FERTILITY associates | a better understanding

TE RAUHANGA O TE WHARETANGATA

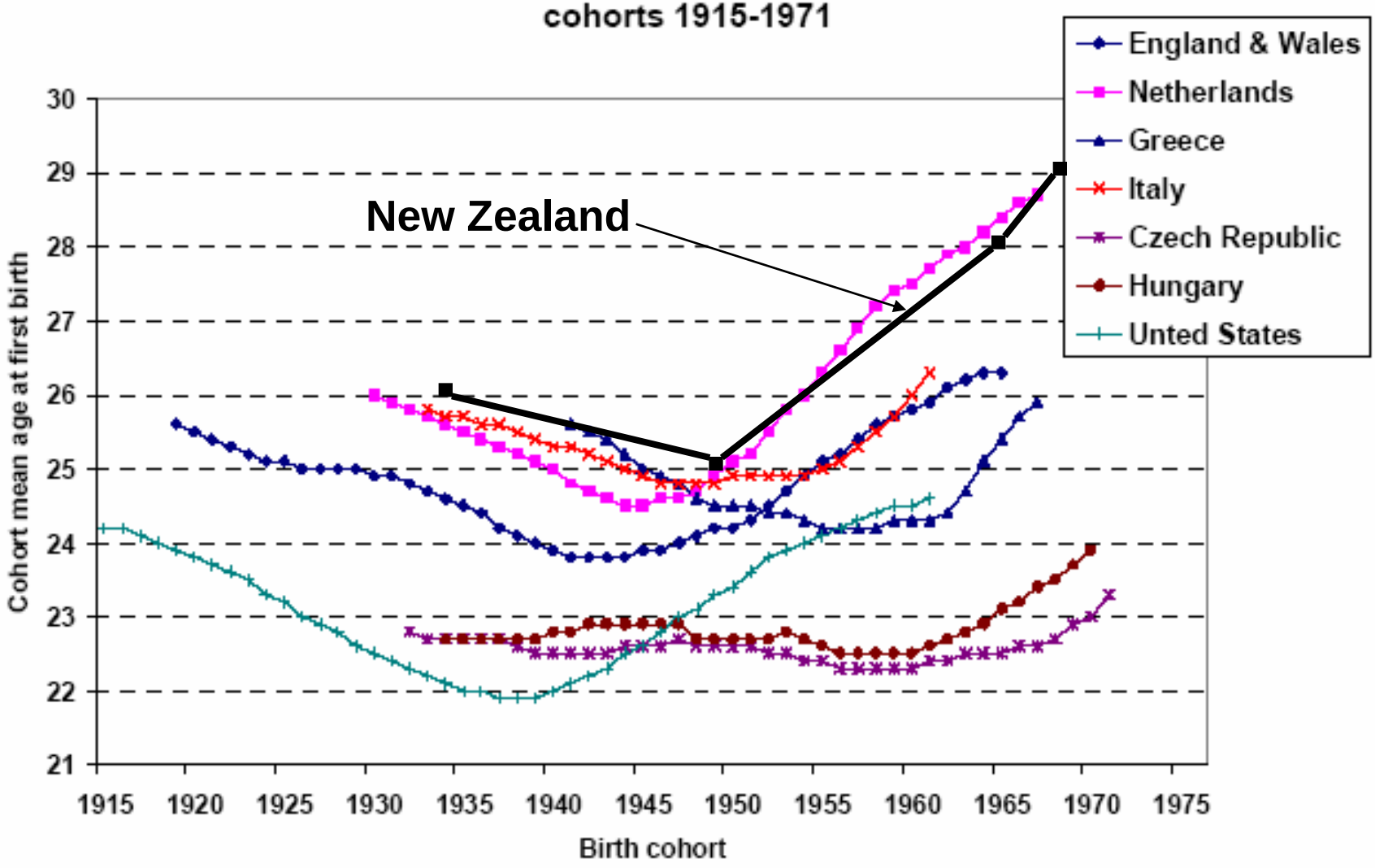
LEADERS IN FERTILITY

Fertility 2010

What do GP's need to know?

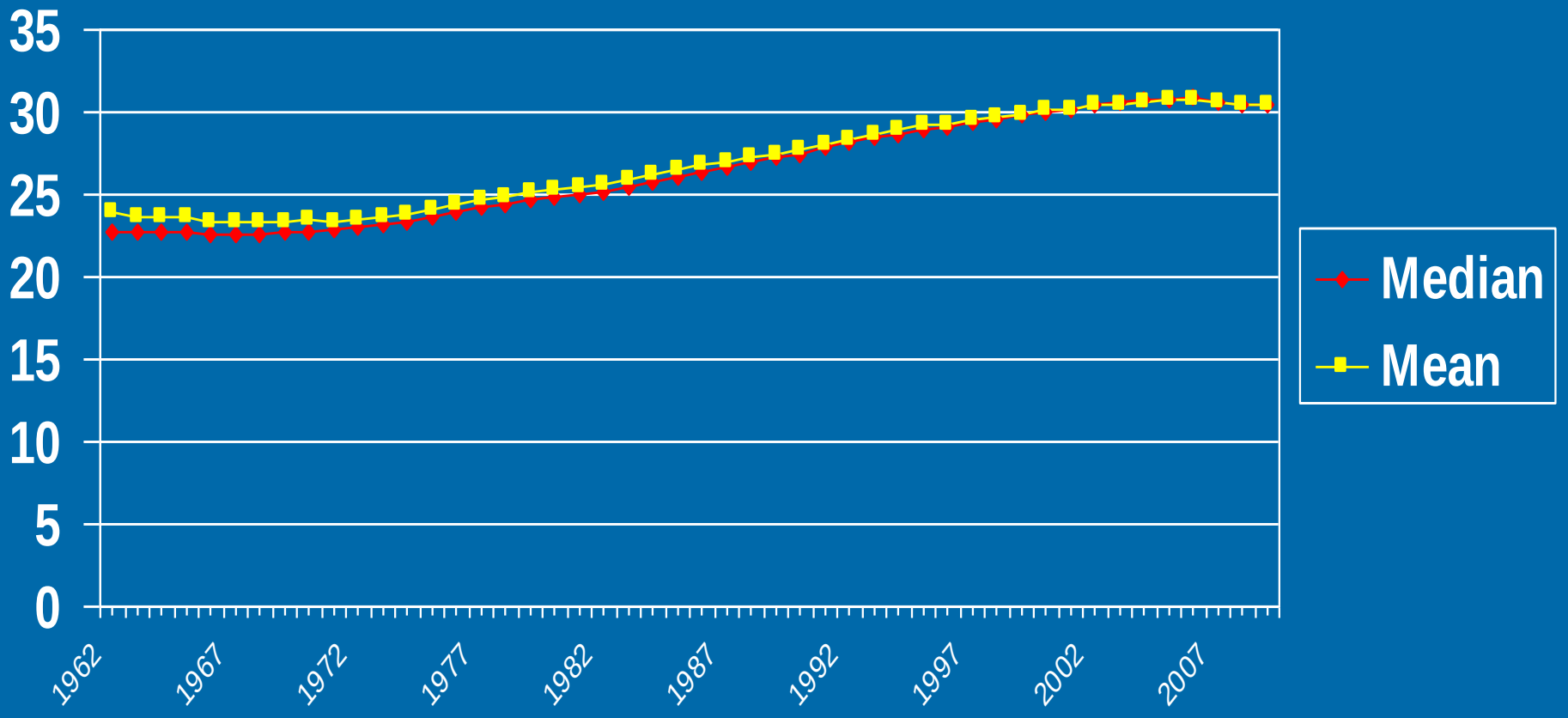
Richard Fisher
Fertility Associates

Figure 4 - Cohort mean age at first birth, selected countries, birth cohorts 1915-1971



Source: Max Planck Institute

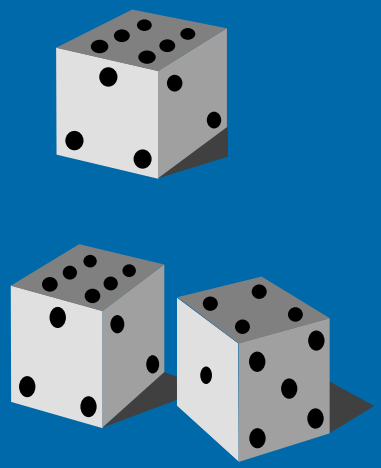
Average age of mother at first birth in New Zealand



Source: Statistics New Zealand 2009

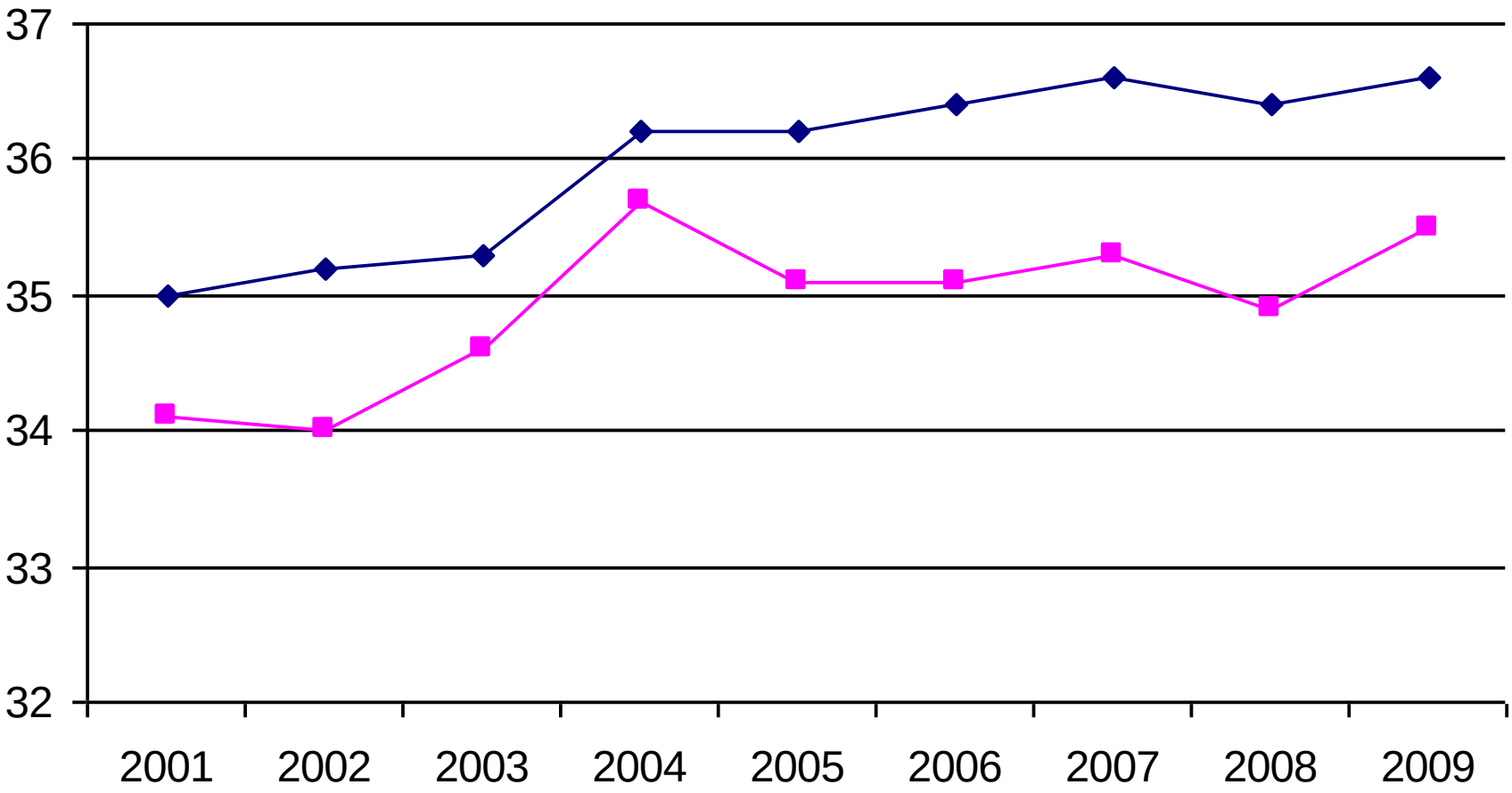
Monthly fecundity by age

Years	%
25	25
30	20
35	16
37	11
40	6
42	4
44	2

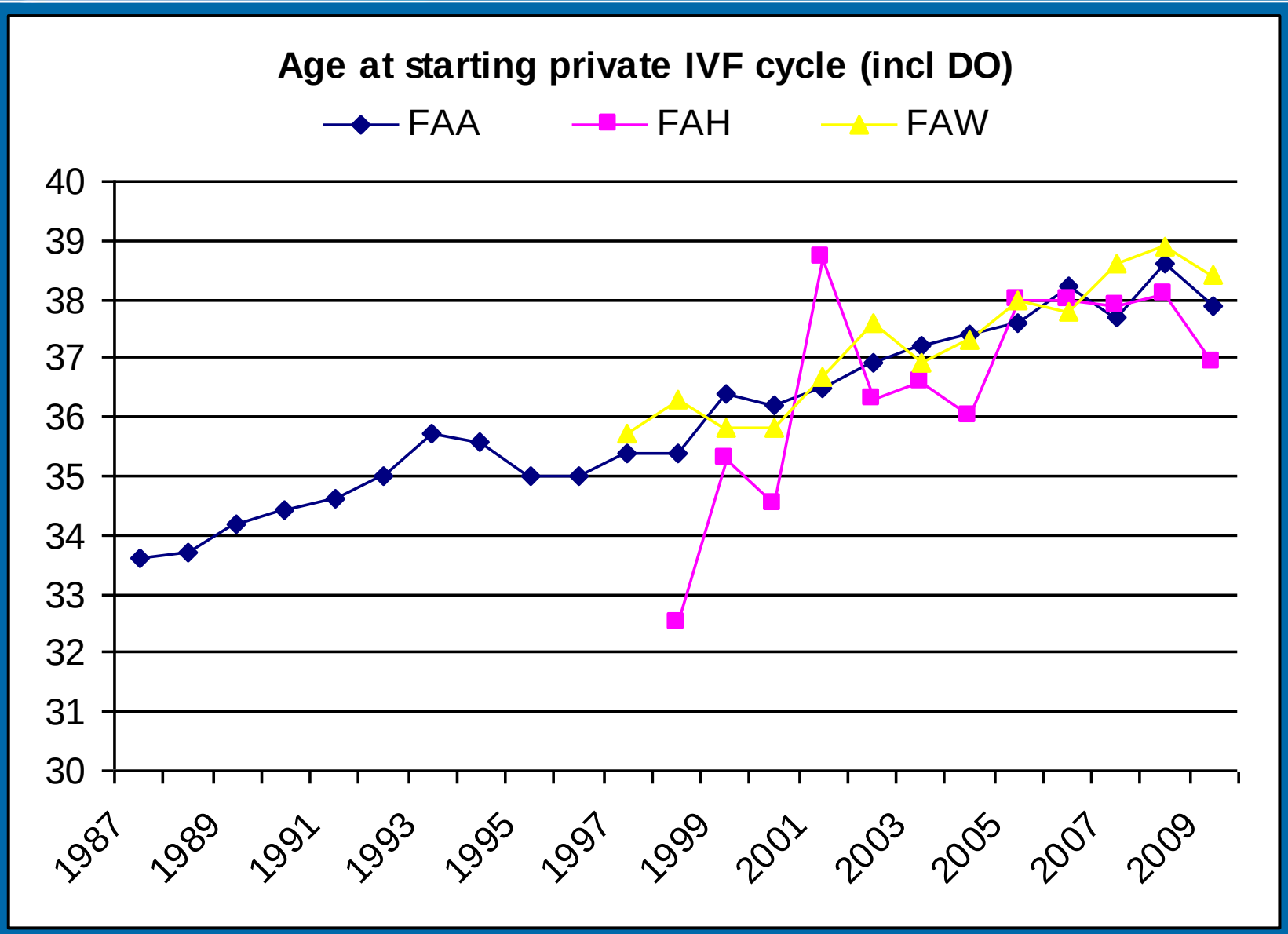


Source: Fertility Associates

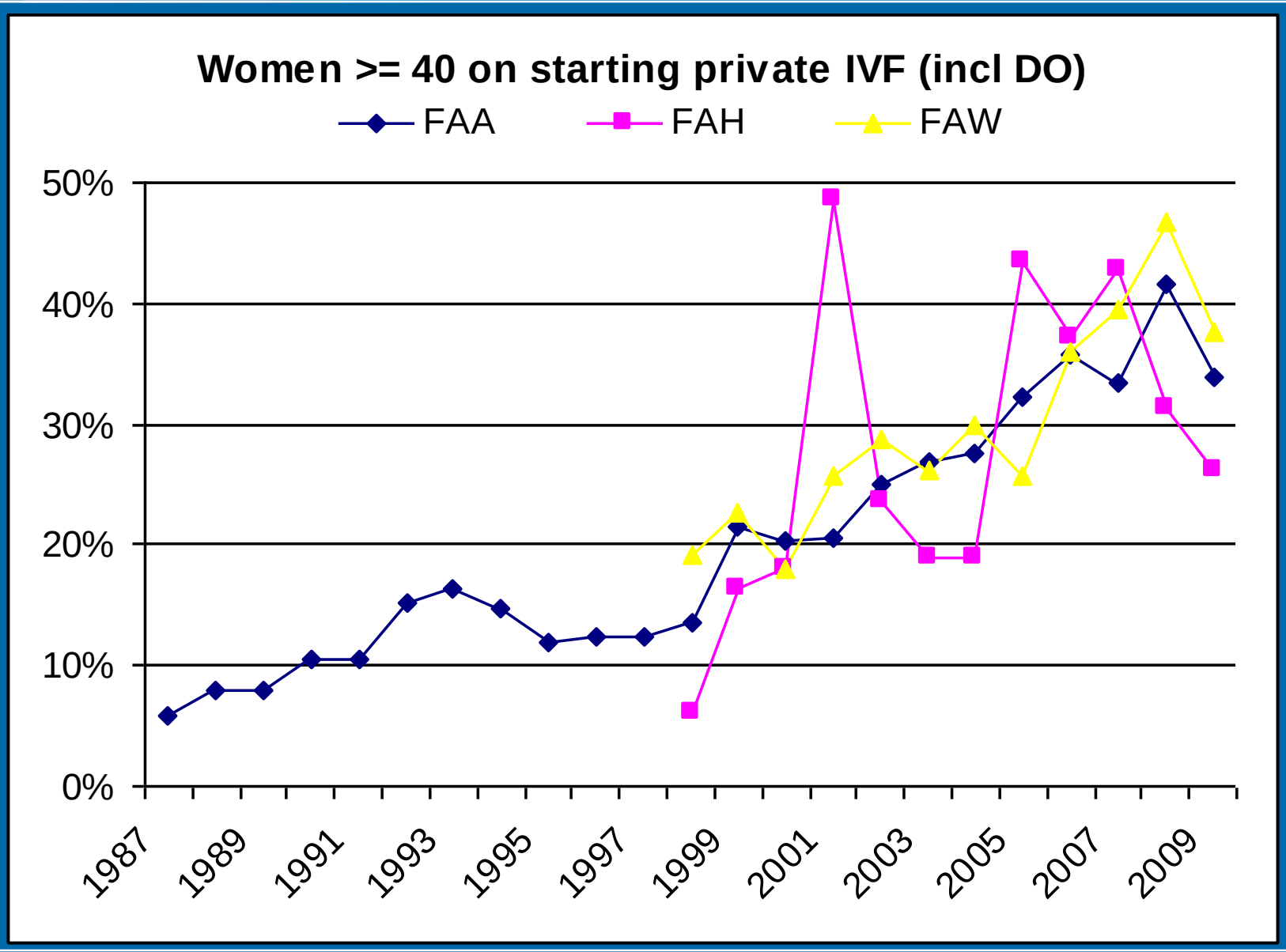
Average age at consultation



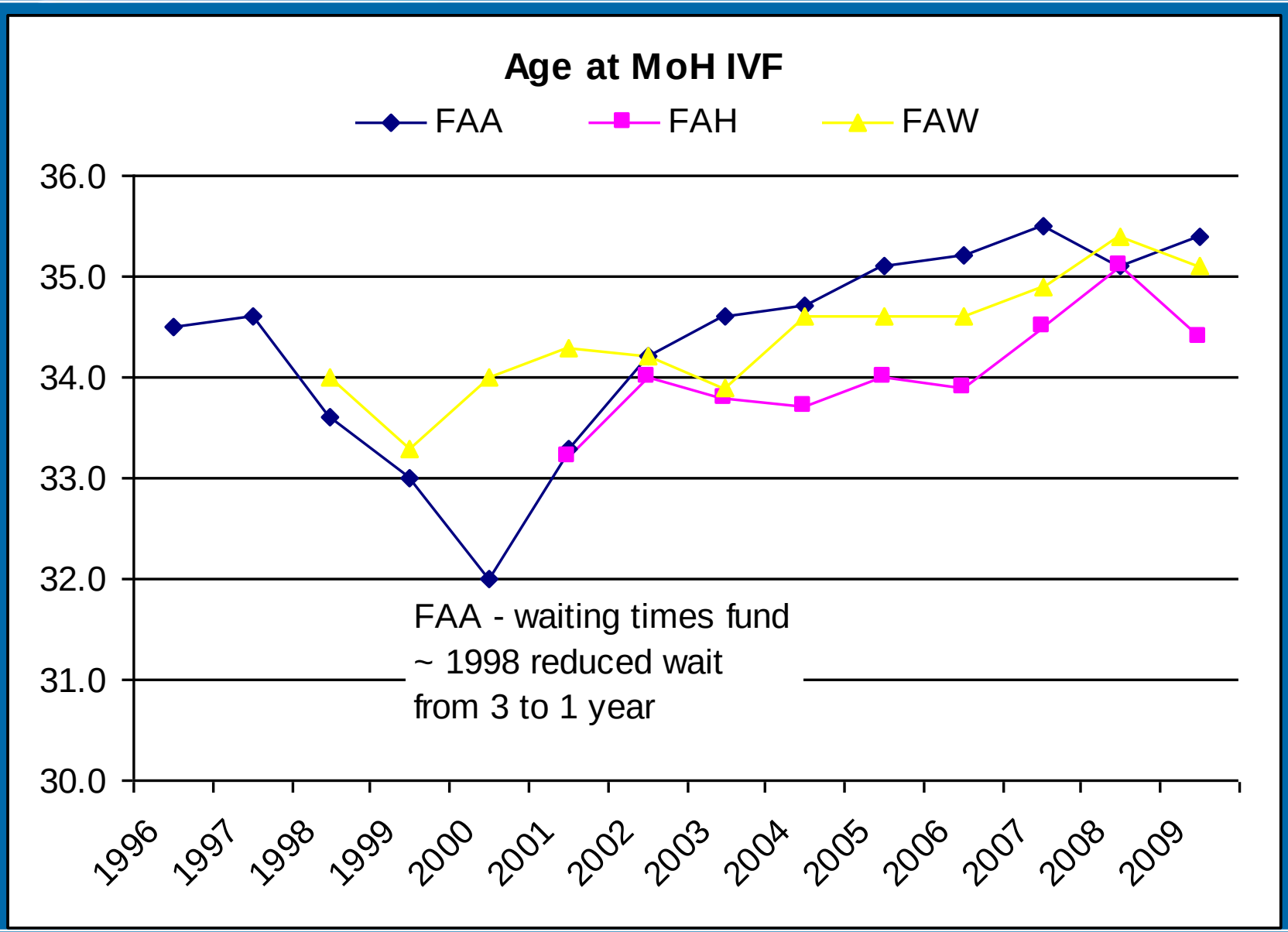
Source: Fertility Associates



Source: Fertility Associates

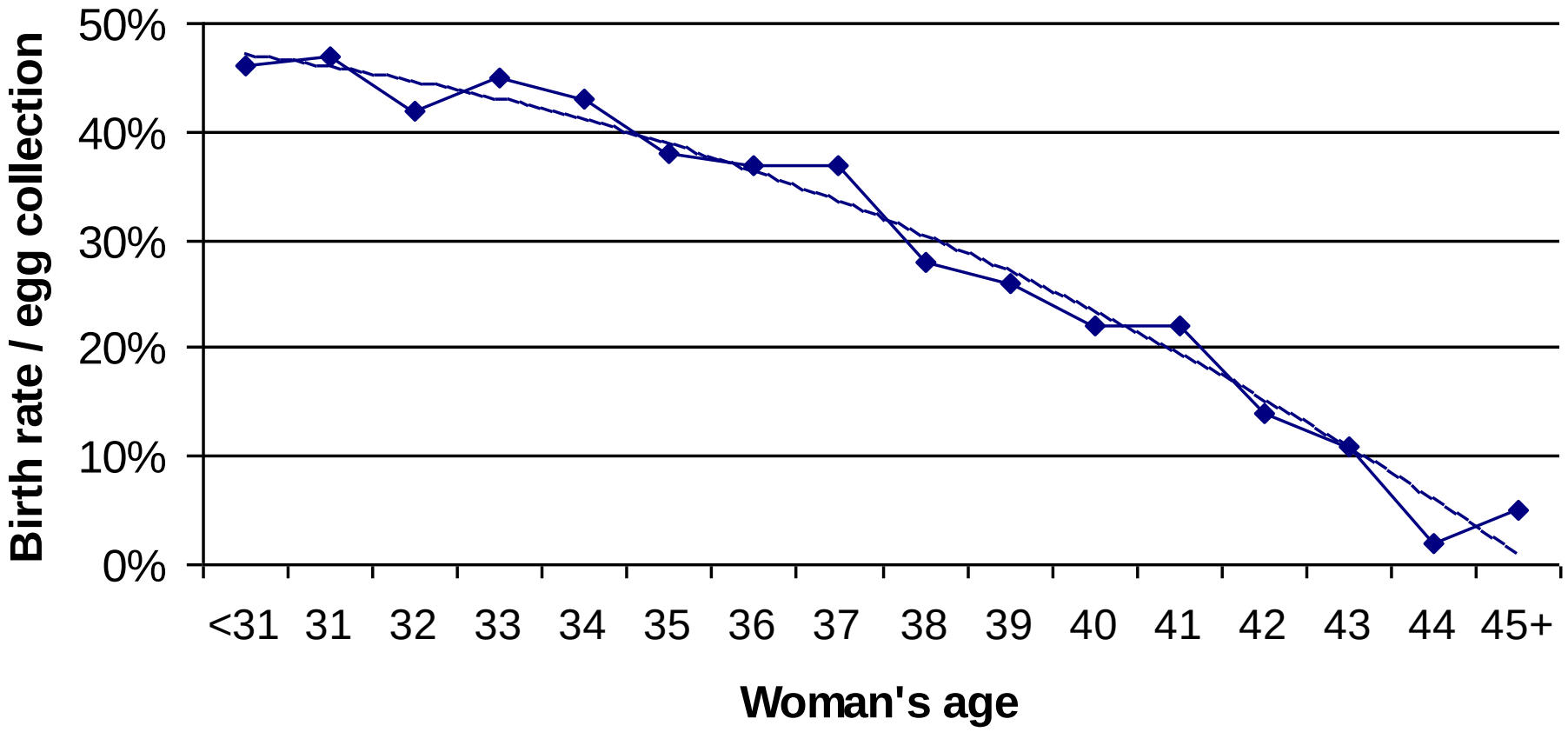


Source: Fertility Associates



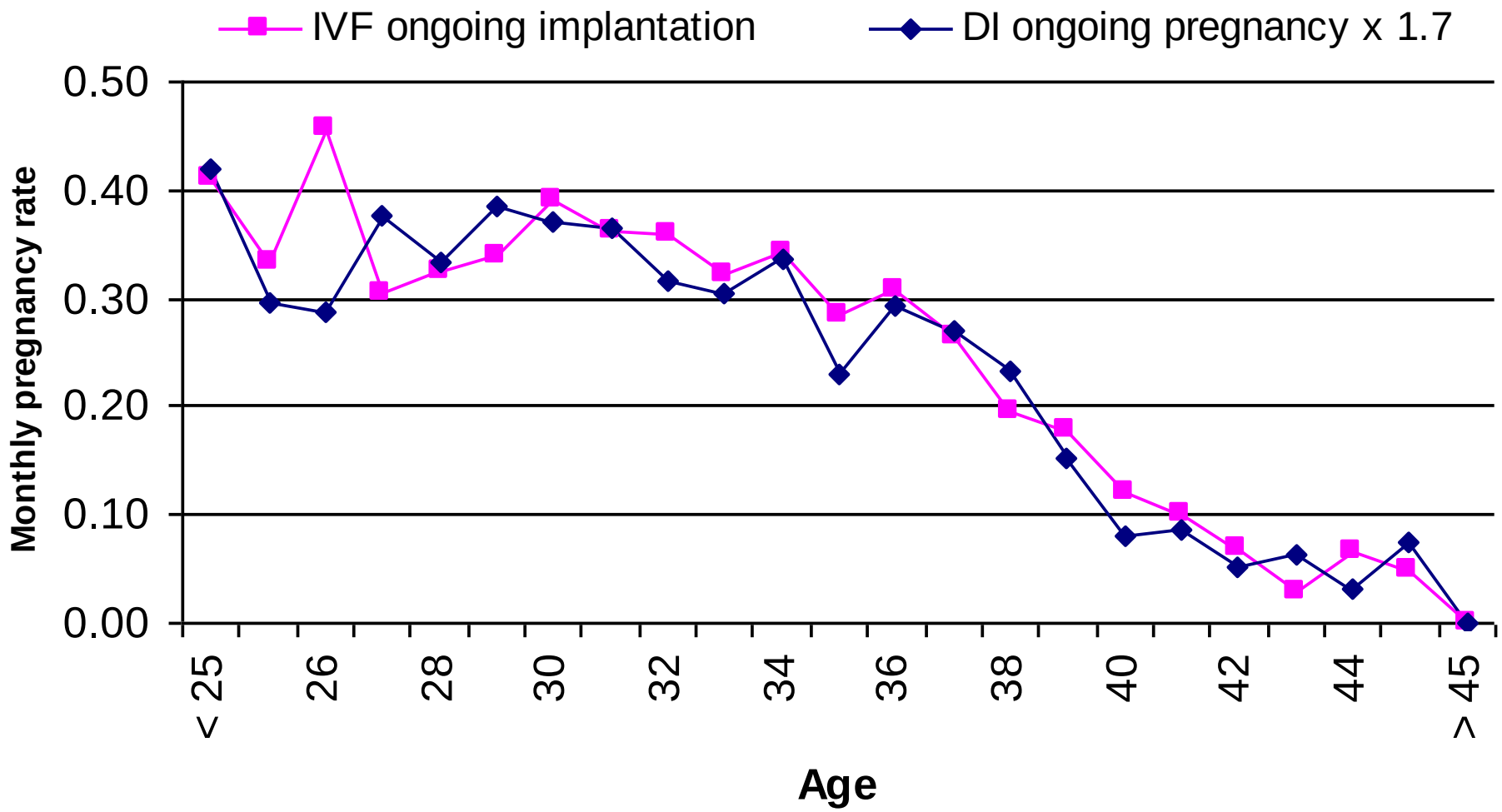
Source: Fertility Associates

Chance of baby, own eggs

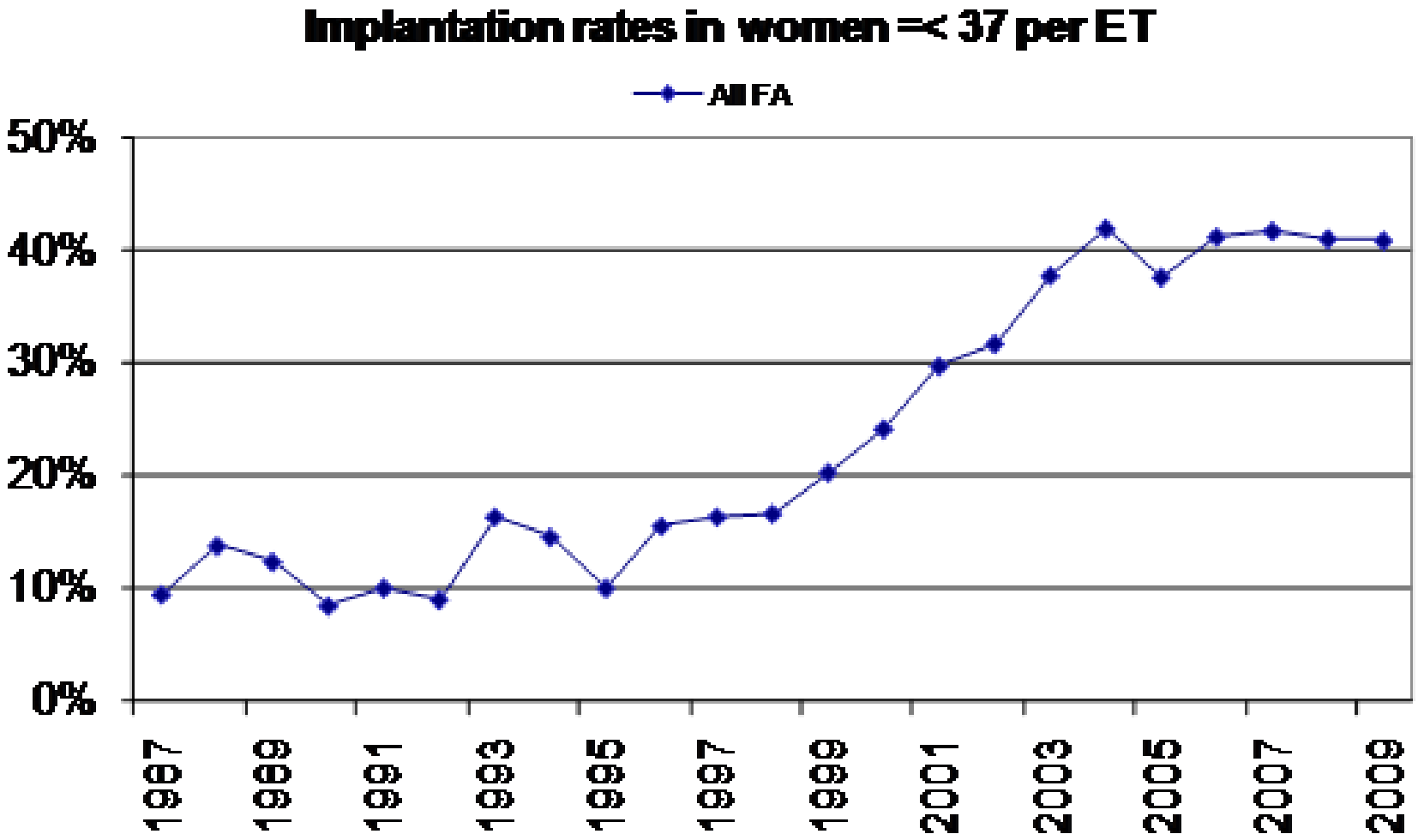


Source: Fertility Associates

Decline in fertility with age

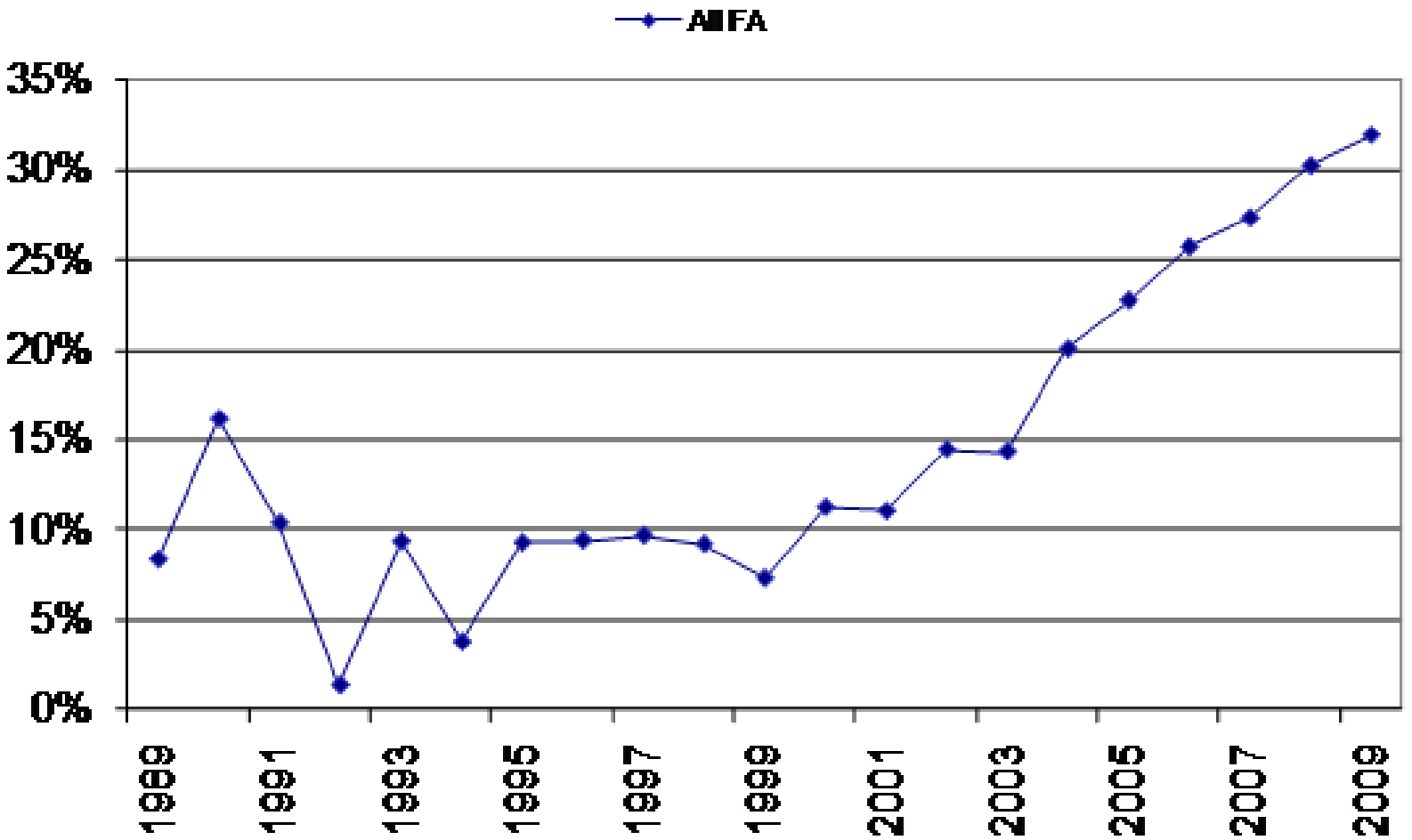


Source: Fertility Associates



Source: Fertility Associates

Implantation rates in women =< 37 per TER



Source: Fertility Associates

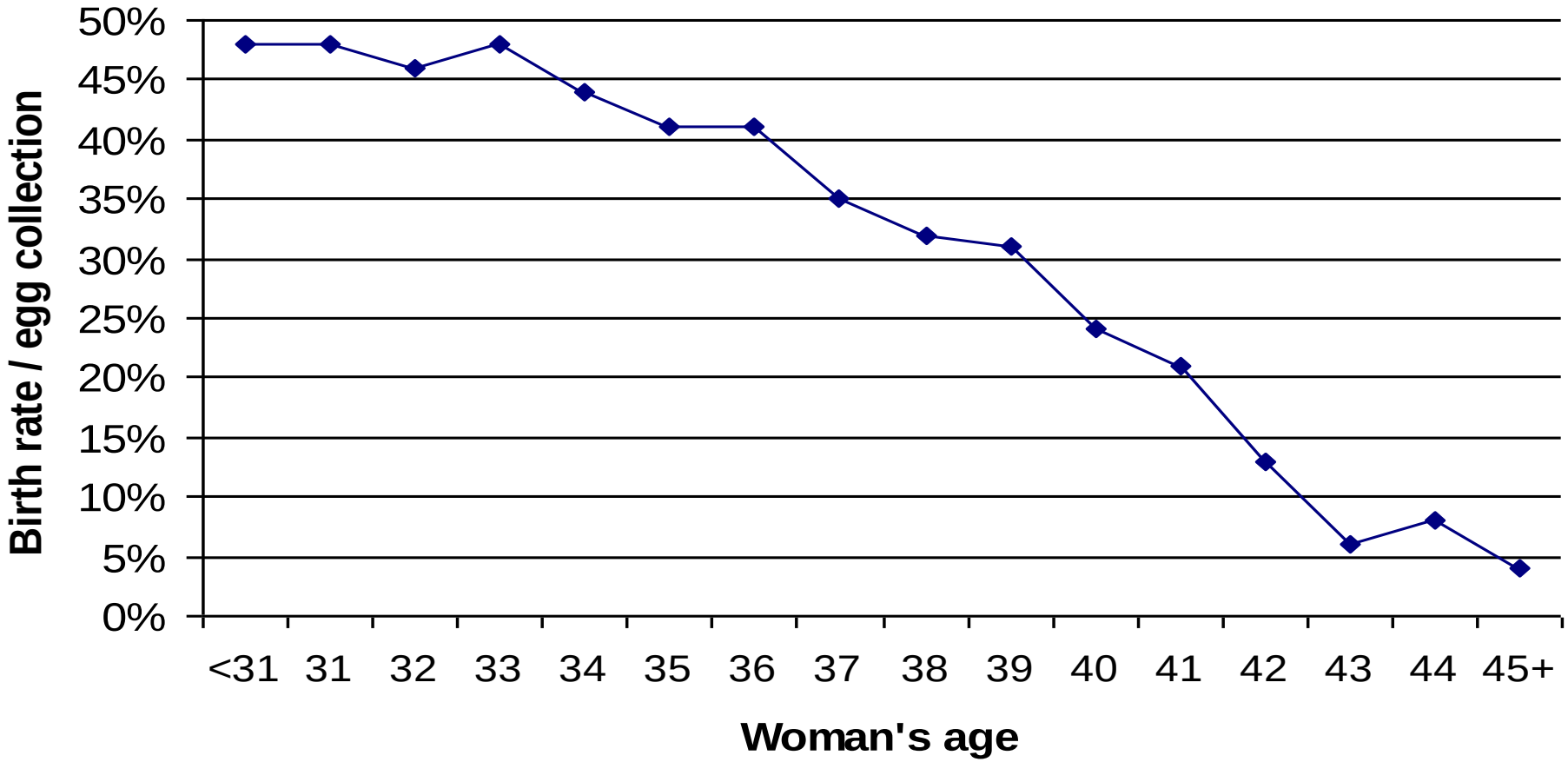
A new species?

IVF-lings…

- Girls born lighter
- Taller when compared to MPH
- There is a trend towards a lower BMI in the IVF groups
- Lower fasting triglycerides and LDL levels
- Higher HDL levels
- Trend to lower fasting insulin levels
- Trend towards higher IGF I levels

Source: Fertility Associates and Liggins Institute

IVF success rates



Source: Fertility Associates

AMH

- Anti Mullerian Hormone
- Produced in the gonads alone
- In female rises from zero at birth to modest levels at puberty and see slow and steady decline thereafter
- Can be measured at any time of cycle and while on oral contraceptives

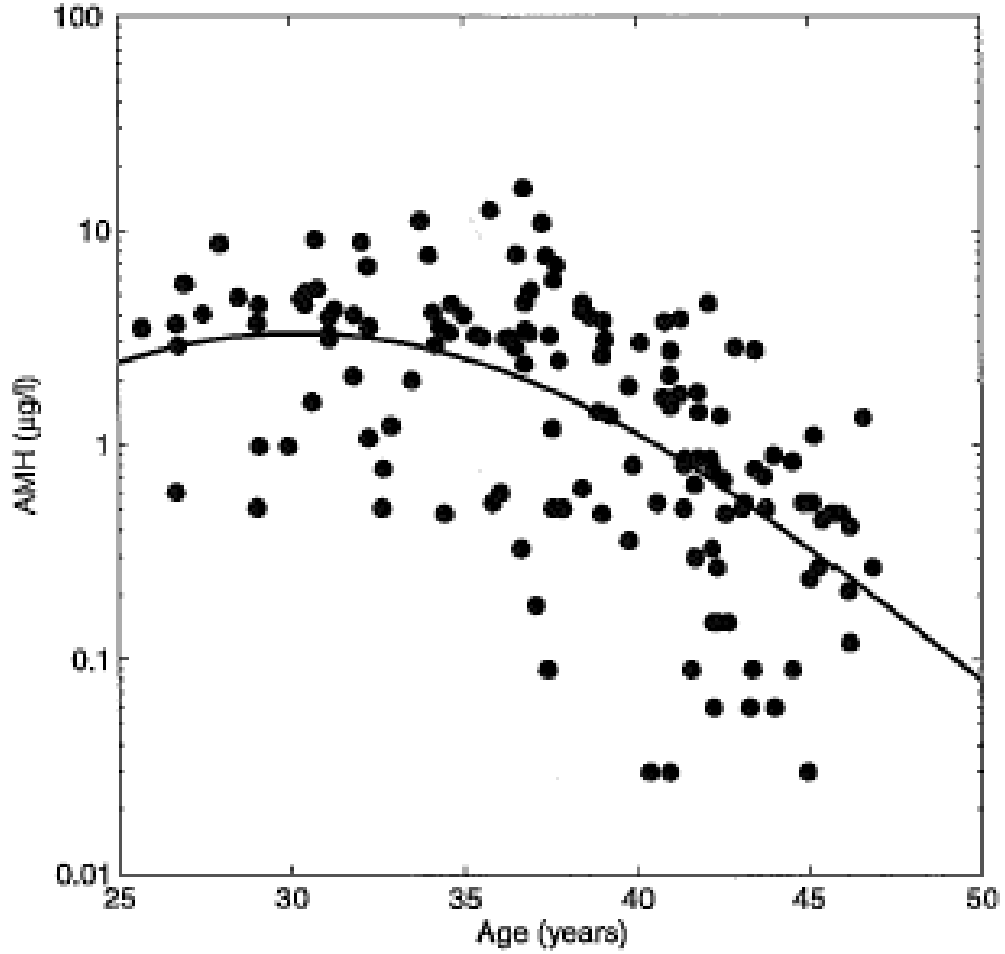
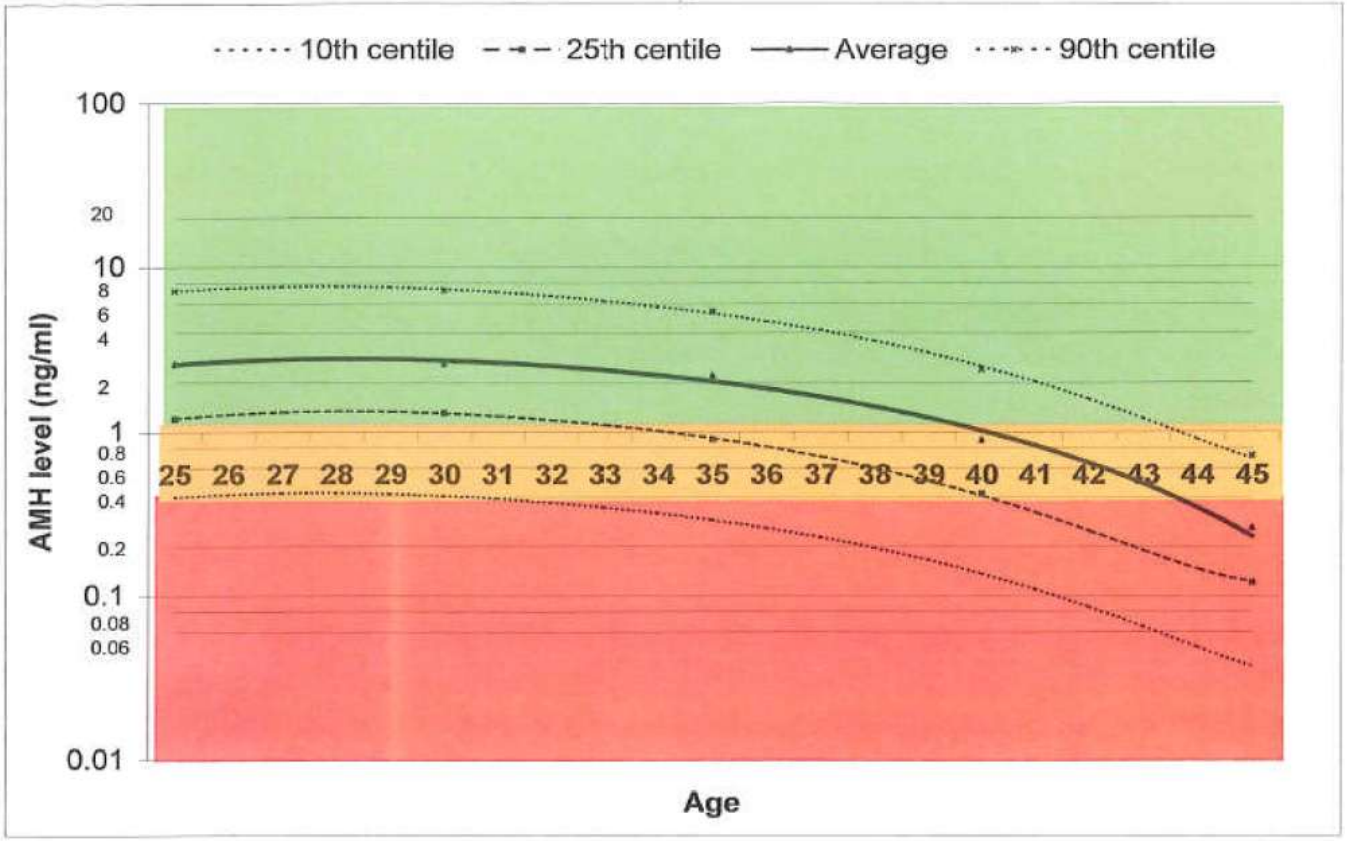


FIG. 1. Age-dependent AMH levels (●) plotted on a logarithmic scale to show more homogeneous variation (n = 144). The *solid line* indicates the smoothed estimate of mean AMH level as a function of age.

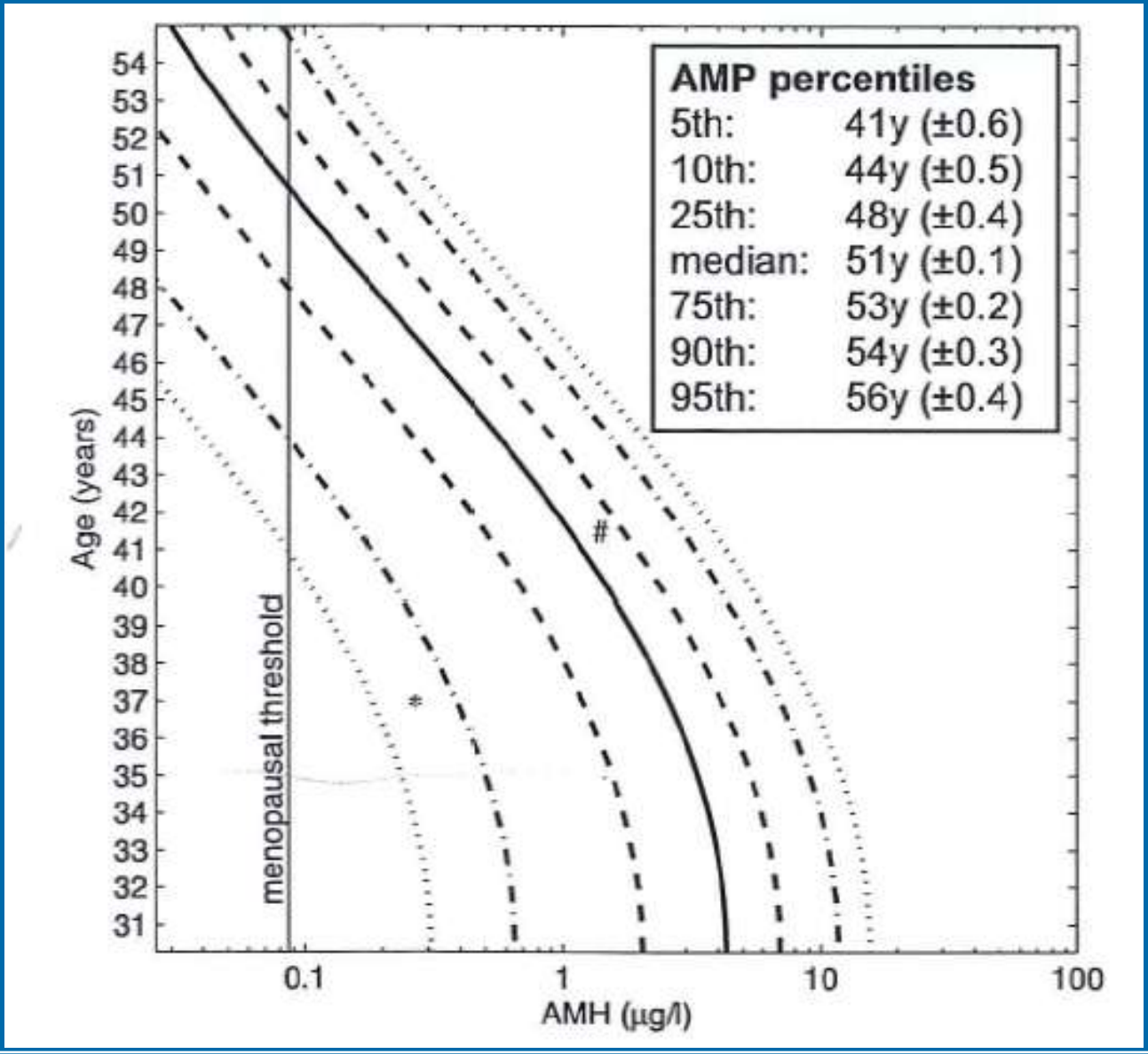
AMH

- Useful to assist in estimating likely age at menopause and consequently ovarian reserve
- Changes before FSH starts to rise
- Helpful in managing patients likely to hypo or hyperstimulate in response to gonadotrophin
- Current evidence doesn't support its use in determining clinical outcomes in treatment



Green zone	Above the 25th centile for younger, fertile women	Very likely normal ovarian reserve - age is the best predictor of your future fertility	80% chance of 6 or more eggs in IVF
Orange	Between the 25th and 10th centiles for younger, fertile women	Some women in this range will have reduced ovarian reserve	50% chance of 6 or more eggs in IVF
Red zone	Below the 10th centile for younger, fertile women	Very likely reduced ovarian reserve	20% chance of 6 or more eggs in IVF

Source: Fertility Associates



Source: van Disseldorp et al AMH Predicts Age at Menopause

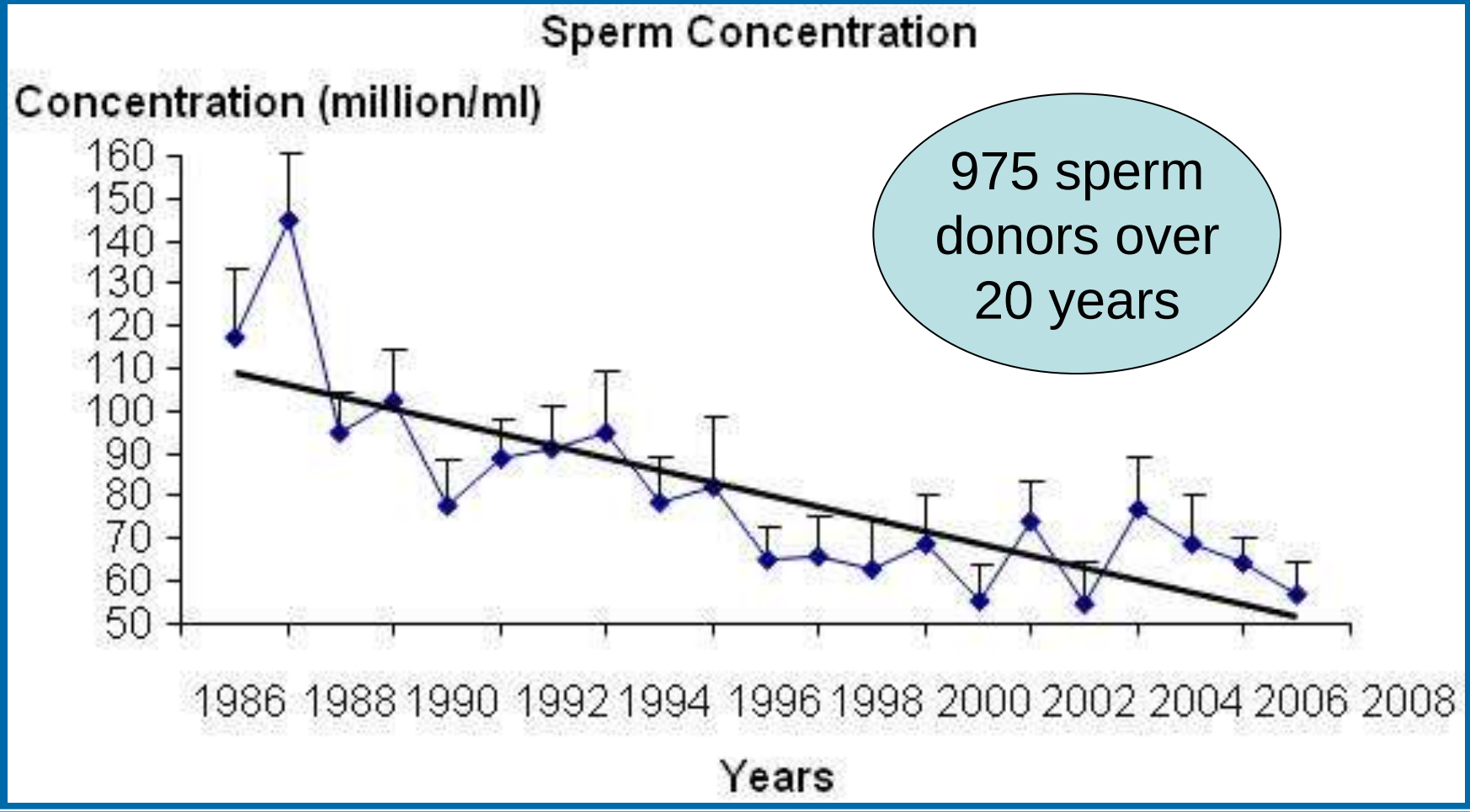
Effect of age on outcome

But what about men?

Some Facts about Ageing, Men and Sperm

- As men age the testes get smaller and softer, sperm morphology and motility tend to decline
- DNA fragmentation increases
- IVF pregnancy rate decreases as DNA fragmentation increases
- Paternal age >50 leads to doubling the chance of fetal death
- Paternal age >40 leads to increased rate of miscarriage independent of maternal age

Changes in sperm



Source: Fertility Associates – Rebecca Shine, Mary Birdsall, John Peek

Changes in sperm

- DNA fragmentation
  - Age
  - ROS – heat
  - Chemo and radiation
  - Environmental toxins
  - Higher in ejaculate than testicular sperm
- Tests
  - TUNEL
  - SCSA
  - HALO

Changes in sperm

Some Facts about Ageing, Men and Sperm

Conception rate adjusted for female age

Years	Rate
< 25	1.00
30-34	0.62
35-39	0.50
> 40	0.51

Some Facts about Ageing, Men and Sperm

Paternal age is a robust risk factor for the incidence of:

- Schizophrenia in offspring
  - At 45+ odds ratio 3.0 = 1:46 chance (Malaspina 2001)
  - Specific for schizophrenia
- Increase in autism
  - Compared with 30 years
  - >40 3 x the risk
  - >50 5 x the risk
- Increase in achondroplasia

Some Facts about Ageing, Men and Sperm

Effect of Weight on Infertility (Nguyen 2007)

Independent of sexual frequency, age, smoking

Normal weight	:	1.0
Overweight	:	1.2
Obese	:	1.36

Effect of Temperature on Infertility (U.S.C. study)

- Infertile men spend >30 mins / week in a hot tub
- Total motile sperm increased 490% at 3-6 months after stopping

Sperm retrieval for IVF

- Very few men in whom sperm are unobtainable
- PESA, TESA, TESE, biopsy, microsurgical biopsy
- Even in Klinefelter's Syndrome

Social consequences of reproductive ageing

- Altered family relationships
- Grandparents
- Have dependents at both end of life scale
- Increased requirements for state social support

The problem is a social one requiring a social solution

A new species?

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Source: Fertility Associates and Liggins Institute

Nutrition in fertility

- Clearly a factor in growth and development
- A factor in incidence of congenital abnormality
- Likely to be important in epigenetic influences
- Perhaps important in ‘ideal’ development

Blastocyst culture

Day 3
8 cell embryo

Day 5
Blastocyst

Day 6
Hatching

- A method for selection
- ‘Best’ embryos transferred
- Fewer transfers and same # of babies

Freezing things

- Embryos
- Eggs
- Sperm

Oocyte freezing – who might benefit?

- Prior to chemotherapy (not the only option)
- Prior to surgical management of endometriosis
- Mosaic Turners Syndrome
- Family history of early menopause (with early evidence)
- ‘Social’

Sperm freezing - who might benefit?

- Prior to chemotherapy
- Prior to vasectomy
- In men with family history of declining sperm counts
- ‘Social’

The future

- Sex for fun
- Insemination for conception
- IVF using frozen eggs for ‘insurance’

Ageing is bad for you and for your gametes

Ageing is a terminal disease

Think probability and time when considering referral

Young sperm is good sperm

Fresh sperm is good sperm

Bonk early and often

Thanks