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ESHRE guideline: ovarian stimulation for IVF/ICSI: an update in 2025†

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ABSTRACT

STUDY QUESTION: What is the recommended management of ovarian stimulation, based on the best available evidence in the literature?

SUMMARY ANSWER: This updated ESHRE guideline on ovarian stimulation for IVF/ICSI provides 121 recommendations, answering 21 key questions on ovarian stimulation for IVF/ICSI.

WHAT IS KNOWN ALREADY?: Before the ESHRE guideline on ovarian stimulation for IVF/ICSI was published in 2019, ovarian stimulation for IVF/ICSI had only been discussed briefly in the National Institute for Health and Care Excellence guideline on fertility problems and in a statement by the Royal Australian and New Zealand College of Obstetricians and Gynaecologists.

STUDY DESIGN, SIZE, DURATION: The guideline was developed according to the structured methodology for ESHRE guidelines. The 18 key questions from the 2019 version of the guideline were revised by the Guideline Development Group (GDG). This resulted in the addition of one new key question, the splitting of the key question on fertility preservation in three separate key questions (fertility preservation for women facing gonadotoxic treatment, elective oocyte cryopreservation, and oocyte donation) and several new interventions being added to the existing key questions. Papers published between 31 October 2018 and 2 February 2025 and written in English were included. The critical outcomes for this guideline were efficacy in terms of cumulative live birth rate per started cycle or live birth rate per started cycle, as well as safety in terms of the rate of occurrence of moderate and/or severe ovarian hyperstimulation syndrome (OHSS).

PARTICIPANTS/MATERIALS, SETTING, METHODS: Based on the available evidence, recommendations were formulated and discussed until consensus was reached within the GDG. Following stakeholder review of the initial draft, the final version was approved by the GDG and ultimately by the ESHRE Executive Committee.

MAIN RESULTS AND THE ROLE OF CHANCE: The guideline provides a total of 121 recommendations: 42 recommendations remained unchanged in 2019, 4 recommendations were reworded for better understanding, 29 recommendations were updated in view of new evidence, and 46 new recommendations for 2025 have been formulated. The guideline provides 4 recommendations on pre-stimulation evaluation, 7 recommendations on pre-treatment therapies, 50 recommendations on pituitary suppression and

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ovarian stimulation, 17 recommendations on monitoring, 18 recommendations on triggering of final oocyte maturation and luteal support, and 8 recommendations on the prevention of OHSS. In addition, the guideline provides 17 recommendations on fertility preservation, both oncologic and elective, and oocyte donation. These include 90 evidence-based recommendations, of which only 42 were formulated as strong recommendations and 48 as conditional, as well as 29 good practice points and 2 research-only recommendations. Of the evidence-based recommendations, none were supported by high-quality evidence, 6 by moderate-quality evidence, 36 by low-quality evidence, and 148 by very low-quality evidence. To support future research on ovarian stimulation for IVF/ICSI, a list of research recommendations was provided.

LIMITATIONS, REASONS FOR CAUTION: Several newer interventions are not well studied yet. For most of these interventions, a recommendation against the intervention or a research-only recommendation was formulated based on insufficient evidence. Future studies may require these recommendations to be revised.

WIDER IMPLICATIONS OF THE FINDINGS: The guideline provides clinicians with clear advice on best practice in ovarian stimulation, based on the best evidence available. In addition, a list of research recommendations is provided to promote further studies in ovarian stimulation.

STUDY FUNDING/COMPETING INTEREST(S): The guideline was developed by ESHRE, who funded the guideline meetings, literature searches, and dissemination of the guideline. The guideline group members did not receive any financial incentives; all work was provided voluntarily. BA reports speaker's fees from Gedeon-Richter, Ferring, IBSA, Intas, Merck, Organon, consulting fees from Merck, Organon, Oxolife, stock options from Global Fertility Solutions LLC (employee co-investment), and was chair of the Turkish Society of Reproductive Medicine. EB reports research grants from Roche Diagnostics and IBSA, consulting fees from MSD, Abbot, Gedeon-Richter, Roche, speaker's fees from IBSA, MSD, Ferring Pharmaceuticals, Abbot, Gedeon-Richter, Merck, Roche, participation in the advisory board of Ferring Pharmaceuticals, IBSA and Merck, and ownership interest from IVI-RMS Valencia. GG was part of the ESHRE working group on Recurrent Implantation Failure and the ESHRE working group on clinical KPISs, reports travel support from Merck, Organon, Ferring, Theramex, Gedeon-Richter, Abbott, consulting fees from Organon, Ferring, Merck, Gedeon-Richter, Theramex, Abbott, ReproNovo, Igyxos, OxoLife, Philipps, ReprodWissen, PregLem, Guerbet, Roche, IBSA, and Besins, speaker's fees from Organon, Ferring, Merck, Gedeon-Richter, Theramex, Abbott, ReproNovo, Igyxos, OxoLife, Philipps, ReprodWissen, PregLem, Guerbet, Roche, IBSA, and Besins, and research grants from Besin, Merck, Abbott, Ferring, Theramex. MG reports speaker's fees from Merck Serono, Ferring, and Gedeon Richter. EK reports travel/hotel expenses from Ferring, Merck SERONO, Vianex, speaker's fees from Ferring, Merck SERONO, Vianex, and is chair of the Greek Society of Fertility and Sterility. MK reports travel support and speaker's fees from Ferring. ALM reports research grants from Merck, Ferring, IBSA, Roche, Organon, Theramex, Beckman Coulter, and Gedeon-Richter, consulting fees from Merck, Ferring, IBSA, Roche, Organon, Theramex, Beckman Coulter, and Gedeon-Richter, speaker's fees from Merck, Ferring, IBSA, Roche, Organon, Theramex, Beckman Coulter, Gedeon-Richter, and participation on an advisory board of Merck, Organon, Ferring, Theramex, Gedeon Richter, and IBSA. GL reports consulting fees from Ferring and Merck, speaker's fees from Ferring, Merck, Gedeon-Richter, Organon, and Vianex, expert testimony fees from Cook, travel support from ESHRE, Ferring, Merck, Gedeon-Richter, Organon, and Vianex, is on the advisory board of Merck and Ferring, and participated in an ESHRE committee and on the Greek Fertility and Sterility Committee. NM reports research grants from IBSA, Organon, consulting fees from Organon, Merck, GE, Ferring, Abbott, and Cooper, and speaker's fees from Ferring, GE, Organon, IBSA, Merck, Theramex. NPP reports research grants from Besins Healthcare, Ferring Pharmaceutical, Merck Serono, Organon, Roche Diagnostics, and Theramex, consulting fees from Besins Healthcare, Alife, Ferring, IBSA, Merck Serono, Organon, Abbott, FertilAI, and speaker's fees from Besins Healthcare, Roche Diagnostics, Ferring Pharmaceuticals, Gedeon-Richter, IBSA, Merck Serono, Organon, and Theramex. SKS reports a research grant from Ferring, travel support from Merck and INTAS, consulting fees from Merck, and speaker's fees from Merck, MSD, INTAS, and Ferring. TT reports travel support from Merck, speaker's fees from Merck, Organon, MSD and is editor-in-chief of a Bulgarian journal, *Reproductive Health*. MT reports travel support from IBSA, Ferring, and Merck, consulting fees from Abbott and is a member of the board of the Finnish Endocrine Society. JU is a member of the Steering Committee of Richter Reproduction Network and received travel support from IBSA. FB reports a research grant from Besins, is on the advisory board of Merck and Abbott, reports speaker's fees from Ferring, Merck, Besins, Intas Fermaceuticals, PREIS School; he is the owner of FRANKSCHOOL RforL. The other authors have nothing to disclose.

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DISCLAIMER: This guideline represents the views of ESHRE, which were achieved after careful consideration of the scientific evidence available at the time of preparation. In the absence of scientific evidence on certain aspects, a consensus between the relevant ESHRE stakeholders has been obtained.

Adherence to these clinical practice guidelines does not guarantee a successful or specific outcome, nor does it establish a standard of care. Clinical practice guidelines do not replace the need for application of clinical judgment to each individual presentation, nor variations based on locality and facility type.

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Keywords: ovarian stimulation / ESHRE / guideline / IVF / ICSI / fertility preservation / oocyte donation / ovarian hyperstimulation syndrome / poor responder / high responder

Introduction

Ovarian stimulation (OS) is defined as pharmacological treatment with the intention of inducing the development of a few, several, or many ovarian follicles. It can be used (i) for timed intercourse or insemination and (ii) in assisted reproduction, to obtain multiple oocytes at follicular aspiration (Zegers-Hochschild *et al.*, 2017).

OS for IVF/ICSI has not been addressed by existing evidence-based guidelines. It is discussed briefly in the National Institute for Health and Care Excellence guideline on fertility problems and the Royal Australian and New Zealand Colleges of Obstetricians and Gynaecologists have published a statement on OS in assisted reproduction. Based on the lack of guidelines, the ESHRE Special Interest Group Reproductive Endocrinology initiated the development of an ESHRE guideline focusing on all aspects of OS for IVF/ICSI.

In 2019, ESHRE published a guideline on OS for IVF/ICSI, aiming to provide clinicians with evidence-based information on the different options for OS for IVF/ICSI, taking into account issues such as the 'optimal' ovarian response, live birth rates (LBR),

safety, patient compliance, and individualization. In this new guideline, special attention has also been given to pre- and adjuvant treatments in LOW responders and the prevention of ovarian hyperstimulation syndrome (OHSS) in HIGH responders.

The current guideline is an update of the version from 2019, with amendments to the recommendations based on recently published data. Where amendments were made, this is labelled as such [updated]. If the GDG felt rewording of a recommendation was necessary without new evidence on the topic, this was also indicated [reworded].

Materials and methods

The guideline was developed according to a well-documented methodology that is universal to ESHRE guidelines (Vermeulen *et al.*, 2020).

In the terminology part, it was decided to replace the term POOR response by LOW response in order to refrain from making any suggestion on prognosis or safety for this specific group.

In short, the 18 key questions from the 2019 version of the guideline were revised by the Guideline Development Group (GDG). This resulted in the addition of one new key question, the splitting of the key question on fertility preservation into three separate key questions (fertility preservation for women facing gonadotoxic treatment, elective oocyte cryopreservation and oocyte donation), and several new interventions being added to the existing key questions. The final guideline was built from a list of 21 key questions, all answered with systematic reviews as PICO (Patient, Intervention, Comparison, Outcome) questions. For each PICO question, databases (PUBMED/MEDLINE and the Cochrane library) were searched from the date of the last searches of the 2019 version of the guideline (31 October 2018) up to 2 February 2025, with the limitation of studies written in English. From the literature searches, studies were selected based on the PICO questions, assessed for quality, and summarized in evidence tables and summary of findings tables. The critical outcomes for this guideline are efficacy in terms of cumulative live birth rate (CLBR) per started cycle and LBR per started cycle, as well as safety in terms of moderate and/or severe OHSS. GDG meetings were organized (primarily online) where the evidence and draft recommendations were presented by the assigned GDG member and discussed until consensus was reached within the group.

Each recommendation was labelled as strong or conditional, and a grade was assigned (Andrews *et al.*, 2013) based on the strength of the supporting evidence (high ⊕⊕⊕⊕, moderate ⊕⊕⊕◯, low ⊕⊕◯◯, and very low ⊕◯◯◯). In the absence of evidence, the GDG formulated no recommendation or a good practice point (GPP) based on clinical expertise.

Strong recommendations suggest that the recommended option applies in most circumstances, whereas conditional recommendations are dependent on specific factors, which need to be considered with benefits/risks weighed before applying a given option (Fig. 1).

The guideline draft and an invitation to participate in the stakeholder review were published on the ESHRE website between 5 May 2025 and 16 June 2025. In addition, all relevant stakeholders received a personal invitation to review by e-mail. We received 486 comments from 156 reviewers. All comments were processed by the GDG, either by adapting the content of the guideline and/or by replying to the reviewer. The review process was summarized in the review report, which is published on the ESHRE website (www.eshre.eu/guidelines).

This guideline will be considered for update four years after publication, with an intermediate assessment of the need for updating two years after publication.

Results

Key questions and recommendations

The current document summarizes all the key questions and the recommendations from the 2025 update of the ESHRE guideline on 'ovarian stimulation for IVF/ICSI'. Further background information and the supporting evidence for each recommendation can be found in the full version of the guideline available at www.eshre.eu/OSguideline. For easy reference, the recommendations have been summarized in schematic overviews (Figs 2 and 3).

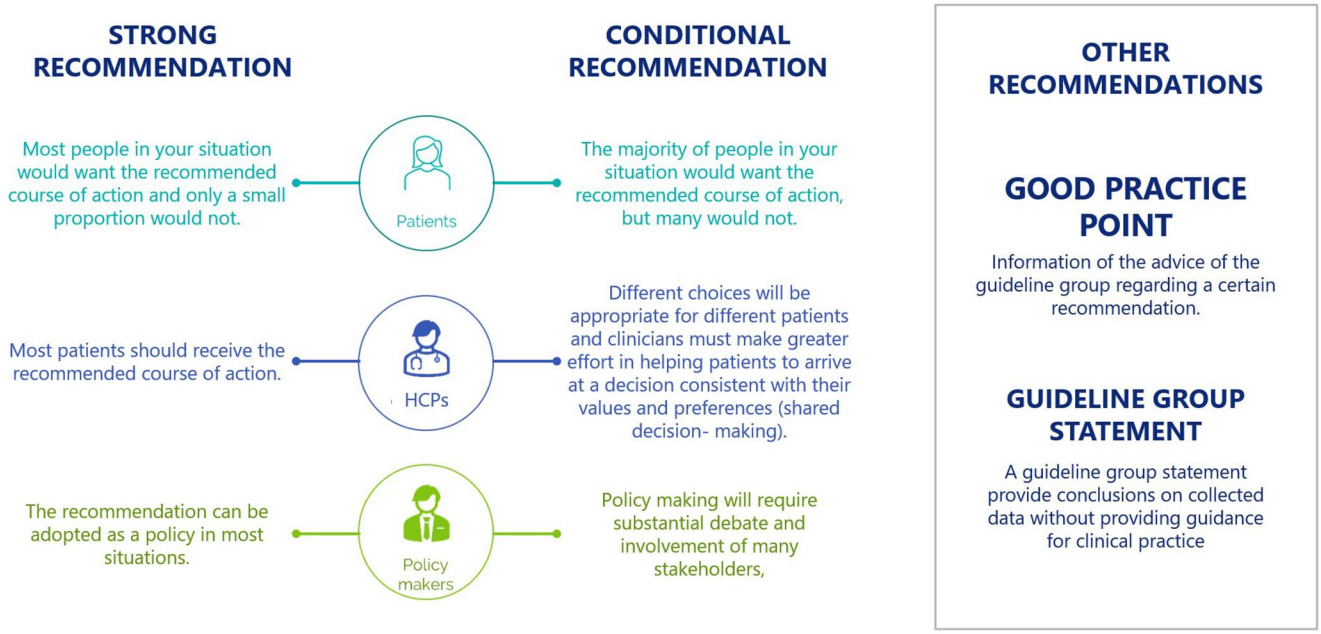

Figure 1. Suggested interpretation of the strong and conditional recommendations included in the guideline by patients, health care professionals (HCPs) and health care policy makers.

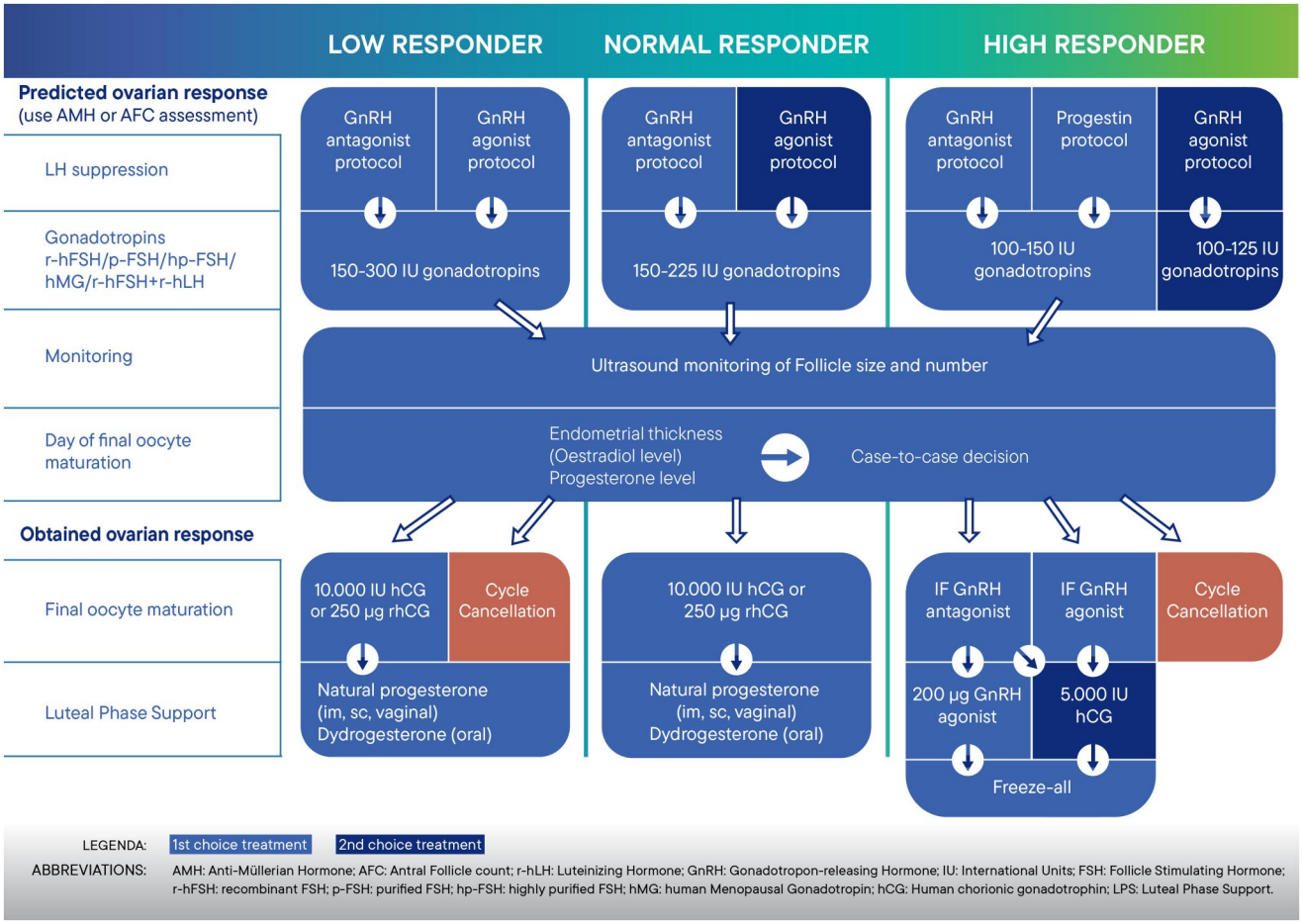

Figure 2. Schematic overview of recommendations from the guideline 'Ovarian stimulation for IVF/ICSI' for high, normal, and low responders. AMH: anti-Müllerian hormone; AFC: antral follicle count; r-hLH: luteinizing hormone; GnRH: gonadotropin-releasing hormone; IU: international units; FSH: follicle-stimulating hormone; r-hFSH: recombinant FSH; p-FSH: purified FSH; hp-FSH: highly purified FSH; hMG: human menopausal gonadotropin; hCG: human chorionic gonadotropin; LPS: luteal phase support.

Pre-stimulation evaluation

Is the assessment of the predicted response to ovarian stimulation sufficiently reliable?

For predicting high and low response to ovarian stimulation, the use of either antral follicle count (AFC) or anti-Müllerian hormone (AMH) is recommended. [updated] (Liu *et al.*, 2023b)	Strong ⊕◯◯◯
Age, BMI, basal FSH, inhibin B, basal oestradiol, basal progesterone, and basal LH are not recommended for the prediction of ovarian response. [2025] (Broekmans *et al.*, 2006; Broer *et al.*, 2013a,b)	Strong ⊕◯◯◯

What is the prognostic value of hormonal assessment at baseline?

AFC, AMH, basal FSH, basal LH, basal oestradiol, basal progesterone, and inhibin B are not recommended for the prediction of pregnancy and live birth. [updated] (Broekmans *et al.*, 2006; Doody *et al.*, 2010; Broer *et al.*, 2013b; Sun *et al.*, 2018; Wang *et al.*, 2022; Liu and Wang, 2023; Lim *et al.*, 2024; Zhang *et al.*, 2024)	Strong ⊕◯◯◯
Female age and BMI are predictors of pregnancy and live birth. [2025] (Broer *et al.*, 2013b)	Strong ⊕◯◯◯

Pre-treatment therapies

Does hormone pre-treatment improve efficacy and safety of ovarian stimulation?

Pre-treatment with oestrogen before ovarian stimulation using the GnRH antagonist protocol is not recommended for improving efficacy. [updated] (Zhu *et al.*, 2022)	Strong ⊕⊕◯◯
Pre-treatment with progesterone before ovarian stimulation is probably not recommended for improving efficacy. [reworded] (Farquhar *et al.*, 2017)	Conditional ⊕⊕◯◯
Oestrogen or progesterone pre-treatment can be used for scheduling purposes, given the data on efficacy and safety. [reworded]	GPP
Combined oral contraceptive pill (COCP) pre-treatment is not recommended in the GnRH antagonist protocol with FSH alone stimulation, because of reduced efficacy. [updated] (Farquhar *et al.*, 2017)	Strong ⊕⊕◯◯
A minimal washout period of 5 days may be applied if COCP is used for programming cycle in the case of a fresh transfer. [2025]	GPP
GnRH antagonist pre-treatment before ovarian stimulation in a delayed-start gonadotropin protocol is probably not recommended. [2019] (Blockeel *et al.*, 2011a, Eftekhar *et al.*, 2018; Zhang *et al.*, 2021)	Conditional ⊕◯◯◯
hCG pre-treatment can only be used in the context of a clinical trial. [2025] (Beretsos *et al.*, 2009)	Research only

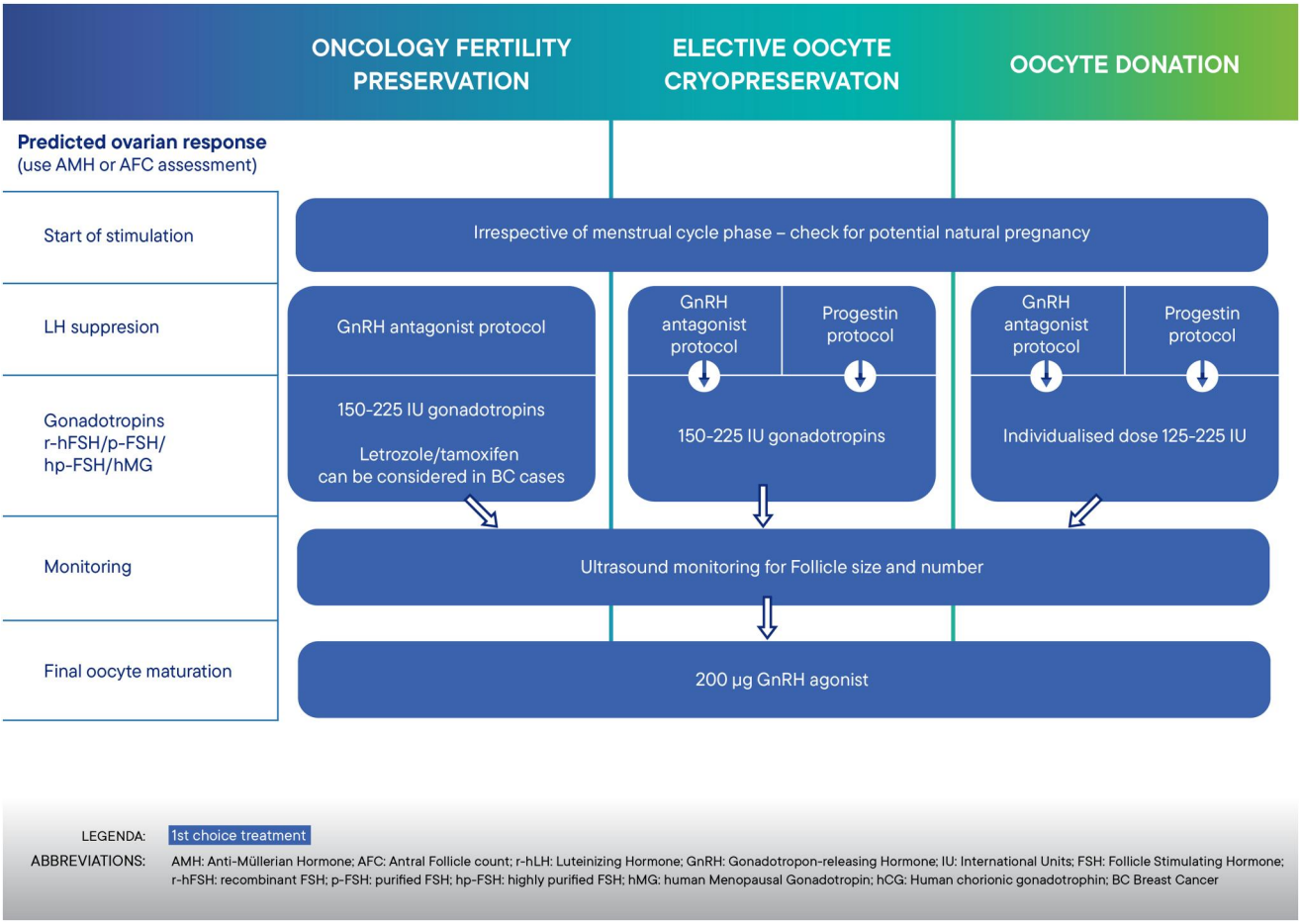

Figure 3. Schematic overview of recommendations from the guideline 'Ovarian stimulation for IVF/ICSI' for fertility preservation in women facing gonadotoxic therapies, elective cryopreservation, and oocyte donation. AMH: anti-Müllerian hormone; AFC: antral follicle count; r-hLH: luteinizing hormone; GnRH: gonadotropin-releasing hormone; IU: international units; FSH: follicle-stimulating hormone; r-hFSH: recombinant FSH; p-FSH: purified FSH; hp-FSH: highly purified FSH; hMG: human menopausal gonadotropin; hCG: human chorionic gonadotropin; BC: breast cancer.

Pituitary suppression and ovarian stimulation

According to predicted response-based stratification, which stimulation protocol is most efficient and safe?

High responder

Delayed-start ovarian stimulation is probably not recommended routinely in predicted high responders to decrease the risk of OHSS. [2025] (Casano *et al.*, 2012; Revelli *et al.*, 2020)	Conditional ⊕◯◯◯
A reduced gonadotropin dose (100 to <150 IU) is probably recommended to decrease the risk of OHSS in predicted high responders. [2025] (Arce *et al.*, 2014; Oudshoorn *et al.*, 2017; Ishihara *et al.*, 2021)	Conditional ⊕◯◯◯
The GnRH antagonist protocol is recommended for predicted high responders. [updated] (Oudshoorn *et al.*, 2017)	Strong ⊕◯◯◯

Normal responder

Delayed-start ovarian stimulation is probably not recommended over a conventional gonadotropin dose for predicted normal responders. [2025] (Hohmann *et al.*, 2003; Baart *et al.*, 2007; Lou and Huang, 2010; Blockeel *et al.*, 2011b; Revelli *et al.*, 2020)	Conditional ⊕◯◯◯
Neither a reduced nor an increased gonadotropin dose is probably recommended over a conventional gonadotropin dose (equivalent to 150-225 IU) for predicted normal responders. [updated] (Ngwenya *et al.*, 2024)	Conditional ⊕◯◯◯

Low responder

Delayed start ovarian stimulation is probably not recommended for predicted low responders. [2025] (Revelli *et al.*, 2020)	Conditional ⊕◯◯◯
The use of modified natural cycle is probably not routinely recommended over conventional stimulation for low responders. [updated] (Morgia *et al.*, 2004; Kim *et al.*, 2009; De Marco *et al.*, 2021)	Conditional ⊕◯◯◯
The GDG recognizes that low responders are a heterogeneous group and in women with very low ovarian reserve, clinicians could choose to use a modified natural cycle. [2025]	GPP
A gonadotropin dose higher than 300 IU is not recommended for predicted low responders. [2019] (Ngwenya *et al.*, 2024)	Strong ⊕◯◯◯

Which pituitary suppression protocol is preferable?

If GnRH agonists are used, the long GnRH agonist protocol is recommended over the short or ultrashort GnRH agonist protocol. [updated] (Siristatidis *et al.*, 2025)	Strong ⊕⊕◯◯
The GnRH antagonist protocol is recommended over the GnRH agonist protocols, given the comparable efficacy and higher safety in the general IVF/ICSI population. [2019] (Liu *et al.*, 2023a)	Strong ⊕⊕⊕◯

(continued)

The fixed GnRH antagonist protocol is probably recommended over the flexible GnRH antagonist protocol. [2025] (Venetis et al., 2023)	Conditional ⊕⊕◯◯
If freeze-all is planned, the use of progestin for pituitary suppression is probably equally recommended to GnRH analogues. [updated] (Glujovsky et al., 2023)	Conditional ⊕◯◯◯

Is the type of stimulation drug associated with efficacy and safety?

The use of recombinant human FSH (r-hFSH) and human menopausal gonadotropin (hMG) for ovarian stimulation is equally recommended. [2019] (Bordewijk et al., 2019)	Strong ⊕⊕⊕◯
The use of recombinant human FSH (r-hFSH) and purified FSH (p-FSH) for ovarian stimulation in the GnRH agonist protocol is equally recommended. [2019] (van Wely et al., 2011)	Strong ⊕⊕◯◯
The use of either recombinant human FSH (r-hFSH) or highly purified FSH (hp-FSH) for ovarian stimulation in the GnRH agonist protocol is equally recommended. [2019] (Bordewijk et al., 2019)	Strong ⊕⊕◯◯
The combination of r-hFSH with r-hLH and r-hFSH alone is probably equally recommended for the general IVF population. [2025] (Mochtar et al., 2017)	Conditional ⊕⊕◯◯
The combination of r-hFSH with r-hLH and r-hFSH alone is probably equally recommended for low responders. [2025] (Ferraretti et al., 2014; Humaidan et al., 2017)	Conditional ⊕⊕◯◯
The combination of r-hFSH with r-hLH and r-hFSH alone is probably equally recommended for women of advanced age (≥35 years). [2025] (Conforti et al., 2021)	Conditional ⊕⊕◯◯
The combined use of recombinant human FSH (rFSH) with human menopausal gonadotropin (hMG), either from the start or mid-phase of ovarian stimulation, is probably not recommended over the use of either r-hFSH or hMG alone in normal and low responders. [2025] (Taronger et al., 2018; Shu et al., 2019; Decleer et al., 2020)	Conditional ⊕⊕◯◯
The use of long-acting and daily recombinant human FSH (r-hFSH) is equally recommended in GnRH antagonist cycles for normal responders. [2019] (Cozzolino et al., 2019)	Strong ⊕◯◯◯
Follitropin delta and follitropin alpha/beta are equally recommended for ovarian stimulation. [2025]	Strong ⊕◯◯◯
The use of highly purified FSH (hp-FSH) and human menopausal gonadotropin (hMG) for ovarian stimulation in GnRH agonist protocols is equally recommended. [2019] (Duijkers et al., 1993; Westergaard et al., 1996; Parsanezhad et al., 2017)	Conditional ⊕⊕◯◯
The use of recombinant human LH + recombinant human FSH (r-hFSH+r-hLH) for ovarian stimulation is probably not recommended over human menopausal gonadotropin (hMG) in GnRH agonist protocols with regard to safety. [2019] (Pacchiarotti et al., 2010)	Conditional ⊕◯◯◯
Adding low dosages of hCG to the FSH stimulation is probably not recommended. [2025] (Koichi et al., 2006; Serafini et al., 2006; Madani et al., 2012; Thuesen et al., 2012; Zhu and Fu, 2019; Decleer et al., 2020; Siristatidis et al., 2022)	Conditional ⊕◯◯◯
The addition of letrozole to gonadotropins in stimulation protocols for predicted high responders is probably not recommended. [updated] (Yang et al., 2019; Tshzmachyan and Hambartsoumian, 2020; Ghasemi Tehrani et al., 2022; Lotfy et al., 2022)	Conditional ⊕◯◯◯
The addition of letrozole to gonadotropins in stimulation protocols is probably not recommended for predicted normal responders. [2019] (Mukherjee et al., 2012; Eftekhar and Saeed, 2020; Bülow et al., 2022)	Conditional ⊕◯◯◯
The addition of letrozole to gonadotropins in stimulation protocols is probably not recommended for predicted low responders. [2019] (Qin, 2021)	Conditional ⊕⊕◯◯
The addition of clomiphene citrate to gonadotropins in stimulation protocols is probably not recommended for predicted high responders. [2019] (Lotfy et al., 2022)	Conditional ⊕⊕◯◯
The addition of clomiphene citrate to gonadotropins in stimulation protocols is probably not recommended for predicted normal responders. [2025] (Datta et al., 2021)	Conditional ⊕⊕⊕◯
Clomiphene citrate alone or in combination with gonadotropins, and gonadotropin stimulation alone are probably equally recommended for predicted low responders. [updated] (Montoya-Botero et al., 2021)	Conditional ⊕⊕◯◯

Is adjustment of the gonadotropin dosage during the stimulation phase meaningful in terms of efficacy and safety?

Adjustment (increase or decrease) of the gonadotropin dose in the mid-stimulation phase during ovarian stimulation is probably not recommended. [2019] (van Hooff et al., 1993; Aboulghar et al., 2000; Cedrin-Durnerin et al., 2000; Aboulghar et al., 2004; Martin et al., 2006; Lawrenz et al., 2021; Xu et al., 2024)	Conditional ⊕◯◯◯
Given the lack of evidence of the value of dose adjustments during ovarian stimulation, it is important that the gonadotropin starting dose is appropriate based on patient characteristics and desired outcome. [2025]	GPP

Is the addition of adjuncts in ovarian stimulation meaningful in terms of efficacy and safety?

Routine use of adjunct metformin before and/or during ovarian stimulation is probably not recommended when using the GnRH antagonist protocol for women with PCOS. [updated] (Tso et al., 2020)	Conditional ⊕⊕◯◯
Use of adjunct growth hormone before and/or during ovarian stimulation is not recommended for normal responders. [2025] (Sood et al., 2021)	Strong ⊕◯◯◯
Use of adjunct growth hormone before and/or during ovarian stimulation is probably not recommended for low responders. [updated] (Liu et al., 2025)	Conditional ⊕◯◯◯
Use of adjunct growth hormone before and/or during ovarian stimulation is not recommended for women with PCOS. [2025] (Gong et al., 2020)	Strong ⊕⊕◯◯
Use of testosterone before ovarian stimulation is probably not recommended for low responders. [updated] (Naik et al., 2024)	Conditional ⊕⊕⊕◯
Use of DHEA before and/or during ovarian stimulation is not recommended for low responders. [2019] (Huang et al., 2025)	Strong ⊕⊕◯◯
Use of DHEA before and/or during ovarian stimulation is not recommended for normal responders. [2025] (Huang et al., 2025)	Strong ⊕⊕◯◯

(continued)

Use of aspirin before and/or during ovarian stimulation is not recommended in the general IVF/ICSI population, nor for low responders. [2019] (Siristatidis *et al.*, 2016)	Strong ⊕⊕⊕◯
Use of sildenafil before and/or during ovarian stimulation is not recommended for low responders. [2019] (Ataalla *et al.*, 2016)	Strong ⊕◯◯◯
Use of myo-inositol before and/or during ovarian stimulation is probably not recommended for women with PCOS undergoing IVF. [2025] (Showell *et al.*, 2018)	Conditional ⊕◯◯◯
Use of myo-inositol before and/or during ovarian stimulation is not recommended in low responders. [2025] (Nazari *et al.*, 2020; Mohammadi *et al.*, 2021)	Strong ⊕⊕◯◯
Use of myo-inositol before and/or during ovarian stimulation is not recommended in non-PCOS women undergoing IVF. [2025] (Seyedoshohadaei *et al.*, 2022)	Strong ⊕⊕◯◯

What is the safety and efficacy of non-conventional start stimulation compared to standard early follicular phase stimulation?

Random-start ovarian stimulation could be used when a fresh transfer is not intended; nonetheless, the risk of OHSS in case of concurrent spontaneous conception should always be discussed with the patient. [reworded] (Qin *et al.*, 2016; Pereira *et al.*, 2017)	GPP
Luteal start ovarian stimulation could be used when a fresh transfer is not intended, and there is no possibility of natural conception. [updated] (Cerrillo *et al.*, 2023; Massin *et al.*, 2023; Suñol *et al.*, 2023; Boudry *et al.*, 2024; Dastjerdi *et al.*, 2024; Saharkhiz *et al.*, 2024)	Conditional ⊕◯◯◯
Late luteal phase start of gonadotropins with fresh transfer is probably not recommended for low responders. [updated] (Rombauts *et al.*, 1998; Kansal Kalra *et al.*, 2008; Kucuk *et al.*, 2008)	Conditional ⊕◯◯◯
Double stimulation can be considered for urgent fertility preservation cycles. [2019]	GPP
Double stimulation can be used with the intention to accumulate oocytes or embryos when a fresh transfer is not planned. [updated] (Cerrillo *et al.*, 2023; Massin *et al.*, 2023)	Strong ⊕⊕◯◯

Fertility preservation and oocyte donation

What is the preferred stimulation protocol for fertility preservation in patients facing gonadotoxic treatment?

For patients facing gonadotoxic treatment, ovarian stimulation for fertility preservation should be started irrespective of the menstrual cycle phase. [updated] (Boots *et al.*, 2016; Chen *et al.*, 2022; Sönmezer *et al.*, 2023)	Strong ⊕◯◯◯
For ovarian stimulation in women seeking fertility preservation for medical reasons, the GnRH antagonist protocol is recommended. [2019] (Boots *et al.*, 2016; Rodgers *et al.*, 2017)	Strong ⊕◯◯◯
In ovarian stimulation for fertility preservation in oestrogen-sensitive diseases, the concomitant use of anti-oestrogen therapy, such as letrozole or tamoxifen, can be considered. [2019] (Chen *et al.*, 2022; Yoshida *et al.*, 2023)	GPP
For final oocyte maturation in patients facing gonadotoxic treatment, a GnRH agonist is preferred. [2025] (Hong *et al.*, 2022; Massarotti *et al.*, 2023)	GPP

What is the preferred stimulation protocol for elective oocyte cryopreservation?

Ovarian stimulation for elective oocyte preservation can be started irrespective of the menstrual cycle phase. [2025] (Pereira *et al.*, 2017)	Conditional ⊕◯◯◯
GnRH antagonist or progestin protocols are probably recommended over GnRH agonist protocols for pituitary suppression in elective oocyte cryopreservation. [2025] (Vaiarelli *et al.*, 2024)	Conditional ⊕◯◯◯
For final oocyte maturation in elective oocyte cryopreservation, a GnRH agonist is preferred. [2025] (Kim *et al.*, 2020; Maslow *et al.*, 2020; Herzberger *et al.*, 2021)	GPP

What is the preferred stimulation protocol for oocyte donation?

Conventional follicular start or random-start ovarian stimulation is equally recommended for oocyte donation cycles. [2025] (Martinez *et al.*, 2022; De Rijdt *et al.*, 2024; Guerrero *et al.*, 2024)	Strong ⊕◯◯◯
If random-start ovarian stimulation is used, oocyte donors need to adopt contraceptive measures to prevent the possibility of a natural pregnancy. [2025]	GPP
Any type of contraception (hormonal, non-hormonal, oral, vaginal, or intrauterine) can be used before initiation of ovarian stimulation in oocyte donors. [2025]	GPP
Progestin or intrauterine contraception can be used during ovarian stimulation in oocyte donors. [2025]	GPP
For pituitary suppression in oocyte donors, the GnRH antagonist and progestin protocol is probably equally recommended. [2025] (Bodri *et al.*, 2011; Martinez *et al.*, 2021)	Conditional ⊕⊕◯◯
A GnRH agonist protocol for pituitary suppression is not recommended in oocyte donors. [2025]	GPP
The use of recombinant human FSH (r-hFSH), purified FSH, long-acting r-hFSH, or hMG is probably equally recommended in oocyte donors undergoing ovarian stimulation. [2025] (Söderström-Anttila *et al.*, 1996; Tesarik and Mendoza, 2002; Acevedo *et al.*, 2004; Melo *et al.*, 2010;Cruz *et al.*, 2017; Alvarado Franco *et al.*, 2023)	Conditional ⊕◯◯◯
Gonadotropin dose should be individualized based on ovarian reserve, with the goal to maintain donors' safety and also to obtain an optimal number of oocytes. [2025]	GPP
The routine use of a GnRH agonist trigger is recommended in oocyte donors using the GnRH antagonist or progestin protocols for pituitary suppression. [2025] (Youssef *et al.*, 2014)	Strong ⊕⊕◯◯
The use of an hCG trigger is not routinely recommended in oocyte donation cycles. [2025] (Youssef *et al.*, 2014)	Strong ⊕⊕◯◯

Monitoring

Is the addition of hormonal assessment (oestradiol/progesterone/LH) to ultrasound monitoring improving efficacy and safety?

The addition of oestradiol measurements to ultrasound monitoring is probably not recommended. [2019] (Kwan *et al.*, 2021)	Conditional ⊕⊕◯◯

(continued)

The addition of a hormonal panel consisting of a combination of oestradiol, progesterone, and LH measurements to ultrasound monitoring is probably not recommended. [2019] (Golan et al., 1994; Wiser et al., 2012)	Conditional ⊕◯◯◯

Does monitoring of endometrial thickness affect the efficacy and safety?

Routine monitoring of endometrial thickness during controlled ovarian stimulation is probably not recommended. [2019] (Kasius et al., 2014; Gao et al., 2020)	Conditional ⊕◯◯◯
The guideline group suggests performing a single measurement of the endometrium during ultrasound assessment on the day of triggering or oocyte pick-up to counsel patients on the potential lower pregnancy chance. [2019]	GPP

Is the outcome of ovarian stimulation dependent on the criteria for final oocyte maturation?

The association of follicle size as a triggering criterion with outcome has not been sufficiently studied. Physicians may choose the follicle size upon which final oocyte maturation is triggered on a case-by-case basis. [2019] (Chen et al., 2014)	Conditional ⊕⊕◯◯
The decision on timing of triggering in relation to follicle size is multi-factorial, taking into account the size of the growing follicle cohort, the hormonal data on the day of the pursued trigger, duration of stimulation, embryo transfer strategy, patient burden, financial costs, experience of previous cycles, and organizational factors for the centre. Most often, final oocyte maturation is triggered at sizes of several of the leading follicles between 16 and 22 mm. [reworded]	GPP
The GDG does not recommend to base timing of final oocyte maturation triggering on oestradiol levels alone. [2019]	GPP
The GDG does not recommend to base timing of final oocyte maturation on oestradiol/follicle ratio alone. [2019]	GPP

Is hormonal assessment on the day of final oocyte maturation recommended?

It is probably recommended to measure serum progesterone levels on the day of final oocyte maturation in cycles aimed for a fresh embryo transfer. [2025] (Venetis et al., 2013)	Conditional ⊕◯◯◯
If serum progesterone levels are high, the patient should be counselled about potentially lower ongoing pregnancy/live birth rates. The decision to defer embryo transfer should include other factors (number of oocytes, number of embryos, and embryo quality). [2025]	GPP
It is not recommended to routinely measure serum oestradiol levels on the day of hCG trigger in ovarian stimulation cycles with the intent for a fresh embryo transfer. [2025] (Karatasiou et al., 2020)	Strong ⊕◯◯◯
It is not recommended to measure serum LH levels on the day of hCG trigger in ovarian stimulation cycles aimed for a fresh embryo transfer. [2025] (Zhang et al., 2022; Luo et al., 2023; Zhou et al., 2023)	Strong ⊕◯◯◯
It is not recommended to measure serum oestradiol, progesterone, or luteinizing hormone levels on the day of a GnRH agonist trigger in freeze-all cycles. [2025] (Kummer et al., 2013; Lu et al., 2016; Popovic-Todorovic et al., 2019; Gambini et al., 2024)	Strong ⊕◯◯◯

Which criteria for cycle cancellation are meaningful regarding predicted low/high oocyte yield?

A low response to ovarian stimulation alone is not a reason to cancel a cycle. [2019] (Oudendijk et al., 2012)	Strong ⊕◯◯◯
The physician should counsel the individual unexpected low responder regarding pregnancy prospects and decide individually whether to continue this cycle. [updated]	GPP
In GnRH agonist cycles with an ovarian response of ≥19 follicles of ≥11 mm, there is an increased risk of OHSS and preventative measures are recommended, which should include primarily cancelling the final oocyte maturation trigger. [updated] (Mathur et al., 2000; Papanikolaou et al., 2006; Steward et al., 2014; Griesinger et al., 2016)	Strong ⊕◯◯◯
In GnRH antagonist cycles, withholding GnRH agonist triggering may still be considered in women with extremely high ovarian response. [2025]	GPP

Triggering ovulation and luteal support

What is the preferred drug for triggering final oocyte maturation in terms of efficacy and safety in the overall IVF/ICSI population?

The use of recombinant hCG and urinary hCG is equally recommended for triggering final oocyte maturation in ovarian stimulation protocols. [2019] (Youssef et al., 2016)	Strong ⊕⊕◯◯
A reduced dose of 5000 IU urinary hCG for final oocyte maturation is probably recommended over a 10 000 IU dose in GnRH agonist protocols, as it may improve safety. [2019] (Shaltout et al., 2006; Kolibianakis et al., 2007; Madani et al., 2013)	Conditional ⊕◯◯◯
It is not recommended to administer recombinant human LH for triggering final oocyte maturation. [2019] (Youssef et al., 2016)	Strong ⊕◯◯◯
The use of GnRH agonist for final oocyte maturation is not recommended in the general IVF/ICSI population with fresh transfer, regardless of luteal phase support (with or without LH-activity). [updated] (Beebeejaun et al., 2025)	Strong ⊕⊕◯◯
If the GnRH agonist trigger with triptorelin is applied, dosages ranging between 0.1 and 0.4 mg can be chosen. [2019]	GPP
The addition of a GnRH agonist to hCG as a dual trigger for final oocyte maturation is probably not recommended for predicted normal responders. [2019] (Beebeejaun et al., 2025)	Conditional ⊕⊕◯◯
The addition of a GnRH agonist to hCG as a dual trigger for final oocyte maturation is probably not recommended for low responders. [2025] (He et al., 2023; Keskin et al., 2023)	Conditional ⊕⊕◯◯

What is the efficacy and safety of luteal support protocols?

Progesterone is recommended for luteal phase support after IVF/ICSI. [2019] (Hurd et al., 1996; Abate et al., 1999)	Strong ⊕◯◯◯
Any of the previously mentioned administration routes (non-oral) for natural progesterone as luteal phase support can be used. [2019]	GPP

(continued)

The dosing of natural progesterone has evolved empirically, usually dosages used include: 50 mg once daily for intramuscular progesterone 25 mg once daily for subcutaneous progesterone 90 mg once daily for vaginal progesterone gel 200 mg three times daily for micronized vaginal progesterone in-oil capsules 100 mg two or three times daily for micronized vaginal progesterone in starch suppositories 400 mg two times daily for vaginal pessary. [2019]	GPP
Starting progesterone for luteal phase support should be in the window between the evening of the day of oocyte retrieval and day 3 post oocyte retrieval. [2019]	GPP
Progesterone support should be administered until at least the day of the pregnancy test. [2019]	GPP
Dydrogesterone is probably recommended for luteal phase support. [2019] (Griesinger *et al.*, 2020) *There are reports on a relation between dydrogesterone exposure and the occurrence of congenital malformations. These observed relations cannot be translated into a conclusion on causality, and therefore are considered as potential associations.*	Conditional ⊕⊕⊕◯
The addition of oestradiol to progesterone for luteal phase support is probably not recommended. [2019] (van der Linden *et al.*, 2015)	Conditional ⊕⊕◯◯
In hCG-triggered ovarian stimulation cycles, hCG as luteal phase support in standard dosages of 1500 IU is not recommended. [updated] (van der Linden *et al.*, 2015)	Strong ⊕⊕◯◯
A GnRH agonist bolus, in addition to progesterone for luteal phase support in hCG-triggered cycles is probably not recommended. [updated] (Liu *et al.*, 2022)	Conditional ⊕⊕◯◯
Repeated GnRH agonist injections, alone or in addition to progesterone for luteal phase support in hCG-triggered cycles is probably not recommended. [reworded] (van der Linden *et al.*, 2015)	Conditional ⊕◯◯◯
The addition of LH to progesterone for luteal phase support can only be used in the context of a clinical trial. [2019]	Research only

Prevention of OHSS

Which is the best strategy to reduce OHSS in the observed high responder regarding ovulation triggering and embryo transfer strategy?

A GnRH agonist trigger is recommended for final oocyte maturation in women at risk of OHSS combined with a freeze-all strategy to minimize the risk of severe OHSS. [updated] (Babayof *et al.*, 2006; Engmann *et al.*, 2008; Humaidan *et al.*, 2013; Youssef *et al.*, 2014; Aflatoonian *et al.*, 2018; Santos-Ribeiro *et al.*, 2020)	Strong ⊕◯◯◯
If a GnRH agonist protocol with hCG trigger is used in high responders, a freeze-all strategy is recommended to decrease the risk of late-onset OHSS. [updated]	GPP
The addition of hCG to GnRH agonist as a dual trigger for final oocyte maturation is probably not recommended for high responders. [2025] (He *et al.*, 2022; Wang *et al.*, 2024)	Conditional ⊕◯◯◯
In patients at risk of OHSS, the use of a GnRH agonist for final oocyte maturation is probably recommended over hCG in cases where no fresh transfer is performed. [2019] (Borges *et al.*, 2016; Tannus *et al.*, 2017)	Conditional ⊕◯◯◯
A GnRH agonist trigger for final oocyte maturation with or without a freeze-all strategy is preferred over a coasting strategy in patients at risk of OHSS. [2019] (DiLuigi *et al.*, 2010; Herrero *et al.*, 2011)	GPP
Dopamine agonists are recommended to decrease the risk of early OHSS, particularly in patients receiving hCG for final oocyte maturation. [2025] (Tang *et al.*, 2021)	Strong ⊕⊕◯◯

Is the freeze-all protocol meaningful in the prevention of ovarian hyper-stimulation syndrome also with regards to efficacy?

A freeze-all strategy is recommended to minimize the risk of late-onset OHSS. [updated] (Zaat *et al.*, 2021)	Strong ⊕⊕◯◯
Prior to the start of ovarian stimulation, a risk assessment for high response is advised with the purpose of applying personalised treatment choices on pituitary suppression protocol, FSH dosage, final oocyte maturation trigger, and embryo transfer strategy. [updated]	GPP

Discussion

The updated ESHRE guideline on ovarian stimulation for IVF/ICSI aims to supply healthcare providers with the best available evidence for approaches in the various steps and phases of OS for IVF/ICSI.

All recommendations in the guideline were formulated after an assessment of the best available evidence in the literature and discussion within the GDG, taking into account the balance of benefits versus harms, patient preferences, clinicians' expertise, and resource use. The guideline provides a total of 121 recommendations: 42 recommendations remained unchanged, 4 recommendations were reworded for better understanding, 29 recommendations were updated in view of new evidence, and 46 new recommendations for 2025 have been formulated. The guideline provides 4 recommendations on pre-stimulation evaluation, 7 recommendations on pre-treatment therapies, 50 recommendations on pituitary suppression and ovarian stimulation, 17 recommendations on monitoring, 18 recommendations on triggering of final oocyte maturation and luteal support, and 8 recommendations on the prevention of OHSS. In addition, the guideline provides 17 recommendations on fertility preservation, both oncologic and elective, and oocyte donation. These include 90 evidence-based recommendations, of which only 42 were formulated as strong recommendations, as well as 29 good practice points and 2 research-only recommendations. Of the evidence-based recommendations, none were supported by high-quality evidence, 6 by moderate-quality evidence, 36 by low-quality evidence, and 148 by very low-quality evidence. To support future research on ovarian stimulation for IVF/ICSI, a list of research recommendations was provided.

With this update of the ovarian stimulation guideline, the guideline development group (GDG) would like to highlight their preference in changing the terminology for the different types of responders from poor, normal, and excessive to low, normal, and high. In addition, they would like to advice clinicians to refrain from using non-standardized terminology, such as 'healthy' responders, 'kind' stimulation, etc.

The GDG also took the opportunity to improve its structure to make it even more clear and even more user-friendly. This resulted in adaptations in the chapter on pre-stimulation evaluation, where now the same diagnostic tests are discussed for assessment of ovarian response as for pregnancy prediction. In addition, the key question on fertility preservation was split up into three parts: fertility preservation for women facing gonadotoxic treatment, elective oocyte cryopreservation, and oocyte donation. Even though freeze-all cycles are used in most cases for all three indications, it is clear that these are three different patient populations, requiring a different strategy for ovarian stimulation and thus separate recommendations were in order.

The section on stimulation protocols for high, normal, and low responders was also reviewed from a different perspective by the GDG. For starters, the GDG wanted to highlight in this updated guideline that a conventional gonadotropin dose is equivalent to 150–225 IU. Secondly, after much consideration, the GDG decided to discard the concept of 'mild stimulation' from the guideline. Mild stimulation is defined by ICMART as a protocol with the intention of limiting the number of oocytes following stimulation for IVF (Zegers-Hochschild *et al.*, 2017). However, as it is an intended approach, it is difficult to decide on a gonadotropin starting dose to obtain this limited number of oocytes. Furthermore, studies published on the topic are very heterogeneous, often unclear in methodology, or using a total gonadotropin dose that is equivalent to conventional stimulation. Comparing and combining these studies to be able to make relevant and evidence-based decisions is therefore not feasible. Lastly, dose comparisons of gonadotropins were introduced. In the previous version of the guideline, dose comparisons were not explicitly presented, and comparisons with higher gonadotropin dosages were only included for low responders. It has been made clear now that there are limited indications to deviate from conventional gonadotropin dosing.

Several new interventions were added to the chapter on gonadotropins, such as follitropin delta, combinations of FSH with hMG, and combinations of FSH and hCG. With regard to follitropin delta, there was some discussion about the RCTs comparing follitropin delta to follitropin alpha. Some GDG members felt that these RCTs included two interventions, i.e. different follitropin medications and individualized versus conventional dosing of the follitropin medications. Other GDG members disagreed, arguing that, in order to show non-inferiority, the new follitropin delta medications, which can only be administered by individualized, algorithm-based dosing, had to be compared to conventional dosing in the control arm. Because of the non-inferiority in efficacy outcomes, and improved safety profile in terms of OHSS (because of the individualized dosing), a strong recommendation in favour of follitropin delta was issued. With regard to the combination of FSH with hMG or hCG, while the GDG understands the rationale of adding LH-activity in the mid-follicular phase during ovarian stimulation with recombinant human FSH, the evidence clearly shows no benefit in terms of (cumulative) live birth rates. Therefore, it is not surprising that these combinations are not recommended by the GDG.

One completely new key question that was introduced in the guideline is the need for hormonal assessment (progesterone, oestrogen, or LH) on the day of final oocyte maturation. The GDG felt this question was overlooked in the previous version of the guideline. The evidence is consistently showing lower live birth rates with elevated progesterone, resulting in the expectation of a strong recommendation in favour of measuring progesterone on the day of final oocyte maturation. However, the GDG felt the recommendation had to be very nuanced. For diagnostic tests, the GDG feels strongly that unless an intervention or treatment is available to rectify the abnormality, the test should not be recommended. In the case of elevated progesterone levels on the day of final oocyte maturation, current evidence shows that the reduction in live birth rates is not seen after a frozen embryo transfer. However, when considering the freeze-all strategy, several factors need to be taken into account, such as the number of oocytes, the number of embryos, and embryo quality. Therefore, only a conditional (weak) statement was formulated in favour of measuring progesterone levels on the day of final oocyte maturation.

Research gaps were detected in several areas, and the top three topics are documented in a list of recommendations for further research (Supplementary Data File S1).

Despite the limitations of guidelines in general, and the limitations in the evidence supporting the current guideline, the guideline group is confident that this document will help best practice in ovarian stimulation for IVF/ICSI.

Supplementary data

Supplementary data are available at *Human Reproduction* online.

Data availability

The data underlying this article are available in the article and in its online supplementary material.

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Authors' roles

FB chaired the GDG and hence fulfilled a leading role in collecting the evidence, writing the manuscript, and dealing with reviewer comments. NLC, as the methodological expert, performed all literature searches for the guideline, provided methodological support, and coordinated the guideline development. All other authors, listed in alphabetical order, as GDG members, contributed equally to the manuscript by drafting key questions, synthesizing evidence, writing different parts of the guideline, and discussing recommendations until consensus within the group was reached.

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