



Annex 8: Summary of evidence

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EXPLANATIONS

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.

Moderate certainty: 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 certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

Very low certainty: 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



III. Treatment

III.1 Expectant management

PICO QUESTION: WHAT IS THE VALUE OF EXPECTANT MANAGEMENT COMPARED TO ACTIVE TREATMENT FOR PATIENTS WITH UI?

CLOMIPHENE CITRATE WITH TIMED INTERCOURSE (+/- OVULATION TRIGGER)

CC + timed intercourse compared to expectant management for unexplained infertility

Patient or population: Couples with unexplained infertility
Intervention: CC + timed intercourse
Comparison: Expectant management

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with expectant management	Risk with CC + timed intercourse				
Live birth rate (Bhattacharya et al., 2008)	156 per 1,000	0 per 1,000 (0 to 0)	not estimable	340 (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 sample size with a low event rate and effect estimate with a wide confidence interval.

INTRA-UTERINE INSEMINATION (IUI) IN A NATURAL CYCLE VS. EXPECTANT MANAGEMENT

IUI in a natural cycle compared to expectant management for unexplained infertility

Patient or population: Couples with unexplained infertility
Intervention: IUI in a natural cycle
Comparison: Expectant management

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with expectant management	Risk with IUI in a natural cycle				
Live birth rate (Bhattacharya, et al., 2008)	156 per 1,000	0 per 1,000 (0 to 0)	not estimable	332 (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 sample size with a low event rate and effect estimate with a wide confidence interval.



OVARIAN STIMULATION WITH IUI VS. EXPECTANT MANAGEMENT

OS+IUI compared to expectant management for unexplained infertility

Patient or population: Couples with unexplained infertility
Intervention: OS+IUI
Comparison: Expectant management

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with expectant management	Risk with OS+IUI				
Cumulative live birth rate, poor prognosis patients (Ayeleke et al., 2020)	90 per 1,000	307 per 1,000 (165 to 497)	OR 4.48 (2.00 to 10.01)	201 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Cumulative live birth rate, moderate prognosis patients (Ayeleke, et al., 2020)	238 per 1,000	204 per 1,000 (123 to 318)	OR 0.82 (0.45 to 1.49)	253 (1 RCT)	⊕⊕○○ Low ^{a,c}	
Multiple pregnancy rate (Ayeleke, et al., 2020)	4 per 1,000	13 per 1,000 (2 to 79)	OR 3.01 (0.47 to 19.28)	454 (2 RCTs)	⊕⊕○○ Low ^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. Small sample size with a low event rate.
- c. Small sample size with a low event rate and effect estimate which includes the point of no effect.

IVF VS. EXPECTANT MANAGEMENT

IVF compared to expectant management for unexplained infertility

Patient or population: Couples with unexplained infertility
Intervention: IVF
Comparison: Expectant management

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with expectant management	Risk with IVF				
Live birth rate (Pandian et al., 2015)	37 per 1,000	458 per 1,000 (90 to 879)	OR 22.00 (2.56 to 189.37)	51 (1 RCT)	⊕○○○ Very 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 sample size with a low event rate and a wide confidence interval.



III.2 Active treatment

PICO QUESTION: IF ACTIVE TREATMENT IS PURSUED, WHICH TYPE OF ACTIVE TREATMENT FOR UI?

TIMED INTERCOURSE

Letrozole + timed intercourse compared to CC + timed intercourse for unexplained infertility

Patient or population: Couples with unexplained infertility

Intervention: Letrozole + timed intercourse

Comparison: CC + timed intercourse

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with CC + timed intercourse	Risk with Letrozole + timed intercourse				
Ongoing PR (Harira, 2018)	81 per 1,000	0 per 1,000 (0 to 0)	not estimable	172 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Multiple pregnancy rate (Harira, 2018)	23 per 1,000	0 per 1,000 (0 to 0)	not estimable	172 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Multiple pregnancy rate (Ibrahim et al., 2012)	214 per 1,000	0 per 1,000 (0 to 0)	not estimable	44 (1 RCT)	⊕⊕○○ 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. Small sample size with low event rate.

c. Very low event rate.

TIMED INTERCOURSE VS. IUI IN A NATURAL CYCLE

Natural cycle + IUI compared to CC + timed intercourse for unexplained infertility

Patient or population: Couples with unexplained infertility

Intervention: Natural cycle + IUI

Comparison: CC + timed intercourse

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with CC + timed intercourse	Risk with natural cycle + IUI				
Live birth rate (Bhattacharya, et al., 2008)	133 per 1,000	0 per 1,000 (0 to 0)	not estimable	338 (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 sample size with a low event rate



TIMED INTERCOURSE VS. OVARIAN STIMULATION AND IUI

OS+IUI compared to CC + timed intercourse for unexplained infertility

Patient or population: Couples with unexplained infertility

Intervention: OS+IUI

Comparison: CC + timed intercourse

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with CC + timed intercourse	Risk with OS+IUI				
Conception rate (Agarwal and Mittal, 2004)	182 per 1,000	0 per 1,000 (0 to 0)	not estimable	113 (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 bias and unknown risk of performance bias.
- b. Serious risk of inconsistency because only 1 RCT.
- c. Small sample size and calculation of optimal information size was not stated.

OS+IUI compared to Gonadotropins + timed intercourse for unexplained infertility

Patient or population: Couples with unexplained infertility

Intervention: OS+IUI

Comparison: Gonadotropins + timed intercourse

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with Gonadotropins + timed intercourse	Risk with OS+IUI				
Live birth rate (Ayeleke, et al., 2020)	255 per 1,000	352 per 1,000 (231 to 496)	OR 1.59 (0.88 to 2.88)	208 (2 RCTs)	⊕⊕○○ Low ^{a,b}	
Multiple pregnancy rate (Ayeleke, et al., 2020)	38 per 1,000	59 per 1,000 (17 to 188)	OR 1.61 (0.44 to 5.89)	208 (2 RCTs)	⊕⊕○○ 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. Statistically significant heterogeneity between studies ($I^2=72\%$)
- b. Large confidence intervals in the individual studies, and the effect estimate includes the point of no effect.
- c. Small sample size with a very low event size.



IUI IN A NATURAL CYCLE VS. OVARIAN STIMULATION AND IUI

OS+IUI compared to natural cycle IUI for unexplained infertility

Patient or population: Couples with unexplained infertility
Intervention: OS+IUI
Comparison: Natural cycle IUI

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with natural cycle IUI	Risk with OS+IUI				
Live birth rate (Ayeleke, et al., 2020)	139 per 1,000	251 per 1,000 (165 to 361)	OR 2.07 (1.22 to 3.50)	396 (4 RCTs)	⊕⊕○○ Low ^{a,b}	
Multiple pregnancy rate (Ayeleke, et al., 2020)	0 per 1,000	0 per 1,000 (0 to 0)	OR 3.00 (0.11 to 78.27)	39 (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 included studies.
- b. Small sample size with a very low event rate.
- c. Unknown risk of performance and attrition bias.
- d. Serious risk of inconsistency because only 1 RCT.
- e. Serious imprecision because only 1 event, very large confidence intervals.

IVF

IVF compared to natural cycle + IUI for unexplained infertility

Patient or population: Couples with unexplained infertility
Intervention: IVF
Comparison: Natural cycle + IUI

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with natural cycle + IUI	Risk with IVF				
Live birth rate (Pandian, et al., 2015)	184 per 1,000	358 per 1,000 (211 to 536)	OR 2.47 (1.19 to 5.12)	156 (2 RCTs)	⊕⊕○○ Low ^a	
Multiple pregnancy rate (Pandian, et al., 2015)	30 per 1,000	31 per 1,000 (1 to 460)	OR 1.03 (0.04 to 27.29)	43 (1 RCT)	⊕○○○ Very 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. The quality rating was downgraded by 2 levels due to serious imprecision. There were only 44 events and there was substantial statistical heterogeneity ($I^2=60%$) though the direction of effect was consistent.
- b. Serious risk of inconsistency due to only 1 study.
- c. There was only 1 event and the pooled estimate includes the line of no effect.



IVF compared to OS+IUI for unexplained infertility

Patient or population: Couples with unexplained infertility

Intervention: IVF

Comparison: OS+IUI

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with OS+IUI	Risk with IVF				
Live birth rate (Nandi et al., 2022)	318 per 1,000	490 per 1,000 (331 to 726)	RR 1.54 (1.04 to 2.28)	1391 (7 RCTs)	⊕⊕○○ Low ^{a,b}	
Multiple pregnancy rate (Nandi, et al., 2022)	126 per 1,000	105 per 1,000 (63 to 174)	RR 0.83 (0.50 to 1.38)	507 (6 RCTs)	⊕⊕○○ 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. Risk of bias because blinding of participants and personnel and of outcome assessment was not specified or not blinded in most studies.
- b. Significant heterogeneity among included studies ($I^2=83\%$).
- c. Wide confidence intervals in the individual studies and the pooled estimate includes the point of no effect.

PICO QUESTION: WHAT IS THE VALUE OF IVF VERSUS ICSI?

IVF compared to ICSI for unexplained infertility

Patient or population: Couples with unexplained infertility

Intervention: IVF

Comparison: ICSI

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with ICSI	Risk with IVF				
Live birth rate (Foong et al., 2006)	500 per 1,000	0 per 1,000 (0 to 0)	not estimable	60 (1 RCT)	⊕○○○ Very low ^{a,b,c}	
Live birth rate (Dang et al., 2021)	367 per 1,000	378 per 1,000 (290 to 495)	RR 1.03 (0.79 to 1.35)	382 (1 RCT)	⊕⊕○○ Low ^{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 performance bias due to poor reporting of methodology.
- b. Serious risk of inconsistency because only 1 study.
- c. Very small sample size, no calculation of optimal information size reported.
- d. The CI crosses the clinical decision threshold between recommending and not recommending treatment



III.3 Mechanical-surgical procedures

PICO QUESTION: WHAT IS THE VALUE OF MECHANICAL-SURGICAL PROCEDURES?

RESECTION OF POLYPS OR FIBROIDS

Resection of polyps/fibroids compared to expectant management for unexplained infertility

Patient or population: Couples with unexplained infertility
Intervention: Resection of polyps/fibroids
Comparison: Expectant management

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with expectant management	Risk with resection of polyps/fibroids				
Ongoing PR (Seyam et al., 2015)	100 per 1,000	430 per 1,000 (229 to 807)	RR 4.30 (2.29 to 8.07)	200 (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. Risk of selection and performance bias.
- b. Serious risk of inconsistency because only 1 RCT.

TUBAL FLUSHING

Tubal flushing with oil-based contrast media compared to expectant management for unexplained infertility

Patient or population: Couples with unexplained infertility
Intervention: Tubal flushing with oil-soluble contrast media (OSCM)
Comparison: No tubal flushing

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with expectant management	Risk with tubal flushing with OSCM				
Live birth rate (Wang et al., 2020)	111 per 1,000	290 per 1,000 (164 to 461)	OR 3.27 (1.57 to 6.85)	204 (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. Small sample size with a low event rate
- b. Optimal information size not met.



Tubal flushing with water-based contrast media compared to expectant management for unexplained infertility

Patient or population: Couples with unexplained infertility

Intervention: Tubal flushing with water-soluble contrast media (WSCM)

Comparison: No tubal flushing

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with expectant management	Risk with tubal flushing with WSCM				
Live birth rate (Wang, et al., 2020)	205 per 1,000	225 per 1,000 (147 to 330)	OR 1.13 (0.67 to 1.91)	334 (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 sample size with a low event rate

ENDOMETRIAL INJURY/SCRATCH

Endometrial scratching compared to no endometrial scratching for unexplained infertility

Patient or population: Couples with unexplained infertility

Intervention: Endometrial scratching

Comparison: No endometrial scratching

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no endometrial scratching	Risk with endometrial scratching				
Live birth (Wong et al., 2022)	65 per 1,000	89 per 1,000 (34 to 220)	OR 1.39 (0.50 to 4.03)	220 (1 RCT)	⊕⊕○○ Low ^{a,b}	
Ongoing PR (Wong, et al., 2022)	65 per 1,000	89 per 1,000 (34 to 220)	OR 1.39 (0.50 to 4.03)	220 (1 RCT)	⊕⊕⊕○ Moderate ^b	
Ongoing PR (Parsanezhad et al., 2013)	58 per 1,000	149 per 1,000 (62 to 317)	OR 2.83 (1.07 to 7.49)	217 (1 RCT)	⊕⊕○○ Low ^{c,d}	
Ongoing PR (Yildiz et al., 2021)	48 per 1,000	0 per 1,000 (0 to 0)	not estimable	96 (1 RCT)	⊕⊕○○ Low ^{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. Serious risk of inconsistency because only 1 RCT.

b. Small number of events, and the optimal information size was not met.

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

d. Small number of events with a wide confidence interval.

e. Small number of patients with a small event rate, no calculation of optimal information size provided.



III.4 Alternative therapeutic approaches

PICO QUESTION: WHAT IS THE EFFECTIVENESS OF ALTERNATIVE THERAPEUTIC APPROACHES?

ANTIOXIDANTS

Antioxidants compared to placebo/no treatment for unexplained infertility

Patient or population: Couples with unexplained infertility

Intervention: Antioxidants

Comparison: Placebo/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/no treatment	Risk with Antioxidants				
Live birth rate (Showell et al., 2020)	150 per 1,000	209 per 1,000 (96 to 396)	OR 1.50 (0.60 to 3.72)	133 (2 RCTs)	⊕○○○ Very low ^{a,b}	
Multiple pregnancy (Showell, et al., 2020)	30 per 1,000	20 per 1,000 (8 to 48)	OR 0.65 (0.26 to 1.62)	804 (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. Possible risk of selection and publication bias, risk of performance, detection and attrition bias in one study.
- b. Very small sample size, and the cumulative effect crosses the line of no effect.
- c. Serious inconsistency because only 1 study.
- d. Low number of events and the cumulative effect crosses the line of no effect.

ACUPUNCTURE

Accupuncture compared to no treatment for unexplained infertility

Patient or population: Couples with unexplained infertility

Intervention: Acupuncture

Comparison: No treatment

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	No of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no treatment	Risk with Acupuncture				
Live birth rate (Guyen et al., 2020)	278 per 1,000	0 per 1,000 (0 to 0)	not estimable	72 (1 RCT)	⊕⊕○○ 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 study.
- c. Small sample size, optimal information size not met.



NUTRACEUTICALS (INOSITOL)

Inositol compared to placebo for unexplained infertility

Patient or population: Couples with unexplained infertility

Intervention: Inositol

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 Inositol				
Live birth rate (Montanino Oliva et al., 2020)	70 per 1,000	0 per 1,000 (0 to 0)	not estimable	86 (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 selection and performance bias due to incomplete reporting of methodology.

b. Serious inconsistency because only 1 study.

c. Low number of patients and a low number of events.

REFERENCES

- Agarwal S, Mittal S. A randomised prospective trial of intrauterine insemination versus timed intercourse in superovulated cycles with clomiphene. *The Indian journal of medical research* 2004;120: 519-522.
- Ayeleke RO, Asseler JD, Cohlen BJ, Veltman-Verhulst SM. Intra-uterine insemination for unexplained subfertility. *The Cochrane database of systematic reviews* 2020;3: Cd001838.
- Bhattacharya S, Harrild K, Mollison J, Wordsworth S, Tay C, Harrold A, McQueen D, Lyall H, Johnston L, Burrage J et al. Clomifene citrate or unstimulated intrauterine insemination compared with expectant management for unexplained infertility: pragmatic randomised controlled trial. *BMJ (Clinical research ed)* 2008;337: a716.
- Dang VQ, Vuong LN, Luu TM, Pham TD, Ho TM, Ha AN, Truong BT, Phan AK, Nguyen DP, Pham TN et al. Intracytoplasmic sperm injection versus conventional in-vitro fertilisation in couples with infertility in whom the male partner has normal total sperm count and motility: an open-label, randomised controlled trial. *Lancet* 2021;397: 1554-1563.
- Foong SC, Fleetham JA, O'Keane JA, Scott SG, Tough SC, Greene CA. A prospective randomized trial of conventional in vitro fertilization versus intracytoplasmic sperm injection in unexplained infertility. *Journal of assisted reproduction and genetics* 2006;23: 137-140.
- Guyen PG, Cayir Y, Borekci B. Effectiveness of acupuncture on pregnancy success rates for women undergoing in vitro fertilization: A randomized controlled trial. *Taiwanese journal of obstetrics & gynecology* 2020;59: 282-286.
- Harira M. Use of Letrozole versus clomiphene-estradiol for treating infertile women with unexplained infertility not responding well to clomiphene alone, comparative study. *Middle east fertility society journal* 2018;23: 384-387.
- Ibrahim MI, Moustafa RA, Abdel-Azeem AA. Letrozole versus clomiphene citrate for superovulation in Egyptian women with unexplained infertility: a randomized controlled trial. *Archives of gynecology and obstetrics* 2012;286: 1581-1587.
- Montanino Oliva M, Buonomo G, Carra MC, Lippa A, Lisi F. Myo-inositol impact on sperm motility in vagina and evaluation of its effects on foetal development. *European review for medical and pharmacological sciences* 2020;24: 2704-2709.



- Nandi A, Raja G, White D, Tarek ET. Intrauterine insemination+controlled ovarian hyperstimulation versus in vitro fertilisation in unexplained infertility: a systematic review and meta-analysis. *Archives of gynecology and obstetrics* 2022;305: 805-824.
- Pandian Z, Gibreel A, Bhattacharya S. In vitro fertilisation for unexplained subfertility. *The Cochrane database of systematic reviews* 2015;2015: Cd003357.
- Parsanezhad ME, Dadras N, Maharlouei N, Neghaban L, Keramati P, Amini M. Pregnancy rate after endometrial injury in couples with unexplained infertility: A randomized clinical trial. *Iranian journal of reproductive medicine* 2013;11: 869-874.
- Seyam EM, Hassan MM, Mohamed Sayed Gad MT, Mahmoud HS, Ibrahim MG. Pregnancy Outcome after Office Microhysteroscopy in Women with Unexplained Infertility. *International journal of fertility & sterility* 2015;9: 168-175.
- Showell MG, Mackenzie-Proctor R, Jordan V, Hart RJ. Antioxidants for female subfertility. *The Cochrane database of systematic reviews* 2020;8: Cd007807.
- Wang R, Watson A, Johnson N, Cheung K, Fitzgerald C, Mol BWJ, Mohiyiddeen L. Tubal flushing for subfertility. *The Cochrane database of systematic reviews* 2020;10: Cd003718.
- Wong TY, Lensen S, Wilkinson J, Glanville EJ, Acharya S, Clarke F, Das S, Dawson J, Hammond B, Jayaprakasan K *et al.* Effect of endometrial scratching on unassisted conception for unexplained infertility: a randomized controlled trial. *Fertility and sterility* 2022;117: 612-619.
- Yildiz G, Kurt D, Mat E, Yildiz P. The effect of local endometrial injury on the success of intrauterine insemination. *Journal of Experimental and Clinical Medicine (Turkey)* 2021;38: 521-524.