Annex 2: 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)	№ 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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with pre-treatment with oestradiol				
Cumulative LBR (Cédrin-Durnerin et al., 2024)	229 per 1,000	**0 per 1,000** (0 to 0)	not estimable	291 (1 RCT)	⨁⨁◯◯ Low[a,b]	
LBR (Cédrin-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)	№ 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)	№ 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)	№ 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)	№ 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)	№ 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)	№ 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: poor responder 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)	№ 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)	№ 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)	№ 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)	№ 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)	№ 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)	№ 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)	№ 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)	№ 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)	№ 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)	№ 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)	№ 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 Progestin compared to GnRH antagonist protocol for pituitary suppression

Patient or population: women undergoing COS for IVF/ICSI
Intervention: progestin protocol
Comparison: GnRH antagonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GnRH antagonist	Risk with short GnRH agonist 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 Progestin compared to GnRH agonist protocol for pituitary suppression

Patient or population: women undergoing COS for IVF/ICSI
Intervention: progestin protocol
Comparison: GnRH agonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GnRH antagonist	Risk with short GnRH agonist 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 Progestin compared to GnRH antagonist protocol for pituitary suppression in low responders

Patient or population: low responder women undergoing COS for IVF/ICSI
Intervention: progestin protocol
Comparison: GnRH antagonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GnRH antagonist	Risk with short GnRH agonist 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 Progestin compared to GnRH analogue protocol for pituitary suppression for high responders

Patient or population: high responder women undergoing COS for IVF/ICSI
Intervention: progestin protocol
Comparison: GnRH analogue protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GnRH antagonist	Risk with short GnRH agonist protocol				
Cumulative LBR (Chen)	485 per 1,000	**0 per 1,000** (0 to 0)	not estimable	784 (1 RCT)	⊕⊕◯◯ Low[a,b]	
Live birth rate (Yang)	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)	327 per 1,000	**0 per 1,000** (0 to 0)	not estimable	784 (1 RCT)	⊕⊕◯◯ Low[a,b]	
OHSS (Yang)	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 rFSH compared to hMG for ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI
Intervention: rFSH
Comparison: hMG

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hMG	Risk with rFSH				
Cumulative LBR						Not reported
LBR/ongoing PR (van Wely et al., 2011)	255 per 1,000	**223 per 1,000** (198 to 253)	**OR 0.84** (0.72 to 0.99)	3197 (11 RCTs)	⊕⊕⊕⊕ HIGH	
Cumulative LBR (Devroey et al., 2012)	401 per 1,000	**0 per 1,000** (0 to 0)	not estimable	749 (1 RCT)	⊕⊕⊕◯ MODERATE [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 (van Wely, et al., 2011)	10 per 1,000	**10 per 1,000** (6 to 18)	**OR 1.00** (0.58 to 1.71)	4197 (11 RCTs)	⊕⊕⊕◯ MODERATE [c]	
OHSS (Devroey, et al., 2012)	27 per 1,000	**0 per 1,000** (0 to 0)	not estimable	749 (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 events
c. The pooled effect crosses the line of no effect.

15 purified FSH compared to rFSH for ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI
Intervention: purified FSH
Comparison: rFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with rFSH	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 rFSH for ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI
Intervention: highly purified FSH
Comparison: rFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with rFSH	Risk with hp-FSH				
Cumulative LBR						Not reported
LBR/ongoing PR (van Wely, et al., 2011)	266 per 1,000	**272 per 1,000** (238 to 307)	**OR 1.03** (0.86 to 1.22)	2712 (13 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 (van Wely, et al., 2011)	27 per 1,000	**30 per 1,000** (19 to 46)	**OR 1.11** (0.70 to 1.75)	3053 (16 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 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 rFSH+rLH compared to rFSH for controlled ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI
Intervention: rFSH+rLH
Comparison: rFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with rFSH	Risk with rFSH+rLH				
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 rFSH+rLH compared to rFSH in low responders

Patient or population: low responder women undergoing COS for IVF/ICSI
Intervention: rFSH+rLH
Comparison: rFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with rFSH	Risk with rFSH+rLH				
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 rFSH+rLH compared to rFSH for women of advanced age

Patient or population: women of advanced age undergoing COS for IVF/ICSI
Intervention: rFSH+rLH
Comparison: rFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with rFSH	Risk with rFSH+rLH				
Cumulative LBR						Not reported
Live birth rate	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 rFSH combined with hMG compared to rFSH for ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI
Intervention: rFSH+hMG
Comparison: rFSH alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ 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 rFSH compared to rFSH for ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI
Intervention: rFSH+mid-phase hMG supplementation
Comparison: rFSH alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with daily rFSH	Risk with long-acting rFSH				
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 (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 rFSH compared to daily rFSH for ovarian stimulation

Patient or population: women undergoing COS for IVF/ICSI
Intervention: long-acting rFSH
Comparison: daily rFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ 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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no letrozole	Risk with letrozole				
Cumulative LBR (50 IU) Thuesen	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	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	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	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	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	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	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	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	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	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 2007	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	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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no letrozole	Risk with letrozole				
Cumulative LBR (Decleer)	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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no letrozole	Risk with letrozole				
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)	№ 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)	№ 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 (Hossein Rashidi et al., 2022)	196 per 1,000	**0 per 1,000** (0 to 0)	not estimable	214 (1 RCT)	⨁⨁◯◯ Low[a,b]	
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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with FSH	Risk with clomiphene citrate				
Cumulative LBR - not reported						
Live birth rate (Lotfy)	280 per 1,000	**0 per 1,000** (0 to 0)	not estimable	100 (1 RCT)	⨁⨁⨁◯ Moderate[a,b]	
OHSS (Lotfy)	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)	№ 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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with testosterone				
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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with testosterone				
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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with testosterone				
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)	№ 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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no DHEA	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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no DHEA	Risk with DHEA				
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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no DHEA	Risk with DHEA				
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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no DHEA	Risk with DHEA				
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)	№ 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)	№ 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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG	Risk with GnRH agonist				
Cumulative LBR						Not reported
Live birth rate (Beebeejaun 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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG	Risk with GnRH agonist				
Cumulative LBR						Not reported
Live birth rate (Beebeejaun, 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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG	Risk with GnRH agonist				
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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG	Risk with GnRH agonist				
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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG	Risk with GnRH agonist				
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 Progestins compared to placebo or no intervention for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI
Intervention: progestins
Comparison: placebo or no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo/no intervention	Risk with progesterone				
Cumulative LBR						Not reported
Live birth/ongoing PR (van der Linden et al., 2015)	101 per 1,000	**165 per 1,000** (109 to 243)	**OR 1.77** (1.09 to 2.86)	642 (5 RCTs)	⊕◯◯◯ 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)	№ 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)	№ 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)	№ 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)	№ 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)	№ 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)	№ 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)	№ 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)	№ 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)	№ 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]	
Live birth rate (Atarieh et al., 2024)	413 per 1,000	**0 per 1,000** (0 to 0)	not estimable	207 (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 bias due to incomplete reporting of methodology in primary studies.
b. Significant risk of performance bias.
c. Serious risk of inconsistency because only 1 RCT.

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)	№ 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)	№ 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)	№ 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)	№ 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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone	Risk with progesterone+repeated GnRHa				
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)	№ 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)	№ 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)	№ 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)	№ 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)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with albumin	Risk with Freeze-all				
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)	№ 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.

REFERENCES

Abdalmageed OS, Farghaly TA, Abdelaleem AA, Abdelmagied AE, Ali MK, Abbas AM. Impact of Metformin on IVF Outcomes in Overweight and Obese Women With Polycystic Ovary Syndrome: A Randomized Double-Blind Controlled Trial. *Reproductive sciences (Thousand Oaks, Calif)* 2019;26: 1336-1342.

Aflatoonian A, Mansoori-Torshizi M, Farid Mojtahedi M, Aflatoonian B, Khalili MA, Amir-Arjmand MH, Soleimani M, Aflatoonian N, Oskouian H, Tabibnejad N, Humaidan P. Fresh versus frozen embryo transfer after gonadotropin-releasing hormone agonist trigger in gonadotropin-releasing hormone antagonist cycles among high responder women: A randomized, multi-center study. *International journal of reproductive biomedicine (Yazd, Iran)* 2018;16: 9-18.

Al-Inany HG, Youssef MA, Ayeleke RO, Brown J, Lam WS, Broekmans FJ. Gonadotrophin-releasing hormone antagonists for assisted reproductive technology. *The Cochrane database of systematic reviews* 2016;4: Cd001750.

Atarieh M, Javadian M, Basirat Z, Kashifard M, Yazdani S, Adib-Rad H, Abdollahzade-Delavar M, Gholinia H. Comparison of the effect of dydrogesterone and natural micronized progesterone for luteal-phase support in assisted reproductive technology cycles: A single-blind randomized clinical trial study. *Health Sci Rep* 2024;7: e2296.

Babayof R, Margalioth EJ, Huleihel M, Amash A, Zylber-Haran E, Gal M, Brooks B, Mimoni T, Eldar-Geva T. Serum inhibin A, VEGF and TNFalpha levels after triggering oocyte maturation with GnRH agonist compared with HCG in women with polycystic ovaries undergoing IVF treatment: a prospective randomized trial. *Human reproduction (Oxford, England)* 2006;21: 1260-1265.

Beebeejaun Y, Copeland T, Duffy JMN, Sarris I, Showell M, Wang R, Sunkara SK. Triggering oocyte maturation in in vitro fertilization treatment in healthy responders: a systematic review and network meta-analysis. *Fertility and sterility* 2024.

Bülow NS, Skouby SO, Warzecha AK, Udengaard H, Andersen CY, Holt MD, Grøndahl ML, Nyboe Andersen A, Sopa N, Mikkelsen ALE *et al.* Impact of letrozole co-treatment during ovarian stimulation with gonadotrophins for IVF: a multicentre, randomized, double-blinded placebo-controlled trial. *Human reproduction (Oxford, England)* 2022;37: 309-321.

Casano S, Guidetti D, Patriarca A, Pittatore G, Gennarelli G, Revelli A. MILD ovarian stimulation with GnRH-antagonist vs. long protocol with low dose FSH for non-PCO high responders undergoing IVF: a prospective, randomized study including thawing cycles. *Journal of assisted reproduction and genetics* 2012;29: 1343-1351.

Cédrin-Durnerin I, Carton I, Massin N, Chevalier N, Dubourdieu S, Bstandig B, Michelson X, Goro S, Jung C, Guivarc'h-Lévêque A. Pretreatment with luteal estradiol for programming antagonist cycles compared to no pretreatment in advanced age women stimulated with corifollitropin alfa: a non-inferiority randomized controlled trial. *Human reproduction (Oxford, England)* 2024.

Cozzolino M, Vitagliano A, Cecchino GN, Ambrosini G, Garcia-Velasco JA. Corifollitropin alfa for ovarian stimulation in in vitro fertilization: a systematic review and meta-analysis of randomized controlled trials. *Fertility and sterility* 2019;111: 722-733.

Datta AK, Maheshwari A, Felix N, Campbell S, Nargund G. Mild versus conventional ovarian stimulation for IVF in poor, normal and hyper-responders: a systematic review and meta-analysis. *Human reproduction update* 2021;27: 229-253.

Decleer W, Comhaire F, Balduyck J, Ameye A, Osmanagaoglu K, Devroey P. Replacing HMG/FSH by low-dose HCG to complete corifollitropin alfa stimulation reduces cost per clinical pregnancy: a randomized pragmatic trial. *Reproductive biomedicine online* 2020;40: 468-474.

Devroey P, Pellicer A, Nyboe Andersen A, Arce JC. A randomized assessor-blind trial comparing highly purified hMG and recombinant FSH in a GnRH antagonist cycle with compulsory single-blastocyst transfer. *Fertility and sterility* 2012;97: 561-571.

Doblinger J, Cometti B, Trevisan S, Griesinger G. Subcutaneous Progesterone Is Effective and Safe for Luteal Phase Support in IVF: An Individual Patient Data Meta-Analysis of the Phase III Trials. *PloS one* 2016;11: e0151388.

Eftekhar M, Bagheri RB, Neghab N, Hosseinisadat R. Evaluation of pretreatment with Cetrotide in an antagonist protocol for patients with PCOS undergoing IVF/ICSI cycles: a randomized clinical trial. *JBRA assisted reproduction* 2018;22: 238-243.
Eftekhar M, Saeed L. Effect of adding letrozole to gonadotropin on in vitro fertilization outcomes: an RCT. *International journal of reproductive biomedicine* 2020;18: 287-294.
Farquhar C, Rombauts L, Kremer JA, Lethaby A, Ayeleke RO. Oral contraceptive pill, progestogen or oestrogen pretreatment for ovarian stimulation protocols for women undergoing assisted reproductive techniques. *The Cochrane database of systematic reviews* 2017;5: Cd006109.
Fernández-Prada S, Martín-Cameán M, Armijo O, Diez-Sebastián J, Iniesta S, Lobo S, Silva P, Sanz C, Sánchez MJ, Hernández A. Use of steroid pre-treatments in IVF-ICSI cycles with GnRH antagonist protocol and their impact on gestational outcomes. *Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology* 2022;42: 478-484.
Gao J, Gu F, Miao BY, Chen MH, Zhou CQ, Xu YW. Effect of the initiation of progesterone supplementation in in vitro fertilization-embryo transfer outcomes: a prospective randomized controlled trial. *Fertility and sterility* 2018;109: 97-103.
Gao J, Mai Q, Zhong Y, Miao B, Chen M, Luo L, Zhou C, Mol BW, Yanwen X. Pretreatment with oral contraceptive pills in women with PCOS scheduled for IVF: a randomized clinical trial. *Human Reproduction Open* 2024;2024: hoae019.
Ghasemi Tehrani H, Aasasi K, Mardanian F, Mehrabian F, Movahedi M, Naghshineh E. Evaluation of The Effect of Letrozole in the Ovarian Hyperstimulation Syndrome Prevention in Participants at Risk of Treatment with Ovulation-Stimulating Drugs:A Randomized Controlled Trial. *Reports of biochemistry & molecular biology* 2022;11: 386-393.
Glujovsky D, Pesce R, Miguens M, Sueldo C, Ciapponi A. Progestogens for prevention of luteinising hormone (LH) surge in women undergoing controlled ovarian hyperstimulation as part of an assisted reproductive technology (ART) cycle. *Cochrane Database of Systematic Reviews* 2023.
Gordts S, Van Turnhout C, Campo R, Puttemans P, Valkenburg M, Gordts S. A prospective randomised study comparing a GnRH-antagonist versus a GnRH-agonist short protocol for ovarian stimulation in patients referred for IVF. *Facts, views & vision in ObGyn* 2012;4: 82-87.
Griesinger G, Blockeel C, Kahler E, Pexman-Fieth C, Olofsson JI, Driessen S, Tournaye H. Dydrogesterone as an oral alternative to vaginal progesterone for IVF luteal phase support: A systematic review and individual participant data meta-analysis. *PloS one* 2020;15: e0241044.
Hossein Rashidi B, Shahrokh Tehraninejad E, Amanpour S, Bandarian F, Bandarian M. The impact of letrozole on oocyte quality in assisted reproductive technology (ART); a randomized double-blind clinical trial. *Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology* 2022;38: 1087-1092.
Huang L, Gao Y, Liang S, Jiang M. Administration of dehydroepiandrosterone improves endometrial thickness in women undergoing IVF/ICSI: a systematic review and meta-analysis. *Journal of ovarian research* 2025;18: 35.
Humaidan P, Alsbjerg B, Elbaek HO, Povlsen BB, Laursen RJ, Jensen MB, Mikkelsen AT, Thomsen LH, Kol S, Haahr T. The exogenous progesterone-free luteal phase: two pilot randomized controlled trials in IVF patients. *Reproductive biomedicine online* 2021;42: 1108-1118.
Humaidan P, Chin W, Rogoff D, D'Hooghe T, Longobardi S, Hubbard J, Schertz J. Efficacy and safety of follitropin alfa/lutropin alfa in ART: a randomized controlled trial in poor ovarian responders. *Human reproduction (Oxford, England)* 2017;32: 544-555.
Humaidan P, Polyzos NP, Alsbjerg B, Erb K, Mikkelsen AL, Elbaek HO, Papanikolaou EG, Andersen CY. GnRHa trigger and individualized luteal phase hCG support according to ovarian response to stimulation: two prospective randomized controlled multi-centre studies in IVF patients. *Human reproduction (Oxford, England)* 2013;28: 2511-2521.
Hussein RS, Elnashar I, Amin AF, Zhao Y, Abdelmagied AM, Abbas AM, Abdelaleem AA, Farghaly TA, Abdalmageed OS, Youssef AA *et al.* Effect of Metformin on Premature Luteinization and Pregnancy Outcomes in Intracytoplasmic Sperm Injection-Fresh Embryo Transfer Cycles: A Randomized Double-Blind Controlled Trial. *International journal of fertility & sterility* 2021;15: 108-114.

Keskin M, Ecemiş T, Atik A, Yeğen P, Kalkan E, Yücel GS. Cycle outcomes of dual trigger (GnRH agonist+hCG) versus human chorionic gonadotropin trigger alone in POSEDION group 3-4 poor-responders and normo-responders: A prospective randomized study. *Journal of gynecology obstetrics and human reproduction* 2023;52: 102633.
Lahoud R, Ryan J, Illingworth P, Quinn F, Costello M. Recombinant LH supplementation in patients with a relative reduction in LH levels during IVF/ICSI cycles: a prospective randomized controlled trial *European journal of obstetrics gynecology and reproductive biology*. 2017, pp. 300-305.
Li J, Chen Q, Wang J, Huang G, Ye H. Does growth hormone supplementation improve oocyte competence and IVF outcomes in patients with poor embryonic development? A randomized controlled trial. *BMC pregnancy and childbirth* 2020;20: 310.
Liu Y, Ding F, Yang Y, Ma B. Growth hormone improves the pregnancy outcomes in poor ovarian responders undergoing in vitro fertilization: an umbrella review. *Journal of assisted reproduction and genetics* 2025.
Liu Y, Wu Y, Pan Z, Jiang F, Lu Y, Meng Y. Single-Dose Versus Multiple-Dose GnRH Agonist for Luteal-Phase Support in Women Undergoing IVF/ICSI Cycles: A Network Meta-Analysis of Randomized Controlled Trials. *Frontiers in endocrinology* 2022;13: 802688.
Lotfy M, Saleh MM, Elshahat AM, Elserour GA, Taha OT. GONADOTROPINS- LETROZOLE, GONADOTROPIN- CLOMIPHENE CITRATE, AND GONADOTROPINS ONLY FOR CONTROLLED OVARIAN SUPER STIMULATION IN WOMEN WITH POLYCYSTIC OVARY SYNDROME UNDERGOING INTRACYTOPLASMIC SPERM INJECTION. *Journal of pharmaceutical negative results* 2022;13: 4568-4576.
Lou HY, Huang XY. Modified natural cycle for in vitro fertilization and embryo transfer in normal ovarian responders. *The Journal of international medical research* 2010;38: 2070-2076.
Madani T, Mohammadi Yeganeh L, Khodabakhshi S, Akhoond MR, Hasani F. Efficacy of low dose hCG on oocyte maturity for ovarian stimulation in poor responder women undergoing intracytoplasmic sperm injection cycle: a randomized controlled trial. *Journal of assisted reproduction and genetics* 2012;29: 1213-1220.
Mochtar MH, Danhof NA, Ayeleke RO, Van der Veen F, van Wely M. Recombinant luteinizing hormone (rLH) and recombinant follicle stimulating hormone (rFSH) for ovarian stimulation in IVF/ICSI cycles. *The Cochrane database of systematic reviews* 2017;5: Cd005070.
Mochtar MH, Van Wely M, Van der Veen F. Timing luteal phase support in GnRH agonist down-regulated IVF/embryo transfer cycles. *Human reproduction (Oxford, England)* 2006;21: 905-908.
Mourad A, Jamal W, Hemmings R, Tadevosyan A, Phillips S, Kadoch IJ. Empirical use of growth hormone in IVF is useless: the largest randomized controlled trial. *Human reproduction (Oxford, England)* 2025;40: 77-84.
Mukherjee S, Sharma S, Chakravarty BN. Letrozole in a low-cost in vitro fertilization protocol in intracytoplasmic sperm injection cycles for male factor infertility: A randomized controlled trial. *Journal of human reproductive sciences* 2012;5: 170-174.
Murber A, Fancsovits P, Ledo N, Szakacs M, Rigo J, Urbancsek J. Impact of highly purified versus recombinant follicle stimulating hormone on oocyte quality and embryo development in intracytoplasmic sperm injection cycles. *Acta biologica Hungarica* 2011;62: 255-264.
Naik S, Lepine S, Nagels HE, Siristatidis CS, Kroon B, McDowell S. Androgens (dehydroepiandrosterone or testosterone) for women undergoing assisted reproduction. *The Cochrane database of systematic reviews* 2024;6: Cd009749.
Ngwenya O, Lensen SF, Vail A, Mol BWJ, Broekmans FJ, Wilkinson J. Individualised gonadotropin dose selection using markers of ovarian reserve for women undergoing in vitro fertilisation plus intracytoplasmic sperm injection (IVF/ICSI). *The Cochrane database of systematic reviews* 2024;1: Cd012693.
Niu Y, Liu H, Li X, Zhao J, Hao G, Sun Y, Zhang B, Hu C, Lu Y, Ren C *et al.* Oral micronized progesterone versus vaginal progesterone for luteal phase support in fresh embryo transfer cycles: a multicenter, randomized, non-inferiority trial. *Human reproduction (Oxford, England)* 2023;38: ii24-ii33.

Oudshoorn SC, van Tilborg TC, Eijkemans MJC, Oosterhuis GJE, Friederich J, van Hooff MHA, van Santbrink EJP, Brinkhuis EA, Smeenk JMJ, Kwee J *et al.* Individualized versus standard FSH dosing in women starting IVF/ICSI: an RCT. Part 2: The predicted hyper responder. *Human reproduction (Oxford, England)* 2017;32: 2506-2514.
Papanikolaou EG, Verpoest W, Fatemi H, Tarlatzis B, Devroey P, Tournaye H. A novel method of luteal supplementation with recombinant luteinizing hormone when a gonadotropin-releasing hormone agonist is used instead of human chorionic gonadotropin for ovulation triggering: a randomized prospective proof of concept study. *Fertility and sterility* 2011;95: 1174-1177.
Parsanezhad M, Jahromi B, Rezaee S, Kooshesh L, Alaee S. The effect of four different gonadotropin protocols on oocyte and embryo quality and pregnancy outcomes in IVF/ICSI cycles; a randomized controlled trial *Iranian journal of medical sciences*. 2017, pp. 57-65.
Revelli A, Gennarelli G, Sestero M, Canosa S, Carosso A, Salvagno F, Pittatore G, Filippini C, Benedetto C. A prospective randomized trial comparing corifollitropin-α late-start (day 4) versus standard administration (day 2) in expected poor, normal, and high responders undergoing controlled ovarian stimulation for IVF. *Journal of assisted reproduction and genetics* 2020;37: 1163-1170.
Santos-Ribeiro S, Mackens S, Popovic-Todorovic B, Racca A, Polyzos NP, Van Landuyt L, Drakopoulos P, de Vos M, Tournaye H, Blockeel C. The freeze-all strategy versus agonist triggering with low-dose hCG for luteal phase support in IVF/ICSI for high responders: a randomized controlled trial. *Human reproduction (Oxford, England)* 2020;35: 2808-2818.
Selman H, Pacchiarotti A, Rinaldi L, Crescenzi F, Lanzilotti G, Lofino S, El-Danasouri I. Simultaneous administration of human acidic and recombinant less acidic follicle-stimulating hormone for ovarian stimulation improves oocyte and embryo quality, and clinical outcome in patients with repeated IVF failures. *European review for medical and pharmacological sciences* 2013;17: 1814-1819.
Seyedoshohadaei F, Abbasi S, Rezaie M, Allahvaisi A, Jafar Rezaie M, Soufizadeh N, Rahmani K. Myo-inositol effect on pregnancy outcomes in infertile women undergoing in vitro fertilization/intracytoplasmic sperm injection: A double-blind RCT. *International journal of reproductive biomedicine* 2022;20: 643-650.
Showell MG, Mackenzie-Proctor R, Jordan V, Hodgson R, Farquhar C. Inositol for subfertile women with polycystic ovary syndrome. *Cochrane Database of Systematic Reviews* 2018.
Shu L, Xu Q, Meng Q, Dai X, Zhang Y, Zhou W, Yi H, Liu J, Wu C, Hou Z *et al.* Clinical outcomes following long GnRHa ovarian stimulation with highly purified human menopausal gonadotropin plus rFSH or rFSH in patients undergoing in vitro fertilization-embryo transfer: a multi-center randomized controlled trial. *Annals of translational medicine* 2019;7: 146.
Siristatidis CS, Basios G, Pergialiotis V, Vogiatzi P. Aspirin for in vitro fertilisation. *The Cochrane database of systematic reviews* 2016;11: Cd004832.
Siristatidis CS, Yong LN, Maheshwari A, Ray Chaudhuri Bhatta S. Gonadotropin-releasing hormone agonist protocols for pituitary suppression in assisted reproduction. *The Cochrane database of systematic reviews* 2025;1: Cd006919.
Sood A, Mohiyiddeen G, Ahmad G, Fitzgerald C, Watson A, Mohiyiddeen L. Growth hormone for in vitro fertilisation (IVF). *The Cochrane database of systematic reviews* 2021;11: Cd000099.
Tang H, Mourad SM, Wang A, Zhai SD, Hart RJ. Dopamine agonists for preventing ovarian hyperstimulation syndrome. *The Cochrane database of systematic reviews* 2021;4: Cd008605.
Taronger R, Martínez-Cuenca S, Ferreros I, Rubio JM, Fernández-Colom PJ, Martínez-Triguero ML, Pellicer A. Ovarian stimulation with corifollitropin alfa followed by hp-hMG compared to hp-hMG in patients at risk of poor ovarian response undergoing ICSI: A randomized controlled trial. *European journal of obstetrics, gynecology, and reproductive biology* 2018;231: 192-197.
Toftager M, Bogstad J, Bryndorf T, Lossl K, Roskaer J, Holland T, Praetorius L, Zedeler A, Nilas L, Pinborg A. Risk of severe ovarian hyperstimulation syndrome in GnRH antagonist versus GnRH agonist protocol: RCT including 1050 first IVF/ICSI cycles. *Human reproduction (Oxford, England)* 2016;31: 1253-1264.
Tshzmachyan R, Hambartsoumian E. The role of Letrozole (LE) in controlled ovarian stimulation (COS) in patients at high risk to develop ovarian hyper stimulation syndrome (OHSS). A prospective

randomized controlled pilot study. *Journal of gynecology obstetrics and human reproduction* 2020;49: 101643.
Tso LO, Costello MF, Albuquerque LET, Andriolo RB, Macedo CR. Metformin treatment before and during IVF or ICSI in women with polycystic ovary syndrome. *The Cochrane database of systematic reviews* 2020;12: Cd006105.
van der Linden M, Buckingham K, Farquhar C, Kremer JA, Metwally M. Luteal phase support for assisted reproduction cycles. *The Cochrane database of systematic reviews* 2015: Cd009154.
van Wely M, Kwan I, Burt AL, Thomas J, Vail A, Van der Veen F, Al-Inany HG. Recombinant versus urinary gonadotrophin for ovarian stimulation in assisted reproductive technology cycles. *The Cochrane database of systematic reviews* 2011: Cd005354.
Watters M, Noble M, Child T, Nelson S. Short versus extended progesterone supplementation for luteal phase support in fresh IVF cycles: a systematic review and meta-analysis. *Reproductive biomedicine online* 2020;40: 143-150.
Wu L, Yin H, Guan L, Li G, Zhang J, Shen Q, Ni X, Wang C, Wang T, Geng H *et al.* The first multiple center prospective study of rhFSH CTP in patients undergoing assisted reproductive technology in China. *Scientific reports* 2025;15: 2666.
Yan MH, Sun ZG, Song JY. Dual trigger for final oocyte maturation in expected normal responders with a high immature oocyte rate: a randomized controlled trial. *Frontiers in medicine* 2023;10.
Yang X, Lin G, Lu G, Gong F. Letrozole supplementation during controlled ovarian stimulation in expected high responders: a pilot randomized controlled study. *Reproductive biology and endocrinology : RB&E* 2019;17: 43.
Ye H, Shi L, Quan X, Hou M, Ma H, Xue S, Yu Z, Chen Q, Sun L. Cumulative live birth rate of in vitro fertilization cycle via progestin-primed ovarian stimulation versus gonadotropin-releasing hormone antagonist protocol in infertile women with normal ovarian reserve: an open-label, randomized controlled trial. *Human fertility (Cambridge, England)* 2024;27: 2316005.
Youssef MA, Abou-Setta AM, Lam WS. Recombinant versus urinary human chorionic gonadotrophin for final oocyte maturation triggering in IVF and ICSI cycles. *The Cochrane database of systematic reviews* 2016;4: Cd003719.
Youssef MA, Van der Veen F, Al-Inany HG, Mochtar MH, Griesinger G, Nagi Mohesen M, Aboulfoutouh I, van Wely M. Gonadotropin-releasing hormone agonist versus HCG for oocyte triggering in antagonist-assisted reproductive technology. *The Cochrane database of systematic reviews* 2014: Cd008046.
Zaat T, Zagers M, Mol F, Goddijn M, van Wely M, Mastenbroek S. Fresh versus frozen embryo transfers in assisted reproduction. *Cochrane Database of Systematic Reviews* 2021.
Zhang Y, Liu L, Qin J, Huang H, Xue L, Wang S, Tan W. Evaluation of GnRH antagonist pretreatment before ovarian stimulation in a GnRH antagonist protocol in normal ovulatory women undergoing IVF/ICSI: a randomized controlled trial. *Reproductive biology and endocrinology : RB&E* 2021;19: 158.
Zhou C, Yang X, Wang Y, Xi J, Pan H, Wang M, Zhou Y, Xiao Y. Ovulation triggering with hCG alone, GnRH agonist alone or in combination? A randomized controlled trial in advanced-age women undergoing IVF/ICSI cycles. *Human reproduction (Oxford, England)* 2022;37: 1795-1805.
Zhu S, Lv Z, Song L, Zhang Q, Fan Y, Li J. Estradiol pretreatment in GnRH antagonist protocol for IVF/ICSI treatment. *Open medicine (Warsaw, Poland)* 2022;17: 1811-1820.
Zhu X, Fu Y. Randomized, Controlled Pilot Study of Low-Dose Human Chorionic Gonadotropin Administration Beginning From the Early Follicular Phase for Women With Polycystic Ovarian Syndrome Undergoing Ovarian Stimulation Using the Progesterone Protocol. *Frontiers in endocrinology* 2019;10: 875.