Annex 8: Evidence tables

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

Reference	Study Type	Patients	Diagnostic test evaluated Reference standard test	Outcome measures	Effect size	Comments
Liu, Y., Pan, Z., Wu, Y., Song, J., & Chen, J. (2023). Comparison of anti-Müllerian hormone and antral follicle count in the prediction of ovarian response: a systematic review and meta-analysis. *Journal of ovarian research*, *16*(1), 117.	SR	Systematic review	AMH AFC	Sensitivity AUC	**Poor response:** AMH Sens 0.80 AFC sens 0.74 **High response**: AMH sens 0.81, AFC sens 0.87 **Poor response** : AMH AUC 0.85 AFC AUC 0.85 **High response** : AMH AUC 0.86 AFC AUC 0.87	
Bosch, E., Labarta, E., Zuzuarregui, J., Iliodromiti, S., & Nelson, S. M. (2023). Prediction of ovarian response using the automated Elecsys anti-Müllerian hormone assay in gonadotrophin-releasing hormone antagonist cycles. *Reproductive biomedicine online*, *46*(2), 295–301.	CS	**Inclusion criteria:** 1248: Eligible women were aged over 18 years, presenting for ovarian stimulation cycles for the purpose of IVF, fertility preservation or oocyte donation. **No exclusion criteria.** Patients were divided into four categories based on the number of oocytes retrieved (ovarian response): low (zero to three oocytes), suboptimal (four to nine oocytes), optimal (10–15 oocytes), and high (>15 oocytes).	AMH	Threshold levels of AMH for different response categories	**Low response** AMH: 74.4 sensitivity and 79.8 specificity **High response** Sens: 88.3, spec 74.8 Poor response AMH 0.85 **High response** AMH 0.85 low 6.4 pmol/L = 0.89 ng/ml high 14.2 pmol/L = 1.99 ng/ml	NB in table and text other sens and spec % mentioned for low response prediction. used from table.

Hochberg, A., Esteves, S. C., Yarali, H., Vuong, L. N., & Dahan, M. H. (2025). Antimüllerian hormone and antral follicle count thresholds for hyperresponse risk assessment in in vitro fertilization: a Hyperresponse Risk Assessment consensus study. *Fertility and sterility*, *123*(5), 827–837.	CS	4220: Women with infertility aged 22–45 years undergoing their first IVF/intracytoplasmic sperm injection (ICSI) cycle at 3 centers: ANDROFERT, Andrology and Human Reproduction Clinic (Campinas, Brazil); Anatolia IVF (Ankara, Turkey); and IVFMD, My Duc Hospital (Ho Chi Minh City, Vietnam), between 2015 and 2017. **Inclusion criteria:** Participants included consecutive individuals who met the following criteria: had their ovarian reserve evaluated through both AMH and AFC within 3 months before commencing the IVF cycle; demonstrated adequate pre-stimulation ovarian reserve markers according to the POSEIDON thresholds (AMH level of ≥1.2 ng/mL and AFC of ≥5); underwent standard OS with a gonadotropin-releasing hormone (GnRH) antagonist protocol and daily FSH doses ranging from 150 to 300 IU; and underwent oocyte retrieval **Exclusion criteria:** patients lacking assessment of both ovarian reserve markers, those with low AMH and AFC values according to the POSEIDON thresholds (AMH level of <1.2 ng/mL and/or AFC of <5), individuals undergoing IVF/ICSI for infertility purposes (e.g., donor cycles, preimplantation genetic testing for monogenic diseases, and fertility preservation cycles), and those treated with natural cycle IVF or mild stimulation protocols	AMH, AFC	determine the threshold values of serum AMH and AFC indicating an increased risk of hyper response to OS for IVF on the basis of the HERA Delphi Consensus definition, using receiver operating characteristic (ROC) curves; stratify these threshold values based on patients' age (<35 andR35 years); and evaluate the factors associated with an HERA hyper response.	hyper response: An AMH level of 4.38 ng/mL (area under the curve [AUC], 0.71; sensitivity, 0.77; specificity, 0.68; Fig. 1B) and AFC of 16 (AUC, 0.80; sensitivity, 0.83; specificity, 0.63; Fig. 2B) were identified for the entire cohort.	

Huang, J., Lin, J., Gao, H., Wang, Y., Zhu, X., Lu, X., Wang, B., Fan, X., Cai, R., & Kuang, Y. (2019). Anti-müllerian Hormone for the Prediction of Ovarian Response in Progestin-Primed Ovarian Stimulation Protocol for IVF. *Frontiers in endocrinology*, *10*, 325.	CS	523 women who underwent the PPOS treatment protocol for their first IVF/ICSI cycle were included in the study. **Inclusion criteria:** The inclusion was limited to patients with a regular cycle who underwent their first IVF/ICSI cycle with PPOS protocol regardless of age. **Exclusion criteria:** Patients were excluded from the study if they met one of the following criteria: (1) diagnosis of PCOS in accordance with the modified Rotterdam diagnostic criteria (34); (2) documented history of ovarian surgery (i.e., laparoscopic ovarian drilling, ovarian endometrioma stripping ,and unilateral oophorectomy); (3) use of hormonal contraceptives for pretreatment before the study cycle; (4) core data missing in the medical records (e.g., without endometrial thickness on the day of embryo transfer).	AMH	ovarian response in progestin primed ovarian stimulation protocols	AUC 0.861 for poor response AUC 0.773 for high response AMH 1.26 ng/ml for poor response and 4.34 ng/ml for high response	different protocol of stimulation however supports test accuracy
Lee, R. W. K., Khin, L. W., Hendricks, M. S., Tan, H. H., Nadarajah, S., Tee, N. W. S., Loh, S. F., Tai, B. C., & Chan, J. K. (2020). Ovarian biomarkers predict controlled ovarian stimulation for in vitro fertilisation treatment in Singapore. *Singapore medical journal*, *61*(9), 463–468.	CS	Women undergoing fresh IVF/ICSI cycles at KK Women's and Children's Hospital in Singapore were prospectively recruited from March 2009 to January 2012. 263 women included **Inclusion criteria:** primary or secondary subfertility diagnoses of: male factor, tubal factors, anovulatory cycles, endometriosis or unexplained fertility. **Exclusion criteria:** Women who were more than 45 years of age or those with endocrine disorders such as diabetes mellitus and thyroid dysfunction were excluded. **poor** ovarian response: cancellation of cycles with > 2 follicles of > 11 mm in diameter, or < 4	AMH AFC Age FSH BMI E2	Sensitivity Specificity AUC	**Poor response** AMH: cut-off value of ≤ 0.69 ng/mL, sens 70.6, spec 76%, AUC: 0.85 AFC cut-off value of ≤ 5, sens 75, spec 68.2%, AUC: 0.82 Age: cutoff ≥ 35, sens 69.6, spec 80.3%, AUC: 0.68 FSH: cutoff ≥ 5.7, sens 72, spec 80.5%, AUC: 0.73 BMI: cutoff ≥ 25, sens 17.1, spec 82.1%, AUC: 0.54 E2: cutoff ≥ 82, sens 70.5, spec 24.1%, AUC: 0.66 **Hyper response** AMH: cutoff ≥ 3.06, sens 76, spec 66.2%, AUC: 0.80	

		oocytes retrieved at oocyte retrieval **excessive** ovarian response: > 19 oocytes retrieved during oocyte retrieval			AFC: cut-off of ≥ 12, sens 72, spec 63%, AUC: 0.81 Age: cutoff ≤ 35, sens 70.1, spec 76.9%, AUC: 0.65 FSH: cutoff ≤ 4.5, sens 80, spec 94.1%, AUC: 0.63 BMI: cutoff ≥ 30, sens 6, spec 94.5%, AUC: 0.52 E2: cutoff ≤ 87, sens 71, spec 33%, AUC: 0.52	
Sun, X., Xiong, W., Liu, L., Xiong, J., Liao, C., Lan, Y., Li, F., Tao, S., Meng, M., Sun, C., & Mao, X. (2022). Comparison of the predictive capability of antral follicle count vs. the anti-Müllerian hormone for ovarian response in infertile women. *Frontiers in endocrinology*, *13*, 862733.	CS	2585: retrospective study of data from infertile women who underwent the first cycle of IVF/ICSI cycles at the reproductive center of the affiliated hospital of Southwest Medical University (Luzhou, China); **Inclusion criteria:** 1.Infertile women treated with IVF-ET or ICSI-ET treatment at the reproductive center; 2. Use of different protocols; 3. The presence of bilateral ovaries confirmed by color Doppler ultrasonography. **Exclusion criteria:** 1. Ovarian surgery or ovarian lesions; 2. Ultrasonography showing unclear and absent ovaries; 3. Systemic endocrine diseases such as PCOS, hyperprolactinemia, etc. 4. Severe endometriosis Low ovarian response group: number of eggs retrieved ≤3 or cancelled due to low ovarian response; Normal ovarian response group: 3< number of eggs retrieved ≤15; High ovarian response group: number of eggs retrieved >15.	AFC AMH BMI Age	Sensitivity AUC	**Low response:** AFC: Sens 95.5, spec 70.8% AMH: Sens 88, spec 58.2% BMI: sens 56.2, spec 57% Age: sens 69.4, spec 69.3% **high response:** AFC: Sens 91.4, spec 45.1 AMH: Sens 69.5, spec 63.5 BMI: sens 74.4, spec 0.3% age: sens 0.67, spec 0.56 **low response** AFC: 0.916 AMH 0.791 BMI 0.575 age 0.752 **high response** AFC 0.731 AMH 0.733 BMI 0.511 Age 0.654	

Wang, X., Jin, L., Mao, Y. D., Shi, J. Z., Huang, R., Jiang, Y. N., Zhang, C. L., & Liang, X. Y. (2021). Evaluation of Ovarian Reserve Tests and Age in the Prediction of Poor Ovarian Response to Controlled Ovarian Stimulation-A Real-World Data Analysis of 89,002 Patients. *Frontiers in endocrinology*, *12*, 702061.	CS	89,001 cycles: first oocyte retrieval IVF/ICSI cycle of all patients. VERY large population AMH group 48642 AFC group 84884 **Inclusion criteria:** Female patients with regular menstruation and bilateral ovaries at one of the five reproductive centers with first-time fresh cycles of IVF **Exclusion criteria:** 1. PCOS (according to Rotterdam Criteria); 2. history of ovarian surgery; 3. history of chemotherapy and pelvic radiotherapy; 4. pretreatment of oral contraceptives within 2 months before conducting the IVF cycle; 5. natural cycle IVF and mild stimulation cycle with daily gonadotropin <150; 6. canceled oocyte retrieval cycle that isn't due to poor ovarian response.	AMH AFC AGE basal FSH	Sensitivity Specificity AUC	**poor response** AFC ≤5, sens 0.559, spec 0.908, AUC : 0.862 AMH ≤ 1.18 ng/ml, sens 0.633, spec 0.900, AUC: 0.842 Age: ≤38, sens 0.407, spec 0.890, AUC: 0.723 bFSH: ≤9.8, sens 0.384, spec 0.900, AUC: 0.689	Chinese patients retrospective but very large group of patients.

2. WHAT IS THE PROGNOSTIC VALUE OF HORMONAL ASSESSMENT AT BASELINE?

Reference	Study Type	Patients	Diagnostic test evaluated Reference standard test	Outcome measures	Effect size	Comments
Lim, Y. C., Hamdan, M., Maheshwari, A., & Cheong, Y. (2024). Progesterone level in assisted reproductive technology: a systematic review and meta-analysis. *Scientific reports*, *14*(1), 30826.	SR	**Inclusion criteria** a) studies on fresh IVF/ICSI cycles or natural/modified natural/medicated FET cycles, (b) controlled ovarian stimulation (COS) with gonadotrophins and GnRH analogues in fresh cycle, or using trigger in modified natural FET cycle, or using hormonal replacement therapy in medicated FET cycle (c) the study provided extractable per woman data on pregnancy outcomes which included live birth rate (LBR), ongoing pregnancy rate (OPR), clinical pregnancy rate (CPR), miscarriage rate (MR) and (d) where serum progesterone was monitored **Exclusion criteria** (a) any intervention that leads to cycle cancellation or freeze-all embryos in the follicular phase or further progesterone supplementation in the luteal phase of fresh and FET cycles, (b) studies involving donor cycles, (c) studies without control groups and (d) studies providing per cycle data on pregnancy outcomes. Any intervention in the studies that influence the clinical decision and change the pregnancy outcome	Elevated progesterone at baseline compared to non-elevated progesterone at baseline.	LBR CPR	**LBR:** There was no difference in LBR in the EP compared to the NEP at threshold level >1.5 ng/ml, (OR 0.76, 95% CI 0.39–1.49, I=0%, 2 studies, N=309, very low quality. **Clinical pregnancy rate:** Three studies reported CPR over two different threshold levels (>0.65 ng/ml and>1.5 ng/ml). There was no difference in CPR in the EP compared to the NEP (P>0.65 ng/ml, OR 1.41, 95% CI 0.93–2.13, 1 study, N=464; P>1.5 ng/ml, OR 0.81, 95% CI 0.38-1.71, I=23%, 2 studies, N=309, very low quality).	

Broekmans, F. J., Kwee, J., Hendriks, D. J., Mol, B. W. and Lambalk, C. B. Hum Reprod Update. 2006; 12 (6): 685-718.	SR	(9 studies) Variation among the definitions of poor response and study quality and design characteristics is clearly present but logistic regression analysis revealed that none of the items significantly impacted the predictive performance of the test	Inhibin B Basal oestradiol	Non-pregnancy	Inhibin B: Extreme threshold levels were necessary to obtain a modest positive likelihood ratio of ~4–5, resulting in a post-test pregnancy rate of approximately 5% Oestradiol: For prediction of non-pregnancy no clear threshold levels could be identified for that would lead to an adequate combination of LR, post-test probability and abnormal test rate.	
Broer, S. L., van Disseldorp, J., Broeze, K. A., Dolleman, M., Opmeer, B. C., Bossuyt, P., Eijkemans, M. J., Mol, B. W. and Broekmans, F. J. Hum Reprod Update. 2013; 19 (1): 26-36.	SR	55 studies	AFC AMH Basal FSH Age BMI	OPR	AFC: AUC 0.50, 95% CI 0.40-0.59 AMH: AUC 0.55, 95% CI 0.45-0.64 Basal FSH: AUC 0.53, 95% CI 0.43-0.62 Age: OR 0.94, 95% CI 0.89-0.99 BMI: OR 0.91, 95% CI 0.85-0.97	
Doody, K., Devroey, P., Gordon, K., Witjes, H., & Mannaerts, B. (2010). LH concentrations do not correlate with pregnancy in rFSH/GnRH antagonist cycles. *Reproductive biomedicine online*, *20*(4), 565–567.	CS	**Inclusion criteria** See ENGAGE trial **Exclusion criteria** See ENGAGE trial **Total: N=696** **Control (n=348):** LH percentile on day 1 of stimulation P25-P75 **Study group 1 (n=174):** LH percentile on day 1 of stimulation <P25 **Study group 2 (n=174):** LH percentile on day 1 of stimulation >P75	influence of endogenous LH concentrations on ongoing pregnancy rates in a larger study population.	OPR	**Control:** - Ongoing pregnancy rate: 36.8 (95%CI: 31.7-42.1) **Study group 1:** - Ongoing pregnancy rate: 36.8 (95%CI: 29.6-44.4) **Study group 2:** - Ongoing pregnancy rate: 37.9 (95%CI: 30.7-45.6)	

Frazier, L. M., Grainger, D. A., Schieve, L. A., & Toner, J. P. (2004). Follicle-stimulating hormone and estradiol levels independently predict the success of assisted reproductive technology treatment. *Fertility and sterility*, *82*(4), 834–840.	CS	**Inclusion criteria** patient's oocytes were used, and the embryos were fresh. We limited our analysis to data from clinics that reported FSH, E2, and their laboratory upper limits of normal. We further limited the analysis to data from only the clinics that reported values within the nonextreme ranges listed above for 75% or more of their cycles **Exclusion criteria** FSH values of 0 or 100, laboratory upper limit of normal values for FSH of 0 or 30, E2 values of 0 or 500, and laboratory upper limit of normal values for E2 of 0 or 300	To evaluate the relationship between early follicular phase levels of FSH and E2 and outcomes of therapy with assisted reproductive technologies			
Kaya, C., Pabuccu, R., & Satıroglu, H. (2010). Serum antimüllerian hormone concentrations on day 3 of the in vitro fertilization stimulation cycle are predictive of the fertilization, implantation, and pregnancy in polycystic ovary syndrome patients undergoing assisted reproduction. *Fertility and sterility*, *94*(6), 2202–2207.	CS	A total of 60 infertile PCOS patients underwent 80 controlled ovarian hyperstimulation–intracytoplasmic sperm injection (ICSI) cycles. **Inclusion criteria** Diagnosis of PCOS was according to the Rotterdam Consensus Meeting **Exclusion criteria** Patients with congenital adrenal hyperplasia, Cushing syndrome, androgen-secreting tumors, or thyroid disease were excluded, and all patients had normal prolactin levels **Control (n=39 cycles):** Average (25th to 75th percentile) **Study group 1 (n=21 cycles):** Low (<25th percentile) **Study group 2 (n=20 cycles):** High (>75th percentile)	To determine the possible relationship between AMH concentrations on day 3 and reproductive outcomes in women with PCOS	CPR Nr of MII oocytes	**Control:** - Clinical pregnancy rate: 46.1% -number of MII oocytes: 12.3+-2.9 **Study group 1:** - Clinical pregnancy rate: 33.3% -number of MII oocytes: 8.2+-2.4 **Study group 2:** - Clinical pregnancy rate: 60% -number of MII oocytes: 17.8+-3.1	

Li, Y., Nie, M., Liu, Y., Zhang, W., & Yang, X. (2015). The dynamic changes of anti-Mullerian hormone and inhibin B during controlled ovarian hyperstimulation in decreased ovarian reserve women and the effect on clinical outcome.*Gynecological endocrinology : 31*(6), 450–453.	CS	124 patients who were under their first COH cycle. **Inclusion criteria** NOR group (52 patients): the age range was 20-39 years, body mass index (BMI) of 18-29 kg/m2 normal basal endocrine, regular menstrual cycle. DOR group (72 patients): the age range was 20-39 years, BMI of 18-29 kg/m2 and regular menstrual cycles. The basal FSH level was 10-20 mIU/ml and AFC<4. **Exclusion criteria** Patients with polycystic ovary syndrome, leiomyoma, endometriosis and/or endometrioma, uterine ovarian abnormalities, and with relevant systemic and chronic diseases.	to determine whether AMH or INHB levels are associated with ovarian response and clinical outcomes in IVF cycles.	Oocyte retrieved CPR	There was a positive correlation between serum AMH and INHB levels on D2/3 and AFC, oocytes retrieval (r=0.598, r= 0.500 and r =0.380, r = 0.359, respectively, p<0.001), but no direct correlation was observed between serum AMH and INHB levels on D2/3 and clinical pregnancy.	
Liu Z, Wang KH. Effect of basal luteinizing hormone (bLH) level on in vitro fertilization/intra-cytoplasmic injections (IVF/ICSI) outcomes in polycystic ovarian syndrome (PCOS) patients. BMC pregnancy and childbirth 2023;23: 618.	CS	Women were divided into two groups based on basal LH levels, i.e. high basal LH (LH≥12.455 IU/L; n=59) and low basal LH (LH<12.455 IU/L, n=176). **Inclusion criteria:** (1) Patients aged 20–40 years; (2) Patients who had fulfilled the diagnostic criteria for PCOS; (3) Patients who underwent IVF/ICSI treated and the men's semen showed no abnormality; **Exclusion criteria:** (1) Patients with bilateral or unilateral hydrosalpinx detected by B-ultrasound or hysterosalpingography; (2) Patients with submucosal fibroids or intrauterine adhesions, endometrial polyps, etc.; (3) Patients with a history of recurrent miscarriage; (4) Patients with thyroid dysfunction, elevated prolactin and autoimmune diseases; (5) Patients with diabetes, cushing syndrome, and other	Basal LH association with IVF/ICSI outcomes in PCOS patients	Cumulative LBR OHSS	cumulative live birth rate: 61.82% (34/55) vs. 60% (99/165) incidence of OHSS: 3.39% (2/59) vs. 1.14% (2/176)	

		endocrine disease; (6) congenital or acquired uterine anomalies, history of ovarian surgery; (7) abnormal parental karyotypes or medical conditions that contraindicated assisted reproductive technology and/or pregnancy; (8) previous medication of combined oral contraceptive pills or glucocorticosteroids within 2–3 months before ovarian stimulation; (9) repeated cycles, one patient with more than one time of COH.				
Shan, D., Zhao, J., Lu, X., Zhang, H., Lu, J., & Shen, Q. (2024). Effect of basal luteinizing hormone/follicle-stimulating hormone ratio on clinical outcome of *In Vitro* fertilization in patients with polycystic ovarian syndrome: a retrospective cohort study. *PeerJ*, *12*, e18635.	CS	**Inclusion criteria** PCOS diagnostic by Rotterdam criteria **Exclusion criteria** Not reported **Control (n=176):** low basal LH group: LH<12.455 IU/L **Study group 1 (n=59):** high basal LH group: LH≥12.455 IU/L **Study group 2 (n=21):** oral contraceptive group	The effect of basal LH rise on ovulation induction and pregnancy outcomes in PCOS patients in the GnRH antagonist protocol.	Cumulative LBR OHSS Cumulative CPR	**Control:** -Cumulative live birth rate: 60% (99/165) -Incidence of different grades of OHSS (%,N): 1.14% (2/176) - Clinical pregnancy rate: Cumulative 79.39% (131/165) **Study group 1:** -Cumulative live birth rate: 61.82% (34/55), NS -Incidence of different grades of OHSS (%,N): 3.39% (2/59) - Clinical pregnancy rate: Cumulative: 80% (44/55), NS **Study group 2:** -Cumulative live birth rate: 55% (11/20), NS -Incidence of different grades of OHSS (%,N): 0% (0/21) - Clinical pregnancy rate: Cumulative: 85% (17/20), NS	

Sun, L., Ye, J., Wang, Y., Chen, Q., Cai, R., Fu, Y., Tian, H., Lyu, Q., Lu, X., & Kuang, Y. (2018). Elevated basal luteinizing hormone does not impair the outcome of human menopausal gonadotropin and medroxyprogesterone acetate treatment cycles. *Scientific reports*, *8*(1), 13835.	CS	PCOS patients undergoing IVF/ICSI. **Inclusion criteria** women with PCOS according to the Rotterdam consensus meeting criteria **Exclusion criteria** Not reported Included women were categorised based on their basal LH level: < 5 mIU/mL (n=575), between 5 and 7.5 mIU/mL (n=216), between 7.5 and 10 mIU/mL (n=115), and ≥ 10 mIU/mL (n=105)	The effect of elevated LH on IVF cycle outcomes	CPR Nr of MII oocytes	**Clinical pregnancy rate :** LH <5: 47.7% (288/604) LH 5-7.5: 46.5% (112/241) LH 7.5-10: 58.8% (70/119) LH ≥10: 55.5% (61/110) **Number of MII oocytes:** LH <5: 11.10±7.24 LH 5-7.5: 13.97±8.65 LH 7.5-10: 13.47±9.38 LH ≥10: 17.18±9.60	
Umarsingh, S., Adam, J. K., & Krishna, S. B. N. (2020). The relationship between anti-Müllerian hormone (AMH) levels and pregnancy outcomes in patients undergoing assisted reproductive techniques (ART). *PeerJ*, *8*, e10390.	CS	Fifty women (n = 50), aged 20–45 years were recruited. **Inclusion criteria** The population of the study included female patients ranging between the ages of 20–45. **Exclusion criteria** Patients undergoing cancer therapy and patients on immune suppressant drugs were excluded from study. **Control (n=17):** Normal AMH: <1 ng/ml **Study group 1 (n=22):** High AMH: <3 ng/ml **Study group 2 (n=3):** Low to normal AMH: 0.3 - 0.9 ng/ml	To investigate the relationship between AMH levels and pregnancy outcomes in patients undergoing IVF/ICSI	CPR	**Control:** - Clinical pregnancy rate: 35.3% **Study group 1:** - Clinical pregnancy rate: 27.3% **Study group 2:** - Clinical pregnancy rate: 0%	
Wang, J., Ding, J., Qu, B., Zhang, Y., & Zhou, Q. (2022). Does Serum LH Level Influence IVF Outcomes in Women with PCOS Undergoing GnRH-Antagonist Stimulation: A Novel Indicator. *Journal of*	CS	**Inclusion criteria** women with PCOS according to Rotterdam criteria aged between 21 and 35 using the GnRH-antagonist stimulation protocol **Exclusion criteria** (1) congenital or acquired uterine anomalies; (2) history of ovarian surgery; (3) abnormal parental karyotypes or medical	Serum LH and relationship with reproductive outcomes	LBR CPR	**LBR:** ≤5 mIU/mL: 23.08 (15/65) 5-10 mIU/mL: 31.48% (17/54) ≥10 mIU/mL: 17.39% (4/23) **Clinical pregnancy rate :** Cumulative ≤5 mIU/mL: 61.54% (40/65) 5-10 mIU/mL: 68.52% (37/54) ≥10 mIU/mL: 56.52% (13/23)	

clinical medicine, *11*(16), 4670.		conditions that contraindicated ART and/or pregnancy; (4) two or more previous recurrent spontaneous abortions; (5) other known endocrine disorders; (6) previous medication of COCP or glucocorticosteroids within 2–3 months before ovarian stimulation; (7) repeated cycles, i.e., one patient with more than one time of COH Patients were divided in three groups according to their baseline LH level, i.e. ≤5 mIU/mL (n=65), 5-10 mIU/mL (n=54), ≥10 mIU/mL (n=23)				
Xi, W., Gong, F., & Lu, G. (2012). Correlation of serum Anti-Müllerian hormone concentrations on day 3 of the in vitro fertilization stimulation cycle with assisted reproduction outcome in polycystic ovary syndrome patients. *Journal of assisted reproduction and genetics*, *29*(5), 397–402.	CS	164 PCOS patients undergoing their first IVF treatment cycle. **Control (n=82):** Between the 25th and the 75th percentiles (average AMH) 4.85 - 8.82 ng/ml **Study group 1 (n=41):** Below the 25th percentile (low AMH) <4.85 ng/ml **Study group 2 (n=41):** Above the 75th percentile (high AMH). >8.82 ng/ml	To investigate whether serum AMH on day 3 could predict controlled ovarian stimulation and reproductive outcomes in women with PCOS.	CPR	**Control:** - Clinical pregnancy rate: 66.7% **Study group 1:** - Clinical pregnancy rate: 65%, NS **Study group 2:** - Clinical pregnancy rate: 45.9%, NS	
Zhang, L. J., Liu, D., Xu, L. Q., Wei, J. Y., Fan, L., Zhang, X. Q., & Liu, F. H. (2025). Impact of Luteinizing Hormone on IVF/ICSI Assisted Reproduction on the Initiation Day of Gonadotropin-releasing Hormone Antagonist Protocol. *Endocrine,*	CS	The data of 1361 cycles of IVF/ICSI using the GnRH-antagonist protocol. **Inclusion criteria** (1) IVF/ICSI cycles with fresh embryo transfer; (2) Cycles with trigger drugs using hCG 10000IU (ZHUHAI LIVZON, China); (3) The basic sex hormone value is detected on the 2nd, 3rd or 4th day of menstrual cycle; (4) The number of transferred embryos is 1 or 2 **Exclusion criteria**	The relationship between serum LH level on the Gn initiation day and IVF/ICSI outcomes was analyzed	OHSS CPR	**Study group:** -Incidence of different grades of OHSS (%,N): poor: 0.00 (0/270) normal: 0.89 (3/338) high: 3.42 (5/146) - Clinical pregnancy rate: poor: 49.63 (134/270) normal: 58.0 (196/338) high: 59.60 (87/146)	

metabolic & immune disorders drug targets, *25*(5), 400–410.		(1) Age ≥ 45 years old; (2) PGT cycles; (3) Fresh embryo transfer cancelled. (4) Cycles with missing data or incomplete follow-up. **Study group:** poor: 270 normal: 338 high: 146 **Control group:** poor: 157 normal: 232 high: 251			**Control group:** -Incidence of different grades of OHSS (%,N): poor: 2.55 (4/157), p=0.018 normal: 3.45 (8/232), p=0.058 (NS) high: 5.98 (15/251), NS - Clinical pregnancy rate: poor: 47.77 (75/157), NS normal: 53.45 (124/232), NS high:68.92 (173/251), p= 0.059 (NS)	

3. DOES HORMONE PRE-TREATMENT IMPROVE EFFICACY AND SAFETY OF OVARIAN STIMULATION?

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Zhu, S., Lv, Z., Song, L., Zhang, Q., Fan, Y., & Li, J. (2022). Estradiol pretreatment in GnRH antagonist protocol for IVF/ICSI treatment. *Open medicine (Warsaw, Poland)*, *17*(1), 1811–1820.	SR	Systematic review, including 7 RCTs	oestrogen pre-treatment compared to no pre-treatment in the GnRH antagonist protocol	LBR Cumulative OPR	**LBR:** 4 RCTs, OR: 0.98 (95% CI:0.74–1.30; P = 0.90, 919 women) between patients with and those without estradiol pretreatment in GnRH antagonist protocol. **Cumulative ongoing pregnancy:** 7 RCT N=1236 no significant difference in ongoing pregnancy rate (odds ratio (OR): 0.92 (95% CI: 0.69–1.21; P = 0.53)	Luteal estradiol pretreatment in IVF/ICSI cycles with GnRH antagonist protocol in normal ovary responding population does not affect the reproductive outcomes
Beretsos, P., Partsinevelos, G. A., Arabatzi, E., Drakakis, P., Mavrogianni, D., Anagnostou, E., Stefanidis, K., Antsaklis, A., & Loutradis, D. (2009). "hCG priming" effect in controlled ovarian stimulation through a long protocol. *Reproductive biology and endocrinology : RB&E*, *7*, 91.	RCT	Patients with a history of at least one previous unsuccessful ICSI cycle. **Inclusion criteria:** 25-40 years of age and a normal hormonal profile **Exclusion criteria:** ovulation induction or any other hormone treatment for less than three months preceding the study. **Control (n=27):** **Study group (n=19):**	**Study group:** long luteal (intranasal) protocol with rFSH + 7 days hCG 200 IU/day before rFSH fixed dose of 200 IU daily **Control:** long luteal (intranasal) protocol with rFSH fixed dose of 200 IU daily	CPR No of MII oocytes	**Control:** - Clinical pregnancy rate (%, N) 31.8 - Number of MII oocytes (mean ± SD) 7(3) **Study group:** - Clinical pregnancy rate (%, N) 46.2, p=<0.05 - Number of MII oocytes (mean ± SD) 8(2), N/A	pilot study, poor quality

Cédrin-Durnerin, I., Carton, I., Massin, N., Chevalier, N., Dubourdieu, S., Bstandig, B., Michelson, X., Goro, S., Jung, C., & Guivarc'h-Lévêque, A. (2024). Pretreatment with luteal estradiol for programming antagonist cycles compared to no pretreatment in advanced age women stimulated with corifollitropin alfa: a non-inferiority randomized controlled trial. *Human reproduction (Oxford, England)*, *39*(9), 1979–1986.	RCT	Women with advanced age, first or second IVF/ICSI cycle. **Inclusion criteria:** Patients aged between 38 and 42 years, regular cycles (26–35 days) with no limitation on antral follicle count (AFC) or anti-Mullerian hormone (AMH) levels, weight >50 kg and body mass index (BMI) <32, first or second IVF or ICSI cycle **Exclusion criteria:** No known polycystic ovarian syndrome, history of ovarian hyperstimulation, dysovulation with irregular cycles, presence of a hydrosalpinx or uterine malformation, or stage 3 or 4 endometriosis. Patients having already undergone two cycles of IVF/ICSI were excluded. **Control (n=144):** **Study group (n=147):**	**Study group:** E2 pre-treatment started between Day 20 (D20) and D24 of the cycle and continued until Wednesday evening following the onset of menses and stimulation was started on Friday. Stimulation with corifollitropin alpha 150 IU single dose. Fixed GnRH antagonist from d6 0.25 mg/day up to the day of hCG. **Control:** No pre-treatment. stimulation was started on D2 or D3 of the spontaneous menstrual cycle. Stimulation with corifollitropin alpha 150 IU single dose. Fixed GnRH antagonist from d6 0.25 mg/day up to the day of hCG.	Cumulative LBR LBR CPR No of MII oocytes	**Control:** - Cumulative live birth rate (%, N) 22.9% (33/144) - Live birth rate (%, N) 18.5% (17/92) - Number of MII oocytes (mean ± SD) 7.3 (5.2) **Study group:** - Cumulative live birth rate (%, N) 17.7 (26/147), NS - Live birth rate (%, N) 16.2% (16/99), NS - Number of MII oocytes (mean ± SD) 7.0 (5.5), NS	
Gao, J., Mai, Q., Zhong, Y., Miao, B., Chen, M., Luo, L., Zhou, C., Mol, B. W., & Yanwen, X. (2024). Pretreatment with oral contraceptive pills in women with PCOS scheduled for IVF: a randomized clinical trial. *Human reproduction open*, *2024*(2), hoae019.	RCT	PCOS according to the 2003 Rotterdam PCOS diagnostic criteria. **Inclusion criteria:** patient age 20–40 years; and scheduled for a first or second IVF/ICSI cycle **Exclusion criteria:** endometriosis, endometrioma or submucous myoma, uterine malformations such as bicornuate uterus and uterine cavity adhesion, ovarian tumors, recurrent spontaneous abortion, and chromosomal abnormalities	**Study group:** ethinyl estradiol (0.03 mg) and drospirenone (3 mg). OCPs were administered daily for 21 days to induce menstruation, followed by 7 days of washout. Recombinant FSH (rFSH) was started on Day 7 of the washout period **Control:** rFSH was started immediately regardless of the day of the menstrual cycle	Cumulative LBR LBR OHSS CPR No of MII oocytes	**Control:** - Cumulative live birth rate (%, N) ITT: 77,7% (94/121) - Live birth rate (%, N) per protocol: 55.1% (60/109) - Incidence of different grades of OHSS (%, N) ITT: 10.74% (13/121) - Clinical pregnancy rate (%, N) per protocol: 68.8% (75/109) - Number of MII oocytes (mean ± SD) 26.6 **Study group:** - Cumulative live birth rate (%, N) ITT: 74,4% (90/121), p=0.652	non inferior washout 7d, freeze all

		Control (n=118): **Study group (n=119):**			- Live birth rate (%, N) per protocol: 52.8% (56/106), p=0.785 - Incidence of different grades of OHSS (%, N) ITT: 6.61% (8/121), p=0.361 - Clinical pregnancy rate (%, N) per protocol: 67.9% (72/106), n=1 - Number of MII oocytes (mean ± SD) 22.8, n=0.01	
Eftekhar, M., Bagheri, R. B., Neghab, N., & Hosseinisadat, R. (2018). Evaluation of pretreatment with Cetrotide in an antagonist protocol for patients with PCOS undergoing IVF/ICSI cycles: a randomized clinical trial. *JBRA assisted reproduction*, *22*(3), 238–243.	RCT	Women with PCOS based on the Rotterdam criteria. **Inclusion criteria:** Patients with at least two of the following findings were included in the study: oligo-ovulation or anovulation; clinical or biochemical hyperandrogenism; and polycystic ovaries on ultrasound examination **Exclusion criteria:** Women aged 40 years or older, presence of severe male factor or systemic disease, use of hormone medication other than OCP, individuals on systemic drug therapy or with recurring IVF failure, recurrent pregnancy loss or uterine anomalies. **Control (n=50)** **Study group (n=38)**	**Study group:** 3 days of antagonist starting on day 2 before GnRH flexible antagonist protocol with rFSH 150 IU on cycle day 5 **Control:** GnRH flexible antagonist protocol with rFSH 150 IU on cycle day 2	Incidence of OHSS CPR No of MII oocytes	**Control:** - Incidence of different grades of OHSS (%, N): 36% (18) - Clinical pregnancy rate (%, N): 9% (2) - Number of MII oocytes (mean ± SD) 14.1 (8) **Study group:** - Incidence of different grades of OHSS (%, N): 39% (15), p=0.74 - Clinical pregnancy rate (%, N): 32% (7), p=0.05 - Number of MII oocytes (mean ± SD) 14.6(8), p=0.76	abnormally low CPR in control group and high number of loss of follow up

Fernández-Prada, S., Martín-Cameán, M., Armijo, O., Diez-Sebastián, J., Iniesta, S., Lobo, S., Silva, P., Sanz, C., Sánchez, M. J., & Hernández, A. (2022). Use of steroid pre-treatments in IVF-ICSI cycles with GnRH antagonist protocol and their impact on gestational outcomes. *Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology*, *42*(3), 478–484.	RCT	**Inclusion criteria:** age between 18 and 40 years, BMI 30 kg/m2, less than two previous IVF attempts, basal FSH <14 UI/l basal E2 < 80 pg/ml. **Exclusion criteria:** AFC less than 4, endometriosis grades III and IV, uterus disorders previously diagnosed, uncorrected hydrosalpinx severe male factor (mobile sperm count <1 million). **Control (n=27):** **Study group (n=34):**	**Study group:** OCP 30 mg ethinyl E2/150 mg levonorgestrel, from day 1 of the cycle to five days before the scheduled ovarian stimulation **Control:** No premedication, start of the stimulation on day 2 or 3 of the menstrual cycle		**Control:** - Cumulative live birth rate (%, N) 47.6% (10/21) - Live birth rate (%, N) 46.7% (7/15) - Number of MII oocytes (mean ± SD) 6.15 ±4.68 **Study group 1 :** - Cumulative live birth rate (%, N) 38.7% (12/31), NS - Live birth rate (%, N) 31.8% (7/22), NS - Number of MII oocytes (mean ± SD) 6.32±5.16, NS **Study group 2:** - Cumulative live birth rate (%, N) 27.3% (6/22), NS - Live birth rate (%, N) 28.6% (4/14), NS - Number of MII oocytes (mean ± SD) 5.76±3.67, NS	underpower, need for larger study or meta-analysis
Ghasemzadeh et al. Effect of Estrogen Priming in Antagonist Cycles in Women With Poor Response to IVF Treatment. Crescent Journal of Medical and Biological Sciences, Vol. 7, No. 1, January 2020	RCT	POR based on center's own definition. **Inclusion criteria:** Women in the age group of 19 to 42 years with low ovarian reserve, borderline FSH (over 10), low AMH (below 1), and low number of antral follicles who had previously not responded to treatment with short-term antagonist and gonadotropin protocol or their retrieved oocytes was ≤ 3 **Exclusion criteria:** women who had not responded to treatment at all, had a follicle or a canceled cycle or changed into IUI,	**Study group:** From the 21st day of the previous IVF cycle, a daily dosage of oral estradiol valerate (4 mg) was prescribed for these patients. This continued to the second day of the cycle, day of starting HMG and FSH **Control:** the second day of the cycle, day of starting HMG and FSH	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD) 2.8±0.3 **Study group:** - Number of MII oocytes (mean ± SD) 3.6±0.3, p=0.05	very poor quality and high heterogeneity in ET

		or had certain diseases such as hypothyroidism or hyperprolactinemia. **Control (n=53)** **Study group (n=53)**				
Zhang, S., Tang, Y., Wang, X., Zong, Y., Li, X., Cai, S., Ma, H., Guo, H., Song, J., Lin, G., Lu, G., & Gong, F. (2022). Estrogen valerate pretreatment with the antagonist protocol does not increase oocyte retrieval in patients with low ovarian response: a randomized controlled trial. *Human reproduction (Oxford, England)*, *37*(7), 1431–1439.	RCT	women with low response according to the Bologna criteria who requested IVF treatment. **Inclusion criteria:** women under 45 years of age with a low ovarian response (according to the Bologna criteria) and a BMI between 18 and 28 kg/m2 **Exclusion criteria:** PGT cycle; donor cycle; family history of thrombosis or a high risk of thrombosis; previous history of hypertension or hypertension, systolic blood pressure 150 mmHg, diastolic blood pressure 90 mmHg; hyperlipidemia;estrogen-dependent breast disease; and cervical biopsy showing cervical intraepithelial neoplasia grade III or above. **Control (n=224):** **Study group (n=209):**	**Study group:** on Day 7 after ovulation patients were administered oral estrogen valerate (2 mg twice a day) until Day 2 of their next menstruation. Ovary stimulation was performed using rFSH, and a flexible GnRH antagonist **Control:** No pretreatment, start at D2 A fixed dose of 300 IU recombinant FSH	CPR No of MII oocytes	**Control:** - Clinical pregnancy rate (%, N) per first transfer: 28.7%, 43/276 - Number of MII oocytes (mean ± SD) 3.1±2.4 **Study group:** - Clinical pregnancy rate (%, N) per first transfer: 19.3% 23/276, p=0.08 - Number of MII oocytes (mean ± SD) 2.9±2.5, p=0.16	well powered for oocyte number, no difference in oocyte number, not powered for CPR or LBR
Zhang, Y., Liu, L., Qin, J., Huang, H., Xue, L., Wang, S., & Tan, W. (2021). Evaluation of GnRH antagonist pretreatment before ovarian stimulation in a GnRH antagonist protocol in normal ovulatory women	RCT	All consecutive women who underwent their first or second cycle of IVF/ICSI were included, and the first cycle included only normal responders. **Inclusion criteria:** age<40years; anti-Mullerian hormone (AMH) ≥1.2ng/	**Study group:** ovarian stimulation was initiated after 3 days of GnRH antagonist pretreatment followed by 150–225IU of recombinant FSH in flexible antagonist **Control:**	LBR OHSS OPR CPR No of MII oocytes	**Control:** - Live birth rate (%, N) per ET cycle 43.1%, 25/58 - Incidence of different grades of OHSS (%, N): 2.9%, 2/68 - ongoing pregnancy rate (%, N): 45.6% (26/58) - Clinical pregnancy rate (%, N): 53.4%	No difference

undergoing IVF/ICSI: a randomized controlled trial. *Reproductive biology and endocrinology : RB&E*, *19*(1), 158.		ml; antral follicle count (AFC) >7; regular menstrual cycles over the 3 months before the study (25–35days in duration); and a basal serum FSH concentration lower than 12IU/L. **Exclusion criteria:** endometriosis grade III to IV (American Fertility Society classification of endometriosis); adenomyosis; diagnoses of PCOS ; decreased ovarian reserve function (FSH >12U/L or AFC <8 or AMH <1.1ng/ml) or a poor ovarian response (<4 oocytes being retrieved in a previous IVF or ICSI cycle); BMI >30kg/m2; severe male oligospermia or obstructive azoospermia; and use of hormone therapy within the 3 months before the study. **Control (n=68):** **Study group (n=68):**	ovarian stimulation with Gn was initiated on day 2 of the menstrual cycle		- Number of MII oocytes (mean ± SD) 9.0 (5.3-12.0) **Study group:** - Live birth rate (%, N) per ET cycle 33.9%, 20/59, p=0.19 - Incidence of different grades of OHSS (%, N): 1.5%, 1/68, p=0.56 - ongoing pregnancy rate (%, N): 33.9 (20/59) - Clinical pregnancy rate (%, N): 45.8% (27/59), p=0.4 - Number of MII oocytes (mean ± SD) 7.0 (6.0-11.0), p=0.48	

4A. ACCORDING TO PREDICTED RESPONSE-BASED STRATIFICATION, WHICH STIMULATION PROTOCOL IS MOST EFFICIENT AND SAFE FOR HIGH RESPONDERS?

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Arce JC, Andersen AN, Fernández-Sánchez M, Visnova H, Bosch E, García-Velasco JA, Barri P, de Sutter P, Klein BM, Fauser BC. Ovarian response to recombinant human follicle-stimulating hormone: a randomized, antimüllerian hormone-stratified, dose-response trial in women undergoing in vitro fertilization/intracytoplasmic sperm injection. Fertility and sterility 2014;102: 1633-1640.e1635.	RCT	Inclusion criteria Women diagnosed with tubal infertility, unexplained infertility, infertility related to endometriosis stage I/II, or with partners diagnosed with male factor infertility, age 18–37 years; BMI 18.5–32.0 kg/m2; infertility for at least 1 year before randomization; regular menstrual cycles of 24–35 days, presumed to be ovulatory; HSG, hysteroscopy, or transvaginal ultrasound documenting a uterus consistent with expected normal function; transvaginal ultrasound documenting presence and adequate visualization of both ovaries, without evidence of significant abnormality; early follicular phase FSH serum concentration of 1–12 IU/L and total AFC (diameter 2–10 mm) count R6 and %25 for both ovaries combined; serum AMH concentration of 5.0–44.9 pmol/L (0.7–6.3 ng/mL); willing to accept transfer of one blastocyst in the fresh cycle; and willing to accept transfer of one blastocyst in frozen	Study group: ovarian stimulation with either 5.2 (=23), 6.9 (n=26), 8.6 (n=24), 10.3 (n=24), or 12.1 µg (n=26) of r-hFSH Control group: ovarian stimulation with 11 µg (150 IU, n=25)) of follitropin alfa All women received a GnRH antagonist cycle.	Cumulative LBR LBR OHSS No of oocytes	**Study groups vs control** -cumulative live birth rate (43% (10/23), 54% (14/26), 46% (11/24), 38% (9/24), 50% (13/26) vs. 56% (14/25)) -live birth rate (39% (9/23), 42% (11/26), 38% (9/24), 25% (6/24), 46% (12/26) vs. 48% (12/25). -A statistically significant dose–response relationship with respect to number of oocytes retrieved was established for r-hFSH (5.9±3.9, 9.1±6.4, 10.6±4.8, 13.6±7.8, 14.4±5.8 vs. 12.4±5.4). -Two cases of early OHSS were reported in the highest r-hFSH dose groups (10.3 and 12.1 µg, respectively), and three late OHSS (one in the 8.6 µg group and two in the 12.1 µg group).	

		embryo replacement cycles initiated within 6 months after randomization. **exclusion criteria** known PCOS-associated with anovulation; known endometriosis stage III–IV; three or more COS cycles for IVF/ICSI; poor ovarian response in a previous COS cycle using an average daily FSH dose R150 IU (<4 follicles R15 mm or cycle cancellation due to limited follicular response); excessive ovarian response in a previous COS cycle using an average daily FSH dose <225 IU (>25 oocytes retrieved or cycle cancellation due to excessive ovarian response, including risk of OHSS); severe OHSS in a previous COS cycle; history of recurrent miscarriage; current or past (up to 1 year before randomization) abuse of alcohol or drugs; and intake of more than 14 units of alcohol per week during the past month or smoking more than 10 cigarettes per day within 3 months before randomization.				

Casano, S., Guidetti, D., Patriarca, A., Pittatore, G., Gennarelli, G., & Revelli, A. (2012). MILD ovarian stimulation with GnRH-antagonist vs. long protocol with low dose FSH for non-PCO high responders undergoing IVF: a prospective, randomized study including thawing cycles. *Journal of assisted reproduction and genetics*, *29*(12), 1343–1351.	RCT	women younger than 38 with good ovarian reserve **Inclusion criteria:** patients younger than 38 years, with basal (day 3) follicle-stimulating hormone (FSH) <8 U/l, anti-Mullerian hormone (AMH) >2 ng/ml and antral follicle count (AFC) >16, at their first IVF attempt, **Exclusion criteria:** not specified **Control (n=207):** **Study group (n=205):**	**Study group:** 150 IU/d of recombinant FSH from day 4 of a spontaneous menstrual cycle; the GnRH antagonist cetrorelix was then given from the fifth day of stimulation (day 8 of the cycle). **Control:** The classical "long" protocol was performed administering the GnRH agonist buserelin from day 21 of the cycle. After approximately two weeks, pituitary suppression was verified and rFSH was started at a daily dose of 150 IU	LBR Incidence of OHSS CPR No of MII oocytes	**Control:** - Live birth rate (%, N): 26,6%, NS - Incidence of different grades of OHSS (%, N): 2%, NS - Clinical pregnancy rate (%, N) 33.8%, NS - Number of MII oocytes (mean ± SD) 10.3+-4.6, NS **Study group:** - Live birth rate (%, N): 24,9 % - Incidence of different grades of OHSS (%, N): 1,6% - Clinical pregnancy rate (%, N): 31.5% - Number of MII oocytes (mean ± SD) 9.9+-5.1	
Ishihara, O., Klein, B. M., Arce, J. C., & Japanese Follitropin Delta Phase 2 Trial Group (2021). Randomized, assessor-blind, antimüllerian hormone-stratified, dose-response trial in Japanese in vitro fertilization/intracytoplasmic sperm injection patients undergoing controlled ovarian stimulation with follitropin delta. *Fertility and sterility*, *115*(6), 1478–1486.	RCT	**Inclusion criteria:** Japanese women, 20–39 years of age and eligible for IVF/ICSI treatment, who were diagnosed with tubal infertility, unexplained infertility, or infertility related to endometriosis stage I/II or with partners diagnosed with male factor infertility. BMI of 17.5–32.0 kg/m2, regular menstrual cycles of 24–35 days, presence of both ovaries, AMH serum concentration of 5.0–44.9 pmol/L, and early follicular phase FSH serum concentration of 1–12 IU/L **Exclusion criteria:** endometriosis stage III/IV, three or more, history of recurrent miscarriage, and use of hormonal preparations (except for thyroid medication) during the last	**Study group:** fixed daily subcutaneous injections of 6 mg, 9 mg, or 12 mg follitropin delta. The assigned daily dose was fixed throughout the stimulation period. GnRH antagonist 0.25 mg was initiated on stimulation day 6 and maintained throughout the stimulation period **Control:** 150 IU/d follitropin beta. The assigned daily dose was fixed throughout the stimulation period. GnRH antagonist 0.25 mg was initiated on stimulation day 6 and maintained throughout the stimulation period	LBR Incidence of OHSS OPR CPR	**Control:** - Live birth rate (%, N): 15% (6/41) - Incidence of different grades of OHSS (%, N): 22% (9/41) - ongoing pregnancy rate (%, N): 15% (6/41) - Clinical pregnancy rate (%, N): 20% (8/41) **Study group:** - Live birth rate (%, N) 6 µg: 16% (6/37) 9 µg: 18% (7/40) 12 µg: 23% (9/40) - Incidence of different grades of OHSS (%, N) 6 µg: 11% (4/37) 9 µg: 8% (3/40) 12 µg: 18% (7/40) - ongoing pregnancy rate (%, N)	all outcomes are per started cycle

		menstrual cycle before randomization **Control (n=41)** **Study group** 6 µg: 37 9 µg: 40 12 µg: 40			6 µg: 16% (6/37) 9 µg: 18% (7/40) 12 µg: 25% (10/40) - Clinical pregnancy rate (%, N) 6 µg: 24% (9/37) 9 µg: 20% (8/40) 12 µg: 33% (13/40)	
Oudshoorn SC, van Tilborg TC, Eijkemans MJC, Oosterhuis GJE, Friederich J, van Hooff MHA, van Santbrink EJP, Brinkhuis EA, Smeenk JMJ, Kwee J et al. Individualized versus standard FSH dosing in women starting IVF/ICSI: an RCT. Part 2: The predicted hyper responder. Human reproduction (Oxford, England) 2017;32: 2506-2514.	RCT		**Study group**: ovarian stimulation with 100 IU FSH (n=255) **Control group**: ovarian stimulation with 150 IU FSH (n=266) Either in a GnRH agonist or GnRH antagonist protocol was used for pituitary suppression	18 month cumulative LBR 1st cycle LBR OHSS	**Study group vs control** - ongoing pregnancy within 18 months of follow-up resulting in live birth 66.3% vs. 69.5%; RR 0.953, 95% CI 0.85–1.07, NS -1st cycle live birth (fresh and cryopreserved embryos) 36.0% vs. 39.1%, NS -OHSS rate 5.2% vs. 11.8%, p<0.05	
Revelli, A., Gennarelli, G., Sestero, M., Canosa, S., Carosso, A., Salvagno, F., Pittatore, G., Filippini, C., & Benedetto, C. (2020). A prospective randomized trial comparing corifollitropin-α late-start (day 4) versus standard administration (day 2) in expected poor, normal, and high responders undergoing controlled ovarian stimulation for IVF. *Journal of assisted*	RCT	included 113 patients aged 18–43 years undergoing IVF to treat male or tubal-related infertility **Inclusion criteria:** According to the biomarkers assessed during the diagnostic workout AMH and AFC, enrolled patients were expected high responders to COS (AFC > 15 and AMH > 3.5 ng/ml; n = 43) **Exclusion criteria:** BMI > 28, PCOS; indications to IVF other than male and/or tubal factor; IVF treatment completed in the previous 2 months; history of	**Study group:** corifollitropin on day4 **Control:** corifollitropin on day2	Cumulative LBR CPR No of MII oocytes	**Control:** - Cumulative live birth rate (%, N): 37.7% - Clinical pregnancy rate (%, N): 31.6% - Number of MII oocytes (mean ± SD) : 7.1+-4.8 **Study group:** - Cumulative live birth rate (%, N): 29.2%, NS - Clinical pregnancy rate (%, N): 25%, NS - Number of MII oocytes (mean ± SD): 7+-4.7, NS	

reproduction and genetics, *37*(5), 1163–1170.		OHSS; previous IVF cycle with more than 30 growing follicles ≥ 11 mm; presence of ovarian cyst or malignant ovarian tumor; known breast, uterus, or central nervous system cancer; systemic diseases potentially affecting ovarian response to gonadotropins. **Control (n=21)** **Study group (n=21)**				

4B. ACCORDING TO PREDICTED RESPONSE-BASED STRATIFICATION, WHICH STIMULATION PROTOCOL IS MOST EFFICIENT AND SAFE FOR NORMAL RESPONDERS?

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Ngwenya O, Lensen SF, Vail A, Mol BWJ, Broekmans FJ, Wilkinson J. Individualised gonadotropin dose selection using markers of ovarian reserve for women undergoing in vitro fertilisation plus intracytoplasmic sperm injection (IVF/ICSI). The Cochrane database of systematic reviews 2024;1: Cd012693.	SR	Systematic review of 12 RCTS	Dose comparisons of gonadotropins during ovarian stimulation for IVF/ICSI	LBR/OPR Incidence of OHSS No of oocytes	**200 vs. 100 IU** - LBR/OPR: OR 0.88, 95% CI 0.57-1.36, 2 RCTs, 522 women, NS -severe OHSS: peto OR 0.14, 95% CI 0.00-6.96, 2 RCT, 522 women, NS - moderate to severe OHSS: peto OR 0.62, 95% CI 0.21-1.87, 2 RCTs, 522 women, NS -Ratio of mean oocytes 1.58, 95% CI 1.43-1.77, 2 RCTs, 330 women **225/200 vs. 150 IU** -LBR/OPR: OR 0.98, 95% CI 0.70-1.36, 2 RCTs, 211 women, NS -severe OHSS: peto OR 1.00, 95% CI 0.20-5.02, 4 RCT, 740 women, NS - moderate to severe OHSS: peto OR 1.21, 95% CI 0.51-2.85, 4 RCTs, 740 women, NS Ratio of mean oocytes 1.16, 95% CI 1.08-1.25, 6 RCTs, 872 women **300 vs. 150 IU** -LBR: OR 0.80, 95% 0.19-3.42, 1 RCT, 37 women, NS -The ratio of mean oocytes was 1.23, 95% CI 0.89-1.72, 57 women **300 vs. 225 IU** LBR: OR 0.65, 95% 0.32-1.32, 1 RCT, 47 women, NS	

					- severe OHSS: peto OR 0.14, 95% CI 0.00-6.92, 1 RCT, 135 women, NS - moderate to severe OHSS: peto OR 0.67, 95% CI 0.11-3.99, 1 RCT, 135 women - ratio of mean oocytes 1.03, 95% CI 0.84-1.26, 1 RCT, 135 women	
Lou, H. Y., & Huang, X. Y. (2010). Modified natural cycle for in vitro fertilization and embryo transfer in normal ovarian responders. *The Journal of international medical research*, *38*(6), 2070–2076.	RCT	**Inclusion criteria:** Women with a regular menstrual cycle were recruited using the following inclusion criteria: age < 35 years; no previous IVF treatment; a baseline serum FSH concentration < 10 IU/l; a regular and proven ovulatory menstrual cycle of 28 – 30 days; a BMI of 18 – 28 kg/m2; and tubal pathology as the indication for IVF treatment. **Exclusion criteria:** Patients requiring ICSI. **Control (n=30)** **Study group (n=30)**	**Study group:** HMG 150 U daily without GnRH analog. **Control:** Long GnRH protocol + 150-300 U FSH.	OHSS OPR CPR No of MII oocytes	**Control:** -grades of OHSS (%, N): 6.7% (2/30) - ongoing pregnancy rate (%, N) : 23.3% (7/30) - Clinical pregnancy rate (%, N) : 30,0% (9/30) - Number of MII oocytes (mean ± SD) : 12.2+-8.6 **Study group:** - grades of OHSS (%, N): 0%, NS - ongoing pregnancy rate (%, N):26.7 (8/30), NS - Clinical pregnancy rate (%, N): 30,0 (9/30), NS - Number of MII oocytes (mean ± SD) : 7.8+-4.5, p<0.05	
Revelli, A., Gennarelli, G., Sestero, M., Canosa, S., Carosso, A., Salvagno, F., Pittatore, G., Filippini, C., & Benedetto, C. (2020). A prospective randomized trial comparing corifollitropin-α late-start (day 4) versus standard administration (day 2) in expected poor, normal, and high responders undergoing controlled ovarian	RCT	included 113 patients aged 18–43 years undergoing IVF to treat male or tubal-related infertility **Inclusion criteria:** According to the biomarkers assessed during the diagnostic workout AMH and AFC, enrolled patients were expected normal responders (AFC 7–15 and AMH 1.1–3.5 ng/ml; n = 39); **Exclusion criteria:** BMI > 28, PCOS; indications to IVF other than male and/or tubal	**Study group:** corifollitropin on day4 **Control:** corifollitropin on day2	Cumulative LBR CPR	**Study group vs controls** - cumulative live birth per oocyte pick-up: 16.7% (3/18) vs. 26.3% (5/19), NS - clinical pregnancy rate per started cycle: 16.7% (3/18) vs. 26.3% (5/19), NS	

stimulation for IVF. *Journal of assisted reproduction and genetics*, *37*(5), 1163–1170.		factor; IVF treatment completed in the previous 2 months; history of OHSS; previous IVF cycle with more than 30 growing follicles ≥ 11 mm; presence of ovarian cyst or malignant ovarian tumor; known breast, uterus, or central nervous system cancer; systemic diseases potentially affecting ovarian response to gonadotropins. **Control (n=20)** **Study group (n=19)**				

4C. ACCORDING TO PREDICTED RESPONSE-BASED STRATIFICATION, WHICH STIMULATION PROTOCOL IS MOST EFFICIENT AND SAFE FOR LOW RESPONDERS?

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Ngwenya O, Lensen SF, Vail A, Mol BWJ, Broekmans FJ, Wilkinson J. Individualised gonadotropin dose selection using markers of ovarian reserve for women undergoing in vitro fertilisation plus intracytoplasmic sperm injection (IVF/ICSI). The Cochrane database of systematic reviews 2024;1: Cd012693.	SR	Systematic review of 6 RCTS	Dose comparisons of gonadotropins during ovarian stimulation for IVF/ICSI	LBR/OPR Moderate or severe OHSS No of oocytes	**300/450 IU vs 150 IU** - LBR/OPR: 3 RCT, OR 1.20, 95% CI 0.78-1.86, 538 women, NS - moderate or severe OHSS: none reported - ratio of mean oocytes 1.97, 95% CI 1.70 to 2.29, 3 RCT, 947 women, p<0.05 **400/450 IU vs 300 IU** - OPR: OR 0.77, 95% CI 0.19-3.19, 1 RCT, 62 women, NS - moderate or severe OHSS: none reported - ratio of mean oocytes 0.97, 95% CI 0.74 to 1.27, 2 RCT, 110 women **600 IU vs 450 IU** -LBR: OR 1.33, 95% CI 0.71-2.52, 1 RCT, 356 women, NS - 1 case of moderate OHSS in the 600 IU dose group - ratio of mean oocytes 1.08, 95% CI 0.96 to 1.22, 1 RCT, 356 women	

De Marco, M. P., Montanari, G., Ruscito, I., Giallonardo, A., Ubaldi, F. M., Rienzi, L., Costanzi, F., Caserta, D., Schimberni, M., & Schimberni, M. (2021). Natural Cycle Results in Lower Implantation Failure than Ovarian Stimulation in Advanced-Age Poor Responders Undergoing IVF: Fertility Outcomes from 585 Patients. *Reproductive sciences (Thousand Oaks, Calif.)*, *28*(7), 1967–1973.	CS	**Inclusion criteria:** Advanced maternal age: patients over 40 years old and at least one of the following: (1) Abnormal ovarian reserve biomarker: AMH < 0.5–1.1 ng/mL; AFC < 5–7 (2) Previous POR: ≤ 3 oocytes with conventional stimulation (3) Two episodes of POR after maximal stimulation **Exclusion criteria:** (1) BMI greater than 35 kg/m2, (2) Irregular menstrual cycles, (3) Previous mono lateral oophorectomy, (4) The presence of untreated endocrine abnormalities, (5) The presence of comorbidities, (6) Patients who underwent PGT **Control (n=355)** **Study group (n=230)**	natural cycle IVF (n=230) was compared to conventional ovarian stimulation in GnRH antagonist protocol (n=355)	Cumulative LBR OPR	**Study group:** **-** Cumulative live birth rate (%, N) **:** 22/230(9.6) - ongoing pregnancy rate (%, N) : (36/230) 15.65% **Control:** **-** Cumulative live birth rate (%, N) **:** 51/355 (14.4) - ongoing pregnancy rate (%, N) : (70/355) 19.72%	
Kim, C. H., Kim, S. R., Cheon, Y. P., Kim, S. H., Chae, H. D., & Kang, B. M. (2009). Minimal stimulation using gonadotropin-releasing hormone (GnRH) antagonist and recombinant human follicle-stimulating hormone versus GnRH antagonist multiple-dose protocol in low responders undergoing in vitro fertilization/intracytoplasmic sperm injection. *Fertility and sterility*, *92*(6), 2082–2084.	RCT	**Inclusion criteria:** A low responder was defined as a patient who failed to produce three or fewer follicles with a mean diameter of at least 16 mm with the result that three or fewer oocytes were retrieved despite the use of a high gonadotropin dose (>2500 IU) in previous failed IVF/ICSI cycles. All patients had regular ovulatory cycles (duration 21–35 days). They were in good health with normal thyroid, hepatic, and renal functions, and they had experienced spontaneous onset of puberty and normal	**Study group:** Minimal stimulation MNC 0.25 mg GnRH antagonist cetrorelix + 150 IU rFSH as soon as the lead follicle reached 13–14 mm. **Control:** Flexible antagonist protocol rFSH 225IU D3 / 0.25 antagonist as soon as follicle of 13-14mm.	CPR No of MII oocytes	**Control:** - Clinical pregnancy rate (%, N) : 17.8 (8/45) - Number of MII oocytes (mean ± SD) : 3.1+/-1.6 **Study group:** - Clinical pregnancy rate (%, N) : 13.3 (6/45) - Number of MII oocytes (mean ± SD) : 1.5+/-0.9	

		sexual development. None of the subjects had taken any infertility medications (clomiphene and/or gonadotropins) within the preceding 3 months. **Exclusion criteria:** infertility medications (clomiphene and/or gonadotropins) within the preceding 3 months. Irregular cycles. **Control (n=45)** **Study group (n=45)**				
Revelli, A., Gennarelli, G., Sestero, M., Canosa, S., Carosso, A., Salvagno, F., Pittatore, G., Filippini, C., & Benedetto, C. (2020). A prospective randomized trial comparing corifollitropin-α late-start (day 4) versus standard administration (day 2) in expected poor, normal, and high responders undergoing controlled ovarian stimulation for IVF. *Journal of assisted reproduction and genetics*, *37*(5), 1163–1170.	RCT	included 113 patients aged 18–43 years undergoing IVF to treat male or tubal-related infertility **Inclusion criteria:** According to the biomarkers assessed during the diagnostic workout AMH and AFC, enrolled patients were expected poor responders (fulfilling at least two out of the three Bologna criteria for poor response, AMH < 1.1 ng/ml and AFC < 7; n = 31) **Exclusion criteria:** BMI > 28, PCOS; indications to IVF other than male and/or tubal factor; IVF treatment completed in the previous 2 months; history of OHSS; previous IVF cycle with more than 30 growing follicles ≥ 11 mm; presence of ovarian cyst or malignant ovarian tumor; known breast, uterus, or central nervous system cancer; systemic diseases potentially affecting ovarian	**Study group:** corifollitropin on day4 **Control:** corifollitropin on day2	Cumulative LBR CPR	**Study group vs controls** Cumulative LBR: 0% (0/9) vs. 23.1% (3/13), p<0.05 CPR: 0% (0/15) vs. 18.7% (3/16), p<0.05	

		response to gonadotropins. **Control (n=16)** **Study group (n=15)**				

5. WHICH PITUITARY SUPPRESSION PROTOCOL IS PREFERABLE?

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Glujovsky, D., Pesce, R., Miguens, M., Sueldo, C., & Ciapponi, A. (2023). Progestogens for prevention of luteinising hormone (LH) surge in women undergoing controlled ovarian hyperstimulation as part of an assisted reproductive technology (ART) cycle. *The Cochrane database of systematic reviews*, *11*(11), CD013827.	SR	Systematic review of 4 RCTs	Progestins for pituitary suppression vs GnRH analogues	LBR/OPR OHSS CPR No of MII oocytes	**PPOS vs. GnRH agonist in normal responders** - LBR/OPR:59/130 vs. 61/130; OR 0.94, 95% 0.58-1.53, NS - OHSS rate: 0/130 vs. 3/130; OR 0.14, 95% CI 0.01-2.73, NS - CPR: 65/130 vs. 69/130; OR 0.88, 95% CI 0.54-1.44, NS - No of MII oocytes (10.3±5.8 vs. 10.1±5.2; MD 0.20, 95% CI -1.14 to 1.54), NS. **PPOS vs. GnRH antagonist in normal responders** No of MII oocytes: 10.8±5.8 vs. 7±4.2; MD 3.80, 95% CI 1.82, 5.78, p<0.05. **PPOS vs. GnRH antagonist in poor responders:** LBR/OPR: 37/170 vs. 31/170; OR 1.25; 95% CI 0.73-2.13, NS, CPR: 48/170 vs. 39/170; OR 1.32; 95% CI 0.81-2.16, NS, No of MII oocytes: 3.2±2.4 vs. 2.8±2.2; MD 0.40; 95% CI -0.09 to 0.89, NS.	

Liu, C., Tian, T., Lou, Y., Li, J., Liu, P., Li, R., Qiao, J., Wang, Y., & Yang, R. (2023). Live birth rate of gonadotropin-releasing hormone antagonist versus luteal phase gonadotropin-releasing hormone agonist protocol in IVF/ICSI: a systematic review and meta-analysis. *Expert reviews in molecular medicine*, *26*, e2.	SR	women undergoing ovarian stimulation for IVF/ICSI with either the GnRH antagonist or long GnRH agonist protocol. **Inclusion criteria:** (1) studies comparing a standard luteal long GnRH-a protocol with the GnRH-ant protocol; (2) RCT as the study design and (3) studies written in English. **Exclusion criteria:** (1) single-dose GnRH-a or GnRH-ant; (2) reviews, comments, conference abstracts, short articles or study protocols or (3) articles including donor oocyte cycles.	**Study group:** Women undergoing ovarian stimulation with the GnRH antagonist protocol. **Control:** Women undergoing ovarian stimulation with the long GnRH agonist protocol.	LBR Incidence of OHSS	**Control:** - Live birth rate (%, N) : subgroup analyses of different population types, hormonal pretreatments, fixed or flexible protocols and types of agonists and antagonists, there were no differences in the live birth rates between the GnRH-ant and GnRH-a groups **Study group:** - Live birth rate (%, N) : RR of 0.95, 95% CI: 0.86–1.06, 13 RCTs, 3336 cycles, p=0.96 - Incidence of different grades of OHSS (%, N) : RR: 0.79, 95% CI 0.71–0.88, 23 RCTs, 5471 cycles, p=0.24 -moderate-to-severe OHSS rate: RR: 0.49, 95% CI 0.37–0.64, 22 RCTs, 5637 cycles, p<0.01	
Siristatidis, C. S., Yong, L. N., Maheshwari, A., & Ray Chaudhuri Bhatta, S. (2025). Gonadotropin-releasing hormone agonist protocols for pituitary suppression in assisted reproduction. *The Cochrane database of systematic reviews*, *1*(1), CD006919.	SR	**Inclusion criteria:** We included randomized controlled trials (RCTs) comparing any two protocols of GnRHa, or variations of the protocol in terms of different doses or duration, used in in vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) cycles in sub fertile women **Exclusion criteria:** non-RCTs	To evaluate the effectiveness and safety of different GnRHa protocols used as adjuncts to COH in women undergoing ART	LBR/OPR CPR	**Long vs short GnRH agonist protocol:** LBR/OPR: OR 1.45, 95% CI 0.83-2.52, 5 RCT, 381 women, NS **Long vs ultrashort GnRH agonist protocol:** LBR: 1 RCT, OR 1.78, 95% CI 0.72-4.36, 150 women, NS **Short vs ultrashort GnRH agonist protocol** CPR: 1 RCT, OR 1.33, 95% CI 0.47-3.81, 82 women, NS **Long GnRH agonist protocol: luteal vs follicular start** : LBR/OPR: 1 RCT, OR 1.89, 95% CI 0.87-4.10, 223 women, NS	

					Long GnRH agonist protocol: continuation vs stopping GnRH agonist at start of stimulation OPR: OR 0.66, 95% CI 0.30-1.49, 2 RCT, 194 women, NS CPR: OR 0.76, 95% CI 0.40-1.44, 3 RCT, 264 women, NS **Long agonist protocol: continuation of same-dose vs reduced-dose GnRH agonist until trigger**: LBR/OPR: OR 1.59, 95% CI 0.66-3.87, 1 RCT, 96 women, NS	
Venetis, C. A., Storr, A., Chua, S. J., Mol, B. W., Longobardi, S., Yin, X., & D'Hooghe, T. (2023). What is the optimal GnRH antagonist protocol for ovarian stimulation during ART treatment? A systematic review and network meta-analysis. *Human reproduction update*, *29*(3), 307–326.	SR	Systematic review of 6 RCTs and 907 participants	Comparing fixed and flexible GnRH antagonist protocols	OPR	Ongoing pregnancy rate was significantly lower with a flexible GnRH antagonist protocol compared to a fixed (RR 0.76, 95% CI 0.62-0.94, 6 RCTs; 907 women).	
Yang, L., Liang, F., Yuan, Y., Luo, X., Wang, Q., Yao, L., & Zhang, X. (2023). Efficacy of progestin-primed ovarian stimulation in women with polycystic ovary syndrome undergoing *in vitro* fertilization: a systematic review and meta-analysis. *Frontiers in endocrinology*, *14*, 1224858.	SR	**Inclusion criteria:** 1) RCTs or observational studies published in English; 2) infertile women diagnosed with PCOS undergoing IVF or ICSI; 3) the intervention group used PPOS protocol without discrimination of progestin types, and the control group included GnRH analogue protocols, involving the GnRH antagonist and the GnRH agonist (GnRH-a) protocol; and 4) primary outcomes included: live birth rate; the incidence of moderate or	**Study group:** Progestins **Control:** GnRH agonist or antagonist protocol	LBR OHSS OPR CPR No of MII oocytes	- Live birth rate (%, N) : 1 RCT: OR 1.46, 95% CI 0.79-2.71, 167 cycles, p=0.23 - Incidence of different grades of OHSS (%, N) : OR 0.19, 95% CI 0.01-4.11, 2 RCT, 240 patients, p=0.29 - ongoing pregnancy rate (%, N) : OR 0.98, 95% CI 0.43-2.24, 3 RCT, 418 patients, p=0.97 - Clinical pregnancy rate (%, N) : OR 1.00, 95% CI 0.51-1.94, 3 RCT, 418 cycle, p=1.00 -Number of MII oocytes (mean ± SD)	

		severe OHSS; and the number of metaphase II (MII) oocytes; Secondary outcomes included the number of oocytes retrieved; the number of good-quality embryos; the total dose of gonadotropin (Gn) stimulation; the incidence of premature LH surge; cycle cancellation rate (due to no viable embryos); implantation rate (IR); clinical pregnancy rate (CPR); and ongoing pregnancy rate (OPR). **Exclusion criteria:** not reported			MD -0.85, 95% CI -3.40 to 1.71, 3 RCT, 358 patients, p=0.52	
Cai, H., Shi, Z., Liu, D., Bai, H., Zhou, H., Xue, X., Li, W., Li, M., Zhao, X., Ma, C., Wang, H., Wang, T., Li, N., Wen, W., Wang, M., Zhang, D., Mol, B. W., Shi, J., & Tian, L. (2025). Flexible progestin-primed ovarian stimulation versus a GnRH antagonist protocol in predicted suboptimal responders undergoing freeze-all cycles: a randomized non-inferiority trial. *Human reproduction (Oxford, England)*, *40*(2), 319–327.	RCT	**Inclusion criteria:** women under 40 years old with a predicted suboptimal response based on antral follicle count (AFC) (2–10 mm) of <10 and a basal serum FSH level of <12 mIU/ml **Exclusion criteria:** Women with functional ovarian cysts (estrogen over 80 pg/ml) on Day 2 of the menstrual cycle, diagnosed uterine malformations, a history of two or more spontaneous miscarriages, cycles involving oocyte or sperm donation, couples with abnormal karyotypes, or undergoing PGT were excluded from the study. Additionally, individuals with contraindications to ovarian stimulation or those participating in other clinical trials were not eligible to participate.	**Study group:** PPOS protocol **Control:** GnRH antagonist protocol	Cumulative LBR LBR	**Control:** **-** Cumulative live birth rate (%, N) **:** in 12 months: 48.9% (114/233) - Live birth rate (%, N) : first transfer 34.3% (80/240) **Study group:** **-** Cumulative live birth rate (%, N) **:** in 12 months: 44.4% (96/216), RR 0.91, 95% CI 0.74-1.11 - Live birth rate (%, N) : first transfer: 32.9% (71/216), RR 0.96, 95% CI 0.74-1.24	

		Control (n=233) **Study group (n=216)**				
Chen, Z. Q., Ai, A., Zhang, Y., Li, H., Wang, J. Y., Wang, L., & Ng, E. H. Y. (2024). A randomized controlled trial to compare the live birth rate of the first frozen embryo transfer following the progestin-primed ovarian stimulation protocol vs. the antagonist protocol in women with an anticipated high ovarian response. *Fertility and sterility*, *121*(6), 937–945.	RCT	**Inclusion criteria:** women aged <43 years at the time of ovarian stimulation; those under-going the first IVF cycle; and those having an antral follicle count of >15 by transvaginal scanning on days 2–5 of the period. women with PCOS (Rotter-dam diagnostic criteria). **Exclusion criteria:** donor eggs or sperm used, the presence of hydrosalpinges shown on scanning and not treated, the presence of a functional ovarian cyst with a serum estradiol level of >100 pg/mL on days 2–5 of the period, an abnormal chromosome in either or both partners, an uncorrected congenital uterine anomaly, PGT, and moderate or severe endometriosis. **Control (n=327)** **Study group (n=330)**	**Study group:** PPOS protocol **Control:** GnRH antagonist protocol	Cumulative LBR LBR	**Control:** **-** Cumulative live birth rate (%, N) **:** ITT: 48.5% (190/392) Per protocol: 58.1% (190/327) - Live birth rate (%, N) : ITT: 32.7% (128/392) Per protocol: 39.1% (128/327) **Study group:** **-** Cumulative live birth rate (%, N) **:** ITT: 54.6% (214/392) Per protocol 64.8% (214/330) - Live birth rate (%, N) : ITT: 37.5% (147/392) Per protocol: 44.5% (147/330)	
Ye, H., Shi, L., Quan, X., Hou, M., Ma, H., Xue, S., Yu, Z., Chen, Q., & Sun, L. (2024). Cumulative live birth rate of in vitro fertilization cycle via progestin-primed ovarian stimulation versus gonadotropin-releasing hormone antagonist protocol in infertile women with normal ovarian reserve: an	RCT	**Inclusion criteria:** Infertile women aged 20–40 years who were undergoing their first cycle of IVF and had a spontaneous menstrual cycle (25–35 days), serum AMH levels > 1.1 ng/ml, bilateral AFC 8–20, basal FSH < 10 mIU/mL were enrolled. **Exclusion criteria:** Women who had basal oestradiol levels > 80 pg/mL, a recurrent	**Study group:** PPOS protocol **Control:** GnRH antagonist protocol	LBR Cumulative CPR No of MII oocytes	**Control:** - Live birth rate (%, N) : 52.9% (92/174) - Clinical pregnancy rate (%, N) : cumulative 55.9% (109/195) - Number of MII oocytes (mean ± SD) : 7.49 ± 4.23 **Study group:** - Live birth rate (%, N) : 55.7% (97/174)	

open-label, randomized controlled trial. *Human fertility (Cambridge, England)*, *27*(1), 2316005.		miscarriage with two or more spontaneous abortions, requiring preimplantation genetic testing, or any contraindications for COS or were diagnosed with endometriosis (grade 3 or higher), PCOS, hydrosalpinx, genital tract tumors, abnormal karyotype, abnormal uterine anatomical structure were excluded. **Control (n=172)** **Study group (n=170)**			- Clinical pregnancy rate (%, N) : cumulative 57% (114/200) - Number of MII oocytes (mean ± SD): 8.13 ± 4.66, NS	

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

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Bordewijk, E. M., Mol, F., van der Veen, F., & Van Wely, M. (2019). Required amount of rFSH, HP-hMG and HP-FSH to reach a live birth: a systematic review and meta-analysis. s*Human reproduction open*, *2019*(3), hoz008.	SR	**Inclusion criteria:** Randomized controlled trials comparing rFSH with HP- hMG or HP-FSH for ovarian stimulation in couples with an indication for IVF or ICSI treatment. **Exclusion criteria:** Studies that compare rFSH with hMG or pituitary extract-FSH, because these products are no longer available for ovarian stimulation.	**Study group 1:** r FSH **Study group 2:** HP-FSH **Control:** HP-hMG	Cumulative LBR LBR CPR	The MDs in total amount were −37 IU (seven studies; N = 3220; 95% CI, −115 to 41; I2 = 68%) for rFSH versus HP-hMG and −31 IU (17 studies; N = 3629; 95% CI, −290 to 228; I2 = 97%) for rFSH versus HP-FSH. For rFSH versus HP-hMG, the RR for clinical pregnancy, live birth and cumulative live birth were 0.90 (95% CI, 0.81–1.00), 0.88 (95% CI, 0.78–0.99) and 0.91 (95% CI, 0.80–1.04), respectively. For rFSH versus HP-FSH, the RR for clinical pregnancy and live birth were 1.03 (95% CI, 0.94–1.13) and 1.03 (95% CI, 0.90–1.18), respectively; the data on cumulative live birth rate were lacking.	
Conforti, A., Esteves, S. C., Humaidan, P., Longobardi, S., D'Hooghe, T., Orvieto, R., Vaiarelli, A., Cimadomo, D., Rienzi, L., Ubaldi, F. M., Zullo, F., & Alviggi, C. (2021). Recombinant human luteinizing hormone co-treatment in ovarian stimulation for assisted reproductive technology in women of advanced	SR	**Inclusion criteria:** RCTs in which recombinant FSH (r-hFSH) alone protocols were compared to r-hFSH/r-hLH co-treatment in women aged 35 years or above undergoing fresh IVF cycles.	R-hFSH vs r-hFSH+r-hLH	LBR CPR No of MII oocytes	**LBR:** OR 1.53, 95% CI 0.50-4.65, 2 RCT, 371 women, p=0.45. **Clinical pregnancy rates:** OR 1.11, 95% CI 0.89-1.38, 11 RCT, 1670 women, NS **Number of MII oocytes:** (MD -0.47, 95 CI -1.07 to + 0.12, 7 RCT, 997 women, p= ns.	This is not in agreement with the PROSPERO research question

reproductive age: a systematic review and meta-analysis of randomized controlled trials. *Reproductive biology and endocrinology : RB&E*, *19*(1), 91.						
Cozzolino, M., Vitagliano, A., Cecchino, G. N., Ambrosini, G., & Garcia-Velasco, J. A. (2019). Corifollitropin alfa for ovarian stimulation in in vitro fertilization: a systematic review and meta-analysis of randomized controlled trials. *Fertility and sterility*, *111*(4), 722–733.	SR	**Inclusion criteria:** Randomized controlled trials (RCTs) of infertile women undergoing a single IVF/ICSI cycle with either corifollitropin alfa or a conventional ovarian stimulation protocol based on daily injections.	**Study group:** Two studies focused on a population of poor responders, one of which only accepted patients fulfilling the Bologna criteria for poor ovarian response (11), and the other only included subjects with a previous poor response stimulation defined as <4 cumulus-oocyte complexes with at least 450 IU of rFSH per day.	LBR/OPR Incidence of OHSS CPR No of MII oocytes	**Study group:** - LBR/OPR: no difference RR, 0.92; 95% CI, 0.80–1.05, 8 RCT, 4340 cycles, p=0.21 - Incidence of different grades of OHSS (%, N) : overall: RR 1.15, 95% CI 0.83-1.57, 5 RCT, 3749 cycles, p=0.40 moderate/severe: RR 1.17, 95% CI 0.54-2.56, 4 RCT, 3349 cycles, p=0.69 - Clinical pregnancy rate (%, N) : RR 0.96, 95%CI 0.88-1.05, 7 RCT, 4242 cycles, p=0.33 - Number of MII oocytes (mean ± SD) : higher in study group MD 1.13 [95% CI, +0.33 to +1.92, 5 RCT, 3848 cycles, p=0.006	
Datta AK, Maheshwari A, Felix N, Campbell S, Nargund G. Mild versus conventional ovarian stimulation for IVF in poor, normal and hyper-responders: a systematic review and meta-analysis. Human.reproduction.update 2021;27: 229-253.	SR	studies from January 1990 (since the introduction of the concept of poor or high ovarian response in IVF) to April 2020. Abstracts or conference proceedings were also reviewed and included, avoiding duplication, only if all required information was available. Studies were excluded if complete information was not obtained despite personal request.	to evaluate MD-IVF (150 IU daily dose of gonadotrophin alone, or in combination with oral compounds) in randomised studies by comparing its clinical effectiveness, risks and cost with those of conventional (higher-dose stimulation) IVF protocols (CD-IVF) in patients identified as poor, normal and hyper-responders to IVF.	LBR Incidence of OHSS	live birth rate: RR 0.88, 95 % CI 0.69-1.12, 3 RCTs, 573 women, NS. Incidence of OHSS: RR 0.12, 95% CI 0.03-0.51, 3 RCTs, 623 women, p<0.05	

Montoya-Botero, P., Drakopoulos, P., González-Foruria, I., & Polyzos, N. P. (2021). Fresh and cumulative live birth rates in mild versus conventional stimulation for IVF cycles in poor ovarian responders: a systematic review and meta-analysis. *Human reproduction open*, *2021*(1), hoaa066.	SR	Although all RCTs clearly defined inclusion of women with POR, the definition was consistently different (14 different definitions) (Supplementary Table SIII), with only 3 out of 15 RCTs (18.8%) employing the Bologna criteria as an inclusion criterion. **Inclusion criteria:** only RCTs that compared the reproductive outcomes between the different protocols of mild (i.e. oral compounds, lower doses or shorter treatments) and conventional IVF stimulation in POR	**Study group:** Among the eligible studies, 12 compared an anti-oestrogen (clomiphene citrate (CC), n = 6) or an aromatase inhibitor (letrozole, n = 6) with COS. Finally, no studies were included in the delayed-start group. **Control:** In the control arm, nine RCTs used the long GnRH agonist protocol and three used the antagonist protocol.	Cumulative LBR LBR	**Study group:** **CLBR:** RR 1.15; 95% CI: 0.73 - 1.81; I2= 0% **LBR:** RR 1.01; 95% CI: 0.97- 1.04; I2 = 0%	
Qin Y. (2021). Effects of using letrozole in combination with the GnRH antagonist protocol for patients with poor ovarian response: A meta-analysis. *Journal of gynecology obstetrics and human reproduction*, *50*(8), 102139.	SR	**Inclusion criteria:** (1) all women subjected to the GnRH antagonist protocol in IVF/ICSI cycles, (2) adjunctive letrozole administration in the study group, (3) conventional GnRH antagonist protocol without letrozole in the control group (4) all patients characterized as poor ovarian responders. POR was determined as having at least one of the following criteria:(i) Retrieval of ≤3 oocytes during previous COH protocol; (ii) an abnormal ovarian reserve test(basal FSH <12 IU/mL, or antral follicle count (AFC) < 5−7 follicles or AMH< 1.1 ng/ml, or E2 <450pg/ml on the day of HCG). **Exclusion criteria:**	**Study group:** Letrozole + various types of FSH **Control:** FSH	CPR	- CPR: RR 1.57, 95% CI 1.00−2.44, 6 RCT, 564 women, NS. Low-dose: CPR: RR 1.65, 95% CI 0.85−3.18, 3 RCT, 270 women, NS High dose: CPR: RR 1.5, 95% CI 0.82−2.73, 3 RCT, 294 women, NS	Incorrect data

		1) retrospective cohort study, 2) non-comparative clinical trials, 3) publications in a language other than English, 4) studies with no data that we aimed to evaluate				
Berkkanoglu, M., Isikoglu, M., Aydin, D., & Ozgur, K. (2007). Clinical effects of ovulation induction with recombinant follicle-stimulating hormone supplemented with recombinant luteinizing hormone or low-dose recombinant human chorionic gonadotropin in the midfollicular phase in microdose cycles in poor responders. *Fertility and sterility*, *88*(3), 665–669.	RCT	**Inclusion criteria:** women who had <12 antral follicles and were undergoing a microdose protocol with GnRH-a followed by recombinant FSH administration had > three growing follicles (from 170 patients 35 were excluded on day 7 of stimulation) **Exclusion criteria:** women older than 42 years, women with only one ovary, and women with a basal FSH concentration of >12 IU/L < three growing follicles on day 7 of stimulation **Control (n=48)** **Study group (n=51)**	**Study group 1:** Group B: 600 IU rFSH + 75 IU rLH **Study group 2:** Group C: 600 IU rFSH + 75 IU rhCG **Control:** Group A: 600 IU of recombinant FSH	CPR No of MII oocytes	**Study group 1:** - Clinical pregnancy rate (%, N) : per transfer: 27.5% - Number of MII oocytes (mean ± SD) : 4.8 ±0.6 **Study group 2:** - Clinical pregnancy rate (%, N) : per transfer: 21.8% - Number of MII oocytes (mean ± SD) : 3.8 ± 0.4 **Control:** - Clinical pregnancy rate (%, N) : per transfer: 27.1% - Number of MII oocytes (mean ± SD) : 5.6 ± 0.7 **p-value CPR:** 0.65 **p-value oocytes:** 0.19	percentages reported in Table 3 cannot be used to arrive at raw data
Bülow, N. S., Skouby, S. O., Warzecha, A. K., Udengaard, H., Andersen, C. Y., Holt, M. D., Grøndahl, M. L., Nyboe Andersen, A., Sopa, N., Mikkelsen, A. L. E., Pinborg, A., & Macklon, N. S. (2022). Impact of letrozole co-treatment during ovarian stimulation with gonadotrophins for IVF: a multicentre, randomized,	RCT	**Inclusion criteria:** Age 18–40 years, a BMI <35 kg/m2, expected normal ovarian reserve, which was defined as AMH ranging 8–32 nmol/ml, and a regular menstrual cycle between 21 and 35 days. There were no restrictions on causes of infertility, fertilization method or the number of previous IVF/ICSI cycles. **Exclusion criteria:**	**Study group:** Fixed dose of rFSH 150 IU/day + 5 mg letrozole **Control:** Fixed dose of rFSH 150 IU/day + placebo	OPR No of MII oocytes	**Control:** ongoing pregnancy rate (%, N) : per randomized: 33% (26/79) - Number of MII oocytes (mean ± SD) : 6.6 ± 3.4. per protocol **Study group:** ongoing pregnancy rate (%, N) : per randomized: 26% (21/80), p=0.53 - Number of MII oocytes (mean ± SD) : 5.8 ± 3.9 per protocol, p=0.48	

double-blinded placebo-controlled trial. *Human reproduction (Oxford, England)*, *37*(2), 309–321.		A previous stimulation with <4 oocytes, PCOS (Rotterdam criteria) or a known allergy toward letrozole or were in treatment for fertility preservation. **Control (n=62)** **Study group (n=67)**				
Bülow, N. S., Warzecha, A. K., Nielsen, M. V., Andersen, C. Y., Holt, M. D., Petersen, M. R., Sopa, N., Zedeler, A., Englund, A. L., Pinborg, A., Grøndahl, M. L., Skouby, S. O., & Macklon, N. S. (2023). Impact of letrozole co-treatment during ovarian stimulation on oocyte yield, embryo development, and live birth rate in women with normal ovarian reserve: secondary outcomes from the RIOT trial. *Human reproduction (Oxford, England)*, *38*(11), 2154–2165.	RCT	**Inclusion criteria:** Age 18–40 years, a BMI <35 kg/m2, expected normal ovarian reserve, which was defined as AMH ranging 8–32 nmol/ml, and a regular menstrual cycle between 21 and 35 days. There were no restrictions on causes of infertility, fertilization method or the number of previous IVF/ICSI cycles. **Exclusion criteria:** A previous stimulation with <4 oocytes, PCOS according to the Rotterdam criteria or a known allergy toward letrozole or were in treatment for fertility preservation. **Control (n=62)** **Study group (n=67)**	**Study group:** Fixed dose of 150 IU rFSH + 5mg Letrozole **Control:** Fixed dose of 150 IU rFSH + placebo	LBR CPR Cumulative CPR	**Control:** - Live birth rate (%, N) : 37% (23/62) per randomized: 30% (24/79) - Clinical pregnancy rate (%, N) : 39% (24/62) Cumulative CPR after 4.8y after OPU: 34% (50/147) **Study group:** - Live birth rate (%, N): 28% (19/67) per randomized: 24% (19/80), p=0.60 - Clinical pregnancy rate (%, N) : 31 % (21/67), p=0.65 Cumulative CPR after 4.8y after OPU: 38% (53/140), p=0.70	
Decleer, W., Comhaire, F., Balduyck, J., Ameye, A., Osmanagaoglu, K., & Devroey, P. (2020). Replacing HMG/FSH by low-dose HCG to complete corifollitropin alfa stimulation reduces cost per clinical pregnancy: a randomized	RCT	**Inclusion criteria:** <40 years of age, had undergone no more than three previous IVF attempts and did not present with major endocrinological disorders. **Exclusion criteria:**	**Study group:** Patients in the HCG group (n = 50) received a daily injection of 150 IU HCG from Day 7 onwards. **Control:** those belonging to the FSH group (n = 55) received a daily	LBR OPR CPR No of MII oocytes	**Control:** - Live birth rate (%, N) : fresh: 9/55 cryo: 0/12; fresh+frozen, NS - ongoing pregnancy rate (%, N) : fresh: 8/55 cryo: 1/12, fresh+frozen, NS - Clinical pregnancy rate (%, N) :	

pragmatic trial. *Reproductive biomedicine online*, *40*(3), 468–474.		Patients with PCOS were excluded because different doses of FSH may be needed in comparison to the general population. **Control (n=55)** **Study group (n=50)**	injection of three ampoules of menotropin 75 IU (225 IU in total)		fresh: 11/55 cryo: 1/12, fresh+frozen, NS - Number of MII oocytes (mean ± SD) : 9.8 ± 6.7 **Study group:** - Live birth rate (%, N) : fresh: 10/50 cryo: 1/11, fresh+frozen, NS - ongoing pregnancy rate (%, N) : fresh: 10/50 cryo: 1/11 - Clinical pregnancy rate (%, N) : fresh: 13/50 cryo: 2/11 - Number of MII oocytes (mean ± SD) : 10.4 ± 6.5	
Drakakis, P., Loutradis, D., Beloukas, A., Sypsa, V., Anastasiadou, V., Kalofolias, G., Arabatzi, H., Kiapekou, E., Stefanidis, K., Paraskevis, D., Makrigiannakis, A., Hatzakis, A., & Antsaklis, A. (2009). Early hCG addition to rFSH for ovarian stimulation in IVF provides better results and the cDNA copies of the hCG receptor may be an indicator of successful stimulation. *Reproductive biology and endocrinology : RB&E*, *7*, 110.	RCT	Women undergoing IVF. **Inclusion criteria:** all were between 36 and 42 years old, had a BMI of 32 or less, a menstrual cycle lasting between 21 and 35 days, normal serum levels of FSH, prolactin and TSH and a normal uterine cavity confirmed by hysteroscopy or hysterosalpingography. The causes for entering the program were: tubal factor, male factor, mild endometriosis (AFS classification stage I or II) or unexplained infertility (with a history of at least 3 years of infertility). **Exclusion criteria:** any other treatment with clomiphene citrate or	**Study group:** Group A patients (final n = 58, two cycles were cancelled) were administered hCG in addition to rFSH in the first days of ovarian stimulation. **Control:** Group B patients (final n = 56, four cycles were cancelled) were administered rLH in addition to rFSH. **Control (n=56)** **Study group (n=58)**	Incidence of OHSS CPR No of MII oocytes	**Control:** - Incidence of different grades of OHSS (%, N) : 12% - Clinical pregnancy rate (%, N) : 10.7% (6/56) PER PROTOCOL - Number of MII oocytes (mean ± SD) : 66.7% (66.7-100) **Study group:** - Incidence of different grades of OHSS (%, N) : 12%, NS - Clinical pregnancy rate (%, N) : 27.6% (16/58) PER PROTOCOL, p=0.022 - Number of MII oocytes (mean ± SD) : 75% (57.1-100), NS	

		gonadotrophins for at least 3 months before screening				
Eftekhar, M., & Saeed, L. (2020). Effect of adding letrozole to gonadotropin on in vitro fertilization outcomes: An RCT. *International journal of reproductive biomedicine*, *18*(4), 287–294.	RCT	**Inclusion criteria:** aged from 18-40 yr, with normal ovarian response. (AFC>7, and AMH from 1.1- to 3.5 ng/ml). **Exclusion criteria:** • A history of endocrine abnormalities • Intrauterine disorders (intrauterine adhesions, submucosal fibroma, and uterine polyp) • Azoospermia of the husband • Severe endometriosis **Control (n=50)** **Study group (n=50)**	**Study group:** Gonadotropin + letrozole + antagonist. **Control:** gonadotropin + antagonist	Incidence of OHSS CPR No of MII oocytes	**Control:** - Incidence of different grades of OHSS (%, N): 4% 2/ 50 - Clinical pregnancy rate (%, N) : 22.0% (11/50) - Number of MII oocytes (mean ± SD) : 6.96 ± 4.09 **Study group:** - Incidence of different grades of OHSS (%, N): 4% 2/ 50 - Clinical pregnancy rate (%, N) : 20% (10/50), p=0.8 - Number of MII oocytes (mean ± SD) : 8.46 ± 4.73, p=0.093	
Fernández Sánchez, M., Višnová, H., Larsson, P., Yding Andersen, C., Filicori, M., Blockeel, C., Pinborg, A., Khalaf, Y., Mannaerts, B., & Rainbow Study Group (2022). A randomized, controlled, first-in-patient trial of choriogonadotropin beta added to follitropin delta in women undergoing ovarian stimulation in a long GnRH agonist protocol. *Human reproduction (Oxford, England)*, *37*(6), 1161–1174.	RCT	**Inclusion criteria:** Women (age 30–42 years) who were undergoing their first or second IVF/ICSI cycle due to unexplained infertility, tubal infertility, endometriosis stage I/II or with partners diagnosed with male factor infertility, BMI 17.5–32.0 kg/m2, regular menstrual cycles of 24–35 days and AMH levels at screening of 5.0–35.0 pmol/l **Exclusion criteria:** Poor or excessive ovarian response in a previous COS cycle, endometriosis stage III–IV, history of recurrent miscarriage and use of hormonal preparations (except for thyroid medication) during	**Study group:** 1, 2, 4, 8 and 12 ug, equivalent to injections of 50, 100, 200, 400 and 600 ul hCG All randomized subjects received an individualized fixed daily dose of follitropin delta, determined based on their AMH level at screening and their body weight at stimulation Day 1. **Control:** 50, 100, 200, 400 and 600 ul placebo All randomized subjects received an individualized fixed daily dose of follitropin delta, determined based on their	Incidence OHSS OPR CPR No of MII oocytes	**Study group:** - Incidence of different grades of OHSS (%, N) : 4: 1 case 8: 1 case 12: 1 case - ongoing pregnancy rate (%, N) : 1: 28.4%* 2: 29.1%* 4: 39.2% 8: 37.4% 12: 30.4% - Clinical pregnancy rate (%, N) : 1: 28.4%* 2: 30.1% 4: 41.3% 8: 40.3% 12: 35.3% - Number of MII oocytes (mean ± SD) :	

		the last menstrual cycle before randomization.	AMH level at screening and their body weight at stimulation Day 1. **Control (n=92)** **Study group:** 1: 94 2: 87 4: 78 8: 85 12: 84		1: 8.2 ± 0.85 2: 8.3 ± 0.86 4: 8.0 ± 0.83 8: 8.4 ± 0.87 12: 7.3 ± 0.75 **Control:** - Incidence of different grades of OHSS (%, N): 2 cases - (cumulative) ongoing pregnancy rate (%, N): 42.9% - Clinical pregnancy rate (%, N): 42.9% - Number of MII oocytes (mean ± SD) : 9.7 **p-value OHSS:** * p<0.05 all others NS **p-value CPR:** * p<0.05 all others NS	
Ghasemi Tehrani, H., Aasasi, K., Mardanian, F., Mehrabian, F., Movahedi, M., & Naghshineh, E. (2022). Evaluation of The Effect of Letrozole in the Ovarian Hyperstimulation Syndrome Prevention in Participants at Risk of Treatment with Ovulation-Stimulating Drugs:A Randomized Controlled Trial. *Reports of biochemistry & molecular biology*, *11*(3), 386–393.	RCT	**Inclusion criteria:** 1) age between 20-40 years, 2) candidate for treatment with OHSS and IVF, 3) history of at least one year of infertility, 4) BMI< 25 kg/m² and, 5) AMH levels> 5 ng/ml. **Exclusion criteria:** History of any hormone therapy during the previous three months, history of allergy to Letrozole and other aromatase inhibitors, history of heart disease, kidney failure, liver disease, and other endocrine diseases. **Control (n=25)** **Study group (n=25)**	**Study group:** six doses of r-hFSH 150 IU/day from the second day of the menstrual cycle (days 2, 3, 4, 5, 6, and 7) and Intramuscular hMG 75 IU/day from day four of the menstrual cycle until the trigger day. + 5 mg letrozole daily in the case group (n=25) on the second day of the menstrual cycle for five consecutive days. **Control:** six doses of r-hFSH 150 IU/day from the second day of the menstrual cycle (days 2, 3, 4, 5, 6, and 7) and Intramuscular hMG 75 IU/day from day four of the menstrual cycle until the	Incidence of OHSS CPR	**Control:** - Incidence of different grades of OHSS (%, N) : Mild: 4/25 Moderate: 9/25 Severe: 0 - Clinical pregnancy rate (%, N): 52% (13/25) **Study group:** - Incidence of different grades of OHSS (%, N) : p=0.01 Mild: 6/25 Moderate: 1/25 Severe: 0 - Clinical pregnancy rate (%, N): 60% (15/25), p=0.56	

			trigger day + placebo identical to study group.			
Jiahui Qiu, Shan Luo, Yu Bai, Xun Zeng, Xiaohong Li. Human Menopausal Gonadotropins in Combination for Stimulation does not Improve IVF Outcomes in POSEIDON Group 4 Patients, When Compared to Recombinant Follicle Stimulating Hormone Alone: A Prospective Randomized, Non-Blinded, Controlled Pilot Trial. *Clin. Exp. Obstet. Gynecol* **2023**, 50(11), 235.	RCT	**Inclusion criteria:** between the ages of 35 and 44 years and were classified as having poor ovarian reserve parameters (AFC <5 or AMH <1.2 ng/mL) based on the POSEIDON Group 4 classification **Exclusion criteria:** natural cycles or mild stimulation cycles, PGT cycles or oocyte donation cycles, hypogonadotropic hypogonadism, history of exogenous LH allergy, tumor history or suspected tumor, and unexplained ovarian enlargement **Control (n=94)** **Study group (n=78)**	**Study group:** Menotropins for Injection, 75 IU per day in addition to FSH until hCG was triggered. long GnRHa or GnRH antagonist (97%) protocol. **Control:** The control group was administered FSH alone. log GnRHa or GnRH antagonist (97%) protocol.	OPR CPR	**Control:** - ongoing pregnancy rate (%, N) : per completed cycle: 27.1% (19/70) - Clinical pregnancy rate (%, N) : per completed cycle: 28.6% (20/70) **Study group:** - ongoing pregnancy rate (%, N) : per completed cycle: 26.1% (23/88), p=0.887 - Clinical pregnancy rate (%, N) : per completed cycle: 29.5% (26/88), p=0.894	
Koichi, K., Yukiko, N., Shima, K., & Sachiko, S. (2006). Efficacy of low-dose human chorionic gonadotropin (hCG) in a GnRH antagonist protocol. *Journal of assisted reproduction and genetics*, *23*(5), 223–228.	RCT	women undergoing COS **Inclusion criteria:** <40-years old with BMI <27 kg/m2) **Control (n=66)** **Study group (n=63)**	**Study group 1:** (NhCGP, n = 63), a full dose of uhFSH administered until reaching a follicular diameter of 14 mm, at which point Fertinorm P dosage was increased to 300 IU/day and GnRH antagonist was initiated. **Study group 2:** hCGP, n = 63), using the same protocol as NhCGP until reaching a follicular diameter of 14 mm, at which point Fertinorm P dosage was decreased to 75 IU/day and Cetrorelix (0.25 mg/day)	Incidence of OHSS CPR	**Control:** - Incidence of severe OHSS (%, N) : 9.1% (6/66) - Clinical pregnancy rate (%, N) : 56.9% (33/58) **Study group 1:** - Incidence of severe OHSS (%, N) : 1.6% (1/63), NS - Clinical pregnancy rate (%, N) : 36.8% (21/57), NS **Study group 2:** - Incidence of severe OHSS (%, N) : 1.6% (1/63), NS - Clinical pregnancy rate (%, N) : 39.0 (23/59), NS	

			with 200 IU/day of hCG was initiated. **Control:** long protocol (LP, n = 66), uhFSH after midluteal pituitary desensitization with nasal GnRH agonist (900 µg/day)			
Liu, Y., Chen, Q., Yu, S., Wang, Y., He, W., Chang, H. Y., Wang, B., Gao, H., Long, H., Wang, L., Lyu, Q., Ai, A., & Kuang, Y. (2018). Progestin-primed ovarian stimulation with or without clomiphene citrate supplementation in normal ovulatory women undergoing in vitro fertilization/intracytoplasmic sperm injection: A prospective randomized controlled trial. *Clinical endocrinology*, *88*(3), 442–452.	RCT	**Inclusion criteria:** 1] age between 22 and 40 years, [2] regular menstrual cycles over the 3-month period prior to the study (24-35 days in duration), [3] an antral follicle count (AFC) higher than 5 on menstrual cycle days (MC) 3, and [4] a basal serum FSH concentration lower than 10 IU/L. **Exclusion criteria:** [1] endometriosis grade 3 or higher, [2] diagnosis of PCOS, [3] presence of hormonal treatments within the 3-month period prior to the study, and [4] any contraindications for ovarian stimulation treatment. **Control (n=132)** **Study group (n=144)**	**Study group:** medroxyprogesterone acetate (MPA) and human menopausal gonadotropin (hMG) were simultaneously administered on menstrual cycle day 3. + CC **Control:** medroxyprogesterone acetate (MPA) and human menopausal gonadotropin (hMG) were simultaneously administered on menstrual cycle day 3. without CC	Cumulative OPR Cumulative CPR No of MII oocytes	**Control:** **- cu**mulative OPR per patient: 53.1% (85/160) - cumulative CPR per patient: 66.9% (107/160) - Number of MII oocytes (mean ± SD) : 8.9±6.59 **Study group:** **-** cumulative OPR per patient: 60.6% (97/160), p=0.176 - cumulative CPR per patient: 68.8% (110/160), p=0.72 - Number of MII oocytes (mean ± SD) : 8.71±5.28, p=0.608	
Lotfy M, Saleh MM, Elshahat AM, Elserour GA, Taha OT. GONADOTROPINS-LETROZOLE, GONADOTROPIN-CLOMIPHENE CITRATE, AND GONADOTROPINS ONLY FOR CONTROLLED OVARIAN SUPER STIMULATION IN WOMEN WITH POLYCYSTIC	RCT	**Inclusion criteria:** women with PCOS according to the Rotterdam criteria a) women aged 20- 40 years, b) BMI 20- 35, c) the first trial for ICSI, d) presenting with primary infertility, e) euthyroid, and f) normal serum prolactin **Exclusion criteria:**	**Study group 1:** CC+hMG **Study group 2:** Ltz+hMG **Control:** hMG alone	LBR Incidence of OHSS CPR No of MII oocytes	**Study group 1:** - Live birth rate (%, N): 24% (12/50) - Incidence of different grades of OHSS (%, N) : 0 - Clinical pregnancy rate (%, N) : 48% (24/50) - Number of MII oocytes (mean ± SD) : 6.06±1.27 **Study group 2:**	

OVARY SYNDROME UNDERGOING INTRACYTOPLASMIC SPERM INJECTION. Journal of pharmaceutical negative results 2022;13: 4568-4576.		a) previous pelvic surgery, b) chronic illnesses, and c) women refusing to participate in the study **Control (n=50)** **Study group (n=50)**			- Live birth rate (%, N): 20% (10/50) - Incidence of different grades of OHSS (%, N) : 2% (1/50) - Clinical pregnancy rate (%, N) : 46% (23/50) - Number of MII oocytes (mean ± SD) : 6.08±1.29 **Control:** - Live birth rate (%, N): 28% (14/50) - Incidence of different grades of OHSS (%, N) : 10% (5/50) - Clinical pregnancy rate (%, N) : 52% (26/50) - Number of MII oocytes (mean ± SD) : 6.04±1.31 **p-value LBR:** 0.899 **p-value OHSS:** 0.058 **p-value CPR:** 0.830 **p-value oocytes:** 0.979	
Madani, T., Mohammadi Yeganeh, L., Khodabakhshi, S., Akhoond, M. R., & Hasani, F. (2012). Efficacy of low dose hCG on oocyte maturity for ovarian stimulation in poor responder women undergoing intracytoplasmic sperm injection cycle: a randomized controlled trial. *Journal of assisted reproduction and genetics*, *29*(11), 1213–1220.	RCT	**Inclusion criteria:** 1- Poor responders to ovarian stimulation according to the existence of at least two of the following criteria: Advanced maternal age (37 to 43 years), AFC <5, prior history of poor response to COS (peak E2 <500 pg/ml and/or ≤3 oocytes retrieved) 2- Indication for ICSI treatment, second or third cycle 3- BMI ≤30 kg/m2 4- The presence of two functional ovaries and no previous ovarian surgery 5- The presence of normal uterine cavity and 2 normal tubes based on recent	**Study group 1:** hCG 100. Long GnRHa protocol. Fixed dose of 300 IU r-FSH for the first 5 days. d6: addition of 100 IU hCG **Study group 2:** hCG 200. Long GnRHa protocol. Fixed dose of 300 IU r-FSH for the first 5 days. d6: addition of 200 IU hCG. **Control:** Long GnRHa protocol. Fixed dose of 300 IU r-FSH for the first 5 days. rFSH alone.	LBR CPR No of MII oocytes	**Study group 1:** - Live birth rate (%, N) : per ET: 14.3% (3/21) - Clinical pregnancy rate (%, N) : per ET: 19.0% (4/21) - Number of MII oocytes (mean ± SD) : 5.2±2.1 **Study group 2:** - Live birth rate (%, N) : per ET: 21.1% (4/19) - Clinical pregnancy rate (%, N) : per ET: 26.3% (5/19) - Number of MII oocytes (mean ± SD) : 5.2±4.4 **Control:** - Live birth rate (%, N) : 13% (3/23) per ET	

		HSG or hystroscopic evaluation 6- Basal (day 2 or 3) serum FSH levels ≤13 IU/L 7- Normal semen analysis 8- No history or signs of endometriosis 9- No untreated endocrinologic disease **Control (n=26)** **Study group (n=24)**			- Clinical pregnancy rate (%, N) : per ET: 13% (3/23) - Number of MII oocytes (mean ± SD) : 3.4±1.7 **p-value LBR:** 0.75 **p-value CPR:** 0.55 **p-value oocytes:** 0.16	
Nasrin Saharkhiz et al. Comparing Corifollitropin Alfa to Recombinant Follicle-STIMULATING Hormone in Poor Responder Patients Undergoing Intracytoplasmic Injection: A Randomized Clinical Trial. Vol. 11, No. 4, October 2024, 176–182	RCT	**Inclusion criteria:** AFC<5, AMH<1.2 ng/dL, at least three oocytes in the previous cycle, and fulfilled Bologna criteria for poor ovarian response. **Exclusion criteria:** Uterine anomalies, a history of untreated endocrine problems, cardiovascular diseases, any disorder related to the lung and liver, severe and uncontrolled underlying diseases, unilateral or bilateral hydrosalpinx, and prohibition of gonadotropin use, egg donors, severe male infertility (azoospermia, oligoasthenoteratospermia), stage 4 endometriosis, and patients with extremely low or high BMI <18 or >30.	**Study group:** Corifollitropin **Control:** rFSH	CPR No of MII oocytes	**Control:** - Clinical pregnancy rate (%, N) : 22.0% - Number of MII oocytes (mean ± SD) : 4.2±1.7 **Study group:** - Clinical pregnancy rate (%, N) : 28.8%, NS - Number of MII oocytes (mean ± SD) : 5.0±2.1, p=0.021	
Serafini, P., Yadid, I., Motta, E. L., Alegretti, J. R., Fioravanti, J., & Coslovsky, M. (2006). Ovarian stimulation with daily late follicular phase administration of low-dose human chorionic	RCT	**Inclusion criteria:** (1) indication for either IVF or ICSI; (2) age 21 to 39 years; (3) the presence of two functional ovaries; (4) the presence of an anatomically normal uterine cavity on the basis of recent HSG	**Study group 1:** r-hFSH beginning on either day 2 or 3 of the menstrual cycle, continuing with the full dose until either two codominant follicles reached 13–14 mm or the patient reached day 6 of	OHSS CPR No of MII oocytes	**Control:** - Incidence of different grades of OHSS (%, N):4, - Clinical pregnancy rate (%, N) : 40.7% (35/86) - Number of MII oocytes (mean ± SD) : 11.6±0.8	

gonadotropin for in vitro fertilization: a prospective, randomized trial. *Fertility and sterility*, *86*(4), 830–838.		or hysteroscopic evaluation (6 months); (5) history of 3 attempts at IVF/ICSI; (6) early follicular phase (day 2 or 3) serum FSH levels 15 IU/L and E2 levels 60 pg/mL; (7) no history of low ovarian response in previous IVF/ICSI treatment; (8) BMI 25 kg/m2; (9) no untreated endocrinologic disease; (10) no treatment with gonadotropin therapy for 3 months preceding the study; and (11) male partner should have ejaculated spermatozoa with 1% strict morphology. **Control (n=96)** **Study group (n=106)**	stimulation, when the r- hFSH dose was lowered to 75 IU daily and SC injections of 200 IU of hCG were begun, along with daily administration of 0.25 mg of cetrorelix. **Study group 2:** Daily SC injections of Leuprolide acetate 0.5 mg were administered in the midluteal phase of the previous menstrual cycle after which recombinant hFSH was initiated. **Control:** r-hFSH beginning on either day 2 or 3 of the menstrual cycle, continuing with the full dose until 2 codominant follicles reached 18 mm in the largest diameter. Daily SC injection of 0.25 mg CTD began either when two codominant follicles reached 13–14 mm or the patient reached day 6 of stimulation.		**Study group 1:** - Incidence of different grades of OHSS (%, N): 3, NS - Clinical pregnancy rate (%, N) : 54.9% (56/102), NS - Number of MII oocytes (mean ± SD) : 10.3±0.5, NS **Study group 2:** - Incidence of different grades of OHSS (%, N): 6, NS - Clinical pregnancy rate (%, N) : 44.0% (41/92), NS - Number of MII oocytes (mean ± SD) : 10.6±0.5, NS	
Shu, L., Xu, Q., Meng, Q., Dai, X., Zhang, Y., Zhou, W., Yi, H., Liu, J., Wu, C., Hou, Z., Cui, Y., Li, T. C., & Liu, J. (2019). Clinical outcomes following long GnRHa ovarian stimulation with highly purified human menopausal gonadotropin plus rFSH or rFSH in patients undergoing *in vitro* fertilization-embryo	RCT	**Inclusion criteria:** I) aged 20–37 years, BMI 18–24 kg/m2 and weight 40–80 kg, with regular menstrual cycle (21–35 days); (II) infertility (more than 1 year of free intercourses) with no history of IVF treatment; (III) basal FSH <10 U/L and LH <10 U/L; (IV) normal uterine anatomy confirmed by TVU examination and in some cases HSG and	**Study group:** HP-HMG+rFSH in long GnRHa protocol **Control:** rFSH in long GnRHa protocol **Control (n=305)** **Study group (n=305)**	Incidence of OHSS CPR No of MII oocytes	**Control:** - Incidence of moderate/severe: 3.6% (11/305) - Clinical pregnancy rate (%, N) : per initiated cycle: 23.9% (73/305) - Number of MII oocytes (mean ± SD) : 11.4±5.2 **Study group:** - Incidence of moderate/severe OHSS: 3.3% (10/305), p=0.824	

transfer: a multi-center randomized controlled trial. *Annals of translational medicine*, *7*(7), 146.		hysteroscopy; (V) no evidence of hydrosalpinx or ovarian cyst or endometrioma; (VI) antral follicle count (AFC) >6; and (VII) signed written informed consent. **Exclusion criteria:** (I) had PCOS, endometriosis of stage III/IV, hyperprolactinemia or other significant systemic disease (endocrine or metabolic abnormalities); (II) use of the following drugs within 1 month prior to randomization: clomiphene citrate, metformin, gonadotropin or GnRH analogues; (III) smokes >10 cigarettes per day within 3 months of recruitment; (IV) history of chemotherapy, radiotherapy, or ovarian surgery.			- Clinical pregnancy rate (%, N) : per cycle initiated: 29.2% (89/305), p=0.142 - Number of MII oocytes (mean ± SD) : 10.6±5.7, p=0.074	
Siristatidis, C., Stavros, S., Dafopoulos, K., Sergentanis, T., Domali, E., Drakakis, P., & Loutradis, D. (2022). A Randomized Controlled Trial on the Efficacy and Safety of Low-Dose hCG in a Short Protocol with GnRH Agonist and Ovarian Stimulation with Recombinant FSH (rFSH) During the Follicular Phase in Infertile Women Undergoing ART. *Reproductive sciences (Thousand Oaks, Calif.)*, *29*(2), 497–505.	RCT	**Inclusion criteria:** age 35 -40 years, physiological menstrual cycles (24–35 days), normal endocrine function (normal PRL and TSH, FSH ≤ 15 IU / ml), TVU without pathological findings, free personal medical history, indication for IVF/ICSI [36], and first or second IVF/ICSI cycle **Exclusion criteria:** endocrine or metabolic disorders, e.g., PCO (S), pathology of the uterus and/or endometrium, basal FSH levels> 15 IU / ml, surgery in the ovaries, BMI ≥ 35	**Study group:** adding hCG with the initiation of standard short GnRH agonist protocol for IVF/ICSI with 200 IU rFSH **Control:** application of the same protocol, adding placebo **Control (n=41)** **Study group (n=40)**	Incidence of OHSS CPR No of MII oocytes	**Control:** - Incidence of different grades of OHSS (%, N): 2.4% (1/41) - Clinical pregnancy rate (%, N) : 24.4% (10/41) - Number of MII oocytes (mean ± SD) : 3 (IQR 2) **Study group:** - Incidence of different grades of OHSS (%, N): 7.5% (3/40), p=0.359 - Clinical pregnancy rate (%, N) : 25% (10/40), p=0.949 - Number of MII oocytes (mean ± SD) : 3 (IQR 5), p=0.735	

		kg/ m2, and age <35 years and > 40 years old				
Taronger, R., Martínez-Cuenca, S., Ferreros, I., Rubio, J. M., Fernández-Colom, P. J., Martínez-Triguero, M. L., & Pellicer, A. (2018). Ovarian stimulation with corifollitropin alfa followed by hp-hMG compared to hp-hMG in patients at risk of poor ovarian response undergoing ICSI: A randomized controlled trial. *European journal of obstetrics, gynecology, and reproductive biology*, *231*, 192–197.	RCT	**Inclusion criteria:** < 40 years of age with indication of IVF/ICSI, who were at risk of poor ovarian response because they met at least one of the following three criteria: a history of medical or surgical treatment as a risk factor for POR; a previous poor response with a conventional stimulation (3 oocytes); an abnormal ovarian ORT, AMH < 8 pmol/L or AFC < 7. **Exclusion criteria:** anovulation, presence of uterine pathology, uncorrected hydrosalpinx, severe male factor, FSH >20 mIU/ml, non-detectable AMH levels, or AFC<3 **Control (n=109)** **Study group (n=112)**	**Study group:** CFA group (n = 117) received a single injection of 150mg CFA (Elonva 1), after the assessment of ovarian response on day 8th, 300 IU of hp-hMG was added until the criteria for ovulation triggering were accomplished; In both groups, Ganirelix at a dose of 0.25 mg/24 h was added when follicles were >=14 mm. **Control:** p-hMG group (n = 117) received 300 IU of hp-hMG at continuous daily dose. In both groups, Ganirelix at a dose of 0.25 mg/24 h was added when follicles were >=14 mm.	Cumulative LBR LBR/OPR CPR No of MII oocytes	**Control:** - cumulative OPR and LBR: 22% - OPR and LBR per started cycle: 20.2% (22/109) - Clinical pregnancy rate (%, N): 23.9 Cumulative: 26.6% (29/109) - Number of MII oocytes (mean ± SD) : 3.8 (2.61) **Study group:** - cumulative OPR and LBR: 15.2%, p=0.19 - OPR and LBR per started cycle: 15.2% (17/112), p=0.33 - Clinical pregnancy rate (%, N): 18.8%, p=0.35 Cumulative: 19.6% (22/112), p=0.22 - Number of MII oocytes (mean ± SD) : 3.1 (2.25), p=0.04	
Thuesen, L. L., Loft, A., Egeberg, A. N., Smitz, J., Petersen, J. H., & Andersen, A. N. (2012). A randomized controlled dose-response pilot study of addition of hCG to recombinant FSH during controlled ovarian stimulation for in vitro fertilization. *Human reproduction (Oxford, England)*, *27*(10), 3074–3084.	RCT	**Inclusion criteria:** (i) women with indication for COS and IVF; (ii) age 25–37 years; (iii) BMI .18 -30 kg/m2; (iv) a regular menstrual cycle of 24–35 days, presumed to be ovulatory; (v) two ovaries; (vi) tubal or unexplained infertility, including endometriosis Stage I/II and mild male factor; (vii) a uterus consistent with expected normal function (e.g. no clinically interfering uterine fibroids) documented by TVU at the	**Study group:** rFSH 150 IU/day in a fixed dose regimen on Day 1 of stimulation. Supplementation with different doses of hCG started on Day 1 of stimulation after the randomization. (G1) hCG low dose (D50): 150 IU/day of rFSH + 50 IU/day of hCG, (G2) hCG medium dose (D100): 150 IU/day of rFSH + 100 IU/day of hCG and (iv) hCG high dose (D150): 150 IU/day of rFSH + 150 IU/day of hCG.	Cumulative LBR LBR Incidence of OHSS CPR	**Control:** - Cumulative live birth rate (%, N) **:** per started fresh cycle: 31% (n=5) - Live birth rate (%, N): Fresh: 25% (4/16) Frozen: n=1 - Incidence of different grades of OHSS (%, N): 1 case of mild OHSS - Clinical pregnancy rate (%, N): 25% (4/16) **Study group:** - Cumulative live birth rate (%, N) **:** per started fresh cycle, p=0.89 50 IU: 33% (n=5)	

		screening; (viii) male partner with sperm quality compatible with fertilization via an IVF procedure or previous clinical pregnancy; (ix) early follicular phase serum FSH levels of 1–12 IU/l; (x) early follicular phase total antral follicle (2–10 mm) count ≥6 **Exclusion criteria:** (i) history of or current PCOS, endometriosis Stage III/IV or severe male factor requiring ICSI; (ii) history of severe OHSS; (iii) presence of unilateral or bilateral hydrosalpinx at ultrasound; (iv) more than three previous COS cycles; (v) previous poor response on an IVF cycle.(20 days of gonadotrophin stimulation, cancellation due to limited follicular response or less than four follicles of ≥15 mm diameter); (vi) previous IVF cycle with unsuccessful fertilization, (fertilization of ≤20% of the retrieved oocytes); (vii) history of recurrent miscarriage; (viii) FSH >12 IU/l or LH >12 UI/l (early-follicular phase); (ix) contraindications for the use of gonadotrophins or GnRH analogues; (x) recent history of current epilepsy, HIV infection, diabetes or cardiovascular, gastrointestinal, hepatic, renal or pulmonary disease; (xi) pregnancy, lactation or contra-	**Control:** All the randomized patients were treated with rFSH 150 IU/day in a fixed dose regimen on Day 1 of stimulation. **Control (n=16)** **Study group:** 50 IU: 15 100 IU: 16 150 IU: 13		100 IU: 44% (n=7) 150 IU: 39% (n=5) - Live birth rate (%, N) : p=0.98 Fresh 50 IU: 27% (4/15) 100 IU: 25% (4/16) 150 IU: 31% (4/13) Frozen 50 IU: n=1 100 IU: n=3 150 IU: n=1 - Incidence of different grades of OHSS (%, N) : 50 IU: 1 moderate case - Clinical pregnancy rate (%, N) : per started cycle: p=0.87 50 IU: 27% (4/15) 100 IU:38% (6/16) 150 IU: 31% (4/13)	

		indication to pregnancy; (xii) current or past (last 12 months) abuse of alcohol or drugs; (xiii) history of chemotherapy (except for gestational conditions) or radiotherapy; (xiv) undiagnosed vaginal bleeding; (xv) tumors of the ovary, breast, adrenal gland, pituitary or hypothalamus and malformation of sexual organs incompatible with pregnancy; (xvi) abnormal karyotype of the patient (if karyotyping was performed) and (xvii) hypersensitivity to any trial product.				
Tshzmachyan, R., & Hambartsoumian, E. (2020). The role of Letrozole (LE) in controlled ovarian stimulation (COS) in patients at high risk to develop ovarian hyper stimulation syndrome (OHSS). A prospective randomized controlled pilot study. *Journal of gynecology obstetrics and human reproduction*, *49*(2), 101643.	RCT	**Inclusion criteria:** PCOS (Rotterdam criteria), ages between 21 and 38, no hormonal treatment during last 3 months, BMI below <25 kg/m2, AMH > 50 pmol/L. **Exclusion criteria:** Subjects with any known systemic diseases or endocrine disorders, including obesity. **Control (n=24)** **Study group (n=24)**	**Study group:** Conventional antagonist protocol and LE: 150 IU of human gonadotropins for 6 days followed by Menopur 150 IU from d4 to trigger day Addition of LE to the COS protocol, at a dosage of 5 mg per day starting from day 3 to day 7 of the cycle. **Control:** conventional multiple-dose GnRH-antagonist protocol only. 150 IU of human gonadotropins for 6 days followed by Menopur 150 IU from d4 to trigger day	LBR OHSS	**Control:** - Live birth rate (%, N) : 33.3% (8/24) - Incidence of different grades of OHSS (%, N) : mild: 9 cases moderate: 1 case **Study group:** - Live birth rate (%, N): 37.5% (9/24), p=0.769 - Incidence of different grades of OHSS (%, N): mild: 2 cases, OR 7.86; 1.49-41.3 p=0.008	

Yang, X., Lin, G., Lu, G., & Gong, F. (2019). Letrozole supplementation during controlled ovarian stimulation in expected high responders: a pilot randomized controlled study. *Reproductive biology and endocrinology : RB&E*, *17*(1), 43.	RCT	**Inclusion criteria:** (1) medical indication for IVF treatment; (2) AFC between 15 - 23; (3) age 21–35 years; (4) at the first or the second treatment cycle; and (5) BMI 18–28. **Exclusion criteria:** (1) medical contraindication to IVF treatment (< 4 oocytes obtained); (2) previously documented poor response to ovary in IVF-stimulated cycles; (3) presence of endometriosis or uterine malformations; and (4) a history of unexplained miscarriages. **Control (n=64)** **Study group (n=60)**	**Study group:** Standard short GnRH-agonist protocol, which was daily intramuscular injections of 100–225 IU recFSH from stimulation day 1 until the day of hCG administration and co-treatment with letrozole 2.5 mg daily from stimulation day 5 until the day of hCG administration. **Control:** 100–225 IU of recFSH was injected intramuscularly daily from day 1 of stimulation to the day of hCG administration.	LBR OHSS CPR	**Control:** - Live birth rate (%, N) : 62.5% (30/48) - Incidence of different grades of OHSS (%, N) : 1.5% (1/65) - Clinical pregnancy rate (%, N) : 72.9% (35/48) **Study group:** - Live birth rate (%, N): 42.9% (21/49), p=0.053 - Incidence of different grades of OHSS (%, N): 0/65, p=1.000 - Clinical pregnancy rate (%, N) : 53.1% (26/49), p=0.043	
Witz, C. A., Daftary, G. S., Doody, K. J., Park, J. K., Seifu, Y., Yankov, V. I., Heiser, P. W., & Menopur in GnRH Antagonist Cycles with Single Embryo Transfer – High Responder (MEGASET-HR) Trial Group (2020). Randomized, assessor-blinded trial comparing highly purified human menotropin and recombinant follicle-stimulating hormone in high responders undergoing intracytoplasmic sperm injection. *Fertility and sterility*, *114*(2), 321–330.	RCT	**Inclusion criteria:** age 21-35 years with menstrual cycles of 21 45 days, BMI 18-30 kg/m2, infertility for ≥ year, day 2 or 3 serum FSH levels of 1-12 IU/L, total testosterone, prolactin, and thyroid stimulating hormone within normal limits, and serum AMH ≥5 ng/mL at screening. **Exclusion criteria:** Women with stage III IV endometriosis; history of recurrent miscarriage; previous ART failure from poor response; AFC (diameter 2 10 mm) <10 for both ovaries combined and/or	**Study group:** HP-hMG. Treatment was initiated on day 2 or 3 of the menstrual cycle at a dose of 150 IU HP-hMG for the first 5 days. Starting at day 6, the dose could be adjusted daily by 75 IU. The maximum daily dose was 300 IU/d and the maximum treatment duration was 20 days. **Control:** rFSH. Treatment was initiated on day 2 or 3 of the menstrual cycle at a dose of 150 IU rFSH for the first 5 days. Starting at day 6, the dose could be adjusted daily by 75 IU. The	Cumulative LBR LBR Incidence of OHSS No of MII oocytes	**Control:** **-** Cumulative live birth rate (%, N) **:** per started cycle: 51.5% - Live birth rate (%, N) : fresh: 48.7% frozen: 50.8% - Incidence of different grades of OHSS (%, N) : Total: 21.4% (66/309) Mild: 5.8% (18/309) Moderate: 12.6% (39/309) Severe: 2.9% (9/309) - OPR per started cycle: 30.7% - Number of MII oocytes (mean ± SD) : 15.9±9.01 **Study group:** **-** Cumulative live birth rate (%, N) **:** per started cycle: 50.6%,	

		use of hormonal birth control <3 months prior to screening **Control (n=309)** **Study group (n=308)**	maximum daily dose was 300 IU/d and the maximum treatment duration was 20 days.		- Live birth rate (%, N): fresh: 52.2% frozen: 63.4% - Incidence of different grades of OHSS (%, N) : Total: 9.7% (30/310) Mild: 2.3% (7/310) Moderate: 4.8% (15/310) Severe: 2.6% (8/310) - OPR per started cycle: 35.5% - Number of MII oocytes (mean ± SD) : 10.1±7.18	
Wu, L., Yin, H., Guan, L., Li, G., Zhang, J., Shen, Q., Ni, X., Wang, C., Wang, T., Geng, H., Xu, C., Cao, Y., He, X., & Song, B. (2025). The first multiple center prospective study of rhFSH CTP in patients undergoing assisted reproductive technology in China. *Scientific reports*, *15*(1), 2666.	RCT	**Inclusion criteria:** females aged 20–35 undergoing IVF, ICSI, or a combination, with serum levels of FSH, estradiol, progesterone, and LH within normal ranges, regular menstrual cycles lasting 25–34 d and a BMI of 18.5–28.0 kg/m were required. **Exclusion criteria:** patients with a prior history of recurrent miscarriage (i.e., ≥3 consecutive miscarriages), OHSS, or active pelvic inflammatory disease, potentially affecting embryo implantation and pregnancy outcomes, a low or no ovarian response or those who had undergone >3 unsuccessful cycles of ovarian stimulation since the establishment of the last sustained pregnancy	**Study group:** rFSH-CTP **Control:** rFSH **Control (n=141)** **Study group (n=142)**	LBR OHSS OPR	**Control:** - Live birth rate (%, N) : 36% - Incidence of different grades of OHSS (%, N) : severe OHSS: 1.4% (2/141) - ongoing pregnancy rate (%, N) : 36.9% **Study group:** - Live birth rate (%, N) : 31.7%, NS - Incidence of different grades of OHSS (%, N) :severe OHSS: 0% - ongoing pregnancy rate (%, N) : 31.7%, NS	

Zhu, X., & Fu, Y. (2019). Randomized, Controlled Pilot Study of Low-Dose Human Chorionic Gonadotropin Administration Beginning From the Early Follicular Phase for Women With Polycystic Ovarian Syndrome Undergoing Ovarian Stimulation Using the Progesterone Protocol. *Frontiers in endocrinology*, *10*, 875.	RCT	**Inclusion criteria:** Women with PCOS <38 years and had a BMI <28 kg/m2 and planning to undergo treatment with IVF/ICSI with the freeze-all strategy were eligible to participate. **Exclusion criteria:** Women with a history of IVF/ICSI, severe endometriosis (grade 3 or higher), significant systemic disease, or other situations unsuitable for ovarian stimulation **Control (n=20)** **Study group (n=20)**	**Study group:** hMG and progesterone soft capsule 100 mg/d were added simultaneously beginning from menstrual cycle day 3 for all participants. Low dose hCG (200 IU) was injected every 3 days in the study group from the first day of ovarian stimulation until trigger. **Control:** HMG + Utrogestan protocol	OHSS CPR No of MII oocytes	**Control:** - Incidence of severe OHSS (%, N): 0 cases - Clinical pregnancy rate (%, N) : per transfer: 41.94% (13/31) per patient: 65% (13/20) - Number of MII oocytes (mean ± SD) : 13.4 ± 6.34 **Study group:** - Incidence of severe OHSS (%, N): 0 cases - Clinical pregnancy rate (%, N) : per transfer: 65.52% (19/29), p=0.067 per patient: 95% (19/20), p=0.044 - Number of MII oocytes (mean ± SD) : 13.55 ± 6.56, p=0.818	all frozen transfer, no fresh

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

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Xu, B., Geerts, D., Yuan, J., Wang, M., Li, Z., Lai, Q., Zheng, Y., Liu, S., Yang, S., Zhu, G., & Jin, L. (2024). A modified flexible GnRH antagonist protocol using antagonist early cessation and a gonadotropin step-down approach improves live birth rates in fresh cycles: a randomized controlled trial. *Human reproduction (Oxford, England)*, *39*(9), 1969–1978.	RCT	**Inclusion criteria:** Age <40 years, a normal menstrual cycle, body mass index (BMI) 18.5–30 kg/m2, antral follicle count (AFC) >5 follicles, anti-Mullerian hormone (AMH) >1.1 ng/ml, and basal FSH level < 10 IU/ml. **Exclusion criteria:** Patients with the presence of 12 or more follicles in at least one ovary, or with chromosomal aberrations, recurrent miscarriage, hyperprolactinemia, adenomyosis, hydrosalpinx, uterine abnormalities, congenital adrenal hyperplasia, or thyroid disease were excluded, as well as patients using oral contraceptives (OC), or receiving sperm from TESE, TESA or micro-TESE. **Control (n=273)** **Study group (n=273)**	**Study group:** modified GnRH antagonist protocol. 50–225 IU/day of rFSH, dose adjustments allowed, flexible GnRH antagonist started when at least one of the following criteria was met: (i) the presence of at least one follicle measuring ≥13mm; (ii) serum estradiol (E2) levels ≥600 pg/ml; (iii) serum LH levels ≥10 IU/l. When the leading follicles reached 14 mm, Gn dose reduced by 30–50%. GnRH antagonist administration was suppressed on the day of the hCG. **Control group:** conventional protocol. 50–225 IU/day of rFSH, dose adjustments allowed, flexible GnRH antagonist started when at least one of the following criteria was met: (i) the presence of at least one follicle measuring ≥13mm; (ii) serum estradiol (E2) levels ≥600 pg/ml; (iii) serum LH levels ≥10 IU/l	LBR Incidence of OHSS OPR CPR No of MII oocytes	**Control group:** -Live birth rate (%, N) 27.5% (75/273) -Incidence of different grades of OHSS (%, N): 1.8 (5/273) -ongoing pregnancy rate (%, N) 27.8% (76/273) -Clinical pregnancy rate (%, N) 31.9% (87/273) -Number of MII oocytes (mean ± SD): 10.75 (4.53) **Study group:** -Live birth rate (%, N): 38.1% (104/273), RR 1.39 (1.09-1.77) p=0.008 -Incidence of different grades of OHSS (%, N): 1.1% (3/273), RR 0.60 (0.14-2.49), p=0.725 -ongoing pregnancy rate (%, N): 38.8% (106/273), RR 1.39 (1.09-1.78), p=0.006 -Clinical pregnancy rate (%, N) 43% (118/273), RR 1.36 (1.09-1.69), p=0.006 -Number of MII oocytes (mean ± SD): 10.95 (4.43)	

Lawrenz, B., Coughlan, C., Melado, L., Digma, S., Sibal, J., Jean, A., & Fatemi, H. M. (2021). Step-Down of FSH-Dosage During Ovarian Stimulation - Basic Lessons to Be Learnt From a Randomized Controlled Trial. *Frontiers in endocrinology*, *12*, 661707.	RCT	**Inclusion criteria:** Age between 18 and 40 years, a weight of 60 kg up to and including 90 kg, which results in a BMI of 18–32 kg/m2 and a regular menstrual cycle length of 24–35 days. **Exclusion criteria:** presence or history of an endocrine abnormality, abnormal serum biochemistry or hematology, relevant ovarian-, tubal- or uterine-pathology which may adversely affect ovarian stimulation treatment, a history of ovarian hyper response (more than 30 follicles ≥ 11 mm) or OHSS, PCOS, a history of poor ovarian response, according to the Bologna- criteria and ovarian reserve parameters' indicating the risk of poor ovarian response (AFC < 5 and AMH < 0,5ng/ml) (12) as well as according to the POSEIDON criteria (13) and endometriosis stage III/IV. **Control (n=55)** **Study group (n=53)**	**Study group:** To reduce the gonadotropin dosage daily by 12.5 IU rec-FSH as soon as ≥ 3 follicles ≥ 14 mm were present until the criteria for final oocyte maturation were met. GnRH antagonist protocol + rFSH **Control:** Constant stimulation dose; GnRH antagonist protocol + rFSH	Number of MII oocytes	**Study group vs controls** - Number of MII oocytes (mean ± SD) 12 (IQR8) vs 12 (IQR 6), p=0.783	

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

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Huang, L., Gao, Y., Liang, S., & Jiang, M. (2025). Administration of dehydroepiandrosterone improves endometrial thickness in women undergoing IVF/ICSI: a systematic review and meta-analysis. *Journal of ovarian research*, 1*8*(1), 35.	SR	women undergoing IVF/ICSI **Inclusion criteria:** (i) parallel-controlled RCT design; (ii) women underwent IVF/ICSI, the experimental group received DHEA administration, while the control group received with or without placebo; and (iii) the outcomes included reproductive or endometrial function. The reproductive outcomes consisted of LBR, (OPR as a surrogate), CPR, and miscarriage rate (MR). Endometrial outcomes included endometrial thickness (EMT) and endometrial morphology. The primary outcomes included LBR/ongoing pregnancy rate (or CPR if LBR/ongoing pregnancy rate was not reported) and EMT. The secondary outcomes were MR, endometrial morphology, oocyte and embryo quality **Exclusion criteria:** studies include laboratory or animal studies, reviews, cohort or case-control studies, case reports or quasi-randomized trials.	**Study group:** DHEA pre-treatment **Control:** no pre-treatment/placebo	LBR No of MII oocytes	**LBR:** OR 1.33, 95% CI 0.98-1.82, 10 RCTs, 1217 women, NS. **Number of MII oocytes:** MD 0.56, CI -0.06 to 1.18, 8 RCTs, 842 women, NS.	

Liu, Y., Ding, F., Yang, Y., & Ma, B. (2025). Growth hormone improves the pregnancy outcomes in poor ovarian responders undergoing in vitro fertilization: an umbrella review. *Journal of assisted reproduction and genetics*, *42*(3), 721–736.	SR	**Inclusion criteria:** women with POR undergoing IVF treatment aged 20 to 45 years old. The intervention groups must receive GH treatment, while the control groups should be treated without GH or with placebo, with no restrictions on dosage, duration, or course of treatment. The primary out-comes were live birth rate and clinical pregnancy rate, while secondary outcomes included total dose of Gn for ovarian stimulation, number of retrieved oocytes and MII oocytes, number of transferred embryos, endometrial thickness (EDM) on hCG day, and adverse effects such as multiple pregnancy, ectopic pregnancy, miscarriage, cycle cancellation, local injection site reactions, and severe physical side effects **Exclusion criteria:** network meta-analysis, literature lacking complete data or inaccessible original text, GH combined with other drugs, and updated meta-analyses	**Study group:** GH treatment **Control:** placebo/no treatment	LBR CPR No of MII oocytes	**LBR:** OR=1.80, 95% CI (1.22, 2.64), 9 RCTs, p<0.05, the improvements were more obvious in patients with advanced age (over 40 years old), while no benefits were noted in young patients. **CPR** 19 RCTs involving 1763 patients OR 1.92, 95% CI 1.51-2.43, 19 RCTs, 1763 women, p<0.05 **Number of MII oocytes:** 11 RCT involving 1358 patients MD = 1.63, 95%CI (1.13, 2.13), p<0.05	

Naik S, Lepine S, Nagels HE, Siristatidis CS, Kroon B, McDowell S. Androgens (dehydroepiandrosterone or testosterone) for women undergoing assisted reproduction. The Cochrane database of systematic reviews 2024;6: Cd009749.	SR	**Inclusion criteria:** Randomized controlled trials (RCTs) comparing Testosterone as an adjunct treatment to any other active intervention, placebo, or no treatment in women undergoing assisted reproduction **Exclusion criteria:** non-RCTs	**Study group:** testosterone pre-treatment **Control:** no pre-treatment	LBR/OPR	LBR/OPR: OR 2.53, 95% CI 1.61-3.99, 8 RCT, 716 women, p<0.05	
Showell, M. G., Mackenzie-Proctor, R., Jordan, V., Hodgson, R., & Farquhar, C. (2018). Inositol for subfertile women with polycystic ovary syndrome. *The Cochrane database of systematic reviews*, *12*(12), CD012378.	SR	Sub fertile women with PCOS (defined by the Rotterdam consensus) who were trying to become pregnant **Inclusion criteria:** Oral inositol versus: * placebo or no treatment All trials included in the meta-analyses enrolled women who were taking myo-inositol versus standard treatment (folic acid) and were undergoing IVF or ICSI.	**Study group:** Myo-inositol plus folic acid **Control:** Folic acid Long GnRH agonist protocol	LBR	No significant difference in live birth rates have been found with myo-inositol compared to standard treatment (folic acid) (2 RCT, OR 2.42; 95% CI 0.75-7.83; 84 women).	Note - only data for IVF studies has been extracted for the guideline evidence synthesis.
Sood, A., Mohiyiddeen, G., Ahmad, G., Fitzgerald, C., Watson, A., & Mohiyiddeen, L. (2021). Growth hormone for in vitro fertilisation (IVF). *The Cochrane database of systematic reviews*, *11*(11), CD000099.	SR	Women with infertility undergoing ovarian stimulation for IVF **Inclusion criteria:** Data from primary trials was combined in the following comparisons. • GH versus no adjuvant treatment: routine use of adjuvant GH for IVF	**Study group:** GH **Control:** No GH Long GnRH agonist protocol	LBR OHSS CPR	**LBR:** OR 1.32, 95% CI 0.40 to 4.43; I2 = 0%; 2 trials, 80 participants; very low-certainty evidence, NS. **OHSS:** Only one study reported OHSS as an outcome (Younis 1992) in normal responders. There were no cases of OHSS in the study and control group" **CPR:** Routine use in IVF: Only one RCT was conducted in	

					women who were not identified as poor responders (Younis 1992), hence meta-analysis could not be performed.	
Tso, L. O., Costello, M. F., Albuquerque, L. E. T., Andriolo, R. B., & Macedo, C. R. (2020). Metformin treatment before and during IVF or ICSI in women with polycystic ovary syndrome. *The Cochrane database of systematic reviews*, *12*(12), CD006105.	SR	Sub fertile women with PCOS undergoing IVF or ICSI **Inclusion criteria:** Women of reproductive age with anovulation attributed to PCOS, with or without another cause of couple infertility, who were treated with metformin before and during an IVF or ICSI cycle. PCOS (Rotterdam criteria) **Exclusion criteria:** Other causes of hyperandrogenism that mimic PCOS (such as congenital adrenal hyperplasia, Cushing's syndrome, or androgen- secreting tumors) should have been excluded	**Study group:** Testosterone gel **Control:** Lubricant gel	LBR OHSS CPR	**LBR:** RR 1.30, 95% CI 0.94 to 1.79; 6 RCTs; 651 women; I2 = 47%; low-quality evidence, NS. One study used GnRH antagonist protocol (Jacob 2016) which reported lower live birth rate with metformin compared to the control group (RR 0.48, 95% CI 0.29 to 0.79). **OHSS:** RR 0.40, 95% CI 0.26 to 0.760; 10 RCTs; 898 women; I2 = 13%, p<0.05. GnRH antagonist protocol: RR 0.97; 95% CI 0.32 to 2.98; 2 RCTs; 193 women; I2 - 26%, NS. **CPR:** long GnRH-agonist protocol: RR 1.32, 95% CI 1.08 to 1.63; 10 studies; 915 women; I2 = 13%; low-quality evidence, p<0.05 GnRH antagonist protocol: RR 1.38, 95% CI 0.21 to 9.14; 2 studies; 177 women; I2 = 87%; very low quality evidence, NS	

Aliakbar, V. H., Tanha, F. D., Asbagh, F. A., Ebrahimi, M., & Shahraki, Z. (2024). The effect of methyltestosterone on in vitro fertilization outcomes: A randomized clinical trial on patients with low ovarian response. *Clinical and experimental reproductive medicine*, *51*(2), 158–162.	RCT	**Inclusion criteria:** women aged 35 to 42 years with a poor ovarian response, an AFC of less than 5, and a serum AMH level of less than 1.2, as per the Poseidon criteria for poor ovarian reserve **Exclusion criteria:** Patients with a history of ovarian surgery, systemic disease, thyroid disorders, renal or hepatic dysfunction, as well as ovum donors were excluded from the study. **Control (n=60)** **Study group (n=60)**	**Study group:** Methyl testosterone pre-treatment **Control:** placebo pre-treatment		**Control:** - ongoing pregnancy rate (%, N) : 3.3% (2/60) - Clinical pregnancy rate (%, N) : 6.67% (4/60) **Study group:** -ongoing pregnancy rate (%, N) : 13.3% (8/60), p=0.05 - Clinical pregnancy rate (%, N) : 15% (9/60), NS	
Gong, Y., Luo, S., Fan, P., Jin, S., Zhu, H., Deng, T., Quan, Y., & Huang, W. (2020). Growth hormone alleviates oxidative stress and improves oocyte quality in Chinese women with polycystic ovary syndrome: a randomized controlled trial. *Scientific reports*, *10*(1), 18769.	RCT	**Inclusion criteria:** Study group: patients (aged 20–40 years) diagnosed with PCOS according to the Rotterdam criteria38 and undergoing IVF treatment were enrolled Control group: inclusion criterion for control patients required the absence of all the Rotterdam criteria **Exclusion criteria:** (1) hydrosalpinx; (2) congenital uterine malformations and/or endometrial disease, tuberculosis, hyperplasia; (3) systemic lupus erythematosus and/or sicca syndrome; (4) uncontrolled endocrinopathy such as diabetes, hyperthyroidism, hypothyroidism, and	**Study group:** On the same day as the rFSH administration, only patients in the PCOS-T group were subcutaneously injected with 4 IU/day of rhGH for pharmaceutical use until the trigger day **Control:** No placebo	CPR No of MII oocytes	**Study group 1:** - Clinical pregnancy rate (%, N) : 54% (27/50) - Number of MII oocytes (mean ± SD) : 12.30±6.80 **Study group 2:** - Clinical pregnancy rate (%, N) : 42% (21/50) - Number of MII oocytes (mean ± SD) :10.02±6.48 **Control:** - Clinical pregnancy rate (%, N) : 50% (25/50) - Number of MII oocytes (mean ± SD) :9.94±5.30	

		hyperprolactinemia; (5) cigarette smoking and/or alcohol consumption; (6) supplementation with vitamin E, vitamin C, or CoQ10, which influence OS markers. **Control (n=50)** **Study group 1 (n=50)** **Study group 2 (n=50)**				
Hussein, R. S., Elnashar, I., Amin, A. F., Zhao, Y., Abdelmagied, A. M., Abbas, A. M., Abdelaleem, A. A., Farghaly, T. A., Abdalmageed, O. S., Youssef, A. A., Badran, E., & Abou-Taleb, H. A. (2021). Effect of Metformin on Premature Luteinization and Pregnancy Outcomes in Intracytoplasmic Sperm Injection-Fresh Embryo Transfer Cycles: A Randomized Double-Blind Controlled Trial. *International journal of fertility & sterility*, *15*(2), 108–114.	RCT	**Inclusion criteria:** (1) Women aged between 20 and 38 year, (2) AMH ≥1 ng/ml, (3) Day-3 FSH <10 mIU/ml, (4) Normal levels of prolactin and thyroid-stimulating hormone **Exclusion criteria:** Patients who were known to have (1) diabetes, (2) renal and liver diseases (3) alcoholism, (4) drug abuse (5) poor responders, defined according to Bologna criteria, (6) Patients whose BMI was more than 30 kg/m2, were advised to have 5-10% weight loss through lifestyle modification and exercises for 3 months. **Control (n=160)** **Study group (n=160)**	**Study group:** Low dose aspirin (100 mg) **Control:** Placebo IVF cycles were conducted for all of the patients by the long GnRH agonist protocol	LBR Incidence of OHSS Number of MII oocytes	**Control:** - Live birth rate (%, N): 44/160 (27.5%) - Incidence of different grades of OHSS (%, N): 1 (0.63%) - Number of MII oocytes (mean ± SD): Median (IQR) 0 (9) **Study group:** - Live birth rate (%, N): 61/160 (38.1%), p=0.04 - Incidence of different grades of OHSS (%, N): 1 (0.63%) - Number of MII oocytes (mean ± SD): Median (IQR) 12 (8), p=0.103	

Lisi, F., Carfagna, P., Oliva, M. M., Rago, R., Lisi, R., Poverini, R., Manna, C., Vaquero, E., Caserta, D., Raparelli, V., Marci, R., & Moscarini, M. (2012). Pretreatment with myo-inositol in non polycystic ovary syndrome patients undergoing multiple follicular stimulation for IVF: a pilot study. *Reproductive biology and endocrinology : RB&E*, *10*, 52.	RCT	Non-PCOS patients undergoing ovarian stimulation and IVF or ICSI **Inclusion criteria:** 1. Female age < 40 years 2. Basal FSH level <10mUI/m 3. BMI between 18 and 28 **Exclusion criteria:** 1. Patients presenting diagnostic criteria for PCOS 2. Concomitant endocrine and metabolic diseases such as hypothyroidism, hyperthyroidism, diabetes mellitus, androgen-secreting tumors, adrenal hyperplasia, Cushing's syndrome, hyperprolactinemia 3. Patients that underwent hormonal treatment in the previous 3 months were excluded from the study 4. Obese women (BMI greater than 30 kg/m2) **Control (n=50)** **Study group (n=50)**	**Study group:** 3 tablets of metformin 500 mg per day (Cidophage®, Chemical Industries Development Co, Egypt) with the start of contraceptive pills in the preceding cycle until the day of ovulation triggering. GnRH antagonist regimen **Control:** 3 corn flour placebo tablets for the same regimen and period and regimen. GnRH antagonist regimen	CPR No MII oocytes	**Control:** - Clinical pregnancy rate (%, N) : 12/50 (24%) - calculated as ITT - Number of MII oocytes (mean ± SD) : 6.3 ± 2.9 (No. metaphase II/patient) **Study group:** - Clinical pregnancy rate (%, N) : 14/50 (28%) - calculated as ITT, NS - Number of MII oocytes (mean ± SD) : 4.8 ± 2.2 (No. metaphase II/patient), p<0.05	
Mohammadi, S., Eini, F., Bazarganipour, F., Taghavi, S. A., & Kutenaee, M. A. (2021). The effect of Myo-inositol on fertility rates in poor ovarian responder in women undergoing assisted reproductive technique: a randomized clinical trial. *Reproductive biology and*	RCT	**Inclusion criteria:** 1. Infertile women aged 20–43 years who have one of the criteria of poor ovarian responder as below: AFC < 7 or AMH < 1.2 ng/ml 2. BMI of 19–25 **Exclusion criteria:** (1) PCOS (2) Endocrine disorders such as hyperprolactinemia, diabetes and thyroid dysfunction	**Study group:** Patients received a daily dose of 4,000 mg of myo-inositol into two administrations/day in addition to 400 µg of folic acid for the 3 months before and during rFSH administration, following the long protocol. **Control:**	CPR No of MII oocytes	**Control:** - Clinical pregnancy rate (%, N) : 0/30 - Number of MII oocytes (mean ± SD) : 1.87 ± 1.07 **Study group:** - Clinical pregnancy rate (%, N) : 2/30 (6.6%), p=0.15 - Number of MII oocytes (mean ± SD) : 2.36 ± 1.64, p=0.24	

endocrinology : RB&E, *19*(1), 61.		(3) Pelvic pathology such as hydrosalpinx, uterine anomaly Stages III to IV endometriosis and fibroma (4) Male factors infertility such as Oligo-Astheno-Teratozoospermia (OAT) or Azoospermia (5)Patients who become pregnant spontaneously in pretreatment period and had no desire for cooperation **Control (n=30)** **Study group (n=30)**	Patients received 400 µg of folic acid for the 3 months before and during rFSH administration, following the long protocol. Both groups had the long GnRH agonist protocol			
Mourad, A., Jamal, W., Hemmings, R., Tadevosyan, A., Phillips, S., & Kadoch, I. J. (2025). Empirical use of growth hormone in IVF is useless: the largest randomized controlled trial. *Human reproduction (Oxford, England)*, *40*(1), 77–84.	RCT	**Inclusion criteria:** women aged between 30 and 42 years with primary or secondary infertility, undergoing a GnRH antagonist protocol, who had not previously been treated with GH during an IVF cycle, and had an AMH measurement in the last 24 months. **Exclusion criteria:** those with a contraindication to GH, BMI ≥35 kg/m2, concurrent participation in another trial, AMH <0.5 ng/ml, diabetic, at risk for gestational diabetes, undergoing egg donation, received experimental medication within 3 months, positive HIV/Hepatitis B or C screening, history of recurrent implantation failure (defined as: age 30 to 34 years having had 3 or more day-3 embryos transferred or 2 blastocysts transferred without a positive	**Study group:** GH adjunct **Control:** no adjunct therapy	LBR CPR No of MII oocytes	**Control:** - Live birth rate (%, N) : PP fresh: 33% (30/90) - Clinical pregnancy rate (%, N) : PP fresh: 50% (45/90) - Number of MII oocytes (mean ± SD) : ITT: 8.6 (6.3) **Study group:** - Live birth rate (%, N) : PP fresh: 32% (25/78), NS - Clinical pregnancy rate (%, N) : PP fresh: 44% (34/78), NS - Number of MII oocytes (mean ± SD) : ITT: 8.5 (6.2), NS	

		pregnancy test, or age 35–42 years having had 4 or more day-3 embryos transferred or 3 blastocysts transferred without a positive pregnancy test), inability to communicate in French or English, undergoing endometrial receptivity evaluations, or undergoing PGT **Control (n=105)** **Study group (n=105)**				
Namavar Jahromi, B., Zolghadri, J., Rahmani, E., Alipour, S., Anvar, Z., Zarei, A., & Keramati, P. (2019). Effect of low-dose aspirin on the development of ovarian hyperstimulation syndrome and outcomes of assisted reproductive techniques in the women with PCOS, a randomized double-blinded clinical trial. *Taiwanese journal of obstetrics & gynecology*, *58*(2), 255–260.	RCT	**Inclusion criteria:** PCOS was diagnosed according to the modified Rotterdam criteria **Exclusion criteria:** 1. Women with history of gastritis, gastrointestinal bleeding or hypersensitivity to aspirin 2. Abnormal semen parameters (according to WHO 2010 criteria) **Control (n=105)** **Study group (n=109)**	**Study group:** 100 mg low dose aspirin daily from the 21st day of their menstrual cycle prior to the cycle that was planned to start gonadotropins **Control group:** Placebo from the 21st day of their menstrual cycle prior to the cycle that was planned to start gonadotropins	Incidence of OHSS CPR	**Control:** - Incidence of different grades of OHSS (%, N) : 32/105 (30.5%) Moderate to severe OHSS - Clinical pregnancy rate (%, N) : 24/105 (22.9%) **Study group:** - Incidence of different grades of OHSS (%, N) : 38/109 (34.9%) Moderate to severe OHSS - Clinical pregnancy rate (%, N) : 31/109 (28.4%), p=0.350	
Nazari, L., Salehpour, S., Hosseini, S., Saharkhiz, N., Azizi, E., Hashemi, T., & Ghodssi-Ghassemabadi, R. (2020). Effect of myo-inositol supplementation on ICSI outcomes among poor ovarian responder patients: A randomized controlled trial. *Journal of gynecology*	RCT	Poor responder patients classifiable in POSEIDON group 3 or 4 undergoing IVF + ICSI. Patients <35 years with pre-stimulation parameters of AFC < 5 and AMH < 1.2 ng/ml are placed in POSEIDON group 3. Older patients >35 years with	**Study group:** Infolic powder (myo-inositol + folic acid) **Control:** Folic acid powder like the form of Inofolic Both groups had GnRH antagonist protocol	OPR No of MII oocytes	**Control:** - ongoing pregnancy rate (%, N) : 3.6% - Number of MII oocytes (mean ± SD) : Result not given as mean and SD Result stated as total number - 97.4 **Study group:**	

obstetrics and human reproduction, *49*(5), 101698.		pre-stimulation parameters of AFC < 5 and AMH < 1.2 ng/ml are placed in POSEIDON group 4. **Inclusion criteria:** (1) Women aged between 20 and 45 years old, (2) Normal ovulatory cycles of 24–35 days in length, (3) Basal FSH <15 mIU/ml (4) BMI between 18 and 30 **Exclusion criteria:** (1) Any pelvic pathology such as hydrosalpinx uterine anomaly, advanced endometriosis of stage III to IV, fibroids with uterine cavity distortion, (2) Endocrine and metabolic disorders such as hyperprolactinemia, diabetes, and thyroid dysfunction, (3) Partner had severe oligoasthenozoospermia or azoospermia **Control (n=56)** **Study group (n=56)**			-ongoing pregnancy rate (%, N) : 7.1%, p=0.6 - Number of MII oocytes (mean ± SD) : Result not given as mean and SD Result stated as total number – 96.7, p=0.9	
Saharkhiz, N., Zademodares, S., Salehpour, S., Hosseini, S., Nazari, L., & Tehrani, H. G. (2018). The effect of testosterone gel on fertility outcomes in women with a poor response in *in vitro* fertilization cycles: A pilot randomized clinical trial. *Journal of research in medical sciences : the official journal of Isfahan University of Medical Sciences*, *23*, 3.	RCT	Poor responders to gonadotropins in IVF cycles according to the Bologna criteria **Inclusion criteria:** 1. Candidates for IVF cycles 2. Patients older than 40 years 3. A cycle with early poor response, i.e., to obtain 3 or <3 oocytes of the cycles by normal stimulating 4. AFC <5–7, AMH <0.5–1.1 ng/ml 5. male factor normal-FSH <15 6. Individual's consent to	**Study group:** Testosterone pre-treatment **Control group:** No pre-treatment/placebo	CPR No of MII oocytes	**Control group** - CPR: Reported as pregnancy outcome (not defined pregnancy):0/23 - MII oocytes: Reported number of oocytes - 1.17±1.27, p=0.004 **Study group** -CPR: Reported as pregnancy outcome (not defined pregnancy): 4/25, p=0.04 - MII oocytes: Reported number of oocytes - 2.48±1.64, p=0.004	

		participate in the research project **Exclusion criteria:** (1) Endocrine disorders (thyroid, prolactin, etc.), (2) Endometrioma, (3) Any history of surgery on the ovaries, (4) Reluctance to participate in project (5) New clinical conditions or a change in a treatment procedure, (6) Sensitivity to testosterone gel and its complications. **Control (n=23)** **Study group (n=25)**				
Seyedoshohadaei, F., Abbasi, S., Rezaie, M., Allahvaisi, A., Jafar Rezaie, M., Soufizadeh, N., & Rahmani, K. (2022). Myo-inositol effect on pregnancy outcomes in infertile women undergoing in vitro fertilization/intracytoplasmic sperm injection: A double-blind RCT. *International journal of reproductive biomedicine*, *20*(8), 643–650.	RCT	Infertile women referred for IVF **Inclusion criteria:** 1. Age 20-40 yr, 2. Infertility for at least 1 year 3. Candidates for IVF/ICSI treatments 4. Not used contraception methods for at least 1 year 4. Agonist cycles 5. Regular menstrual cycle (24-35 days) **Exclusion criteria:** 1. Women with metabolic or endocrine disorders, 2. Uterine anomaly, 3. Frozen embryo transfer cycle 4. Recurrent miscarriages **Control (n=30)** **Study group (n=30)**	**Study group:** Myo-inositol (4 g) and folic acid (400mg) daily **Control:** Folic acid (400 mg) daily GnRH antagonist protocol with dual trigger (250mg of hCG plus 0.2 mg triptorelin acetate (Decapeptyl)	LBR CPR No of MII oocytes	**Control:** - Live birth rate (%, N) : 3/30 (10.0) - Clinical pregnancy rate (%, N) : 7 (23.33) - Number of MII oocytes (mean ± SD): 5.43 ± 2.50 **Study group:** - Live birth rate (%, N) : 8/30 (26.66) , p=0.04 - Clinical pregnancy rate (%, N) : 17 (56.66), p=0.04 - Number of MII oocytes (mean ± SD): 7.53 ± 3.71, p=0.04	

Tehraninejad, Ensieh & Khazaei, Noushin & Ayati, Elnaz & Movafegh, Ali & Azimaraghi, Omid. (2018). Effect of vaginal sildenafil on in vitro fertilization success rates in women with previous failed in vitro fertilization attempts. Asian Journal of Pharmaceutical and Clinical Research. 11. 486.	RCT	**Inclusion criteria:** Women who had previously at least two IVF failure attempts and women aged below 45 years of age. **Exclusion criteria:** Patients are 45 years of age or older and patients with a history of heart failure (function class III or higher), signs of severe or chronic ischemia of the lower extremities, or pulselessness on physical examination, a previously diagnosed hematological, renal, hepatic or endocrinal disorder, medical history of acute/chronic heart disease, or high blood pressure **Control (n=36)** **Study group (n=36)**	**Study group:** Daily 100 mg vaginal sildenafil suppositories were also administered to the patients in the case group from the 3 days of menstruation which continued until to the date of human chorionic gonadotropin (HCG) administration.	CPR	**Study group:** - Clinical pregnancy rate (%, N) : 33.3%, 12/36 **Control:** - Clinical pregnancy rate (%, N) : 27.8%, 10/36	

9. WHAT IS THE SAFETY AND EFFICACY OF NON-CONVENTIONAL START STIMULATION COMPARED TO STANDARD EARLY FOLLICULAR PHASE STIMULATION?

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Boudry, L., Mateizel, I., Wouters, K., Papaleo, E., Mackens, S., De Vos, M., Racca, A., Adriaenssens, T., Tournaye, H., & Blockeel, C. (2024). Does dual oocyte retrieval with continuous FSH administration increase the number of mature oocytes in low responders? An open-label randomized controlled trial. *Human reproduction (Oxford, England)*, *39*(3), 538–547.	RCT	**Inclusion criteria:** Women aged ≥25 and ≤40 years and with a low ovarian reserve (AMH level of ≤1.5 ng/ml, or AFC of ≤6 follicles, or ≤5 oocytes retrieved in a previous cycle following standard conventional OS). **Exclusion criteria:** more than 3 consecutive previous failed IVF/ICSI cycles. BMI >35 and <20 kg/m² testicular sperm being used for ICSI; oral contraceptives being used <3 months prior to the start of the treatment; a diagnosis of PCOS according to the Rotterdam criteria; OS for PGT; medical/social freezing; IVM; a history of untreated autoimmune, endocrine, or metabolic disorders; or a history of an ovarian cystectomy or oophorectomy. **Control (n=23)** **Study group (n=14)**	**Study group:** a continuous OS with a first and second oocyte retrieval (OR), with cryopreservation of all embryos **Control:** a single OS followed by a fresh embryo transfer (ET)	LBR CPR No of MII oocytes	**Control:** - Live birth rate (%, N) : 26% (6/23) - Clinical pregnancy rate (%, N) : 30% (7/23) - Number of MII oocytes (mean ± SD) :4.1 (2.4) **Study group:** - Live birth rate (%, N) : 35% (8/23), p=0.52 - Clinical pregnancy rate (%, N) : 52% (12/23), p=0.13 - Number of MII oocytes (mean ± SD) : 4.3 (2.7), p=0.77	

Cerrillo, M., Cecchino, G. N., Toribio, M., García-Rubio, M. J., & García-Velasco, J. A. (2023). A randomized, non-inferiority trial on the DuoStim strategy in PGT-A cycles. *Reproductive biomedicine online*, *46*(3), 536–542.	RCT	patients aged ≥38 years old with poor reproductive prognosis undergoing PGT-A **Inclusion criteria:** as defined by the POSEIDON criteria (6): AMH <1.2 ng/ml, AFC <5, and previous ovarian response of <4 or 4–9 eggs retrieved **Control (n=28)** **Study group (n=28)**	**Study group:** FPS started 5 days after the last contraceptive pill or 3 days after the onset of menstruation with flexible antagonist trigger agonist oocytes vitrification LPS started 5 days after picking up no antagonist trigger agonist ICSI with frozen and fresh **Control:** first ovarian stimulations started 5 days after the last contraceptive pill or 3 days after the onset of menstruation trigger agonist oocytes vitrification second stimulation after menstruation trigger agonist ICSI with frozen and fresh	LBR No of MII oocytes	**Control:** - Live birth rate (%, N) : 23.1% - Number of MII oocytes (mean ± SD): 8.7 **Study group:** - Live birth rate (%, N) : 19.5%, p=0.49 - Number of MII oocytes (mean ± SD): 6.8	no difference, stop on interim due to under-powered
Dastjerdi, M. V., Ansaripour, S., Ataei, M., Gharedaghi, R., Hoseini, S. M. M., Mohazzab, A., & Zafardoust, S. (2024). Comparison of luteal phase stimulation with follicular phase stimulation in poor ovarian response: a single-blinded randomized controlled trial. *Contraception and reproductive medicine*, *9*(1), 6.	RCT	Bologna poor responders **Inclusion criteria:** History of one ICSI failed cycle with less than four oocytes and AMH<1.1 ng/ml **Exclusion criteria:** Women with infectious diseases, sexually transmitted diseases, autoimmune disorders, tubal factor infertility, endometriosis, chronic inflammatory diseases, hormonal or anatomical disorders, endometriosis, presence of space-occupying lesions, history of ectopic pregnancy or miscarriage, myomas, polyps, adhesions, previous pelvic surgeries, cancer	**Study group:** Luteal phase stimulation **Control:** Follicular phase stimulation	CPR No of MII oocytes	**Control:** - Clinical pregnancy rate (%, N) : 0% (0/11) - Number of MII oocytes (mean ± SD) : 2 (0-5) **Study group:** - Clinical pregnancy rate (%, N) : 9.1% (1/11), NS - Number of MII oocytes (mean ± SD) :3 (0-8), p=0.041	

		diagnosis, thrombophilic disorders, anemia and body mass index (BMI)≥30 kg/m2, participants with chromosomal abnormalities and severe male factors of their spouses **Control (n=33)** **Study group (n=31)**				
Massin, N., Abdennebi, I., Porcu-Buisson, G., Chevalier, N., Descat, E., Piétin-Vialle, C., Goro, S., Brussieux, M., Pinto, M., Pasquier, M., & Bry-Gauillard, H. (2023). The BISTIM study: a randomized controlled trial comparing dual ovarian stimulation (duostim) with two conventional ovarian stimulations in poor ovarian responders undergoing IVF. *Human reproduction (Oxford, England)*, *38*(5), 927–937.	RCT	Women with POR were defined with adjusted Bologna criteria i.e. AFC < 5 and/or AMH < 1.1 ng/ml was mandatory. These criteria correspond to the Poseidon criteria group 3 (<35 years) and group 4 (>or = 35y) **Inclusion criteria:** 20 to 41 years, with BMI from 19 to 32 kg/m2, with no more than two previous IVF cycles were recruited **Exclusion criteria:** menorrhea, FSH > 20 IU/L or AFC 1 and women with a partner with an extremely severe sperm anomaly or sperm donor use **Control (n=41)** **Study group (n=39)**	**Study group:** FPS pre-treated with estradiol 4 mg/day starting 7 days before expected date of menses HMG 300 IU/day at fixed dose. Flexible Antagonist. trigger rHCG oocyte vitrification LPS started the day after, HMG 300 IU/day. No antagonist. natural progesterone 400 mg/day started after 7 days of stimulation trigger rHCG ICSI fresh and frozen embryos, freeze all **Control:** pre-treated with estradiol 4 mg/day starting 7 days before expected date of menses first and second stimulation HMG 300 IU/day at fixed dose. Flexible Antagonist. trigger rHCG ICSI with a fresh transfer The first cycle was consecutively followed by a second similar cycle if no pregnancy was achieved.	Cumulative LBR No of MII oocytes	**Control:** - Cumulative live birth rate (%, N)**:** 34.1% - Number of MII oocytes (mean ± SD) : 3.1 **Study group:** - Cumulative live birth rate (%, N)**:** 17.9%, p=0.1 - Number of MII oocytes (mean ± SD) : 3.8, p=0.29	The cLBR was not statistically different, comparing controls versus the duostim

Saharkhiz, N., Salehpoor, S., Hosseini, S., Nazari, L., Sheibani, S., & Doohandeh, T. (2024). Comparison *In Vitro* Fertilization Outcomes between DouStim and Minimal Stimulation Protocols in Poor Ovarian Responders: A Randomized Clinical Trial. *International journal of fertility & sterility*, *18*(2), 135–139.	RCT	women with low functional ovarian reserve candidates for IVF with a history of poor ovarian response were included **Inclusion criteria:** Age ≥35 years, antral follicle count (AFC) level <5, and anti-mullerian hormone (AMH) level <1.2 ng/ml). **Exclusion criteria:** Cycles with the only dominant follicle formation, it means produce one dominant follicle during menstrual cycle, uterus malformation and/or abnormalities, intrauterine adhesions, endometriosis, and history of tuberculosis or pelvic surgery **Control (n=21)** **Study group (n=21)**	**Study group:** Double stimulation protocol **Control:** Minimal stimulation protocol	No of MII oocytes	**Study group:** - Number of MII oocytes (mean ± SD) : FP: 1.63 ± 1.40 LP: 1.72 ± 1.72 **Control:** - Number of MII oocytes (mean ± SD) : 3.36 ± 2.42	
Suñol, J., Castillo, J. C., Ortiz, J. A., Ten, J., Fuentes, A., Moliner, B., Martínez, M., Llácer, J., Guerrero, J., Pitas, A., Bernabeu, A., & Bernabeu, R. (2023). Conventional follicular-phase ovarian stimulation vs. luteal-phase stimulation in suboptimal responders: a randomized controlled trial. *F&S reports*, *4*(4), 344–352.	RCT	POSEIDON group 1b/2b **Inclusion criteria:** 4–9 cumulus-oocyte complexes (COCs) retrieved after conventional stimulation in the presence of adequate ovarian reserve marker 18–41 years with regular menstrual cycles (21–35 days), the presence of both ovaries. **Exclusion criteria:** ovarian follicles > 10 mm in the randomization visit, endometriosis stage III/IV, concurrent uterine pathology (e.g., adenomyosis, submucosal	**Study group:** Four days after the detection of luteinizing hormone peak, patients received 150 mg of corifollitropin alfa fixed (GnRH) antagonist on day 6. On day 8, a fixed daily dose of 300 IU of rFSH trigger agonist freeze all oocytes or embryos **Control:** 150 mg of corifollitropin alfa on days 1–3 of the cycle fixed (GnRH) antagonist on day 6. On day 8, a fixed daily dose of 300	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD) : 5.46 (3.63) **Study group:** - Number of MII oocytes (mean ± SD) : 5.22 (2.80), p=0.669	

		myomas, and Asherman syndrome), and simultaneous participation in another study **Control (n=39)** **Study group (n=39)**	IU of rFSH trigger agonist freeze all oocytes or embryos			

10A. WHAT IS THE PREFERRED STIMULATION PROTOCOL FOR FERTILITY PRESERVATION IN PATIENTS FACING GONADOTOXIC TREATMENT?

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Chen, C. N., Chang, L. T., Chen, C. H., & Tam, K. W. (2022). Fertility preservation for women with breast cancer before chemotherapy: a systematic review and meta-analysis. *Reproductive biomedicine online*, *44*(2), 357–369.	SR	**Inclusion criteria** studies that evaluated the outcomes of FP and presented data on oocyte yield, retrieval, cryopreservation, or fertilization before chemotherapy in women with breast cancer, with clear reporting of the following: patient inclusion and exclusion criteria, FP strategies, and OS protocols, and oocyte or embryo cryopreservation results with more than one breast cancer case. **exclusion criteria**: (1) studies recruiting >50% of patient with non-breast cancers, (2) studies with fewer than 10 cases, and (3) duplicate reporting of patient cohorts.	**Study group:** Random start **Control:** Conventional start	No of oocytes	**No of oocytes:** (MD = −0.84; 95% CI: −2.40 to 0.71)	
Sönmezer, M., Şükür, Y. E., Ateş, C., Saçıntı, K. G., Sönmezer, M., Aslan, B., Atabekoğlu, C. S., Özmen, B., & Oktay, K. H. (2023). Random start ovarian stimulation before gonadotoxic therapies in women with cancer: a	SR	**Inclusion criteria:** All comparative studies evaluating the stimulation and cycle outcome parameters of both RSOS and CSOS before gonadotoxic treatments in cancer patients were included.	**Study group:** Random start **Control:** Conventional start	No of MII oocytes No of embryos	- **Number of MII oocytes** (mean ± SD) : SMD 0.11, 95% CI 0.44 to 0.21; P = 0.49 **- No of embryos:** SMD 0.22, 95% CI 0.59 to 0.15; P = 0.25	

systematic review and meta-analysis. *Reproductive biomedicine online*, *47*(6), 103337.						
Yoshida, T., Takahashi, O., Suzuki, Y., Ota, E., & Hirata, T. (2023). The effectiveness of controlled ovarian stimulation with tamoxifen for patients with estrogen-sensitive breast cancer: A systematic review and meta-analysis. *Reproductive medicine and biology*, *22*(1), e12543.	SR	women with estrogen-sensitive breast cancer undergoing ovarian stimulation for fertility preservation **Control (n=117)** **Study group (n=39)**	**Study group:** tamoxifen supplementation **Control:** letrozole supplementation	No of MII oocytes	No significant difference was reported for the number of oocytes retrieved (MD -0.47, 95% CI -3.84 to 2.90, 2 RCT) or MII oocytes (MD 0.22, 95% CI -2.20 to 2.64, 2 RCT).	
Baig, A. S., Camuñas, N. G., Sánchez, P. P., Nadal, J. S., Fabuel, S. M., & Rubio Rubio, J. M. (2023). Controlled Ovarian Stimulation Initiated at Different Phases of the Menstrual Cycle for Fertility Preservation in Oncological Patients: a Retrospective Study. *Reproductive sciences (Thousand Oaks, Calif.)*, *30*(8), 2547–2553.	CS	All patients who underwent oocyte vitrification due to malignant disease or borderline ovarian tumors and who met the inclusion criteria. **Inclusion criteria:** age less than 40 years, no previous healthy children, reasonable survival rate (≥50% in 5 years) no contraindication for pregnancy after disease. **Control (n=176)** **Study group (n=8)**	**Study group 1:** LFP (a dominant or periovulatory follicle greater than or equal to 14 mm.) Patients received a single dose of GnRH agonist (0.2 mg triptorelin acetate) to trigger ovulation of that follicle and started stimulation as described above between the following two and four days, corresponding to the luteal phase. **Study group 2:** LP (defined by the presence of a corpus luteum on ultrasound and/or serum progesterone levels consistent with ovulation (>3 ng/ml). Patients started stimulation with gonadotropins directly.	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD) : 9.0 (6.0 – 13.0) **Study group 1:** - Number of MII oocytes (mean ± SD) : 7.0 (2.3 – 13.3), NS **Study group 2:** - Number of MII oocytes (mean ± SD) : 11.5 (7.0 – 16), NS	

			Control: early EFP (conventional initiation of ovarian stimulation, day 1-5 of menstrual cycle). Patients started stimulation with gonadotropins directly.			
Dezellus, A., Mirallie, S., Leperlier, F., Sauterey, B., Bouet, P. E., Dessaint, A., Duros, S., Gremeau, A. S., Mouret-Reynier, M. A., Durand, L. M., Venat, L., De Blay, P., Robert, M., Freour, T., Campone, M., Blanc-Lapierre, A., & Bordes, V. (2024). Use of tamoxifene-controlled ovarian hyperstimulation for fertility preservation before breast cancer treatment: A prospective cohort study with a 5-year follow-up. *Breast (Edinburgh, Scotland)*, *77*, 103776.	CS	**Inclusion criteria:** patients aged 18–40, a stage I, II, and III BC undergoing chemotherapy in an adjuvant or neoadjuvant setting **Exclusion criteria:** Women with a previous history of BC or other malignancies in the past five years, pregnancy at the time of inclusion, and a thrombo-embolic event in the past 6 months were also excluded **Control (n=43)** **Study group 1 (n=17)** **Study group 2 (n=35)**	**Study group 1:** Late follicular phase **Study group 2:** Luteal phase **Control:** Early follicular phase	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD) : 10.0 ± 7.3 [1–35] **Study group 1:** - Number of MII oocytes (mean ± SD) : 7.7 ± 4.0 [1–13], NS **Study group 2:** - Number of MII oocytes (mean ± SD) : 10.4 ± 5.3 [1–22], NS	
Filippi, F., Reschini, M., Polledri, E., Cecchele, A., Guarneri, C., Vigano, P., Fustinoni, S., Platteau, P., & Somigliana, E. (2023). Progestin-primed ovarian stimulation for fertility preservation in women with cancer: A comparative study. *PloS one*, *18*(3), e0280238.	CS	women with a first diagnosis of cancer **Control (n=76)** **Study group (n=46)**	**Study group:** PPOS hMG Double trigger **Control:** Corifollitropin + rFSH antagonist	No of MII oocytes	**No of MII oocytes:** **Control:** 9 [4–14] **Study group:** 10 [6–18], p=0.05	

Hong, Y. H., Kim, S. K., Lee, J. R., Jee, B. C., & Suh, C. S. (2022). Clinical efficacy of dual trigger with human chorionic gonadotropin and a gonadotropin-releasing hormone agonist for women undergoing fertility preservation. *Reproductive medicine and biology*, *21*(1), e12440.	CS	**Inclusion criteria:** Fertility preservation for cancer / benign diseases / Elective **Control (n=225)** **Study group (n=148)**	**Study group:** Dual trigger hCG + 0.2 GnRHa **Control:** hCG	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD) :n 4.8 ± 3.8 **Study group:** - Number of MII oocytes (mean ± SD) : 5.7 ± 4.9, p=0.052	
Jochum, F., Sananès, N., Teletin, M., Lichtblau, I., Rongières, C., & Pirrello, O. (2019). Luteal phase stimulation, the future of fertility preservation? Retrospective cohort study of luteal phase versus follicular phase stimulation. *Journal of gynecology obstetrics and human reproduction*, *48*(2), 91–94.	CS	**Inclusion criteria:** Cancer patients < 40 years **Exclusion criteria:** AMH <0.75mg/L and/or AFC < 5 **Control (n=20)** **Study group (n=80)**	To assess if luteal phase stimulation can improve fertility preservation	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD) : 13.1 +/-8.0 **Study group:** - Number of MII oocytes (mean ± SD) : 9.2 +/-5.8, p=0.01	
Lalami, I., Labrosse, J., Cedrin-Durnerin, I., Comtet, M., Vinolas, C., Krief, F., Sifer, C., Peigne, M., & Grynberg, M. (2022). Is letrozole during ovarian stimulation useful in breast cancer patients undergoing fertility preservation to reduce early luteal progesterone levels following GnRH-agonist trigger?. *Reproductive biology*	CS	Patients who underwent COS for FP with GnRH antagonist protocol with GnRHa trigger were included. COSTLES for Breast Cancer / Controls with breast cancer, DOR, Endometriosis, auto immune disease. **Inclusion criteria:** Breast cancer 18-42 y. **Exclusion criteria:** Prior chemotherapy **Control (n=162)**	**Study group:** Letrozole **Control:** No letrozole	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD) : 11.1±0.7 **Study group:** - Number of MII oocytes (mean ± SD) : 10.1±0.6, p=0.28	

and endocrinology : RB&E, *20*(1), 87.		**Study group (n=84)**				
Massarotti, C., Stigliani, S., Gazzo, I., Lambertini, M., & Anserini, P. (2023). Long-acting gonadotropin-releasing hormone agonist trigger in fertility preservation cycles before chemotherapy. *ESMO open*, *8*(4), 101597.	CS	**Control (n=34)** **Study group (n=22)**	To assess whether the long-acting GnRHa triggering would lead to the retrieval of mature oocytes with a maturation rate, expressed as mature metaphase II (MII) oocytes/total oocytes retrieved, comparable with the other triggering methods	No of MII oocytes	**Study group 1:** - Number of MII oocytes (mean ± SD) : 11.1 +/- 4 **Study group 2:** - Number of MII oocytes (mean ± SD) : 14 +/-8.4 **Control:** - Number of MII oocytes (mean ± SD) : 8.8 +/- 5.8	
Melo, V. D., Liseth, O. Y., Schmidt, W. M., Pruthi, R. K., Marshall, A. L., & Shenoy, C. C. (2022). Risk of thrombosis in women with cancer undergoing controlled ovarian hyperstimulation for fertility preservation. *Journal of assisted reproduction and genetics*, *39*(12), 2847–2856.	CS	**Inclusion criteria:** Adult women of reproductive age with an active cancer diagnosis or cancer treatment who received controlled ovarian hyperstimulation for fertility preservation. Thrombosis groups vs No thrombosis within 6 months. **Control (n=123)** **Study group (n=4)**	**Study group:** Thrombosis within 6 months after COS **Control:** No Thrombosis within 6 months after COS	No of MII oocytes Incidence of OHSS	**Study group:** - Number of MII oocytes (mean ± SD) : 11.5 (6.0–23.0) - Incidence of different grades of OHSS (%, N) : 0%, 0 **Control:** - Number of MII oocytes (mean ± SD) : 17.0 (0.0–89.0) - Incidence of different grades of OHSS (%, N) : 7.3%, 9	
Nazarenko, T. A., Martirosyan, Y. O., Birukova, A. M., Korneeva, I. E., Sokolova, J., & Khubaeva, D. G. (2021). Outcomes of ovarian stimulation in the follicular and luteal phases of the menstrual cycle in cancer patients. *Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology*, *37*(sup1), 13–16.	CS	**Inclusion criteria:** Cancer **Exclusion criteria:** Extremely reduced ovarian reserve level, recurrent oncological diseases, distant metastases, prior gonadotoxic treatment. **Control (n=72)** **Study group (n=68)**	**Study group:** Follicular phase stim **Control:** Luteal phase stim	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD) : 557 (72.6%) **Study group:** - Number of MII oocytes (mean ± SD) : 520 (72.8%), p=0.521	

Sahin, G., Goker, E. N. T., Gokmen, E., Yeniay, L., Acet, F., Zekioglu, O., & Tavmergen, E. (2022). Controlled ovarian stimulation outcomes of fertility preservation procedures in newly diagnosed breast cancer patients: a retrospective study from a single-tertiary-IVF centre. *Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology*, *42*(3), 518–523.	CS	**Inclusion criteria:** Age between 18 and 45, newly diagnosed Stage 0 3 breast ca/DCIS patients who underwent oocyte/embryo cryopreservation before oncological treatments **Exclusion criteria:** Advanced stage and/or metastatic disease **Study group (n=61)**	**Study group:** Early foll phase start **Control:** Random start	No of MII oocytes	**Study group 1:** - Number of MII oocytes (mean ± SD) : 8.7 ± 6.1 **Control:** - Number of MII oocytes (mean ± SD) : 9.4 ± 5.8	
Shulman, Y., Almog, B., Kalma, Y., Fouks, Y., Azem, F., & Cohen, Y. (2021). Effects of letrozole or tamoxifen coadministered with a standard stimulation protocol on fertility preservation among breast cancer patients. *Journal of assisted reproduction and genetics*, *38*(3), 743–750.	CS	**Inclusion criteria:** Histologically confirmed diagnosis of breast cancer or being a carrier of the BRCA1 or the BRCA 2 gene. **Exclusion criteria:** Age younger than 18 years or older than 42 years, having undergone chemotherapy or pelvic radiation, or a history of ovarian surgery with a possible effect on the ovarian reserve. **Control (n=52)** **Study group 1 (n=36)** **Study group 2 (n=30)**	**Study group 1:** Letrozole **Study group 2:** Tamoxifen **Control:** No letrozole No Tamoxifen	No of MII oocytes	**Study group 1:** - Number of MII oocytes (mean ± SD) : 79% (468/592) **Study group 2:** - Number of MII oocytes (mean ± SD) : 78.6% (264/336) **Control:** - Number of MII oocytes (mean ± SD) :81.5% (396/486	

Sii, S., Polyakov, A., Rozen, G., Agresta, F., & Stern, K. (2023). Controlled ovarian hyperstimulation in breast cancer patients: Does oestrogen receptor status make a difference?. *The Australian & New Zealand journal of obstetrics & gynaecology*, *63*(6), 774–779.	CS	**Inclusion criteria:** 18 and 45 years of age, referred with a breast cancer diagnosis and underwent fertility preservation in the form of egg or embryo cryopreservation or a combination of both **Exclusion criteria:** No ER status, prior gonadotoxic therapy or did not complete fertility preservation due to cycle cancellation prior to egg collection. **Control (n=60)** **Study group (n=154)**	To study the association between oestrogen receptor (ER) status in breast cancer patients and fertility preservation outcomes in a major tertiary referral centre	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD) : 8.9 (7.3–10.5) **Study group:** - Number of MII oocytes (mean ± SD) : 10.5 (9.1–12.0), p=0.19	
Sonigo, C., Sermondade, N., Calvo, J., Benard, J., Sifer, C., & Grynberg, M. (2019). Impact of letrozole supplementation during ovarian stimulation for fertility preservation in breast cancer patients. *European journal of obstetrics & gynecology and reproductive biology: X*, *4*, 100049.	CS	**Inclusion criteria:** Breast cancer **Exclusion criteria:** Prior chemotherapy **Control (n=83)** **Study group (n=94)**	**Study group:** COSTLES **Control:** Conventional antagonist protocol without letrozole	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD) : 10.3 +/- 8.5 **Study group:** - Number of MII oocytes (mean ± SD) : 7.8 +/- 5.3, p= <0.001	
Suzuki, R., Horage-Okutsu, Y., Kawahara, T., Nakamura, K., Shiraishi, E., Iwahata, H., Suzuki-Takahashi, Y., Sugishita, Y., Takae, S., & Suzuki, N. (2023). The effect of aromatase inhibitor on controlled ovarian stimulation for oocyte	CS	**Inclusion criteria:** 73 cancer patients (17-44 yo) **Exclusion criteria:** Endometriosis / AMH > 8 ng/mL **Control (n=26)** **Study group (n=55)**	**Study group:** Aromatase inhibitors COS **Control:** Non aromatase inhibitors	No of MII oocytes	**Study group:** - Number of MII oocytes (mean ± SD) : 7.4 ± 5.9 **Control:** - Number of MII oocytes (mean ± SD) : 6.5 ± 4.5	With or without AI, similar results with Follicular phase stimulation or random start

cryopreservation in adolescent and young cancer patients. *The journal of obstetrics and gynaecology research*, *49*(3), 973–979.						
Takeuchi, H., Maezawa, T., Hagiwara, K., Horage, Y., Hanada, T., Haipeng, H., Sakamoto, M., Nishioka, M., Takayama, E., Terada, K., Kondo, E., Takai, Y., Suzuki, N., & Ikeda, T. (2023). Investigation of an efficient method of oocyte retrieval by dual stimulation for patients with cancer. *Reproductive medicine and biology*, *22*(1), e12534.	CS	The choice of each ovarian stimulation method in dual stimulation was based on each institution's criteria, including patient age, follicle count, and anti-Mullerian hormone (AMH) level. Because this was a multicenter,retrospective study, some centers did not measure AMH values orovarian diameter after oocyte retrieval and were excluded from the present endpoints	To examine the optimal timing of second ovarian stimulation using the dual stimulation method for good ovarian responders with cancer undergoing oocyte retrieval for fertility preservation	No of MII oocytes	**Study group:** - Number of MII oocytes (mean ± SD) : 5.3 ± 3.9	
Turan, V., Gayete-Lafuente, S., Bang, H., & Oktay, K. H. (2023). Outcomes of random-start letrozole protocol with PGT-A in women with breast cancer undergoing fertility preservation. *Journal of assisted reproduction and genetics*, *40*(10), 2401–2408.	CS	**Inclusion criteria:** Breast cancer < 45 yo **Exclusion criteria:** Prior chemotherapy or ovarian surgery **Study group (n=22)**	To compare the cycle characteristics and outcomes of random-start-controlled ovarian stimulation (RSCOS) protocols to the outcomes of standard-start-controlled ovarian stimulation (SSCOS) cycles and to report the utility of PGT-A in these cycles.	No of MII oocytes No of embryos	**Control:** - Number of MII oocytes (mean ± SD) : 10.1±5. - Number of embryos (mean ± SD) : 7.7±4. **Study group:** - Number of MII oocytes (mean ± SD) : 10.9±4.2, p=0.4 - Number of embryos (mean ± SD) : 7.7±4.0, p=0.99	

Oliveira, R., Maya, B. G., Nogueira, M. B. S., Conceição, G. S., Bianco, B., & Barbosa, C. P. (2021). Fertility preservation in breast cancer with oral progestin: is it an option? A pilot study. *Einstein (Sao Paulo, Brazil)*, *19*, eAO5859.	Cross-sectional study	**Inclusion criteria:** Patients with breast cancer who underwent assisted reproduction technologies (ART). **Exclusion criteria:** Use of hormonal contraceptives in the last 3 months preceding treatment, previous ovarian surgery and previous chemotherapy or radiotherapy. **Control (n=20)** **Study group (n=20)**	The patients were divided into two groups, according to the immunohistochemical result of the progesterone receptors testing breast cancer: if positive, ant-GnRH treatment was used, comprising the Control Group; if negative, oral progestin treatment was used, comprising the Progestin Group. **Study group:** PPOS **Control:** GnRH Antagonist	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD) : 4 (2.1-9.8) **Study group:** - Number of MII oocytes (mean ± SD) : 7.5 (3.1-10), p=0.34	
Puthur, S. J., Tracey, S., Gould, D., & Fitzgerald, C. T. (2023). DuoStim protocol- a novel fertility preservation strategy for female oncology patients. *Human fertility (Cambridge, England)*, *26*(5), 1361–1367.	Case series	**Inclusion criteria:** Cancer patients / Random start antagonist **Study group (n=36)**	To evaluate the effectiveness of a modified 'DuoStim' COS protocol in 36 female oncology patients	No of MII oocytes	**No of MII oocytes** 184 (COS#1)+ 184 (COS#2)	

10B. WHAT IS THE PREFERRED STIMULATION PROTOCOL FOR ELECTIVE OOCYTE CRYOPRESERVATION?

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Herzberger, E. H., Knaneh, S., Amir, H., Reches, A., Ben-Yosef, D., Kalma, Y., Azem, F., & Samara, N. (2021). Gonadotropin-Releasing Hormone Agonist Versus Recombinant Human Chorionic Gonadotropin Triggering in Fertility Preservation Cycles. *Reproductive sciences (Thousand Oaks, Calif.)*, *28*(12), 3390–3396.	CS	fertility preservation cycles for social reasons. Ovarian stimulation was performed using the GnRH antagonist protocol in all patients. Gonadotropins were started on early follicular phase. **Control (n=29)** **Study group (n=40)**	**Study group:** GnRHa trigger. The decision was made according to laboratory and sonographic results on the day of triggering, with the risk of OHSS considered **Control:** hCG group	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD): 0.8 (0.7-1.0) **Study group :** - Number of MII oocytes (mean ± SD): 0.8 (0.7-0.9), NS	
Kim, S. J., Kim, T. H., Park, J. K., Eum, J. H., Lee, W. S., & Lyu, S. W. (2020). Effect of a dual trigger on oocyte maturation in young women with decreased ovarian reserve for the purpose of elective oocyte cryopreservation. *Clinical and experimental reproductive medicine*, *47*(4), 306–311.	CS	**Inclusion criteria:** women 35 years old and younger who underwent elective oocyte cryopreservation for FP due to DOR (DOR was defined when the serum AMH level was lower than 1.2 ng/mL at the time of COS initiation **Exclusion criteria:** women on more than their second cycle, a natural cycle, mild stimulation with oral medication, and retrieval failure. **Control (n=36)** **Study group (n=40)**	**Study group:** Dual trigger **Control:** hCG trigger	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD): 2.3 ± 1.7 **Study group :** - Number of MII oocytes (mean ± SD): 3.7 ± 2.7, p=0.010	

Maslow, B. L., Guarnaccia, M., Stefanacci, C., Ramirez, L., & Klein, J. U. (2020). The use of GnRH-agonist trigger for the final maturation of oocytes in normal and low responders undergoing planned oocyte cryopreservation. *Human reproduction (Oxford, England)*, *35*(5), 1054–1060.	CS	all PI-OC cycles **Control (n=671)** **Study group 1 (n=959)** **Study group 2 (n=50)**	**Study group 1:** GnRHa trigger, typically for patients having GnRH antagonist cycles with baseline LH >2.5 IU/L **Study group 2:** dual trigger for patients with baseline LH <2.5 IU/L in GnRH antagonist cycles **Control:** hCG for patients with baseline LH <2.5 IU/L in GnRH antagonist cycles or patients having GnRHa cycles	No of MII oocytes	**Study group 1:** - Number of MII oocytes (mean ± SD) : 13.3 ± 9.1 **Study group 2:** - Number of MII oocytes (mean ± SD) : 13.0 ± 7.8 **Control:** - Number of MII oocytes (mean ± SD) : 8.4 ± 5.9	
Orvieto, R., Aizer, A., Saar-Ryss, B., Marom-Haham, L., Noach-Hirsh, M., Haas, J., & Nahum, R. (2022). Elective egg freezing patients may benefit from increasing the maximal daily gonadotropin dose above 300IU. *Reproductive biology and endocrinology : RB&E*, *20*(1), 171.	CS	all consecutive women admitted to our IVF unit. All women underwent the multiple dose GnRH-antagonist protocol with GnRH-agonist for triggering final follicular maturation. **Inclusion criteria:** First cycle with gonadotropin dose of 300 IU **Control (n=217)** **Study group (n=217)**	**Study group:** Second IVF cycle with adapted dose (increase, decrease, no change) **Control:** first IVF cycle with 300 IU gonadotropins	No of MII oocytes	**Study group :** - Number of MII oocytes (mean ± SD): 8.96±5.19 **Control:** - Number of MII oocytes (mean ± SD): 8.04±4.7	
Pereira, N., Voskuilen-Gonzalez, A., Hancock, K., Lekovich, J. P., Schattman, G. L., & Rosenwaks, Z. (2017). Random-start ovarian stimulation in women desiring elective cryopreservation of oocytes. *Reproductive biomedicine online*, *35*(4), 400–406.	CS	**Inclusion criteria:** Only women desiring oocyte cryopreservation for elective reasons **Exclusion criteria:** underlying medical or gynecological diseases. Women undergoing ovarian stimulation for cancer-related indications, utilizing letrozole-based	**Study group:** Random start stimulation with rFSH and urinary gonadotropins started at the time of GnRH antagonist (flexible) **Control:** Conventional start stimulation day 2/3 with rFSH and flexible GnRH antagonist or GnRH agonist flare protocol	No of MII oocytes	**Study group :** - Number of MII oocytes (mean ± SD) : early follicular: 10.8 (2.7) late follicular: 11.1 (3.0) luteal: 10.9 (3.2) **Control:** - Number of MII oocytes (mean ± SD) : 13.1 (2.3)	

		protocols, or those recently treated with chemotherapy or radiation were excluded. **Control (n=859)** **Study group:** early follicular: 342 late follicular: 42 luteal: 59				

11. WHAT IS THE PREFERRED STIMULATION PROTOCOL FOR OOCYTE DONATION?

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Bodri, D., Sunkara, S. K., & Coomarasamy, A. (2011). Gonadotropin-releasing hormone agonists versus antagonists for controlled ovarian hyperstimulation in oocyte donors: a systematic review and meta-analysis. *Fertility and sterility*, *95*(1), 164–169.	SR	**Inclusion criteria:** Studies were selected if the target population was women undergoing oocyte-donation IVF treatment and the interventions were GnRH agonist versus antagonist-based protocols for COH.	**Study group:** GnRH antagonist protocols **Control:** GnRH agonist protocols	No of MII oocytes Incidence of OHSS	**Study group:** - Number of MII oocytes (mean ± SD) : WMD 0.60, 95% CI 2.26 to 1.07, 7 RCT, 932 donors, NS - Incidence of different grades of OHSS (%, N): RR 0.61 (95% CI 0.18 to 2.15; p=.45; heterogeneity p=.45; I2 0%, fixed effects model).	
Martinez, F., Racca, A., Rodríguez, I., & Polyzos, N. P. (2021). Ovarian stimulation for oocyte donation: a systematic review and meta-analysis. *Human reproduction update*, *27*(4), 673–696.	SR	Systematic review and meta-analysis to summarize current evidence on ovarian stimulation in oocyte donors	clinical outcomes were compared between the use of progestins and GnRH antagonist protocols for pituitary suppression in oocyte donors	No of oocytes CPR	Meta-analysis of the 2 RCTs comparing PPOS with GnRH antagonist protocols for the treatment in 490 oocyte donors showed no differences in mean number of retrieved oocytes (MD 0.33, 95% CI -1.30 to 1.96) and in clinical pregnancy rate among 625 recipients (OR 0.83, 95% CI 0.33-2.06).	Did not meta-analyze any studies for number of MII oocytes retrieved.
Youssef MA, Van der Veen F, Al-Inany HG, Mochtar MH, Griesinger G, Nagi Mohesen M, Aboulfoutouh I, van Wely M. Gonadotropin-releasing hormone agonist versus HCG for oocyte triggering in antagonist-assisted reproductive technology. The.Cochrane.database.of.	SR	Systematic review including 3 RCTs, 372 donors	comparing hCG trigger with GnRH agonist for final oocyte maturation in oocyte donors	Incidence of OHSS No of oocytes LBR	The incidence of OHSS was lower with GnRH agonist compared to hCG for final oocyte maturation (OR 0.05, 95% CI 0.01-0.28, 3 RCT, 372 donors) and mild-moderate OHSS was observed only after hCG triggering. No significant difference was found for the number of retrieved oocytes	

systematic.reviews 2014: Cd008046.					between GnRH agonist and hCG for final oocyte maturation. Live birth rate was similar between hCG and GnRH agonist trigger (OR 0.92, 95% CI 0.53-1.61, 1 RCT, 212 women).	
Acevedo, B., Sanchez, M., Gomez, J. L., Cuadros, J., Ricciarelli, E., & Hernández, E. R. (2004). Luteinizing hormone supplementation increases pregnancy rates in gonadotropin-releasing hormone antagonist donor cycles. *Fertility and sterility*, *82*(2), 343–347.	RCT	Female donors **Inclusion criteria:** older than 18 years **Exclusion criteria:** younger than 35 years donors with PCO, endometriosis, hydrosalpinges, and severe male factor infertility (total number <5,000,000 spermatozoa) **Study group (n=20)** **Control (n=22)**	**Study group:** On the third or fourth day of their menstrual period, a fixed dose of 225 IU/day of recombinant FSH was given for 5 days. On day 6 of ovarian stimulation, 0.25 mg/day of GnRH-a was subcutaneously injected until hCG was given. Subsequently, a step-down protocol was initiated and follicle development observed by sequential ultrasound scans. When the recruited follicles were >18 mm in diameter and if the E2 serum levels were 5,000 pg/mL, follicular maturation with 250 g/mL rhCG and oocyte retrieval was carried 32-34 hours later. **Control:** same GnRH-a/recombinant FSH step-down protocol, except that when the GnRH-a was initiated, 75 IU/day of recombinant LH was added and maintained until the GnRH-a was discontinued.	No of oocytes No of embryos Incidence of OHSS	**Control:** - Number of MII oocytes (mean ± SD): 80% - Number of embryos (mean ± SD): Grade 1: 17 Grade 2: 40 Grade 3: 16 - Incidence of different grades of OHSS (%, N) : 0 **Study group:** - Number of MII oocytes (mean ± SD): 71%, p<0.05 - Number of embryos (mean ± SD): Grade 1: 3, p<0.05 Grade 2: 48, NS Grade 3: 26, NS - Incidence of different grades of OHSS (%, N) : 0	

Alvarado Franco, C. A., Bernabeu García, A., Suñol Sala, J., Guerrero Villena, J., Albero Amorós, S., Llacer, J., Delgado Navas, R. A., Ortiz, J. A., Pitas, A., Castillo Farfan, J. C., & Bernabeu Pérez, R. (2023). Conventional ovarian stimulation vs. delayed single dose corifollitropin alfa ovarian stimulation in oocyte donors: a prospective randomized study. Tail trial. *Frontiers in reproductive health*, *5*, 1239175.	RCT	**Inclusion criteria:** healthy women 18-32 years, with a BMI between 18 and 29 kg/m2, an AFC > 12, both ovaries present, with regular menstrual cycle **Exclusion criteria:** endometriosis, AFC > 20, PCOS and concurrent participation in another study **Study group (n=68)** **Control (n=81)**	**Study group:** TAIL group, only a single dose of 150 ugs of CFA for ovarian stimulation administrated 7 days after OCP cessation. **Control:** a single dose of 150 ugs of CFA plus additional 225 UI of rFSH supplementation from 8th day of COS (if required) were administrated 5 days after OCP discontinuation.		**Control:** - Number of MII oocytes (mean ± SD): 12 (9-17) **Study group:** - Number of MII oocytes (mean ± SD): 9 (4-13), p<0.001	
Cruz, M., Alamá, P., Muñoz, M., Collado, D., Blanes, C., Solbes, E., & Requena, A. (2017). Economic impact of ovarian stimulation with corifollitropin alfa versus conventional daily gonadotropins in oocyte donors: a randomized study. *Reproductive biomedicine online*, *34*(6), 605–610.	RCT	**Inclusion criteria:** Oocyte donors were healthy women aged 18 - 35 years, with regular menstrual cycles, with normal karyotype, at least six antral follicles per ovary at the beginning of the cycle. **Exclusion criteria:** hereditary or chromosomal diseases, sexually transmitted diseases, polycystic ovary syndrome based on Rotterdam criteria or multifollicular ovaries **Study group (n=63)** **Control (n=59)**	**Study group 1:** Collifollitropin alfa 100µg followed by daily administration of recombinant FSH beginning on day 8 if instructed by the researcher. **Study group 2:** 225 IU HP-HMG **Control:** daily doses of 150 IU recombinant FSH	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD): 12.1±1.4 **Study group 1:** - Number of MII oocytes (mean ± SD): 12.2±1.1, NS **Study group 2:** - Number of MII oocytes (mean ± SD): 12.3±2.1, NS	
Clua, E., Martínez, F., Tur, R., Sanmartín, P., Chueca, A., & Barri, P. N. (2012). Triggering ovulation with 250 µg or 500 µg of r-hCG in oocyte donors	RCT	**Inclusion criteria:** aged between 18 and 35 years; with normal screening prior to donation, including karyotype and molecular	**Study group:** 250 µg rhCG **Control:** 500 µg rhCG	No of MII oocytes Incidence of OHSS	**Control:** - Number of MII oocytes (mean ± SD): 9.2±3.4 - Incidence of different grades of OHSS (%, N): mild: 23 (39%)	

treated with antagonist protocol has no effect on the number of mature oocytes retrieved: a randomized clinical trial. *Gynecological endocrinology*, *28*(9), 678–681.		analysis of cystic fibrosis mutations **Exclusion criteria:** Those donors with a history of hyperstimulation or showing a hyper response (14 follicles-11mm). **Study group (n=59)** **Control (n=59)**			**Study group:** - Number of MII oocytes (mean ± SD): 10.1±3.2 - Incidence of different grades of OHSS (%, N): mild: 17 (29%), NS	
De Rijdt, S., Illingworth, K., De Munck, N., Tournaye, H., Mackens, S., De Vos, M., & Blockeel, C. (2024). Early versus late follicular phase ovarian stimulation: a randomized controlled trial. *Reproductive biomedicine online*, *49*(2), 103889.	RCT	Oocyte donors **Inclusion criteria:** 18-36 years old Regular cycles (24 35 days) and BMI of 19 35 kg/m2. **Exclusion criteria:** Women with a low ovarian reserve [AMH <1.1 ng/ml and/or AFC <7] and presumed hyper-responders [number of follicles per ovary 119 and/or AMH >5 ng/ml] were excluded, as were women with endometriosis grade 3 or more, oligomenorrhoea and untreated endocrine abnormalities. **Study group (n=32)** **Control (n=35)**	**Study group:** Late follicular start: Starting stimulation if a dominant follicle and late follicular hormonal values were observed at thesecond evaluation (before rise of LH due to impending ovulation) 225rFSH + GnAnt 0.25 when serum LH levels >10IU/l after 8 days of stimulation. **Control:** Early follicular start: Day 2 of the follicular phase Fixed GnRH antagonist protocol 225rFSH + GnAnt 0.25 D6 (fixed).	No of MII oocytes	**Study group:** - Number of MII oocytes (mean ± SD): 12.7 (8.5) **Control:** - Number of MII oocytes (mean ± SD): 14.1 (8.1)	
Giles, J., Alama, P., Gamiz, P., Vidal, C., Badia, P., Pellicer, A., & Bosch, E. (2021). Medroxyprogesterone acetate is a useful alternative to a gonadotropin-releasing hormone antagonist in oocyte donation: a randomized,	RCT	**Inclusion criteria:** healthy women aged 18-35 years with regular menstrual cycles, no hereditary or chromosomal diseases, a BMI of 18-28 kg/m2, normal karyotype, no sexually transmitted diseases, and a	**Study group:** MPA **Control:** Ganirelix	No of MII oocytes Incidence of OHSS	**Study group:** - Number of MII oocytes (mean ± SD): 16.7 +/- 9 - Incidence of different grades of OHSS (%, N): No moderate-severe **Control:**	

controlled trial. *Fertility and sterility*, *116*(2), 404–412.		normal ovarian reserve characterized by an AMH level of >10 pmol/L or AFC of >12 follicles in both the ovaries at the beginning of the cycle **Exclusion criteria:** PCOS, a chronic medical condition (e.g., diabetes, Crohn disease, thyroid disease, hepatitis B, or sexually transmitted diseases), or had participated in another clinical trial in the previous 3 months **Study group (n=161)** **Control (n=156)**			- Number of MII oocytes (mean ± SD): 16.9 +/- 7.7 - Incidence of different grades of OHSS (%, N): No moderate-severe	
Melo, M., Bellver, J., Garrido, N., Meseguer, M., Pellicer, A., & Remohí, J. (2010). A prospective, randomized, controlled trial comparing three different gonadotropin regimens in oocyte donors: ovarian response, in vitro fertilization outcome, and analysis of cost minimization. *Fertility and sterility*, *94*(3), 958–964.	RCT	**Inclusion criteria:** Donors were healthy women of 18 to 34 years of age, with regular menstrual cycles, normal karyotype, and BMI 18 to 29 kg/m2. **Exclusion criteria:** Family history of hereditary or chromosomal disease, sexually transmitted disease, PCOS. **Study group (n=346)** **Control (n=333)**	**Study group 1:** rFSH in long GnRH agonist protocol **Study group 2:** rFSH+hMG in long GnRH agonist protocol **Control:** hMG in long GnRH agonist protocol	No of embryos Incidence of OHSS	**Study group 1:** - Number of embryos (mean ± SD): 3.4±0.4 - Incidence of different grades of OHSS (%, N): 7.04% (20/284) **Study group 2:** - Number of embryos (mean ± SD): 3.6±0.4 - Incidence of different grades of OHSS (%, N): 5.52% (16/290) **Control:** - Number of embryos (mean ± SD): 3.5±0.5 - Incidence of different grades of OHSS (%, N): 6.78% (19/280)	
Söderström-Anttila, V., Foudila, T., & Hovatta, O. (1996). A randomized comparative study of highly purified follicle stimulating hormone and human	RCT	**Inclusion criteria:** good health, age <35 years, and regarded as psychologically suitable for oocyte donation **Exclusion criteria:**	**Study group:** hp-FSH **Control:** hMG	Incidence of OHSS	**Study group:** - Incidence of different grades of OHSS (%, N): 1/19 **Control:** - Incidence of different grades of OHSS (%, N): 1/20	

menopausal gonadotrophin for ovarian hyperstimulation in an oocyte donation programme. *Human reproduction (Oxford, England)*, *11*(9), 1864–1870.		history of familial genetic disorders, detectable antibodies against hepatitis B, hepatitis C or human immunodeficiency virus, **Study group (n=20)** **Control (n=21)**			53% of the donors in the FSH-HP group (10/19) and 42% in the HMG group (8/19) had complaints about side-effects and discomfort (headache, tiredness, abdominal swelling and pain, nausea and irritability). One donor in the FSH-HP group and two donors in the HMG group experienced a mild fever reaction.	
Tesarik, J., & Mendoza, C. (2002). Effects of exogenous LH administration during ovarian stimulation of pituitary down-regulated young oocyte donors on oocyte yield and developmental competence. *Human reproduction (Oxford, England)*, *17*(12), 3129–3137.	RCT	**Inclusion criteria:** healthy volunteers with normal pituitary and ovarian function	**Study group:** rFSH+hMG in long GnRH agonist protocol (hMG on days 5-7 of stimulation) **Control:** rFSH alone in long GnRH agonist protocol	No of MII oocytes No of embryos	The number of MII oocytes per donor was significantly higher in all groups co-stimulated with LH when compared with corresponding groups stimulated with FSH alone. In women with baseline LH < 1 IU/L, the number of good-quality cleavage-stage embryos was significantly higher with LH activity supplementation. No differences in pregnancy rates were detected between any comparable groups with and without the inclusion of exogenous LH to the stimulation protocol.	

Boniface, C., Schnorr, J. N., Gray, J., McLaughlin, J., Cook, H., Slowey, M., & Schnorr, J. (2023). The role of elagolix in the suppression of ovulation in donor oocyte cycles. *F&S reports*, *4*(2), 179–182.	CS	**Inclusion criteria:** age 21-30 years, nonsmokers, with a BMI of <35 kg/m2, AMH level of >2 ng/mL and an FSH of <10 mIU/mL. All participants had a negative drug screen and underwent psychiatric screening. In addition, participants underwent a full history and physical evaluation, and were excluded if they had chronic medical conditions, first-degree relatives with hereditary disorders, or known carriers of X-linked disorders. Infectious disease testing was required to be negative within 30 days of oocyte retrieval. **Study group (n=75)** **Control (n=75)**	**Study group:** Elagolix for LH control **Control:** Ganirelix for LH control	No of MII oocytes	**Study group:** - Number of MII oocytes (mean ± SD) : 24.73 (no SD given) **Control:** - Number of MII oocytes (mean ± SD): 25.42 (no SD given)	Incomplete data reporting blastulation rates 62.9% in study group and 57.2% in control group.
Christianson, M. S., Barker, M. A., Schouweiler, C., & Lindheim, S. R. (2007). A retrospective comparison of clinical outcomes and satisfaction using reconstituted recombinant gonadotropins (rFSH) or cartridge rFSH with a pen device in donor oocyte cycles. *Current medical research and opinion*, *23*(4), 865–870.	CS	Oocyte donors using GnRH antagonist protocol Aged 20-33. **Study group (n=57)** **Control (n=17)**	**Study group:** Cartridge pen device rFSH **Control:** reconstituted rFSH	No of MII oocytes	**Study group:** - Number of MII oocytes (mean ± SD): 23.1 ± 1.3 **Control:** - Number of MII oocytes (mean ± SD): 23.7 ± 3	

Galvão, A., Karakus, G., Racca, A., Santos-Ribeiro, S., De Munck, N., Drakopoulos, P., De Vos, M., Verheyen, G., Tournaye, H., & Blockeel, C. (2019). Oocyte donation in donors with levonorgestrel intrauterine device: a good match?. *Reproductive biomedicine online*, *39*(4), 641–647.	CS	**Inclusion criteria:** All women who visit the center for cycles of oocyte donation. **Exclusion criteria:** hormonal contraception methods other than LNG-IUD donors who gave oocytes to more than one recipient, cycles not performed using GnRH antagonist suppression and GnRH agonist triggering and sperm retrieved by surgical methods. Cycles of fresh oocyte donation were also excluded **Study group: 103 cycles** **Control: 388 cycles**	**Study group:** LNG-IUD **Control:** no LNG-IUD	No of MII oocytes No of embryos	**Control:** - Number of MII oocytes (mean ± SD): 14.2 (7.3) - Number of embryos (mean ± SD): top quality embryos 2.3 (1.3) **Study group:** - Number of MII oocytes (mean ± SD): 14.5 (6.9), NS - Number of embryos (mean ± SD): top quality embryos 2.3 (1.2), NS	given the low number of donors with LNG-IUD, potentially biasing the interpretation of the results.
Guerrero, J., Castillo, J. C., Ten, J., Ortiz, J. A., Lledó, B., Orozco, D., Quereda, F., Bernabeu, A., & Bernabeu, R. (2024). Random-start ovarian stimulation in an oocyte donation programme: a large, single-centre, experience. *Reproductive biomedicine online*, *48*(1), 103572.	CS	Oocyte donors **Inclusion criteria:** Age <32 years, with BMI between 18 and 28 kg/m2, with regular menstrual cycles, i.e. between 26 and 35 days, recruited according to the clinical and legal requirements of the Spanish Assisted Human Reproduction act (RD 9/2014), which includes a psychological interview, gynecological examination and a rigorous screening for infectious diseases and genetic abnormalities **Study group (n=668)** **Control (n=223)**	**Study group:** Starting ovarian stimulation on day 4 of cycle **Control:** Starting ovarian stimulation on day 1-3 of cycle	No of MII oocytes Incidence of OHSS	**Control:** - Number of MII oocytes (mean ± SD): 13.8 (7.1) - Incidence of different grades of OHSS (%, N): 0 **Study group:** - Number of MII oocytes (mean ± SD): 13.5 (7.0), p=0.6 - Incidence of different grades of OHSS (%, N): 1 severity unknown	OHSS was in a luteal phase start in a pregnant patient
Jones, B. P., Al-Chami, A., Gonzalez, X., Arshad, F.,	CS	Oocyte donors **Inclusion criteria:**	**Study group 1:** GnRH agonist trigger	No of MII oocytes Incidence of OHSS	**Study group 1:**	

Green, J., Bracewell-Milnes, T., Saso, S., Smith, R., Serhal, P., & Ben Nagi, J. (2021). Is oocyte maturity influenced by ovulation trigger type in oocyte donation cycles?. *Human fertility (Cambridge, England)*, *24*(5), 360–366.		All oocyte donors were between the ages of 18-35 years, had a BMI <30 kg/m2 and did not have any infectious or genetic disorders in their personal or family history. **Study group (n=232)** **Control (n=42)**	**Study group 2:** Dual trigger **Control:** hCG trigger		- Number of MII oocytes (mean ± SD): 11.2 ± 5.5 - Incidence of different grades of OHSS (%, N) : 1 **Study group 2:** - Number of MII oocytes (mean ± SD): 7.1 ± 3.4 - Incidence of different grades of OHSS (%, N): 5 **Control:** - Number of MII oocytes (mean ± SD) : 11 6.0 - Incidence of different grades of OHSS (%, N): 0 **p-value oocytes:** <0.001 **p-value OHSS:** <0.001	
Martinez, F., Clua, E., Roca, M., Garcia, S., & Polyzos, N. P. (2022). Comparison of blastocyst euploidy rates following luteal versus follicular phase stimulation in a GnRH antagonist protocol: a prospective study with repeated ovarian stimulation cycles. *Human reproduction (Oxford, England)*, *37*(12), 2777–2786.	CS	Oocyte donors **Inclusion criteria:** good general health, normal karyotype, family medical history without inheritable disease, age 18-34 years, AFC >12, AMH >1.5 ng/ml and BMI 19-28 kg/m2. **Exclusion criteria:** Candidates with endometriosis, PCOS, low ovarian reserve, endocrine abnormalities, contraindication of hormonal treatment, history of OHSS or hyper-response (>30 follicles 11 mm) or body weight <60 kg were excluded. **Study group (n=44)**	**Study group:** Follicular stimulation. **Control:** Luteal stimulation.	No of MII oocytes No of embryos	**Study group:** - Number of MII oocytes (mean ± SD): 20.27 (9.60) - Number of embryos (mean ± SD) : euploid embryos: 1.59±1.30 **Control:** - Number of MII oocytes (mean ± SD): 20.73 (8.65) - Number of embryos (mean ± SD) : euploid embryos: 1.61±1.17	

Martinez G, Sanguineti F, Sepulveda J, Dorey J, Arici A, Patrizio P. A comparison between follitropin alpha filled by mass and follitropin alpha filled by bioassay in the same egg donors. Reproductive.biomedicine. online 2007;14: 26-28.	CS	Inclusion criteria: Healthy donors, with basal cycle 3 FSH<10 IU/L and 17b oestradiol <50pg/ml, who fulfilled the egg donor requirements at screening and had 2 consecutive stimulation cycles, one with rFSH-bio and the second with rFSH-fbm.	clinical outcomes were compared between r-hFSH filled by mass (n=12 cycles) compared to r-hFSH filled by conventional bioassay (n=11 cycles) in the same oocyte donors	No of oocytes No of embryos Incidence of OHSS	The number of oocytes retrieved was significantly higher with r-hFSH filled by mass compared to r-hFSH filled by bioassay (23.8±8.7 vs. 17.1±8.5). The number of day-5 embryos was similar in both groups (5.4±3.1 vs. 5.1±3.0). There were no cases of OHSS reported in either group.	
Pérez-Calvo, A., Martínez, F., Blockeel, C., Clúa, E., Rodríguez, I., Barri, P. N., & Coroleu, B. (2017). Importance of a 5- versus 7-day pill-free interval in a GnRH antagonist protocol using corifollitropin alfa: a prospective cohort study in oocyte donors. *Reproductive biomedicine online*, *35*(4), 425–431.	CS	**Inclusion criteria:** healthy oocyte donor patients aged between 18 and 35 years, with regular menstrual cycles (i.e. between 26 and 35 days), and BMI between 18 and 28 kg /m2 without any relevant personal or family history. The patients had a normal karyotype and negative screening for sexually transmitted diseases. The patients agreed to participate in the study and signed an informed consent. **Exclusion criteria:** Oocyte donors with an AFC over 20, hypersensitivity to the active substance or to any of its excipients, abnormal vaginal bleeding of unknown cause, presence of ovarian cysts or enlarged ovaries, history of OHSS, a previous ovarian stimulation cycle with more than 30 follicles of 11 mm or wider.	**Study group:** Group D5 included oocyte donors, who started ovarian stimulation with corifollitropin alfa 5 days after OCP discontinuation. **Control:** Group D7, the oocyte donors started 7 days after OCP discontinuation.		**Control:** - Number of MII oocytes (mean ± SD): 12.4 (7.4) **Study group:** - Number of MII oocytes (mean ± SD): 10.6 (4.9), NS	

		Study group (n=42) **Control (n=50)**				
Rubio, C., Mercader, A., Alamá, P., Lizán, C., Rodrigo, L., Labarta, E., Melo, M., Pellicer, A., & Remohí, J. (2010). Prospective cohort study in high responder oocyte donors using two hormonal stimulation protocols: impact on embryo aneuploidy and development. *Human reproduction (Oxford, England)*, *25*(9), 2290–2297.	CS	**Inclusion criteria:** 32 high responder donors (>20 oocytes or serum E2 levels .3000 pg/ml on the day of hCG in a previous cycle with standard stimulation, without developing OHSS), age 18 -35 year, normal menstrual cycles of 26 - 34 days duration, normal weight (BMI of 18 -28 Kg/m2, no endocrine treatment (including gonadotrophins and oral contraception) in the 3 months preceding the study, and normal uterus and ovaries at transvaginal ultrasound. **Exclusion criteria:** diagnosis of PCOS according to Rotterdam criteria. **Study group (n=22)** **Control (n=22)**	**Study group:** Reduced Gn dose **Control:** Standard Gn dose	No of MII oocytes	**Control:** - Number of MII oocytes (mean ± SD): 19.5 +/- 4.7 **Study group:** - Number of MII oocytes (mean ± SD): 11.9 +/- 3.3, p= <0.0001	Excluded 10 donors from the study group who had cycles cancelled due to low response to stimulation. All patients had standard dose first, then reduced dose second.
Singh, A., Bhandari, S., Agrawal, P., Gupta, N., & Munaganuru, N. (2016). Use of clomiphene-based stimulation protocol in oocyte donors: A comparative study. *Journal of human reproductive sciences*, *9*(3), 159–163.	CS	Oocyte donors **Inclusion criteria:** Fertile females w previous at least 1 live birth, aged 21-35 years, undergoing COH for the first time, total AFC in both the ovaries 10, with no known or family history of heritable medical disorder, infection screen negative (HIV, and HBsAg) were included in the study. **Exclusion criteria:**	**Study group:** Clomiphene/FSH protocol **Control:** Antagonist/FSH protocol	No of MII oocytes No of embryos Incidence of OHSS	**Control:** - Number of MII oocytes (mean ± SD): 12.96±6.08 - Number of embryos (mean ± SD): 11.21±5.76 fertilized embryos 7.95±4.77 grade 1 embryos d3 - Incidence of different grades of OHSS (%, N): 9 – mild **Study group:** - Number of MII oocytes (mean ± SD): 13.04±5.73, p=0.924	

		The exclusion criteria were no previous live birth, age <21 or >35 years, history of oocyte donation, poor ovarian reserve (total AFC <10), known case of or family history of heritable diseases, HIV or HBsAg positive. **Study group (n=133)** **Control (n=100)**			- Number of embryos (mean ± SD): p=0.973 11.18±5.16 fertilized embryos 8.32±5.09 grade 1 embryos d3 - Incidence of different grades of OHSS (%, N): 10 – mild, p=0.594	

12A. When to start monitoring of follicular development?

No relevant studies identified.

12B. Is the addition of hormonal assessment (oestradiol/progesterone/LH to ultrasound monitoring improving efficacy and safety?

No new relevant studies identified.

13. Does monitoring of endometrial thickness affect the efficacy and safety?

Reference	Study Type	Patients	Diagnostic test evaluated Reference standard test	Outcome measures	Effect size	Comments
Gao G, Cui X, Li S, Ding P, Zhang S, Zhang Y. Endometrial thickness and IVF cycle outcomes: a meta-analysis. Reproductive. biomedicine.online 2020;40: 124-133.	SR	**Inclusion criteria:** (1) participants: all women after IVF; (2) exposure and control: EMT should be divided into higher and lower groups based on the cutoff values of EMT; (3) outcomes: pregnancy rate, implantation rate, abortion rate, live births or ongoing pregnancies, and ectopic pregnancy rate; (4) study design: prospective or retrospective design; and (5) publication language: English.	To explore whether EMT could predict pregnancy outcomes after IVF	CPR	women with lower EMT had a lower chance of clinical pregnancy than those with a higher EMT (OR 0.61, 95% CI 0.52-0.70) irrespective of fresh or frozen embryo transfer. Prospective CS only: no significant association between EMT and pregnancy rates were found	

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

No new relevant studies identified.

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

Reference	Study Type	Patients	Diagnostic test evaluated Reference standard test	Outcome measures	Effect size	Comments
Karatasiou GI, Bosdou JK, Venetis CA, Zepiridis L, Chatzimeletiou K, Tarlatzi TB, Lainas G, Tarlatzis BC, Grimbizis G, Kolibianakis EM. Is the probability of pregnancy after ovarian stimulation for IVF associated with serum estradiol levels on the day of triggering final oocyte maturation with hCG? A systematic review and meta-analysis. *Journal of assisted reproduction and genetics* 2020;37: 1531-1541.	SR	Systematic review and meta-analysis including 3 cohort studies and 641 cycles	To investigate whether the probability of live birth/ongoing pregnancy (≥12 weeks of gestation) or clinical pregnancy (up to 6–8 weeks of gestation) after ovarian stimulation for IVF, using gonadotropin-releasing hormone (GnRH) analogues and gonadotrophins is associated with serum oestradiol levels on the day of triggering final oocyte maturation with hCG	CPR	While the odds of achieving a clinical pregnancy gradually declined with higher oestradiol levels, demonstrating a gradient effect, the difference was not statistically significant.	
Venetis CA, Kolibianakis EM, Bosdou JK, Tarlatzis BC. Progesterone elevation and probability of pregnancy after IVF: a systematic review and meta-analysis of over 60 000 cycles. *Human reproduction update* 2013;19: 433-457.	SR	**Inclusion criteria** (a) the study had to evaluate women undergoing fresh or FET or women undergoing embryo transfer with donated oocytes; (b) the study had to provide extractable data on pregnancy rates among women classified as those with, and those without, PE on the day of hCG administration; and (c) ovarian stimulation should have been performed with the use of gonadotrophins and GnRH analogues.	evaluate the association of PE and the probability of pregnancy achievement	No of oocytes Probability of pregnancy	Based on an analysis of 37 studies reporting the number of oocytes collected, the mean number of cumulus oocyte complexes retrieved was significantly increased in patients with progesterone elevation compared with those without progesterone elevation. serum progesterone elevation on the day of HCG trigger in the stimulation cycle was not	

		Studies in which ovarian stimulation was performed with the concomitant use of anti-estrogens or without the use of GnRH analogues were not eligible.			associated with the probability of pregnancy achievement in a subsequent frozen–thawed cycle	
Bu Z, Zhao F, Wang K, Guo Y, Su Y, Zhai J, Sun Y. Serum progesterone elevation adversely affects cumulative live birth rate in different ovarian responders during in vitro fertilization and embryo transfer: a large retrospective study. *PloS one* 2014;9: e100011.	CS	This retrospective cohort study included 4,651 patients under-going their first IVF/ICSI cycles carried out between January 2011 and December 2012. Cycles carried out for pre-implantation genetic diagnosis (PGD) or those with donor gametes were excluded from this analysis	To investigate the relationship between serum P level on the day of HCG administration during IVF/ICSI and the cumulative live birthrate per oocyte retrieval cycle in patients with different ovarian response.	Cumulative LBR	Adjusted analyses demonstrated an inverse relationship between serum progesterone levels on the day of HCG trigger and cumulative live birth rates in all groups	
Gambini S, Sonigo C, Robin G, Cedrin-Durnerin I, Vinolas C, Sifer C, Boumerdassi Y, Mayeur A, Gallot V, Grynberg M, Peigné M. Risk factors for poor oocyte yield and oocyte immaturity after GnRH agonist triggering. *Human reproduction (Oxford, England)* 2024;39: 963-973.	CS	Retrospective cohort study all patients aged 18–43years who underwent a COH with a GnRH antagonist protocol for IVF with ICSI or FP who were triggered by GnRHa only and who had a “freeze all” strategy between January 2015 and December 2021. Only patients who had undergone ICSI or FP with cryopreservation of mature oocytes, assessed on the day of oocyte retrieval. Patients who received hCG (in combination with GnRHa or in case of suboptimal hormonal response to GnRHa), patients who underwent a fresh embryo transfer after GnRHa trigger, patients who underwent IVF–ICSI cycles with testicular sperm, patients who had no oocyte retrieval	to explore the risk factors for poor oocyte yield and oocyte immaturity after GnRHa trigger in a large cohort of patients undergoing COH in the GnRH antagonist protocol.	Adequate response to GnRH agonist trigger	serum LH level on the day of trigger was not associated the risk of low oocyte maturation rate, defined as <75% of all oocytes collected being at MII stage, or the risk of having a low oocyte recuperation rate, defined as the ratio of collected oocytes over the number of follicles measuring ≥12 mm on the day of trigger below the 10th percentile	

		despite triggering, patients who underwent cycles with the use of letrozole, and patients in whom the pretreatment before COH was unknown were excluded.				
Kummer NE, Feinn RS, Griffin DW, Nulsen JC, Benadiva CA, Engmann LL. Predicting successful induction of oocyte maturation after gonadotropin-releasing hormone agonist (GnRHa) trigger. *Human reproduction (Oxford, England)* 2013;28: 152-159.	CS	Retrospective cohort study All autologous and oocyte donation cycles utilizing a GnRH antagonist protocol where GnRHa was used for the induction of oocyte maturation between 1 April 2003 and 31 December 2011 were considered for analysis. Cycles that were triggered with both GnRHa and hCG were excluded from the analyses.	To evaluate if the magnitude of the endogenous LH surge and progesterone rise after the GnRHa trigger are predictive of the total number of oocytes and mature oocytes retrieved	Adequate response to GnRH agonist trigger	serum oestradiol levels on the day of trigger were significantly different between cycles with and without an adequate post-trigger LH response defined as serum LH level >15 IU/L 12 hours after the GnRH agonist trigger (3242 ± 1233 vs. 2564 ± 1257 pg/ml, respectively)	
Li X, Zeng C, Shang J, Wang S, Gao XL, Xue Q. Association between serum estradiol level on the human chorionic gonadotrophin administration day and clinical outcome. *Chinese medical journal* 2019;132: 1194-1201.	CS	Retrospective study. A total of 2998 patients undergoing their first IVF cycles from January 2011 to January 2016 were reviewed. Of these, 453 patients were excluded because of incomplete cycles (no oocyte retrieval, no ET due to fertility preservation, a freeze-all approach due to OHSS or a lack of fertilization), 449patients were excluded because no top-quality embryos were produced, 312 patients were excluded due to a fibroid uterus, adenomyosis or abnormal pregnancy history, and 13 patients were excluded because of congenital uterine anomalies.	To evaluate the association between elevated serum estradiol (E2) levels on the day of human chorionic gonadotrophin (hCG) administration and IVF-ET pregnancy and birth outcomes.	CPR	Clinical pregnancy rate gradually increased from <100 pg/mL group to 4001–5,000 pg/ml and declined in the >5,000 pg/mL group. Similar pattern was observed for number of MII oocyte counts.	

Lu X, Hong Q, Sun L, Chen Q, Fu Y, Ai A, Lyu Q, Kuang Y. Dual trigger for final oocyte maturation improves the oocyte retrieval rate of suboptimal responders to gonadotropin-releasing hormone agonist. *Fertility and sterility* 2016;106: 1356-1362.	CS	Retrospective cohort study no inclusion or exclusion criteria regarding baseline characteristics were applied.	To determine the incidence of patients who do not respond to an adequate LH surge and identified specific characteristics associated with these non responders.	Response to GnRH agonist trigger	**Serum progesterone** serum progesterone levels on the day of trigger were not associated with the risk of inadequate response to the agonist trigger defined as a serum LH level <15 IU/L, 12 h after the agonist trigger. **Serum oestradiol** significantly different serum oestradiol levels on the day of trigger between cycles with an adequate and inadequate response to the GnRH agonist trigger defined as a serum LH level <15 IU/L, 12 h after the agonist trigger (2,753.23 ± 1,616.34 vs. 1,906.41 ± 1,656.87)	
Luo X, Deng B, Li L, Ma R, Mai X, Wu Z. LH level on ovulation trigger day has a different impact on the outcomes of agonist and antagonist regimens during in vitro fertilization. *Journal of ovarian research* 2023;16: 26.	CS	**Inclusion criteria:** first cycle with controlled ovarian stimulation using a GnRH analog and fresh embryo transfer (ET first cycle with controlled ovarian stimulation using a GnRH analog and fresh embryo transfer **exclusion criteria:** 1) the presence of PCOS, luteinized unruptured follicle syndrome, and other endocrinology disorders; 2) the use of oral contraceptives in the last 3 months; 3) a self-reported history of a family genetic disorder or an abnormal chromosomal karyotype; and 4) incomplete medical records	assess the effects of the LH level on the ovulation trigger day (LHOTD) on the overall clinical outcome of both regimens	LBR CPR	Multivariable regression analysis suggested that higher LH levels were associated with significantly higher live birth and clinical pregnancy rates with both protocols. However, in GnRH antagonist cycles, the difference was only significant for when comparing the third tertile with the first tertile	

Popovic-Todorovic B, Santos-Ribeiro S, Drakopoulos P, De Vos M, Racca A, Mackens S, Thorrez Y, Verheyen G, Tournaye H, Quintero L, Blockeel C. Predicting suboptimal oocyte yield following GnRH agonist trigger by measuring serum LH at the start of ovarian stimulation. *Human reproduction (Oxford, England)* 2019;34: 2027-2035.	CS	Retrospective cohort study Patients with known diagnosis of hypothalamic amenorrhoea were excluded from this treatment. Long-acting GnRH agonist was not used prior to start of ovarian stimulation in the GnRH down-regulated antagonist protocol.	to evaluate the relationship between basal serum LH level, measured on the first day of ovarian stimulation, and the oocyte yield in cycles where a GnRH agonist was used to induce an LH surge for final oocyte maturation.	Adequate response to GnRH agonist trigger	**Serum progesterone** similar serum progesterone levels on the day of agonist trigger between cycles with an adequate and with an inadequate response, defined as the ratio between the total number of oocytes retrieved and the number of follicles with a mean diameter >10 mm on the day of/prior to the trigger <45% (1.3 ± 0.8 vs. 1.4 ± 0.9 ng/ml, respectively) **Serum oestradiol** significantly different serum oestradiol levels on the day of trigger between cycles with an adequate and with an inadequate response, defined as the ratio between the total number of oocytes retrieved and the number of follicles with a mean diameter >10 mm on the day of/prior to the trigger <45% (2796.2 ± 1752.6 vs. 2277.5 ± 1728.1 pg/mL, respectively)	
Racca A, Vanni VS, Somigliana E, Reschini M, Viganò P, Santos-Ribeiro S, Drakopoulos P, Tournaye H, Verheyen G, Papaleo E *et al.* Is a freeze-all policy the optimal solution to circumvent the effect of late follicular elevated	CS	Retrospective cohort study patients who had ovarian stimulation under GnRH antagonist suppression and in which a FA policy of embryos on day 3/5/6 of development was applied. In order to evaluate the oocyte maturation rate and minimise the effect of the known differences in terms of fertilisation between conventional IVF and ICSI, only	To compare CLBR of FA cycles from oocytes obtained with or without elevated P on the day of ovulation trigger of the fresh cycle	Cumulative LBR	Cumulative LBR was similar between patients with serum progesterone levels <1.50 ng/mL and >1.50 ng/mL on the day of hCG trigger	

progesterone? A multicentric matched-control retrospective study analysing cumulative live birth rate in 942 non-elective freeze-all cycles. *Human reproduction (Oxford, England)* 2021;36: 2463-2472.		patients who underwent ICSI were included. Patients who had both conventional IVF and ICSI within the same cycle were excluded. Furthermore, women with an unknown live birth outcome, those who were acceptors of donated oocytes and patients who performed blastocyst biopsy for pre-implantation genetic testing were disregarded				
Wang M, Hao C, Bao H, Huang X, Liu Z, Zhang W, Li F. Effect of elevated estradiol levels on the hCG administration day on IVF pregnancy and birth outcomes in the long GnRH-agonist protocol: analysis of 3393 cycles. *Archives of gynecology and obstetrics* 2017;295: 407-414.	CS	Retrospective cohort study Inclusion criteria: (1) patients were \40 years of age and had any etiology of infertility; (2) the fertilization method used was IVF; (3) embryo transfer cycle; (4) the standard pituitary downregulation long protocol was applied in the mid-luteal phase; (5) case data and E2 result on the hCG day were available and complete Exclusion criteria: (1) failed fertilization; (2) no embryos were available for transfer; (3) all embryos had been cryopreserved due to threatened OHSS; (4) fertilization method was ICSI; (5) the clinical records for the case were incomplete	to detect the effects of supraphysiological E2 levels on pregnancy and birth outcomes of assisted reproductive technology	LBR OHSS No of MII oocytes CPR	Cycles with a serum oestradiol level >3,757 pg/mL on the day of HCG trigger were reported to have a significantly higher mean number of oocytes (14.4±5.3 vs. 7.4±3.9), 2PN oocytes (9.56±4.18 vs. 4.98±2.97), good-quality embryos (5.69±3.45 vs. 2.96±2.27), as well as higher risk of OHSS (3.9% vs 0.6%). Live birth (47.4% vs. 43%) and clinical pregnancy (57.2% vs. 52.1%), were significantly higher in the high oestradiol group	
Zhang W, Liu Z, Liu M, Li J, Guan Y. Is it necessary to monitor the serum luteinizing hormone (LH) concentration on the human chorionic gonadotropin (HCG) day among young women during the follicular-	CS	Retrospective cohort study The following inclusion criteria were applied: 1) age<40 years, 2) follicular-phase single-dose GnRH agonist protocol, and 3) fresh cycle transplants. Thin endometrium on HCG day, recurrent miscarriage and endometriosis were excluded. Although GnRH-a has a therapeutic	to determine whether it is necessary to monitor the serum LH concentration on the HCG day (LHHCG), to identify whether the LHHCG has an impact on the clinical outcome and to determine whether there is an optimal LH range to achieve the	LBR No of oocytes	Regression analyses showed that each unit increase in LH levels on the day of HCG trigger was inversely correlated with the number of oocytes retrieved (adjusted OR -0.351, 95% CI -0.453 to -0.249). However LH levels were not associated with live birth rates	

phase long protocol? A retrospective cohort study. *Reproductive biology and endocrinology : RB&E* 2022;20: 24.		effect on endometriosis, patients diagnosed with endometriosis were excluded in this study because endometriosis leads to infertility and affects the outcome of ART outcomes in many ways	expected clinical outcome			
Zhang W, Tian Y, Xie D, Miao Y, Liu J, Wang X. The impact of peak estradiol during controlled ovarian stimulation on the cumulative live birth rate of IVF/ICSI in non-PCOS patients. *Journal of assisted reproduction and genetics* 2019;36: 2333-2344.	CS	Women aged 20–39 years old were with normal ovarian reserve [defined as the basal AFC > 7] and without diagnosis of PCOS according to Rotterdam diagnostic criteria. Donor cycles and patients who had previous IVF treatment(s) and who did not receive embryo transfer were excluded from the cohort	to investigate the impact of the peak E2 level during COH on the cLBR, as well as the miscarriage rate and the preterm delivery rate in non-PCOS population with normal ovarian reserve.	Probability of LBR	peak serum oestradiol level on the day of hCG administration was not associated with cumulative live birth rate in a multivariable analysis (OR 0.995, 95% CI 0.98-1.01)	
Zhou R, Dong M, Huang L, Zhu X, Wei J, Zhang Q, Liu D, Zhang X, Liu F. Association between serum LH levels on hCG trigger day and live birth rate after fresh embryo transfer with GnRH antagonist regimen in different populations. *Frontiers in endocrinology* 2023;14: 1191827.	CS	Retrospective cohort study patients undergoing their first fresh embryo transfer using GnRH antagonist regimen between January 2014 and October 2020. **inclusion criteria**: (i) maternal age ≤ 40 years; (ii)day-3 fresh embryo transfer; (iii) at least one embryo was available. **exclusion criteria**: (i) uterine abnormalities and intrauterine adhesion; (ii) endometrium thickness on hCG trigger day < 7 mm; (iii) recurrent spontaneous abortion; (iv) hypothalamic or pituitary amenorrhea (29, 30); (v) core data missing	To investigate the association between LH levels on hCG trigger day and live birth rate (LBR), with a particular focus on different populations	LBR	Compared to patients with anticipated normal ovarian response and LH levels >75th percentile, patients in <25th percentile (adjusted OR 0.662, 95%CI 0.508-0.863) and 25th-75th percentile categories (adjusted OR 0.791, 95% CI 0.633-0.988) had significantly lower LBR than those in the >75th percentile category. Patients with PCOS and LH levels <25th percentile also had significantly lower LBR in comparison to patients with LH levels >75th percentile (adjusted	

					OR 0.479, 95% CI 0.277-0.828). LBR were not correlated with LH quartiles in patients with an anticipated low ovarian response	

16. WHICH CRITERIA FOR CYCLE CANCELLATION ARE MEANINGFUL REGARDING PREDICTED LOW/HIGH OOCYTE YIELD?

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Shrem, G., Salmon-Divon, M., Mahfoudh, A. M., Balayla, J., Volodarsky-Perel, A., Henderson, S., Zeadna, A., Son, W. Y., Steiner, N., & Dahan, M. H. (2022). Influence of Maternal Age and Ovarian Reserve on the Decision to Continue or to Cancel IVF Cycles in Patients with One or Two Large Follicles: a Dual Effect. *Reproductive sciences (Thousand Oaks, Calif.)*, *29*(1), 291–300.	CS	**Inclusion criteria:** Patients undergoing stimulated IVF or intra-cytoplasmic sperm injection (ICSI)treatments and having only one or two follicles ≥ 14 mm with at least one mature oocyte. **Exclusion criteria:** The presence of untreated uterine or adnexal pathologies such as uterine leiomyomata, endometrial polyps, hydrosalpinx, and adnexal masses or cysts, oocytes donation cycles, thyroid or prolactin abnormalities, severe male factor infertility (less than5 million total motile sperm count), endometriosis, and natural cycle or modified natural cycle IVF.	For our stratified analysis, we divided the cycles into three groups based on the female age: ≤ 34 years old, 35–39 years old, and ≥ 40 years of age (9.8%, 33.3%, and 56.9% out of the total number of cycles, respectively). Twenty-five percent of the cycles in the ≥ 40-year-old group were cancelled versus 17% and 15% in the 35–39-year-old and ≤ 34-year-old groups, respectively (p < 0.05)	LBR CPR No of MII oocytes	**LBR**: 5.2 % per cycle 6.7% per transfer P<0.01 both per cycle and per ET Per cycle (%) 15.6 6.5 2.7 per ET (%) 18.4 7.9 3.6 Total number of live births 7, 10,1 0 **Clinical pregnancy rate:** 13.3% per cycle 16.9% per ET <0.001 regarding per cycle and ET Per cycle(%) 35.5, 14.7, 8.4 per ET (%) 42.1, 18.1, 11.3 Number of c. pregnancies 16, 23, 22	One study group stratified according to age up to 34, 35-39 40 and more years p -value refers to comparison between different age groups

					Number of MII oocytes: 1.7 ± 0.9 p value 0,8 1 1.8 ± 0.7 1.7 ± 1.0 1.7 ± 0.8	

17. WHAT IS THE PREFERRED DRUG FOR TRIGGERING OF FINAL OOCYTE MATURATION IN TERMS OF EFFICACY AND SAFETY IN THE OVERALL IVF/ICSI POPULATION?

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Beebeejaun Y, Copeland T, Duffy JMN, Sarris I, Showell M, Wang R, Sunkara SK. Triggering oocyte maturation in in vitro fertilization treatment in healthy responders: a systematic review and network meta-analysis. Fertility.and. sterility 2024.	SR	Cross-over, quasi-randomized, and non-randomized trials were excluded, as well as studies involving oocyte donation transfer cycles. Studies were restricted to women predicted to be healthy responders defined as normo-gonotrophic, not a polycystic ovary patient or an expected poor responder, with 8–15 follicles over 12 mm at egg collection, and baseline FSH and LH levels <12 IU/L	To compare the efficacy and safety of hCG trigger alone, GnRH agonist trigger alone, the dual trigger, and the double trigger in women defined as healthy responders.	LBR CPR	Higher live birth rates were found with dual trigger (RR 1.31, 95% CI 1.00-1.70, 1 RCT, 496 women clinical pregnancy rate: RR 1.20, 95% CI 0.89–1.60, 3 RCT, 613 participants	
He, F. F., Hu, W., Yong, L., & Li, Y. M. (2023). Triggering of ovulation for GnRH-antagonist cycles in normal and low ovarian responders undergoing IVF/ICSI: A systematic review and meta-analysis of randomized trials. *European journal of obstetrics, gynecology, and reproductive biology*, *289*, 65–73.	SR	normal and poor responders to ovarian stimulation **Inclusion criteria:** infertility due to tubal and/or male factors, BMI ranging from 18.5 to 28 kg/m2, and baseline FSH level <20 IU/l. **Exclusion criteria:** Patients with PCOS, hydrosalpinx, ovarian endometrioma, abnormal uterus or uterine cavity (adenomyosis, uterine malformations, endometrial	**Study group:** dual trigger **Control:** hCG trigger	OPR CPR	**Study group:** - ongoing pregnancy rate (%, N): normal responders: RR = 1.19 (95% CI 0.72–1.97), 2 RCT, 301 women, NS - Clinical pregnancy rate (%, N) : low responders: RR = 2.2 (95% CI 1.05–4.61, 2 RCT, 36 patients, p=0.04 normal responders: RR = 1.37 (955 CI 0.98–1.91), 4 RCT, 227 patients, p=0.07	

		polyps and intrauterine adhesions) or chromosome abnormalities (in either of the couple) **Control (n=444)** **Study group (n=454)**				
Haas, J., Zilberberg, E., Nahum, R., Mor Sason, A., Hourvitz, A., Gat, I., & Orvieto, R. (2019). Does double trigger (GnRH-agonist + hCG) improve outcome in poor responders undergoing IVF-ET cycle? A pilot study. *Gynecological endocrinology*, *35*(7), 628–630.	RCT	poor responders **Control (n=11)** **Study group (n=12)**	**Study group 1:** Double trigger. GnRH-ag and hCG (6500 IU), 40 and 34 h prior to OPU **Study group 2:** GnRH a trigger. GnRH agonist (GnRH-ag) 36 h before (OPU) and hCG (6500 IU) on day of OPU (GnRH-ag trigger) **Control:** hCG trigger. All patients underwent the multiple-dose GnRH-ant COH protocol, with 300 IU of recFSH started on the third day of menses. trigger: hCG (6500 IU) 36 h before oocyte pick-up	OPR No of MII oocytes	**Control:** - ongoing pregnancy rate (%, N): 9.1% (1/11) - Number of MII oocytes (mean ± SD): 1.4 ± 1.5 **Study group 1:** - ongoing pregnancy rate (%, N): 18.2% (2/11), NS - Number of MII oocytes (mean ± SD): 1.8 ± 1.4, NS **Study group 2:** - ongoing pregnancy rate (%, N): 0, NS - Number of MII oocytes (mean ± SD): 2.1 ± 1.6, NS	
Singh, N., Kashyap, A., Malhotra, N., Mahey, R., Vatsa, R., & Patel, G. (2023). Comparison of the effects of two different trigger strategies - dual (hCG + Leuprolide) versus hCG trigger - in antagonist non-donor IVF: a randomized controlled trial.	RCT	**Inclusion criteria:** PG 3/4 PRs and NRs indicated for ICSI using a GnRH-antagonist protocol were included in the study. **Exclusion criteria:** (1) obesity (BMI > 30), (2) documented uterine abnormalities (as determined	**Study group:** 1 mg GnRHa + 250 µg rhCG **Control:** rhCG 250 µg	CPR No of MII oocytes	**Control:** - Clinical pregnancy rate (%, N) : 19.6% - Number of MII oocytes (mean ± SD): 5.92±2.93 **Study group:** - Clinical pregnancy rate (%, N) : 21%, NS	

JBRA assisted reproduction, *27*(3), 467–473.		via HSG or hysteroscopy), and/or (3) co-existing endocrine disorders (congenital adrenal hyperplasia, hyper-prolactinemia. diabetes mellitus, thyroid dysfunction). Couples who needed counseling for PGD or TESE. **Control (n=50)** **Study group (n=50)**			- Number of MII oocytes (mean ± SD): 7.82±3.24, p=0.003	
Yan, M. H., Sun, Z. G., & Song, J. Y. (2023). Dual trigger for final oocyte maturation in expected normal responders with a high immature oocyte rate: a randomized controlled trial. *Frontiers in medicine*, *10*, 1254982.	RCT	**Inclusion criteria:** women between the ages of 21 and 38 years with either tubal factor, male factor or unexplained infertility, with a normal ovarian reserve **Exclusion criteria:** women with a thin endometrium, prior history of uterine anomaly/surgery, PCOS, poor ovarian reserve [AFC<5 and/or serum AMH levels <1.2 ng/ml] and known medical comorbidities such as diabetes/hypertension. **Control (n=34)** **Study group (n=39)**	**Study group:** Double trigger: Patients were triggered with co-administration of 0.2mg GnRH-a (0.1mg, Diphereline, France, Epson) and r-hCG (6,500IU), 40 and 34h prior to OPU **Control:** rhCG, 6,500IU,	Cumulative LBR LBR CPR No of MII oocytes	**Control:** - Cumulative live birth rate (%, N): 36.0% (9/25) - Live birth rate (%, N): 36.4% (4/11) - Clinical pregnancy rate (%, N) : 40% (10/25) - Number of MII oocytes (mean ± SD): 55.5% [19.8%] **Study group:** - Cumulative live birth rate (%, N): 66.7% (24/36), p=0.022 - Live birth rate (%, N) : 50% (2/4), p=1 - Clinical pregnancy rate (%, N) : 69.4% (25/36) - Number of MII oocytes (mean ± SD): 84.0% [14.0%]	
Zhou, C., Yang, X., Wang, Y., Xi, J., Pan, H., Wang, M., Zhou, Y., & Xiao, Y. (2022). Ovulation triggering with hCG alone, GnRH agonist alone or in combination? A randomized controlled trial in	RCT	Patients aged 35 years or older who had undergone IVF or ICSI for no more than five cycles were recruited **Inclusion criteria:** (i) women who received the PPOS protocol; (ii) age under	**Study group 1:** Dual trigger **Study group 2:** GnRH agonist only **Control:** hCG only	LBR/OPR No of MII oocytes	**Control:** - OPR/LBR: 3/22 (13.6) - Number of MII oocytes (mean ± SD): 2.78 (2.10) **Study group 1:** - OPR/LBR: 7/19 (36.8), NS	

advanced-age women undergoing IVF/ICSI cycles. *Human reproduction (Oxford, England)*, *37*(8), 1795–1805.		40 years; and (iii) a normal ovarian reserve (AMH >1.1 ng/ml, AFC >7 and basal FSH <10 IU/l). **Exclusion criteria:** (i) a history of recurrent pregnancy loss, defined as ≥2 previous spontaneous pregnancy losses; (ii) adenomyosis; (iii) congenital or acquired uterine anomalies, including aseptate uterus, duplex uterus, uterus bicomis, uterus unicomis, intrauterine adhesion and submucosal myomas; (iv) an abnormal chromosomal karyotype in either member of the couple; (v) abnormal thyroid function; or (vi) untreated hydrosalpinx. **Control (n=164)** **Study group (n=168)**			- Number of MII oocytes (mean ± SD): 3.54 (2.51), NS **Study group 2:** - OPR/LBR: 1/5 (20.0), NS - Number of MII oocytes (mean ± SD): 3.15 (2.95), NS	
Li, Q., Li, X., Li, T., Xu, L., Wang, Y., & Huang, R. (2022). Comparison of an HCG-only trigger versus dual trigger for final oocyte maturation in a progestin-primed ovarian stimulation protocol. *Reproductive biomedicine online*, *45*(6), 1176–1181.	CS	Women who underwent IVF/ ICSI. All data from one completed oocyte retrieval cycle, including the fresh stimulated cycle and its associated FET cycles, were extracted and analyzed. **Control (n=565)** **Study group (n=501)**	**Study group:** dual trigger with rhCG 250 µg and 0.1 mg GnRHa **Control:** rhCG 250 µg	Cumulative LBR	**Control:** - Cumulative live birth rate (%, N)**:** 43.72% (247/565) **Study group:** - Cumulative live birth rate (%, N): 40.72% (204/501), p=0.354	

18. WHAT IS THE EFFICACY AND SAFETY OF LUTEAL SUPPORT PROTOCOLS?

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Griesinger, G., Blockeel, C., Kahler, E., Pexman-Fieth, C., Olofsson, J. I., Driessen, S., & Tournaye, H. (2020). Dydrogesterone as an oral alternative to vaginal progesterone for IVF luteal phase support: A systematic review and individual participant data meta-analysis. *PloS one*, *15*(11), e0241044.	SR	Inclusion criteria: 1) prospective RCTs (double-blind, single-blind, or open-label); 2) studies including women undergoing IVF with fresh embryo transfer; and 3) studies comparing the efficacy of oral dydrogesterone (20 to 40 mg daily) with MVP capsules (600 to 800 mg daily) or 8% MVP gel (90 mg daily) by evaluating pregnancy rates (OPR for the main meta-analysis of IPD; both OPR and CPR for the secondary meta-analysis of aggregate data) or LBR. Only studies with available IPD and informed consent from patients allowing the sharing of data with other investigators were included in the meta-analysis of IPD. All eligible studies, including those without suitable IPD, were included in the meta-analysis of aggregate study-level data. Studies including women undergoing IVF with FET were not eligible for inclusion. Review articles, animal	Dydrogesterone vs micronized vaginal progesterone for LPS	LBR OPR	**Study group:** - Live birth rate (%, N) : IPD: OR 1.16; 95% CI 0.96-1.41, 2 RCT, X women aggregate data: OR 1.14; 95% CI 0.99-1.32, 5 RCT, X women - ongoing pregnancy rate (%, N) IPD: OR 1.19; 95% CI 0.99-1.44, 2 RCT, X women aggregate: OR 1.13; 95% CI 1.00-1.28, 9 RCT, X women **p-value LBR:** ns	

		studies, retrospective studies, observational studies, non-randomized studies, and conference abstracts were excluded.				
Liu, Y., Wu, Y., Pan, Z., Jiang, F., Lu, Y., & Meng, Y. (2022). Single-Dose Versus Multiple-Dose GnRH Agonist for Luteal-Phase Support in Women Undergoing IVF/ICSI Cycles: A Network Meta-Analysis of Randomized Controlled Trials. *Frontiers in endocrinology*, *13*, 802688.	SR	Studies looking at GnRh single or multiple vs normal LPS	**Study group 1:** GnRha single bolus. **Study group 2:** GnRha multiple bolus. **Control:** No GnRha bolus.	LBR CPR	**Study group 1:** - Live birth rate (%, N) : 1,21 (0,69, 2,03) vs control - Clinical pregnancy rate (%, N) : 1,40 (0,89, 2,19) vs control **Study group 2:** - Live birth rate (%, N) : 2,04 (1,19. 3.93) vs control - Clinical pregnancy rate (%, N) : 2,10 (1,25, 3,54) vs control	The study didn't differentiate the number of patients in each group. There's variation in how many, when and what GnRHa is given in multidose.
Watters, M., Noble, M., Child, T., & Nelson, S. (2020). Short versus extended progesterone supplementation for luteal phase support in fresh IVF cycles: a systematic review and meta-analysis. *Reproductive biomedicine online*, *40*(1), 143–150.	SR	**Inclusion criteria:** RCTs of prolonged progesterone support vs early cessation **Control (n=809)** **Study group (n=818)**	**Study group:** Stop at pregnancy test. **Control:** Continue	LBR OPR	**Study group:** - Live birth rate (%, N) : RR: 0.94, 95% CI: 0.84-1.00 - ongoing pregnancy rate (%, N): RR: 0.98, 95% CI:0.91-1.05.	Paper stated only RR for outcomes.
Ghanem, M. E., Bedairy, M. H., Shaaban, A., & Albahlol, I. A. (2021). Does the Time of Starting Progesterone Luteal Support Affect Embryo Transfer in Long Agonist Protocol Downregulated ICSI Cycles? A Randomized Controlled Trial. *Reproductive sciences (Thousand Oaks, Calif.)*, *28*(3), 897–903.	RCT	**Inclusion criteria:** total of 190 cycles were eligible from 251 cycles for inclusion as they fulfilled the following inclusion criteria: age ≤ 38 years, nulliparous, first ICSI trial, long agonist protocol, average response (5–20 eggs retrieved), and easy mock transfer with no history of cervical dilatation.	**Study group:** Im progesterone started on day 3 after egg retrieval. **Control:** Im progesterone started on egg retrieval day.	OPR No of MII oocytes	**Control:** - ongoing pregnancy rate (%, N) 37,5 - Number of MII oocytes (mean ± SD) : 9+/- 5,9 **Study group:** - ongoing pregnancy rate (%, N) 44,7, p=0.43 - Number of MII oocytes (mean ± SD) : 8,9+/-5,9	Study looked at ongoing pregnancy rate and miscarriage rate. Starting P on day 3 does not influence pr.

		Control (n=86) **Study group (n=85)**				
Humaidan, P., Alsbjerg, B., Elbaek, H. O., Povlsen, B. B., Laursen, R. J., Jensen, M. B., Mikkelsen, A. T., Thomsen, L. H., Kol, S., & Haahr, T. (2021). The exogenous progesterone-free luteal phase: two pilot randomized controlled trials in IVF patients. *Reproductive biomedicine online*, *42*(6), 1108–1118.	RCT	**Inclusion criteria:** Females aged between 18 and 40 years; (ii) BMI >18 and <30 kg/m, (iii) sperm quality suitable for ICSI or IVF, according to the study center's standard clinical criteria. **Exclusion criteria:** OHSS previously, a previous poor ovarian response to stimulation (<4 oocytes retrieved in a previous cycle), uterine abnormalities or chronic medical diseases, e.g. diabetes mellitus or Crohn's disease. **Control (n=65+60)** **Study group 1 (n=65)** **Study group 2 (n=60)**	**Study group:** A GnRha + 1500 uhCG trigger + 1000 Iu hCG boluses (less than 13 follicles) , GnRha + 1000 uhCG trigger + 500 Iu hCG boluses (14-25 follicles). **Control:** 6500 uhcg and vaginal progesterone.	LBR Incidence of OHSS No of MII oocytes	**Study group 1:** - Live birth rate (%, N) : 20 - Number of MII oocytes (mean ± SD) : 4,3 (2,7) **Study group 2:** - Live birth rate (%, N) :25 - Incidence of different grades of OHSS (%, N) : 3 cases - Number of MII oocytes (mean ± SD) : 8,6 (3,5) **Control:** - Live birth rate (%, N) : 25 and 30 - Incidence of different grades of OHSS (%, N) : 4 cases - Number of MII oocytes (mean ± SD) : 4,9(2,8) adn 8,4 (4,0) **p-value OHSS:** 0,68	The study was looking at fresh transfer after stimulation.
Moini, A., Arabipoor, A., Zolfaghari, Z. *et al.* Subcutaneous progesterone (Prolutex) versus vaginal (Cyclogest) for luteal phase support in IVF/ICSI cycles: a randomized controlled clinical trial. *Middle East Fertil Soc J* **27**, 16 (2022).	RCT	**Inclusion criteria:** infertile patients aged 20–39 years who underwent their first IVF/ICSI and fresh embryo transfer at the Royan Institute 7. **Exclusion criteria:** Risk of OHSS or low ovarian response. **Control (n=40)** **Study group (n=40)**	**Study group:** since ovum pickup day, a daily subcutaneous injection of progesterone (25 mg). **Control:** Vaginal progesterone 400 mg 2 times a day.		**Control:** - Clinical pregnancy rate (%, N) : (40/13) 32% - Number of MII oocytes (mean ± SD) : 8.0±3.6 **Study group:** - Clinical pregnancy rate (%, N) : (40/23) 57,5%, p=0.025 - Number of MII oocytes (mean ± SD) : 7.1±3.6, p=.27	

Niu, Y., Liu, H., Li, X., Zhao, J., Hao, G., Sun, Y., Zhang, B., Hu, C., Lu, Y., Ren, C., Yuan, Y., Zhang, J., Lu, Y., Wen, Q., Guo, M., Sui, M., Wang, G., Zhao, D., Chen, Z. J., & Wei, D. (2023). Oral micronized progesterone versus vaginal progesterone for luteal phase support in fresh embryo transfer cycles: a multicenter, randomized, non-inferiority trial. *Human reproduction (Oxford, England)*, *38*(Suppl 2), ii24–ii33.	RCT	**Inclusion criteria:** Women aged 20–40 years who underwent their first or second cycles of oocyte retrieval and planned to undergo fresh embryo transfer were enrolled. The baseline serum FSH level of eligible patients was considered 15 IU/l or lower. Only women with the use of hCG to trigger oocyte maturation were included. **Exclusion criteria:** history of recurrent miscarriage (≥3 continuous miscarriages), who had failed to achieve a CPR after ≥3 embryo transfers, or who underwent PGT, abnormal intrauterine cavity (such as a septate uterus, uterine unicornis, untreated sub mucous myoma or a history of intrauterine adhesion), hyperprolactinemia, hypothyroidism, a history of seizure, uncontrolled hypertension, thrombophlebitis, a history of thrombosis or stroke or allergy to oral micronized progesterone or vaginal progesterone gel. **Control (n=350)** **Study group 1 (n=345)** **Study group 2 (n=365)**	**Study group 1:** Oral micronized progesterone 400 mg/day. **Study group 2:** Oral micronized progesterone 600 mg/day. **Control:** Vaginal progesterone 90 mg/day.	LBR Incidence of OHSS OPR CPR	**Study group 1:** - Live birth rate (%, N) : 144 (33.5% - Incidence of different grades of OHSS (%, N) : 2 (0.5%) - ongoing pregnancy rate (%, N) 152 (35.3%) - Clinical pregnancy rate (%, N) : 168 (39.1%) **Study group 2:** - Live birth rate (%, N) : 131 (29.8%) - Incidence of different grades of OHSS (%, N) : 1 (0.2%) - ongoing pregnancy rate (%, N) 139 (31.6% - Clinical pregnancy rate (%, N) : 159 (36.1%) **Control:** - Live birth rate (%, N): 156 (35.5%) - Incidence of different grades of OHSS (%, N) : 1 (0.2%) - ongoing pregnancy rate (%, N) 167 (38.0%) - Clinical pregnancy rate (%, N) : 183 (41.6%) **p-value LBR:** 0,19 **p-value COPR:** 0,138	

Salehpour, S., Saharkhiz, N., Nazari, L., Sobhaneian, A., & Hosseini, S. (2021). Comparison of Subcutaneous and Vaginal Progesterone Used for Luteal Phase Support in Patients Undergoing Intracytoplasmic Sperm Injection Cycles. *JBRA assisted reproduction*, *25*(2), 242–245.	RCT	**Inclusion criteria:** Women aged 20 to 40 years who were treated with ICSI fresh cycle, had normal endometrial thickness (7mm-12mm) on day of embryo transfer, and had no endometrial pathology when entered the study. **Exclusion criteria:** Women with advanced endometriosis, pelvic duct adhesion, and history of previous ICSI failures were excluded from the present study. **Control (n=100)** **Study group (n=97)**	**Study group:** Prolutex sc 25 mg (sc progesterone) daily. **Control:** Progesterone pessaries 400 mg twice a day.	OPR CPR	**Study group:** - ongoing pregnancy rate (%, N) 36 (37.1%) - Clinical pregnancy rate (%, N) : 36 (37.1%) **Control:** - ongoing pregnancy rate (%, N) 36 (36.0%) - Clinical pregnancy rate (%, N) : 36 (36.0%)	

19. WHICH GNRH AGONIST MEDICATION AS A METHOD OF TRIGGERING WILL ADD TO THE PREVENTION OF THE OVARIAN HYPERSTIMULATION SYNDROME ALSO WITH REGARDS TO OVERALL EFFICACY?

Reference	Study Type	Patients	Interventions + comparisons	Outcome measures	Effect size	Comments
Tang H, Mourad SM, Wang A, Zhai SD, Hart RJ. Dopamine agonists for preventing ovarian hyperstimulation syndrome. The.Cochrane. database.of.systematic. reviews 2021;4: Cd008605.	SR	Systematic review and meta-analysis including 10 RCTs with 1202 participants All published and unpublished RCTs investigating the effectiveness and safety of dopamine agonists compared with placebo/no intervention or another intervention. We handled conference abstracts in the same way as full publications. We excluded quasirandomised trials and, in the case of cross-over trials, included only pre-crossover data.	dopamine agonist to no intervention or placebo	Incidence of OHSS LBR	- **moderate or severe OHSS:** OR 0.32, 95% CI 0.23-0.44, p<0.05 **- LBR** OR 0.96, 95% CI 0.60-1.55m 3 RCT, n=362, NS	
Zaat T, Zagers M, Mol F, Goddijn M, van Wely M, Mastenbroek S. Fresh versus frozen embryo transfers in assisted reproduction. Cochrane.Database.of. Systematic.Reviews 2021.	SR	Systematic review and meta-analysis. published RCTs comparing the 'freeze all' strategy with the conventional IVF/ICSI strategy with fresh embryo transfer regardless of the context of the evaluation (OHSS or susceptibility of the endometrium). We excluded quasi- and pseudo-randomised controlled trials.	Freeze-all vs fresh transfer	Incidence of OHSS LBR	- **OHSS**: 0.8% vs. 3.7% (Peto OR 0.26, 95% CI 0.17-0.39; 6 RCTs, 4478 women), p<0.05 - **LBR**: OR 1.08, 95% CI 0.95-1.22; 8 RCTs, 4712 women, NS	

		We excluded trials published only as abstracts.				
Santos-Ribeiro S, Mackens S, Popovic-Todorovic B, Racca A, Polyzos NP, Van Landuyt L, Drakopoulos P, de Vos M, Tournaye H, Blockeel C. The freeze-all strategy versus agonist triggering with low-dose hCG for luteal phase support in IVF/ICSI for high responders: a randomized controlled trial. *Human reproduction (Oxford, England)* 2020;35: 2808-2818.	RCT	**Inclusion criteria:** Excessive response to ovarian (≥18 follicles of ≥11 mm on the day of GnRH triggering) • GnRH antagonist suppression • Women aged ≥18 and <40 years • First/second ART cycle in the center • Planned replacement of 1 or 2 blastocysts **Exclusion criteria:** Known reasons for impaired implantation (i.e. hydrosalpinx, fibroid distorting the endometrial cavity, Asherman syndrome, thrombophilia or endometrial tuberculosis) • Oocyte / embryos donation acceptors • Embryos planned to undergo embryo biopsy • BMI ≥35 kg/m2 or ≤18 kg/m2 • Previously enrolled in the same clinical trial • Unable to comprehend the investigational nature of the trial	GnRH agonist trigger for final oocyte maturation with our without freeze-all	LBR Incidence of OHSS	LBR: 39.4% (41/104) vs. 41.6% (42/101), NS moderate-to-severe OHSS occurred only in the fresh transfer group that was given an additional single low-dose hCG on the day of the trigger (8.6% (9/105), 95% CI 3.2-13.9% vs. 0% (0/104), 95% CI 0-3.7%)	

He Y, Tang Y, Chen S, Liu J, Liu H. Effect of GnRH agonist alone or combined with different low-dose hCG on cumulative live birth rate for high responders in GnRH antagonist cycles: a retrospective study. BMC. pregnancy.and.childbirth 2022;22: 172.	CS	Retrospective CS **Inclusion criteria:** (1) age ≤ 40 years old; (2) retrieved oocytes ≥15; and (3) freeze-all strategy. **Exclusion criteria:** (1) embryos derived from donated/vitrified oocytes; (2) PGT cycles; (3) stage III-IV endometriosis/ adenomyosis; (4) presence of uterine cavity lesions or anomalies; (5) untreated hydrosalpinx prior to FET; and (6) uncontrolled systemic diseases, such as hypertension, endocrine disorder, autoimmune disease and so on.	Dual trigger with 1000 or 2000 IU hCG compared to GnRH agonist trigger for final oocyte maturation	Cumulative LBR LBR Incidence of OHSS	**cumulative LBR**: 74.4% (429/577) vs. 75.7% (305/403) vs. 69.7% (253/363) **LBR**: 54.2% (302/577) vs. 54.5% (212/389) vs. 54.3% (191/352)). **Moderate to severe OHSS**: 1.5% (6/403) vs. 1.4% (5/363) vs. 0%, p<0.05	
Shrem G, Steiner N, Balayla J, Volodarsky-Perel A, Tannus S, Son WY, Dahan MH. Use of cabergoline and post-collection GnRH antagonist administration for prevention of ovarian hyperstimulation syndrome. Reproductive.biomedicine. online 2019;39: 433-438.	CS	**Inclusion criteria** PCOS, AFC > 8, eighteen follicles > 10 mm in diameter on the HCG administration day, GnRH-antagonist protocol, GnRH-agonist trigger, freezing of all embryos. There were no exclusion criteria.	Controls: GnRH agonist trigger Study group 1: GnRH agonist + dopamine Study group 2: GnRH agonist + dopamine + GnRH antagonist	Incidence of OHSS	Mild or moderate OHSS: GnRHa vs GnRHa+dopamine: 38% vs. 29%, p<0.05 GnRHa vs. GnRHa+dopamine+GnRH antagonist: 38% vs. 18%, p<0.05. GnRHa+dopamine vs GnRHa+dopamine+GnRH antagonist: 29% vs. 18%, p<0.05	

Wang Q, Wan Q, Li T, Wang X, Hu Y, Zhong Z, Pu K, Ding Y, Tang X. Effect of GnRH agonist trigger with or without low-dose hCG on reproductive outcomes for PCOS women with freeze-all strategy: a propensity score matching study. Archives.of. gynecology.and.obstetrics 2024;309: 679-688.	CS	**Inclusion criteria:** (1) aged ≤ 40 years; (2) with freezeall strategy. Exclusion criteria: (1) donated oocytes; (2) PGT; (3) recurrent spontaneous abortion; (4) untreated hydrosalpinx; (5) endocrine disease (diabetes mellitus, thyroid dysfunction, Cushing syndrome, hyperprolactinemia); (6) endometriosis, uterine adhesion, endometrial polyps, or unicorn uterus; and (7) missing data.	Dual trigger compared to GnRH agonist trigger for final oocyte maturation	LBR Incidence of OHSS	- **LBR**: 56.2% (99/176) vs. 63.1% (111/176), NS. - **total OHSS rate**: 14.8% (26/176) vs. 2.8% (5/176), p<0.05 - **moderate/severe OHSS**: 11.4% (20/176) vs. 1.7% (3/176), p<0.05	