

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

SUMMARY OF FINDINGS TABLES 1 – 51

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

Patient or population: women undergoing OS for IVF/ICSI

Intervention: pre-treatment with oestradiol in GnRH antagonist cycles

Comparison: no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with pre-treatment with oestradiol				
Cumulative LBR						Not reported
LBR/ongoing PR (Farquhar, et al., 2017)	299 per 1,000	252 per 1,000 (185 to 333)	OR 0.79 (0.53 to 1.17)	502 (2 RCTs)	⊕⊕○○ LOW ^{a,b,c}	
OHSS (Shahrokh Tehrani Nejad, et al., 2018)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	133 (1 RCT)	⊕○○○ VERY LOW ^{b,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. High risk of bias associated with poor reporting of methods in one or more primary studies.

b. Small number of events.

c. The pooled effect included the line of no effect

d. Serious risk of bias because of 24% of patients lost to follow-up in the study group.

e. Serious inconsistency because only 1 RCT.

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

Patient or population: women undergoing OS for IVF/ICSI

Intervention: pre-treatment with progesterone in GnRH agonist cycles

Comparison: placebo or no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo or no intervention	Risk with pre-treatment with progesterone				
Cumulative LBR						Not reported
LBR/ ongoing PR (<i>GnRH agonist cycles</i>) (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 (<i>GnRH antagonist cycles</i>) (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}	

*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 the line of no effect
- 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 OS for IVF/ICSI

Intervention: pre-treatment with progesterone in GnRH antagonist cycles

Comparison: placebo or no treatment

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

*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 OS for IVF/ICSI

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

Comparison: no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with pre-treatment with COCP				
Cumulative LBR						Not reported
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 ^a	
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 ^{a,b,c}	
OHSS (Shahrokh Tehrani Nejad, et al., 2018)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	123 (1 RCT)	⊕○○○ VERY LOW ^{b,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. Serious risk of bias due to poor reporting of sequence generation and allocation concealment.

b. Small number of events.

c. The pooled effect included the line of no effect

d. Serious risk of bias due to 24% lost to follow-up in the study group

e. Serious inconsistency because only 1 RCT

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

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

Intervention: pre-treatment with combined contraceptives

Comparison: no pre-treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no pre-treatment	Risk with pre-treatment with combined contraceptives				
Cumulative LBR						Not reported
Live birth rate (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}	

*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 OS for IVF/ICSI

Intervention: pre-treatment with GnRH antagonist

Comparison: no pre-treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no pre-treatment	Risk with pre-treatment with GnRH antagonist				
Cumulative LBR						Not reported
Ongoing PR (Bloekeel, et al., 2011)	333 per 1,000	0 per 1,000 (0 to 0)	not estimable	69 (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

4b Pre-treatment with GnRH antagonist compared to no pre-treatment in GnRH antagonist protocols in poor responders

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

Intervention: pre-treatment with GnRH antagonist

Comparison: no pre-treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no pre-treatment	Risk with pre-treatment with GnRH antagonist				
Cumulative LBR						Not reported
Live birth rate (DiLuigi, et al., 2011)	250 per 1,000	0 per 1,000 (0 to 0)	not estimable	54 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Clinical PR (Maged, et al., 2015)	100 per 1,000	0 per 1,000 (0 to 0)	not estimable	160 (1 RCT)	⊕○○○ VERY LOW ^{b,c,d}	
Clinical PR (Aflatoonian, et al., 2017)	33 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. Serious risk of bias due to poor reporting of methodology

b. Serious inconsistency because only 1 RCT

c. Small number of events

d. Serious risk of performance bias

5 GnRH antagonist compared to long GnRH agonist for LH suppression in high responders

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

Intervention: GnRH antagonist protocol

Comparison: long GnRH agonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with long GnRH agonist	Risk with GnRH antagonist				
Cumulative LBR						Not reported
Live birth rate (Lambalk, et al., 2017)	387 per 1,000	348 per 1,000 (267 to 460)	RR 0.90 (0.69 to 1.19)	363 (3 RCTs)	⊕⊕○○ LOW ^{ab}	
OHSS (Lambalk, et al., 2017)	124 per 1,000	66 per 1,000 (37 to 118)	RR 0.53 (0.30 to 0.95)	1294 (9 RCTs)	⊕⊕○○ LOW ^{cd}	
OHSS (Trenkic, et al., 2016)	156 per 1,000	0 per 1,000 (0 to 0)	not estimable	90 (1 RCT)	⊕○○○ VERY LOW ^{b,e,f}	
Moderate/severe OHSS (Shin, et al., 2018)	273 per 1,000	0 per 1,000 (0 to 0)	not estimable	22 (1 RCT)	⊕○○○ VERY LOW ^{b,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).

- The pooled effect included the line of no effect
- Small number of events
- Serious risk of bias due to poor reporting of methodology in primary studies
- Small number of events, wide confidence intervals
- Serious risk of performance and detection bias
- Serious inconsistency because only 1 RCT
- Risk of performance bias.

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

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

Intervention: reduced-dose gonadotropin

Comparison: conventional gonadotropin dose

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with conventional gonadotropin dose	Risk with reduced-dose gonadotropin				
Cumulative LBR (Oudshoorn, et al., 2017)	695 per 1,000	663 per 1,000 (591 to 744)	RR 0.953 (0.850 to 1.070)	521 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Severe OHSS (Oudshoorn, et al., 2017)	11 per 1,000	0 per 1,000 (0 to 0)	not estimable	519 (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).

- Serious risk of performance bias
- Serious inconsistency because only 1 RCT
- The pooled effect included the line of no effect
- Small event rate

7 GnRH antagonist compared to long GnRH agonist for LH suppression in normal responders

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

Intervention: GnRH antagonist protocol

Comparison: long GnRH agonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with long GnRH agonist	Risk with GnRH antagonist				
Cumulative LBR						Not reported
Live birth rate (Lambalk, et al., 2017)	241 per 1,000	219 per 1,000 (190 to 251)	RR 0.91 (0.79 to 1.04)	2590 (10 RCTs)	⊕⊕○○ LOW ^{a,b}	
OHSS (Lambalk, et al., 2017)	62 per 1,000	39 per 1,000 (31 to 50)	RR 0.63 (0.50 to 0.81)	5598 (22 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. Serious risk of bias due to poor reporting of methodology

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

8 Letrozole in stimulation protocol for IVF/ICSI in normal responders

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

Intervention: letrozole addition to gonadotropins

Comparison: gonadotropins alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no letrozole	Risk with letrozole				
Cumulative LBR						Not reported
Ongoing PR (Verpoest, et al., 2006)	200 per 1,000	0 per 1,000 (0 to 0)	not estimable	20 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Clinical pregnancy rate (Mukherjee, et al., 2012)	327 per 1,000	0 per 1,000 (0 to 0)	not estimable	94 (1 RCT)	⊕○○○ VERY LOW ^{b,c,d}	
OHSS (Mukherjee, et al., 2012)	135 per 1,000	0 per 1,000 (0 to 0)	not estimable	94 (1 RCT)	⊕○○○ VERY LOW ^{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 performance bias

b. Serious inconsistency because only 1 RCT

c. Small number of events

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

9a Reduced FSH dose compared to conventional gonadotropin dose in normal responders

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

Intervention: reduced gonadotropin dose

Comparison: conventional gonadotropin dose

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with normal FSH dose	Risk with reduced FSH dose				
Cumulative LBR						Not reported
OHSS (Sterrenburg, et al., 2011)	0 per 1,000	0 per 1,000 (0 to 0)	OR 0.58 (0.18 to 1.90)	(5 RCTs)	⊕⊕○○ LOW ^{a,b}	
Clinical pregnancy rate (Sterrenburg, et al., 2011)	0 per 1,000	0 per 1,000 (0 to 0)	OR 0.95 (0.69 to 1.30)	(5 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 poor reporting of methodology

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

9b Late-start FSH compared to conventional start gonadotropin in normal responders

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

Intervention: late-start gonadotropin

Comparison: conventional start gonadotropin

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with conventional start FSH	Risk with late-start FSH				
Cumulative LBR						Not reported
Ongoing PR (Baart, et al., 2007)	171 per 1,000	0 per 1,000 (0 to 0)	not estimable	104 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Ongoing PR (Bloekeel, et al., 2011)	278 per 1,000	0 per 1,000 (0 to 0)	not estimable	76 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Ongoing PR (Hohmann, et al., 2003)	167 per 1,000	0 per 1,000 (0 to 0)	not estimable	97 (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 one RCT

c. Low number of events

10a GnRH antagonist compared to long GnRH agonist for LH suppression in low responders

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

Intervention: GnRH antagonist

Comparison: long GnRH agonist

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with long GnRH agonist	Risk with GnRH antagonist				
Cumulative LBR						Not reported
Live birth rate (Lambalk, et al., 2017)	238 per 1,000	212 per 1,000 (133 to 336)	RR 0.89 (0.56 to 1.41)	544 (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 poor reporting of methodology in primary studies

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

10b GnRH antagonist compared to short GnRH agonist for LH suppression in low responders

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

Intervention: GnRH antagonist

Comparison: short GnRH agonist

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with short GnRH agonist	Risk with GnRH antagonist				
Cumulative LBR						Not reported
Clinical pregnancy rate (Xiao, et al., 2013)	148 per 1,000	187 per 1,000 (132 to 258)	OR 1.33 (0.88 to 2.01)	735 (7 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 poor reporting of methodology in primary studies

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

11a Clomiphene citrate compared to FSH for ovarian stimulation in low responders

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

Intervention: clomiphene citrate

Comparison: FSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with FSH	Risk with clomiphene citrate				
Cumulative LBR						Not reported
Live birth rate (Ragni, et al., 2012)	48 per 1,000	35 per 1,000 (11 to 106)	RR 0.72 (0.23 to 2.21)	291 (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. Very small number of events, wide confidence interval

11b Clomiphene citrate in stimulation protocols for low responders

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

Intervention: clomiphene citrate addition to gonadotropins

Comparison: no clomiphene citrate

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no clomiphene citrate	Risk with clomiphene citrate				
Cumulative LBR						Not reported
Live birth rate (Bechtejew, et al., 2017)	131 per 1,000	115 per 1,000 (81 to 164)	RR 0.88 (0.62 to 1.26)	874 (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 poor reporting of methodology in primary studies

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

12 Letrozole in stimulation protocols for low responders

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

Intervention: letrozole addition to gonadotropins

Comparison: gonadotropins alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no letrozole	Risk with letrozole				
Cumulative LBR						Not reported
Clinical pregnancy rate (Bechtejew, et al., 2017)	152 per 1,000	143 per 1,000 (65 to 309)	RR 0.94 (0.43 to 2.03)	155 (2 RCTs)	⊕⊕○○ LOW ^{a,b}	
Clinical pregnancy rate (Ebrahimi, et al., 2017)	114 per 1,000	0 per 1,000 (0 to 0)	not estimable	70 (1 RCT)	⊕⊕○○ LOW ^{c,d}	
Clinical pregnancy rate (Eftekhari, et al., 2014)	88 per 1,000	0 per 1,000 (0 to 0)	not estimable	167 (1 RCT)	⊕○○○ VERY LOW ^{c,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. The pooled effect included both the line of no effect and appreciable benefit or harm

b. Very low number of events, wide confidence intervals

c. Serious inconsistency because only 1 RCT

d. Low number of events

e. Serious risk of performance and attrition bias

13 150 IU compared to 300/450 IU for low responder women

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

Intervention: 150IU dose gonadotropins

Comparison: 300/450IU dose gonadotropins

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with 300/450IU	Risk with 150IU				
Cumulative LBR						Not reported
LBR/ongoing PR (Lensen, et al., 2017)	109 per 1,000	80 per 1,000 (38 to 162)	OR 0.71 (0.32 to 1.58)	286 (2 RCTs)	⊕⊕○○ LOW ^{a,b}	
OHSS (Lensen, et al., 2017)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	286 (2 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).

CI: Confidence interval; OR: Odds ratio

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

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

14a 300 IU compared to 400/450 IU for low responder women

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

Intervention: 300IU dose gonadotropins

Comparison: 400/450IU dose gonadotropins

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with 400/450IU	Risk with 300IU				
Cumulative LBR						Not reported
Ongoing PR (Lensen, et al., 2017)	161 per 1,000	129 per 1,000 (35 to 380)	OR 0.77 (0.19 to 3.19)	62 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
OHSS (Lensen, et al., 2017)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	62 (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. The pooled effect included both the line of no effect and appreciable benefit or harm

14b 450IU compared to 600IU for low responder women

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

Intervention: 450IU dose gonadotropins

Comparison: 600IU dose gonadotropins

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with 600IU	Risk with 450IU				
Cumulative LBR						Not reported
Live birth rate (Lensen, et al., 2017)	108 per 1,000	139 per 1,000 (79 to 234)	OR 1.33 (0.71 to 2.52)	356 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
OHSS (Lensen, et al., 2017)	0 per 1,000	0 per 1,000 (0 to 0)	OR 7.23 (0.14 to 364.29)	356 (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. The pooled effect included both the line of no effect and appreciable benefit or harm

15 Modified natural cycle compared to standard stimulation protocol in poor responders

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

Intervention: modified natural cycle

Comparison: standard stimulation protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with standard stimulation protocol	Risk with modified natural cycle				
Cumulative LBR						Not reported
Pregnancy rate (Morgia, et al., 2004)	69 per 1,000	0 per 1,000 (0 to 0)	not estimable	215 (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 poor reporting of methodology

b. Serious inconsistency because only 1 RCT

c. Small number of events

16a Long versus short GnRH agonist protocol for LH surge suppression

Patient or population: women undergoing OS for IVF/ICSI

Intervention: long GnRH agonist protocol

Comparison: short GnRH agonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with short GnRH agonist protocol	Risk with long GnRH agonist protocol				
Cumulative LBR						Not reported
Live birth rate (Siristatidis, et al., 2015)	134 per 1,000	199 per 1,000 (116 to 320)	OR 1.60 (0.85 to 3.03)	295 (4 RCTs)	⊕⊕○○ 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. 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

16b Long GnRH agonist protocol compared to ultrashort GnRH agonist protocol for LH surge suppression

Patient or population: women undergoing OS for IVF/ICSI

Intervention: long GnRH agonist protocol

Comparison: ultrashort GnRH agonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with ultrashort GnRH agonist protocol	Risk with Long GnRH agonist protocol				
Cumulative LBR						Not reported
LBR/ongoing PR (Siristatidis, et al., 2015)	122 per 1,000	198 per 1,000 (91 to 376)	OR 1.78 (0.72 to 4.36)	150 (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. 1 RCT, very small number of patients.

16c Short GnRH agonist protocol compared to ultrashort GnRH agonist protocol for LH surge suppression

Patient or population: women undergoing OS for IVF/ICSI

Intervention: short GnRH agonist protocol

Comparison: ultrashort GnRH agonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with ultrashort GnRH agonist protocol	Risk with short GnRH agonist protocol				
Cumulative LBR						Not reported
Clinical PR (Siristatidis, et al., 2015)	195 per 1,000	244 per 1,000 (102 to 480)	OR 1.33 (0.47 to 3.81)	82 (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 inconsistency because only 1 RCT.

b. Very low number of events.

c. Wide confidence interval, which crosses the line of no effect.

17a Long GnRH agonist compared to GnRH antagonist protocol for LH surge suppression

Patient or population: women undergoing OS for IVF/ICSI

Intervention: long GnRH agonist protocol

Comparison: GnRH antagonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GnRH antagonist protocol	Risk with long GnRH agonist protocol				
Cumulative LBR (Al-Inany, et al., 2016)						Not reported
Cumulative LBR (Toftager, et al., 2017)	341 per 1,000	371 per 1,000 (313 to 434)	OR 1.14 (0.88 to 1.48)	1050 (1 RCT)	⊕⊕○○ LOW ^{a,b}	
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

17b Short GnRH agonist compared to GnRH antagonist protocol for LH surge suppression

Patient or population: women undergoing OS for IVF/ICSI

Intervention: short GnRH agonist protocol

Comparison: GnRH antagonist protocol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with GnRH antagonist	Risk with short GnRH agonist protocol				
Cumulative LBR						Not reported
Live birth rate (Gordts, et al., 2012)	188 per 1,000	0 per 1,000 (0 to 0)	not estimable	160 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Clinical pregnancy rate (Maldonado, et al., 2013)	521 per 1,000	0 per 1,000 (0 to 0)	not estimable	96 (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 poor reporting of methodology
 b. Serious inconsistency because only 1 RCT
 c. Very small number of events.

18 rFSH compared to hMG for ovarian stimulation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: rFSH

Comparison: hMG

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hMG	Risk with 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.

19 p-FSH compared to rFSH for ovarian stimulation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: p-FSH

Comparison: rFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No 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.

20 hp-FSH compared to rFSH for ovarian stimulation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: hp-FSH

Comparison: rFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No 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

21 hp-FSH compared to hMG for ovarian stimulation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: hp-FSH

Comparison: hMG

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hMG	Risk with hp-FSH				
Cumulative LBR						Not reported
Clinical PR (Duijkers, et al., 1993)	100 per 1,000	0 per 1,000 (0 to 0)	not estimable	20 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Clinical PR (Parsanezhad, et al., 2017)	450 per 1,000	0 per 1,000 (0 to 0)	not estimable	80 (1 RCT)	⊕⊕○○ LOW ^{b,c}	
Clinical PR (Westergaard, et al., 1996)	360 per 1,000	0 per 1,000 (0 to 0)	not estimable	218 (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 poor reporting of methodology

b. Serious inconsistency because only 1 RCT

c. Small number of events

22 hMG compared to rFSH+rLH for ovarian stimulation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: hMG

Comparison: rFSH+rLH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with rFSH+rLH	Risk with hMG				
Cumulative live birth rate						Not reported
OHSS (Pacchiarotti, et al., 2010)	132 per 1,000	0 per 1,000 (0 to 0)	not estimable	111 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Pregnancy rate (Pacchiarotti, et al., 2010)	283 per 1,000	0 per 1,000 (0 to 0)	not estimable	111 (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 attrition and detection bias.

b. Serious inconsistency because only 1 RCT

c. Small number of events

23 Substitution of gonadotropins by Letrozole for ovarian stimulation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: substitution of gonadotropins by letrozole

Comparison: conventional gonadotropin stimulation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with conventional gonadotropin stimulation	Risk with letrozole substitution				
Cumulative LBR						Not reported
Ongoing PR (Yasa, et al., 2013)	200 per 1,000	0 per 1,000 (0 to 0)	not estimable	50 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Clinical PR (Ebrahimi, et al., 2017)	114 per 1,000	0 per 1,000 (0 to 0)	not estimable	70 (1 RCT)	⊕⊕○○ LOW ^{b,c}	
Clinical PR (Verpoest, et al., 2006)	200 per 1,000	0 per 1,000 (0 to 0)	not estimable	20 (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 events

24 Long-acting rFSH compared to daily rFSH for ovarian stimulation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: long-acting rFSH

Comparison: daily rFSH

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with daily rFSH	Risk with long-acting rFSH				
Cumulative LBR						Not reported
Live birth rate (Griesinger, et al., 2016)	296 per 1,000	-591 per 1,000 (-1,478 to 325)	Difference -2.0 (-5.0 to 1.1)	3295 (3 RCTs)	⊕⊕⊕○ MODERATE ^a	
OHSS (Griesinger, et al., 2016)	41 per 1,000	53 per 1,000 (34 to 81)	OR 1.29 (0.81 to 2.05)	3295 (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. The pooled effect included the line of no effect

25 Metformin for adjuvant therapy in ovarian stimulation for PCOS patients

Patient or population: PCOS women undergoing OS for IVF/ICSI

Intervention: metformin

Comparison: placebo/no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo/no metformin	Risk with metformin				
Cumulative LBR						Not reported
Live birth rate (Tso, et al., 2014)	309 per 1,000	383 per 1,000 (266 to 518)	OR 1.39 (0.81 to 2.40)	551 (5 RCTs)	⊕⊕○○ LOW ^{a,b}	
Live birth rate (Jacob, et al., 2016)	516 per 1,000	0 per 1,000 (0 to 0)	not estimable	122 (1 RCT)	⊕⊕○○ LOW ^{c,d}	
Live birth rate (Abdalmageed, et al., 2018)	176 per 1,000	0 per 1,000 (0 to 0)	not estimable	102 (1 RCT)	⊕⊕○○ LOW ^{c,e}	
OHSS (Tso, et al., 2014)	217 per 1,000	74 per 1,000 (48 to 120)	OR 0.29 (0.18 to 0.49)	798 (8 RCTs)	⊕⊕⊕○ MODERATE ^e	
OHSS moderate/severe (Jacob, et al., 2016)	118 per 1,000	156 per 1,000 (68 to 319)	OR 1.376 (0.542 to 3.491)	153 (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. Substantial unexplainable statistical heterogeneity of results (I=52%).

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

c. Serious inconsistency because only 1 RCT.

d. Very small number of patients, small number of events.

e. Low number of events

26a Growth hormone for adjuvant therapy in ovarian stimulation, routine use

Patient or population: women undergoing OS for IVF/ICSI

Intervention: growth hormone

Comparison: no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with growth hormone				
Cumulative LBR						Not reported
Live birth rate (Duffy, et al., 2010)	146 per 1,000	185 per 1,000 (64 to 432)	OR 1.32 (0.40 to 4.43)	80 (2 RCTs)	⊕⊕⊕○ MODERATE ^{a,b}	
Adverse events (Duffy, et al., 2010)	195 per 1,000	131 per 1,000 (42 to 343)	OR 0.62 (0.18 to 2.15)	80 (2 RCTs)	⊕⊕⊕○ MODERATE ^{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. sequence generation and allocation concealment unclear

b. Small number of events.

26b Growth hormone for adjuvant therapy in ovarian stimulation in low responders

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

Intervention: growth hormone

Comparison: no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with growth hormone				
Cumulative LBR						Not reported
Live birth rate (Li, et al., 2017)	158 per 1,000	273 per 1,000 (197 to 379)	RR 1.73 (1.25 to 2.40)	562 (9 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. Small number of events.

b. Serious risk of bias because of poor reporting of methodology.

27 Testosterone for adjuvant therapy before ovarian stimulation.

Patient or population: women undergoing OS for IVF/ICSI

Intervention: adjuvant testosterone

Comparison: no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no intervention	Risk with testosterone				
Cumulative LBR						Not reported
LBR/ongoing PR (Nagels, et al., 2015)	92 per 1,000	208 per 1,000 (116 to 344)	OR 2.6 (1.3 to 5.2)	345 (4 RCTs)	⊕⊕⊕○ MODERATE ^a	
Live birth rate (Bosdou, et al., 2016)	83 per 1,000	0 per 1,000 (0 to 0)	not estimable	50 (1 RCT)	⊕⊕○○ LOW ^{b,c}	
Live birth rate 2 weeks treatment (Kim, et al., 2014)	67 per 1,000	0 per 1,000 (0 to 0)	not estimable	60 (1 RCT)	⊕⊕○○ LOW ^{b,c}	
Live birth rate 3 weeks treatment (Kim, et al., 2014)	67 per 1,000	0 per 1,000 (0 to 0)	not estimable	60 (1 RCT)	⊕⊕○○ LOW ^{b,c}	
Live birth rate 4 weeks treatment (Kim, et al., 2014)	67 per 1,000	0 per 1,000 (0 to 0)	not estimable	60 (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. Large confidence intervals, small number of patients.

b. Serious inconsistency because only 1 RCT

c. Small number of patients, very small number of events.

28 Dehydroepiandrosterone (DHEA) for adjuvant therapy in ovarian stimulation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: adjuvant DHEA

Comparison: no DHEA

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no DHEA	Risk with DHEA				
Cumulative LBR						Not reported
LBR/ongoing PR (Nagels, et al., 2015)	128 per 1,000	209 per 1,000 (155 to 277)	OR 1.81 (1.25 to 2.62)	878 (8 RCTs)	⊕⊕⊕○ MODERATE ^a	
Live birth (Narkwichean, et al., 2017)	320 per 1,000	237 per 1,000 (70 to 794)	RR 0.74 (0.22 to 2.48)	52 (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. Large confidence intervals, small number of events.

b. Risk of performance bias.

c. Serious inconsistency because only 1 RCT.

29 Aspirin for adjuvant therapy in ovarian stimulation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: adjuvant aspirin

Comparison: no intervention

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

*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, small number of events

30 Ultrasound and oestradiol measurements for monitoring during ovarian stimulation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: ultrasound and oestradiol measurements

Comparison: ultrasound alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with USS alone	Risk with USS+E2				
Cumulative LBR						Not reported
OHSS (Kwan, et al., 2014)	36 per 1,000	37 per 1,000 (18 to 76)	OR 1.03 (0.48 to 2.20)	781 (6 RCTs)	⊕⊕○○ LOW ^{a,b}	
Clinical pregnancy rate (Kwan, et al., 2014)	361 per 1,000	383 per 1,000 (308 to 465)	OR 1.10 (0.79 to 1.54)	617 (4 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 primary studies.

b. Wide confidence intervals and the pooled effect included the line of no effect.

31 Ultrasound and hormone panel for monitoring during ovarian stimulation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: ultrasound and hormone panel

Comparison: ultrasound alone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with USS alone	Risk with USS+hormone panel				
Cumulative LBR						Not reported
OHSS (Golan, et al., 1994)	70 per 1,000	0 per 1,000 (0 to 0)	not estimable	114 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
OHSS (Wiser, et al., 2012)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	63 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Pregnancy rate (Golan, et al., 1994)	246 per 1,000	0 per 1,000 (0 to 0)	not estimable	114 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Clinical PR (Wiser, et al., 2012)	576 per 1,000	0 per 1,000 (0 to 0)	not estimable	63 (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

32 Early compared to late hCG administration for final oocyte maturation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: early hCG administration

Comparison: late hCG administration

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with late hCG	Risk with early hCG				
Cumulative LBR						Not reported
Live birth rate (Chen, et al., 2014)	272 per 1,000	310 per 1,000 (125 to 770)	RR 1.14 (0.46 to 2.83)	354 (3 RCTs)	⊕○○○ 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 selection and performance bias

b. Significant heterogeneity $I^2=65\%$

c. The pooled effect included the line of no effect

33 Recombinant hCG compared to urinary hCG for final oocyte maturation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: recombinant hCG

Comparison: urinary hCG

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

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

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

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

34a 5.000 IU compared to 10.000 IU urinary hCG for final oocyte maturation**Patient or population:** women undergoing OS for IVF/ICSI**Intervention:** 5.000 IU urinary hCG**Comparison:** 10.000 IU urinary hCG

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with 10.000 IU uhCG	Risk with 5.000 IU uhCG				
Cumulative LBR						Not reported
Severe OHSS (Kolibianakis, et al., 2007)	36 per 1,000	0 per 1,000 (0 to 0)	not estimable	54 (1 RCT)	⊕⊕○○ LOW ^{a,b}	
OHSS (Shaltout, et al., 2006)	83 per 1,000	0 per 1,000 (0 to 0)	not estimable	98 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Ongoing PR (Kolibianakis, et al., 2007)	250 per 1,000	0 per 1,000 (0 to 0)	not estimable	54 (1 RCT)	⊕⊕○○ LOW ^{a,b}	
Pregnancy rate (Shaltout, et al., 2006)	354 per 1,000	0 per 1,000 (0 to 0)	not estimable	98 (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 inconsistency because only 1 RCT
b. Small number of patients, small number of events
c. Serious risk of bias due to incomplete reporting of methodology

34b 250 µg compared to 500 µg recombinant hCG for final oocyte maturation**Patient or population:** women undergoing OS for IVF/ICSI**Intervention:** 250 µg recombinant hCG**Comparison:** 500 µg recombinant hCG

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with 500 µg recombinant hCG	Risk with 250 µg				
Cumulative LBR						Not reported
OHSS (Madani, et al., 2013)	100 per 1,000	0 per 1,000 (0 to 0)	not estimable	120 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Clinical pregnancy rate (Madani, et al., 2013)	345 per 1,000	0 per 1,000 (0 to 0)	not estimable	100 (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. Possible risk of performance bias due to incomplete reporting of methodology
b. Serious inconsistency because only 1 RCT
c. Small number of patients, small number of events

35 Recombinant LH compared to urinary hCG for final oocyte maturation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: recombinant LH

Comparison: urinary hCG

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

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

- One of the two RCT's did not provide information about methods of randomization, allocation concealment or blinding.
- The pooled effect included both the line of no effect and appreciable benefit or harm.
- Small number of events.
- Very wide confidence intervals.

36 GnRH agonist with conventional luteal support compared to hCG for final oocyte maturation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: GnRH agonist without adjusted LPS

Comparison: hCG

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG	Risk with GnRH agonist				
Cumulative LBR						Not reported
Clinical PR (Griesinger, et al., 2006)	301 per 1,000	83 per 1,000 (21 to 266)	OR 0.21 (0.05 to 0.84)	275 (3 RCTs)	⊕○○○ 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).

- 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
- Serious risk of bias due to incomplete reporting of methodology
- Small number of events, large confidence intervals

37 GnRH agonist with modified luteal support compared to hCG for final oocyte maturation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: GnRH agonist with modified LPS

Comparison: hCG

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG	Risk with GnRH agonist				
Cumulative LBR						Not reported
OHSS (Youssef, et al., 2014)	8 per 1,000	6 per 1,000 (1 to 27)	OR 0.79 (0.18 to 3.47)	777 (6 RCTs)	⊕○○○ VERY LOW ^{a,b,c}	
Live birth rate (Humaidan, et al., 2010)	313 per 1,000	0 per 1,000 (0 to 0)	not estimable	302 (1 RCT)	⊕⊕○○ LOW ^{d,e}	
Live birth rate (Papanikolaou, et al., 2011)	222 per 1,000	0 per 1,000 (0 to 0)	not estimable	35 (1 RCT)	⊕○○○ VERY LOW ^{d,e,f}	
Ongoing PR (Humaidan, et al., 2013)	255 per 1,000	0 per 1,000 (0 to 0)	not estimable	266 (1 RCT)	⊕⊕○○ LOW ^{e,f}	
Clinical pregnancy rate (Humaidan, et al., 2006)	462 per 1,000	0 per 1,000 (0 to 0)	not estimable	28 (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. All studies are at high risk of bias in 1 or more domains. None clearly reported blinded outcome assessment.

b. Substantial heterogeneity: $I^2=66\%$

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

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

e. Serious inconsistency because only 1 RCT

f. Small number of events.

38 Dual trigger compared to hCG for final oocyte maturation

Patient or population: women undergoing OS for IVF/ICSI

Intervention: dual trigger

Comparison: hCG

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG	Risk with dual trigger				
Cumulative LBR						Not reported
Pregnancy rate (Ding, et al., 2017)	307 per 1,000	475 per 1,000 (359 to 632)	RR 1.55 (1.17 to 2.06)	320 (2 RCTs)	⊕⊕○○ LOW ^{a,b}	
Ongoing PR (Eftekhar, et al., 2017)	215 per 1,000	0 per 1,000 (0 to 0)	not estimable	192 (1 RCT)	⊕○○○ VERY LOW ^{c,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. Serious risk of bias due to incomplete reporting of methodology in the primary studies

b. Small number of events

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

d. Serious inconsistency because only 1 RCT

e. Small number of events, sample size not reached.

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

Patient or population: women undergoing OS for IVF/ICSI

Intervention: progesterone

Comparison: placebo or no intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo/no intervention	Risk with progesterone				
Cumulative LBR						Not reported
Live birth/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}	

*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.

40 Low-dose compared to high dose vaginal progesterone for luteal support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: low dose vaginal progesterone

Comparison: high dose vaginal progesterone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with high dose	Risk with low dose				
Cumulative LBR						Not reported
Live birth/ongoing PR (van der Linden, et al., 2015)	325 per 1,000	318 per 1,000 (288 to 348)	OR 0.97 (0.84 to 1.11)	3720 (5 RCTs)	⊕⊕○○ LOW ^{a,b}	
Live birth rate (Aslih, et al., 2017)	250 per 1,000	0 per 1,000 (0 to 0)	not estimable	71 (1 RCT)	⊕○○○ VERY LOW ^{a,c,d}	
Live birth rate (Michnova, et al., 2017)	528 per 1,000	0 per 1,000 (0 to 0)	not estimable	100 (1 RCT)	⊕○○○ VERY LOW ^{a,c,d}	
OHSS (van der Linden, et al., 2015)	70 per 1,000	64 per 1,000 (41 to 99)	OR 0.91 (0.57 to 1.46)	1251 (2 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.

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

c. Serious inconsistency because only 1 RCT

d. Small number of patients, required sample size not reached

41a Subcutaneous compared to vaginal progesterone for luteal support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: subcutaneous progesterone

Comparison: vaginal progesterone

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

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

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

41b Vaginal/rectal compared to oral progesterone for luteal support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: vaginal/rectal progesterone

Comparison: oral progesterone

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

*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.

41c Intramuscular compared to vaginal/rectal progesterone for luteal support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: intramuscular progesterone

Comparison: vaginal/rectal progesterone

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

*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: $I^2=71\%$

41d Intramuscular compared to oral progesterone for luteal support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: intramuscular progesterone

Comparison: oral progesterone

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

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

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

42a Progesterone LPS started on the day of OR compared to day after OR

Patient or population: women undergoing OS for IVF/ICSI

Intervention: progesterone LPS started on the day of OR

Comparison: progesterone LPS started on the day after OR

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

*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

42b Progesterone LPS started on the evening of OR compared to evening of ET

Patient or population: women undergoing OS for IVF/ICSI

Intervention: progesterone LPS started on the evening of OR

Comparison: progesterone LPS started on the evening of ET

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone LPS started on evening of ET	Risk with progesterone LPS started on the evening of OR				
Cumulative LBR						Not reported
Live birth rate (Mochtar, et al., 2006)	205 per 1,000	199 per 1,000 (123 to 319)	RR 0.97 (0.60 to 1.56)	255 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Clinical PR (Baruffi, et al., 2003)	288 per 1,000	0 per 1,000 (0 to 0)	not estimable	103 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Clinical PR (Fanchin, et al., 2001)	293 per 1,000	0 per 1,000 (0 to 0)	not estimable	84 (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

42c Progesterone LPS started before OR compared to after OR

Patient or population: women undergoing OS for IVF/ICSI

Intervention: progesterone LPS started before OR

Comparison: progesterone LPS started after OR

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone LPS started after OR	Risk with progesterone LPS started before OR				
Cumulative LBR						Not reported
Live birth rate (Mochtar, et al., 2006)	211 per 1,000	198 per 1,000 (122 to 321)	RR 0.94 (0.58 to 1.52)	258 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Clinical PR (Sohn, et al., 1999)	246 per 1,000	0 per 1,000 (0 to 0)	not estimable	282 (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

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

Patient or population: women undergoing OS for IVF/ICSI

Intervention: Progesterone LPS until pregnancy test

Comparison: Progesterone LPS until week 6/7

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Progesterone LPS until week 6/7	Risk with Progesterone LPS until pregnancy test				
Cumulative LBR						Not reported
Live birth rate (Liu, et al., 2012)	815 per 1,000	774 per 1,000 (701 to 856)	RR 0.95 (0.86 to 1.05)	369 (2 RCTs)	⊕⊕○○ LOW ^{a,b}	
Ongoing pregnancy rate (Liu, et al., 2012)(Liu 2015)	885 per 1,000	858 per 1,000 (796 to 929)	RR 0.97 (0.90 to 1.05)	1166 (6 RCTs)	⊕○○○ 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 in the primary studies

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

c. Serious heterogeneity between trials: $I^2=73\%$

44a Dydrogesterone compared to progesterone for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: dydrogesterone

Comparison: progesterone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone	Risk with dydrogesterone				
Cumulative LBR						Not reported
Live birth/ongoing PR (Barbosa, et al., 2018)	237 per 1,000	256 per 1,000 (218 to 299)	RR 1.08 (0.92 to 1.26)	3386 (8 RCTs)	⊕⊕⊕○ MODERATE ^a	
Live birth rate (Griesinger, et al., 2018)	325 per 1,000	0 per 1,000 (0 to 0)	not estimable	983 (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. 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

44b Dydrogesterone compared to placebo for luteal support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: dydrogesterone

Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo	Risk with dydrogesterone				
Cumulative LBR						Not reported
Ongoing pregnancy (Kupferminc, et al., 1990)	216 per 1,000	0 per 1,000 (0 to 0)	not estimable	105 (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. Unknown risk of bias due to poor reporting of methodology.

b. Serious inconsistency because only 1 RCT.

c. Small number of patients, small event rate.

45 Progesterone compared to progesterone and oestradiol for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: progesterone

Comparison: progesterone + oestradiol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone+oestradiol	Risk with progesterone				
Cumulative LBR						Not reported
Live birth/ongoing PR (van der Linden, et al., 2015)	375 per 1,000	402 per 1,000 (353 to 453)	OR 1.12 (0.91 to 1.38)	1651 (9 RCTs)	⊕⊕⊕○ MODERATE ^a	
Ongoing PR (Ismail Madkour, et al., 2016)	364 per 1,000	0 per 1,000 (0 to 0)	not estimable	220 (1 RCT)	⊕⊕○○ LOW ^{b,c}	
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

46a hCG compared to no intervention for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: hCG

Comparison: no intervention

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

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

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

46b hCG compared to progesterone for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: hCG

Comparison: progesterone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone	Risk with hCG				
Cumulative LBR						Not reported
Live birth/ongoing PR (van der Linden, et al., 2015)	249 per 1,000	234 per 1,000 (152 to 342)	OR 0.92 (0.54 to 1.57)	434 (4 RCTs)	⊕⊕○○ LOW ^{a,b,c}	
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}	

*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. Effect estimate with wide confidence intervals.

46c hCG compared to progesterone and oestradiol for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: hCG

Comparison: progesterone and oestradiol

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone+oestradiol	Risk with hCG				
Cumulative LBR						Not reported
Clinical PR (Smitz, et al., 1988)	320 per 1,000	317 per 1,000 (160 to 614)	RR 0.99 (0.50 to 1.92)	91 (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).

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

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

Patient or population: women undergoing OS for IVF/ICSI

Intervention: progesterone with GnRH agonist bolus

Comparison: progesterone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone	Risk with progesterone+GnRH _a				
Cumulative LBR						Not reported
Live birth/ongoing PR (van der Linden, et al., 2015)	289 per 1,000	193 per 1,000 (137 to 261)	OR 0.59 (0.39 to 0.87)	1536 (5 RCTs)	⊕⊕○○ LOW ^{a,b}	
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)	195 (1 RCT)	⊕○○○ VERY LOW ^{c,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).

- Evidence of significant heterogeneity ($I^2=59\%$)
- Effect estimate with very wide confidence intervals.
- Lack of detail to make a judgement of risk of bias
- Serious inconsistency because only 1 RCT.
- Small number of patients, low event rate

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

Patient or population: women undergoing OS for IVF/ICSI

Intervention: progesterone with repeated doses of GnRH agonist

Comparison: progesterone

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with progesterone	Risk with progesterone+repeated 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

49 LH compared to progesterone for luteal phase support

Patient or population: women undergoing OS for IVF/ICSI

Intervention: LH

Comparison: progesterone

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

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

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

50a GnRH agonist compared to hCG for final oocyte maturation in high responders

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

Intervention: GnRH agonist

Comparison: hCG

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with hCG	Risk with GnRH agonist				
Cumulative LBR						Not reported
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}	
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}	
Ongoing PR (Engmann, et al., 2008)	483 per 1,000	0 per 1,000 (0 to 0)	not estimable	59 (1 RCT)	⊕○○○ VERY LOW ^{c,d,e}	
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 ^{c,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. 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

50b Fresh transfer compared to freeze-all for prevention of OHSS in high responders

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

Intervention: fresh transfer

Comparison: freeze-all

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with freeze-all	Risk with fresh transfer				
Cumulative LBR						Not reported
Live birth rate (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}	
Live birth rate (Karacan, et al., 2017)	417 per 1,000	0 per 1,000 (0 to 0)	not estimable	122 (1 observational study)	⊕○○○ VERY LOW ^{a,b,d}	
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}	
moderate/severe OHSS (Karacan, et al., 2017)	0 per 1,000	0 per 1,000 (0 to 0)	not estimable	122 (1 observational study)	⊕○○○ 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. Risk of selection and/or performance bias
- b. Serious inconsistency because only 1 study
- c. Small number of events
- d. Small number of patients, small number of events

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

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

Intervention: GnRH agonist

Comparison: hCG non-10.000 IU

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

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

- a. Serious risk of bias due to incomplete reporting of methodology
- b. Serious inconsistency because only 1 RCT
- c. Small number of patients, small number of events

52a Freeze-all protocol compared to fresh transfer for prevention of OHSS

Patient or population: women undergoing OS for IVF/ICSI

Intervention: Freeze-all protocol

Comparison: fresh transfer

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with fresh transfer	Risk with Freeze-all protocol				
Cumulative LBR						Not reported
Live birth rate (Wong, et al., 2017)	579 per 1,000	600 per 1,000 (556 to 643)	OR 1.09 (0.91 to 1.31)	1892 (4 RCTs)	⊕⊕⊕○ MODERATE ^a	
Live birth rate (Shi, et al., 2018)	502 per 1,000	487 per 1,000 (447 to 532)	Rate ratio 0.97 (0.89 to 1.06)	2157 (1 RCT)	⊕⊕○○ LOW ^{a,b,c}	
Live birth rate (Vuong, et al., 2018)	315 per 1,000	337 per 1,000 (277 to 412)	RR 1.07 (0.88 to 1.31)	782 (1 RCT)	⊕⊕○○ LOW ^{a,b,c}	
OHSS (Wong, et al., 2017)	70 per 1,000	18 per 1,000 (11 to 28)	OR 0.24 (0.15 to 0.38)	1633 (2 RCTs)	⊕⊕○○ LOW ^{d,e}	
OHSS (Shi, et al., 2018)	20 per 1,000	7 per 1,000 (3 to 15)	Rate ratio 0.32 (0.14 to 0.74)	2157 (1 RCT)	⊕⊕○○ LOW ^{b,c,e}	
OHSS (Vuong, et al., 2018)	10 per 1,000	8 per 1,000 (2 to 34)	RR 0.75 (0.17 to 3.33)	782 (1 RCT)	⊕⊕○○ LOW ^{b,c,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. The confidence interval included the line of no effect.
- b. Possible risk of performance bias.
- c. Serious inconsistency because only 1 RCT.
- d. Data not reported per cycle
- e. Small number of events

52b Freeze-all protocol compared to intra-venous albumin for prevention of OHSS

Patient or population: women undergoing OS for IVF/ICSI

Intervention: Freeze-all protocol

Comparison: intra-venous albumin

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with albumin	Risk with Freeze-all				
Cumulative LBR						Not reported
Moderate/severe OHSS (D'Angelo and Amso, 2007)	308 per 1,000	703 per 1,000 (185 to 962)	OR 5.33 (0.51 to 56.24)	26 (1 RCT)	⊕○○○ VERY LOW ^{a,b,c}	
Clinical PR (D'Angelo and Amso, 2007)	0 per 1,000	0 per 1,000 (0 to 0)	OR 0.06 (0.00 to 1.17)	26 (1 RCT)	⊕⊕○○ 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. Study was not blinded
- b. Serious inconsistency because only 1 RCT
- c. Very wide confidence interval that included the line of no effect
- d. Very wide confidence interval

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