Over Rezervinin Değerlendirilmesi ve Klinik Önemi

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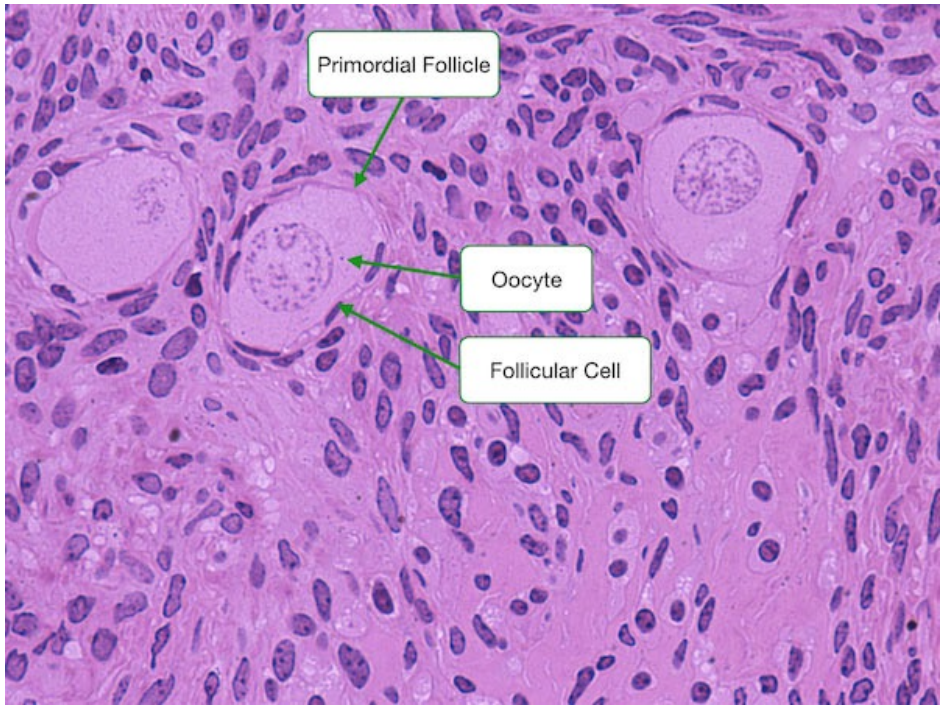
Kadın Hastalıkları ve Doğum AD

Over reserve (OR) tests

- AFC
- AMH
- FSH, E2
- Inhibin
- CCCT



SWOT Analysis

STRENGTHS
Characteristics of the business or project that give it an advantage over others.

WEAKNESSES
Characteristics of the business that place the business or project at a disadvantage relative to others.

OPPORTUNITIES
Elements in the environment that the business or project could exploit to its advantage.

THREATS
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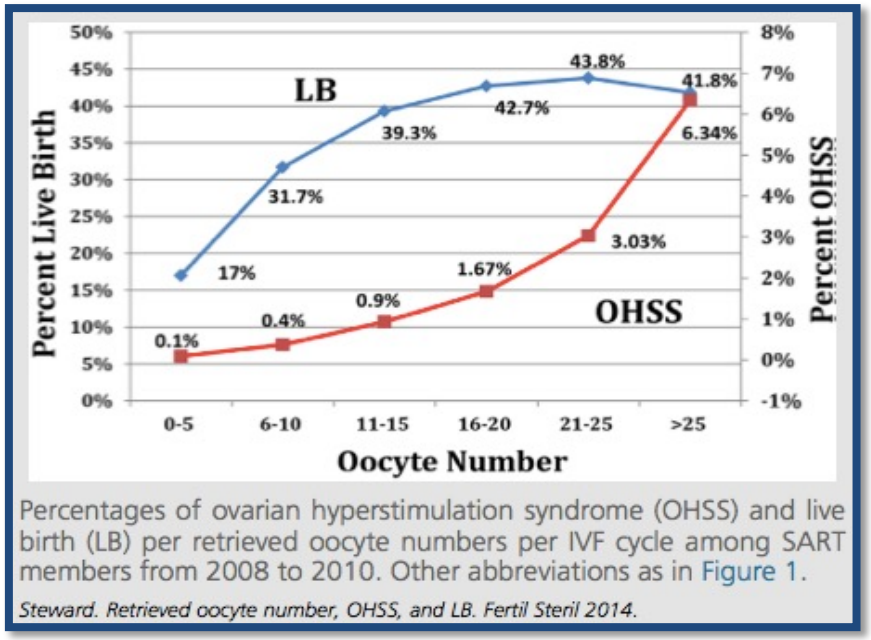
AMH and AFC



Percentages of ovarian hyperstimulation syndrome (OHSS) and live birth (LB) per retrieved oocyte numbers per IVF cycle among SART members from 2008 to 2010. Other abbreviations as in Figure 1.

Steward. Retrieved oocyte number, OHSS, and LB. Fertil Steril 2014.

	Groups	No. of RCT	Finding
Normal response (5 – 15 oocytes)	ORT based vs. 150 IU	3	**1.22 (1.04 – 1.43)**
Moderate/severe OHSS	ORT based vs. 150 IU	4	**0.58 (0.34 – 1.00)**

Lensen et al., Cochrane 2018

AMH or AFC (preclinical studies)

TABLE 3

Multivariate analysis presenting a general linear model for regression of serum AMH and AFC on primordial follicular density.

Parameter	Estimate	SE	τ value	Pr ($>|\tau|$)
(Intercept)	0.69336	0.65267	1.062	0.29
Serum AMH	0.42366	0.14405	2.941	0.005[a]
AFC	0.02792	0.04289	0.651	0.52

Note: AFC = antral follicle count; AMH = antimüllerian hormone; SE = standard error.
[a] $P<.01$.

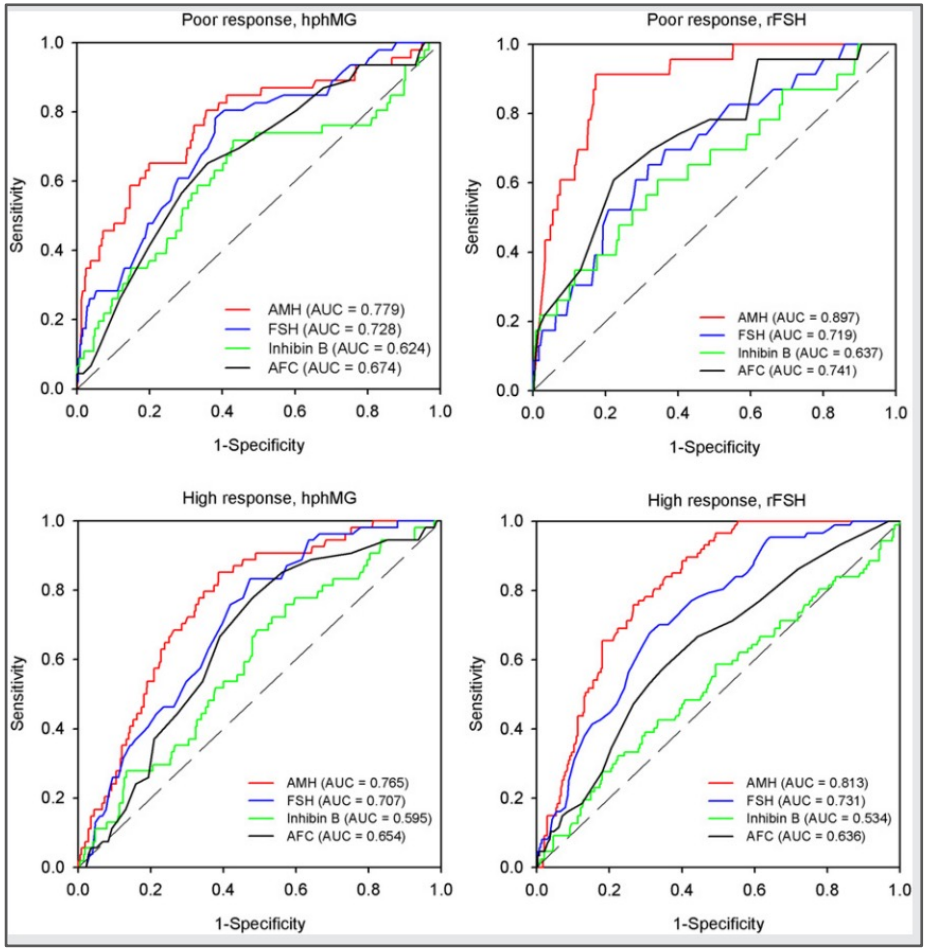
Sermondade. AMH, matured eggs, and follicular density. Fertil Steril 2018.

AMH or AFC (clinical studies)

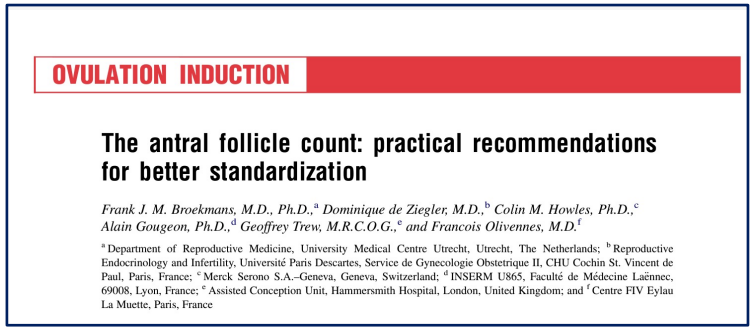
Antimüllerian hormone in gonadotropin releasing-hormone antagonist cycles: prediction of ovarian response and cumulative treatment outcome in good-prognosis patients

Joan-Carles Arce, M.D., Ph.D.,[a] Antonio La Marca, M.D., Ph.D.,[b] Bjarke Mirner Klein, Ph.D.,[c] Anders Nyboe Andersen, M.D.,[d] and Richard Fleming, Ph.D.[e]

[a] Reproductive Health, Ferring Pharmaceuticals A/S, Copenhagen, Denmark; [b] Mother-Infant Department, University of Modena and Reggio Emilia, Modena, Italy; [c] Global Biometrics, Ferring Pharmaceuticals A/S; [d] Fertility Clinic, Rigshospitalet, Copenhagen University Hospital, Copenhagen, Denmark; and [e] Department of Reproductive and Maternal Medicine, University of Glasgow, Glasgow, United Kingdom



AFC



OVULATION INDUCTION

The antral follicle count: practical recommendations for better standardization

Frank J. M. Broekmans, M.D., Ph.D.,[a] *Dominique de Ziegler, M.D.,*[b] *Colin M. Howles, Ph.D.,*[c] *Alain Gougeon, Ph.D.,*[d] *Geoffrey Trew, M.R.C.O.G.,*[e] *and Francois Olivennes, M.D.*[f]

[a] Department of Reproductive Medicine, University Medical Centre Utrecht, Utrecht, The Netherlands; [b] Reproductive Endocrinology and Infertility, Université Paris Descartes, Service de Gynecologie Obstetrique II, CHU Cochin St. Vincent de Paul, Paris, France; [c] Merck Serono S.A.–Geneva, Geneva, Switzerland; [d] INSERM U865, Faculté de Médecine Laënnec, 69008, Lyon, France; [e] Assisted Conception Unit, Hammersmith Hospital, London, United Kingdom; and [f] Centre FIV Eylau La Muette, Paris, France

TABLE 1

The basic clinical and technical requirements for assessment of the antral follicle count in clinical practice.

Clinical considerations
- Select patients with regular menstrual cycles with no coexisting pathologic condition that could technically affect the counting of follicles, such as ovarian endometriosis or previous ovarian surgery
- Count follicles between days 2 and 4 of a spontaneous menstrual or oral contraceptive cycle to avoid the effect of intra-cycle variation
- Include all antral follicles of 2–10 mm in diameter

Technical considerations
- A limited number of personnel, appropriately trained in transvaginal sonography should perform AFCs in each unit
- Real-time two-dimensional imaging is adequate
- Use a transvaginal transducer
- Use a probe with a minimum frequency of 7 MHz, which is maintained in an adequate condition and able to resolve a structure of 2 mm in diameter
- Use a systematic process for counting antral follicles:
  1. Identify the ovary
  2. Explore the dimensions in two planes (perform a scout sweep)
  3. Decide on the direction of the sweep to measure and count follicles
  4. Measure the largest follicle in two dimensions
     - A. If the largest follicle is $\leq$10 mm in diameter:
       - i. Start to count from outer ovarian margin of the sweep to the opposite margin
       - ii. Consider every round or oval transonic structure within the ovarian margins to be a follicle
       - iii. Repeat the procedure with the contralateral ovary
       - iv. Combine the number of follicles in each ovary to obtain the AFC
     - B. If the largest follicle is $>$10 mm in diameter:
       - i. Further ascertain the size range of the follicles by measuring each sequentially smaller follicle, in turn, until a follicle with a diameter of $\leq$10 mm is found
       - ii. Perform a total count (as described) regardless of follicle diameter
       - iii. Subtract the number of follicles of $>$10 mm from the total follicle count

AFC

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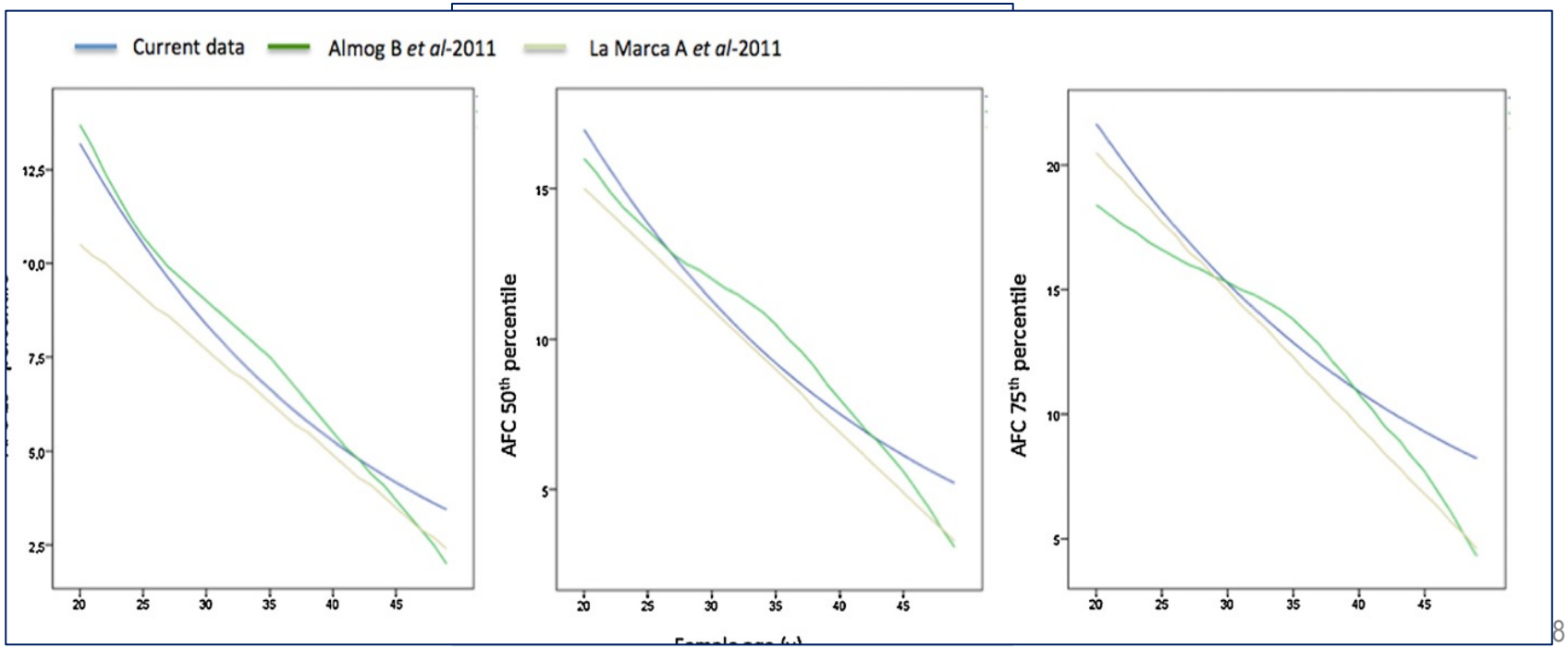
journal homepage: www.elsevier.com/locate/ejogrb

Age related normogram for antral follicle count in general population and comparison with previous studies

Gurkan Bozdag[a,*], Pinar Calis[a], Dila Zengin[a], Atakan Tanacan[a], Sevilay Karahan[b]

[a] Department of Obstetrics and Gynecology, Faculty of Medicine, Hacettepe University, Ankara, Turkey
[b] Department of Biostatistics, Faculty of Medicine, Hacettepe University, Ankara, Turkey

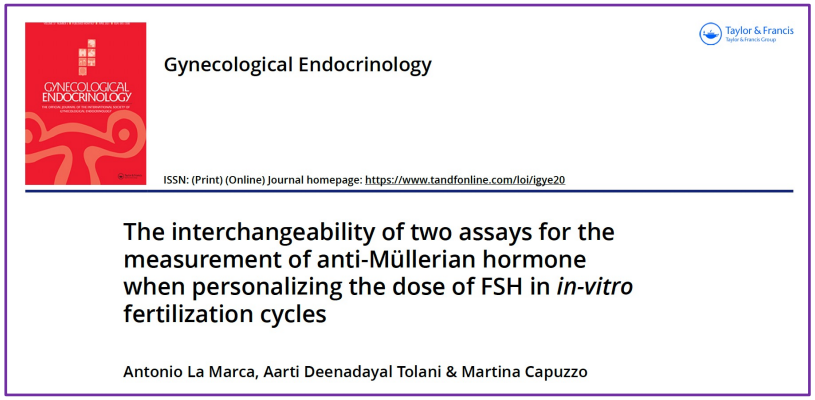


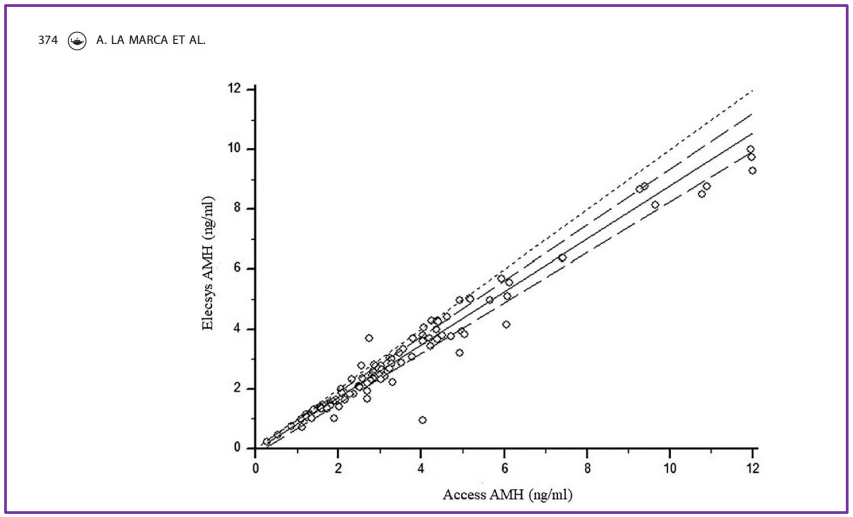
Automated AMH assays

- Faster turnaround time (16 min vs. 6 hrs)
- Higher precision and greater sensitivity
- More stable results in room temperature and after freezing

Loes ME Moolhuijsen and Jenny A. Visser, 2020

Automated AMH assays





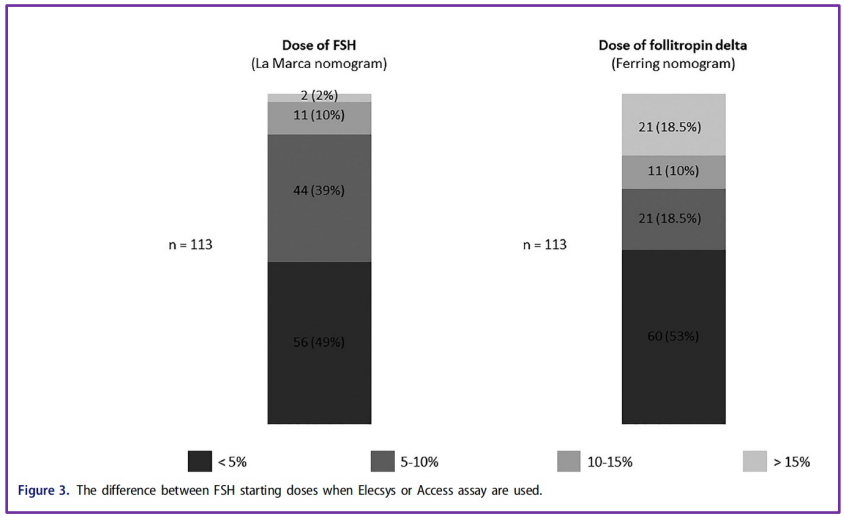


Figure 3. The difference between FSH starting doses when Elecsys or Access assay are used.

*The use of the Roche Elecsys or Beckman Coulter Access leads to **modest differences in AMH values**, which seem to little affect the calibration of FSH dose used for ovarian stimulation*

Strength

- **OR reflect primordial follicle density**
- **OR based iCOS might yield**
  - More “appropriate” response.
  - Less excessive response
- **Better agreement among recent automated assays for AMH**

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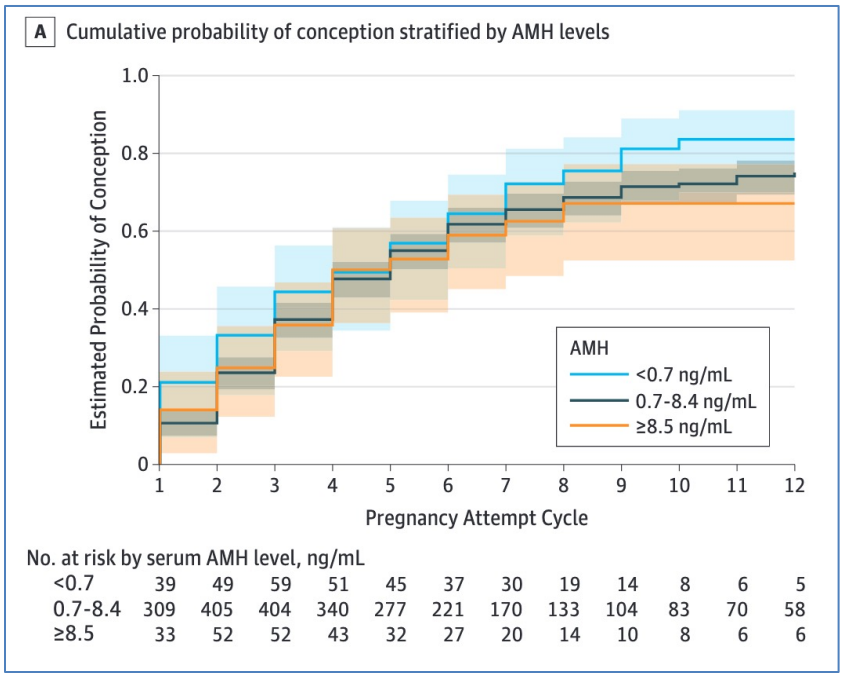
Spontaneous pregnancy

Research

JAMA | Original Investigation

Association Between Biomarkers of Ovarian Reserve and Infertility Among Older Women of Reproductive Age

Anne Z. Steiner, MD, MPH; David Pritchard, MS; Frank Z. Stanczyk, PhD; James S. Kesner, PhD; Juliana W. Meadows, PhD; Amy H. Herring, ScD; Donna D. Baird, PhD, MPH



Spontaneous pregnancy

ORIGINAL ARTICLE: REPRODUCTIVE ENDOCRINOLOGY

Check for updates

Markers of ovarian reserve as predictors of future fertility

Benjamin S. Harris, M.D., M.P.H.,[a] Anne Marie Jukic, Ph.D.,[b] Tracy Truong, M.S.,[c] Caroline T. Nagle, M.P.H.,[d] Alaattin Erkanli, Ph.D.,[c] and Anne Z. Steiner, M.D., M.P.H.[a]

[a] Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, Duke Fertility Center, Morrisville, North Carolina; [b]Epidemiology Branch, National Institute of Environmental Health Sciences, Durham, North Carolina; [c]Department of Biostatistics and Bioinformatics, Duke University Medical Center, Durham, North Carolina; and [d]Clinical Research Unit, Department of Obstetrics and Gynecology, Durham, North Carolina.

TABLE 4

Fecundability ratios associated with pregnancy attempts after Time to Conceive pregnancy attempt

	Fecundability ratio (95% confidence interval)[a]	
Biomarker	Unadjusted	Adjusted[b]
Antimüllerian hormone (ng/mL)		
< 0.7	0.85 (0.48, 1.48)	0.97 (0.59, 1.60)
0.7–8.4	Reference	
≥ 8.5	0.78 (0.43, 1.41)	0.72 (0.39, 1.33)
Serum follicle-stimulating hormone (mIU/mL)		
Missing	—	—
< 10	Reference	
≥ 10	0.86 (0.58, 1.28)	0.86 (0.55, 1.36)
Inhibin B (pg/mL)[c]	1.02 (0.99, 1.04)	1.02 (0.99, 1.04)

[a] All women in the follow-up cohort with attempt time at least 6 months from the end of the original Time to Conceive study (N = 241).
[b] Adjusted model included age at blood draw, age at attempt, race, obesity, use of hormonal contraception, and year of enrollment in original TTC study.
[c] Estimated levels of Inhibin B are based on every 10-unit increase.

Harris. Ovarian reserve and future fertility. Fertil Steril 2022.

Spontaneous pregnancy

Specifically, low AMH levels had reduced fecundability by 57% among women with menstrual cycle irregularity

TABLE 2 ASSOCIATION BETWEEN SERUM ANTI-MÜLLERIAN HORMONE LEVELS AND FECUNDABILITY

	n (%)	Conception *n* (%)	Fecundability ratio[a] (95% CI)		
			Unadjusted	Age-adjusted[b]	Adjusted[c]
AMH strata, ng/ml					
Low (<2.78)	248 (25.0)	151 (25.3)	0.93 (0.75 to 1.17)	0.99 (0.79 to 1.24)	0.96 (0.77 to 1.21)
Intermediate (2.78–6.94)	496 (50.0)	300 (50.2)	Reference	Reference	Reference
High (>6.94)	249 (25.0)	147 (24.5)	1.10 (0.88 to 1.37)	1.08 (0.86 to 1.35)	1.06 (0.84 to 1.32)
P_{trend}			0.232	0.472	0.317

AMH, anti-Müllerian hormone; P_{trend}, *P* for trend.

[a] Probability of conception per cycle. Fecundability ratio less than 1 indicates a reduced fecundability or a longer TTP, whereas fecundability ratio greater than 1 describes increased fecundability or a shorter TTP.

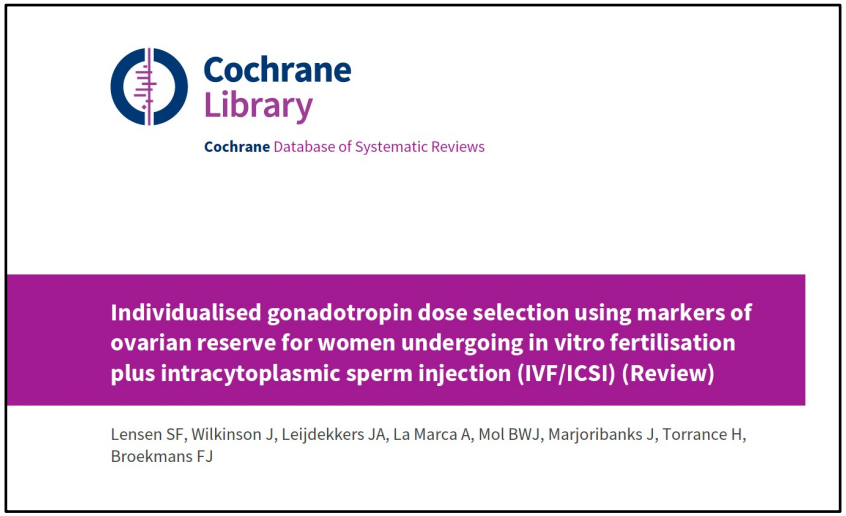
[b] Adjusted for women's age as a continuous covariate.

[c] Adjusted for women's age (continuous), pre-pregnancy body mass index (continuous), education status, smoking status, alcohol consumption and parity.

TABLE 3 EFFECT MODIFICATION BY WOMAN'S AGE, BODY MASS INDEX AND CYCLE REGULARITY ON THE ANTI-MÜLLERIAN HORMONE-FECUNDABILITY ASSOCIATIONS

	Low AMH (<2.78 ng/m)	Intermediate AMH (2.78–6.94 ng/ml)	High AMH (≥6.94 ng/ml)
Women's age, years			
<35			
n (%)	209 (22.8)	467 (51.0)	239 (26.2)
aFR (95% CI)[a]	0.93 (0.73 to 1.18)	Reference	1.10 (0.88 to 1.39)
≥35			
n (%)	39 (50.0)	29 (37.2)	10 (12.8)
aFR (95% CI)[a]	0.77 (0.35 to 1.71)	Reference	0.82 (0.26 to 2.59)
P for interaction	0.252		
Menstrual cycle irregularity			
No			
n (%)	219 (27.5)	402 (50.5)	175 (22.0)
aFR (95% CI)[a]	1.01 (0.80 to 1.28)	Reference	1.11 (0.86 to 1.42)
Yes			
n (%)	29 (14.7)	94 (47.7)	74 (37.6)
aFR (95% CI)[a]	0.43 (0.16 to 1.15)	Reference	1.08 (0.64 to 1.81)
P for interaction	0.064		
Pre-pregnancy BMI, kg/m^2			

OPR/LBR - ART



	Groups	No. of RCT	Finding
OPR/LBR	ORT based vs. 150 IU	4	1.04 (0.88 – 1.23)

Lensen et al., Cochrane 2018

AMH and Aneuploidy

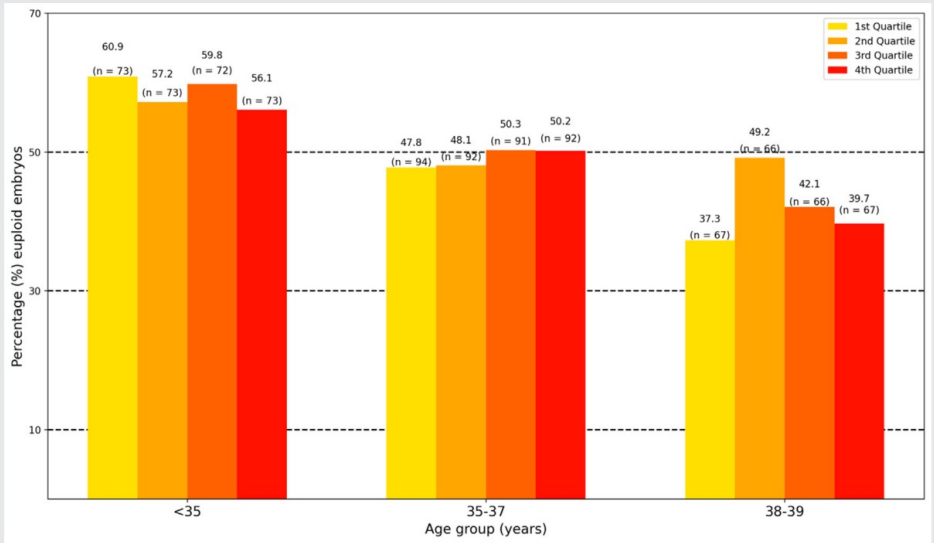
Check for updates

Antimüllerian hormone is not associated with embryo ploidy in patients with and without infertility undergoing in vitro fertilization with preimplantation genetic testing

Yael R. Stovezky, B.A.,[a] Phillip A. Romanski, M.D., M, Sc,[b] Pietro Bortoletto, M.D., M.Sc.,[b] and Steven D. Spandorfer, M.D.[b]

[a] Weill Medical College of Cornell University, New York, New York and [b] The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medical Center, New York, New York

FIGURE 1

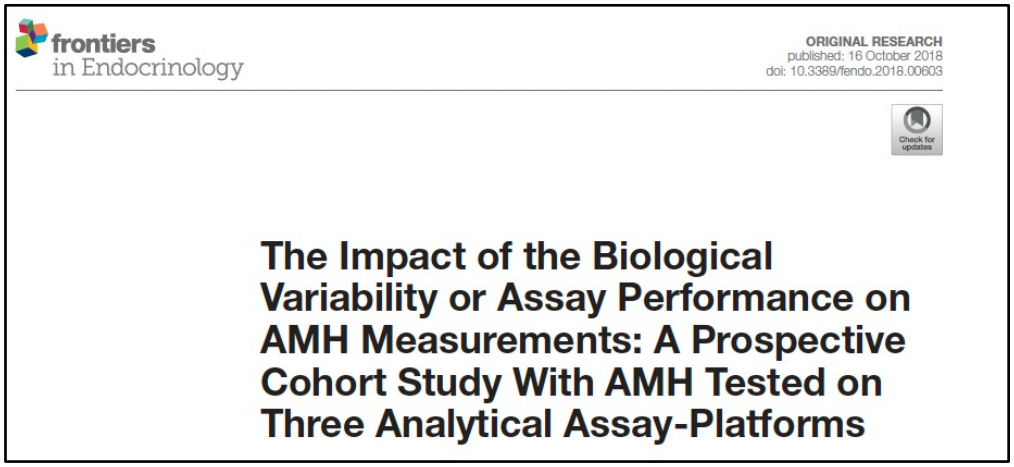


Percentage (%) of euploid embryos in "Infertile" (preimplantation genetic testing for aneuploidy only) patients by antimüllerian hormone quartile and age.

Stovezky. AMH is not associated with embryo ploidy. Fertil Steril 2023.

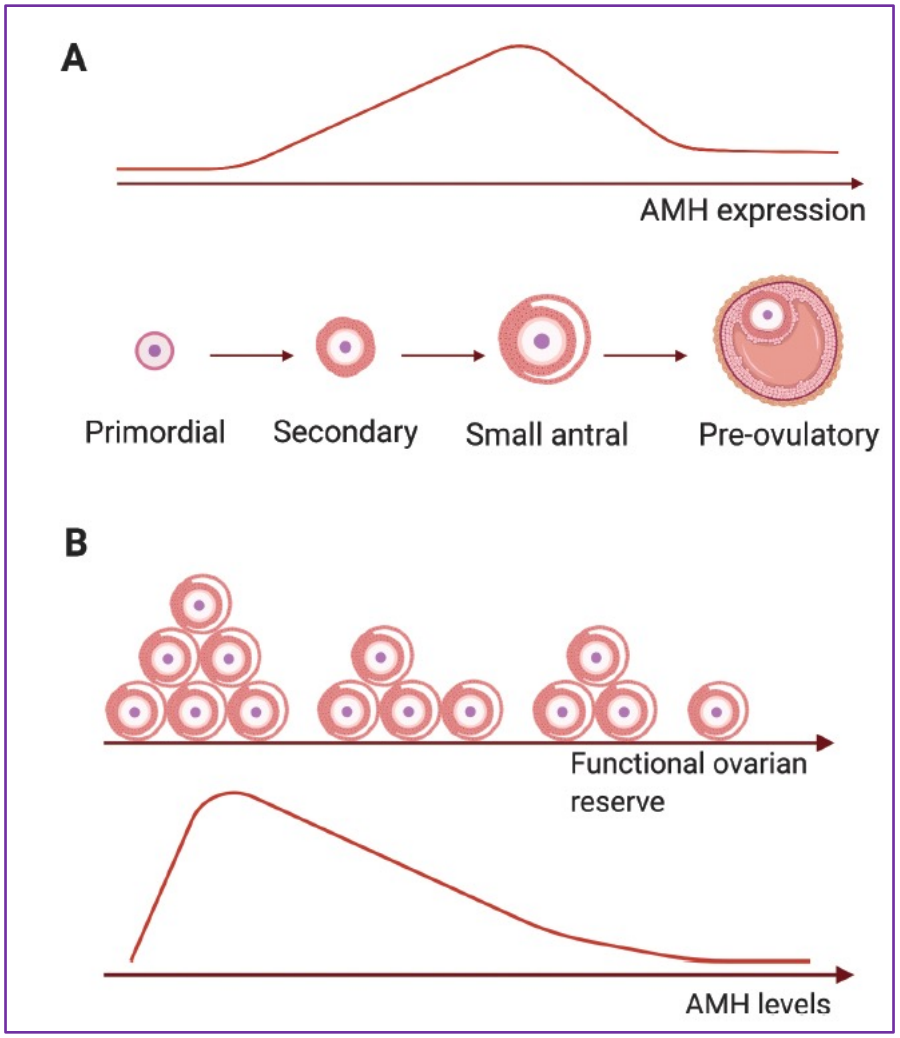
"Infertile" (n= 926) and "Non-infertile" (n= 214) patients

Automated AMH assays

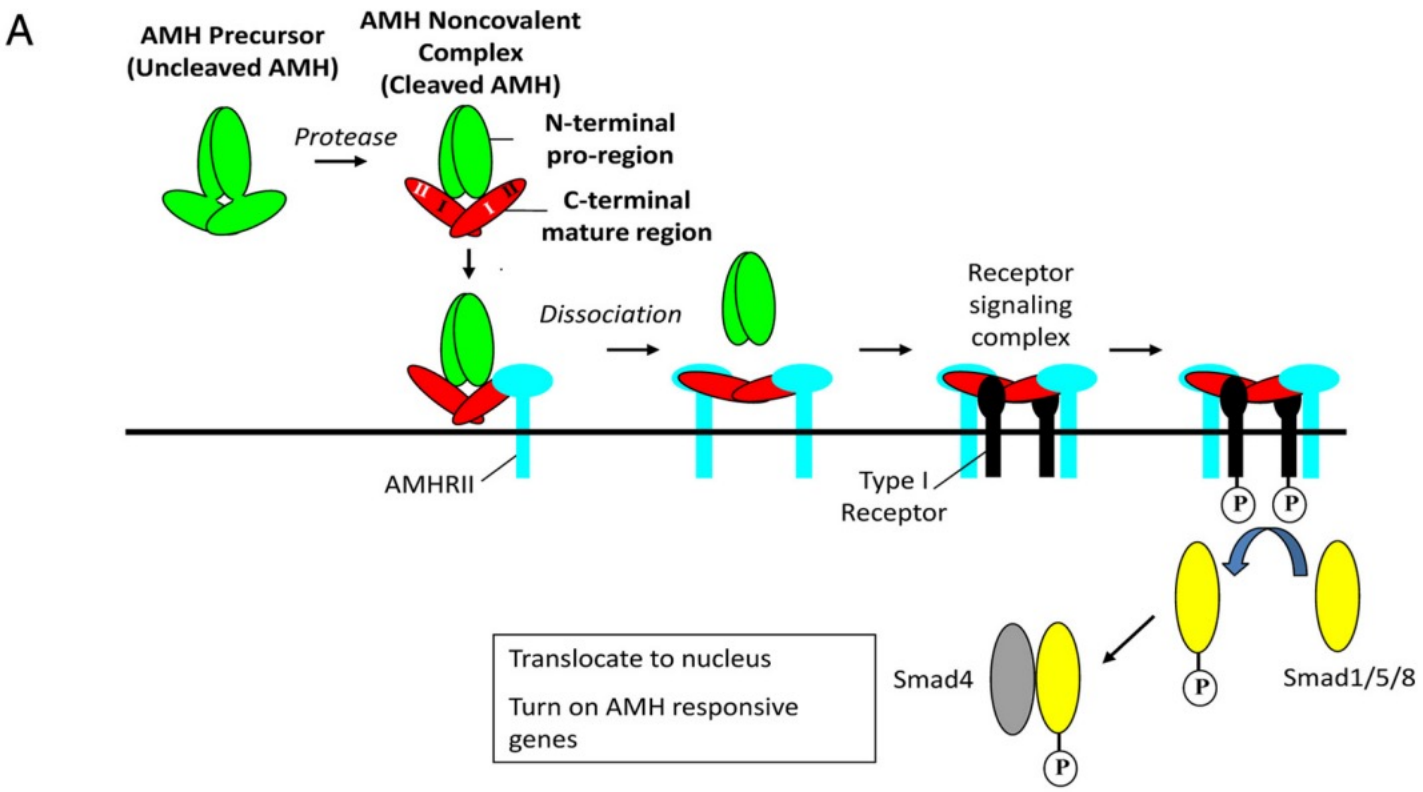


- 5 days intervals during 3 consecutive cycles (n= 26)
  - **Biological variability** : 37 to 728%
  - **Analytical variability** : 1.9 to 25%

AMH-structure



AMH-structure



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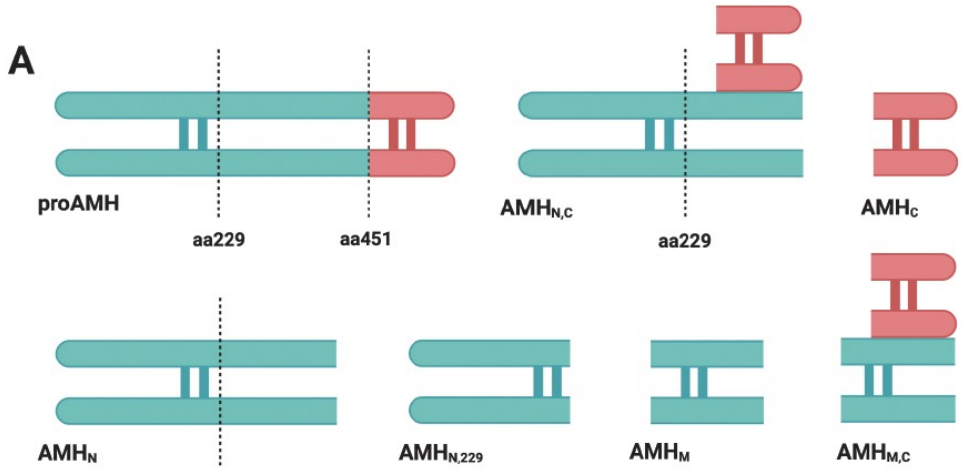

Assay	*Assay type*	*Limit of detection (ng/ml)*	*Measurement range (ng/ml)*
Gen II (Beckman Coulter)	Manual	0.08	0.16 – 22.5
Access (Beckman Coulter)	Automated	0.02	0.08 – 24.0
Elecsys (Roche)	Automated	0.01	0.01 – 23.0

AFC

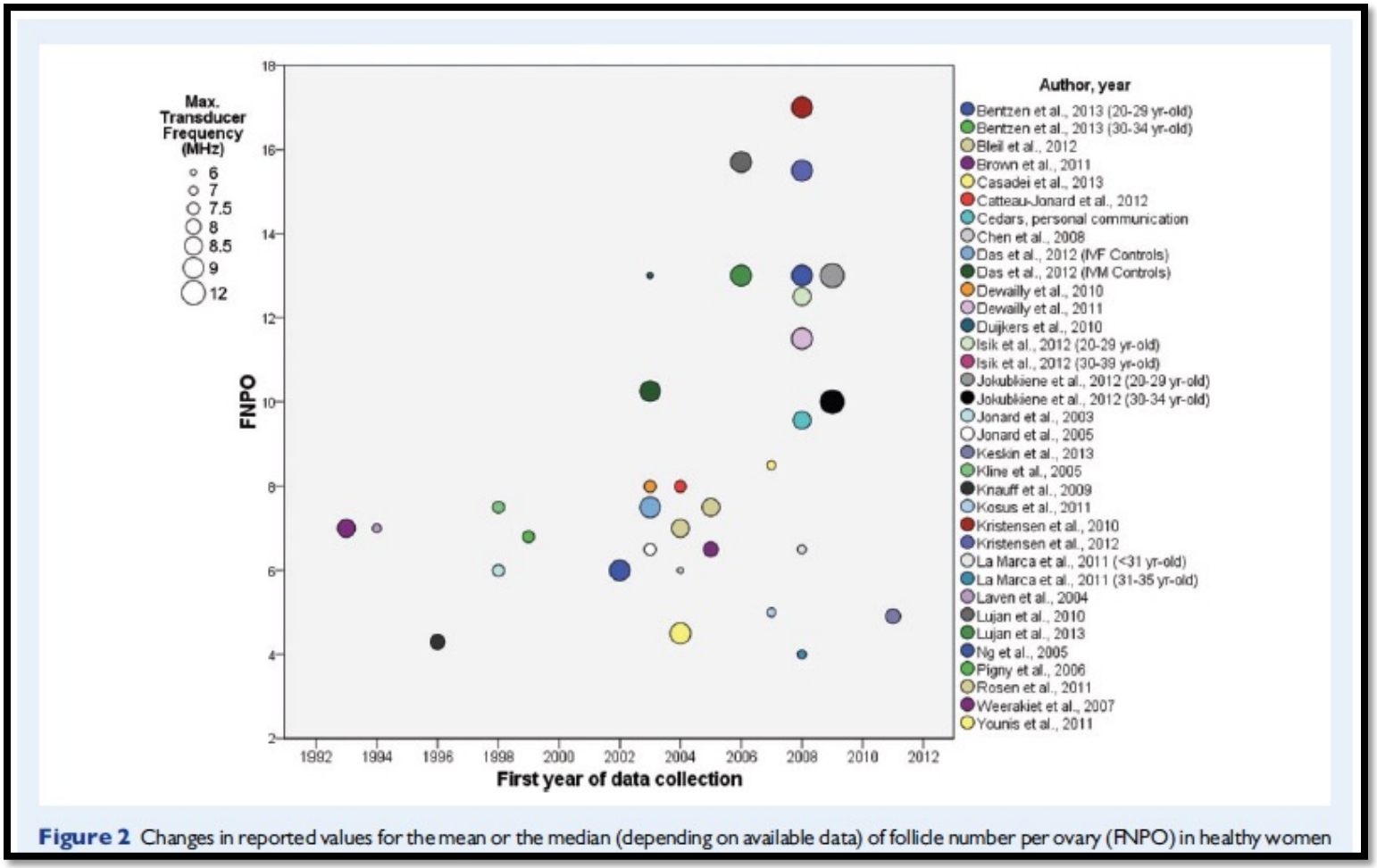

Figure 2 Changes in reported values for the mean or the median (depending on available data) of follicle number per ovary (FNPO) in healthy women

AFC

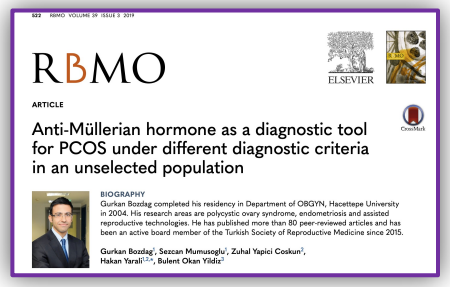

TABLE 1 THE VALIDITY OF AMH TO DIAGNOSE PCOS ACCORDING TO NIH, ROTTERDAM 2003 AND ANDROGEN EXCESS AND PCOS (AE-PCOS) CRITERIA WITH DIFFERENT THRESHOLDS OF AFC

	Definition of PCOM ≥12 AFC or OV ≥10 ml			Definition of PCOM ≥20 AFC or OV ≥10 ml		
	NIH 1990	Rotterdam 2003	AE-PCOS 2006	NIH 1990	Rotterdam 2003	AE-PCOS 2006
Prevalence (*n*, %)	24 (6.1)	78 (19.9)	60 (15.3)	ND	40 (10.2)	35 (8.9)
AMH	4.72 (1.14–13.4)	3.37 (1.41–8.16)	3.46 (1.41–9.76)	ND	3.85 (1.85–12.74)	3.84 (1.65–13.03)
AUC (95% CI)	0.83 (0.75–0.91)	0.81 (0.77–0.86)	0.80 (0.74–0.85)	ND	0.83 (0.77–0.88)	0.82 (0.76–0.88)
aAUC (95% CI)	0.80 (0.71–0.89)	0.74 (0.67–0.81)	0.71 (0.64–0.79)	ND	0.80 (0.73–0.88)	0.79 (0.71–0.87)
AMH threshold (sensitivity and specificity)	5.00 (50.0% and 93.2%)	4.17 (38.5% and 91.1%)	4.38 (33.3% and 91.0%)	ND	4.86 (40.0% and 92.6%)	4.86 (40.0% and 92.2%)
OR (95% CI) for PCOS	13.72 (5.59–33.65)	6.38 (3.51–11.62)	5.03 (2.61–9.67)	ND	8.36 (3.96–17.66)	7.83 (3.60–17.06)

Study group = 392 women.

AMH (ng/ml) levels are given as median (5th–95th percentile).

AFC = antral follicle count; AMH = anti-Müllerian hormone; AUC = area under curve; aAUC = adjusted for age (years) and body mass index (kg/m^2) AUC; CI = confidence interval; ND = no difference; NIH = National Institutes of Health; OR = odds ratio; OV = ovarian volume; PCOM = polycystic ovary morphology; PCOS = polycystic ovary syndrome.

AFC- variability

http://informahealthcare.com/gye
ISSN: 0951-3590 (print), 1473-0766 (electronic)

GYNECOLOGICAL ENDOCRINOLOGY

Gynecol Endocrinol, 2017; 33(7): 515–518
 DOI: 10.1080/09513590.2017.1291614

Taylor & Francis
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ANTRAL FOLLICLE COUNT

Inter-cycle and inter-observer variability of the antral follicle count in routine clinical practice

Jessica Subirá[1,2], Jose Alberola-Rubio[1], María Jose Núñez[1], Alicia Marzal Escrivá[1,2,3], Antonio Pellicer[1,2,3,4], Vicente Montañana[1*], and César Díaz-García[1,2,3,4*]

Table 2. Inter-observer variability results showing ICCs for total AFC and for each ovary separately based on observations performed in 35 patients.

	Observer	*N*	Mean AFC+/-SD	ICC	95% CI	*p*
Right ovary	Observer 1	35	9.06 ± 6.05	0.95	0.90–0.97	<0.05
	Observer 2		9.46 ± 7.16			
Left ovary	Observer 1	35	7.74 ± 6.64	0.94	0.88–0.97	<0.05
	Observer 2		8.97 ± 8.03			
Sum of both ovaries	Observer 1	35	16.33 ± 11.17	0.95	0.91–0.97	<0.05
	Observer 2		17.92 ± 13.80			

Weakness

- **OR-based iCOS does not achieve higher LBR in ART or cycles.**
- **OR have poor predictive validity in the prediction of natural pregnancy.**
- **Complexity of structure for AMH**
  - Biological variability
  - Analytical variability
  - Lack of international standard
- **Variability exists for AFC**

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Treatment burden

RBM ONLINE

ELSEVIER

Article

Live birth rates in various subgroups of poor ovarian responders fulfilling the Bologna criteria

Gurkan Bozdag [a], Mehtap Polat [b], Irem Yarali [b], Hakan Yarali [a,b,]*

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[b] Anatolia Women's Health and IVF Center, Ankara, Turkey

Table 2 – The embryologic data and pregnancy rates of four subgroups of poor ovarian responde each variable in a row, above-given values refer to median (minimum–maximum) and below-given values to coefficient (95% CI) as estimated by multilevel logistic regression analysis.

Variable	Group A (Age ≥40 + previous poor ovarian response)	Group B (Age ≥40 + AFC <7)	Group C (Previous poor ovarian response + AFC <7)	Group D (Age ≥40 + AFC <7 + previous poor ovarian response)	*P*-value
No. of oocyte–cumulus complexes	2 (0–3)[a] −0.44 (−0.74; −0.14)[1]	5 (0–8)[b] 3.28 (3.12; 3.44)[2]	2 (0–3) −1.03 (−1.21; −0.84)[3]	2 (0–3) −0.96 (−1.16; −0.75)[4]	<0.001 0.004[1]/<0.001[2,3,4]
No. of metaphase-II oocytes	2 (0–3) −0.27 (−0.54; 0.003)[1]	4 (0–8)[b] 2.35 (2.19; 2.52)[2]	1 (0–3) −0.83 (−0.99; −0.67)[3]	(0–3) −0.66 (−0.84; −0.47)[4]	<0.001 0.047[1]/<0.001[2,3,4]
Fertilization rate (%)	68.3 −0.005 (−0.18; 0.17)	63.8 0.64 (0.52; 0.77)[1]	66.8 −0.30 (−0.40; −0.20)[2]	63.2 −0.17 (−0.29; −0.05)[3]	0.391 < 0.001[1,2]/0.007[3]
Embryos <10% fragmentation with ≥7 blastomeres (%)	40.2 −0.07 (−0.18; 0.03)	45.9 0.04 (−0.04; 0.11)	46.3 0.02 (−0.05; 0.09)	42.2 −0.02 (−0.10; 0.07)	0.550
No. of cancelled cycles (%)	46 (37.4) −0.35 (−0.82; 0.13)	82 (32.4)[c] −0.71 (−1.07; −0.35)[1]	270 (47.0) 0.28 (−0.003; 0.56)[2]	153 (50.0) 0.40 (0.07; 0.73)[3]	<0.001 <0.001[1]/0.052[2]/0.016[3]
No. of embryos transferred	1 (1–3) −0.12 (−0.30; 0.07)	2 (1–5)[b] 0.70 (0.57; 0.82)[1]	1 (1–3) −0.33 (−0.44; −0.21)[2]	1 (1–3) −0.23 (−0.37; −0.09)[3]	<0.001 <0.001[1,2]/0.001[3]
Clinical pregnancy/cycle (*n*, %)	6 (4.9) −0.83 (−1.89; 0.22)	22 (8.7) 0.07 (−0.54; 0.68)	66 (11.5)[d] 0.84 (0.26; 1.42)[1]	14 (4.6) −1.02 (−1.80; −0.23)[2]	0.002 0.004[1]/0.011[2]
Clinical pregnancy/embryo transfer (*n*, %)	6 (7.8) −0.88 (−1.80; 0.05)[1]	22 (12.9) −0.27 (−0.82; 0.27)	66 (21.6)[e] 0.89 (0.41; 1.37)[2]	14 (9.2) −0.76 (−1.41; −0.10)[3]	<0.001 0.063[1]/<0.001[2]/0.026[3]
Live birth/cycle (*n*, %)	4 (3.3) −0.72 (−1.74; 0.31)	16 (6.3) 0.04 (−0.53; 0.61)	50 (8.7)[d] 0.84 (0.36; 1.32)[1]	7 (2.3) −1.22 (−2.01; −0.43)[2]	0.001 0.001[1]/0.002[2]
Live birth/embryo transfer (*n*, %)	4 (5.2) −0.87 (−1.91; 0.16)	16 (9.4) −0.22 (−0.80; 0.36)	50 (16.4)[e] 1.00 (0.50; 1.49)[1]	7 (4.6) −1.11 (−1.90; −0.31)[2]	<0.001 <0.001[1]/0.007[2]
Implantation rate (%)	6.0 0.02 (−0.22; 0.27)	5.8 −0.21 (−0.36; −0.06)[1]	14.4[f] 0.10 (−0.02; 0.23)	6.3 0.06 (−0.12; 0.24)	0.024 0.006[1]

Treatment burden

Human Reproduction Update, Vol.27, No.2, pp. 229–253, 2021
Advance Access Publication on November 4, 2020 doi:10.1093/humupd/dmaa035

human reproduction update

Mild versus conventional ovarian stimulation for IVF in poor, normal and hyper-responders: a systematic review and meta-analysis

Adrija Kumar Datta [1,*], Abha Maheshwari [2], Nirmal Felix [1], Stuart Campbell [3,4], and Geeta Nargund [4,5]

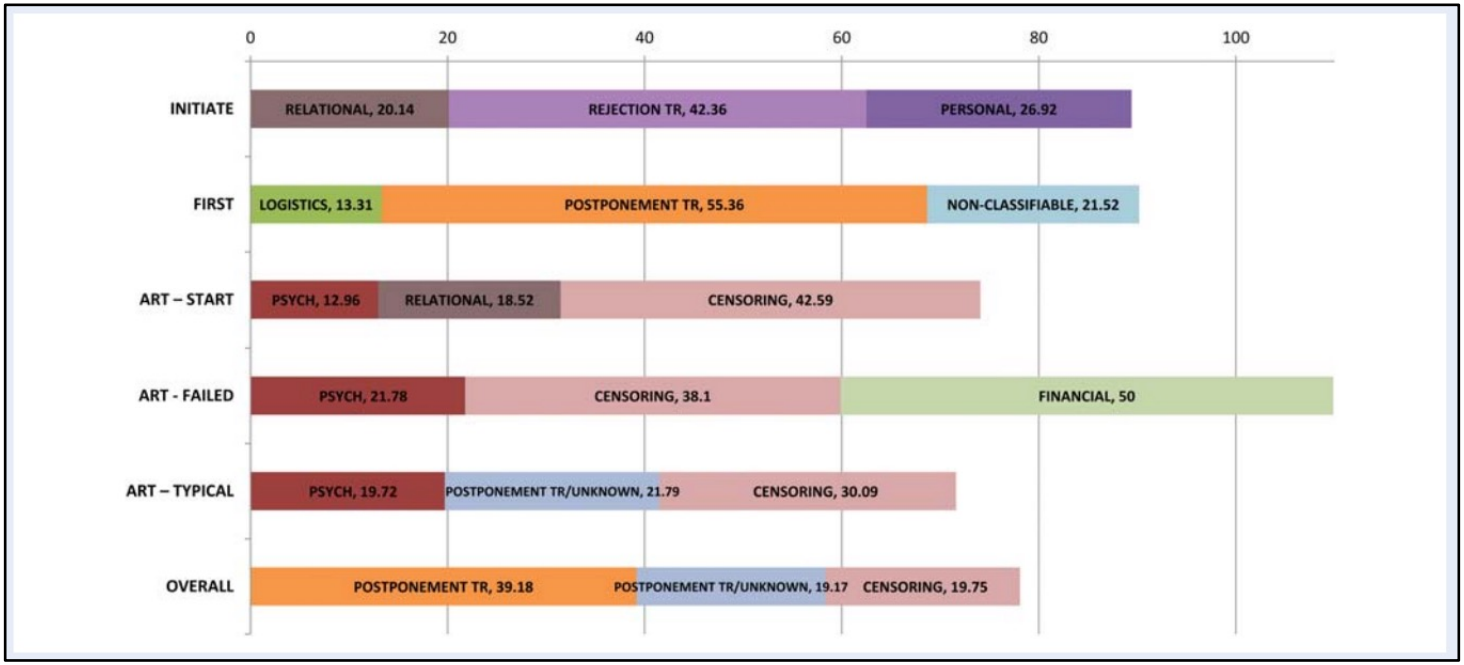
Treatment burden

Human Reproduction Update, Vol.18, No.6 pp. 652–669, 2012
Advanced Access publication on August 6, 2012 doi:10.1093/humupd/dms031

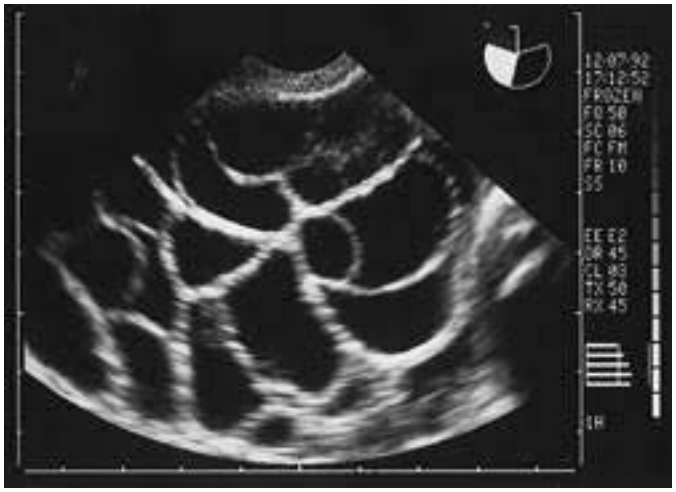
human reproduction update

Why do patients discontinue fertility treatment? A systematic review of reasons and predictors of discontinuation in fertility treatment

S. Gameiro[1,2], J. Boivin[2], L. Peronace[3], and C.M. Verhaak[4,*]

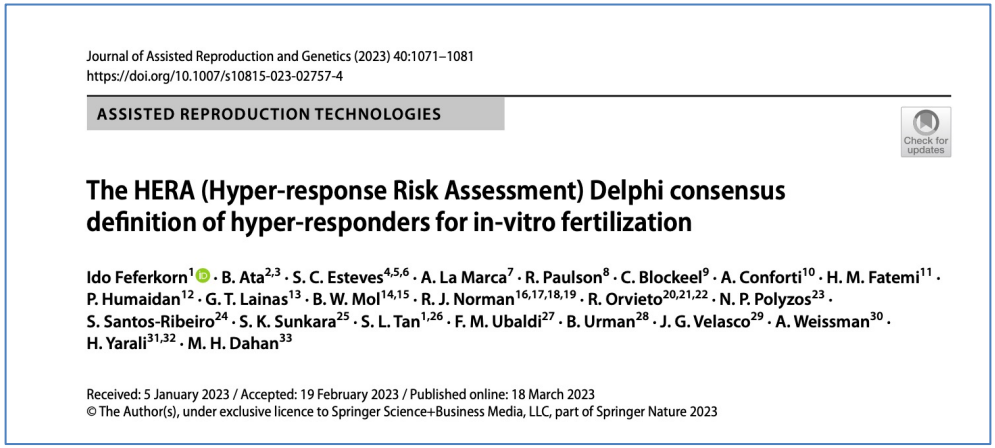


Safety



- The Netherlands National Registry
- Total **~ 100,000** IVF treatment cycles
- 6 deaths directly related to IVF
  - **3** OHSS,
  - 3 thrombosis and sepsis after egg retrieval
- Possibility of underreporting IVF related complications

Safety



Journal of Assisted Reproduction and Genetics (2023) 40:1071–1081
https://doi.org/10.1007/s10815-023-02757-4

ASSISTED REPRODUCTION TECHNOLOGIES

Check for updates

The HERA (Hyper-response Risk Assessment) Delphi consensus definition of hyper-responders for in-vitro fertilization

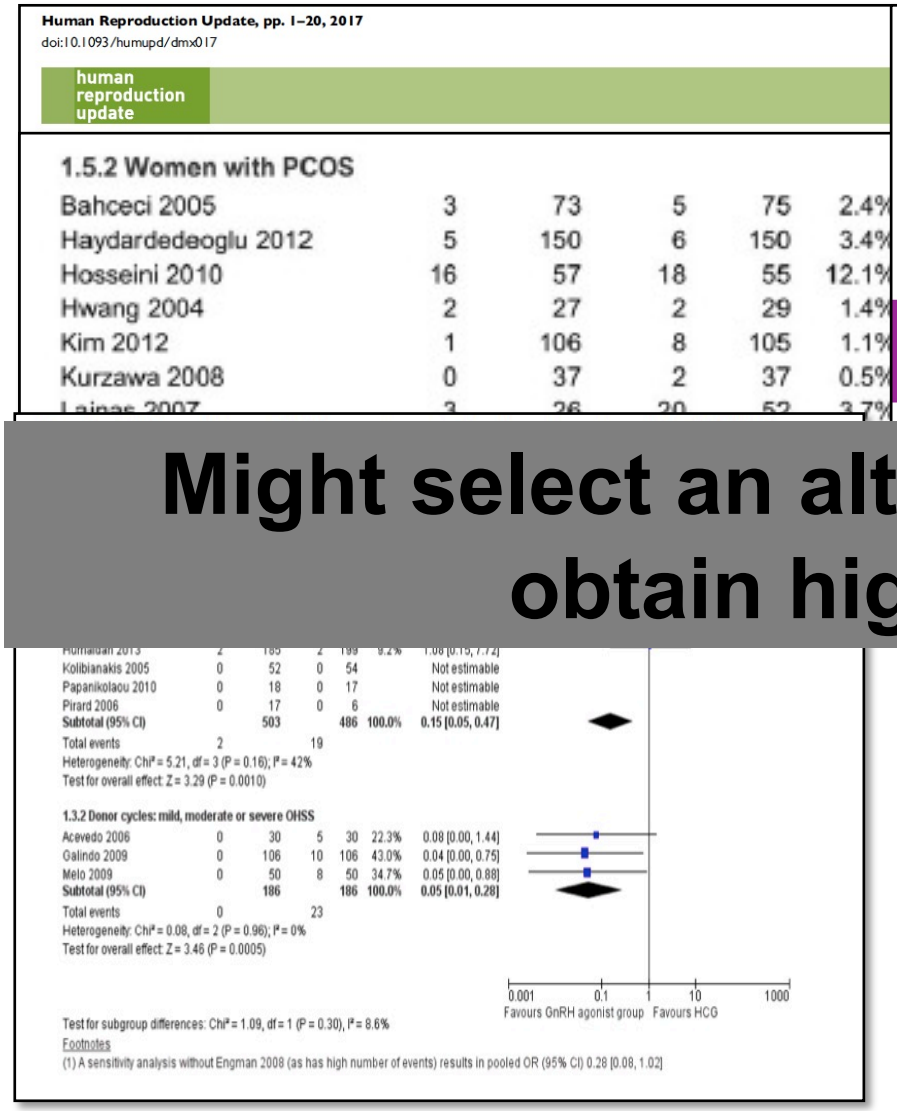
Ido Feferkorn[1] · B. Ata[2,3] · S. C. Esteves[4,5,6] · A. La Marca[7] · R. Paulson[8] · C. Blockeel[9] · A. Conforti[10] · H. M. Fatemi[11] · P. Humaidan[12] · G. T. Lainas[13] · B. W. Mol[14,15] · R. J. Norman[16,17,18,19] · R. Orvieto[20,21,22] · N. P. Polyzos[23] · S. Santos-Ribeiro[24] · S. K. Sunkara[25] · S. L. Tan[1,26] · F. M. Ubaldi[27] · B. Urman[28] · J. G. Velasco[29] · A. Weissman[30] · H. Yarali[31,32] · M. H. Dahan[33]

Received: 5 January 2023 / Accepted: 19 February 2023 / Published online: 18 March 2023

In a patient without previous ovarian stimulation, the most important risk factor for a hyper-response is the antral follicular count (AFC) (68.2% agreement).

In a patient without previous ovarian stimulation, when AMH and AFC are discordant, one suggesting a hyper-response and the other not, AFC is the more reliable marker (68.2% agreement).

Safety



Human Reproduction Update, pp. 1–20, 2017
doi:10.1093/humupd/dmx017

human reproduction update

1.5.2 Women with PCOS

Bahceci 2005	3	73	5	75	2.4%
Haydardedeoglu 2012	5	150	6	150	3.4%
Hosseini 2010	16	57	18	55	12.1%
Hwang 2004	2	27	2	29	1.4%
Kim 2012	1	106	8	105	1.1%
Kurzawa 2008	0	37	2	37	0.5%

Kolibianakis 2005 0 52 0 54 Not estimable
Papanikolaou 2010 0 18 0 17 Not estimable
Pirard 2006 0 17 0 6 Not estimable
Subtotal (95% CI) 503 486 100.0% **0.15 [0.05, 0.47]**
Total events 2 19
Heterogeneity: Chi² = 5.21, df = 3 (P = 0.16); I² = 42%
Test for overall effect: Z = 3.29 (P = 0.0010)

1.3.2 Donor cycles: mild, moderate or severe OHSS

Acevedo 2006	0	30	5	30	22.3%	0.08 [0.00, 1.44]
Galindo 2009	0	106	10	106	43.0%	0.04 [0.00, 0.75]
Melo 2009	0	50	8	50	34.7%	0.05 [0.00, 0.88]
Subtotal (95% CI)		186		186	100.0%	**0.05 [0.01, 0.28]**

Total events 0 23
Heterogeneity: Chi² = 0.08, df = 2 (P = 0.96); I² = 0%
Test for overall effect: Z = 3.46 (P = 0.0005)

0.001 0.1 1 10 1000
Favours GnRH agonist group Favours HCG

Test for subgroup differences: Chi² = 1.09, df = 1 (P = 0.30), I² = 8.6%

Footnotes
(1) A sensitivity analysis without Engman 2008 (as has high number of events) results in pooled OR (95% CI) 0.28 [0.08, 1.02]

Cochrane Library

Cochrane Database of Systematic Reviews

Gonadotropin-releasing hormone agonist versus HCG for oocyte triggering in antagonist-assisted reproductive technology (Review)

Might select an alternative strategy to obtain higher safety.

Cryo-all for excessive responders!

Human Reproduction, Vol.34, No.3 pp. 491–505, 2019
Advanced Access publication on January 28, 2019 doi:10.1093/humrep/dey388

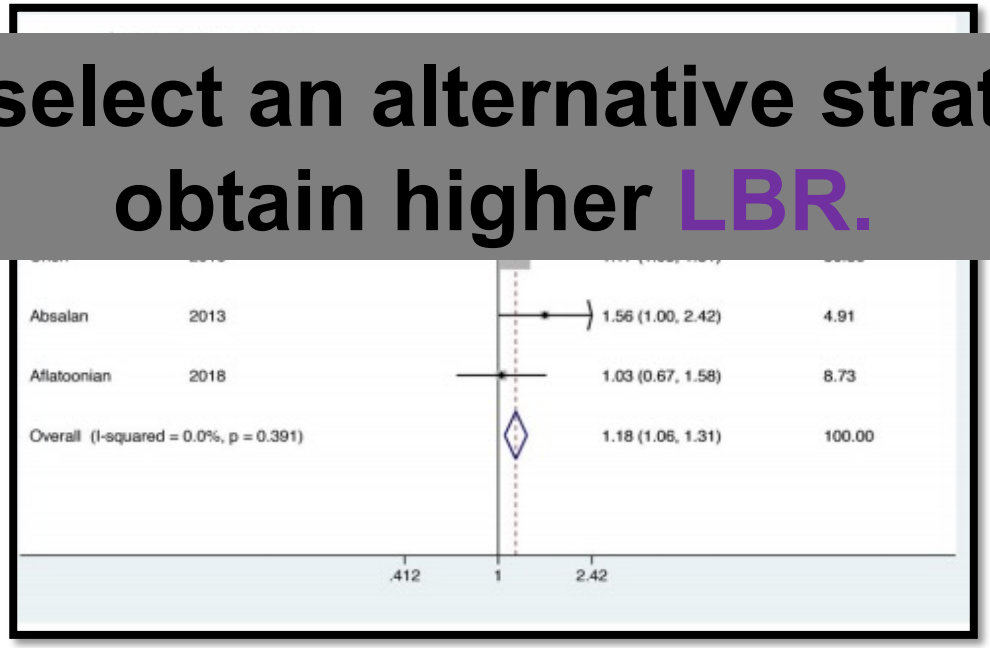
human reproduction

META-ANALYSIS *Infertility*

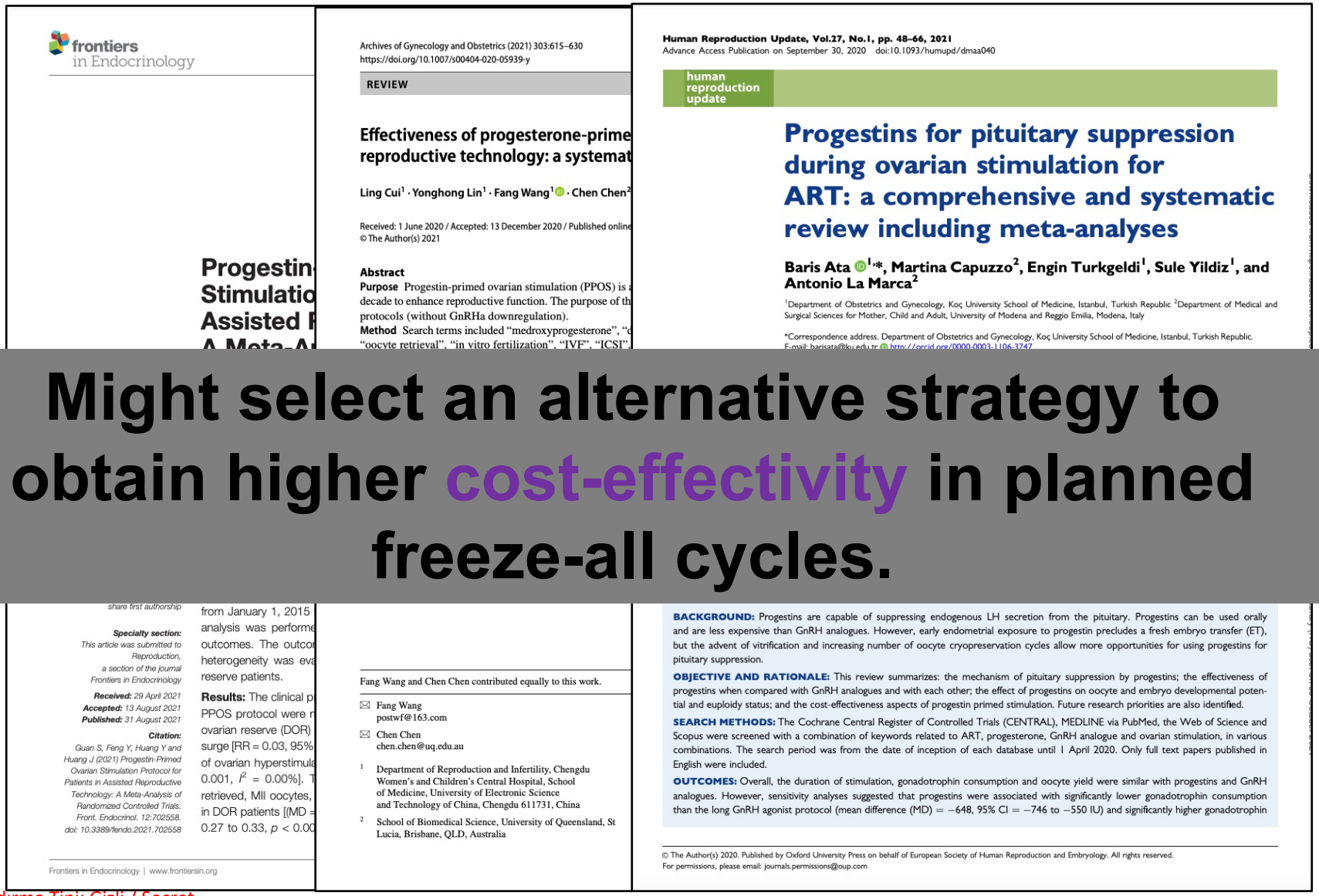
Higher probability of live-birth in high, but not normal, responders after first frozen-embryo transfer in a freeze-only cycle strategy compared to fresh-embryo transfer: a meta-analysis

J.K. Bosdou[1], C.A. Venetis[2], B.C. Tarlatzis[1], G.F. Grimbizis[1], and E.M. Kolibianakis[1,*]

Might select an alternative strategy to obtain higher LBR.



Progestin-primed OS



frontiers in Endocrinology

Archives of Gynecology and Obstetrics (2021) 303:615–630
https://doi.org/10.1007/s00404-020-05939-y

REVIEW

Effectiveness of progesterone-prime
reproductive technology: a systemat

Ling Cui[1] · Yonghong Lin[1] · Fang Wang[1] · Chen Chen[2]

Received: 1 June 2020 / Accepted: 13 December 2020 / Published online
© The Author(s) 2021

Abstract
Purpose Progestin-primed ovarian stimulation (PPOS) is a
decade to enhance reproductive function. The purpose of th
protocols (without GnRHa downregulation).
Method Search terms included "medroxyprogesterone", "
"oocyte retrieval", "in vitro fertilization", "IVF", "ICSI",

Progestin
Stimulatio
Assisted R

share first authorship

Specialty section:
This article was submitted to Reproduction, a section of the journal Frontiers in Endocrinology

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Published: 31 August 2021

Citation:
Guan S, Feng Y, Huang Y and Huang J (2021) Progestin-Primed Ovarian Stimulation Protocol for Patients in Assisted Reproductive Technology: A Meta-Analysis of Randomized Controlled Trials. Front. Endocrinol. 12:702558. doi: 10.3389/fendo.2021.702558

from January 1, 2015
analysis was performe
outcomes. The outcor
heterogeneity was eva
reserve patients.

Results: The clinical p
PPOS protocol were r
ovarian reserve (DOR)
surge [RR = 0.03, 95%
of ovarian hyperstimula
0.001, I^2 = 0.00%]. T
retrieved, MII oocytes,
in DOR patients [(MD =
0.27 to 0.33, p < 0.00

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Human Reproduction Update, Vol.27, No.1, pp. 48–66, 2021
Advance Access Publication on September 30, 2020 doi:10.1093/humupd/dmaa040

human reproduction update

Progestins for pituitary suppression during ovarian stimulation for ART: a comprehensive and systematic review including meta-analyses

Baris Ata[1,*], Martina Capuzzo[2], Engin Turkgeldi[1], Sule Yildiz[1], and Antonio La Marca[2]

[1]Department of Obstetrics and Gynecology, Koç University School of Medicine, Istanbul, Turkish Republic [2]Department of Medical and Surgical Sciences for Mother, Child and Adult, University of Modena and Reggio Emilia, Modena, Italy

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BACKGROUND: Progestins are capable of suppressing endogenous LH secretion from the pituitary. Progestins can be used orally and are less expensive than GnRH analogues. However, early endometrial exposure to progestin precludes a fresh embryo transfer (ET), but the advent of vitrification and increasing number of oocyte cryopreservation cycles allow more opportunities for using progestins for pituitary suppression.

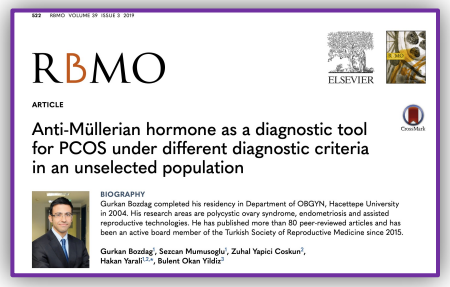
OBJECTIVE AND RATIONALE: This review summarizes: the mechanism of pituitary suppression by progestins; the effectiveness of progestins when compared with GnRH analogues and with each other; the effect of progestins on oocyte and embryo developmental potential and euploidy status; and the cost-effectiveness aspects of progestin primed stimulation. Future research priorities are also identified.

SEARCH METHODS: The Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE via PubMed, the Web of Science and Scopus were screened with a combination of keywords related to ART, progesterone, GnRH analogue and ovarian stimulation, in various combinations. The search period was from the date of inception of each database until 1 April 2020. Only full text papers published in English were included.

OUTCOMES: Overall, the duration of stimulation, gonadotrophin consumption and oocyte yield were similar with progestins and GnRH analogues. However, sensitivity analyses suggested that progestins were associated with significantly lower gonadotrophin consumption than the long GnRH agonist protocol (mean difference (MD) = −648, 95% CI = −746 to −550 IU) and significantly higher gonadotrophin

Might select an alternative strategy to obtain higher cost-effectivity in planned freeze-all cycles.

PCOS - AMH



RBMO

ELSEVIER

ARTICLE

Anti-Müllerian hormone as a diagnostic tool for PCOS under different diagnostic criteria in an unselected population

BIOGRAPHY

Gurkan Bozdag completed his residency in Department of OBGYN, Hacettepe University in 2004. His research areas are polycystic ovary syndrome, endometriosis and assisted reproductive technologies. He has published more than 80 peer-reviewed articles and has been an active board member of the Turkish Society of Reproductive Medicine since 2015.

Gurkan Bozdag[1], Sezcan Mumusoglu[1], Zuhal Yapici Coskun[1], Hakan Yarali[1,2,*], Bulent Okan Yildiz[3]

TABLE 2 THE VALIDITY OF AMH TO DIAGNOSE PCOS ACCORDING TO 2012 NIH WORKSHOP CRITERIA

	Phenotype A (HA+ OD+PCOM)	Phenotype B (HA+OD)	Phenotype C (HA+PCOM)	Phenotype D (OD+PCOM)
Prevalence (*n*, %)	20 (5.1)	4 (1.0)	36 (9.2)	18 (4.6)
Distribution of PCOS phenotypes, % (*n*/*n*)	25.6 (20/78)	5.1 (4/78)	46.2 (36/78)	23.1 (18/78)
AMH	5.64 (2.05–13.54)[a]	2.20 (0.91–2.64)	3.20 (1.39–5.88)	3.10 (1.38–7.42)
AUC (95% CI)	0.91 (0.86–0.96)	0.59 (0.43–0.76)	0.78 (0.72–0.84)	0.81 (0.74–0.89)
aAUC (95% CI)	0.85 (0.77–0.92)	0.59 (0.27–0.93)	0.67 (0.56–0.78)	0.78 (0.64–0.91)
AMH threshold (sensitivity and specificity)	4.35 (65.0% and 92.4%)	2.62 (25.0% and 73.9%)	4.19 (25.0% and 91.4%)	4.33 (38.9% and 92.4%)
OR (95% CI) for PCOS	22.44 (8.18–61.54)	0.94 (0.10–9.19)	3.54 (1.51–8.30)	7.69 (2.73–21.65)

- .90-1 = excellent (A)
- .80-.90 = good (B)
- .70-.80 = fair (C)
- .60-.70 = poor (D)
- .50-.60 = fail (F)

Opportunity

- **OR-based iCOS might decrease treatment burden in POR patients**
  - Financial
  - Physical

- **OR-based iCOS might change the primary strategy in patients with hyper-response risk.**
  - Safer (less risk of OHSS)
  - More efficient (freeze-all)
  - More cost effective (with PPOS)

SWOT Analysis

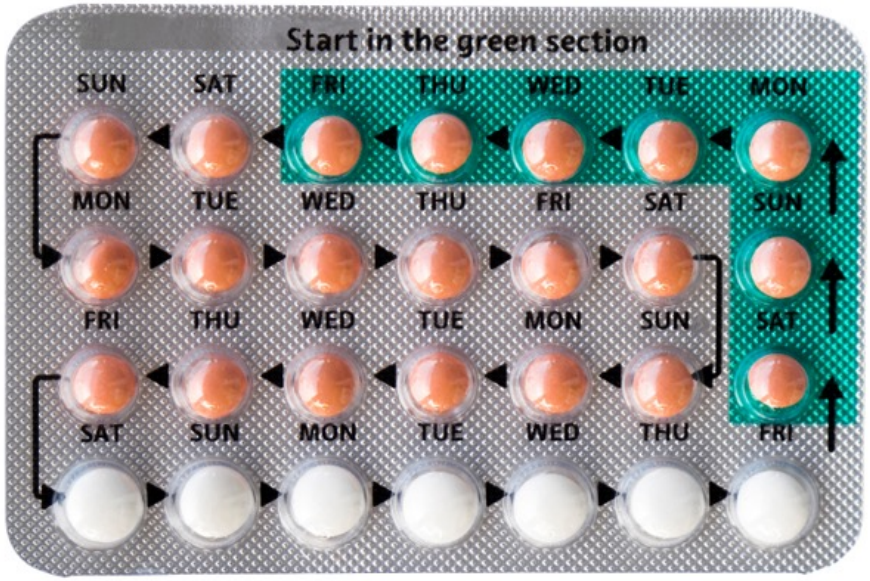
STRENGTHS
Characteristics of the business or project that give it an advantage over others.

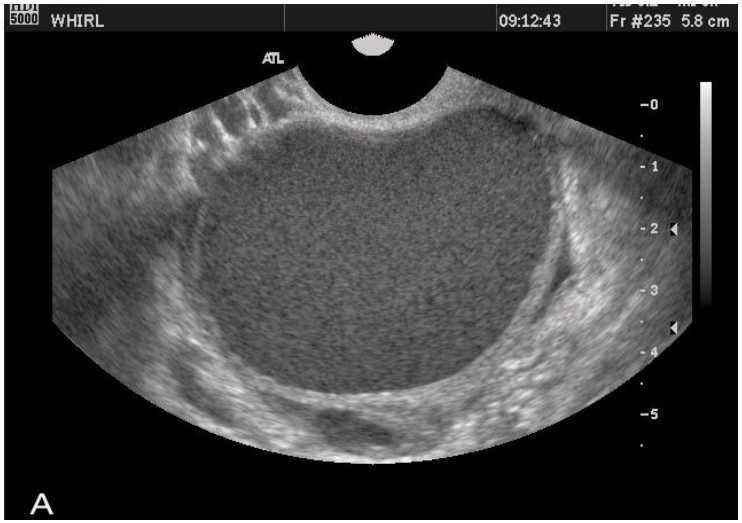
WEAKNESSES
Characteristics of the business that place the business or project at a disadvantage relative to others.

OPPORTUNITIES
Elements in the environment that the business or project could exploit to its advantage.

THREATS
Elements in the environment that could cause trouble for the business or project.

OR tests might be influenced by…





AMH-validity in advanced ages

Journal of Assisted Reproduction and Genetics
https://doi.org/10.1007/s10815-019-01633-4

REPRODUCTIVE PHYSIOLOGY AND DISEASE

Check for updates

Ovarian cortical follicle density in infertile women with low anti-Müllerian hormone

Stine Aagaard Lunding[1] · Susanne Elisabeth Pors[2] · Stine Gry Kristensen[2] · Jane Alrø Bøtkjær[2] · Maja Ramløse[2] · Janni Vikkelsø Jeppesen[1] · Esben Meulengracht Flachs[3] · Anja Pinborg[1,4] · Kirsten Tryde Macklon[1] · Anette Tønnes Pedersen[1,5] · Claus Yding Andersen[2] · Anders Nyboe Andersen[1]

Received: 17 September 2019 / Accepted: 8 November 2019

Table 1 Clinical characteristics of women with DOR (cases) and a control group (controls)

	Cases	Controls
Cohort, *n*	**20**	**100**
Age (years)		
Median (range)	38.3 (30.8–39.8)	29.9 (2.8–42.7)
Diagnoses (%)		
Breast cancer	–	39
Cervical cancer	–	6
Diminished ovarian reserve	100	–
Hodgkin/non-hodgkin disease	–	20
Sarcoma	–	13
Others	–	22
Follicle density (follicles per mm^3 tissue)		
Median (range)	1.9 (0–93.7)	16.3 (0–1578)
Cohort, *n*	**20**	**35**
AMH (pmol/L)		
Median (range)	1.9 (0.21–5.2*)	14.4 (2.7–50.4)
FSH (IU/L)		
Median (range)	10.4 (4.8–25.9)	NA
AFC		
Median (range)	5 (2–9)	NA
Cohort, *n*	**20**	**78**
Ovarian volume (mL) (*n*)		
Median (range)	3.96 (1.77–10.22)	5.87 (0.5–15.10)

Table 2 Estimated follicle density depending on age and serum levels of anti-Mullerian hormone

Follicle density (follicles per mm^3 tissue)					
AMH (pmol/L)	25 years	30 years	35 years	40 years	45 years
0–5	25.3	9.6	3.3	0.7	–
6–0	35.0	13.6	4.9	1.4	–
11–15	47.0	18.4	6.9	2.2	0.3
16–20	63.0	24.9	9.5	3.2	0.7
21–25	84.3	33.5	13.0	4.7	1.3
26–30	112.6	45.0	17.6	6.5	2.0
31–35	150.5	60.3	23.8	9.0	3.1
36–40	200.9	80.7	32.1	12.4	4.4
41–45	268.0	107.9	43.1	16.9	6.2
46–50	357.6	144.2	57.8	22.8	8.6

AMH anti-Müllerian hormone

No of OCC in advanced ages

Human Reproduction, Vol.26, No.7 pp. 1768–1774, 2011
Advanced Access publication on May 10, 2011 doi:10.1093/humrep/der106

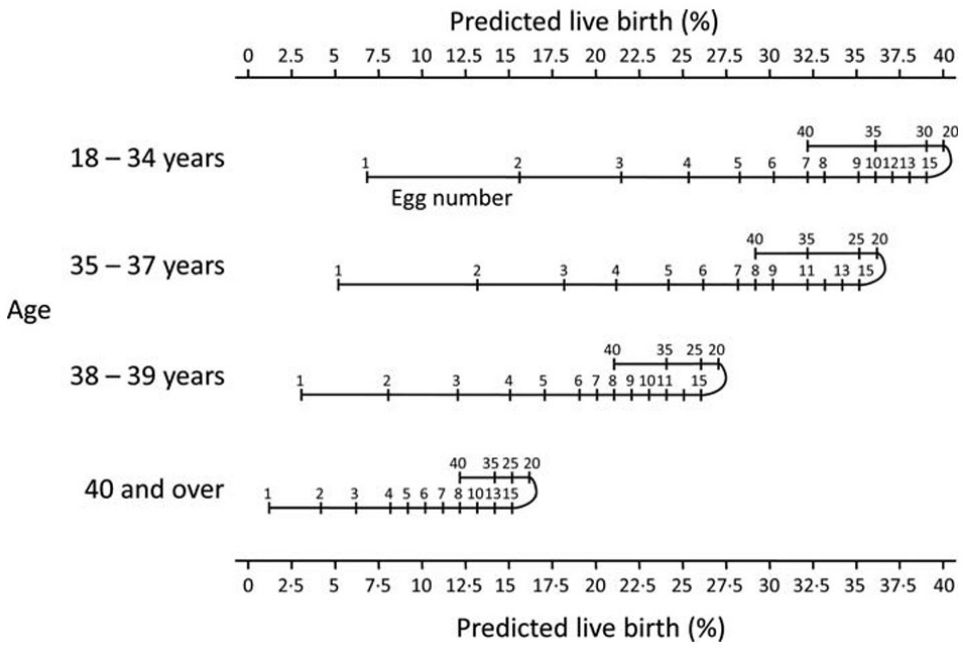
human reproduction

ORIGINAL ARTICLE *Infertility*

Association between the number of eggs and live birth in IVF treatment: an analysis of 400 135 treatment cycles

Sesh Kamal Sunkara[1], Vivian Rittenberg[1], Nick Raine-Fenning[2], Siladitya Bhattacharya[3], Javier Zamora[4], and Arri Coomarasamy[5,*]

[1]Assisted Conception Unit, Guy's and St Thomas' Foundation Trust, King's College London, London, UK [2]Nottingham University Research and Treatment Unit in Reproduction (NURTURE), Division of Human Development, School of Clinical Sciences, University of Nottingham, Nottingham, UK [3]Division of Applied Health Sciences, School of Medicine and Dentistry, University of Aberdeen, Aberdeen, UK [4]Clinical Biostatistics Unit, Hospital Ramon y Cajal. IRYCIS. CIBERESP, University Complutense of Madrid, Spain [5]School of Clinical and Experimental Medicine, College of Medical & Dental Sciences, University of Birmingham, Academic Unit, 3rd Floor, Birmingham Women's Hospital, Birmingham B15 2TG, UK



Discordance Between AMH and AFC

- **Yaxin Guo et al., 2021 (n= 19,239; 6.6%)**

Variable	All normal	Low - AMH	Low - AFC	All - low
No. of OCC	13.7 (6.5)[a]	6.2 (3.6)	6.9 (3.7)	4.3 (2.6)
No. of embryos	8.1 (4.8)[a]	3.8 (2.7)	4.3 (2.8)	2.8 (2.2)
LBR (%)	33.8[a]	28.9	23.5	20.2
CLBR (%)	57.8[a]	37.5	36.3	28.2



[a] $p < 0.001$ for all other groups

Threat

- **Little is known about endogenous and exogenous factors that might impact on OR (obesity, race, vit D level, OCP, hypo-hypo etc).**

- **Age is a better predictor for the achievement of pregnancy than OR tests.**

Strength

- **OR reflect primordial follicle density**
- **OR based iCOS might yield**
  - More “appropriate” response.
  - Less excessive response
- **Better agreement among recent automated assays for AMH**

Weakness

- **OR-based iCOS does not achieve higher LBR in ART or cycles.**
- **OR have poor predictive validity in the prediction of natural pregnancy.**
- **Complexity of structure for AMH**
  - Biological variability
  - Analytical variability
  - Lack of international standard
- **Variability exists for AFC**

Opportunity

- **OR-based iCOS might decrease treatment burden in POR patients**
  - Financial
  - Physical
- **OR-based iCOS might change the primary strategy in patients with hyper-response risk.**
  - Safer (less risk of OHSS)
  - More efficient (freeze-all)
  - More cost effective (with PPOS)

Threat

- **Little is known about endogenous and exogenous factors that might impact on OR (obesity, race, vit D level, OCP, hypo-hypo etc).**
- **Age is a better predictor for the achievement of pregnancy than OR tests.**