

ESHRE Campus Symposium  
Modena, 2008

## Cost effectiveness of ART for women over 35

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A 21<sup>st</sup> century phenomenon?



In "marriages which had lasted five years or more, and in which the husbands were under 75 years of age, ... one marriage in 6.5 was unproductive".

J Y Simpson  
Survey of 495 British Peers, cited in Gibbons (1911)

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## Definition of infertility

What is 'normal' fertility?

- Of couples who will conceive spontaneously
  - 30% of couples conceive in the first month of trying
  - 90% do so within 1 year
  - 95% conceive within 2 years
- Therefore
  - Consider referral after 1- 2 years
  - *Earlier if there is an obvious problem or advancing female age*

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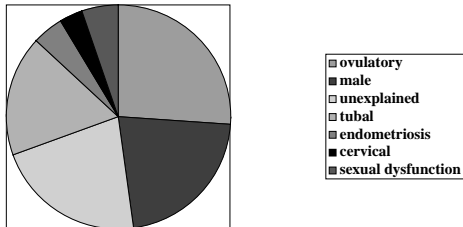
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## Causes of infertility



Hull et al, 1985

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## The business of ART

- ~ £3000 - £8000 per IVF cycle in UK
- ~ 40000 treatments in UK last year
- ~ 25% NHS funded
- > £100 million annual turnover in UK
- > US\$ 1000 million in USA
- ~ 3 million IVF babies Worldwide
- ~ 1 million IVF cycles per year

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“Unexplained” infertility as a consequence of deferring childbirth

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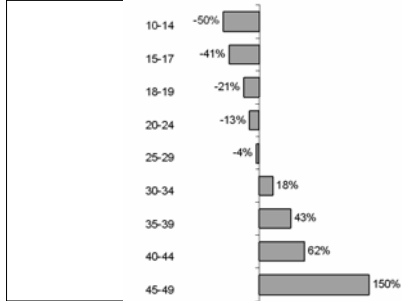
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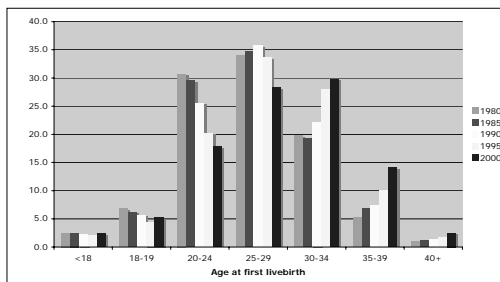
## USA: Changing approaches to childbirth

Infertility Age Birth Rate (%Change)



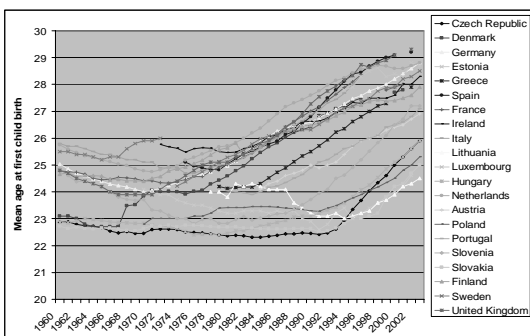
Source: National Vital Statistics Reports, Vol 55, No 1, September 29, 2006

## UK: Changing approaches to childbirth



UK Office of National Statistics, 2004

## Mean age at first child birth



Eurostat database

## Low fertility and population ageing in Europe

- Reasons for the decline in European fertility include
  - High unemployment for young adults
  - High housing costs
  - Young adults living at home for longer
- National policy can slow fertility decline (e.g. in France)
- Policies aimed indirectly at fertility may have beneficial effects
- The prevalence of age related involuntary infertility is likely to rise in the next decade

Grant et al, 2004

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## Can IVF solve the problem for the older patient?

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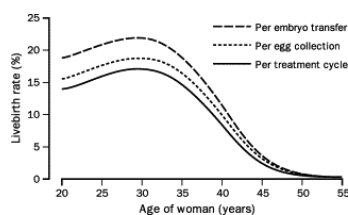
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## Can IVF solve the problem for the older patient?

Not in 1994



Templeton, 1996, Nikolau & Templeton, 2004

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Can IVF solve the problem for the older patient?

Not in 2008

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UK HFEA national statistics

Female age	< 35 years	35 - 37	38 - 39	40 - 42
Live birth rate per cycle started	28.2%	23.6%	18.3%	10.6%

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UK HFEA national statistics

Chance of livebirth after transfer of frozen embryos

Frozen		Below 35	35-37	38-39	40-42	Over 42
	Thaw cycles	17.9% (578/3233)	15.5% (280/1842)	12.3% (150/973)	10.2% (72/707)	10.0% (20/200)

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## Biology of ovarian ageing

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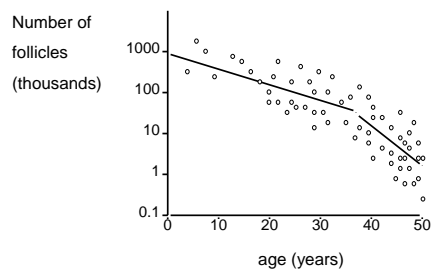
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## Follicle depletion from birth to menopause



Faddy et al, 1992

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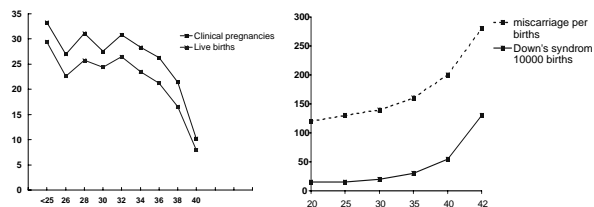
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## Consequences of declining egg 'quantity' and egg 'quality'




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### Miscarriage, aneuploidy and the aging ovary

karyotype of stillbirth      <20, 1.3%    >40, 35.8%

abnormal karyotype in    <35, 25%    >35, 47%  
IVF oocytes

aneuploidy in STOP      <25, <20%    >40, 67%  
tissue

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### Livebirth rate per embryo transfer following transfer of embryos from own or donated oocytes

Age	Live birth rate per embryo transfer	
	Own oocyte	Donor oocyte
< 29	23.7%	21.6%
30 - 34	21.9%	28.2%
35 - 39	17.6%	26.0%
40 - 44	8.1%	18.8%
> 44	3.5%	22.0%

Templeton & Parslow 1996

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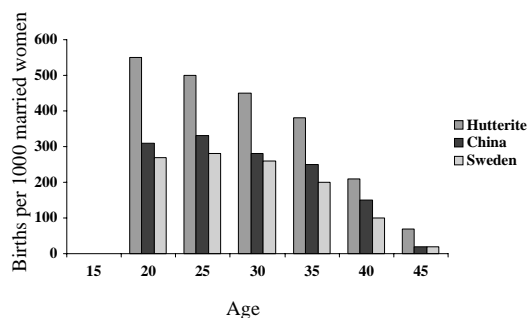
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### Effect of female age on birthrate




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UK National Institute for Health and Clinical Excellence recommends.....

- Optimal female age range for IVF treatment is 23-39 years
- The chance of a live birth following IVF treatment is consistent for the first three cycles, therefore....
- Couples in which the woman is 23-39 years at the time of treatment and who have an identified cause for their fertility problems or who have unexplained infertility of at least three years duration should be offered up to three stimulated cycles of IVF treatment

January 2004

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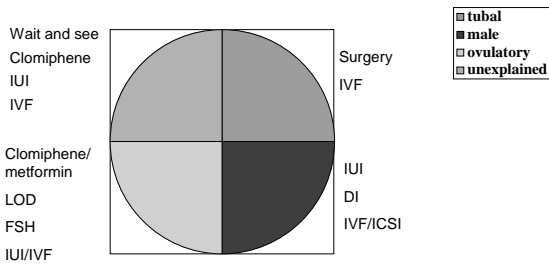
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### What to do about age related infertility?




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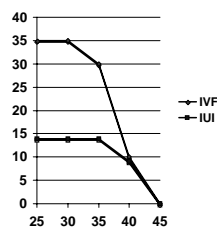
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### Most cost effective 'first line' treatment for infertility

- Tubal disease/endometriosis
  - Severe - IVF, mild - surgery
- Anovulation
  - Medical treatment (LOD)
- Male factor
  - (UI/DI)
- Unexplained infertility
  - IUI



York University Health Economics Consortium  
(Data from RCOG Guidelines)

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### What is the true cost of IVF?

- Detailed costing of all aspects of IVF cycle
  - Staff costs
  - Consumables
  - Premises
  - Heating/ lighting etc
- Low dose predominantly GnRH antagonist protocol
- Formulary costs of drugs

Ledger et al (unpublished)

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### Cost effectiveness of IVF

- £2950 per cycle at age 30
- £3350 per cycle at 40
  - Higher requirement for gonadotropins
  - More monitoring
  - More cycle cancellations
- Cost per baby at age 30
  - £9033
- Cost per cycle at age 40
  - £33500

Ledger et al (unpublished)

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### Scandinavia - cost per live birth at female age 35

Sweden	£10,295
Denmark	£11,858
Norway	£13,413
Finland	£11,211
Iceland	£7,400

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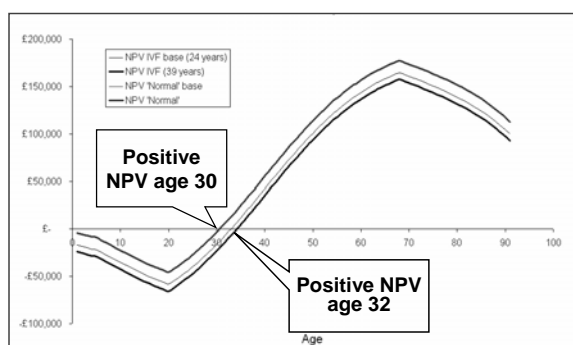
But.... cost effectiveness for patients over 40

Cost per livebirth will increase with

- higher doses of gonadotropins
- adjuvant therapies
- additional embryology costs
  - assisted hatching
  - preimplantation genetic screening

Cost effectiveness from a demographic perspective

NPV estimates- base case



Cost effectiveness of ART for  
the older patient?

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Spend more to....

Improve the number of oocytes?  
Heroic doses of gonadotropins?

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Spend more to....

Improve uterine blood flow?  
Sildenafil, aspirin?

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Spend more to....

Improve endometrial receptivity?  
IVIG, heparin?

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Spend more to....

Improve embryo quality?  
Preimplantation genetic screening?

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Spend more to....

Increase the 'hit' rate  
Replace more embryos?

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Spend more to....

Use some-one else's eggs  
Donor oocyte?

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Spend more to....

'Store' fertility for later?  
Egg or embryo freezing for younger women?

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Or spend more to....

Encourage women to plan to complete their family  
before age 40?

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## Conclusion

- Conventional IVF is rarely successful for women over 40
- This has a large negative impact on the cost effectiveness of IVF in this age group
- Despite much research there are few interventions that significantly increase the chances of livebirth for these patients
- Oocyte donation is successful but, in most cases, not supported by State funding

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Thank you

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