*

Recommendations	Strength rating
Obtain standard karyotype analysis in all men with damaged spermatogenesis (spermatozoa < 10 million/mL) for diagnostic purposes.	Strong
Provide genetic counselling in all couples with a genetic abnormality found on clinical or genetic investigation and in patients who carry a (potential) inheritable disease.	Strong
For all men with Klinefelter's syndrome, provide long-term endocrine follow-up and appropriate medical treatment, if necessary.	Strong
Do not test for microdeletions in men with obstructive azoospermia (OA) since spermatogenesis should be normal.	Strong
Inform men with Yq microdeletion and their partners who wish to proceed with intracytoplasmic sperm injection (ICSI) that microdeletions will be passed to sons, but not to daughters.	Strong
In men with structural abnormalities of the vas deferens (unilateral or bilateral absence with no renal agenesis), test the man and his partner for cystic fibrosis transmembrane conductance regulator gene mutations.	Strong

Obstructive azoospermia

- Less common than NOA and occurs in 15-20% of men with azoospermia
- Normal FSH, normal size testes, and epididymal enlargement
- Obstruction in primary infertile men is frequently present at the epididymal level

Classification

- *Intratesticular*
- *Epididymal*
- *Vas deferens*
- *Ejaculatory duct*
  Congenital or acquired
  low semen volume, decreased or absent seminal fructose, and acid pH
  The seminal vesicles are usually dilated (anterior-posterior diameter > 15 mm)
- *Functional*
  local neuropathy
  selective serotonin re-uptake inhibitor (SSRI) medication

Hormone levels

- Serum FSH levels should be normal, but do not exclude a testicular cause of azoospermia
- FSH level is normal in 40% of men with primary spermatogenic failure
- Inhibin B seems to have a higher predictive value for normal spermatogenesis

Varicocele

- failure of ipsilateral testicular growth and development
- symptoms of pain and discomfort
- male subfertility
- hypogonadism

Varicocele and fertility

- Varicocele is a physical abnormality present in 11.7% of adult men and in 25.4% of men with abnormal semen analysis
- a recent meta-analysis showed that semen improvement is usually observed after surgical correction
- Varicocelectomy can reverse sperm DNA damage

Prophylactic Varicocelectomy

In adolescents with a varicocele, there is a significant risk of over-treatment since most adolescents with a varicocele will have no problem achieving pregnancy later in life
Prophylactic treatment is only advised in case of documented growth deterioration of the testis as documented by serial clinical examinations and impaired semen quality

Recommendations
Treat varicoceles in adolescents with ipsilateral reduction in testicular volume and evidence of progressive testicular dysfunction.
Do not treat varicoceles in infertile men who have normal semen analysis and in men with a subclinical varicocele.
Treat men with a clinical varicocele, oligozoospermia and otherwise unexplained infertility in the couple.

Hypogonadism

- Hypogonadism is characterised by impaired testicular function, which may affect spermatogenesis and/or testosterone synthesis.
- The symptoms of hypogonadism depend on the degree of androgen deficiency and if the condition develops before or after pubertal development of the secondary sex characteristics.

Epidemiology and aetiology

- The aetiological and pathogenetic mechanisms of male hypogonadism can be divided into three main categories:
- Primary (hypergonadotropic) hypogonadism due to testicular failure.
- Secondary (hypogonadotropic) hypogonadism caused by insufficient gonadotropin-releasing hormone (GnRH) and/or gonadotropin (FSH, LH) secretion.
- Androgen insensitivity (end-organ resistance)

Cryptorchidism

- 1% of all full-term male infants
- degeneration of germ cells in maldescended testes is apparent after the first year of life
- depending on the position of the testis

Relationship with fertility

- In men with a history of unilateral cryptorchidism, paternity is almost equal (89.7%)
- in men without cryptorchidism (93.7%)
- In men with bilateral cryptorchidism, oligozoospermia can be found in 31% and azoospermia in 42%. In cases of bilateral cryptorchidism, the rate of paternity is only 35-53%

Germ cell tumours & UDT

- The risk of a germ cell tumour is 3.6-7.4 times higher than in the general population

- 2-6% of men with a history of cryptorchidism will develop a testicular tumour

Round cells

- **Men with increased round cells on SA (>1million/mL)**
- **differentiate white blood cells (pyospermia) from germ cells. (Expert Opinion)**
- **Patients with pyospermia should be evaluated for the presence of infection. (Clinical Principle)**

Male accessory gland infections and infertility

- Infections of the male urogenital tract are potentially curable causes of male infertility . The WHO considers urethritis, prostatitis, orchitis and epididymitis to be male accessory gland infections (MAGIs) . However, specific data are not available to confirm that these diseases have a negative influence? on sperm quality and male fertility in general

Recommendation	Strength rating
Instruct patients with epididymitis that is known or suspected to be caused by *N. gonorrhoeae* or *C. trachomatis* to refer their sexual partners for evaluation and treatment.	Strong

Germ cell malignancy
testicular microcalcification

- most common malignancy in men aged 15-40 years
- untreated ITGCNU will eventually progress to invasive cancer
- risk factors of testicular cancer: Cryptorchidism , hypospadias ,dysgenic testes &Testicular microcalcification (TM) seen on US

- Semen quality ……Azoo 5-8%
- Cryopreservation
- TESE
- Sperm aneuploidy
- Leydig cell dysfunction

Recommendations	Strength rating
Encourage men with testicular microcalcification (TM) to perform self-examination even without additional risk factors as this may result in early detection of testicular germ cell tumour (TGCT).	Weak
Do not perform testicular biopsy, follow-up scrotal ultrasound, routine use of biochemical tumour markers, or abdominal or pelvic computed tomography, in men with isolated TM without associated risk factors (e.g. infertility, cryptorchidism, testicular cancer, and atrophic testis).	Strong
Perform testicular biopsy for men with TM, who belong to one of the following high-risk groups: spermatogenic failure, bilateral TM, atrophic testes (less than 12cc), history of undescended testes and TGCT.	Strong
If there are suspicious findings on physical examination or ultrasound in patients with TM and associated lesions, perform surgical exploration with testicular biopsy or orchidectomy.	Strong
Follow men with TGCT because they are at increased risk of developing hypogonadism and sexual dysfunction.	Strong

Disorders of ejaculation

- *Anejaculation*
- *Anorgasmia*
- *Delayed ejaculation*
- *Retrograde ejaculation*

Anejaculation

- complete absence of antegrade or retrograde ejaculation.
- Failure of semen emission from the seminal vesicles, prostate and ejaculatory ducts into the urethra
- normal orgasmic sensation
- central or peripheral nervous system dysfunction or with drugs

Anorgasmia

- Anorgasmia is the inability to reach orgasm and can give rise to anejaculation

- Anorgasmia is often a primary condition and its cause is usually psychological

Delayed ejaculation

- Delayed ejaculation can be considered a mild form of anorgasmia

1. psychological
2. organic (e.g. incomplete spinal cord lesion or iatrogenic penile nerve damage)
3. pharmacological [e.g. selective serotonin re-uptake inhibitors (SSRIs), antihypertensives, or antipsychotics]

Asthenic ejaculation

- altered propulsive phase, with a normal emission phase
- The orgasmic sensation is reduced
- typically rhythmical contractions associated with ejaculation are missing
- Asthenic ejaculation does not usually affect semen quality

Premature ejaculation

- Ejaculation which always or nearly always occurs prior to or within about one minute of vaginal penetration
- negative personal consequences, such as distress, bother, frustration and/or the avoidance of sexual intimacy

- organic (e.g., prostatitis-related)
- psychogenic
- partner-related
- non-selective

Summary of evidence	LE
Ejaculation disorders can be treated using a wide range of drugs and physical stimulation (eg vibratory stimulation), with a high level of efficacy.	3
Pharmacotherapy includes either dapoxetine on demand (a short-acting SSRI that is the only approved pharmacological treatment for PE) or other off-label antidepressants, i.e. daily SSRIs and clomipramine, that are not amenable to on-demand dosing. Alternatively use topical anaesthetics (LE: 1b) or tramadol (LE: 2a).	1a
In men with spinal cord injury, vibrostimulation and/or electro-ejaculation are effective methods of sperm retrieval.	2

Recommendation	Strength rating
Offer specific treatments for ejaculatory disorders before performing sperm collection and assisted reproduction technique (ART). Premature ejaculation can be treated using dapoxetine (short acting selective serotonin reuptake inhibitor) and/or topical anaesthetics.	Strong

5.12.4 *Summary of evidence and recommendations for semen cryopreservation*

Summary of evidence	LE
The purpose of sperm cryopreservation is to enable future ART procedures.	1b
Cryopreservation techniques are not optimal, and future efforts are needed to improve the outcome of sperm banking.	3

Recommendations	Strength rating
Offer cryopreservation of semen to all men who are candidates for chemotherapy, radiation or surgical interventions that might interfere with spermatogenesis or cause ejaculatory disorders.	Strong
Offer simultaneous sperm cryopreservation if testicular biopsies will be performed for fertility diagnosis.	Strong
If cryopreservation is not available locally, inform patients about the possibility of visiting, or transferring to a cryopreservation unit before therapy starts.	Strong
Take precautions to prevent transmission of viral, sexually transmitted or any other infection by cryostored materials from donor to recipient, and to prevent contamination of stored samples. These precautions include testing of the patient and the use of rapid testing and quarantine of samples until test results are known. Do not store samples from men who are positive for hepatitis virus or HIV in the same container as samples from men who have been tested and are free from infection.	Strong