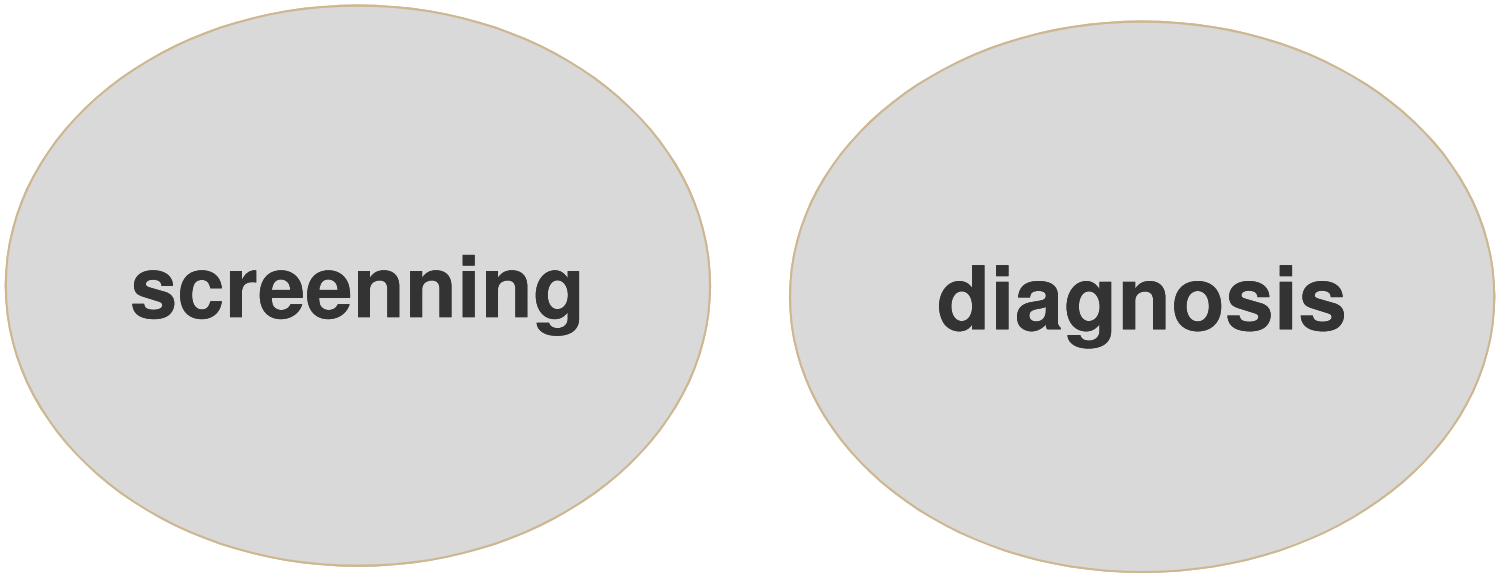
Ovarian reserve testing and prediction for natural and assisted conception

Juan A. Garcia-Velasco, MD

Ovarian reserve testing

- Indirect measure of reproductive age
- Used to define quantity (and quality?) of primordial ovarian follicles at a given age



Ovarian reserve testing

Why is it important?

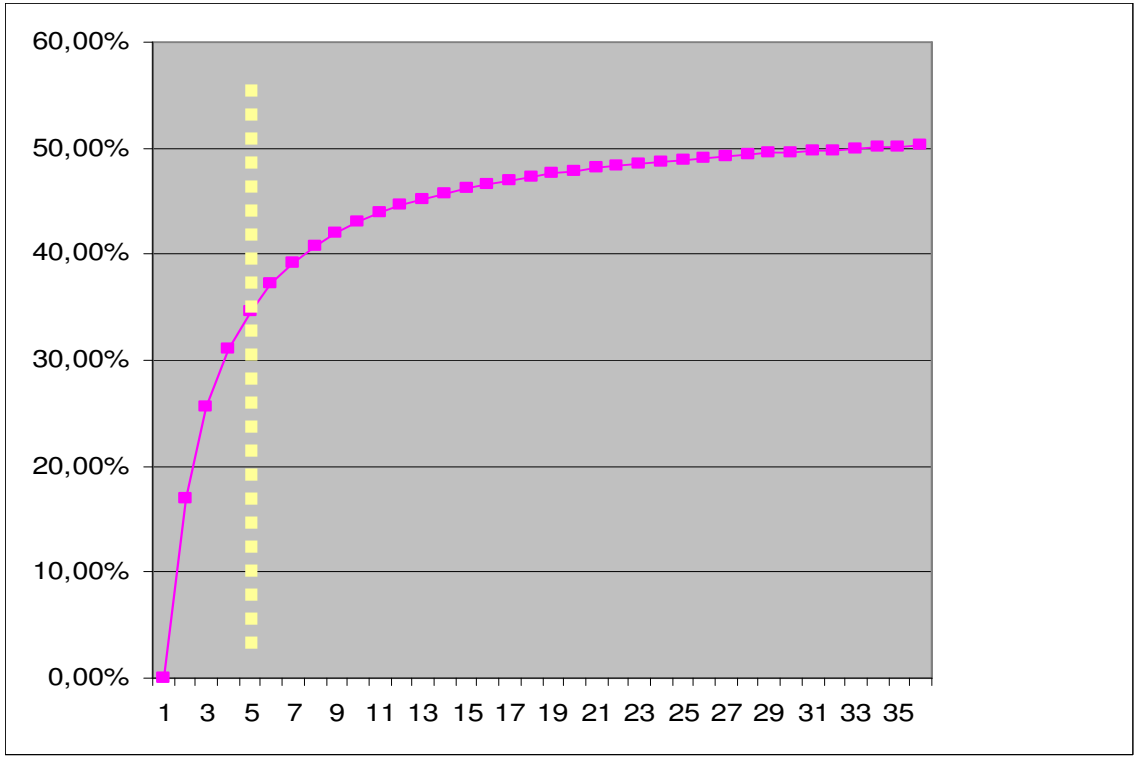
- Adequate counselling of ART outcome
- Tailor stimulation protocols (low, high resp)
- Predict cycle cancellation
- Donor oocytes?
- Previous to oncological treatments /ovarian surgery
- Fertility decline in women with age?

Prediction

- Essential tool for clinical decision-making
- To prevent unnecessary treatment
- Reliable counselling

What is a low response?

n = 6349



% pregnancy= 1/(1.8758 + 4.0406 / nº eggs)

Muñoz et al. ASRM 2007

How big is the problem?

Fresh IVF	2047
Frozen cycles	1076
Egg donation	1005

412 LOW RESPONDERS

0 -	14 cycles
1 -	76 cycles
2 -	84 cycles
3 -	114 cycles
4 -	127 cycles

20.1%

How big is the problem?

Fresh IVF	2047
Frozen cycles	1076
Egg donation	1005

Age

1,404 > 34 y.o

68.6%

Ovarian reserve testing

- Biochemical markers
  - **FSH**
  - **Estradiol**
  - **Inhibin B**
  - **AMH**
  - **FSH/LH ratio**
- Morphometric markers
  - **Ovarian volume**
  - **AFC**
  - **Mean ovarian diameter**
- Dynamic markers
  - **CCCT**
  - **Exogenous FSH ovarian reserve test**
  - **GnRH analogue stimulation test**

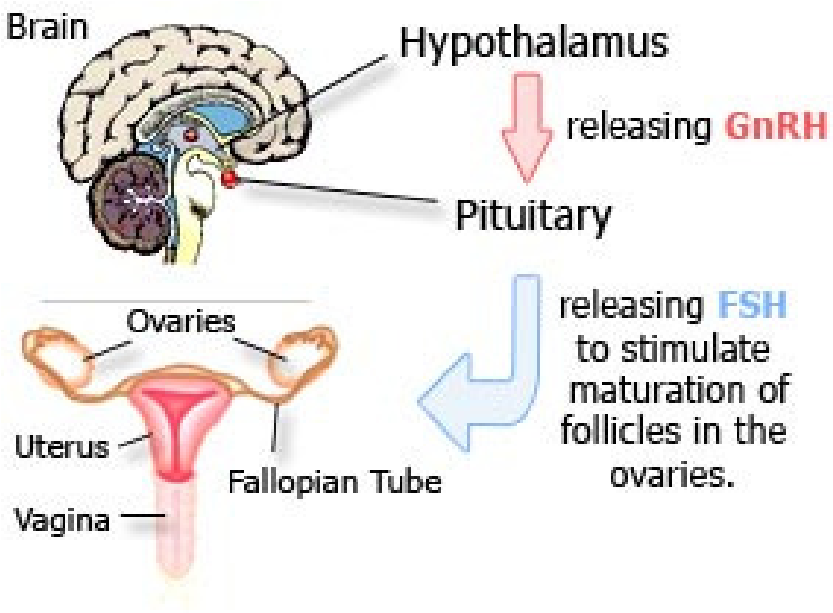
Ovarian Aging: Mechanisms and Clinical Consequences

F. J. Broekmans, M. R. Soules, and B. C. Fauser

The variability of ovarian ageing among women is evident from the large variation in age at menopause. The identification of women who have severely decreased ovarian reserve for their age is clinically relevant. Ovarian reserve tests have appeared to be fairly accurate in predicting response to ovarian stimulation in the assisted reproductive technology (ART) setting. The capacity to predict the chances for spontaneous pregnancy or pregnancy after ART appears very limited.

(*Endocrine Reviews* 30: 465–493, 2009)

Basal FSH



Activin

Estradiol

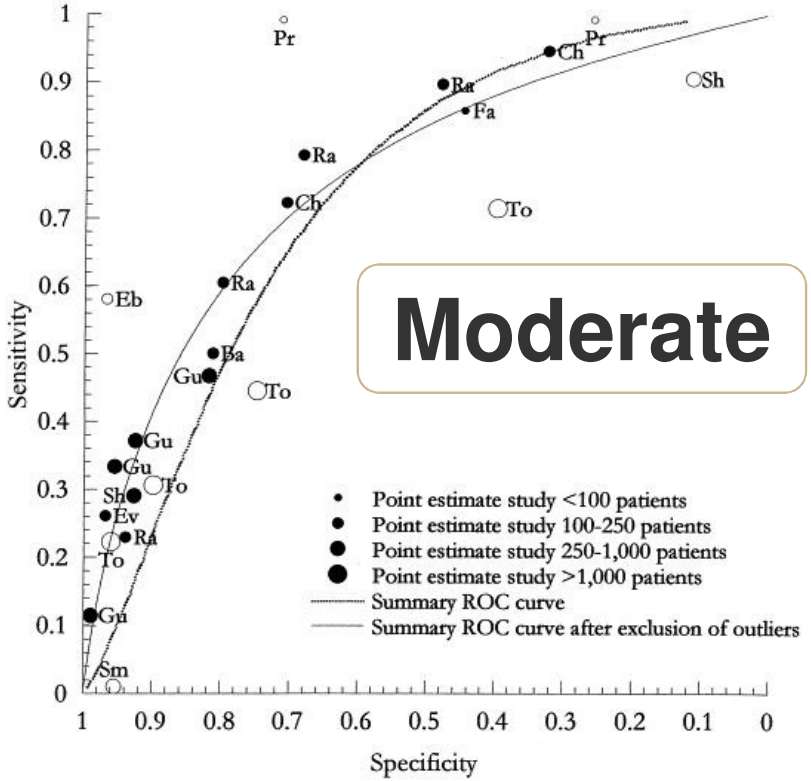
Inhibin

Measuring day 3 FSH is a commonly used test to predict IVF respose

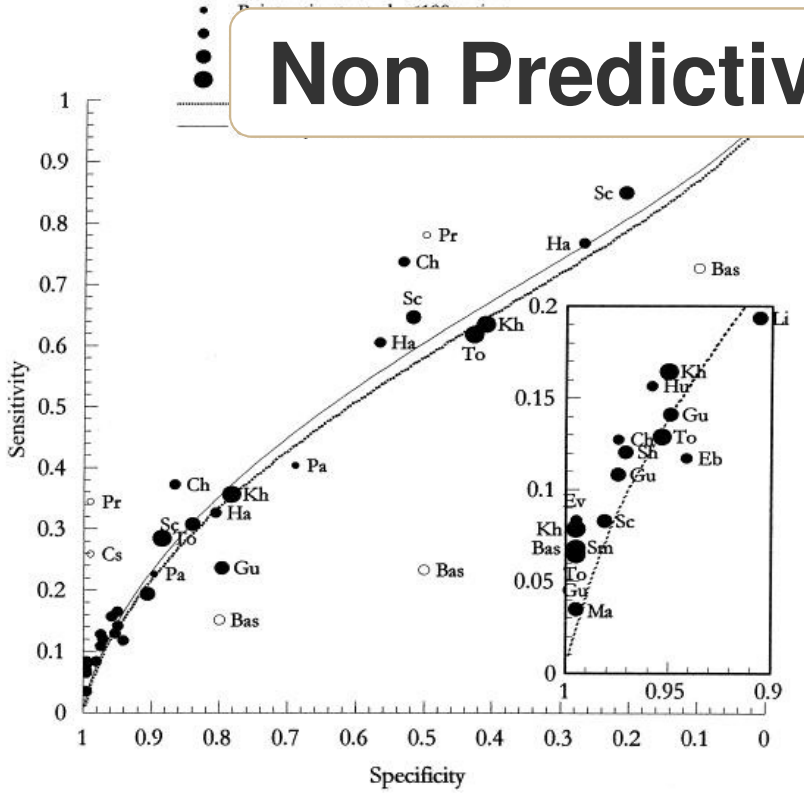
Basal FSH

21 studies
Quality?
Extreme cut-offs
Limited senstivity

Response – Non Pregnancy



Moderate

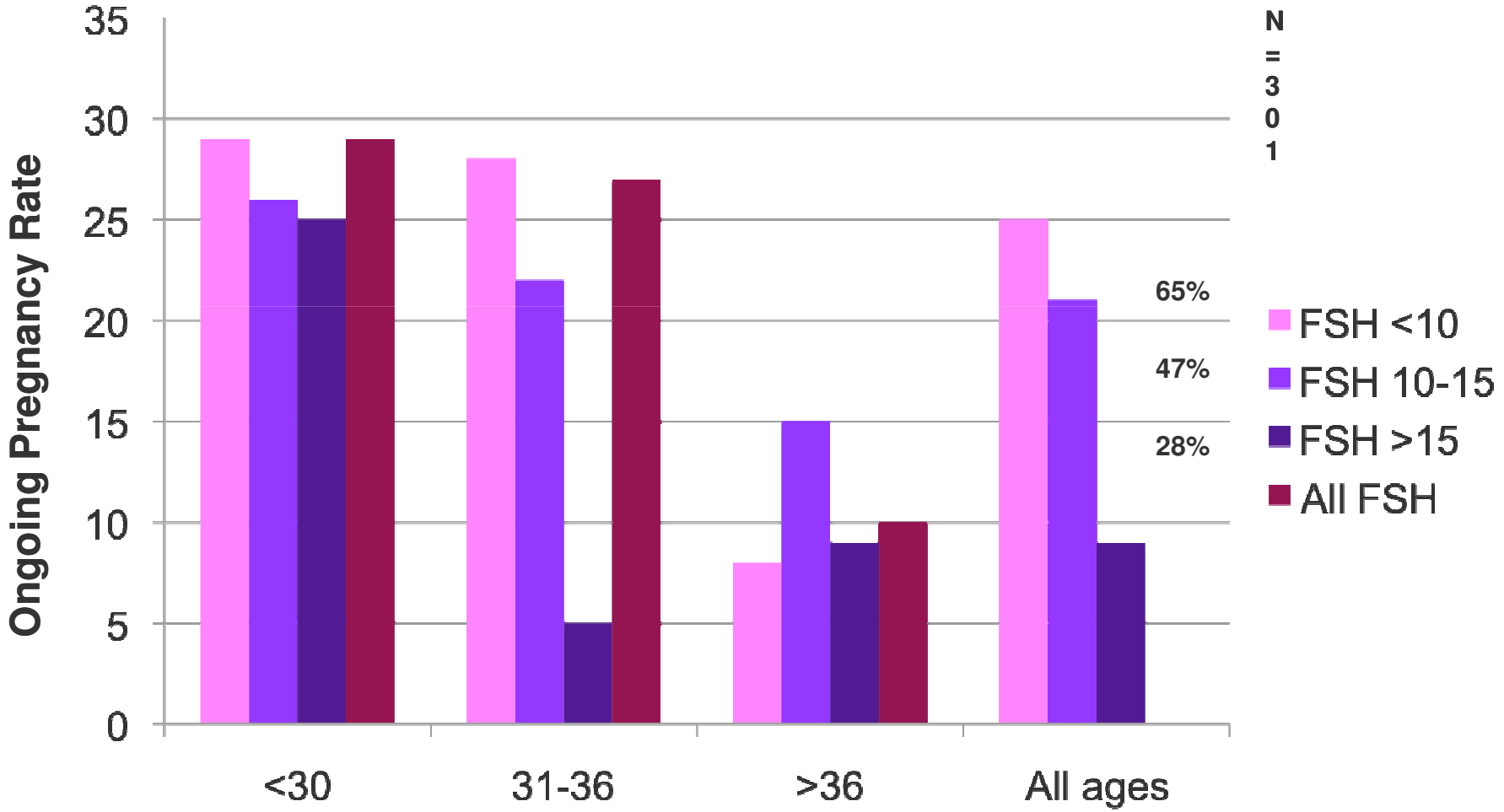


Non Predictive

Bancsi et al. Fertil Steril 2003

Basal FSH

Useless to exclude patients

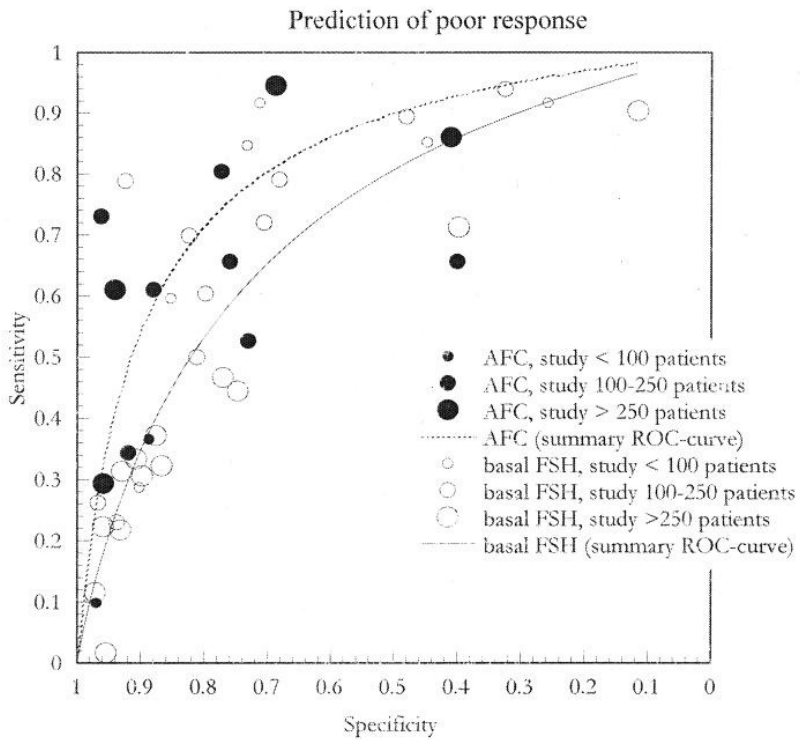


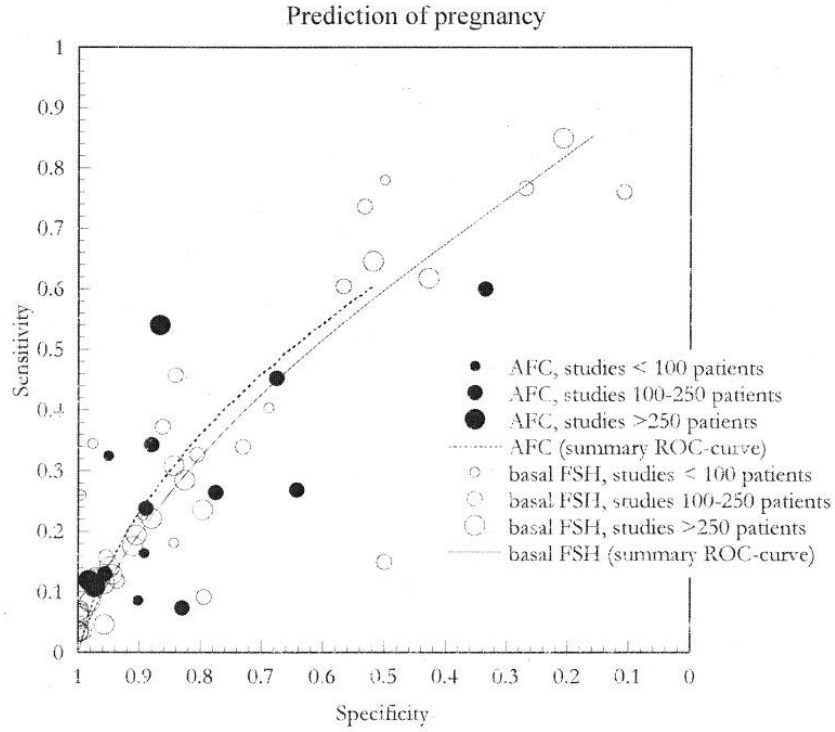
Van Rooij et al. Fertil Steril 2004

FSH vs AFC

Predictive performance of AFC vs FSH as ORT

11 studies on AFC and 32 on FSH





AFC performs better – easy, non invasive, essential

Hendriks et al . Fertil Steril 2005

FSH vs Age

- 1045 patients
- Both markers predicted **quantitative** ovarian response

	Age	FSH	Age + FSH
> 10 oocytes	0.688	0.703	0.718
Pregnancy	0.617	0.545	0.627
Cancellation	0.599	0.601	0.610

- Age was a better predictor of pregnancy rate in women undergoing IVF

Chuang et al. Fertil Steril 2003

Dynamic tests

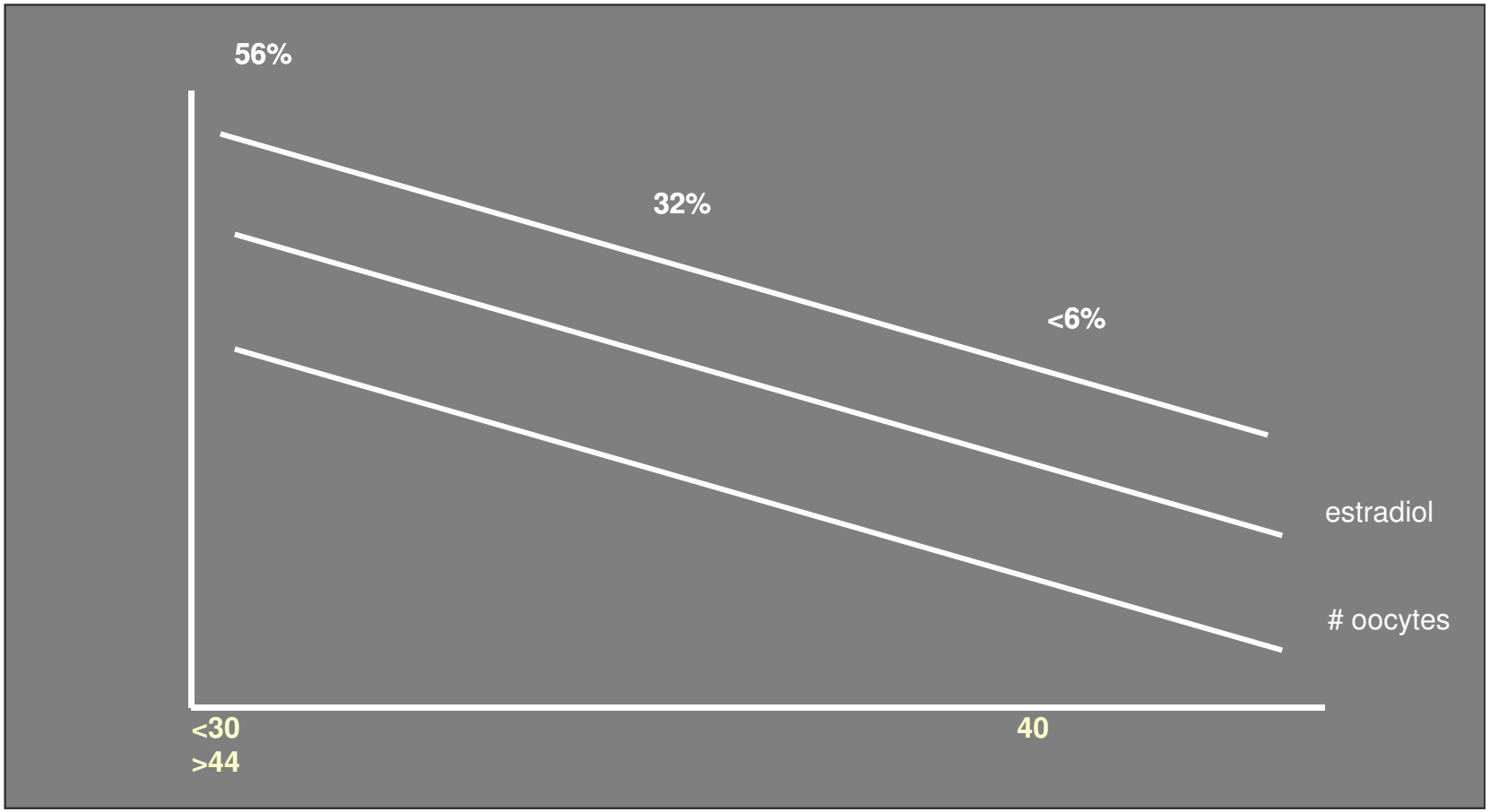
- CCCT adds very little additional value to basal FSH (if any)

  Predictive accuracy not better than FSH + AFC

- GAST or EFFORT should not be advocated as a screening test as it performed similarly to inhibin B or AFC

 Hendriks et al. Fertil Steril 2006; JARG 2005

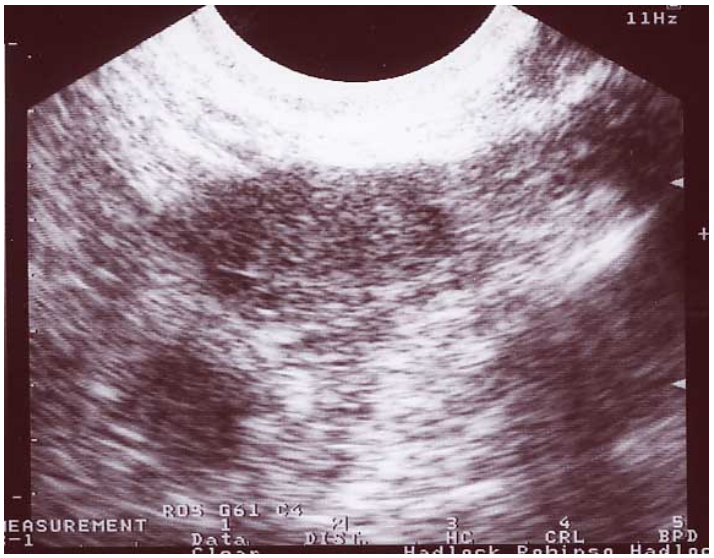
Age influence



Age influence

Ultrasound
AFC

- **Small in diameter (2-8mm)**



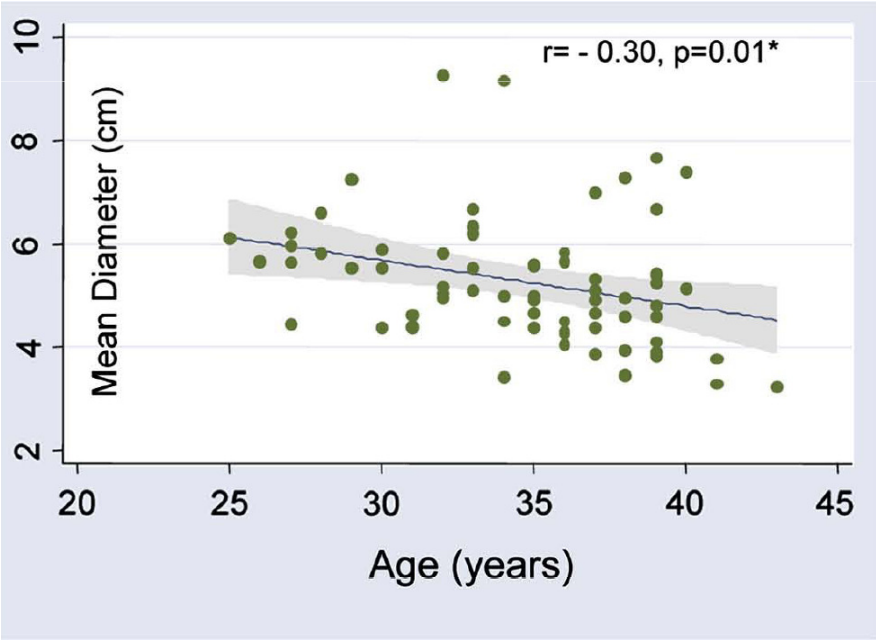
Ultrasound
AFC

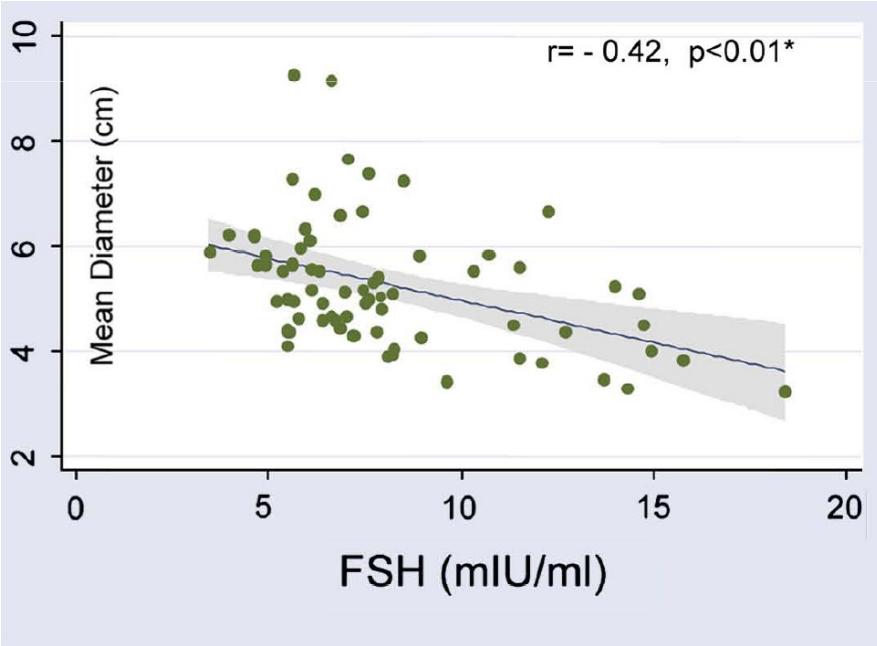
- **2D and 3D similar accuracy**

Scheffer et al. Ultrasound Ob Gyn 2002

Ultrasound
Ovarian volume

- **Limited prognostic value for IVF**
- Simple tool: **(D1 + D2) / 2**

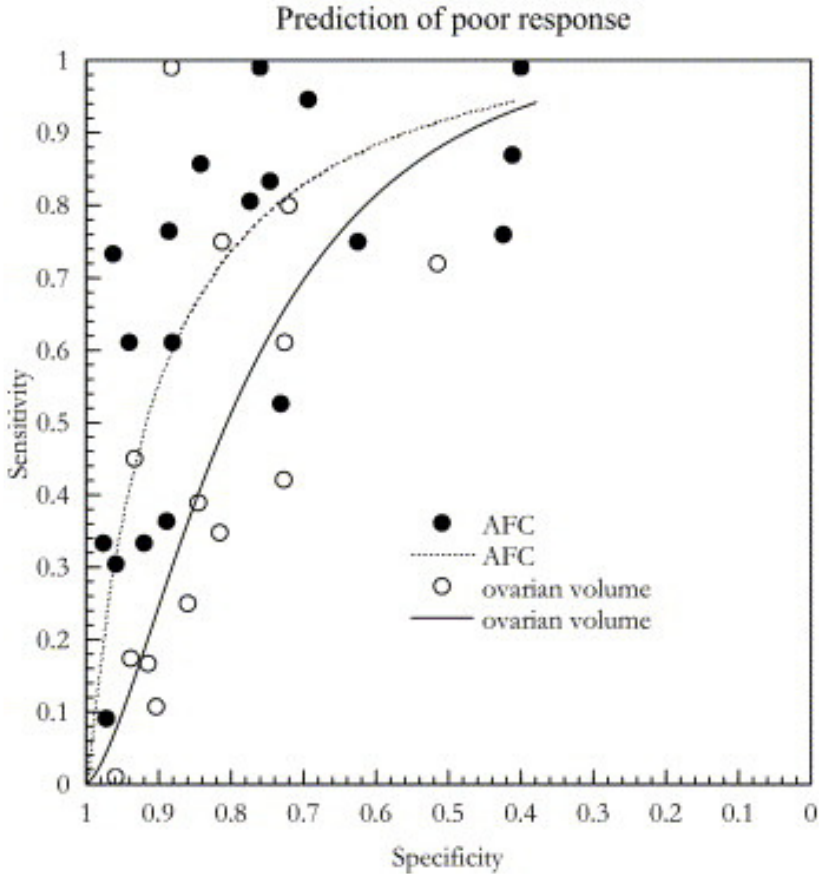




Bowen et al 2007

AFC vs ovarian volume

- 10 studies on OV and 17 on AFC
- AFC better predictor of poor response



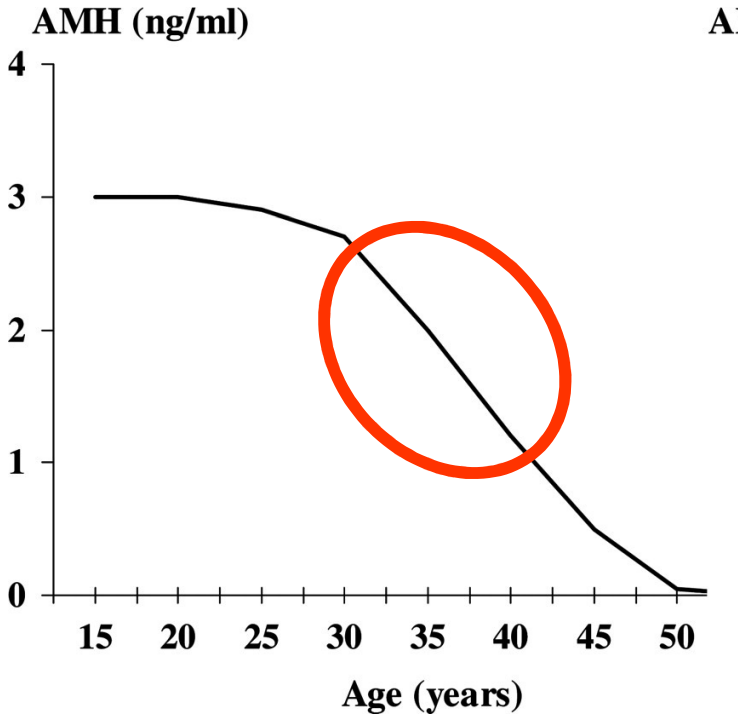
Clinical value in PR prediction only evident in AFC

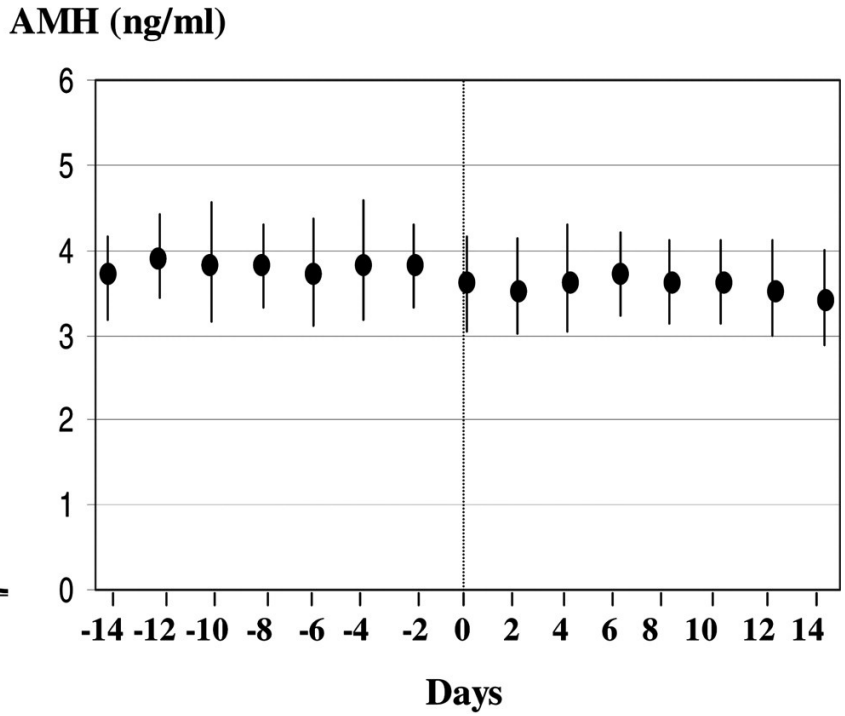
For non-pregnancy absent for both

Hendriks et al 2007

AMH

- **Secreted by GC in primary and preantral fols**

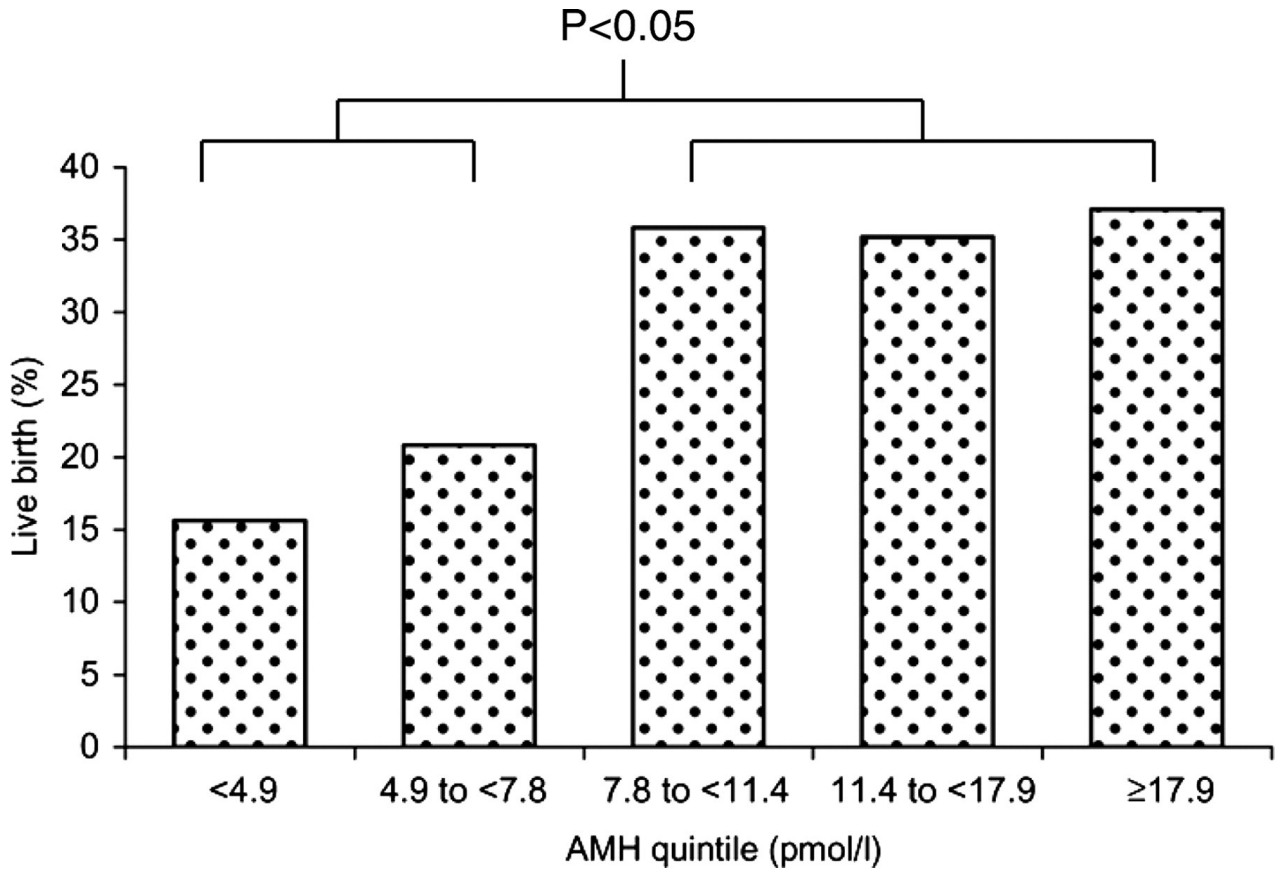




La Marca et al 2010

AMH

- **Live birth rate according to AMH**



Nelson et al 2007

AMH vs AFC

Multivariate models vs AFV as single test

11 studies of MVM

Sens 39-97%

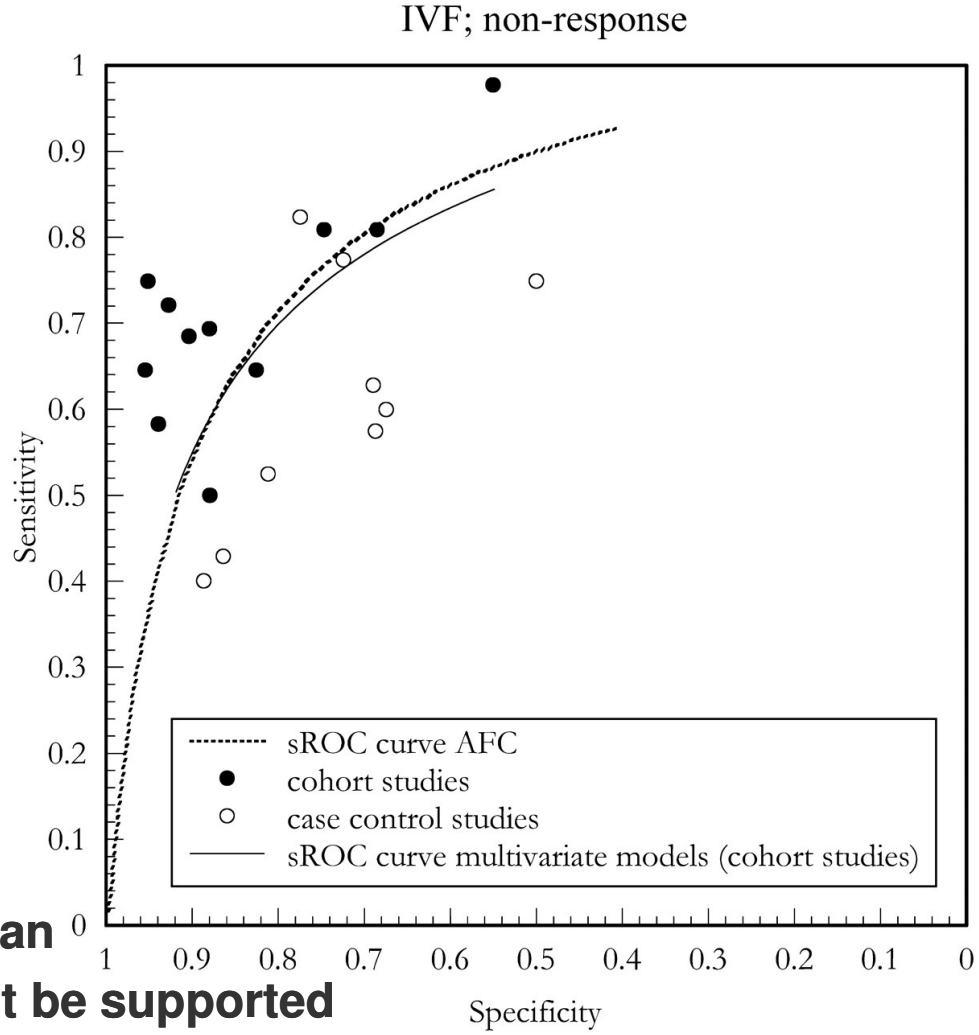
Spec 50-96%

Cohort better than case-control

Similar accuracy of AFC to MVM

No data to predict Pregnancy

The use of more than 1 single test cannot be supported



Verhagen et al. Hum Reprod Update 2008

Simple predictors

Age= egg quality, FSH = egg quantity

Toner J. Fertil Steril 2003

Young, high FSH : > cancellation

< oocytes

average IR / PR

Older, normal FSH: good response

low IR / PR

Conclusions

- **We cannot recruit follicles that do not exist!**

- **Egg quality fundamentally cannot be altered**

Conclusions

- Dynamic tests useless
- Basal FSH – high variability intercycle
- AMH more robust (during cycle, intercycle, OCP… and lower inter/intraassay variability)
- AFC highly reliable and reproducible, low cost
- Age: cheapest and only marker of egg quality

Thank you!

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