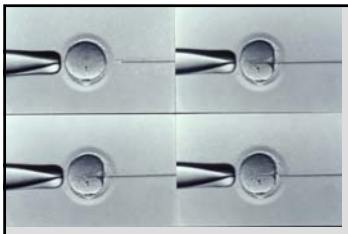


ART@ work

Indications for IVF and ICSI

Professor Allan Templeton

University of Aberdeen

ESHRE, Brussels 2007

Indications for ICSI

- **Too few or dysfunctional sperm**
- **Ejaculated, surgically recovered, cryopreserved**
- **Uncertainty (half oocytes)**
- **Previous fertilisation failure**
- **Non-male factor infertility**
- **Unexplained infertility**
- **PGD**
- **Recurrent miscarriage**

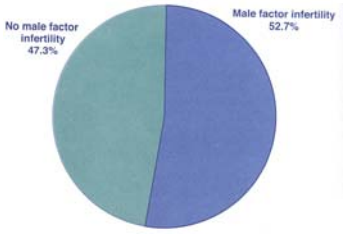
ART in European countries 2002

	Number of cycles (in thousands)	% ICSI
Germany	68.9	57
France	46.7	54
UK	27.6	42
Italy	15.3	58
Netherlands	14.7	35
Spain*	10.7	76
Belgium	8.9	65
Denmark	9.5	39
Sweden	8.9	39
Russia*	7.3	26
Finland	4.3	39
(US	122.9	56)

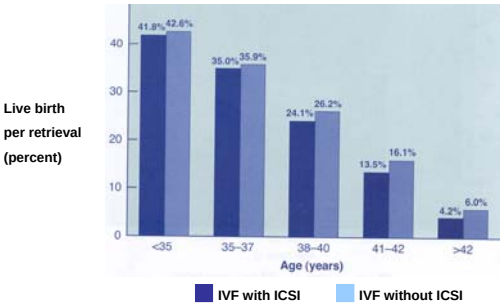
* Highest/Lowest

ESHRE, 2006

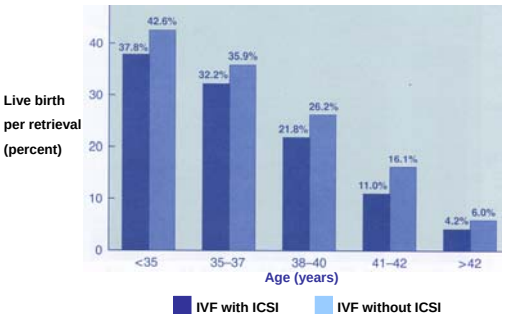
Proportion of ICSI cycles with diagnosis of male factor infertility (US 2003)



Livebirth rates comparing male factor treated with ICSI and IVF without ICSI, US 2003



IVF and ICSI compared in couples not diagnosed with male factor, US 2003



Deliveries per aspiration in Europe, 2002

	IVF %	ICSI %
Belgium	19	17
Finland	20	20
France	17	18
Germany	15	17
Italy	21	20
Spain	22	22
Sweden	24	24
UK	23	24

ESHRE, 2006

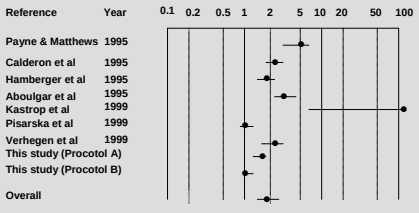
Review of studies comparing IVF and ICSI where indication was borderline semen characteristics

	IVF	ICSI	RR
Fertilisation rate %	36	63	1.9 (1.4 – 2.5)
Fertilisation failure %	34	3	7.5 (3 – 20)

NNT was 3.1 (2 – 12)

Tournaye *et al*, 2002

IVF and ICSI compared in patients with moderate male infertility



Tournaye *et al*, 2002

Two trials where isolated teratozoospermia was problem

	IVF %	ICSI %	RR
Fertilisation rate	57	63	1.1 (0.8 – 1.7)
Fertilisation failure	14	6	2.0 (0.6 – 6.8)

NNT was 12.0 (5 - 35)

Tournaye *et al*, 2002

Fertilisation failure after IVF and ICSI in unexplained and borderline semen infertility

	IVF	ICSI
Unexplained infertility (n = 60)	10	0
Borderline semen (n = 50)	2	1

Herschlag *et al*, 2002

Fertilisation failure after IVF and ICSI in unexplained and borderline semen infertility

	IVF	ICSI
Unexplained infertility (n = 60)	10	0
Borderline semen (n = 50)	2	1

"failed fertilisation after IVF will be a cycle-specific, non-repetitive occurrence … such cases should be treated as occult male-factor infertility"

Herschlag *et al*, 2002

IVF and ICSI in 106 couples with borderline semen – a randomised study using sibling oocytes

	n	%
Fertilisation after both IVF and ICSI	78	73
Fertilisation after ICSI only	26	25
Fertilisation failure	2	2

Van der Westerlaken *et al*, 2006

Comparison of IVF and ICSI in one centre

	IVF n = 478	ICSI n = 271
Fertilisation failure % (95% CI)	2.1 1.0 – 3.8	1.5 0.04 – 3.8

Ola *et al*, 2001

Cost analysis of benefit of ICSI

100 cases to gain extra pregnancy with ICSI (NNT) at a cost of £60K (CNT) for which 29 cycles of IVF could be funded (BIA)

Ola *et al*, 2001

Failed fertilisation after ICSI (n=1779 cycles)

Complete failure **1.3%**

Number of MII oocytes
Increasing patient age

Esfiandiari et al, 2005

Total fertilisation failure in non-male factor infertility. Review of four studies

	Aboulgar	Khamsi	Ruiz	Jun
Cycles (n)	22	35	70	103
Fertilisation failure %				
IVF	23	14	11	7
ICSI	0	1	0	0

Khamsi *et al*, 2000

Fertilisation rate in sibling oocytes allocated to IVF or ICSI in 35 women

	IVF	ICSI
Fertilisation Rate %	57	71
Good quality embryo per assigned oocyte	47	64

Khamsi *et al*, 2001

Comparison of IVF and ICSI in 70 patients with unexplained infertility

	IVF	ICSI
Fertilisation Rate (% oocytes)	54	60
Fertilisation Failure (% cycles)	11	0

Ruiz *et al*, 1997

Comparison of sibling oocytes among patients with tubal disease and normal semen

	IVF	ICSI
Fertilisation failure %	12.5	3.6
(95% CI	5 – 24	0.4 – 12)

Staessen *et al*, 1999

IVF and ICSI in sibling oocytes from patients with PCOS (60 cycles, 1089 COC)

	IVF (n=541)	ICSI (n=548)
Fertilisation rate (%)	45	72
Fertilisation failure (%)	9	0

Hwang et al, 2005

Systematic review by van Rumste *et al* (2003)

- Identified 15 controlled studies
- Eight excluded for randomising oocytes
- Three studies used non-random methods. Three excluded for other reasons
- Identified one study which showed no difference in pregnancy rates
- Concluded use of ICSI for non-male factor infertility remains an open question
- Further research should report livebirth rates and adverse events

Cochrane, 2006

Comparison of IVF and ICSI in non-male infertility (435 cycles)

	IVF (n = 209)	ICSI (n = 206)	95% CI diff
Fertilisation Rate (% retrieved)	58	47	9 to 15
Fertilisation Rate (% injected)	58	65	-10 to -4
Fertilisation Failure (% cycles)	5	2	-0.3 to 7.5

Bhattacharya *et al*, 2001

Comparison of IVF and ICSI in non-male infertility (435 cycles)

	IVF (n = 219)	ICSI (n = 204)	RR (95% CI)
Implantation Rate %	30	22	1.4 (1 – 1.8)
Clinical Pregnancy %	33	26	1.3 (1 – 1.7)

Bhattacharya *et al*, 2001

Subgroup analysis among 100 patients with unexplained infertility

	IVF	ICSI	95% CI diff
Fertilisation Rate (% retrieved)	61	50	5 to 17
Fertilisation Rate (% inseminated)	61	70	2 to 14
Fertilisation Failure (n)	1	0	

Bhattacharya *et al*, 2001

Should ICSI be used for non-male factor infertility?

ICSI has become increasingly popular … and is being adopted … for non-male factor indications. This has arisen because of increasing expectations from infertile couples… moreover the removal of the cumulus cells … more direct feedback on the quality of the stimulation … giving poor morphology oocytes … a much higher chance of success.

In summary both the safety and the scientific viewpoints strongly support the use of ICSI for all indications … confident it will replace other methods.

Orief, 2004

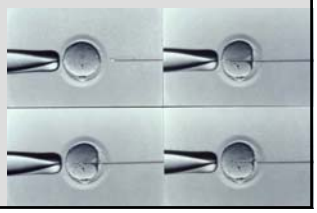
Retrospective analysis of ICSI for non-male factor infertility in 696 couples

	IVF (n=597)	ICSI (n=99)
Oocytes fertilised (n)	6.6	5.1
Fertilisation rate (%)	74	69
Fertilisation failure (%)	3.2	4.0
Live birth rate (%)	22	17

Kim et al, 2007

- Too few or dysfunctional spermatozoa
- Uncertainty about fertilisation (half oocytes)
- PGD

NOT Unexplained or non-male factor infertility



ICSI cycles in Europe

	% ICSI cycles
Spain	76
Belgium	65
Germany	57
UK	42
Sweden	39
Russia	26

ESHRE 2006