



THE UNIVERSITY OF
WESTERN AUSTRALIA
Achieving International Excellence

Fertility options for women with premature ovarian insufficiency (POI) ⁴⁵



Roger Hart

Professor of Reproductive Medicine, UWA, Australia

Fertility Specialists of Western Australia & National Medical
Director of City Fertility



City Fertility

Global CHA IVF Partners

fertilityspecialists
of Western Australia



Disclosures

- National Medical Director of City Fertility
- Medical Director of Fertility Specialists of Western Australia
- Equity interests in CHA SMG
- Educational grant support from MSD, Merck KGaA, and Ferring Pharmaceuticals



What we will cover



THE UNIVERSITY OF
WESTERN AUSTRALIA
Achieving International Excellence

Causes of POI

Egg freezing and IVF in the setting of a limited ovarian reserve

- *unrewarding / unethical?*

Potential for natural conception?

Egg donation treatment



City Fertility

Global CHA IVF Partners

fertilityspecialists
of Western Australia



Causes of POI

- Majority are 'idiopathic'
 - Strong familial link
- Must exclude karyotypic abnormality + Fragile X pre-mutation
- Chemo/radio treatment
- Ovarian surgery- particularly treatment of endometrioma





POI facts

1. POI- Menopause occurring before 40 years (4%)
2. Early menopause- occurs before 45 years (12%)
3. More frequent in low resource countries
4. Significant implications for health, *as well as fertility (Jean Hailes)*
 - Increased risk of cardiovascular disease (50% ↑ cardiovascular event risk)
 - Bone demineralization (50% ↑ fracture risk)
 - All cause mortality increased
 - Quality of life linked to menopausal symptoms
 - Dementia risk not clarified

So should we offer IVF or egg freezing?



THE UNIVERSITY OF
WESTERN AUSTRALIA
Achieving International Excellence

- Depends on the ovarian reserve- antral follicle count or serum AMH
 - Most patients it would be very unrewarding / unethical



Low antral follicle count

vs



high antral follicle count



City Fertility

Global CHA IVF Partners

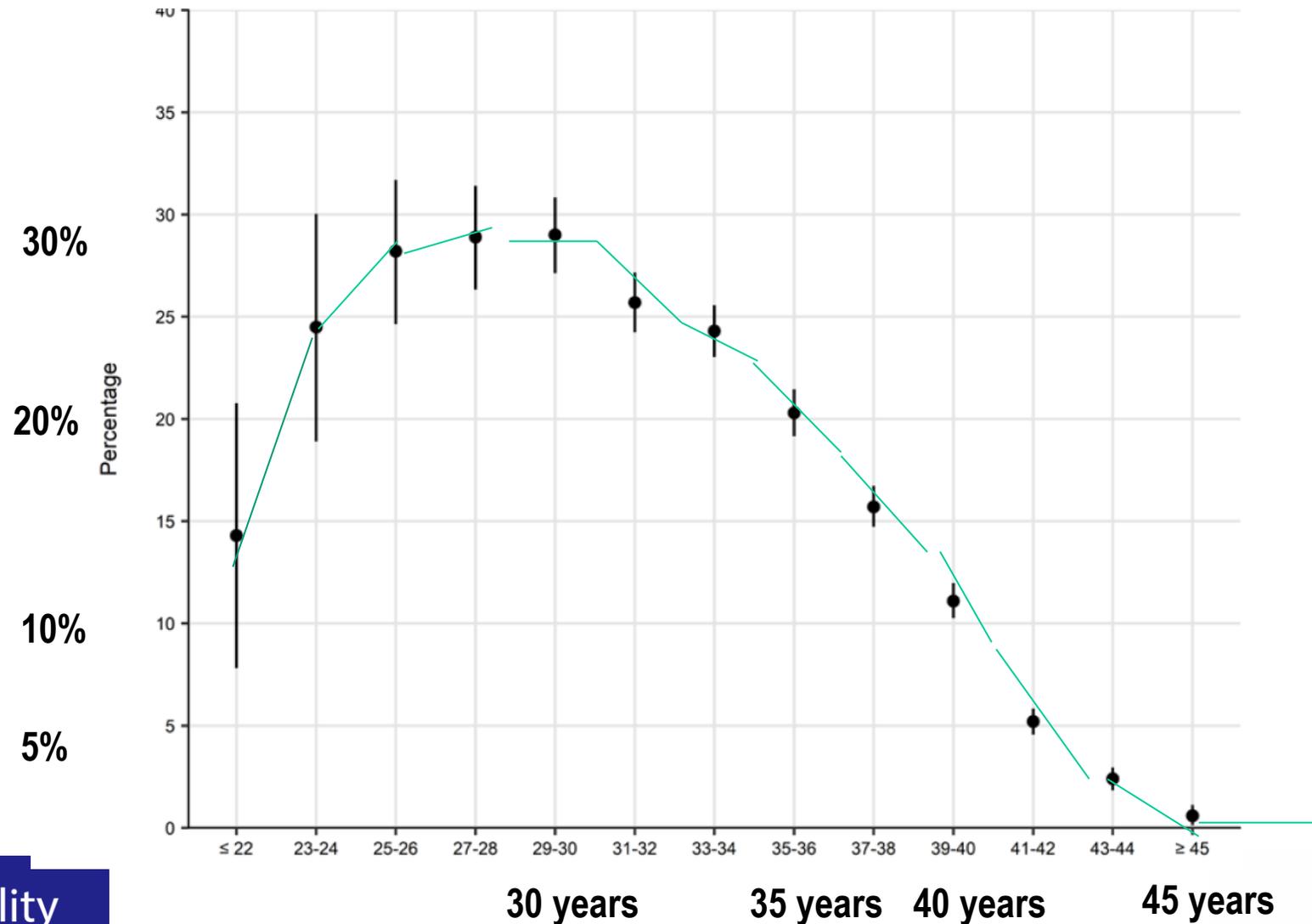
fertilityspecialists
of Western Australia



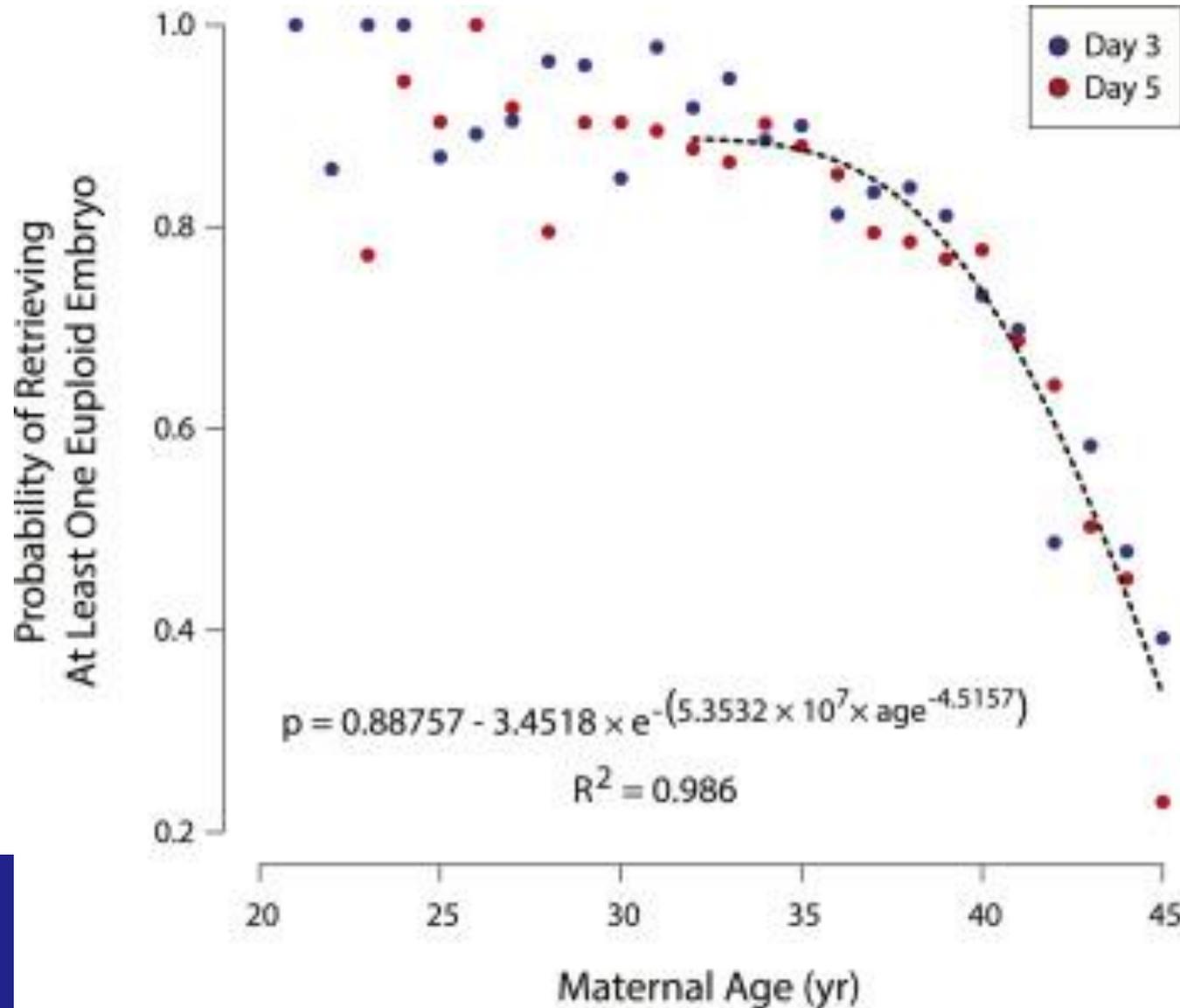
- Before proceed- we must know what 'normal' is..



Chance of livebirth through IVF by age-



For the average patient (normal ovarian reserve) the chance of achieving a chromosomally normal embryo is significantly reduced for women >37 years of age – Demko 2016



City Fertility

Global CHA IVF Partners



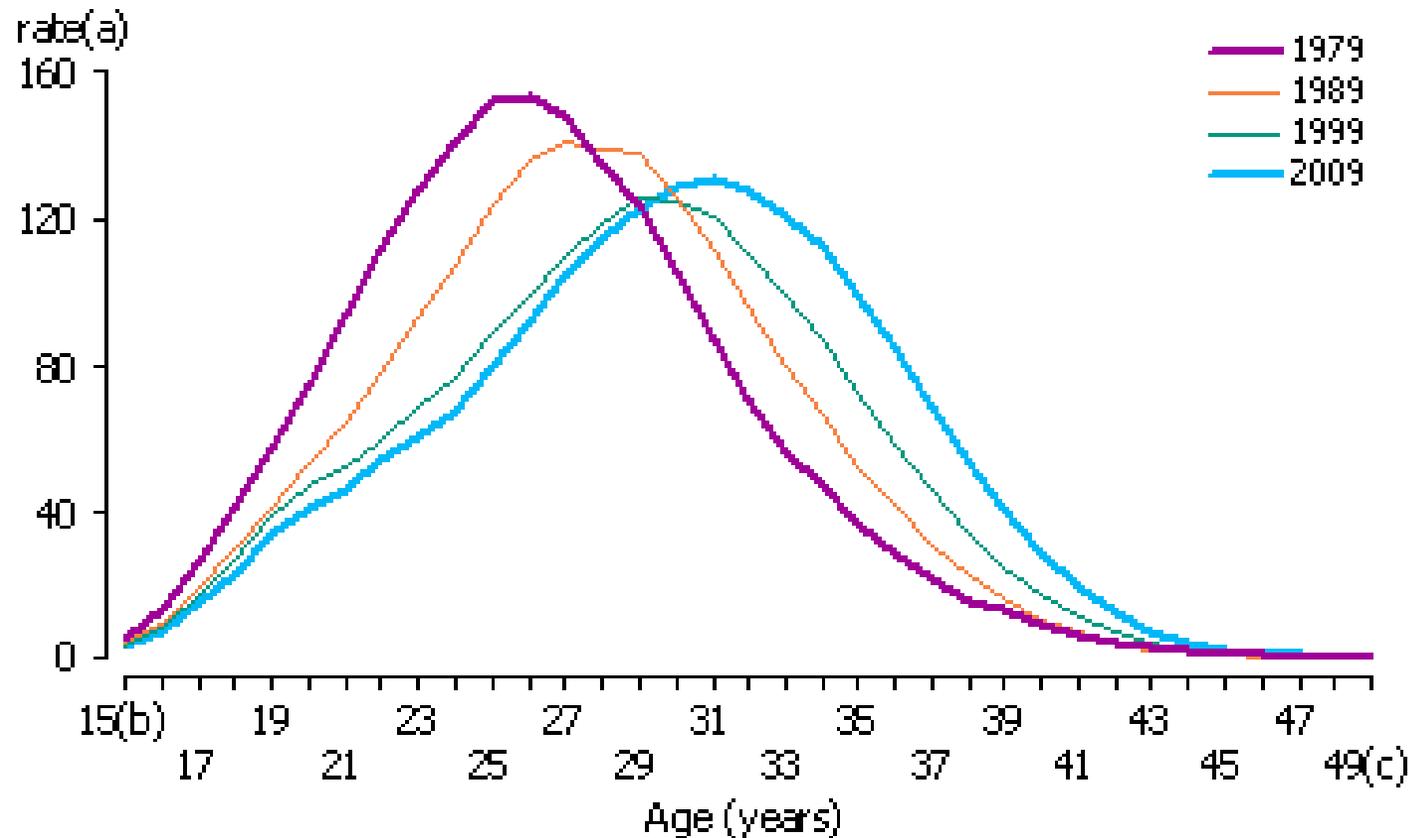


Infertility at the natural age of the perimenopause

- Unfortunately -this is a natural process
- Options
 - IVF *success aged 45yrs 1% per cycle*
 - *Risks of miscarriage, obstetric complications and chromosomal abns*
 - *Plus male age significant influence*
 - *Egg donation treatment –still have the obs risks irrespective of egg age*



increasingly we are postponing the time to start planning to conceive
–*chance more women will present with reduced ovarian reserve and incipient POI*



-increasing by 2 years every decade

Source: ABS Birth registrations collection

But- Younger women going through early menopause
- different to at the usual age



THE UNIVERSITY OF
WESTERN AUSTRALIA
Achieving International Excellence



City Fertility

Global CHA IVF Partners

fertilityspecialists
of Western Australia

Younger women going through early menopause
- different to at the usual age



THE UNIVERSITY OF
WESTERN AUSTRALIA
Achieving International Excellence

Devastating realisation that this is the cause of infertility

Why IVF isn't the solution?



City Fertility

Global CHA IVF Partners

fertilityspecialists
of Western Australia

Younger women going through early menopause
- different to at the usual age



THE UNIVERSITY OF
WESTERN AUSTRALIA
Achieving International Excellence

Devastating realisation that this is the cause of infertility

Why IVF isn't the solution?

Chance of euploid oocyte by age

Consideration of natural conception?



City Fertility

Global CHA IVF Partners

fertilityspecialists
of Western Australia



Younger women going through early menopause
- different to at the usual age

Devastating realisation that this is the cause of infertility

Why linked to infertility?

Chance of euploid oocyte by age

Consideration of natural conception?

Potential to catch an ovulation

Family size





Younger women going through early menopause
- different to at the usual age

Devasting realisation that this is the cause of infertility

Why linked to infertility?

Chance of euploid oocyte by age

Consideration of natural conception?

Potential to catch an ovulation

Family size

Egg donation treatment

Logistics / cost /Processes



Fertility is compromised even when young



THE UNIVERSITY OF
WESTERN AUSTRALIA
Achieving International Excellence

Chance of conceiving spontaneously, in the next cycle, by age

Sozoue and Hartshorne PLoS 2012



City Fertility

Global CHA IVF Partners



Fertility chances



THE UNIVERSITY OF
WESTERN AUSTRALIA
Achieving International Excellence

Chance of conceiving spontaneously, in the next cycle, by age

Age 3 months

25	18%
30	16%
35	12%
40	7%

Sozoue and Hartshorne PLoS 2012



City Fertility

Global CHA IVF Partners





In 30s fertility is compromised

Chance of conceiving spontaneously, in the next cycle, by age

	Age 3 months	6 months
25	18%	15%
30	16%	13%
35	12%	9%
40	7%	5%

Sozoue and Hartshorne PLoS 2012



City Fertility

Global CHA IVF Partners

Fertility chances



Chance of conceiving spontaneously, in the next cycle, by age

	Age 3 months	6 months	12 months
25	18%	15%	10%
30	16%	13%	9%
35	12%	9%	6%
40	7%	5%	3%

Sozoue and Hartshorne PLoS 2012



City Fertility

Global CHA IVF Partners

Fertility chances



Chance of conceiving spontaneously, in the next cycle, by age

	Age 3 months	6 months	12 months	36 months
25	18%	15%	10%	3%
30	16%	13%	9%	2%
35	12%	9%	6%	1%
40	7%	5%	3%	0.5%

Sozoue and Hartshorne PLoS 2012



City Fertility

Global CHA IVF Partners



What positives can we draw?

- That a young woman – irrespective of her ovarian reserve has a reasonably good chance of conception
- Often the challenge is trying to ‘catch’ that infrequent ovulation
- *Plus* often compounded by a poor luteal phase & into pregnancy



Consider egg freezing *attracts a Medicare rebate-* (different to 'social egg' freezing)



THE UNIVERSITY OF
WESTERN AUSTRALIA
Achieving International Excellence

- *Reproductive insurance*



Oocyte vitrification-
*Increasingly being used for
Social indications –reliable*



City Fertility

Global CHA IVF Partners



What is egg freezing?



THE UNIVERSITY OF
WESTERN AUSTRALIA
Achieving International Excellence



Gonadotrophin injections



City Fertility
Global CHA IVF Partners

fertilityspecialists
of Western Australia

What is egg freezing?

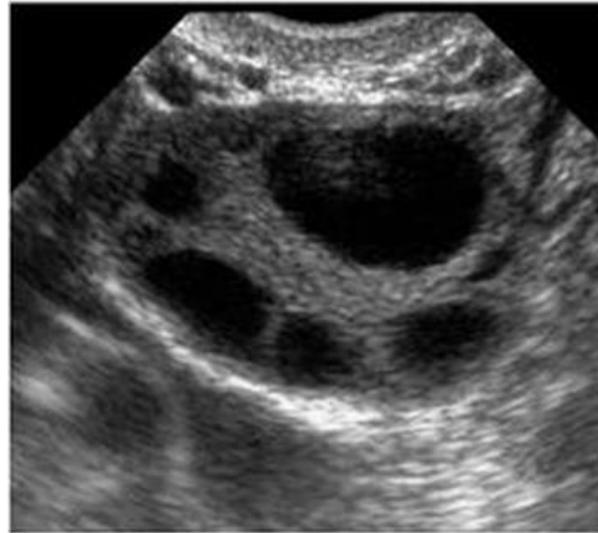


THE UNIVERSITY OF
WESTERN AUSTRALIA
Achieving International Excellence



Gonadotrophin injections

Close cycle monitoring



City Fertility

Global CHA IVF Partners

fertilityspecialists
of Western Australia

What is egg freezing?

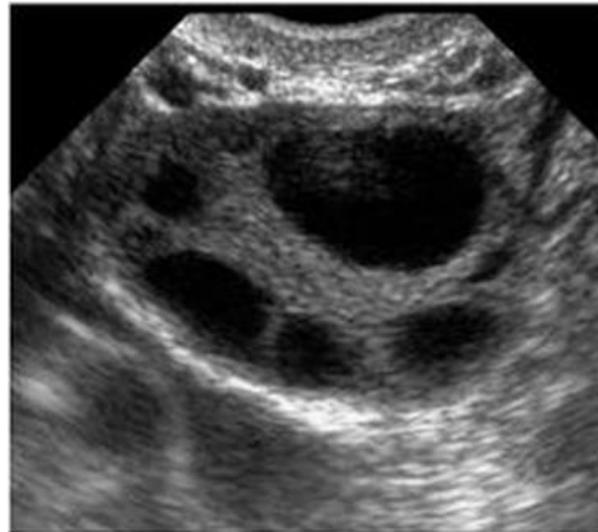


THE UNIVERSITY OF
WESTERN AUSTRALIA
Achieving International Excellence



Gonadotrophin injections

Close cycle monitoring



Oocyte retrieval



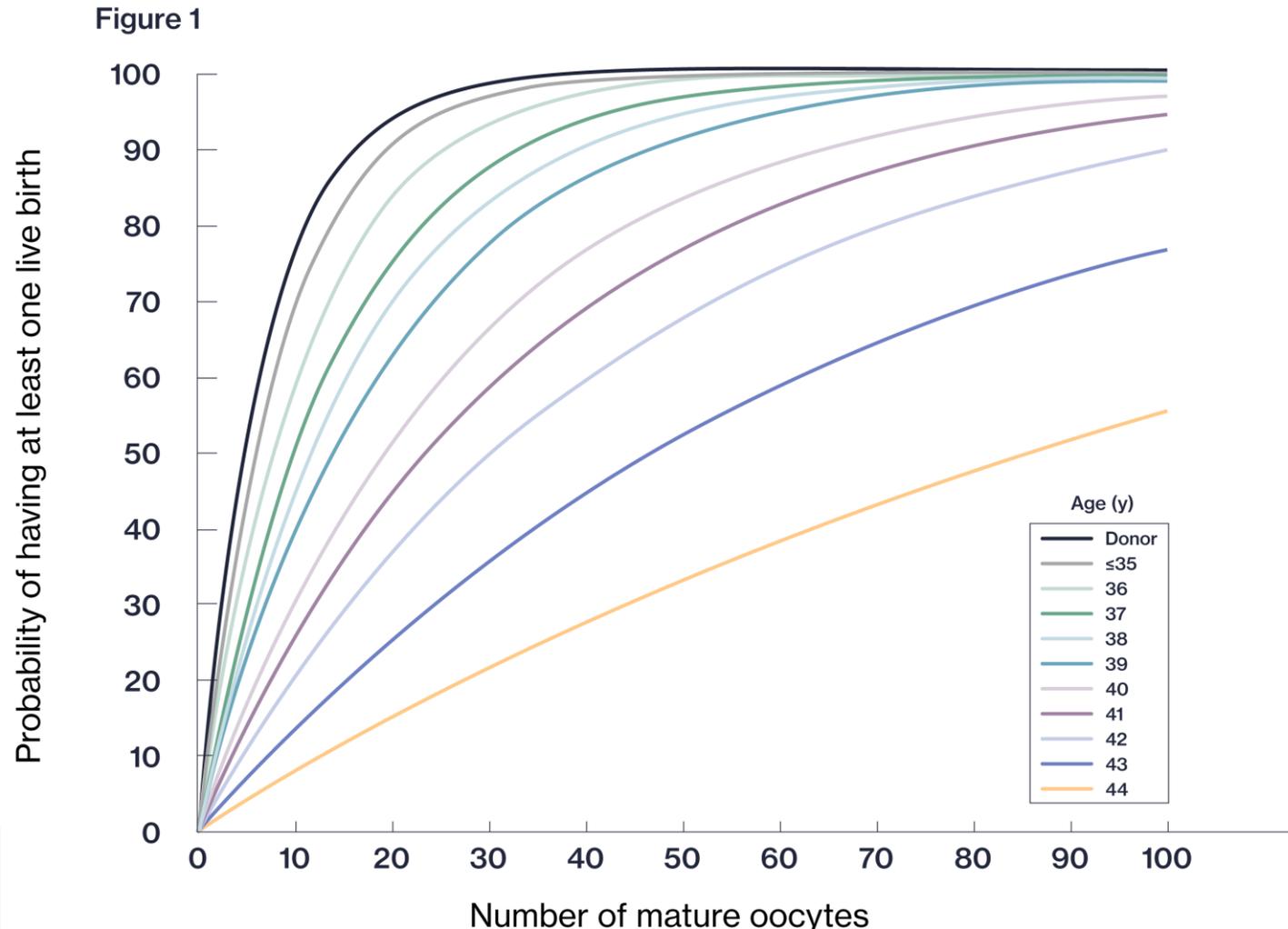
City Fertility

Global CHA IVF Partners

Specialists
of Western Australia



How many eggs are needed by age?



Goldman 2017 <https://doi.org/10.1093/humrep/dex008>

Source: Goldman et al.



City Fertility

Global CHA IVF Partners



Fertility Preservation for women with cancer

- all cancer therapies have potential harmful effects, depending on
 - chemotherapy agent
 - cumulative dose
 - duration of treatment
 - age at treatment

Also could be considered for;

recurrent ovarian cysts & severe endometriosis

requirement for aggressive systemic medication

POI



City Fertility

Global CHA IVF Partners

Effect of 1 -3 cycles of chemo



TABLE 1

IVF outcome in cancer patients during (patients 1–4) or before (patients 5–11) chemotherapy.

Patient	Age (y)	Pathology
1	32	NHL
2	22	AML
3	26	AML
4	24	ALL
5	31	MA
6	24	HL
7	28	HL
8	33	NHL
9	25	BOT
10	26	HL
11	26	OC II

Note: ALL: acute lymphoblastic leukemia; AML: acute myoblastic leukemia; BOT: borderline ovarian tumor; HL: Hodgkin's lymphoma; MA: medullar aplasia; NHL: non-Hodgkin's lymphoma; OC II: ovarian carcinoma, stage II.

^a One regimen of ACVBP (adriamycin, cyclophosphamide, vincristine, bleomycin, prednisone).

^b Two regimens of cytarabine and idarubicin.

^c One regimen of COP followed by two regimens of COPADM (cyclophosphamide, oncovin, prednisone, adriamycin, methotrexate).

Dolmans. Efficacy of IVF after chemotherapy. Fertil Steril 2005.



Effect of 1 -3 cycles of chemo



TABLE 1

IVF outcome in cancer patients during (patients 1–4) or before (patients 5–11) chemotherapy.

Patient	Age (y)	Pathology	Chemotherapy before IVF
1	32	NHL	1 regimen ^a
2	22	AML	2 regimens ^b
3	26	AML	2 regimens ^b
4	24	ALL	3 regimens ^c
5	31	MA	0
6	24	HL	0
7	28	HL	0
8	33	NHL	0
9	25	BOT	0
10	26	HL	0
11	26	OC II	0

Note: ALL: acute lymphoblastic leukemia; AML: acute myoblastic leukemia; BOT: borderline ovarian tumor; HL: Hodgkin's lymphoma; MA: medullar aplasia; NHL: non-Hodgkin's lymphoma; OC II: ovarian carcinoma, stage II.

^a One regimen of ACVBP (adriamycin, cyclophosphamide, vincristine, bleomycin, prednisone).

^b Two regimens of cytarabine and idarubicin.

^c One regimen of COP followed by two regimens of COPADM (cyclophosphamide, oncovin, prednisone, adriamycin, methotrexate).

Dolmans. Efficacy of IVF after chemotherapy. Fertil Steril 2005.



Effect of 1 -3 cycles of chemo



TABLE 1

IVF outcome in cancer patients during (patients 1–4) or before (patients 5–11) chemotherapy.

Patient	Age (y)	Pathology	Chemotherapy before IVF	Oocytes
1	32	NHL	1 regimen ^a	6
2	22	AML	2 regimens ^b	0
3	26	AML	2 regimens ^b	0
4	24	ALL	3 regimens ^c	0
5	31	MA	0	10
6	24	HL	0	13
7	28	HL	0	25
8	33	NHL	0	8
9	25	BOT	0	12
10	26	HL	0	11
11	26	OC II	0	9

Note: ALL: acute lymphoblastic leukemia; AML: acute myoblastic leukemia; BOT: borderline ovarian tumor; HL: Hodgkin's lymphoma; MA: medullar aplasia; NHL: non-Hodgkin's lymphoma; OC II: ovarian carcinoma, stage II.

^a One regimen of ACVBP (adriamycin, cyclophosphamide, vincristine, bleomycin, prednisone).

^b Two regimens of cytarabine and idarubicin.

^c One regimen of COP followed by two regimens of COPADM (cyclophosphamide, oncovin, prednisone, adriamycin, methotrexate).

Dolmans. Efficacy of IVF after chemotherapy. Fertil Steril 2005.



Effect of 1 -3 cycles of chemo



TABLE 1

IVF outcome in cancer patients during (patients 1–4) or before (patients 5–11) chemotherapy.

Patient	Age (y)	Pathology	Chemotherapy before IVF	Cryopreserved embryos
1	32	NHL	1 regimen ^a	1
2	22	AML	2 regimens ^b	0
3	26	AML	2 regimens ^b	0
4	24	ALL	3 regimens ^c	0
5	31	MA	0	6
6	24	HL	0	10
7	28	HL	0	11
8	33	NHL	0	5
9	25	BOT	0	5
10	26	HL	0	4
11	26	OC II	0	4

Note: ALL: acute lymphoblastic leukemia; AML: acute myoblastic leukemia; BOT: borderline ovarian tumor; HL: Hodgkin's lymphoma; MA: medullar aplasia; NHL: non-Hodgkin's lymphoma; OC II: ovarian carcinoma, stage II.

^a One regimen of ACVBP (adriamycin, cyclophosphamide, vincristine, bleomycin, prednisone).

^b Two regimens of cytarabine and idarubicin.

^c One regimen of COP followed by two regimens of COPADM (cyclophosphamide, oncovin, prednisone, adriamycin, methotrexate).

Dolmans. Efficacy of IVF after chemotherapy. Fertil Steril 2005.





Long-term consequences

No evidence in women of increase in oocyte aneuploidy or increase in miscarriage or fetal malformations post chemotherapy.





Cancer patient recommendations

- All patients should be warned regarding the implications of their cancer treatment on their fertility
 - National Institute for Health and Clinical Excellence (NICE) and ASCO.
- If feasible should be offered opportunity to discuss the implications with fertility expert



What options exist for a woman with POI



THE UNIVERSITY OF
WESTERN AUSTRALIA
Achieving International Excellence

1. Try to 'catch' a natural ovulation- *may be 'few and far between'*

Relies on partner 'availability' – FIFO challenge

Need patent fallopian tube and normal semen parameters

Usually significant impairment to luteal phase, requiring support

Different to menopause at natural age as euploid oocytes commoner

2. Egg donation treatment

Expensive

'Anonymous' or known donation

3. Embryo donation treatment

Availability of embryos



Take-home messages

1. There maybe an opportunity to freeze-eggs
2. The success of any fertility treatment in the 40's is very low
Devastating, that the only recourse is oocyte donation treatment
3. A young woman going through going through the menopause- doubly devastating
However, she may have an opportunity to spontaneously conceive although her family size will be limited further compounding her distress

Thanks



THE UNIVERSITY OF
WESTERN AUSTRALIA
Achieving International Excellence

roger.hart@uwa.edu.au

Claremont@fertilitywa.com.au



City Fertility

Global CHA IVF Partners

fertilityspecialists
of Western Australia