



Annex 6: Summary of findings tables

EXPLANATIONS

GRADE Working Group grades of evidence

High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect

Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

CI: Confidence Interval; RR: Risk Ratio ; OR: Odds ratio

3. Pre-treatment therapies

1a Pre-treatment with oestradiol compared to no intervention in normal responders in GnRH antagonist cycles

Patient or population: women undergoing COS for IVF/ICSI

Intervention: pre-treatment with oestradiol in GnRH antagonist cycles

Comparison: no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with pre- treatment with oestradiol				
Cumulative LBR (Fernández-Prada et al., 2022)	476 per 1,000	0 per 1,000 (0 to 0)	not estimable	43 (1 RCT)	⊕○○○ Low ^{a,b,c}	
Live birth rate (Zhu et al., 2022)	316 per 1,000	312 per 1,000 (255 to 376)	OR 0.98 (0.74 to 1.30)	919 (4 RCTs)	⊕⊕○○ Low ^{d,e}	
Live birth rate (Fernández-Prada, et al., 2022)	467 per 1,000	0 per 1,000 (0 to 0)	not estimable	29 (1 RCT)	⊕○○○ Low ^{a,b,c}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Significant risk of attrition bias and risk of performance bias.

b. Serious inconsistency because only 1 RCT.

c. Small number of events

d. Significant risk of performance bias in 3/7 studies and unknown risk of performance bias in 3/7 studies.

e. The pooled effect estimate includes the line of no effect.



1b Pre-treatment with oestradiol compared to no intervention in women of advanced age in GnRH antagonist cycles

Patient or population: women of advanced age undergoing COS for IVF/ICSI

Intervention: pre-treatment with oestradiol in GnRH antagonist cycles

Comparison: no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with pre-treatment with oestradiol				
Cumulative LBR (Cédric-Durnerin et al., 2024)	229 per 1,000	0 per 1,000 (0 to 0)	not estimable	291 (1 RCT)	⊕⊕○○ Low ^{a,b}	
LBR (Cédric-Durnerin, et al., 2024)	118 per 1,000	0 per 1,000 (0 to 0)	not estimable	291 (1 RCT)	⊕⊕○○ Low ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of performance bias

b. Single study.

2a Pre-treatment with progesterone compared to placebo or no intervention in GnRH agonist cycles

Patient or population: women undergoing COS for IVF/ICSI

Intervention: pre-treatment with progesterone in GnRH agonist cycles

Comparison: placebo or no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo or no intervention	Risk with pre-treatment with progesterone				
Cumulative LBR						Not reported
LBR/ ongoing PR (GnRHa cycles) (Farquhar et al., 2017)	170 per 1,000	216 per 1,000 (124 to 351)	OR 1.35 (0.69 to 2.65)	222 (2 RCTs)	⊕⊕○○ LOW ^{a,b,c}	
LBR/ ongoing PR (GnRH anta cycles) (Farquhar, et al., 2017)	292 per 1,000	216 per 1,000 (69 to 511)	OR 0.67 (0.18 to 2.54)	47 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c,d}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. High risk of bias associated with poor reporting of methods in the primary studies.

b. Small number of events

c. The pooled effect included both the line of no effect and appreciable benefit or harm.

d. Serious inconsistency because only 1 RCT



2b Pre-treatment with progesterone compared to placebo or no treatment in GnRH antagonist cycles

Patient or population: women undergoing COS for IVF/ICSI

Intervention: pre-treatment with progesterone in GnRH antagonist cycles

Comparison: placebo or no treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo or no treatment	Risk with pre-treatment with progesterone				
Cumulative LBR						Not reported
LBR/ongoing PR (Farquhar, et al., 2017)	292 per 1,000	216 per 1,000 (69 to 511)	OR 0.67 (0.18 to 2.54)	47 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c,d}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

- a. High risk of bias associated with poor reporting of methods in one or more of the primary studies.
- b. Serious inconsistency because only 1 RCT.
- c. Very small number of events.
- d. Wide confidence interval, which crosses the line of no effect and appreciable benefit or harm.

3a Pre-treatment with combined contraceptives compared to no intervention in GnRH antagonist cycles

Patient or population: women undergoing COS for IVF/ICSI

Intervention: pre-treatment with combined contraceptives in GnRH antagonist cycles

Comparison: no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with pre-treatment with combined contraceptives				
Cumulative LBR (Fernández-Prada, et al., 2022)	476 per 1,000	0 per 1,000 (0 to 0)	not estimable	52 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
LBR/ongoing PR (Farquhar, et al., 2017)	270 per 1,000	215 per 1,000 (177 to 260)	OR 0.74 (0.58 to 0.95)	1335 (6 RCTs)	⊕⊕⊕○ MODERATE ^d	
LBR (Fernández-Prada, et al., 2022)	467 per 1,000	0 per 1,000 (0 to 0)	not estimable	37 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
OHSS (Farquhar, et al., 2017)	16 per 1,000	16 per 1,000 (4 to 52)	OR 0.98 (0.28 to 3.40)	642 (2 RCTs)	⊕⊕○○ LOW ^{d,e,f}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

- a. Significant risk of attrition bias and risk of performance bias.
- b. Serious inconsistency because only 1 RCT.
- c. Small number of events
- d. Serious risk of bias due to poor reporting of sequence generation and allocation concealment.
- e. Small number of events.
- f. The pooled effect included both the line of no effect and appreciable benefit or harm.



3b Pre-treatment with combined contraceptives compared to no pre-treatment in low responders

Patient or population: low responder women undergoing COS for IVF/ICSI

Intervention: pre-treatment with combined contraceptives

Comparison: no pre-treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no pre-treatment	Risk with pre-treatment with combined contraceptives				
Cumulative LBR						Not reported
LBR (Farquhar, et al., 2017)	200 per 1,000	0 per 1,000 (0 to 0)	not estimable	80 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of performance bias

b. Serious inconsistency because only 1 RCT

c. Small number of events

3c Pre-treatment with combined contraceptives compared to no pre-treatment in women with PCOS

Patient or population: women with PCOS undergoing COS for IVF/ICSI

Intervention: pre-treatment with combined contraceptives

Comparison: no pre-treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no pre-treatment	Risk with pre-treatment with combined contraceptives				
Cumulative LBR (Gao et al., 2024)	777 per 1,000	0 per 1,000 (0 to 0)	not estimable	242 (1 RCT)	⊕⊕○○ Low ^{a,b}	
LBR (Gao, et al., 2024)	550 per 1,000	0 per 1,000 (0 to 0)	not estimable	215 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Moderate to severe OHSS (Gao, et al., 2024)	107 per 1,000	0 per 1,000 (0 to 0)	not estimable	242 (1 RCT)	⊕○○○ Very low ^{a,b,c}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of performance bias.

b. Serious inconsistency because only 1 RCT.

c. Small number of events



4a Pre-treatment with GnRH antagonist compared to no pre-treatment in GnRH antagonist protocols

Patient or population: women undergoing COS for IVF/ICSI

Intervention: pre-treatment with GnRH antagonist

Comparison: no pre-treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no pre-treatment	Risk with pre-treatment with GnRH antagonist				
Cumulative LBR						Not reported
LBR (Zhang et al., 2021)	431 per 1,000	0 per 1,000 (0 to 0)	not estimable	117 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Moderate to severe OHSS (Zhang, et al., 2021)	29 per 1,000	0 per 1,000 (0 to 0)	not estimable	136 (1 RCT)	⊕○○○ Very low ^{a,b,c}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Significant risk of performance bias and possible risk of selection bias.

b. Serious inconsistency because only 1 RCT.

c. Small number of events.

4b Pre-treatment with GnRH antagonist compared to no pre-treatment in GnRH antagonist protocols in women with PCOS

Patient or population: women with PCOS undergoing COS for IVF/ICSI

Intervention: pre-treatment with GnRH antagonist

Comparison: no pre-treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no pre-treatment	Risk with pre-treatment with GnRH antagonist				
Cumulative LBR						Not reported
Live birth rate						Not reported
moderate to severe OHSS (Eftekhar et al., 2018)	360 per 1,000	0 per 1,000 (0 to 0)	not estimable	88 (1 RCT)	⊕○○○ Very low ^{a,b,c}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Significant risk of performance bias and possible risk of selection bias.

b. Serious inconsistency because only 1 RCT.

c. Small number of events.



4. Ovarian stimulation protocols

5 Delayed-start ovarian stimulation in high responders

Patient or population: high responder women undergoing COS for IVF/ICSI

Intervention: delayed-start ovarian stimulation

Comparison: conventional start ovarian stimulation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with long GnRH agonist	Risk with GnRH antagonist				
Cumulative live birth rate (Revelli et al., 2020)	571 per 1,000	0 per 1,000 (0 to 0)	not estimable	42 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
Live birth rate (Casano et al., 2012)	266 per 1,000	0 per 1,000 (0 to 0)	not estimable	412 (1 RCT)	⊕⊕⊕○ Moderate ^b	
OHSS (Casano, et al., 2012)	19 per 1,000	0 per 1,000 (0 to 0)	not estimable	412 (1 RCT)	⊕⊕○○ Low ^{b,c}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Risk of performance and attrition bias by incomplete reporting of methodology.

b. Serious inconsistency because only 1 RCT.

c. Small number of events.

6 Reduced-dose gonadotropin compared to conventional gonadotropin dose in high responders

Patient or population: high responder women undergoing COS for IVF/ICSI

Intervention: higher gonadotropin dose

Comparison: lower gonadotropin dose

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with conventional gonadotropin dose	Risk with reduced-dose gonadotropin				
Cumulative LBR (Oudshoorn et al., 2017)	695 per 1,000	663 per 1,000 (591 to 744)	RR 0.953 (0.850 to 1.070)	521 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Live birth rate (Oudshoorn, et al., 2017)	255 per 1,000	251 per 1,000 (184 to 333)	OR 0.98 (0.66 to 1.46)	521 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Severe OHSS (Oudshoorn, et al., 2017)	16 per 1,000	11 per 1,000 (3 to 48)	OR 0.72 (0.16 to 3.19)	521 (1 RCT)	⊕○○○ Very low ^{a,c}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of performance bias due to lack of blinding and/or selective reporting.

b. Small number of events.

c. Very serious imprecision associated with a very small number of events.



7 Delayed-start stimulation compared to conventional start stimulation in normal responders

Patient or population: normal responder women undergoing COS for IVF/ICSI

Intervention: Delayed-start stimulation

Comparison: conventional start stimulation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with conventional start FSH	Risk with late-start FSH				
Cumulative LBR (Revelli, et al., 2020)	263 per 1,000	0 per 1,000 (0 to 0)	not estimable	37 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
OHSS (Lou and Huang, 2010)	67 per 1,000	0 per 1,000 (0 to 0)	not estimable	60 (1 RCT)	⊕○○○ Very low ^{a,b,c}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Risk of performance and attrition bias by incomplete reporting of methodology.

b. Serious risk of inconsistency because only 1 RCT.

c. Small number of events.



8 Higher versus lower gonadotropin dose in normal responders

Patient or population: normal responder women undergoing COS for IVF/ICSI

Intervention: higher gonadotropin dose

Comparison: lower gonadotropin dose

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with higher FSH dose	Risk with lower FSH dose				
Cumulative LBR						Not reported
LBR/Ongoing PR - 200 vs. 100 IU (Ngwenya et al., 2024)	204 per 1,000	184 per 1,000 (127 to 258)	OR 0.88 (0.57 to 1.36)	522 (2 RCTs)	⊕⊕○○ Low ^{a,b}	
Live birth rate - 225/200 vs. 150 IU (Ngwenya, et al., 2024)	309 per 1,000	305 per 1,000 (238 to 378)	OR 0.98 (0.70 to 1.36)	686 (2 RCTs)	⊕⊕○○ Low ^{a,b}	
Live birth rate - 300 vs. 150 IU (Ngwenya, et al., 2024)	294 per 1,000	250 per 1,000 (73 to 588)	OR 0.80 (0.19 to 3.42)	37 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Live birth rate - 300 vs. 225 IU (Ngwenya, et al., 2024)	397 per 1,000	300 per 1,000 (174 to 465)	OR 0.65 (0.32 to 1.32)	135 (1 RCT)	⊕⊕○○ Low ^{a,b}	
moderate to severe OHSS - 200 vs. 100 IU (Ngwenya, et al., 2024)	31 per 1,000	19 per 1,000 (7 to 56)	OR 0.62 (0.21 to 1.87)	522 (2 RCTs)	⊕○○○ Very low ^{a,c}	
moderate to severe OHSS - 225/200 vs. 150 IU (Ngwenya, et al., 2024)	27 per 1,000	32 per 1,000 (14 to 73)	OR 1.21 (0.51 to 2.85)	740 (4 RCTs)	⊕○○○ Very low ^{a,c}	
moderate to severe OHSS - 300 vs. 225 IU (Ngwenya, et al., 2024)	44 per 1,000	30 per 1,000 (5 to 156)	OR 0.67 (0.11 to 3.99)	135 (1 RCT)	⊕○○○ Very low ^{a,c}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of performance bias due to lack of blinding and/or selective reporting and/or selection bias due to unclear methods of randomisation.

b. Small number of events.

c. Very serious imprecision associated with a very small number of events.



9 Delayed-start stimulation compared to conventional start stimulation in low responders

Patient or population: low responder women undergoing COS for IVF/ICSI

Intervention: Delayed-start stimulation

Comparison: Conventional start stimulation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with conventional start FSH	Risk with late-start FSH				
Cumulative LBR (Revelli, et al., 2020)	231 per 1,000	0 per 1,000 (0 to 0)	not estimable	22 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Risk of performance and attrition bias by incomplete reporting of methodology.

b. Serious risk of inconsistency because only 1 RCT.

c. Small number of events.



10 Higher versus lower gonadotropin dose for low responder women

Patient or population: low responder women undergoing COS for IVF/ICSI

Intervention: Higher gonadotropin dose

Comparison: Lower gonadotropin dose

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with 300/450IU	Risk with 150IU				
Cumulative LBR						Not reported
LBR/Ongoing PR - 300/450 IU vs. 150 IU (Ngwenya, et al., 2024)	195 per 1,000	225 per 1,000 (159 to 311)	OR 1.20 (0.78 to 1.86)	538 (3 RCTs)	⊕⊕○○ Low ^{a,b}	
Ongoing PR - 400/450 vs. 300 IU (Ngwenya, et al., 2024)	161 per 1,000	129 per 1,000 (35 to 380)	OR 0.77 (0.19 to 3.19)	62 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Live birth rate - 600 vs. 450 IU (Ngwenya, et al., 2024)	108 per 1,000	139 per 1,000 (79 to 234)	OR 1.33 (0.71 to 2.52)	356 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Moderate or severe OHSS 300/450 vs. 150 IU (Ngwenya, et al., 2024)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	286 (2 RCTs)	⊕○○○ Very low ^{a,c}	
Moderate or severe OHSS 400/450 vs. 300 IU (Ngwenya, et al., 2024)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	62 (1 RCT)	⊕○○○ Very low ^{a,c}	
Moderate OHSS 600 vs. 450 IU (Ngwenya, et al., 2024)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	356 (1 RCT)	⊕○○○ Very low ^{a,c}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of performance bias due to lack of blinding and/or selective reporting.

b. Small number of events.

c. Very serious imprecision associated with a very small number of events.



5. Pituitary suppression regimes

11a Long versus short GnRH agonist protocol for pituitary suppression

Patient or population: women undergoing COS for IVF/ICSI

Intervention: long GnRH agonist protocol

Comparison: short GnRH agonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with short GnRH agonist protocol	Risk with long GnRH agonist protocol				
Cumulative LBR						Not reported
LBR/Ongoing PR (Siristatidis et al., 2025)	143 per 1,000	195 per 1,000 (122 to 296)	OR 1.45 (0.83 to 2.52)	381 (5 RCTs)	⊕⊕○○○ Low ^a	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of bias, poor reporting of methods in primary studies.

11b Long GnRH agonist protocol compared to ultrashort GnRH agonist protocol for pituitary suppression

Patient or population: women undergoing COS for IVF/ICSI

Intervention: long GnRH agonist protocol

Comparison: ultrashort GnRH agonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with ultrashort GnRH agonist protocol	Risk with Long GnRH agonist protocol				
Cumulative LBR						Not reported
Live birth rate (Siristatidis, et al., 2025)	122 per 1,000	198 per 1,000 (91 to 376)	OR 1.78 (0.72 to 4.36)	150 (1 RCT)	⊕○○○○ Very low ^{a,b,c}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of bias.

b. Serious risk of inconsistency because only 1 RCT.

c. Small number of events.



12a Long GnRH agonist protocol compared to GnRH antagonist protocol for pituitary suppression

Patient or population: women undergoing COS for IVF/ICSI

Intervention: long GnRH agonist protocol

Comparison: GnRH antagonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GnRH antagonist protocol	Risk with long GnRH agonist protocol				
Cumulative LBR						Not reported
Live birth rate (Al-Inany et al., 2016)	286 per 1,000	290 per 1,000 (254 to 330)	OR 1.02 (0.85 to 1.23)	2303 (12 RCTs)	⊕⊕⊕○ MODERATE ^a	
Live birth rate (Toftager et al., 2016)	222 per 1,000	0 per 1,000 (0 to 0)	not estimable	1023 (1 RCT)	⊕⊕○○ LOW ^{b,c}	
OHSS (Al-Inany, et al., 2016)	114 per 1,000	73 per 1,000 (62 to 85)	OR 0.61 (0.51 to 0.72)	7944 (36 RCTs)	⊕⊕⊕○ MODERATE ^d	
Moderate/severe OHSS (Al-Inany, et al., 2016)	71 per 1,000	39 per 1,000 (30 to 50)	OR 0.53 (0.40 to 0.69)	5141 (20 RCTs)	⊕⊕○○ LOW ^{d,e}	
Severe OHSS (Toftager, et al., 2016)	51 per 1,000	0 per 1,000 (0 to 0)	not estimable	1023 (1 RCT)	⊕⊕○○ LOW ^{b,f}	
Moderate OHSS (Toftager, et al., 2016)	102 per 1,000	0 per 1,000 (0 to 0)	not estimable	1023 (1 RCT)	⊕⊕○○ LOW ^{b,f}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

- a. The confidence interval crosses the line of no effect.
- b. Serious inconsistency because only 1 RCT
- c. Wide confidence intervals, sample size not met
- d. Very wide confidence intervals, small number of events.
- e. Most domains of the risk of bias were assessed as either 'unclear' or 'high'.
- f. Small number of events, sample size not met

12b Short GnRH agonist protocol compared to GnRH antagonist for pituitary suppression

Patient or population: women undergoing COS for IVF/ICSI

Intervention: short GnRH agonist protocol

Comparison: GnRH antagonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GnRH antagonist	Risk with short GnRH agonist protocol				
Cumulative LBR						Not reported
Live birth rate (Gordts et al., 2012)	188 per 1,000	0 per 1,000 (0 to 0)	not estimable	160 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

- a. Serious risk of bias due to poor reporting of methodology
- b. Serious inconsistency because only 1 RCT
- c. Very small number of events.



13a Progesterin compared to GnRH antagonist protocol for pituitary suppression

Patient or population: women undergoing COS for IVF/ICSI

Intervention: progesterin protocol

Comparison: GnRH antagonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GnRH antagonist	Risk with progesterin protocol				
Cumulative LBR (Ye et al., 2024)	529 per 1,000	0 per 1,000 (0 to 0)	not estimable	348 (1 RCT)	⊕⊕○○ Low ^{a,b}	
OHSS (Ye, et al., 2024)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	348 (1 RCT)	⊕○○○ Very low ^{a,b,c}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of performance bias.

b. Serious risk of inconsistency because only 1 RCT.

c. Small number of events.

13b Progesterin compared to GnRH agonist protocol for pituitary suppression

Patient or population: women undergoing COS for IVF/ICSI

Intervention: progesterin protocol

Comparison: GnRH agonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GnRH agonist	Risk with progesterin protocol				
Cumulative LBR						Not reported
LBR/Ongoing PR (Glujovsky et al., 2023)	469 per 1,000	454 per 1,000 (339 to 575)	OR 0.94 (0.58 to 1.53)	260 (1 RCT)	⊕⊕○○ Low ^{a,b}	
OHSS (Glujovsky, et al., 2023)	23 per 1,000	3 per 1,000 (0 to 61)	OR 0.14 (0.01 to 2.73)	260 (1 RCT)	⊕○○○ Very low ^{a,c}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of inconsistency because only 1 RCT.

b. Low number of participants (n < 400) and very wide confidence intervals including both substantial benefit and harm.

c. Low number of participants (n < 400), very low number of events and very wide confidence intervals including both substantial benefit and harm.



13c Progesterin compared to GnRH antagonist protocol for pituitary suppression in low responders

Patient or population: low responder women undergoing COS for IVF/ICSI

Intervention: progesterin protocol

Comparison: GnRH antagonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GnRH antagonist	Risk with progesterin protocol				
Cumulative LBR						Not reported
LBR/Ongoing PR (Glujovsky, et al., 2023)	182 per 1,000	218 per 1,000 (140 to 322)	OR 1.25 (0.73 to 2.13)	340 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
OHSS (Glujovsky, et al., 2023)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	340 (1 RCT)	⊕○○○ Very low ^{a,b,d}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of performance bias.

b. Serious risk of inconsistency because only 1 RCT.

c. Small number of events and the pooled effect included the line of no effect.

d. Small number of patients, small event rate and the pooled effect included the line of no effect.

13d Progesterin compared to GnRH analogue protocol for pituitary suppression for high responders

Patient or population: high responder women undergoing COS for IVF/ICSI

Intervention: progesterin protocol

Comparison: GnRH analogue protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GnRH analogue	Risk with progesterin protocol				
Cumulative LBR (Chen et al., 2024)	485 per 1,000	0 per 1,000 (0 to 0)	not estimable	784 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Live birth rate (Yang et al., 2023)	378 per 1,000	470 per 1,000 (324 to 622)	OR 1.46 (0.79 to 2.71)	167 (1 RCT)	⊕○○○ Very low ^{b,c,d}	
Live birth rate (Chen, et al., 2024)	327 per 1,000	0 per 1,000 (0 to 0)	not estimable	784 (1 RCT)	⊕⊕○○ Low ^{a,b}	
OHSS (Yang, et al., 2023)	17 per 1,000	3 per 1,000 (0 to 65)	OR 0.19 (0.01 to 4.11)	240 (2 RCTs)	⊕○○○ Very low ^{c,d}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of performance bias.

b. Serious risk of inconsistency because only 1 RCT.

c. Serious risk of bias.

d. Small number of patients, very small number of events, wide confidence intervals and the pooled effect includes the line of no effect.



6. Types of gonadotropins and other ovarian stimulation drugs

14 r-hFSH compared to hMG for ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: r-hFSH

Comparison: hMG

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hMG	Risk with r-hFSH				
Cumulative LBR (Bordewijk et al., 2019)	319 per 1,000	291 per 1,000 (255 to 332)	RR 0.91 (0.80 to 1.04)	2109 (3 RCTs)	⊕⊕⊕○ Moderate ^{a,b}	
Live birth rate (Bordewijk, et al., 2019)	263 per 1,000	231 per 1,000 (205 to 260)	RR 0.88 (0.78 to 0.99)	3397 (7 RCTs)	⊕⊕⊕⊕ High ^a	
Live birth rate (Parsanezhad et al., 2017)	400 per 1,000	0 per 1,000 (0 to 0)	not estimable	80 (1 RCT)	⊕⊕○○ LOW ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious inconsistency because only 1 RCT

b. Small number of events

c. The pooled effect crosses the line of no effect.



15 purified FSH compared to r-hFSH for ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: purified FSH

Comparison: r-hFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with r-hFSH	Risk with p-FSH				
Cumulative LBR						Not reported
LBR/ongoing PR (van Wely et al., 2011)	207 per 1,000	248 per 1,000 (201 to 300)	OR 1.26 (0.96 to 1.64)	1430 (5 RCTs)	⊕⊕○○ LOW ^{a,b}	
OHSS (van Wely, et al., 2011)	28 per 1,000	49 per 1,000 (25 to 95)	OR 1.79 (0.89 to 3.62)	1490 (6 RCTs)	⊕⊕○○ LOW ^{a,b}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. High risk of bias associated with poor reporting of methods in one or more primary studies.

b. The pooled effect crosses the line of no effect.

16 highly purified FSH compared to r-hFSH for ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: highly purified FSH

Comparison: r-hFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with r-hFSH	Risk with hp-FSH				
Cumulative LBR						Not reported
Live birth rate (Bordewijk, et al., 2019)	254 per 1,000	262 per 1,000 (229 to 300)	RR 1.03 (0.90 to 1.18)	2458 (12 RCTs)	⊕⊕○○ Low ^{a,b}	
Live birth rate (Murber et al., 2011)	313 per 1,000	0 per 1,000 (0 to 0)	not estimable	67 (1 RCT)	⊕⊕○○ LOW ^{c,d}	
Live birth rate (Parsanezhad, et al., 2017)	400 per 1,000	0 per 1,000 (0 to 0)	not estimable	80 (1 RCT)	⊕⊕○○ LOW ^{c,d}	
Live birth rate (Selman et al., 2013)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	(1 RCT)	⊕○○○ VERY LOW ^{c,d,e}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. High risk of bias associated with poor reporting of methods in one or more primary studies.

b. The pooled effect included the line of no effect and appreciable benefit or harm.

c. Serious inconsistency because only 1 RCT

d. Small number of events

e. Serious risk of bias due to poor reporting of methodology



17a r-hFSH+r-hLH compared to r-hFSH for controlled ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: r-hFSH+r-hLH

Comparison: r-hFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with r-hFSH	Risk with r-hFSH+r-hLH				
Cumulative LBR						Not reported
Live birth rate (Mochtar et al., 2017)	173 per 1,000	217 per 1,000 (151 to 302)	OR 1.32 (0.85 to 2.06)	499 (4 RCTs)	⊕⊕⊕○ MODERATE ^{a,b}	
Live birth rate (Lahoud et al., 2017)	298 per 1,000	233 per 1,000 (119 to 456)	RR 0.78 (0.40 to 1.53)	100 (1 RCT)	⊕○○○ VERY LOW ^{c,d,e}	
OHSS (Mochtar, et al., 2017)	13 per 1,000	5 per 1,000 (2 to 13)	OR 0.38 (0.14 to 1.01)	2178 (6 RCTs)	⊕⊕⊕○ MODERATE ^{e,f,g}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Small number of patients, small number of events.

b. Effect estimate with wide confidence intervals, the pooled effect crosses the line of no effect and appreciable benefit or harm.

c. Serious risk of bias due to poor reporting of methodology

d. Serious inconsistency because only 1 RCT

e. Small event rate.

f. High risk of bias associated with poor reporting of methodology in one or more primary studies.

g. Effect estimate with wide confidence intervals.

17b r-hFSH+r-hLH compared to r-hFSH in low responders

Patient or population: low responder women undergoing COS for IVF/ICSI

Intervention: r-hFSH+r-hLH

Comparison: r-hFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with r-hFSH	Risk with r-hFSH+r-hLH				
Cumulative LBR						Not reported
Live birth rate (Mochtar, et al., 2017)	48 per 1,000	318 per 1,000 (49 to 808)	OR 9.33 (1.03 to 84.20)	43 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Live birth rate (Humaidan et al., 2017)	117 per 1,000	0 per 1,000 (0 to 0)	not estimable	939 (1 RCT)	⊕⊕○○ LOW ^{b,c}	
Mild OHSS (Humaidan, et al., 2017)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	939 (1 RCT)	⊕⊕○○ LOW ^{b,c}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of bias due to poor reporting of methodology

b. Serious inconsistency because only 1 RCT

c. Small number of events



17c r-hFSH+r-hLH compared to r-hFSH for women of advanced age

Patient or population: women of advanced age undergoing COS for IVF/ICSI

Intervention: r-hFSH+r-hLH

Comparison: r-hFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with r-hFSH	Risk with r-hFSH+r-hLH				
Cumulative LBR						Not reported
Live birth rate (Conforti et al., 2021)	138 per 1,000	197 per 1,000 (74 to 427)	OR 1.53 (0.50 to 4.65)	371 (2 RCTs)	⊕⊕○○ Low ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. High heterogeneity between studies, $I^2=67\%$.

b. Large confidence intervals and the pooled effect includes both appreciable effect and little or no effect.

18a r-hFSH combined with hMG compared to r-hFSH for ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: r-hFSH+hMG

Comparison: r-hFSH alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with daily rFSH	Risk with long-acting rFSH				
Cumulative LBR						Not reported
LBR						Not reported
OHSS (Shu et al., 2019)	36 per 1,000	0 per 1,000 (0 to 0)	not estimable	611 (1 RCT)	⊕⊕○○ Low ^{a,b}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of inconsistency because only 1 RCT.

b. Small number of events.



18b mid-phase hMG supplementation to long-acting r-hFSH compared to r-hFSH for ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: r-hFSH+mid-phase hMG supplementation

Comparison: r-hFSH alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with daily r-hFSH	Risk with long-acting r-hFSH				
Cumulative LBR (Decler et al., 2020)	134 per 1,000	0 per 1,000 (0 to 0)	not estimable	128 (1 RCT)	⊕⊕⊕○ Moderate ^a	
Live birth rate (Taronger et al., 2018)	202 per 1,000	0 per 1,000 (0 to 0)	not estimable	221 (1 RCT)	⊕⊕○○ Low ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of inconsistency because only 1 RCT.

b. Risk of selection and/or performance bias.

19 Long-acting r-hFSH compared to daily r-hFSH for ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: long-acting r-hFSH

Comparison: daily r-hFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with daily rFSH	Risk with long-acting rFSH				
Cumulative LBR						Not reported
LBR/ongoing PR (Cozzolino et al., 2019)	280 per 1,000	258 per 1,000 (224 to 294)	RR 0.92 (0.80 to 1.05)	4340 (8 RCTs)	⊕⊕○○ Low ^{a,b}	
Live birth rate (Wu et al., 2025)	291 per 1,000	0 per 1,000 (0 to 0)	not estimable	283 (1 RCT)	⊕⊕⊕○ Moderate ^c	
OHSS (Cozzolino, et al., 2019)	37 per 1,000	42 per 1,000 (30 to 58)	RR 1.15 (0.83 to 1.57)	3749 (5 RCTs)	⊕○○○ Very low ^{a,b,d}	
OHSS (Wu, et al., 2025)	14 per 1,000	0 per 1,000 (0 to 0)	not estimable	283 (1 RCT)	⊕⊕○○ Low ^{c,d}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of detection bias in all included primary studies and attrition bias in 4/8 primary studies.

b. The pooled effect crosses the line of no effect.

c. Serious risk of inconsistency because only 1 RCT.

d. Small number of events.



20a Combinations with hCG compared to conventional ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: combinations of FSH and hCG

Comparison: FSH alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with FSH alone	Risk with FSH+hCG				
Cumulative LBR (50 IU) (Thuesen et al., 2012)	313 per 1,000	0 per 1,000 (0 to 0)	not estimable	31 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
Cumulative LBR (100 IU) (Thuesen, et al., 2012)	313 per 1,000	0 per 1,000 (0 to 0)	not estimable	32 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
Cumulative LBR (150 IU) (Thuesen, et al., 2012)	313 per 1,000	0 per 1,000 (0 to 0)	not estimable	29 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
Live birth rate (50 IU) (Thuesen, et al., 2012)	250 per 1,000	0 per 1,000 (0 to 0)	not estimable	31 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
Live birth rate (100 IU) (Thuesen, et al., 2012)	250 per 1,000	0 per 1,000 (0 to 0)	not estimable	32 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
Live birth rate (150 IU) (Thuesen, et al., 2012)	250 per 1,000	0 per 1,000 (0 to 0)	not estimable	29 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
OHSS (100 IU) (Siristatidis et al., 2022)	24 per 1,000	0 per 1,000 (0 to 0)	not estimable	81 (1 RCT)	⊕○○○ Very low ^{b,c,d}	
OHSS (50 IU) (Thuesen, et al., 2012)	63 per 1,000	0 per 1,000 (0 to 0)	not estimable	31 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
OHSS (100 IU) (Thuesen, et al., 2012)	63 per 1,000	0 per 1,000 (0 to 0)	not estimable	32 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
OHSS (150 IU) (Thuesen, et al., 2012)	63 per 1,000	0 per 1,000 (0 to 0)	not estimable	29 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
OHSS (200 IU) (Koichi et al., 2006)	16 per 1,000	0 per 1,000 (0 to 0)	not estimable	126 (1 RCT)	⊕○○○ Very low ^{b,c,e}	
OHSS (200 IU) (Serafini et al., 2006)	47 per 1,000	0 per 1,000 (0 to 0)	not estimable	188 (1 RCT)	⊕○○○ Very low ^{a,b,c}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Significant risk of performance bias.

b. Serious risk of inconsistency because only 1 RCT.

c. Small number of events.

d. Possible risk of attrition bias.

e. Serious risk of performance bias and possible risk of attrition bias.



20b Combinations with hCG compared to conventional ovarian stimulation in low responders

Patient or population: low responder women undergoing COS for IVF/ICSI

Intervention: mid-phase hCG supplementation

Comparison: rFSH alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with FSH alone	Risk with I FSH+hCG				
Cumulative LBR (Decleer, et al., 2020)	134 per 1,000	0 per 1,000 (0 to 0)	not estimable	128 (1 RCT)	⊕⊕⊕○ Moderate ^a	
Live birth rate (hCG 100 IU) (Madani et al., 2012)	130 per 1,000	0 per 1,000 (0 to 0)	not estimable	44 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Live birth rate (hCG 200 IU) (Madani, et al., 2012)	130 per 1,000	0 per 1,000 (0 to 0)	not estimable	42 (1 RCT)	⊕⊕○○ Low ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of inconsistency because only 1 RCT.

b. Small number of events.

20c Combinations with hCG compared to conventional ovarian stimulation in women with PCOS

Patient or population: women with PCOS undergoing COS for IVF/ICSI

Intervention: hCG supplementation from start of ovarian stimulation

Comparison: hMG alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with FSH alone	Risk with FSH+hCG				
Cumulative LBR						Not reported
Live birth rate (Zhu and Fu, 2019)	355 per 1,000	0 per 1,000 (0 to 0)	not estimable	60 (1 RCT)	⊕⊕○○ Low ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of inconsistency because only 1 RCT.

b. Small number of events.



21a Letrozole in stimulation protocols for IVF/ICSI in high responders

Patient or population: high responder women undergoing COS for IVF/ICSI

Intervention: letrozole addition to gonadotropins

Comparison: gonadotropins alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no letrozole	Risk with letrozole				
Cumulative LBR						Not reported
Live birth rate (Lotfy et al., 2022)	280 per 1,000	0 per 1,000 (0 to 0)	not estimable	100 (1 RCT)	⊕⊕⊕○ Moderate ^a	
Live birth rate (Tshzmachyan and Hambartsoumian, 2020)	375 per 1,000	0 per 1,000 (0 to 0)	not estimable	48 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
Live birth rate (Yang et al., 2019)	625 per 1,000	0 per 1,000 (0 to 0)	not estimable	97 (1 RCT)	⊕⊕○○ Low ^{a,d}	
OHSS (Ghasemi Tehrani et al., 2022)	360 per 1,000	0 per 1,000 (0 to 0)	not estimable	50 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
OHSS (Lotfy, et al., 2022)	100 per 1,000	0 per 1,000 (0 to 0)	not estimable	100 (1 RCT)	⊕⊕○○ Low ^{a,c}	
OHSS (Tshzmachyan and Hambartsoumian, 2020)	417 per 1,000	849 per 1,000 (516 to 967)	OR 7.86 (1.49 to 41.30)	48 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
OHSS (Yang, et al., 2019)	15 per 1,000	0 per 1,000 (0 to 0)	not estimable	130 (1 RCT)	⊕○○○ Very low ^{a,c,d}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of inconsistency because only 1 RCT.

b. Serious risk of performance bias.

c. Small number of events.

d. Serious risk of attrition bias.



21b Letrozole in stimulation protocols for IVF/ICSI in normal responders

Patient or population: normal responder women undergoing COS for IVF/ICSI

Intervention: letrozole addition to gonadotropins

Comparison: gonadotropins alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no letrozole	Risk with letrozole				
Cumulative LBR						Not reported
Live birth rate (Bülow et al., 2022)	387 per 1,000	0 per 1,000 (0 to 0)	not estimable	129 (1 RCT)	⊕⊕⊕○ Moderate ^a	
OHSS (Eftekhar and Saeed, 2020)	40 per 1,000	0 per 1,000 (0 to 0)	not estimable	100 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
OHSS (Mukherjee et al., 2012)	135 per 1,000	0 per 1,000 (0 to 0)	not estimable	94 (1 RCT)	⊕○○○ Very low ^{a,b,d}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of inconsistency because only 1 RCT.

b. Small number of events.

c. Significant risk of performance bias.

d. Serious risk of bias due to incomplete reporting of methodology .

22a Clomiphene citrate in stimulation protocols for high responders

Patient or population: high responder women undergoing COS for IVF/ICSI

Intervention: clomiphene citrate addition to gonadotropins

Comparison: gonadotropins alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with FSH	Risk with clomiphene citrate				
Cumulative LBR - not reported						
Live birth rate (Lotfy, et al., 2022)	280 per 1,000	0 per 1,000 (0 to 0)	not estimable	100 (1 RCT)	⊕⊕⊕○ Moderate ^{a,b}	
OHSS (Lotfy, et al., 2022)	100 per 1,000	0 per 1,000 (0 to 0)	not estimable	100 (1 RCT)	⊕⊕○○ Low ^{a,b}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of inconsistency because only 1 RCT.

b. Small number of events



22b Clomiphene citrate in stimulation protocols for normal responders

Patient or population: normal responder women undergoing COS for IVF/ICSI

Intervention: clomiphene citrate addition to gonadotropins

Comparison: gonadotropins alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with FSH	Risk with clomiphene citrate				
Cumulative LBR						Not reported
Live birth rate (Datta et al., 2021)	353 per 1,000	310 per 1,000 (243 to 395)	RR 0.88 (0.69 to 1.12)	573 (4 RCTs)	⊕⊕⊕○ Moderate ^a	
OHSS (Datta, et al., 2021)	51 per 1,000	6 per 1,000 (2 to 26)	RR 0.12 (0.03 to 0.51)	623 (3 RCTs)	⊕⊕⊕○ Moderate ^a	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Several primary studies with unclear risk of bias due to incomplete reporting of methodology.



8. Adjunct therapies

23 Metformin compared to placebo/no intervention as adjunct during ovarian stimulation for women with PCOS

Patient or population: women with PCOS undergoing COS for IVF/ICSI

Intervention: adjunct metformin

Comparison: placebo/no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with metformin				
Cumulative LBR						Not reported
Live birth rate - long GnRH agonist protocol (Tso et al., 2020)	283 per 1,000	368 per 1,000 (266 to 507)	RR 1.30 (0.94 to 1.79)	651 (6 RCTs)	⊕⊕○○ Low ^{a,b}	
Live birth rate - GnRH antagonist protocol (Tso, et al., 2020)	434 per 1,000	208 per 1,000 (126 to 343)	RR 0.48 (0.29 to 0.79)	153 (1 RCT)	⊕⊕○○ Low ^{c,e}	
Live birth rate (Hussein et al., 2021)	275 per 1,000	0 per 1,000 (0 to 0)	not estimable	320 (1 RCT)	⊕⊕⊕○ Moderate ^c	
Live birth rate (Abdalmageed et al., 2019)	176 per 1,000	0 per 1,000 (0 to 0)	not estimable	102 (1 RCT)	⊕⊕⊕○ Moderate ^c	
OHSS (Tso, et al., 2020)	196 per 1,000	90 per 1,000 (57 to 141)	RR 0.46 (0.29 to 0.72)	1091 (11 RCTs)	⊕⊕○○ Low ^{a,d}	
OHSS (Hussein, et al., 2021)	6 per 1,000	0 per 1,000 (0 to 0)	not estimable	320 (1 RCT)	⊕⊕○○ Low ^{c,d}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

- a. The majority of the primary studies have unclear or high risk of bias.
- b. Low number of events (total number of events < 300) and 95% CI includes both appreciable effect and little or no effect.
- c. Serious risk of inconsistency because only 1 RCT.
- d. Small number of events.
- e. Low number of events (total number of events < 300).



24a Growth hormone compared to placebo/no intervention as adjunct during ovarian stimulation for normal responders

Patient or population: women undergoing COS for IVF/ICSI

Intervention: adjunct growth hormone

Comparison: placebo/no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with GH				
Cumulative LBR						Not reported
Live birth rate (Sood et al., 2021)	146 per 1,000	185 per 1,000 (64 to 432)	OR 1.32 (0.40 to 4.43)	80 (2 RCTs)	⊕○○○ Very low ^{a,b}	
Live birth rate (Mourad et al., 2025)	333 per 1,000	0 per 1,000 (0 to 0)	not estimable	168 (1 RCT)	⊕⊕○○ Low ^{c,d}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Downgraded one level due to randomisation bias and selective reporting.

b. Downgraded 2 levels due to imprecision, small study numbers and very wide confidence intervals.

c. Serious risk of bias due to randomisation bias and lack of blinding.

d. Serious risk of inconsistency because only 1 RCT.

24b Growth hormone compared to placebo/no intervention as adjunct during ovarian stimulation for low responders

Patient or population: low responder women undergoing COS for IVF/ICSI

Intervention: adjunct growth hormone

Comparison: placebo/no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with GH				
Cumulative LBR						Not reported
Live birth rate (Liu et al., 2025)	104 per 1,000	172 per 1,000 (124 to 234)	OR 1.80 (1.22 to 2.64)	945 (9 RCTs)	⊕○○○ Very low ^{a,b,c}	
Live birth rate (Li et al., 2020)	176 per 1,000	0 per 1,000 (0 to 0)	not estimable	158 (1 RCT)	⊕○○○ Very low ^{d,e,f}	
OHSS (Li, et al., 2020)	20 per 1,000	0 per 1,000 (0 to 0)	not estimable	158 (1 RCT)	⊕○○○ Very low ^{d,e,f}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of attrition bias in the primary studies.

b. Downgraded one level due to imprecision, small numbers and wide confidence intervals.

c. Downgraded one level due to publication bias as per funnel plot.

d. Significant risk of performance bias.

e. Serious risk of inconsistency because only 1 RCT.

f. Small number of patients and small number of events.



25 Testosterone compared to placebo/no intervention as adjunct during ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: adjunct testosterone

Comparison: placebo/no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with testosterone				
Cumulative LBR						Not reported
LBR/ongoing PR (Naik et al., 2024)	98 per 1,000	216 per 1,000 (149 to 303)	OR 2.53 (1.61 to 3.99)	716 (8 RCTs)	⊕⊕⊕○ Moderate ^a	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Downgraded one level for risk of bias: performance and detection bias due to lack of blinding.

26 Dehydroepiandrosterone (DHEA) compared to placebo/no intervention as adjunct during ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: adjunct DHEA

Comparison: placebo/no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with DHEA				
Cumulative LBR						Not reported
LBR/Ongoing PR (Huang et al., 2025)	141 per 1,000	179 per 1,000 (139 to 230)	OR 1.33 (0.98 to 1.82)	1217 (10 RCTs)	⊕⊕○○ Low ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Methods of allocation concealment not clearly described, or too many participants lost to follow-up, or high risk of selective reporting bias.

b. Small sample sizes, or very wide confidence intervals.



27 Aspirin compared to placebo/no intervention as adjunct during ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: adjunct aspirin

Comparison: placebo/no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with aspirin				
Cumulative LBR						Not reported
Live birth rate (Siristatidis et al., 2016)	225 per 1,000	205 per 1,000 (162 to 259)	RR 0.91 (0.72 to 1.15)	1053 (3 RCTs)	⊕⊕⊕○ Moderate ^a	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Downgraded one level for serious imprecision with low event rate. Confidence interval compatible with no effect from the intervention or with clinically meaningful benefit in the control group.

28a Myo-inositol compared to placebo/no intervention as adjunct during ovarian stimulation for women with PCOS

Patient or population: women with PCOS undergoing COS for IVF/ICSI

Intervention: adjunct myo-inositol

Comparison: placebo/no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with myo-inositol				
Cumulative LBR						Not reported
Live birth rate (Showell et al., 2018)	116 per 1,000	242 per 1,000 (90 to 507)	OR 2.42 (0.75 to 7.83)	84 (2 RCTs)	⊕○○○ Very low ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Downgraded one level due to risk of bias, as unclear blinding in one study and unclear selective reporting in both studies.

b. Downgraded two levels due to imprecision, as both studies has small sample sizes and confidence intervals are wide.



28b Myo-inositol compared to placebo/no intervention as adjunct during ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: adjunct myo-inositol

Comparison: placebo/no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with myo-inositol				
Cumulative LBR						Not reported
Live birth rate (Seyedoshohadaei et al., 2022)	100 per 1,000	0 per 1,000 (0 to 0)	not estimable	60 (1 RCT)	⊕⊕○○ Low ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of inconsistency because only 1 RCT.

b. Small number of events.



17. Triggering of final oocyte maturation

29 Recombinant hCG compared to urinary hCG for final oocyte maturation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: recombinant hCG

Comparison: urinary hCG

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with urinary hCG	Risk with recombinant hCG				
Cumulative LBR						Not reported
LBR/ongoing PR (Youssef et al., 2016)	366 per 1,000	399 per 1,000 (339 to 462)	OR 1.15 (0.89 to 1.49)	1136 (7 RCTs)	⊕⊕⊕○ MODERATE ^a	
Moderate/severe OHSS (Youssef, et al., 2016)	10 per 1,000	17 per 1,000 (4 to 77)	OR 1.76 (0.37 to 8.45)	417 (3 RCTs)	⊕⊕○○ LOW ^b	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. The pooled effect included both the line of no effect and appreciable benefit or harm.

b. Very wide confidence intervals, small number of events.

30 Recombinant LH compared to urinary hCG for final oocyte maturation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: recombinant LH

Comparison: urinary hCG

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with urinary hCG	Risk with recombinant LH				
Cumulative LBR						Not reported
LBR/ongoing PR (Youssef, et al., 2016)	191 per 1,000	184 per 1,000 (108 to 297)	OR 0.95 (0.51 to 1.78)	289 (2 RCTs)	⊕○○○ VERY LOW ^{a,b,c,d}	
Moderate OHSS (Youssef, et al., 2016)	121 per 1,000	102 per 1,000 (52 to 189)	OR 0.83 (0.40 to 1.70)	289 (2 RCTs)	⊕○○○ VERY LOW ^{a,b,c,d}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. One of the two RCT's did not provide information about methods of randomization, allocation concealment or blinding.

b. The pooled effect included both the line of no effect and appreciable benefit or harm.

c. Small number of events.

d. Very wide confidence intervals.



31 GnRH agonist compared to hCG for final oocyte maturation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: GnRH agonist trigger

Comparison: hCG trigger

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG	Risk with GnRH agonist				
Cumulative LBR						Not reported
Live birth rate (Beebejaun et al., 2024)	225 per 1,000	185 per 1,000 (133 to 255)	RR 0.82 (0.59 to 1.13)	723 (3 RCTs)	⊕⊕○○○ Low ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of performance bias in the primary studies.

b. Significant heterogeneity between primary studies ($I^2=85\%$).

32a Dual trigger compared to hCG for final oocyte maturation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: Dual trigger

Comparison: hCG trigger

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG	Risk with dual trigger				
Cumulative LBR						Not reported
Live birth rate (Beebejaun, et al., 2024)	279 per 1,000	366 per 1,000 (279 to 475)	RR 1.31 (1.00 to 1.70)	154 (1 RCT)	⊕⊕○○○ Low ^{a,b}	
Live birth rate (Zhou et al., 2022)	321 per 1,000	0 per 1,000 (0 to 0)	not estimable	112 (1 RCT)	⊕⊕○○○ Low ^{b,c}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of performance bias.

b. Serious risk of inconsistency because only 1 RCT.

c. Risk of selection bias.



32b Dual trigger compared to GnRH agonist for final oocyte maturation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: Dual trigger

Comparison: GnRH agonist trigger

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GnRH agonist	Risk with dual trigger				
Cumulative LBR						Not reported
Live birth rate (Zhou, et al., 2022)	67 per 1,000	0 per 1,000 (0 to 0)	not estimable	34 (1 RCT)	⊕⊕○○○ Low ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Risk of selection bias.

b. Serious risk of inconsistency because only 1 RCT.

32c Dual trigger compared to hCG for final oocyte maturation for low responders

Patient or population: low responder women undergoing COS for IVF/ICSI

Intervention: Dual trigger

Comparison: hCG trigger

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG	Risk with dual trigger				
Cumulative LBR						Not reported
Live birth rate (Keskin et al., 2023)	364 per 1,000	0 per 1,000 (0 to 0)	not estimable	112 (1 RCT)	⊕⊕○○○ Low ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Risk of selection bias.

b. Serious risk of inconsistency because only 1 RCT.



33 Double trigger compared to hCG for final oocyte maturation

Patient or population: women undergoing COS for IVF/ICSI

Intervention: Double trigger

Comparison: hCG trigger

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG	Risk with double trigger				
Cumulative LBR	360 per 1,000	0 per 1,000 (0 to 0)	not estimable	61 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Live birth rate (Yan et al., 2023)	364 per 1,000	0 per 1,000 (0 to 0)	not estimable	15 (1 RCT)	⊕⊕○○ Low ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Two of the trials (Humaidan et al., 2005; Kolibianakis et al., 2005) included were prematurely discontinued because of the comparatively lower pregnancy rate observed after GnRH agonist treatment

b. Serious risk of bias due to incomplete reporting of methodology

c. Small number of events, large confidence intervals



18. Luteal phase support (LPS)

34 Progesterone compared to placebo or no intervention for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: progesterone

Comparison: placebo or no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo/no intervention	Risk with progesterone				
Cumulative LBR						Not reported
Live birth rate (Abate et al., 1999)	38 per 1,000	144 per 1,000 (36 to 434)	OR 4.21 (0.93 to 19.18)	156 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Inadequate reporting of study methods. Risk of bias unclear in most domains of most studies.

b. Very small number of events.

c. Effect estimate with very wide confidence intervals.

35a Subcutaneous compared to vaginal progesterone for luteal support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: subcutaneous progesterone

Comparison: vaginal progesterone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with vaginal progesterone	Risk with subcutaneous				
Cumulative LBR						Not reported
Live birth (Doblinger et al., 2016)	376 per 1,000	349 per 1,000 (301 to 400)	OR 0.889 (0.714 to 1.106)	1435 (2 RCTs)	⊕⊕⊕○ MODERATE ^a	
OHSS (Doblinger, et al., 2016)	36 per 1,000	37 per 1,000 (22 to 63)	OR 1.04 (0.60 to 1.81)	1435 (2 RCTs)	⊕⊕⊕○ MODERATE ^a	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. The pooled effect included the line of no effect.



35b Vaginal/rectal compared to oral progesterone for luteal support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: vaginal/rectal progesterone

Comparison: oral progesterone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with oral progesterone	Risk with vaginal/rectal				
Cumulative LBR						Not reported
Live birth/ongoing PR (van der Linden et al., 2015)	217 per 1,000	248 per 1,000 (187 to 319)	OR 1.19 (0.83 to 1.69)	857 (4 RCTs)	⊕⊕○○ LOW ^{a,b}	
Live birth rate (400 mg) (Niu et al., 2023)	355 per 1,000	0 per 1,000 (0 to 0)	not estimable	870 (1 RCT)	⊕⊕⊕○ Moderate ^c	
Live birth rate (600 mg) (Niu, et al., 2023)	355 per 1,000	0 per 1,000 (0 to 0)	not estimable	880 (1 RCT)	⊕⊕⊕○ Moderate ^c	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of bias due to poor reporting of methodology.

b. The pooled effect crosses the line of no effect.

c. Serious risk of inconsistency because only 1 RCT.

35c Intramuscular compared to vaginal/rectal progesterone for luteal support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: intramuscular progesterone

Comparison: vaginal/rectal progesterone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with vaginal/rectal progesterone	Risk with intramuscular				
Cumulative LBR						Not reported
Live birth/ongoing PR (van der Linden, et al., 2015)	306 per 1,000	353 per 1,000 (312 to 398)	OR 1.24 (1.03 to 1.50)	2039 (7 RCTs)	⊕⊕○○ LOW ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of bias due to poor reporting of methodology.

b. Significant heterogeneity of results: $I^2=71\%$



35d Intramuscular compared to oral progesterone for luteal support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: intramuscular progesterone

Comparison: oral progesterone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with oral progesterone	Risk with intramuscular				
Cumulative LBR						Not reported
Live birth/ongoing PR (van der Linden, et al., 2015)	200 per 1,000	151 per 1,000 (34 to 478)	OR 0.71 (0.14 to 3.66)	40 (1 RCT)	⊕○○○ VERY LOW a,b,c,d	
OHSS (van der Linden, et al., 2015)	50 per 1,000	50 per 1,000 (3 to 475)	OR 1.00 (0.06 to 17.18)	40 (1 RCT)	⊕○○○ VERY LOW a,b,c,d	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

- a. Serious risk of bias due to poor reporting of methodology.
- b. Serious inconsistency because only 1 RCT.
- c. Small number of patients, small event rate.
- d. The pooled effect crosses the line of no effect.

36a Progesterone LPS started on the day of OR compared to day after OR

Patient or population: women undergoing OS for IVF/ICSI

Intervention: progesterone LPS started on the day of OR

Comparison: progesterone LPS started on the day after OR

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone LPS started on the day after OR	Risk with progesterone LPS started on the day of OR				
Cumulative LBR						Not reported
Live birth rate (Gao et al., 2018)	457 per 1,000	0 per 1,000 (0 to 0)	not estimable	197 (1 RCT)	⊕⊕○○ LOW a,b	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

- a. Serious inconsistency because only 1 RCT.
- b. Small number of patients, small number of events



36b Progesterone LPS started on the evening of OR compared to evening of ET

Patient or population: women undergoing OS for IVF/ICSI

Intervention: progesterone LPS started on the evening of OR

Comparison: progesterone LPS started on the evening of ET

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone LPS started on evening of ET	Risk with progesterone LPS started on the evening of OR				
Cumulative LBR						Not reported
Live birth rate (Mochtar et al., 2006)	205 per 1,000	199 per 1,000 (123 to 319)	RR 0.97 (0.60 to 1.56)	255 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of bias due to incomplete reporting of methodology

b. Serious inconsistency because only 1 RCT.

c. Small number of patients, small number of events

36c Progesterone LPS started before OR compared to after OR

Patient or population: women undergoing OS for IVF/ICSI

Intervention: progesterone LPS started before OR

Comparison: progesterone LPS started after OR

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone LPS started after OR	Risk with progesterone LPS started before OR				
Cumulative LBR						Not reported
Live birth rate (Mochtar, et al., 2006)	211 per 1,000	198 per 1,000 (122 to 321)	RR 0.94 (0.58 to 1.52)	258 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of bias due to incomplete reporting of methodology

b. Serious inconsistency because only 1 RCT.

c. Small number of patients, small number of events



37 Progesterone LPS until pregnancy test compared to Progesterone LPS until week 6/7

Patient or population: women undergoing OS for IVF/ICSI

Intervention: Progesterone LPS until pregnancy test

Comparison: Progesterone LPS until week 6/7

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Progesterone LPS until week 6/7	Risk with Progesterone LPS until pregnancy test				
Cumulative LBR						Not reported
Live birth rate (Watters et al., 2020)	835 per 1,000	785 per 1,000 (701 to 835)	RR 0.94 (0.84 to 1.00)	830 (3 RCTs)	⊕⊕○○ Low ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of bias due to incomplete reporting of methodology in the primary studies.

b. The pooled effect includes the line of no effect.

38 Dydrogesterone compared to progesterone for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: dydrogesterone

Comparison: progesterone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone	Risk with dydrogesterone				
Cumulative LBR						Not reported
Live birth rate (Griesinger et al., 2020)	259 per 1,000	285 per 1,000 (257 to 316)	OR 1.14 (0.99 to 1.32)	4162 (5 RCTs)	⊕⊕⊕○ Moderate ^a	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of bias due to incomplete reporting of methodology in primary studies.



39 Progesterone compared to progesterone and oestradiol for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: progesterone

Comparison: progesterone + oestradiol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone+oestradiol	Risk with progesterone				
Cumulative LBR						Not reported
Live birth/ongoing PR (van der Linden, et al., 2015)	375 per 1,000	402 per 1,000 (353 to 453)	OR 1.12 (0.91 to 1.38)	1651 (9 RCTs)	⊕⊕⊕○ MODERATE ^a	
OHSS (van der Linden, et al., 2015)	39 per 1,000	23 per 1,000 (8 to 63)	OR 0.58 (0.20 to 1.68)	461 (2 RCTs)	⊕⊕○○ LOW ^{a,d,e}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

- a. Very wide confidence intervals, the pooled effect included both the line of no effect and appreciable benefit or harm.
- b. Risk of performance bias
- c. Serious inconsistency because only 1 RCT
- d. Inadequate reporting of study methods. Risk of bias unclear in most domains of most studies.
- e. Small number of events

40a hCG compared to no intervention for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: hCG

Comparison: no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with hCG				
Cumulative LBR						Not reported
Live birth/ongoing PR (van der Linden, et al., 2015)	119 per 1,000	191 per 1,000 (127 to 278)	OR 1.76 (1.08 to 2.86)	527 (3 RCTs)	⊕⊕○○ LOW ^{a,b,c}	
OHSS (van der Linden, et al., 2015)	41 per 1,000	155 per 1,000 (76 to 292)	OR 4.28 (1.91 to 9.60)	387 (1 RCT)	⊕○○○ VERY LOW ^{a,c,d}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

- a. Inadequate reporting of study methods. Risk of bias unclear in most domains of most studies.
- b. Effect estimate with wide confidence intervals.
- c. Very small number of events.
- d. Serious inconsistency because only 1 RCT.



40b hCG compared to progesterone for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: hCG

Comparison: progesterone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone	Risk with hCG				
Cumulative LBR						Not reported
Live birth/ongoing PR (van der Linden, et al., 2015)	249 per 1,000	234 per 1,000 (152 to 342)	OR 0.92 (0.54 to 1.57)	434 (4 RCTs)	⊕⊕○○ LOW ^{a,b,c}	
Live birth rate (low risk of OHSS) (Humaidan et al., 2021)	463 per 1,000	0 per 1,000 (0 to 0)	not estimable	104 (1 RCT)	⊕⊕⊕○ Moderate ^d	
Live birth rate (risk of OHSS) (Humaidan, et al., 2021)	577 per 1,000	0 per 1,000 (0 to 0)	not estimable	101 (1 RCT)	⊕⊕⊕○ Moderate ^d	
OHSS (van der Linden, et al., 2015)	68 per 1,000	40 per 1,000 (23 to 68)	OR 0.57 (0.32 to 1.00)	615 (4 RCTs)	⊕⊕○○ LOW ^{a,c,d}	
OHSS (low risk of OHSS) (Humaidan, et al., 2021)	577 per 1,000	0 per 1,000 (0 to 0)	not estimable	101 (1 RCT)	⊕⊕○○ Low ^{c,d}	
OHSS (risk of OHSS) (Humaidan, et al., 2021)	77 per 1,000	0 per 1,000 (0 to 0)	not estimable	98 (1 RCT)	⊕⊕○○ Low ^{c,d}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Inadequate reporting of study methods. Risk of bias unclear in most domains of most studies.

b. Effect estimate with wide confidence intervals, the pooled effect included the line of no effect

c. Low event rate

d. Serious risk of inconsistency because only 1 RCT.

41 Progesterone with GnRH agonist bolus compared to progesterone for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: progesterone with GnRH agonist bolus

Comparison: progesterone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone	Risk with progesterone+GnRHa				
Cumulative LBR						Not reported
Live birth rate (Liu et al., 2022)	307 per 1,000	364 per 1,000 (285 to 449)	OR 1.29 (0.90 to 1.84)	1909 (6 RCTs)	⊕⊕○○ Low ^{a,b}	
OHSS						Not reported

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Significant heterogeneity between primary studies ($I^2 = 65\%$).

b. The pooled effect included both the line of no effect.



42 Progesterone with repeated GnRH agonist doses compared to progesterone for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: progesterone with repeated doses of GnRH agonist

Comparison: progesterone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone	Risk with progesterone+repeated GnRH agonist				
Cumulative LBR						Not reported
Live birth/ongoing PR (van der Linden, et al., 2015)	256 per 1,000	180 per 1,000 (126 to 252)	OR 0.64 (0.42 to 0.98)	1325 (5 RCTs)	⊕⊕○○ LOW ^{a,b,c}	
OHSS (van der Linden, et al., 2015)	53 per 1,000	53 per 1,000 (18 to 143)	OR 1.00 (0.33 to 3.01)	179 (1 RCT)	⊕○○○ VERY LOW ^{d,e,f}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

- a. Evidence of significant heterogeneity ($I^2=60\%$)
- b. Effect estimate with wide confidence intervals.
- c. Small number of events.
- d. Lack of detail to make a judgement of risk of bias
- e. Serious inconsistency because only 1 RCT.
- f. Small number of patients, low event rate

43 LH compared to progesterone for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: LH

Comparison: progesterone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone	Risk with LH				
Cumulative LBR						Not reported
Live birth rate (Papanikolaou et al., 2011)	235 per 1,000	0 per 1,000 (0 to 0)	not estimable	35 (1 RCT)	⊕⊕○○ LOW ^{a,b}	
OHSS (Papanikolaou, et al., 2011)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	35 (1 RCT)	⊕⊕○○ LOW ^{a,b}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

- a. Serious inconsistency because only 1 RCT.
- b. Small number of patients, small event rate.



19. Prevention of OHSS

44a GnRH agonist compared to hCG for final oocyte maturation in high responders

Patient or population: high responder women undergoing OS for IVF/ICSI

Intervention: GnRH agonist

Comparison: hCG

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG	Risk with GnRH agonist				
Cumulative LBR						Not reported
Live birth rate (Babayof et al., 2006)	154 per 1,000	0 per 1,000 (0 to 0)	not estimable	28 (1 RCT)	⊕⊕○○ LOW ^{c,d}	
Moderate/severe OHSS (Youssef et al., 2014)	107 per 1,000	11 per 1,000 (2 to 59)	OR 0.09 (0.02 to 0.52)	212 (3 RCTs)	⊕⊕○○ LOW ^{a,b}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of bias due to incomplete reporting of methodology in the primary studies

b. Small number of events

c. Serious inconsistency because only 1 RCT

d. Small number of patients, small number of events

e. Serious risk of bias due to incomplete reporting of methodology



44b Fresh transfer compared to freeze-all for prevention of OHSS in high responders

Patient or population: high responder women undergoing OS for IVF/ICSI

Intervention: fresh transfer

Comparison: freeze-all

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with freeze-all	Risk with fresh transfer				
Cumulative LBR						Not reported
Live birth rate (Santos-Ribeiro et al., 2020)	416 per 1,000	0 per 1,000 (0 to 0)	not estimable	205 (1 RCT)	⊕⊕⊕○ Moderate ^a	
Live birth rate (Aflatoonian et al., 2018)	273 per 1,000	277 per 1,000 (176 to 403)	OR 1.02 (0.57 to 1.80)	240 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Moderate-to-severe OHSS (Santos-Ribeiro, et al., 2020)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	209 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Moderate OHSS (Aflatoonian, et al., 2018)	58 per 1,000	0 per 1,000 (0 to 0)	not estimable	240 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Risk of selection and/or performance bias

b. Serious inconsistency because only 1 study

c. Small number of events

44c GnRH agonist compared to hCG non-10.000 IU for final oocyte maturation in high responders

Patient or population: high responder women undergoing OS for IVF/ICSI

Intervention: GnRH agonist

Comparison: hCG non-10.000 IU

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG non-10.000 IU	Risk with GnRH agonist				
Cumulative LBR						Not reported
OHSS (Humaidan et al., 2013)	34 per 1,000	0 per 1,000 (0 to 0)	not estimable	118 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Ongoing PR (Humaidan, et al., 2013)	259 per 1,000	282 per 1,000 (155 to 512)	RR 1.09 (0.60 to 1.98)	118 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of bias due to incomplete reporting of methodology

b. Serious inconsistency because only 1 RCT

c. Small number of patients, small number of events



45 Dopamine agonists compared to placebo/no treatment for prevention of OHSS

Patient or population: women undergoing OS for IVF/ICSI

Intervention: Dopamine agonists

Comparison: Placebo/no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with Dopamine agonists				
Cumulative LBR						Not reported
Live birth rate (Tang et al., 2021)	324 per 1,000	315 per 1,000 (223 to 426)	OR 0.96 (0.60 to 1.55)	362 (3 RCTs)	⊕⊕○○ Low ^{a,b}	
OHSS (Tang, et al., 2021)	268 per 1,000	105 per 1,000 (78 to 139)	OR 0.32 (0.23 to 0.44)	1202 (10 RCTs)	⊕⊕○○ Low ^{a,b}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Serious risk of bias due to incomplete reporting of methodology in the primary studies.

b. Small number of events.

46 Freeze-all protocol compared to fresh transfer for prevention of OHSS

Patient or population: women undergoing OS for IVF/ICSI

Intervention: Freeze-all protocol

Comparison: fresh transfer

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with fresh transfer	Risk with Freeze-all protocol				
Cumulative LBR (Zaat et al., 2021)	608 per 1,000	626 per 1,000 (595 to 654)	OR 1.08 (0.95 to 1.22)	4712 (8 RCTs)	⊕⊕⊕○ Moderate ^a	
OHSS (Zaat, et al., 2021)	37 per 1,000	10 per 1,000 (6 to 15)	OR 0.26 (0.17 to 0.39)	4478 (6 RCTs)	⊕⊕○○ Low ^{a,b}	

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

a. Downgraded one level due to serious risk of bias associated with lack of power calculation (unclear what determined end of study) and/or use of interim analysis that was calculated per transfer (unit of analysis error) with absence of adequate stopping rules (possible overestimation of treatment effect).

b. Small number of events.



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