National Women & Infants Health Programme

QUICK SUMMARY DOCUMENT

In Vitro Fertilisation (IVF) and Intracytoplasmic Sperm Injection (ICSI)

This QSD is a resource for all clinicians working in healthcare in Ireland who are involved in the provision of IVF and ICSI to women/couples.

Following a comprehensive literature review a number of evidence-based recommendations for fertility investigation and management were agreed upon.

Key Recommendations

Number	Recommendation	Grade of evidence
Section 1: Indications for ART		
1	We recommend taking a detailed clinical history from all people embarking on fertility treatment. Medical and mental health co-morbidities, including body mass index, should be optimised prior to embarking on treatment.	*Best Practice*
2	We recommend that men should have a recent semen analysis (within 12 months of treatment).	*Best Practice*
3	We recommend that referral to a urologist with specialist training in andrology/male infertility should be considered in the following indications: • Azoospermia • Severe oligospermia • Urological symptoms • Treatable or modifiable factor contributing to infertility	*Best Practice*
4	We do not recommend routine sperm DNA fragmentation testing prior to in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) treatment.	*2B*
5	We suggest that women should have testing of ovarian reserve in the form of an anti-müllerian hormone (AMH) level and/or antral follicle count (AFC), to predict ovarian response.	*2B*
6	We suggest that a baseline ultrasound scan may be performed to ensure that ovaries are quiescent and that the endometrial thickness is <5mm prior to starting stimulation. Pregnancy must be out ruled prior to starting stimulation.	*2C*
7	We strongly recommend that IVF should be offered as a first line for complete tubal infertility.	*1A*
8	We recommend that IVF should be offered first line for couples with unexplained infertility when the woman is aged over 38 years.	*1C*

Number	Recommendation	Grade of evidence
9	We suggest that IVF be offered for the following indications: • Mild tubal/partial tubal infertility • Endometriosis with infertility • Following previous unsuccessful treatment (ovulation induction or intrauterine insemination)	*1B*
10	We recommend that individual/couple preferences should be considered when recommending IVF/ICSI treatment.	*Best Practice*
11	We strongly recommend that ICSI should be performed as the fertilisation technique for male factor infertility.	*1A*
12	We recommend that ICSI is performed when a previous IVF cycle resulted in failed fertilisation or suboptimal fertilisation.	*1B*
13	We recommend that ICSI is the fertilisation technique of choice for thawed oocytes.	*1C*
14	We recommend that ICSI should be used as a fertilisation technique for preimplantation genetic testing (PGT) for monogenic disorders (PGT-M) and structural rearrangements (PGT-SR). Conventional IVF is feasible for PGT for aneuploidy (PGT-A).	*1B*
Section 2: IVF/ICSI treatment in practice		
15	We strongly recommend that for women who are predicted to have a high ovarian response, a GnRH antagonist protocol should be used for controlled ovarian hyperstimulation (COH).	*1A*
16	We recommend that for women who are predicted to have a low ovarian response, a GnRH agonist protocol is a reasonable first line choice for COH, the GnRH antagonist protocol may also be used.	*1B*
17	We recommend that all clinics providing IVF/ICSI have their own standard operating procedure (SOP) providing evidence-based guidelines for prescribing medications for ovarian stimulation, taking into account availability of medications.	*Best Practice*
18	We suggest that pre-treatment with oestrogen or progesterone may be used for scheduling purposes as it does not appear to negatively affect outcomes.	*2B*
19	We do not recommend pre-treatment with the combined oral contraceptive pill (COCP) if a fresh embryo transfer is planned.	*1B*
20	We recommend monitoring with pelvic ultrasound, ideally transvaginal, during COH to measure: • Ovarian response (follicular growth) • Endometrial thickness	*1B*
21	We do not recommend monitoring with serum oestradiol in addition to pelvic ultrasound as it has not been shown to reduce the risk of ovarian hyperstimulation syndrome (OHSS).	*1B*
22	We suggest that endometrial thickness should ideally be >7mm before embryo transfer.	*2B*
23	We recommend that an oocyte maturation trigger should be given 36-38 hours prior to egg collection.	*1B*

Number	Recommendation	Grade of evidence
24	We recommend that the decision on when to trigger should be individualised, usually when lead follicles have reached 16-22mm size.	*Best Practice*
25	We recommend that if a fresh embryo transfer is planned, a HCG trigger is given, either alone or combined with a GnRH agonist trigger.	*1A*
26	We suggest that a dual trigger (hCG and GnRH agonist) may be considered in women who have predicted or previous low ovarian response in a GnRH antagonist cycle.	*2B*
27	We recommend that in GnRH antagonist cycles, where there is a high risk of OHSS, a GnRH agonist trigger may be given, along with a 'freeze all' approach as this reduces the risk of OHSS.	*1B*
28	We strongly recommend that progesterone is given for luteal phase support following oocyte retrieval (OCR) when a fresh embryo transfer is planned.	*1A*
29	We recommend that progesterone support is initiated after OCR (from that evening up to 3 days post-OCR) and continued until at least the date of pregnancy testing.	*1C*
30	We recommend that all non-oral routes of administration of progesterone appear to be efficacious and the decision on the route of administration should be decided upon based on clinician and the woman's preferences.	*1B*
31	We recommend embryo cryopreservation to individuals/couples that have surplus embryos suitable to freeze following a fresh embryo transfer.	*1C*
32	We suggest that the endometrial thickness should ideally be >7mm prior to a frozen embryo transfer (FET).	*2B*
33	We recommend that the protocol for endometrial preparation should be individualised, taking into consideration the regularity of the woman's cycle, previous treatment if any and her personal preferences.	*Best practice*
34	We recommend that all women should have an assessment of risk factors for OHSS and other complications of IVF.	*Best Practice*
35	We suggest that cabergoline 0.5mg/day for 5-7 days may be prescribed to women at high risk of OHSS.	*2C*
36	We strongly recommend that the antagonist protocol should be used in women at high risk of OHSS.	*1A*
37	We recommend venous thromboembolism prophylaxis for women who develop OHSS.	*1B*
38	We suggest that antibiotics may be considered at OCR in women who are at increased risk of infection.	*2B*
39	We recommend that the decision to cancel an IVF/ICSI should be addressed on a case-by-case basis, considering the age and ovarian reserve of the woman, previous response to stimulation and the wishes of the individual/couple.	*Best Practice*
40	We suggest that cycle cancellation may be considered when the response to COH is less than expected for the woman's age/ovarian reserve.	*Best Practice*

Number	Recommendation	Grade of evidence
41	We suggest that cycle cancellation may be considered when there is a high risk of OHSS based on a high number of follicles, and the woman's clinical condition.	*Best Practice*
42	We suggest that cycle cancellation should be considered if another medical or social issue arises during stimulation that would make proceeding with treatment unsafe or unacceptable to the woman.	*Best Practice*
43	We do not recommend the transfer of more than 2 embryos under any circumstances.	*1C*
44	We recommend that elective single embryo transfer (eSET) should be the standard procedure whenever more than one good quality embryo is available. Double embryo transfer (DET) may be considered in selected circumstances.	*1B*
45	We recommend that medical risk factors should be considered before a DET due to the higher rates of maternal, fetal, and neonatal complications with multiple pregnancy.	*Best Practice*
46	We recommend that when a DET is considered, the individual/couple should be provided with clear information about the risks associated with multiple pregnancy.	*Best Practice*
Section 3: AHR standards of practice		
47	We recommend that any site in Ireland which carries out AHR procedures must be authorised by the HPRA and practice should follow guidance from the Health Products Regulatory Authority (HPRA).	*Best Practice*

Auditable standards

Audit using the key recommendations as indicators should be undertaken to identify where improvements are required and to enable changes as necessary, and to provide evidence of quality improvement initiatives.

Auditable standards for this guideline include:

1. Outcomes following IVF/ICSI treatment
    - Clinical pregnancy rates
    - Miscarriage rates
    - Ectopic pregnancy rates
    - Live birth rates
2. Rate of multiple births following IVF/ICSI treatment in Ireland
3. Obstetric outcomes following successful IVF/ICSI treatment in Ireland
4. Incidence of OHSS following COH, including number of hospital admissions

Recommended reading:

1. HSE nomenclature/glossary for audit www.hse.ie/eng/about/who/nqpsd/ncca/nomenclature-a-glossary-of-terms-for-clinical-audit.pdf
2. HSE National Framework for developing Policies, Procedures, Protocols and Guidelines at https://www.hse.ie/eng/about/who/qid/nationalframeworkdevelopingpolicies/
3. https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Addons
4. Schäler L OLD, Barry M, Crosby DA. National Clinical Practice Guideline: Fertility-Investigation and Management in Secondary Care.: National Women and Infants Health Programme and The Institute of Obstetricians and Gynaecologists.; October 2023. https://www.hse.ie/eng/about/who/acute-hospitals-division/woman-infants/clinical-guidelines/ncpg-fertility-investigation-guideline.pdf
5. T, Bosch E, Broer S, Griesinger G, Grynberg M, Humaidan P, *et al.* ESHRE guideline: ovarian stimulation for IVF/ICSI(†). Hum Reprod Open. 2020;2020(2):hoaa009. https://pubmed.ncbi.nlm.nih.gov/32395637/
6. Alteri A. AG, Baccino G., Craciunas L., De Geyter C., Ebner T., Koleva M., Kordic K., Mcheik S., Mertes H., Pavicic Baldani D., Rodriguez-Wallberg K., Rugescu I., Santos-Ribeiro S., Tilleman K., Woodward B., Vermeulen N., Veleva Z. The ESHRE guideline group on the number of embryos to transfer during IVF/ICSI, Evidence-based guideline: Number of embryos to transfer during IVF/ICSI.: ESHRE; 2023. https://www.eshre.eu/-/media/sitecore-files/Guidelines/Embryo-transfer/1--ESHRE-ET-Guideline---Main-document.pdf

Authors

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https://www.hse.ie/eng/about/who/acute-hospitals-division/woman-infants/clinical-guidelines/

https://www.rcpi.ie/faculties/obstetricians-and-gynaecologists/national-clinical-guidelines-in-obstetrics-and-gynaecology/