Fertility preservation for young people with cancer: State of the art.

Professor W Hamish Wallace

Consultant Paediatric Oncologist,

Edinburgh

Scotland, UK

hamish.wallace@nhs.net

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Fertility preservation options: established and experimental

Panel 1: Intrinsic and extrinsic factors for fertility preservation strategies in children and young adults[9]

Intrinsic factors

- Health status of patient
- Psychosocial factors
- Consent (patient or parent)
- Assessment of pubertal status
- Assessment of ovarian reserve (female patients)

Extrinsic factors

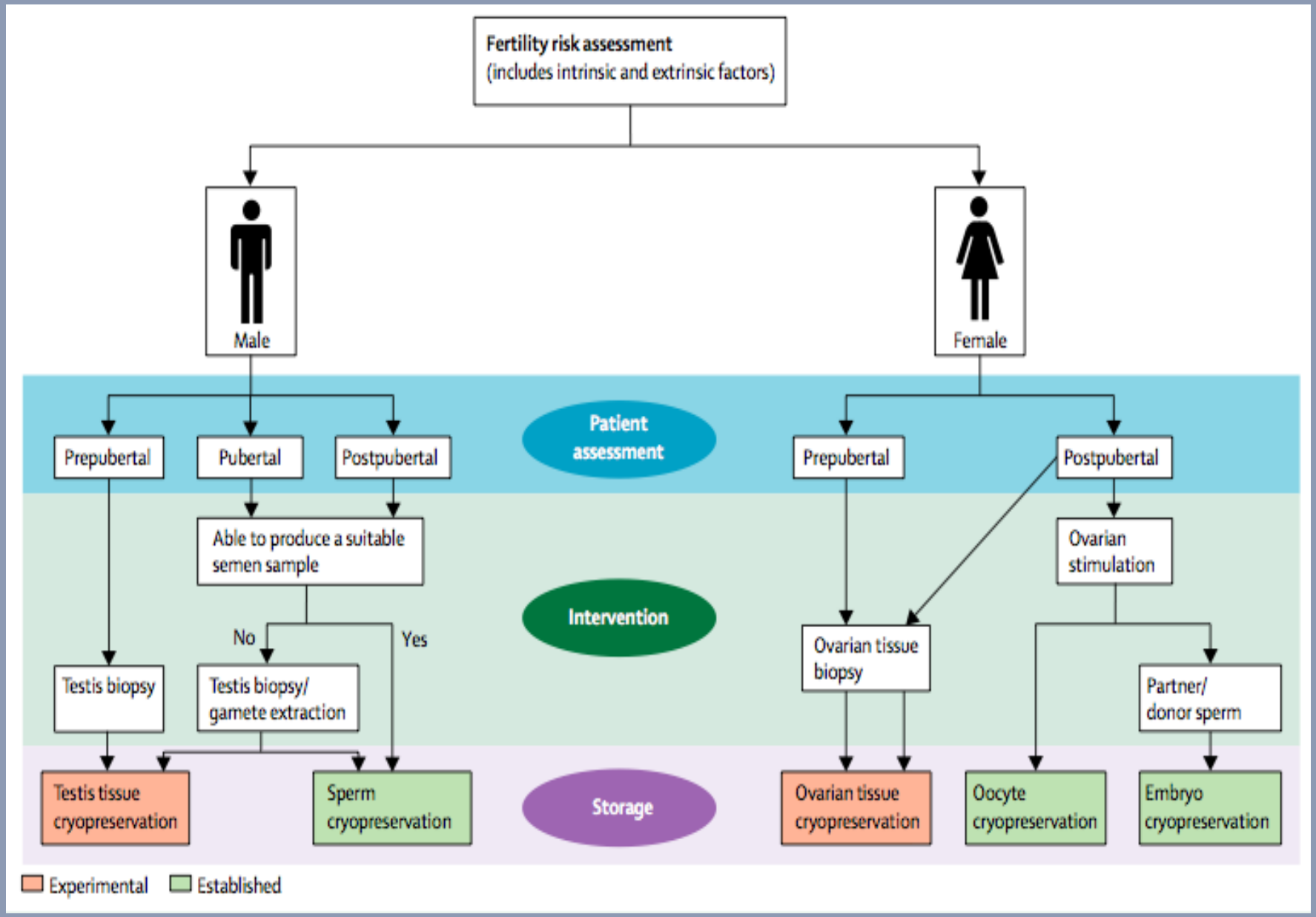
- Risk of predicted treatment (high, medium, low, or uncertain risk)
- Time available
- Expertise and technical options available

Anderson RA…Wallace WH. Lancet Diabetes Endocrinol. 2015

Risk of infertility

Low risk (<20%)	Medium risk	High risk (>80%)
ALL Wilms' tumour Brain tumour Sx, RT < 24Gy Soft tissue sarcoma (stage1) **Hodgkin's Lymphoma HL(Low stage)**	AML Osteosarcoma Ewing's sarcoma STS: stage II/III Neuroblastoma NHL Brain tumour RT>24Gy **HL (High Stage)**	Total Body Irradiation Pelvic/testes RT Chemo pre BMT Metastatic Ewing's **HL (Pelvic RT)**

Wallace, Anderson, Irvine. Lancet Oncology 2005



Anderson RA…Wallace WH. Lancet Diabetes Endocrinol. 2015

Key features of the 3 options for fertility preservation for women

Embryo cryopreservation

- Established but require time and a partner

Oocyte cryopreservation

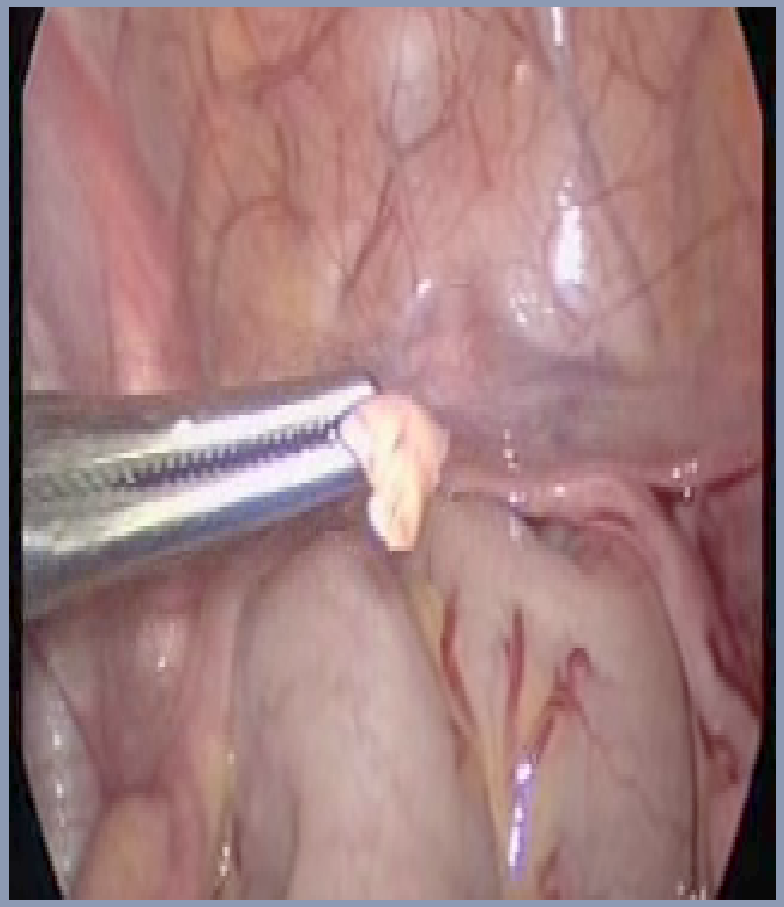
- Established but require time and hormone stimulation (success rate per oocyte low)

Ovarian tissue cryopreservation

- Minimal delay
- No lower age limit
- Surgical procedure
- Allows for future developments

Ovarian tissue cryopreservation: World-wide experience

- At least 60 pregnancies worldwide after othotopic reimplantation of frozen–thawed ovarian cortex
- Success rate is unclear as the denominator is unknown
- No pregnancies reported following the reimplantation of ovarian tissue harvested pre-pubertally
- Young children are potentially ideal candidates



Donnez, J. & Dolmans, M.-M. *Nat. Rev. Endocrinol.* 9, 735–749 (2013)

Cryopreservation: European experience

Three centres (Denmark, Spain and Belgium)

60 cases of orthotopic reimplantation.

Of these women, 11 (21%) became pregnant

Six have delivered 12 healthy babies.

Restoration of ovarian activity was observed in 93% of the patients between 3.5 months and 6.5 months after grafting

The mean duration of ovarian function after trans- plantation is ~4–5 years but can persist for up to 7 years.

Donnez, J. *et al.* *Fertil. Steril.* 99, 1503–1513 (2013).

Outcomes of transplantations of cryopreserved ovarian tissue to 41 women in Denmark

41 women who had thawed ovarian tissue transplanted 53 times over a period of 10 years

Majority had breast cancer or lymphoma, all <39 years at ovarian tissue cryopreservtion

Among 32 women with a pregnancy-wish, 10(31%) had a child/children

The transplanted ovarian tissue can last up to 10 year

Three relapses occurred (2 Breast Ca, 1 Ewings)

Jensen AK…Andersen CY Hum Rep 2015

Transplantation of Ovarian Tissue - The Israeli experience

N= 20 cancer survivors

Ovarian Tissue harvested 14-39 years

N=15 haematological malignancies

N=10 exposed to pre-harvest chemotherapy

93% reported endocrine recovery

N=16 pregnancies(10: IVF, 6 spontaneous)

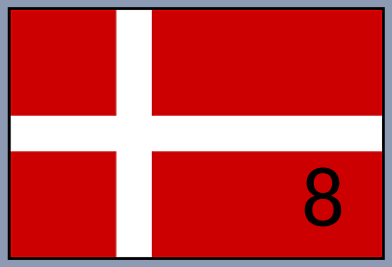
32% had at least one live birth and 53% had a pregnancy

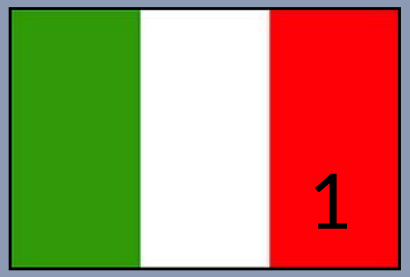
No cancer relapses

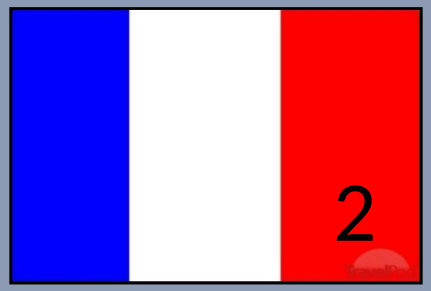
Safe and no longer experimental!

Meirow et al., Fertility and Sterility 2016

Children born from transplantation of frozen/thawed ovarian tissue







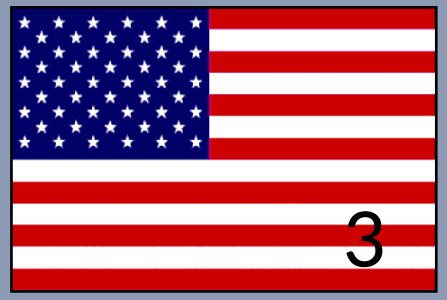
All Normal Babies

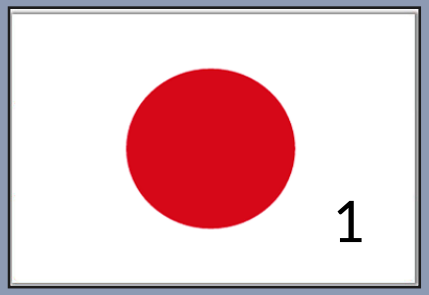
weight and duration

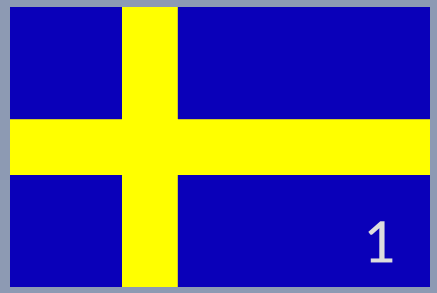
Orthotopic >> heterotopic

All except for one is a result of a slow-freezing protocol

An estimated excess of 150 transplantations have been performed







Induction of puberty by autograft of cryopreserved ovarian tissue

10 year old with Sickle cell disease 2003 before HSCT Rt Oophorectomy and cryopreservation

Aged 13 , developed POI, and requested return for pubertal induction

B2, 4 months; Menstruation, 8 months

Regular menstruation for two years post graft, Normal breast development

This case shows the first restoration of endocrine ovarian function from tissue harvested before puberty.

Poirot et al.Lancet, 2012

Induction of puberty by autograft of cryopreserved ovarian tissue

9 year old with Ewing, intensively treated with CT and RT

OTC before treatment commenced

Developed POI . No pubertal development. In remission

4.5 years later (13.5years) ovarian tissue returned for pubertal induction. Tanner B4 and menstruation within one year.

Graft ceased to function after 19 months

Several years later she relapsed and died from recurrent Ewing sarcoma

No evidence of EWS FLI1 in remaining stored ovarian tissue.

Ernst et al EJC, 2013

Induction of puberty by autograft of cryopreserved ovarian tissue

Induction of puberty with exogenous steroid hormones either orally or trans-dermally is well established

The re-implantation of ovarian tissue in a hypergonadotrophic environment not ideal

Potential waste of a finite number of germ cells

Risk of relapse ..particularly in haematological malignancies

Live birth after autograft of ovarian tissue cryopreserved during childhood

Sickle cell disease Aged 5 from Rep of Congo

Onset of puberty Aged 10, No menstruation

BU/CY HSCT from matched sibling for severe disease

Lap collection of whole ovary Aged 13 and 11 months, October 2000 before HSCT

Developed POI, started on HRT aged 15

Aged 25 ovarian tissue replaced. After five months menstruation, continued for two years. Assisted conception due to male factor. No pregnancy

Aged 27 spontaneous conception with new partner. Healthy male 3.14 Kg.

Demeestere I et al Hum Rep 2015

Ovarian Cryopreservation & Ovarian Function

Edinburgh experience in children (< 18 yrs) 1996-2012

***Panel 2:* The Edinburgh Selection Criteria for gonadal tissue cryopreservation**

These criteria were established with ethics committee review and approval because they refer to experimental procedures, and should be regarded as a starting point for future discussion, research, and refinement.

Female patients[112]

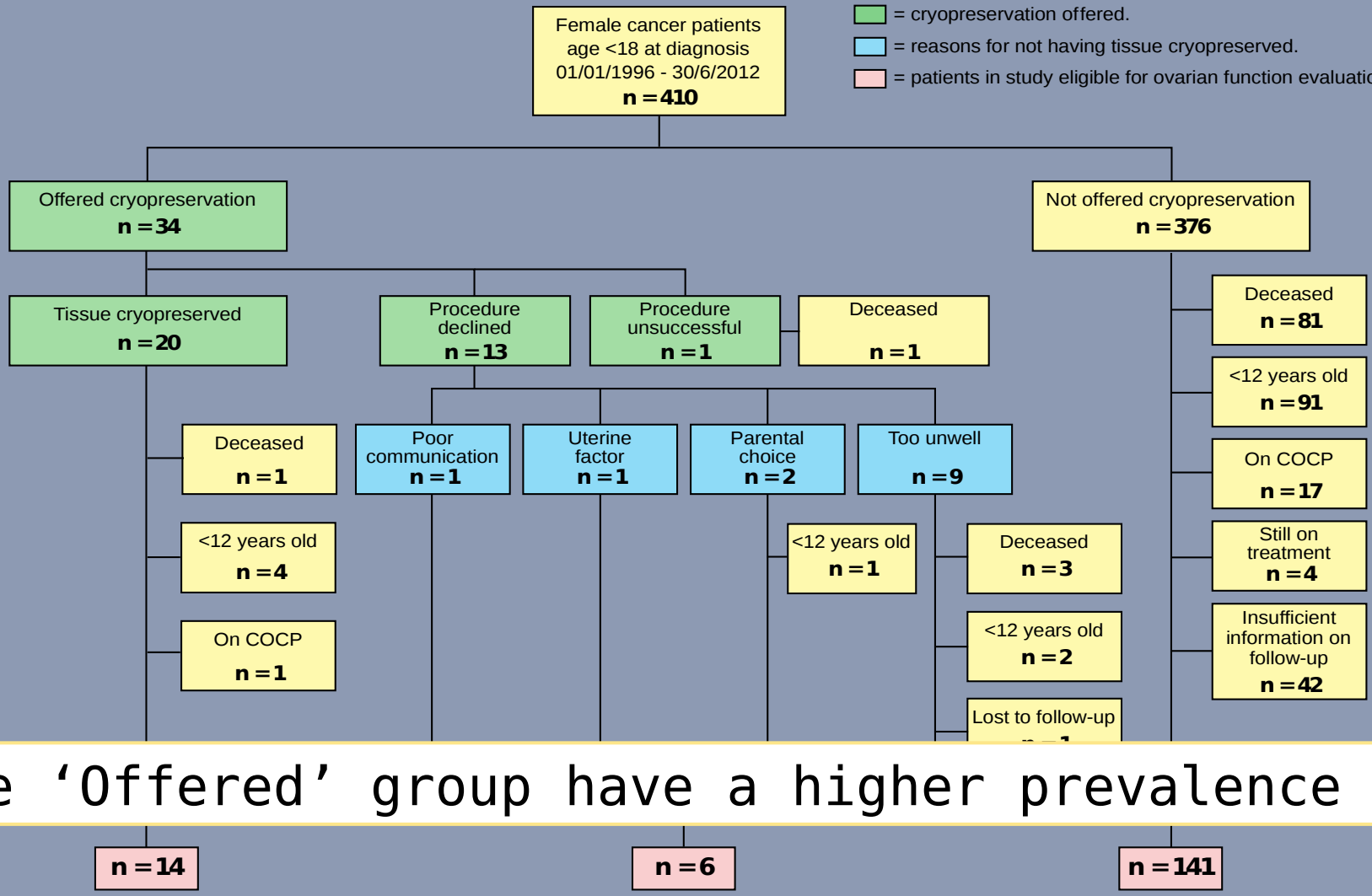
- Age younger than 35 years
- No previous chemotherapy or radiotherapy if aged 15 years or older at diagnosis, but mild, non-gonadotoxic chemotherapy is acceptable if younger than 15 years
- A realistic chance of 5-year survival
- A high risk of premature ovarian insufficiency (>50%)
- Informed consent (parent and, when possible, patient)
- Negative HIV, syphilis, and hepatitis serology
- Not pregnant and no existing children

Male patients

- Age 0–16 years
- A high risk of infertility (>80%)
- Unable to produce a semen sample by masturbation
- No clinically significant pre-existing testicular disease (eg, cryptorchidism)
- Informed consent (parent and, when possible, patient)
- Negative HIV, syphilis, and hepatitis serology

Anderson RA…Wallace WH. Lancet Diabetes Endocrinol. 2015

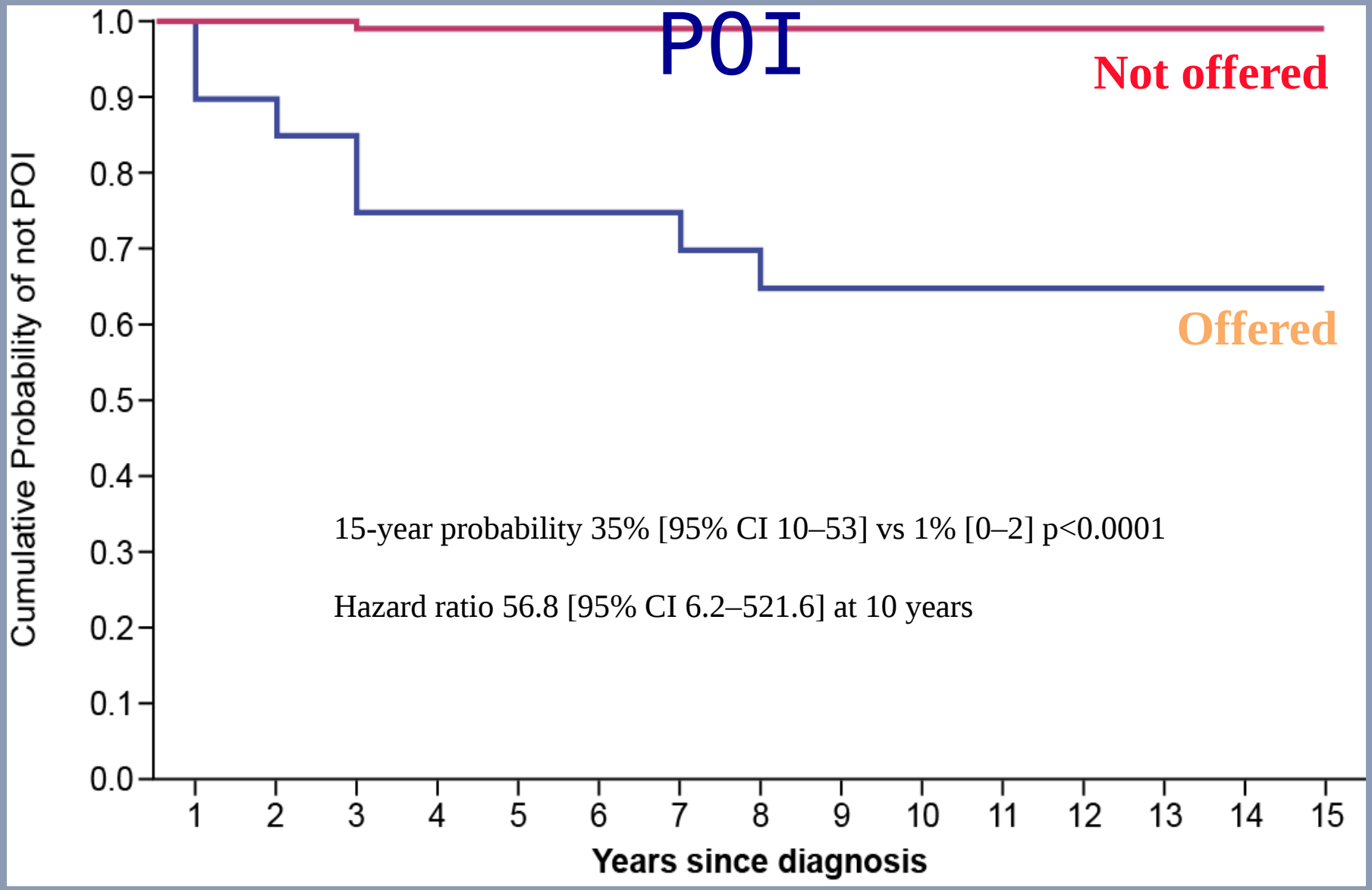
15 year, population-based analysis of criteria for ovarian cryopreservation



the ‘Offered’ group have a higher prevalence of PC

Walllace WH et al. 2014 Lancet Oncology

Cumulative incidence of POI



Walllace…..and Anderson 2014 Lancet Oncology

Conclusion

Ovarian cryopreservation was offered to 9% of our patients, and performed in 5%

The procedure was safe and without complications

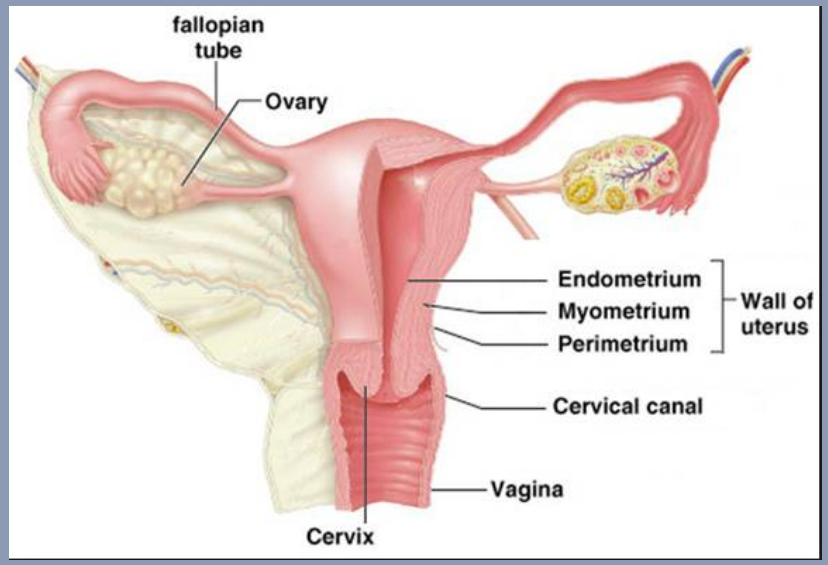
No patients have asked for re-implantation of their tissue – to date

All patients who have thus far developed premature ovarian insufficiency were identified except one patient

The Edinburgh Selection Criteria have proved to be helpful in selecting those patients at highest risk of POI

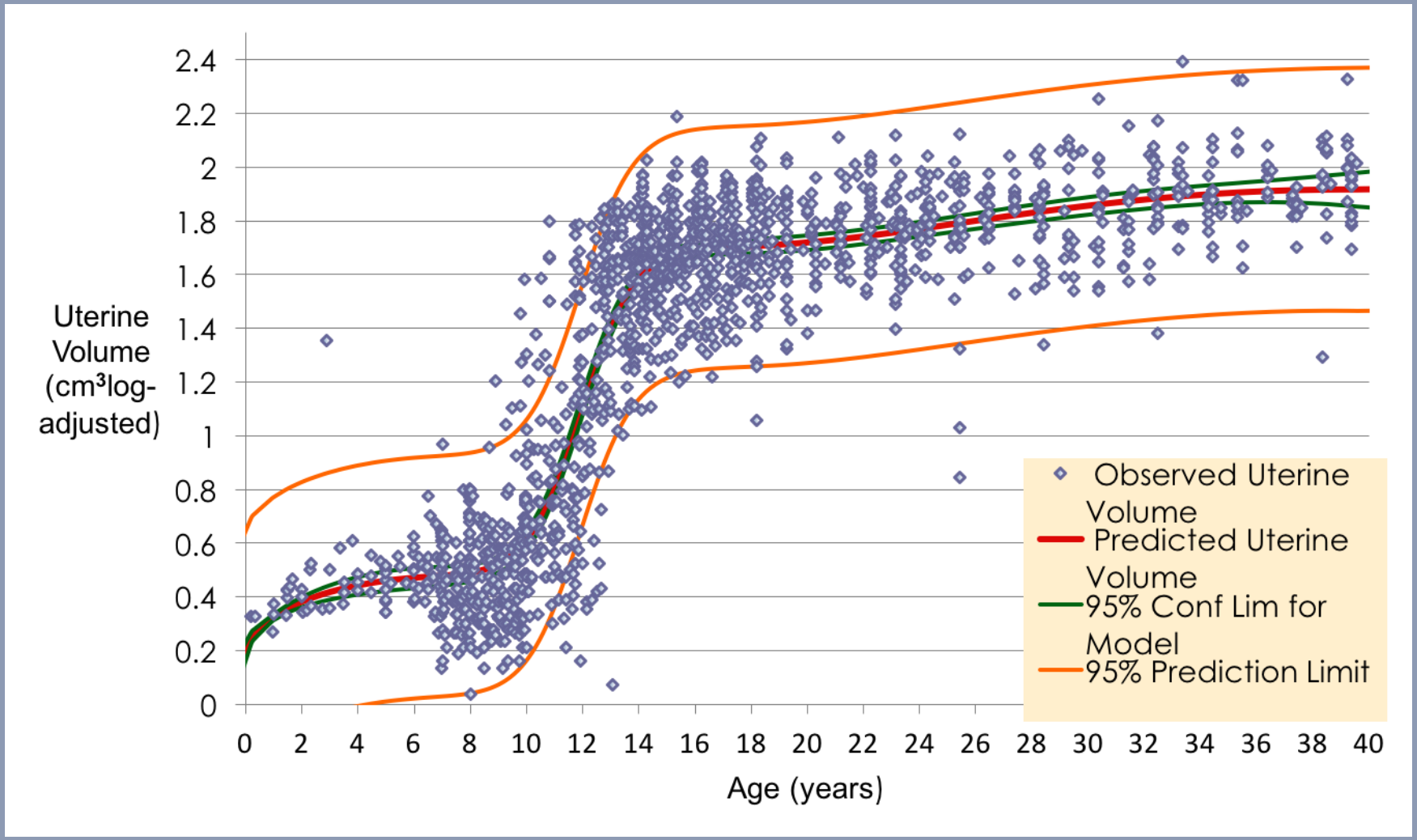
Wallace WH…..and Anderson 2014 Lancet Oncology

The Uterus


fallopian tube
Ovary
Endometrium
Myometrium
Perimetrium
Wall of uterus
Cervical canal
Vagina
Cervix

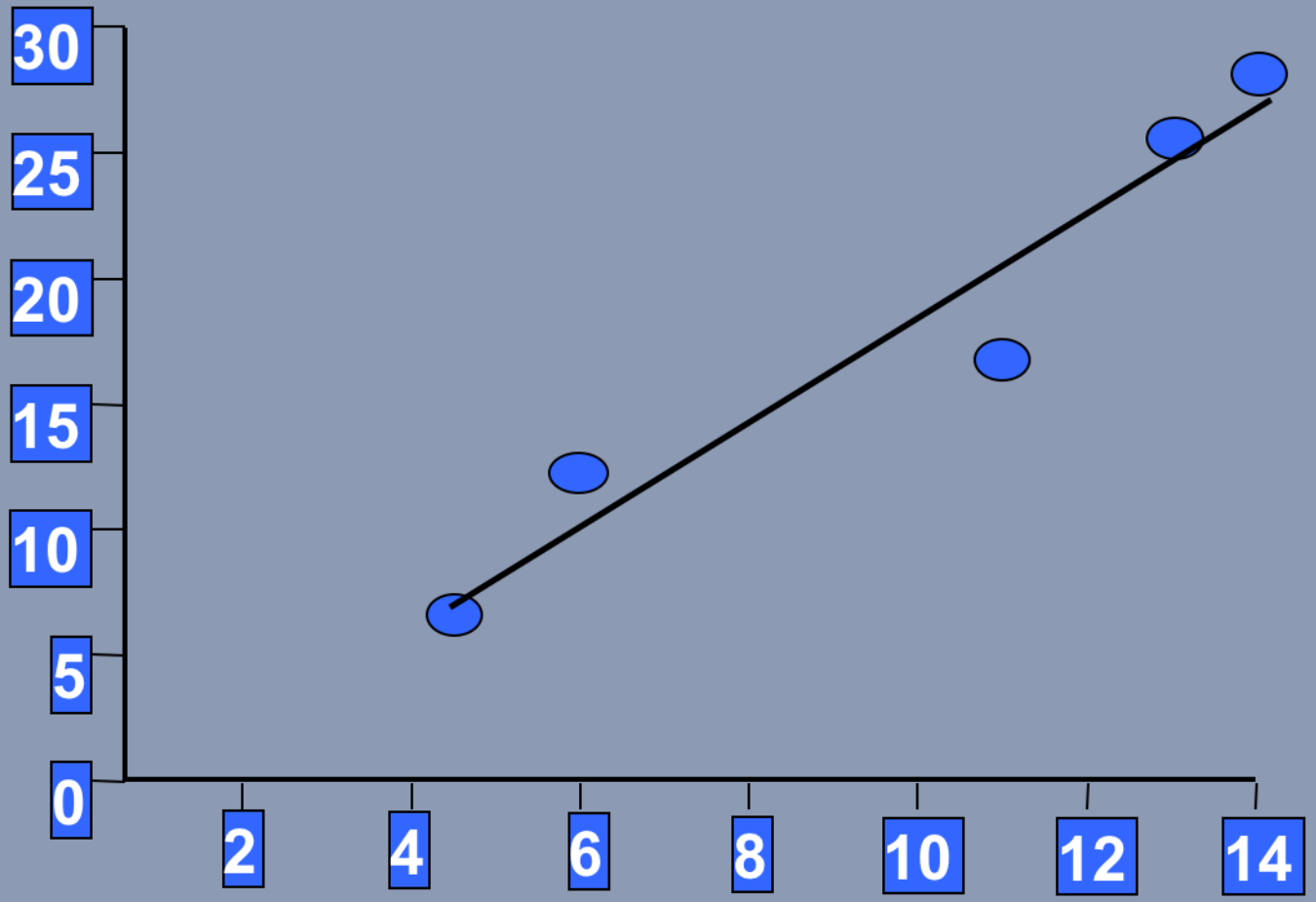

A

Normative model for uterine volume from birth to 40 years. The r^2 is 0.859.



Kelsey et al. unpublished

Uterine volume and age at irradiation (TBI)



Bath et al. BJOG (1999)

Uterine function after cancer treatment

No reports of uterine damage due to chemotherapy

Radiotherapy:

Uterine damage, manifest by impaired growth and blood flow.

Uterine volume correlates with age at irradiation.

Exposure of the pelvis to radiation is associated with an increased risk of miscarriage, mid-trimester pregnancy loss, PPH, pre-term birth and low birth weight.

2016

Ovarian tissue cryopreservation

Established or Experimental?

For pubertal induction…experimental

For fertility preservation in children..experimental

For fertility preservation in adult women…?

Fertility Preservation ASCO Guidelines (2006) and update (2013): General

Discuss fertility preservation with **all** patients of reproductive age (and with parents or guardians of children and adolescents) if infertility is a potential risk of therapy

Refer patients who express an interest in fertility preservation to reproductive specialists

Address fertility preservation as early as possible, before treatment starts

Document fertility preservation discussions in the medical record

Encourage patients to participate in registries and clinical studies

Lee et al. JCO 2006
Loren et al. JCO 2013

Fertility Preservation ASCO Guidelines update (2013) (Females)

Embryo (2006) and oocyte cryopreservation (2013) should be considered as **established** fertility preservation methods

There is insufficient evidence of the effectiveness of ovarian suppression (gonadotropin-releasing hormone analogs) as a fertility preservation method

Other methods (e.g., ovarian tissue cryopreservation) are still **experimental**

Lee et al. JCO 2006
Loren et al. JCO 2013

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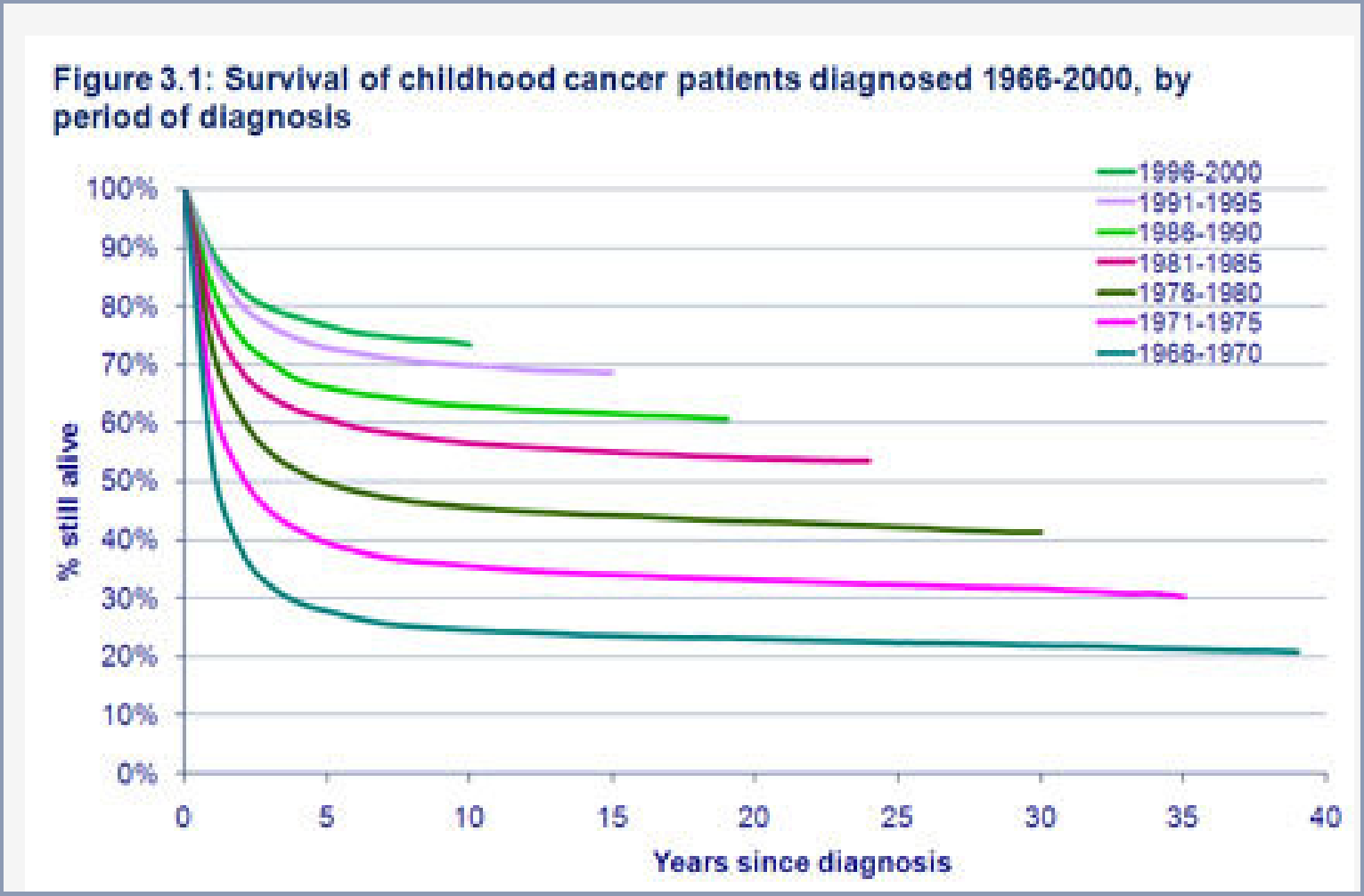
Fraser Munro

Edinburgh Fertility Preservation

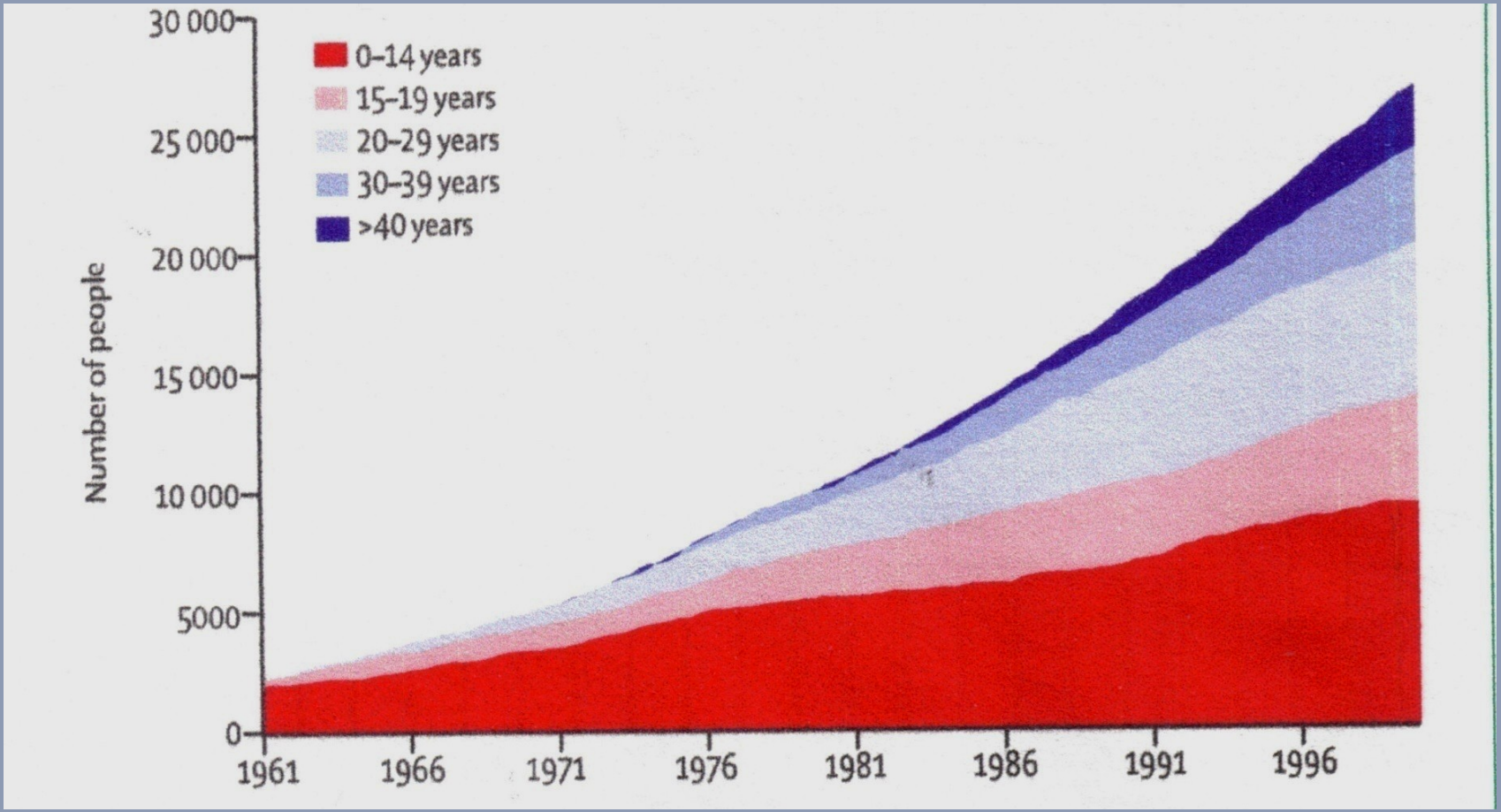
www.ed.ac.uk/Edinburgh-fertility-preservation

@edinfertility

Improved Five Year Survival (1966-2000)



Increasing numbers of five year UK survivors by current age



Skinner, Wallace & Levitt , Lancet Oncology, 20

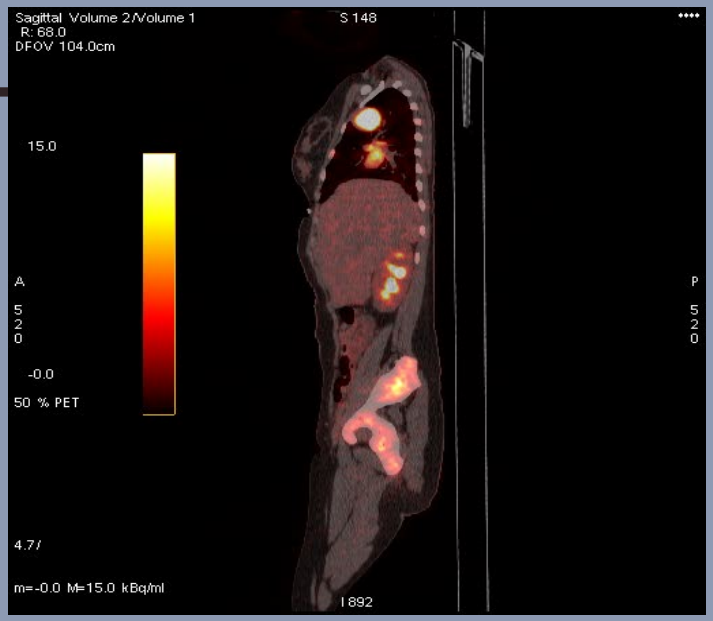
A Patient

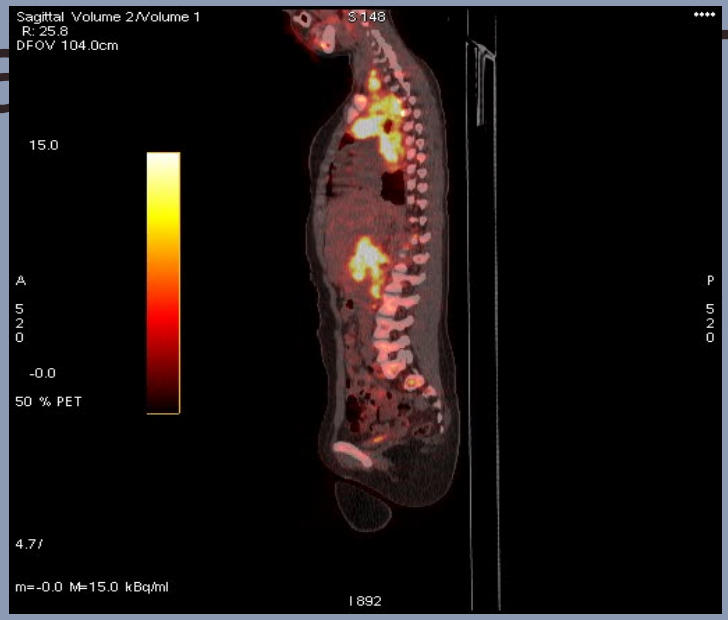
March 2011 (age 15 years)

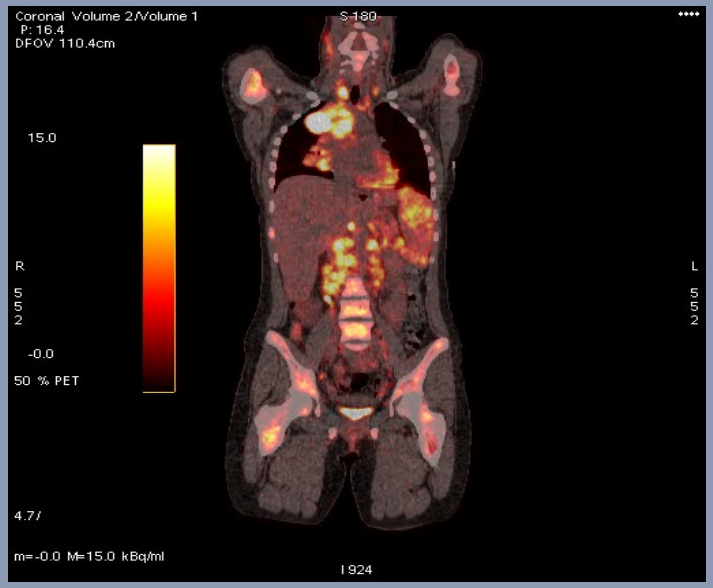
Six month H/O of intense pruritis of her feet

Three month H/O fever, night sweats, lethargy, pallor, poor appetite and weight loss

Widespread LN – lower cervical, mediastinum, abdomen


Sagittal Volume 2/Volume 1
S 148
R: 68.0
DFOV 104.0cm
15.0
A
P
-0.0
50 % PET
4.7/
m=-0.0 M=15.0 kBq/ml
I 892


Sagittal Volume 2/Volume 1
S 148
R: 25.8
DFOV 104.0cm
15.0
A
P
-0.0
50 % PET
4.7/
m=-0.0 M=15.0 kBq/ml
I 892


Coronal Volume 2/Volume 1
S 180
P: 16.4
DFOV 110.4cm
15.0
R
L
-0.0
50 % PET
4.7/
m=-0.0 M=15.0 kBq/ml
I 924


Coronal Volume 2/Volume 1
S 180
P: 7.0
DFOV 110.4cm
15.0
R
L
-0.0
50 % PET
4.7/
m=-0.0 M=15.0 kBq/ml
I 924

Diagnosis and Staging

Mediastinal lymph node biopsy

- Hodgkin's lymphoma

Insertion of double lumen portacath

Laparoscopic ovarian biopsy and cryopreservation of ovarian cortical strips

Laura

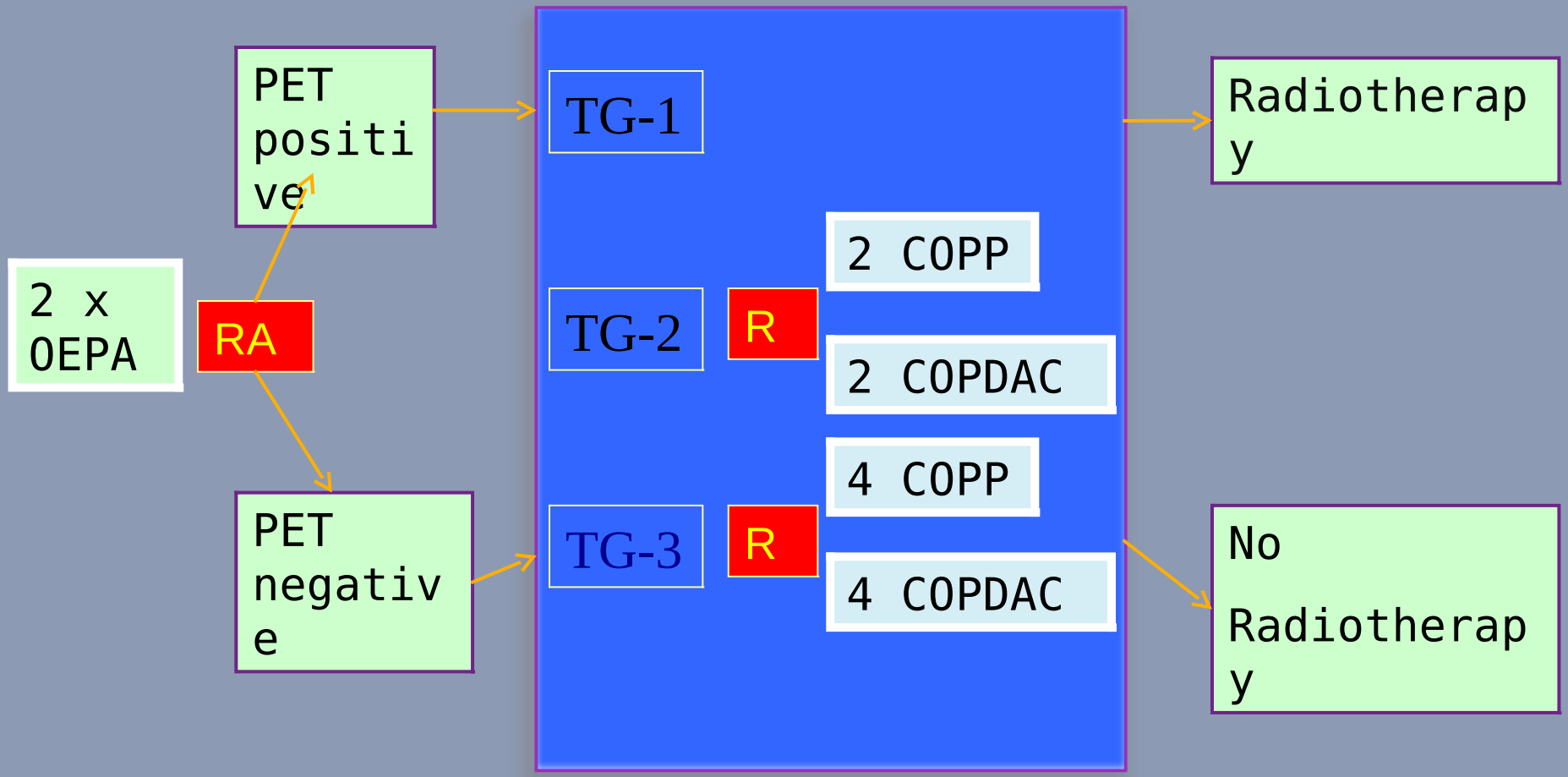
EuroNet-PHL-C1 Protocol:

Treatment Group 3 (TG3)

Two cycles of OEPA

Four cycles of COPDAC or COPP

EuroNet-PHL-C-1



Wallace WH. UK Chief Investigator

CRUK support 400K

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Anderson RA…Wallace WH. Lancet Diabetes Endocrinol. 2015

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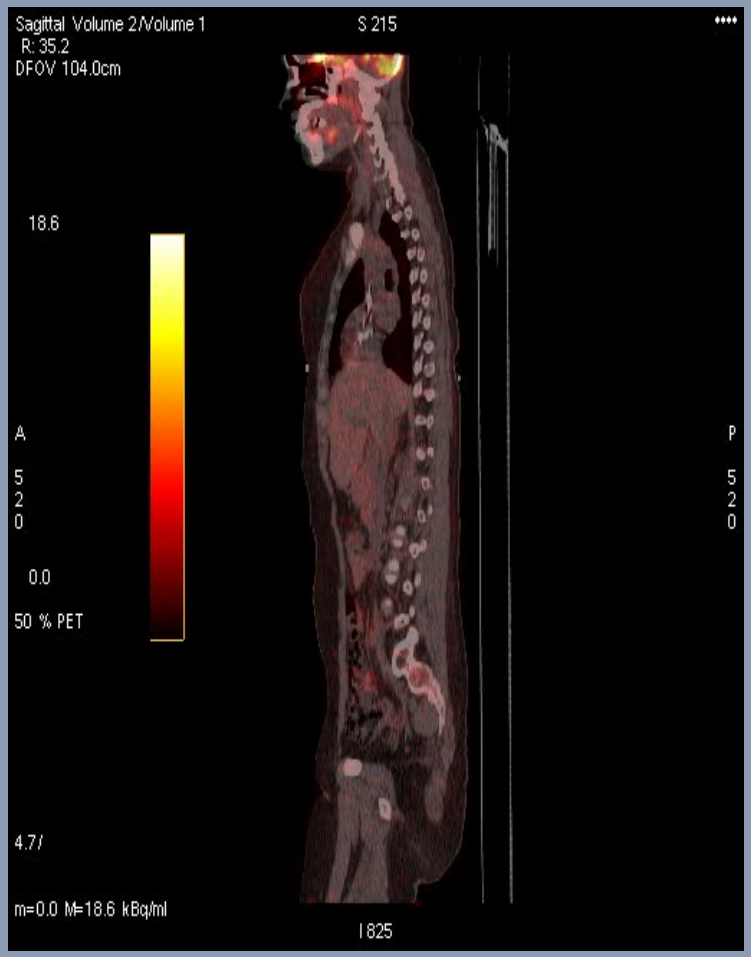
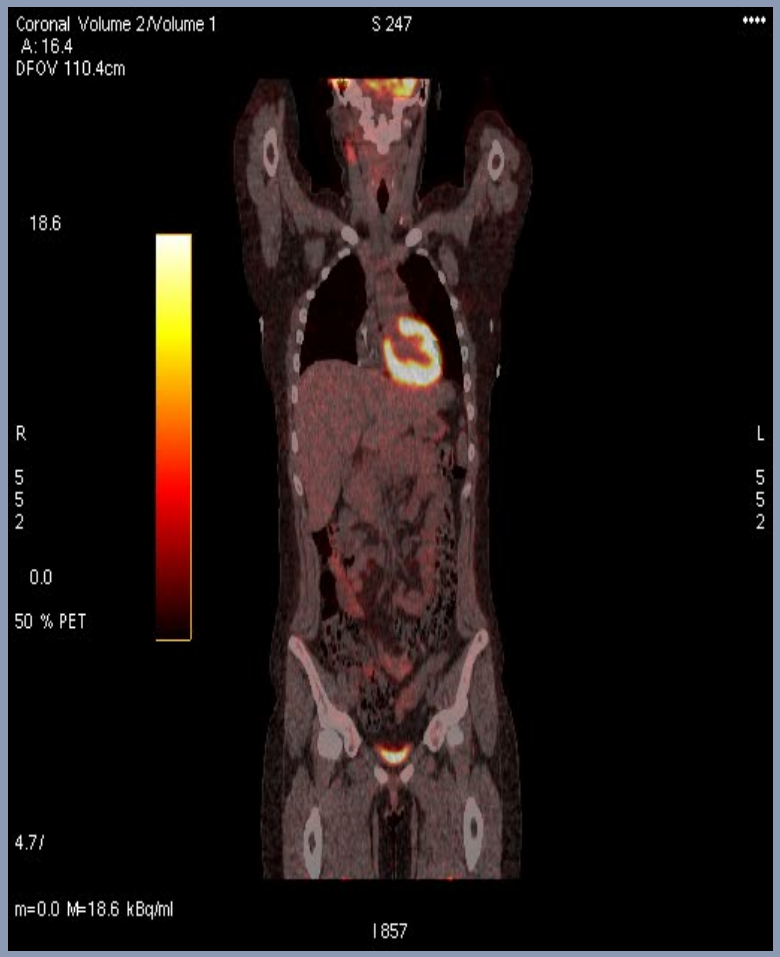
Wallace, Anderson, Irvine. Lancet Oncology 2005

Early Response Assessment PET scan





Radiotherapy Field and estimated doses to organs at

Organs at risk	Maximium dose received	Mean Dose
- spinal cord	2139.7 cGy	1916.2 cGy
- heart	2116.1 cGy	1701.4 cGy
- left kidney	2169.1 cGy	1439.8 cGy
- right kidney	2022.2 cGy	639.3 cGy
- lung	2148.5 cGy	1168.9 cGy
- right breast	2195.1 cGy	476.7 cGy
- left breast	2156.4 cGy	654.6 cGy
- liver	2153.4 cGy	830.2 cGy
- thyroid	2047.2 cGy	1999.0 cGy

Infertility - Risk Factors

RT to HPA or a field that includes testes/ovaries

Busulphan

BCNU

CCNU

Cyclophosphamide

Ifosfamide

Melphalan

Mustine

Nitrogen mustard

Procarbazine

Thiotepa

Chlorambucil

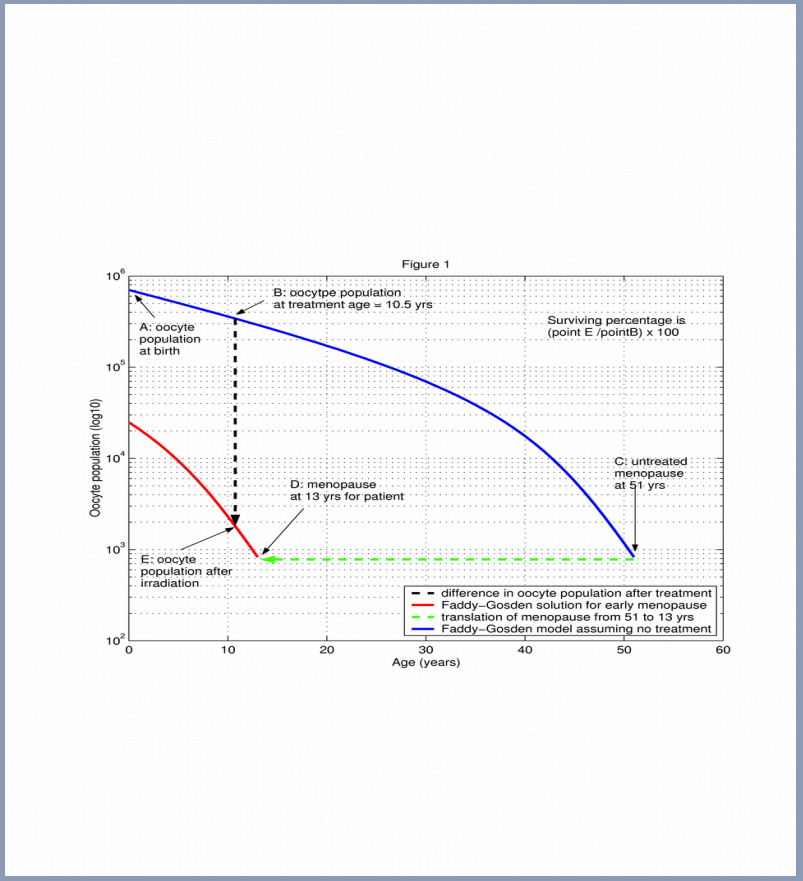
Cytarabine

The pre-pubertal gonad is not protected

Radiation-induced ovarian damage

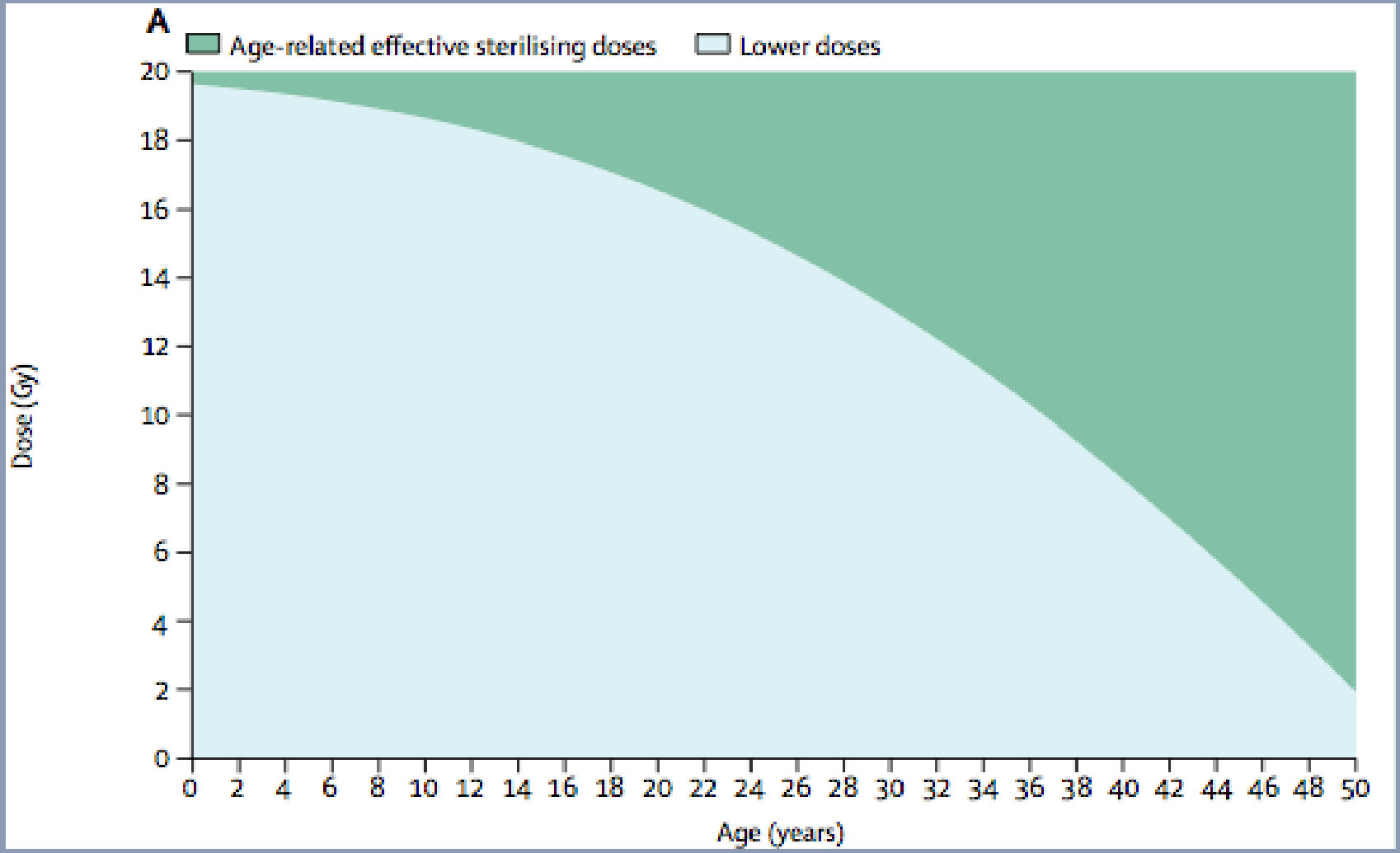
Human oocyte (Primordial follicle)

$LD_{50} < 2$ Gy

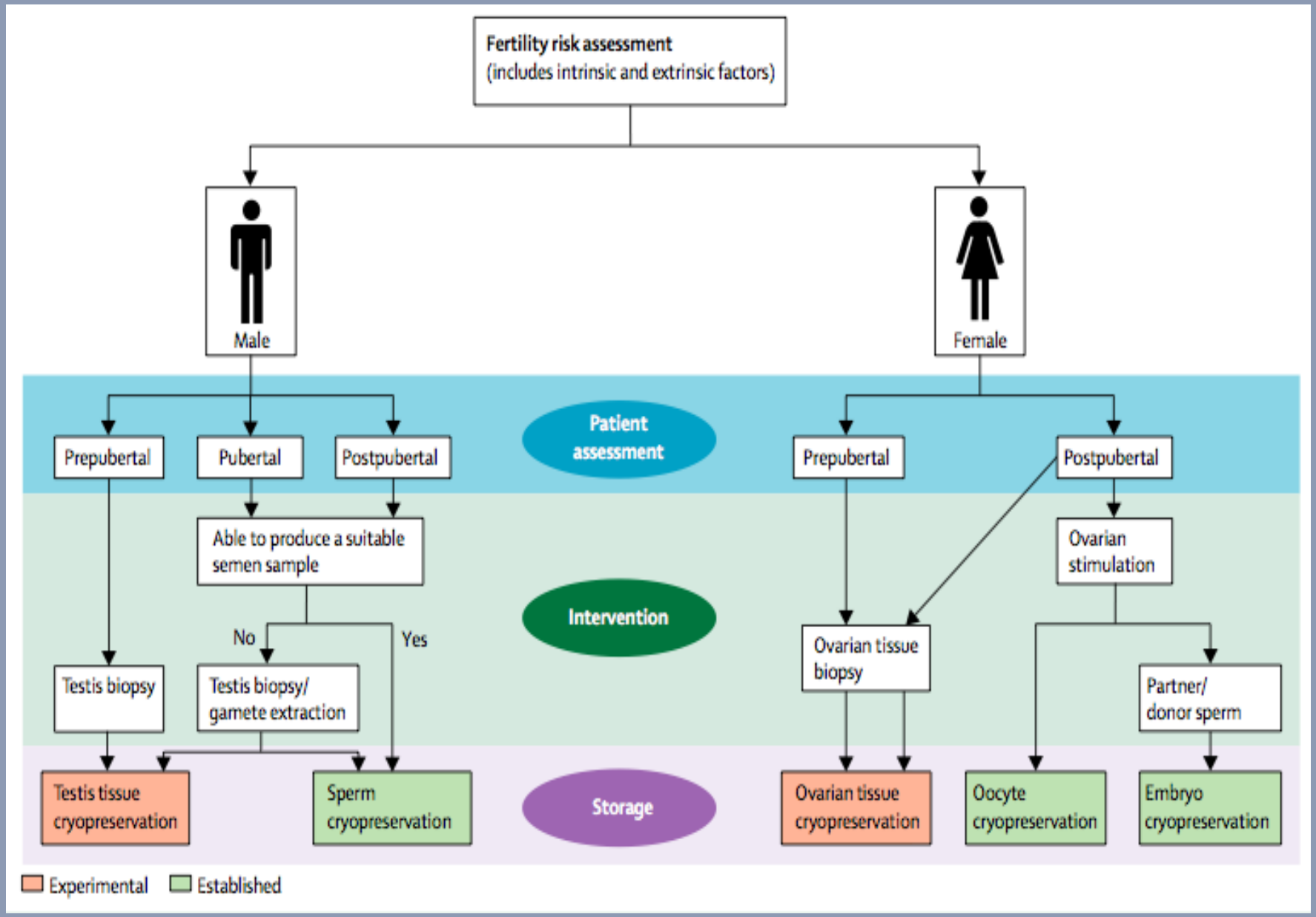


Wallace, Thomson, Kelsey. (2003) Hum Reprod.

Effective ovarian sterilizing doses of radiotherapy with increasing age



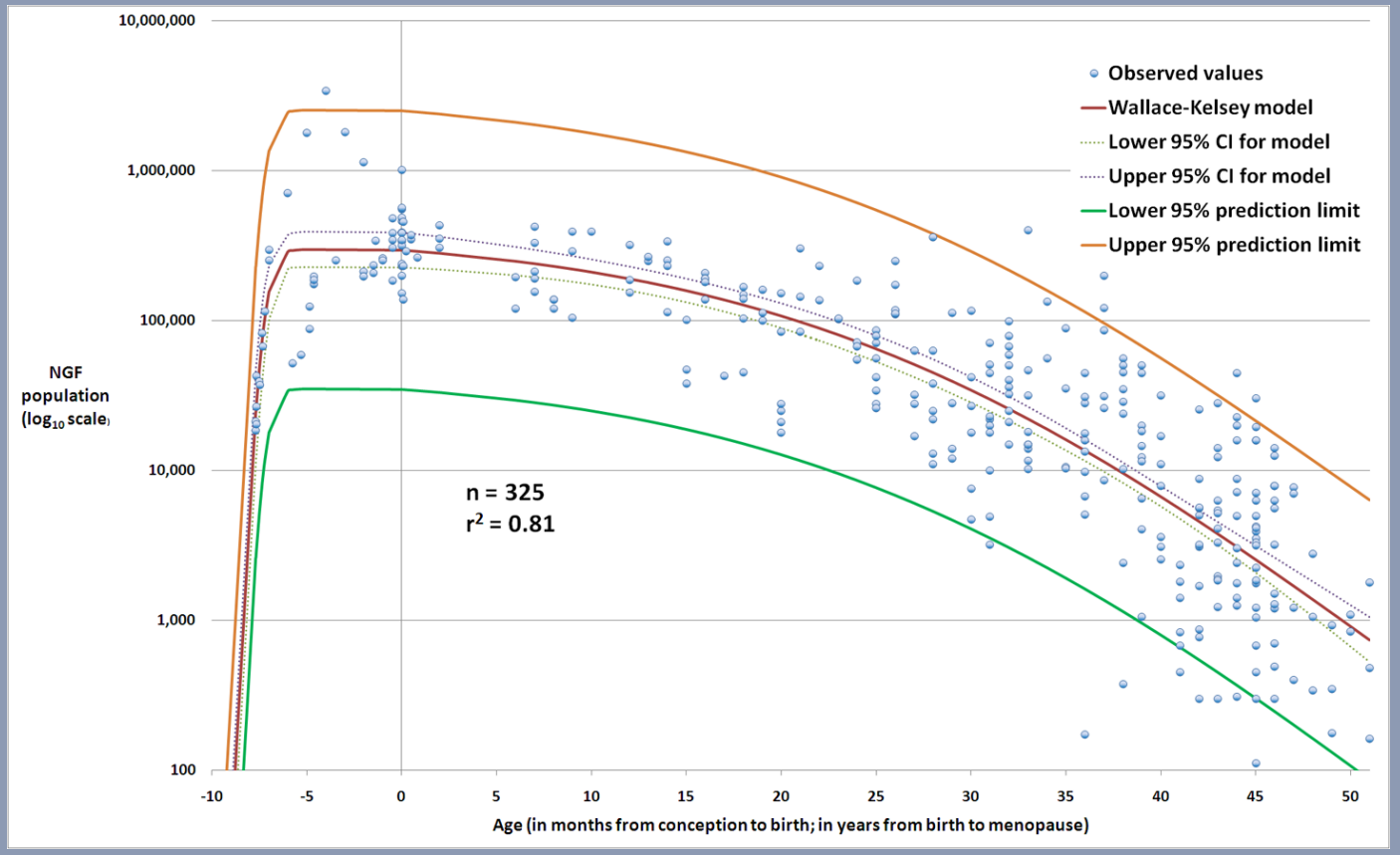
Anderson RA…Wallace WH. Lancet Diabetes Endocrinol. 2015



Anderson RA…Wallace WH. Lancet Diabetes Endocrinol. 2015

Ovarian Reserve?

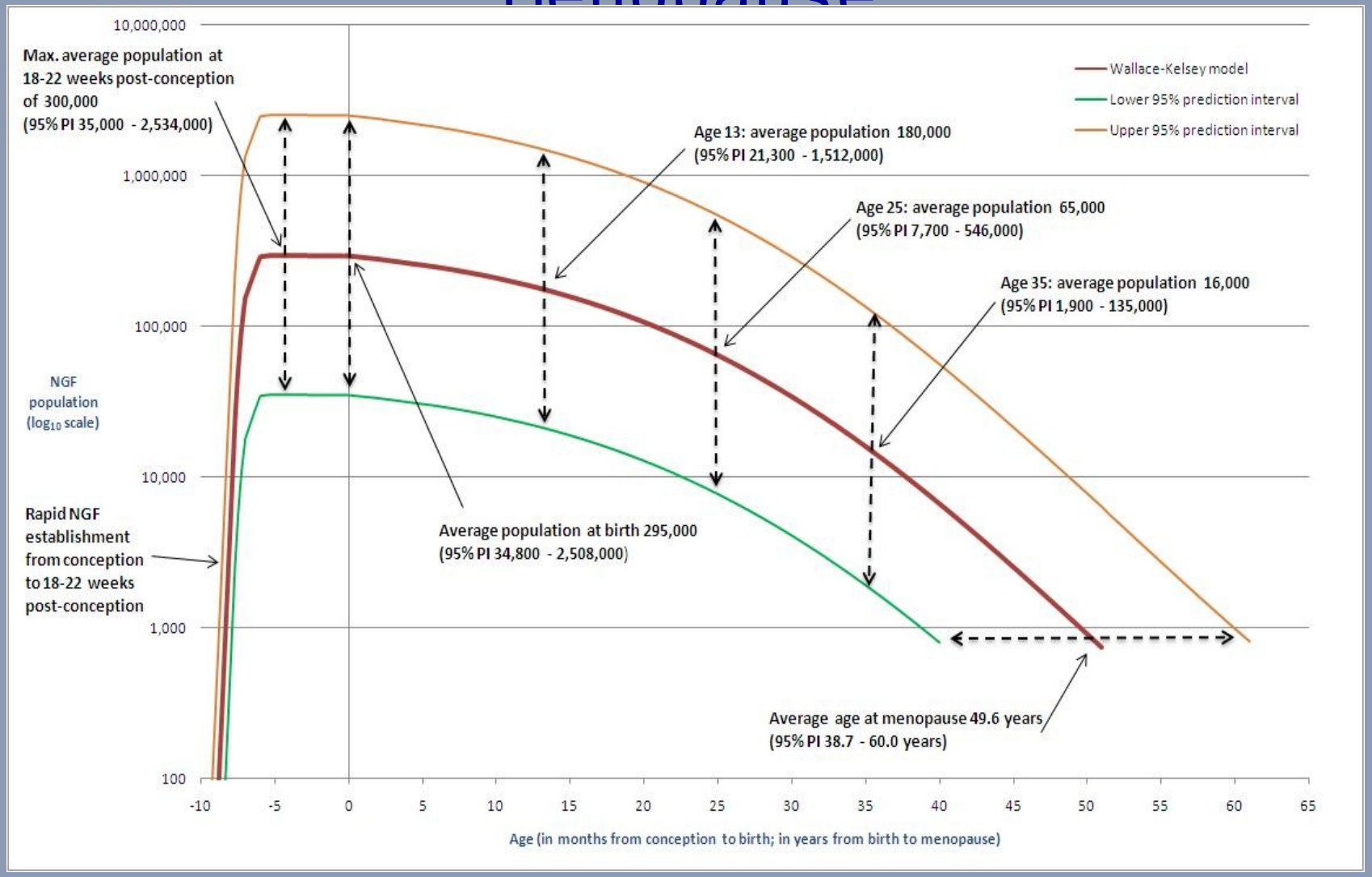
The Wallace-Kelsey Model
(Five parameter asymmetric double-Gaussian cumulative curve)



$$log_{10}(y) = \frac{a}{4}\left[1 + \mathrm{Erf}\left(\frac{x+b+\frac{c}{2}}{d\sqrt{2}}\right)\right]\left[1 - \mathrm{Erf}\left(\frac{x+b-\frac{c}{2}}{e\sqrt{2}}\right)\right]$$

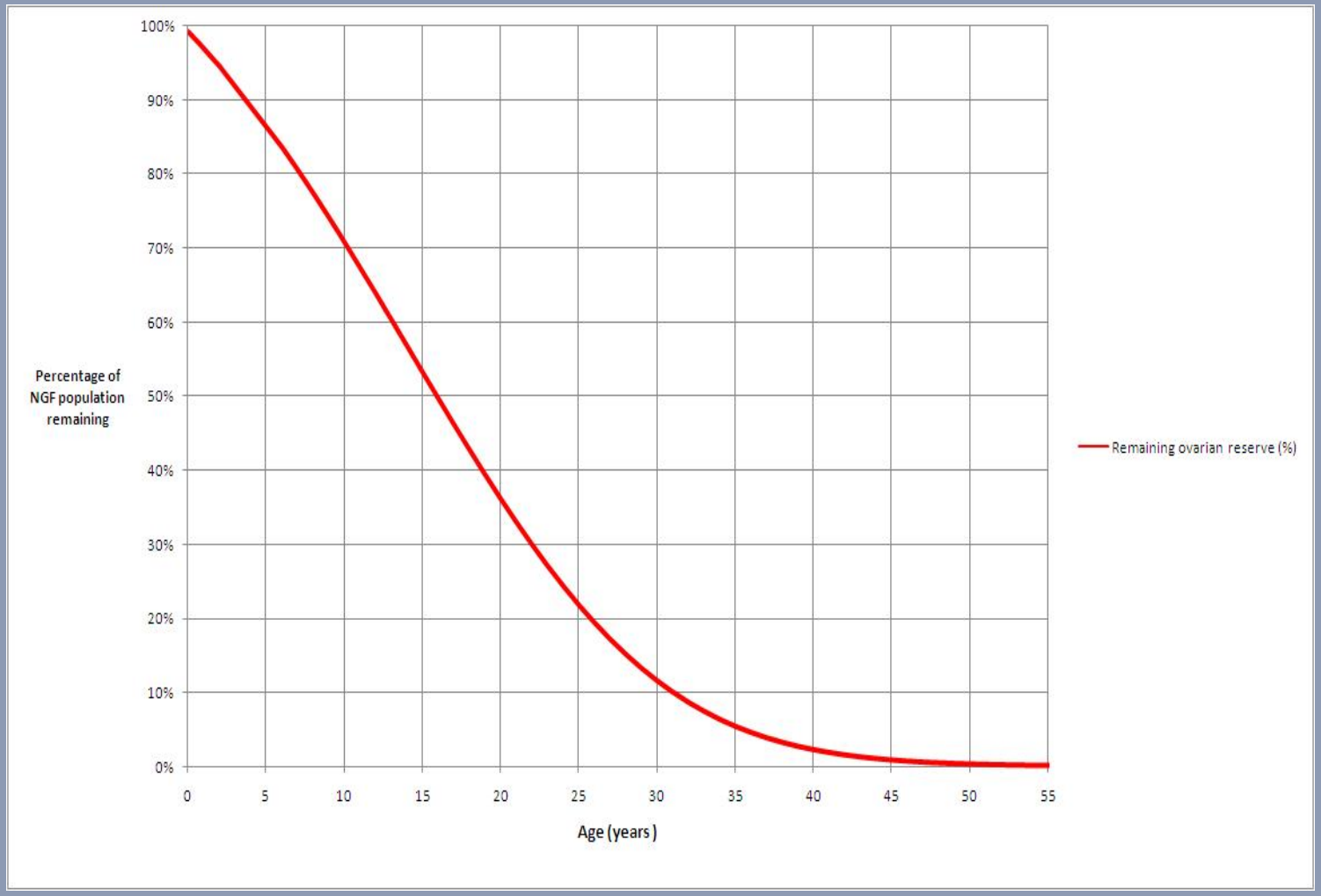
Wallace &Kelsey (2010) PloS ONE

Ovarian reserve: Conception to Menopause



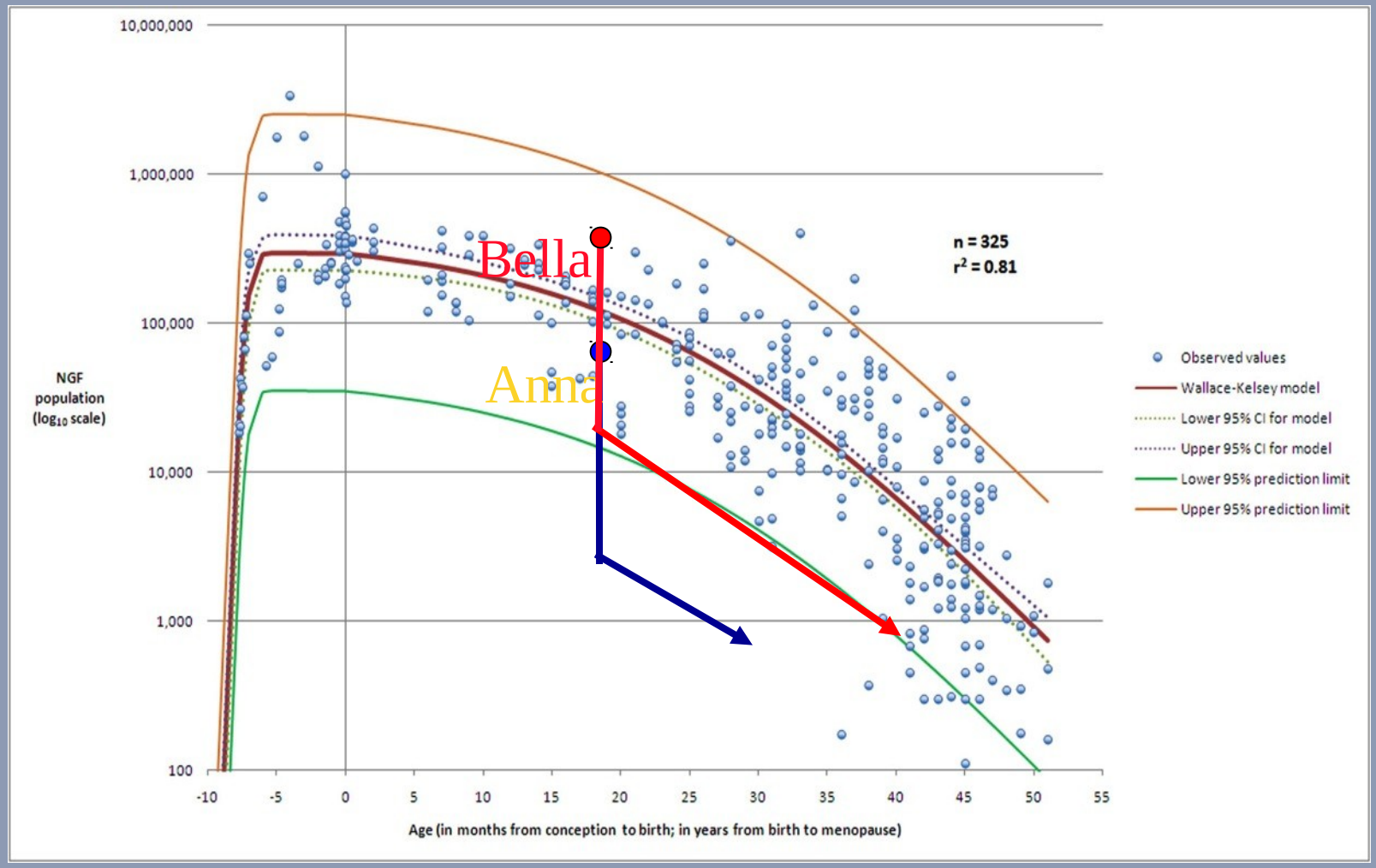
Wallace &Kelsey (2010) PloS ONE

Percentage of NGF population remaining with increasing age



Wallace &Kelsey (2010) PloS ONE

Ovarian reserve: Conception to Menopause



Wallace &Kelsey (2010) PloS ONE

Prediction of Ovarian Reserve (AMH)

Anti Mullerian Hormone (AMH) is an important product of the adult ovary, produced by the granulosa cells of small growing follicles

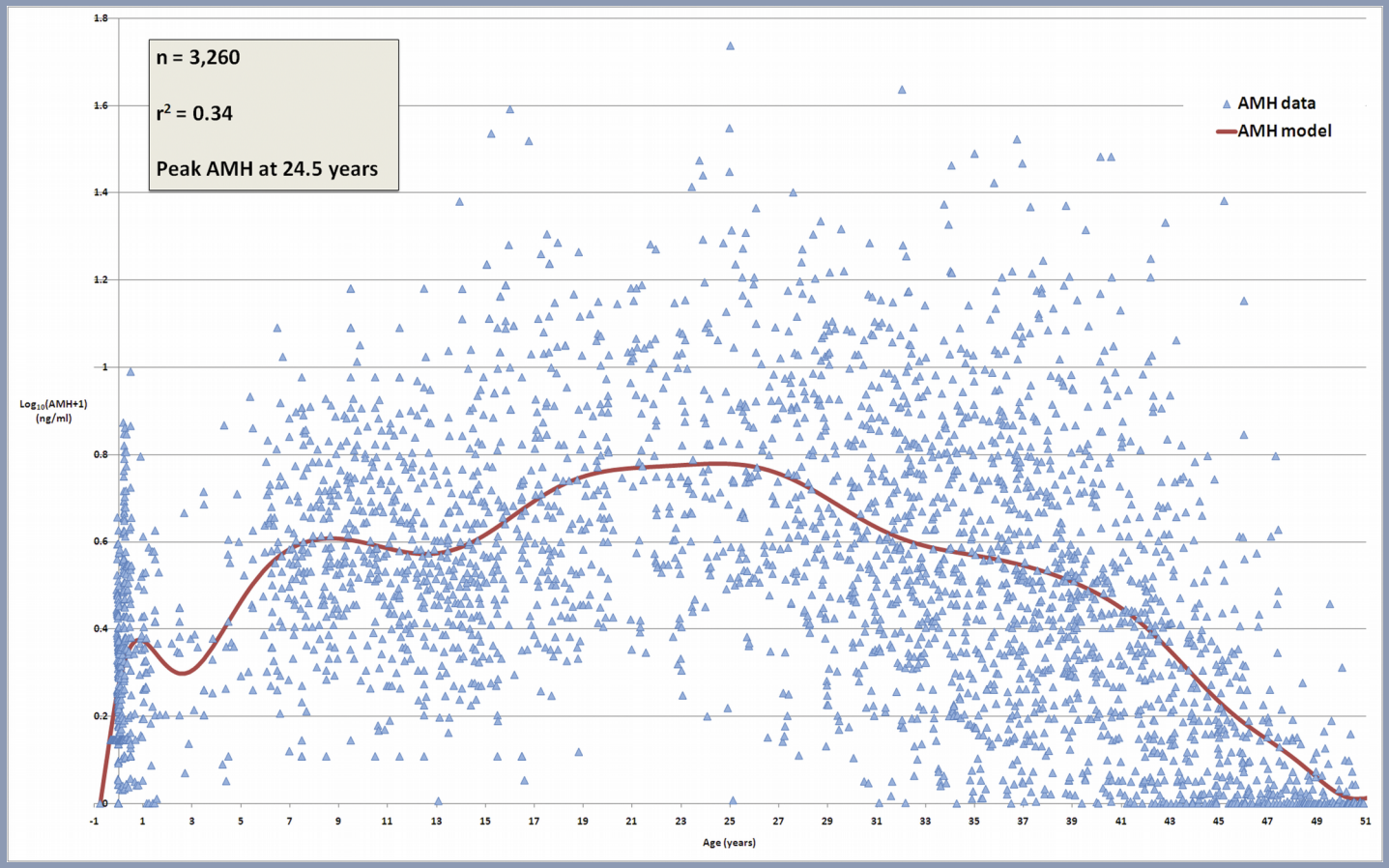
AMH has little variation across and between menstrual cycles

AMH is the best currently available marker of the number of small-growing follicles in the ovary

But there was no validated reference model for AMH available

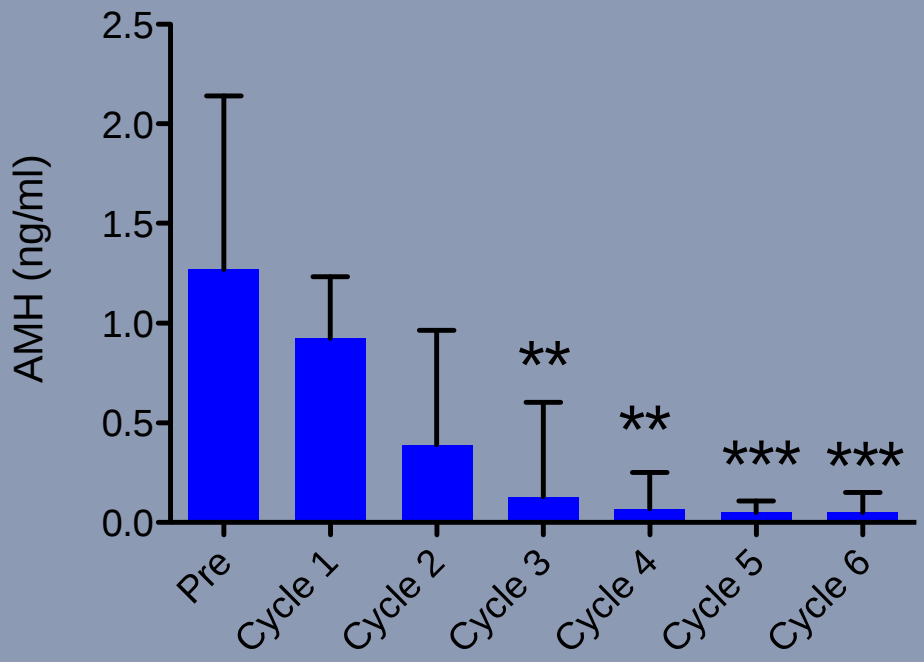
Anderson, Nelson, Wallace (2011) Maturitas

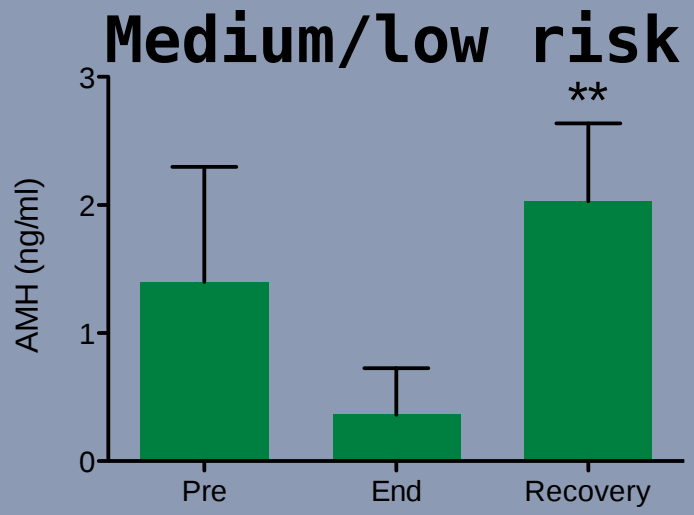
A validated model of serum anti-Mullerian hormone (AMH) from conception to menopause

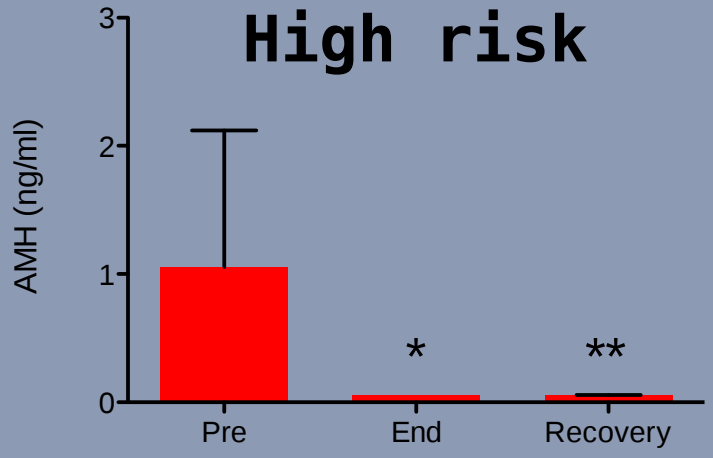


Kelsey et al. PLoS ONE 2011

AMH in childhood cancer



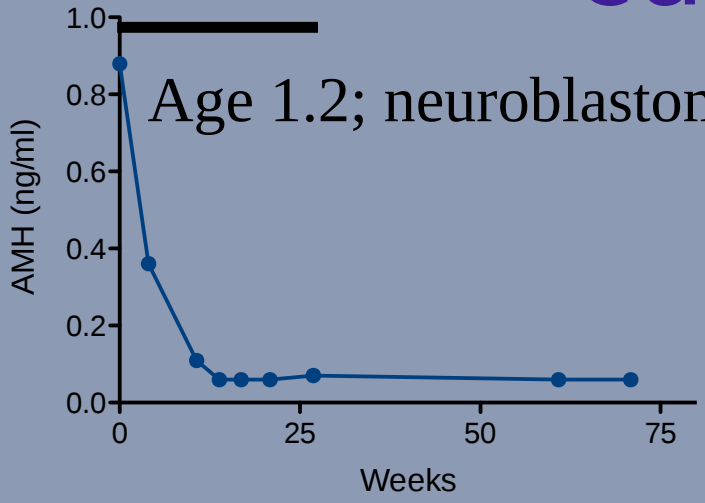


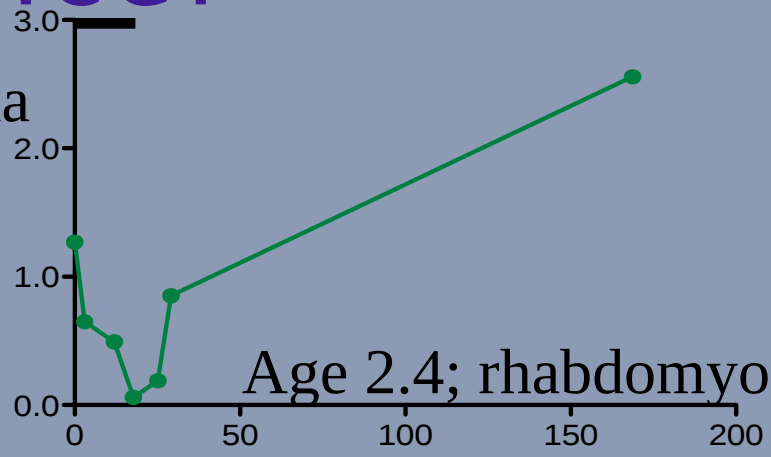


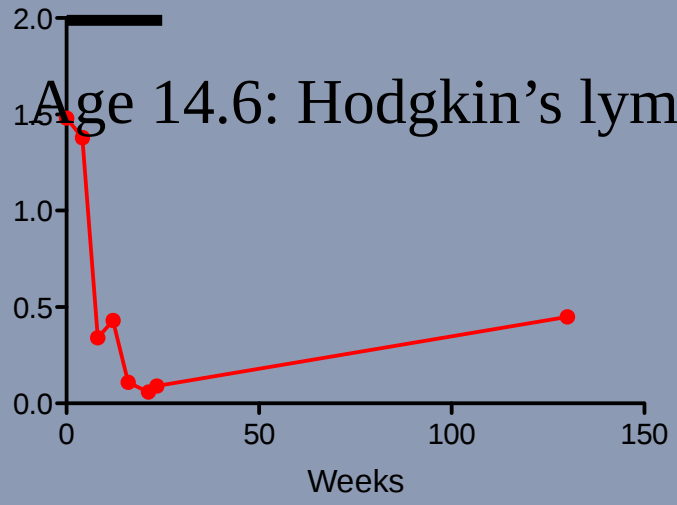
22 girls age 0.3-15yr
17 prepubertal

Brougham et al 2012 JCE&M

AMH in 3 girls with cancer







Brougham et al 2012 JCE&M

Summary

AMH is detectable before puberty

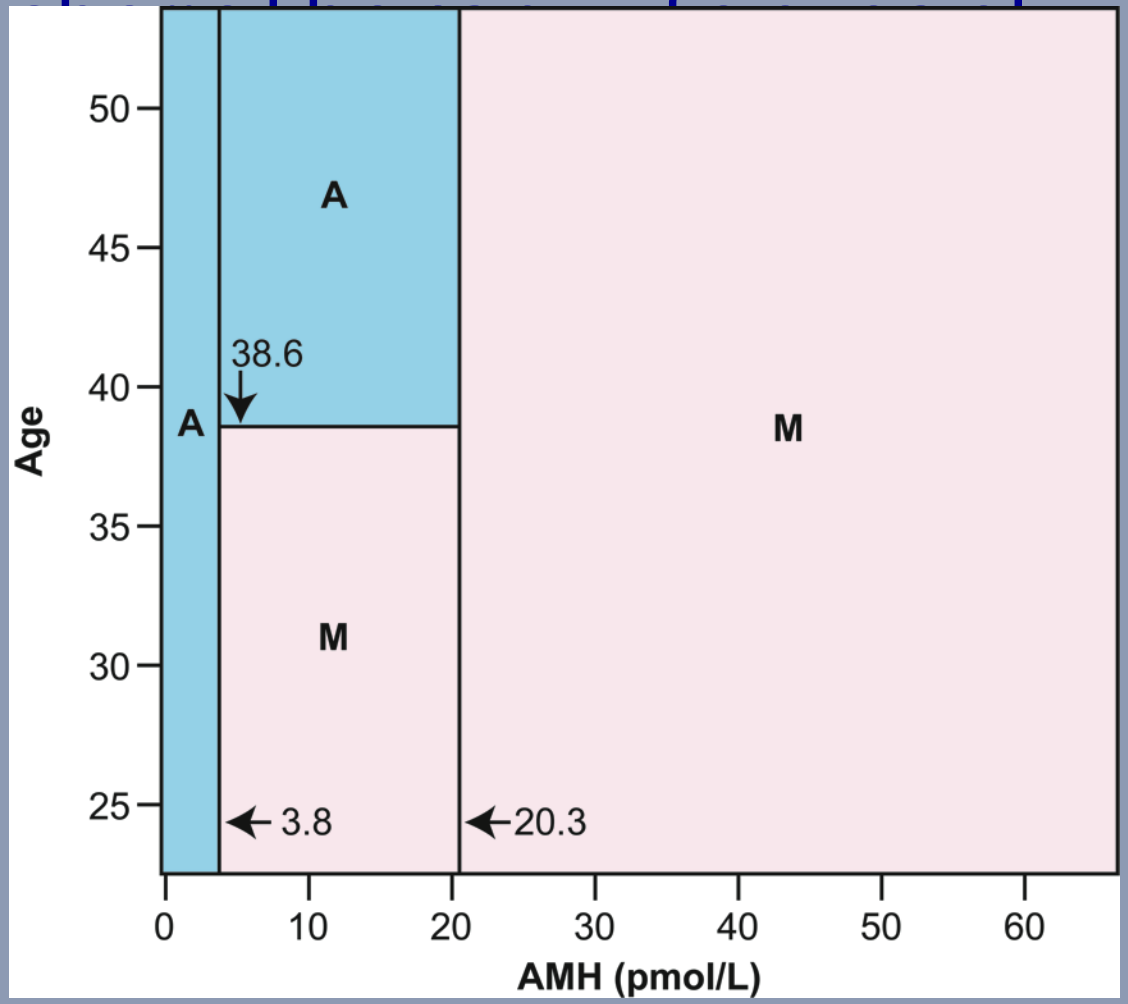
AMH falls rapidly during cancer treatment in both pre-pubertal and pubertal girls

AMH levels recover in those patients at low/medium risk of gonadotoxicity

AMH fails to recover in those at high risk. This could be indicative of future reproductive impairment

Brougham et al 2012 JCE&M

Pretreatment anti-Müllerian hormone predicts for loss of ovarian function after [illegible] breast

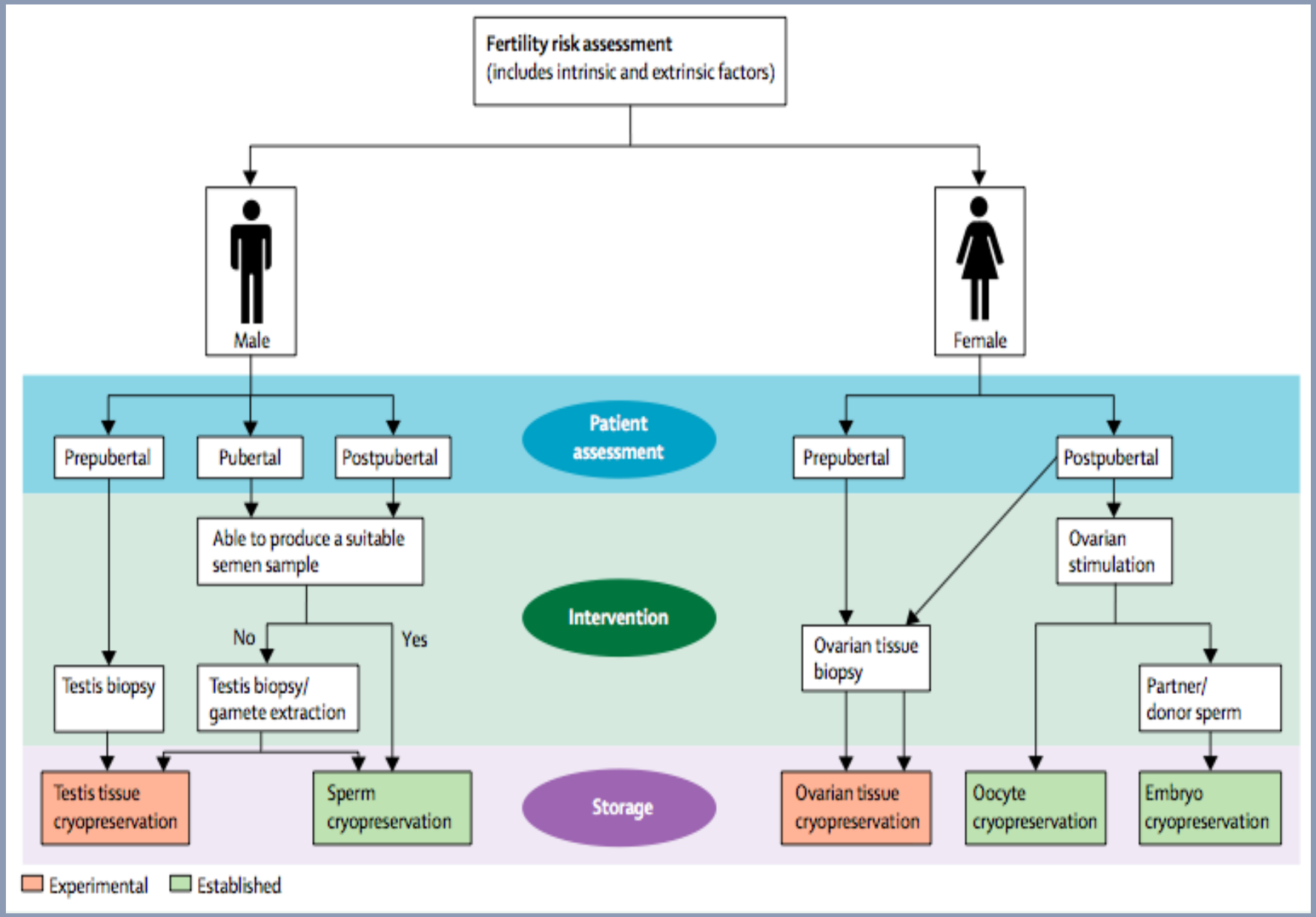


sensitivity 98.2%
specificity 80.0%
for correct classification
of amenorrhoea

n=75

Anderson and Cameron 2011 JCE&M
Anderson et al 2013 Eur J Cancer

Fertility preservation options: established and experimental



Anderson RA…Wallace WH. Lancet Diabetes Endocrinol. 2015

Key features of the 3 options for fertility preservation for women

Embryo cryopreservation

- Established but require time and a partner

Oocyte cryopreservation

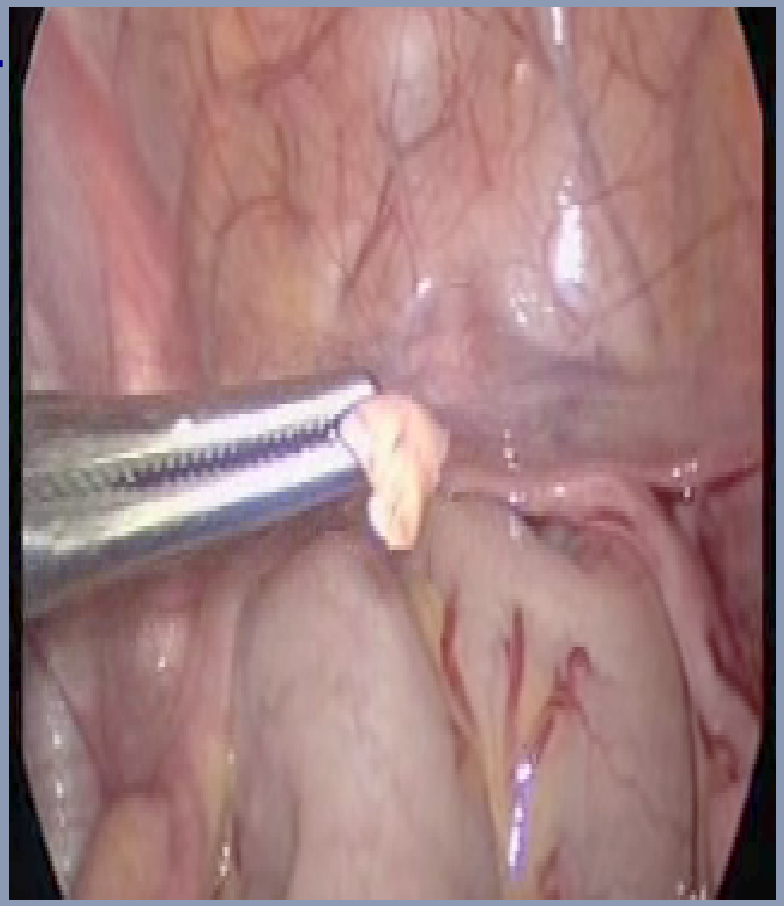
- Established but require time and hormone stimulation (success rate per oocyte low)

Ovarian tissue cryopreservation

- Minimal delay
- No lower age limit
- Surgical procedure
- Allows for future developments

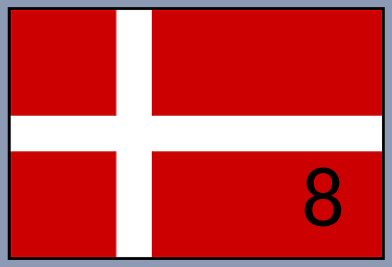
Ovarian tissue cryopreservation: World-wide experi

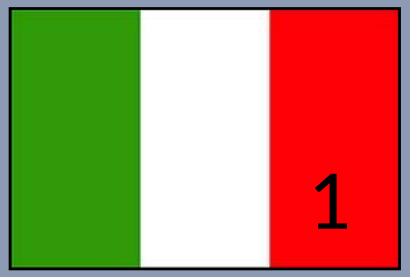
- At least 60 pregnancies worldwide after orthotopic reimplantation of frozen–thawed ovarian cortex
- Success rate is unclear as the denominator is unknown
- No pregnancies reported following the reimplantation of ovarian tissue harvested pre-pubertally
- Young children are potentially ideal candidates

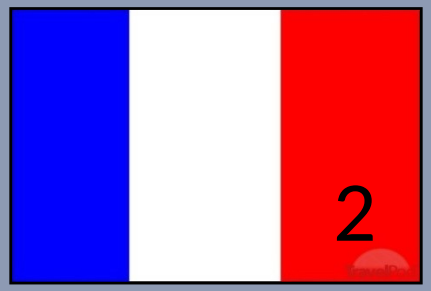


Donnez, J. & Dolmans, M.-M. *Nat. Rev. Endocrinol.* 9, 735–749 (2013)

Children born from transplantation of frozen/thawed ovarian tissue







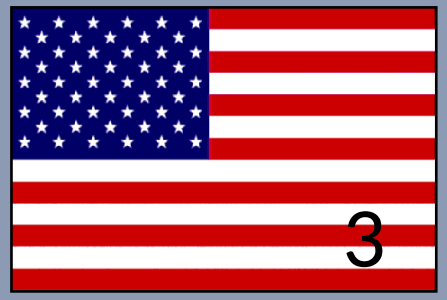
All Normal Babies

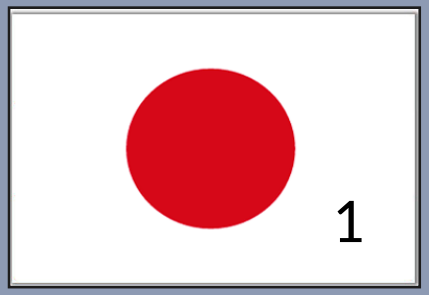
weight and duration

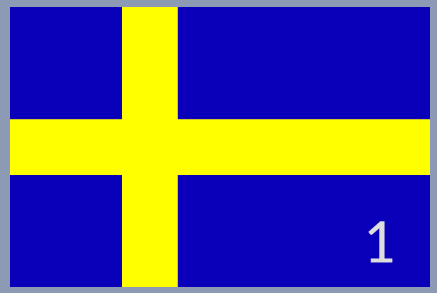
Orthotopic >> heterotopic

All except for one is a result of a slow-freezing protocol

An estimated excess of 150 transplantations have been performed







Cryopreservation: European experience

Three centres (Denmark, Spain and Belgium)

60 cases of orthotopic reimplantation.

Of these women, 11 (21%) became pregnant

Six have delivered 12 healthy babies.

Restoration of ovarian activity was observed in 93% of the patients between 3.5 months and 6.5 months after grafting

The mean duration of ovarian function after trans- plantation is ~4–5 years but can persist for up to 7 years.

Donnez, J. *et al.* *Fertil. Steril.* 99, 1503–1513 (2013).

Ovarian Cryopreservation & Ovarian Function

Edinburgh experience in children (< 18 yrs) 1996-2012

***Panel 2:* The Edinburgh Selection Criteria for gonadal tissue cryopreservation**

These criteria were established with ethics committee review and approval because they refer to experimental procedures, and should be regarded as a starting point for future discussion, research, and refinement.

Female patients[112]

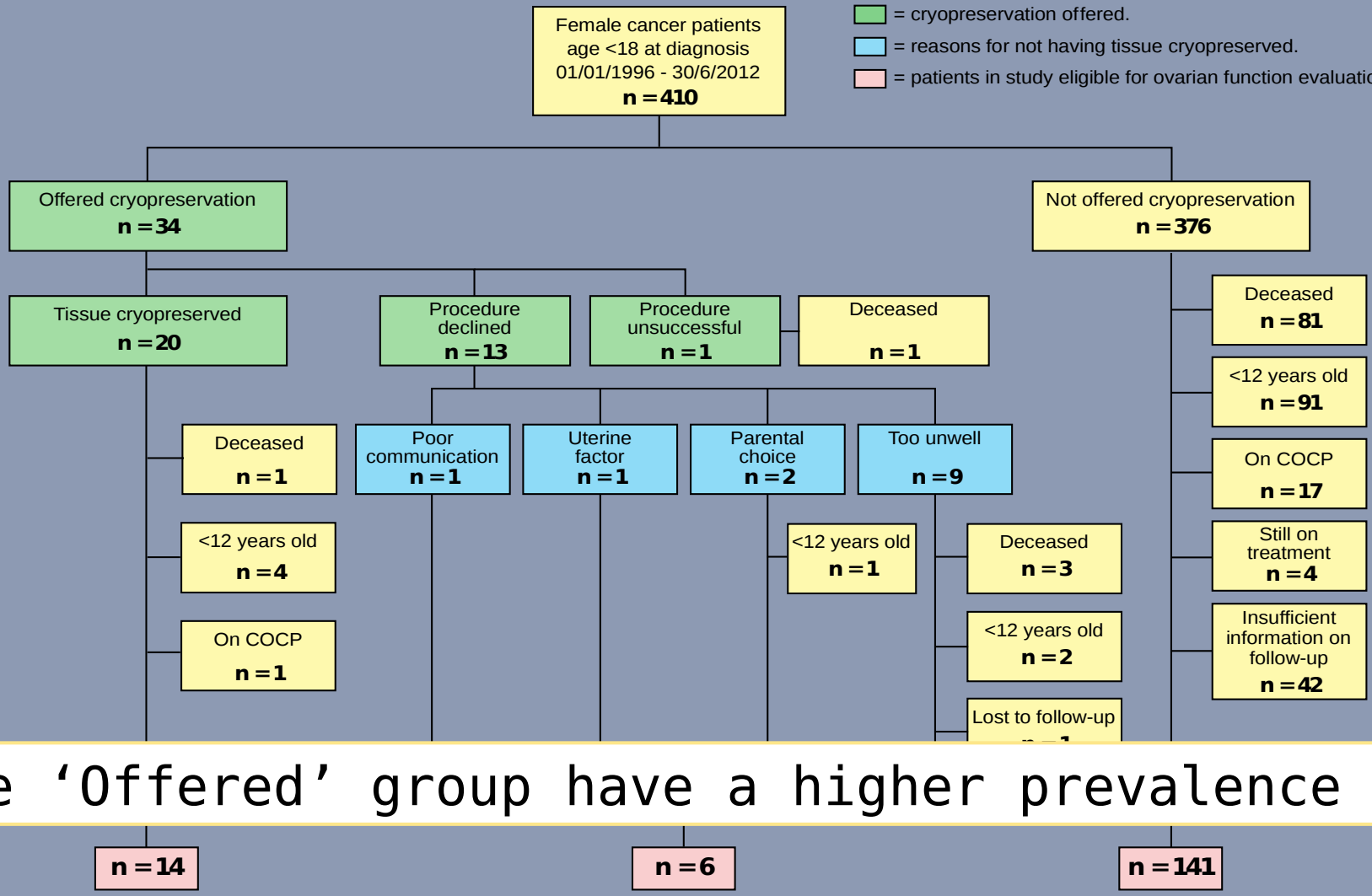
- Age younger than 35 years
- No previous chemotherapy or radiotherapy if aged 15 years or older at diagnosis, but mild, non-gonadotoxic chemotherapy is acceptable if younger than 15 years
- A realistic chance of 5-year survival
- A high risk of premature ovarian insufficiency (>50%)
- Informed consent (parent and, when possible, patient)
- Negative HIV, syphilis, and hepatitis serology
- Not pregnant and no existing children

Male patients

- Age 0–16 years
- A high risk of infertility (>80%)
- Unable to produce a semen sample by masturbation
- No clinically significant pre-existing testicular disease (eg, cryptorchidism)
- Informed consent (parent and, when possible, patient)
- Negative HIV, syphilis, and hepatitis serology

Anderson RA…Wallace WH. Lancet Diabetes Endocrinol. 2015

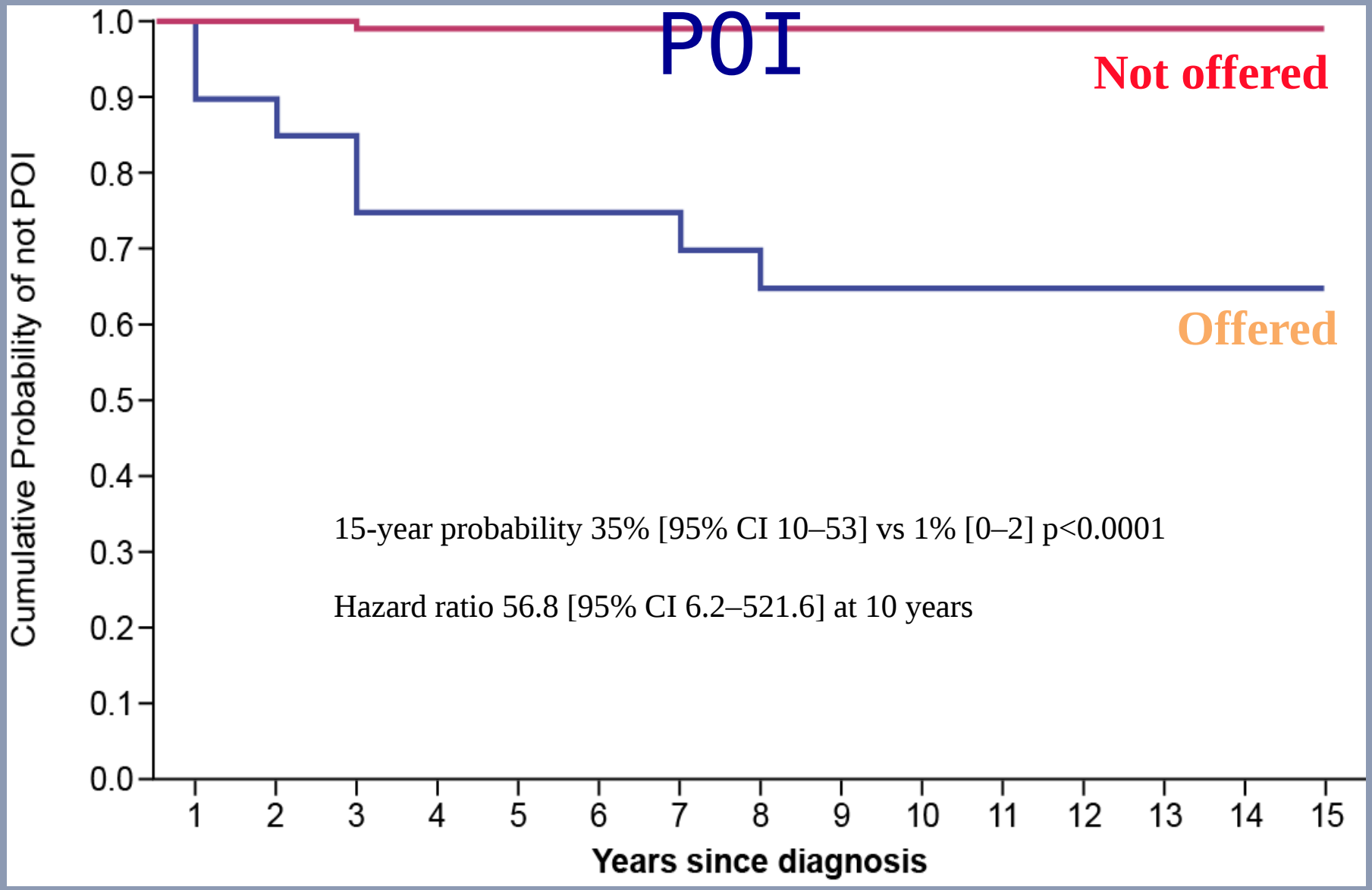
15 year, population-based analysis of criteria for ovarian cryopreservation



the ‘Offered’ group have a higher prevalence of PC

Walllace WH et al. 2014 Lancet Oncology

Cumulative incidence of POI



Walllace…..and Anderson 2014 Lancet Oncology

Conclusion

Ovarian cryopreservation was offered to 9% of our patients, and performed in 5%

The procedure was safe and without complications

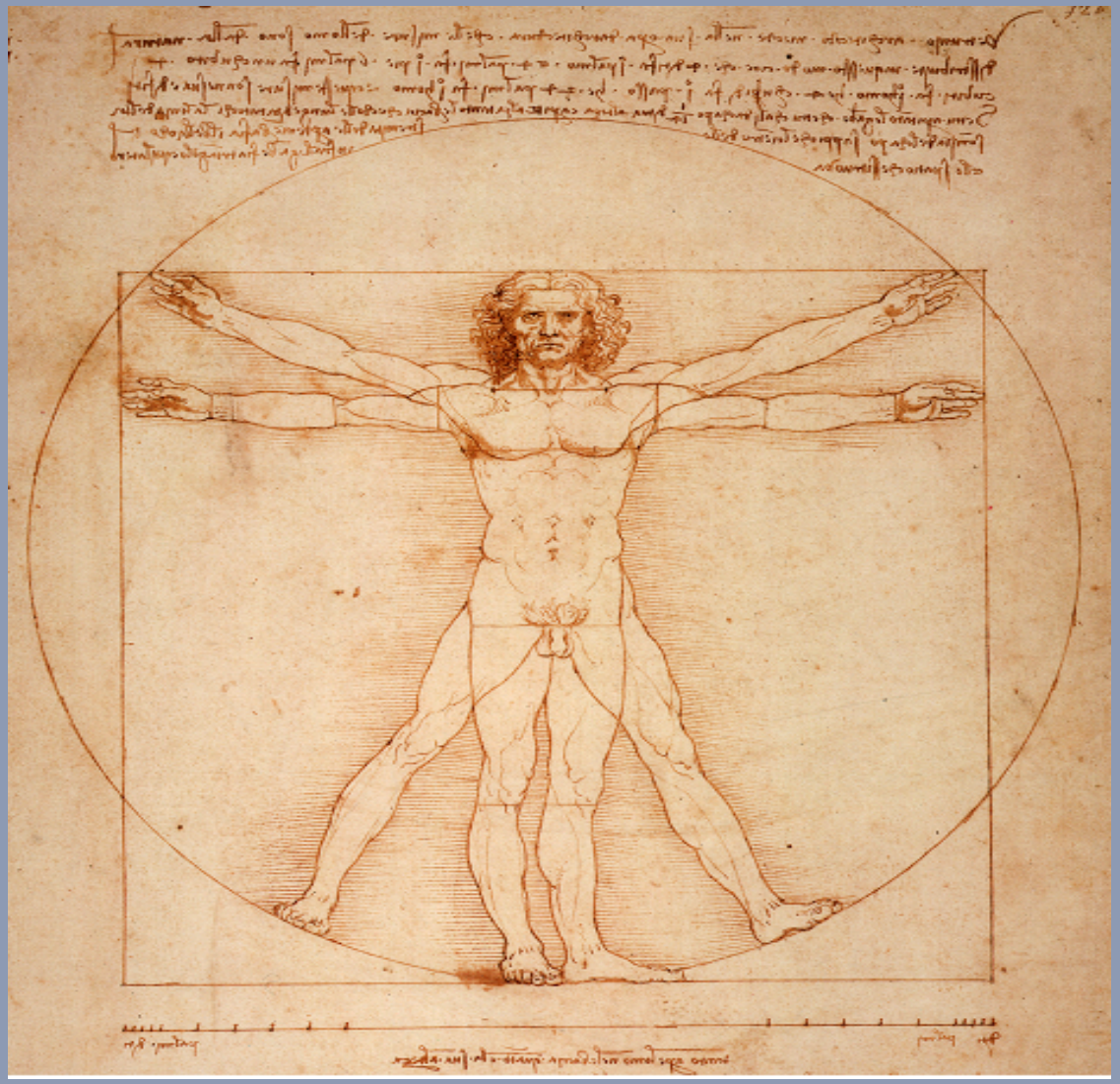
No patients have asked for re-implantation of their tissue – to date

All patients who have thus far developed premature ovarian insufficiency were identified except one patient

The Edinburgh Selection Criteria have proved to be helpful in selecting those patients at highest risk of POI

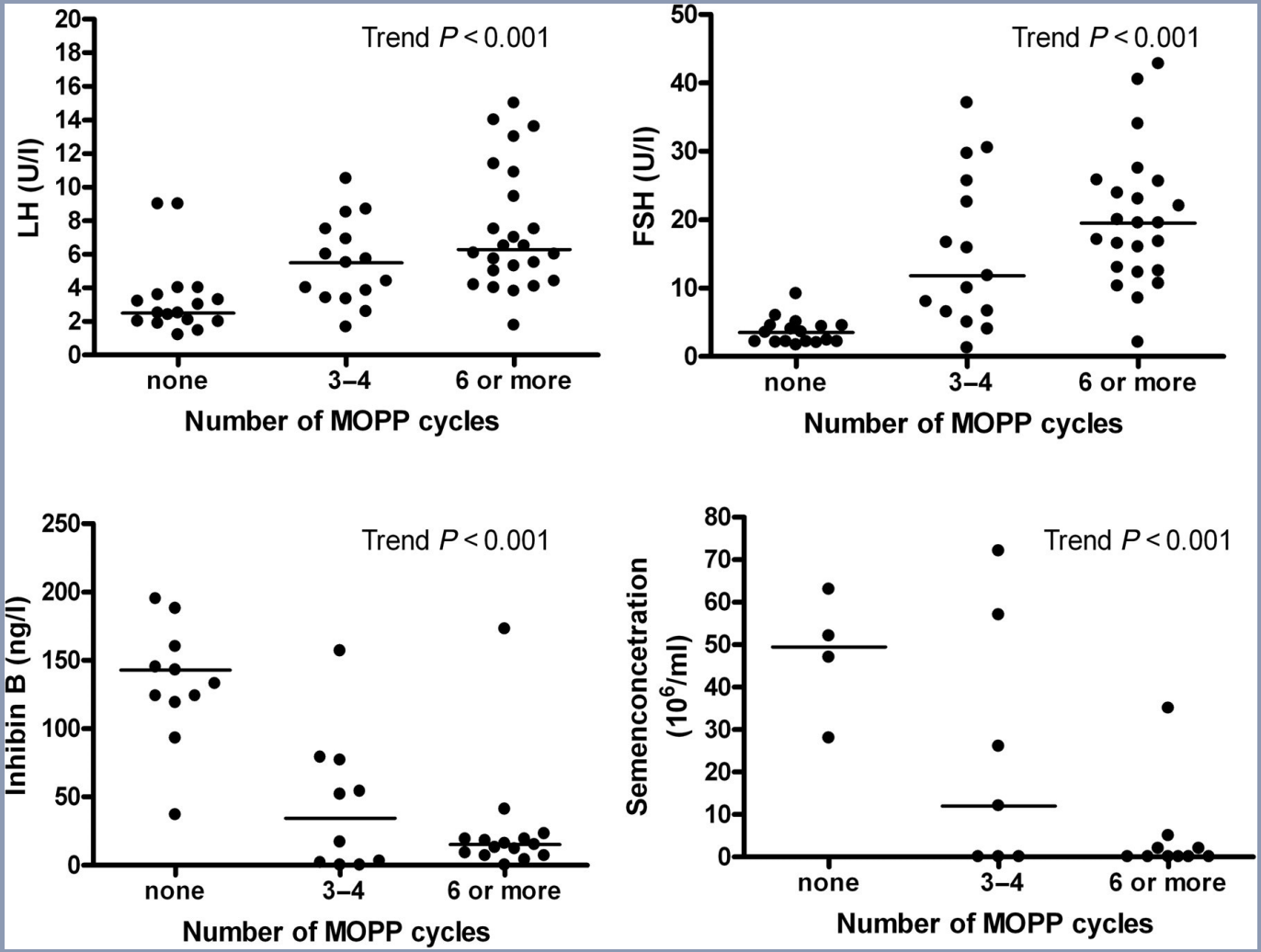
Wallace WH…..and Anderson 2014 Lancet Oncology

Vitruvian man



Leonardo da Vinci 1490

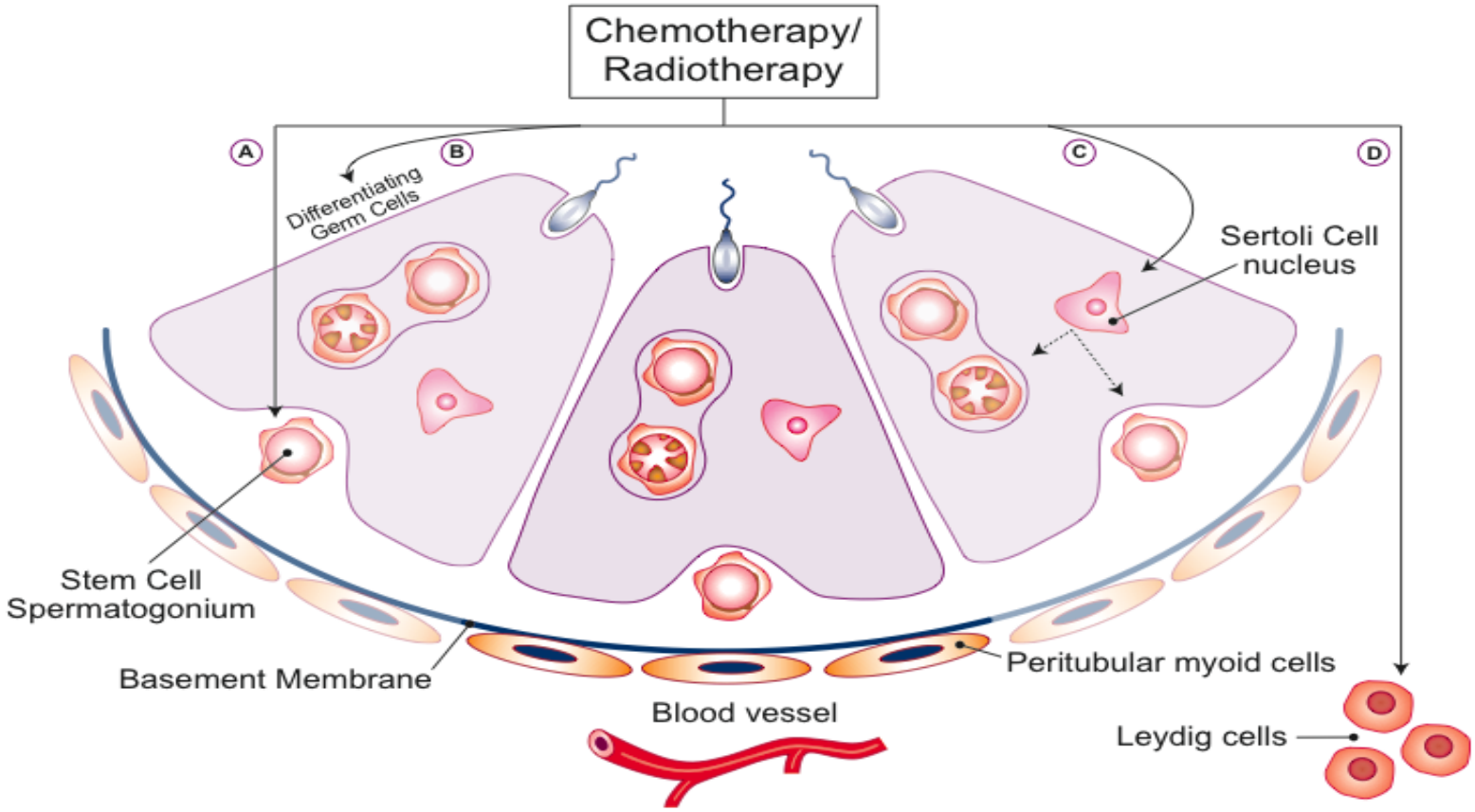
Hormone levels and semen concentration in relation to the number of MOPP cycles in male long-term survivors of childhood Hodgkin's.



van Beek R D et al. Hum. Reprod. 2007;22:3215-3222

human reproduction

Sertoli Cell

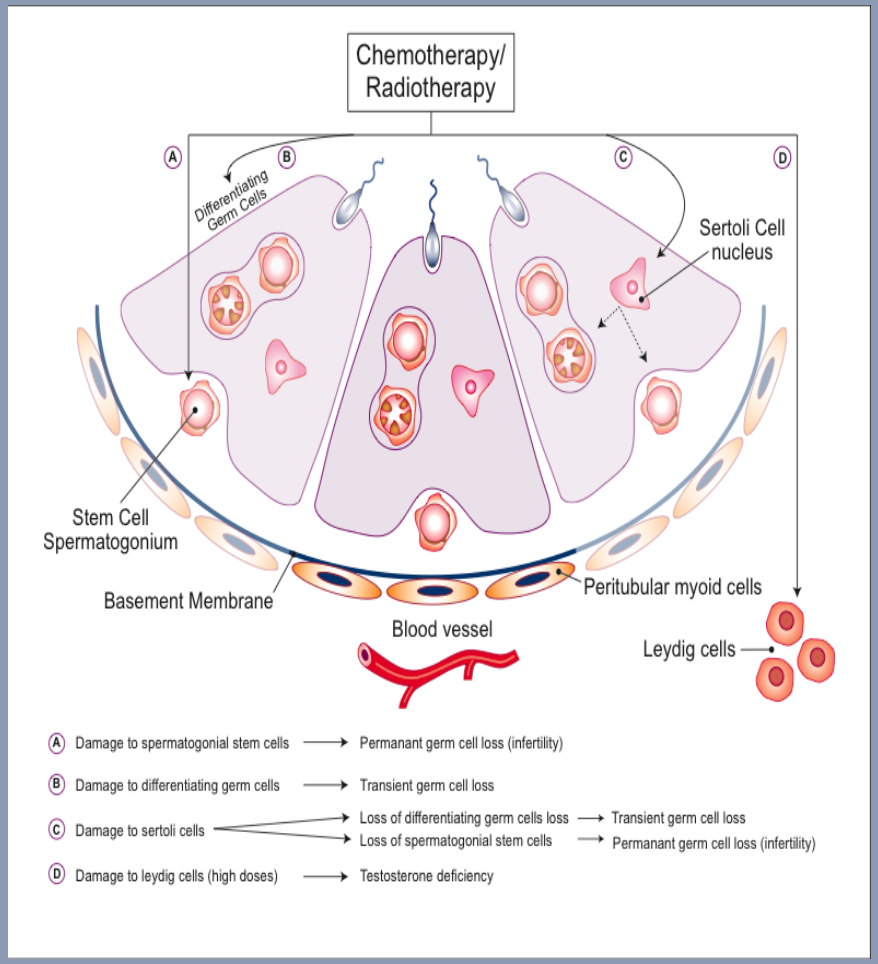


- (A) Damage to spermatogonial stem cells → Permanant germ cell loss (infertility)
- (B) Damage to differentiating germ cells → Transient germ cell loss
- (C) Damage to sertoli cells → Loss of differentiating germ cells loss → Transient germ cell loss
  - Damage to sertoli cells → Loss of spermatogonial stem cells → Permanant germ cell loss (infertility)
- (D) Damage to leydig cells (high doses) → Testosterone deficiency

Radiation-induced testicular damage

Germinal epithelium

>1.2Gy azoospermia



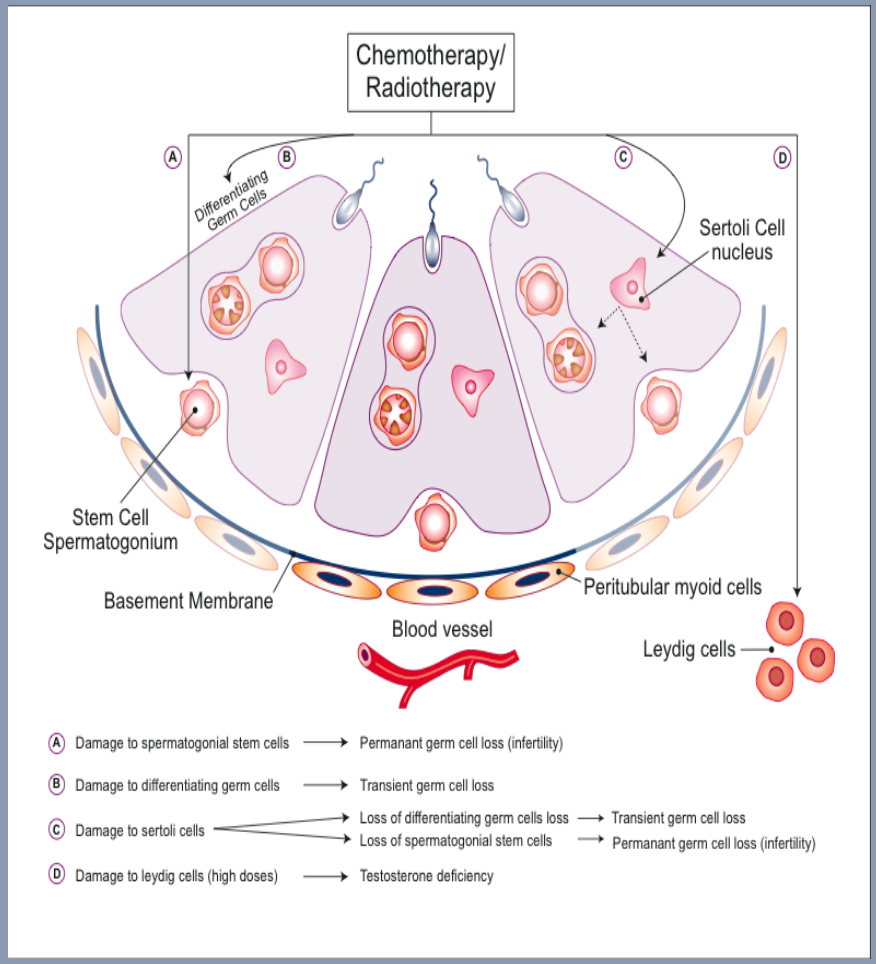
Radiation-induced testicular damage

Leydig cell function

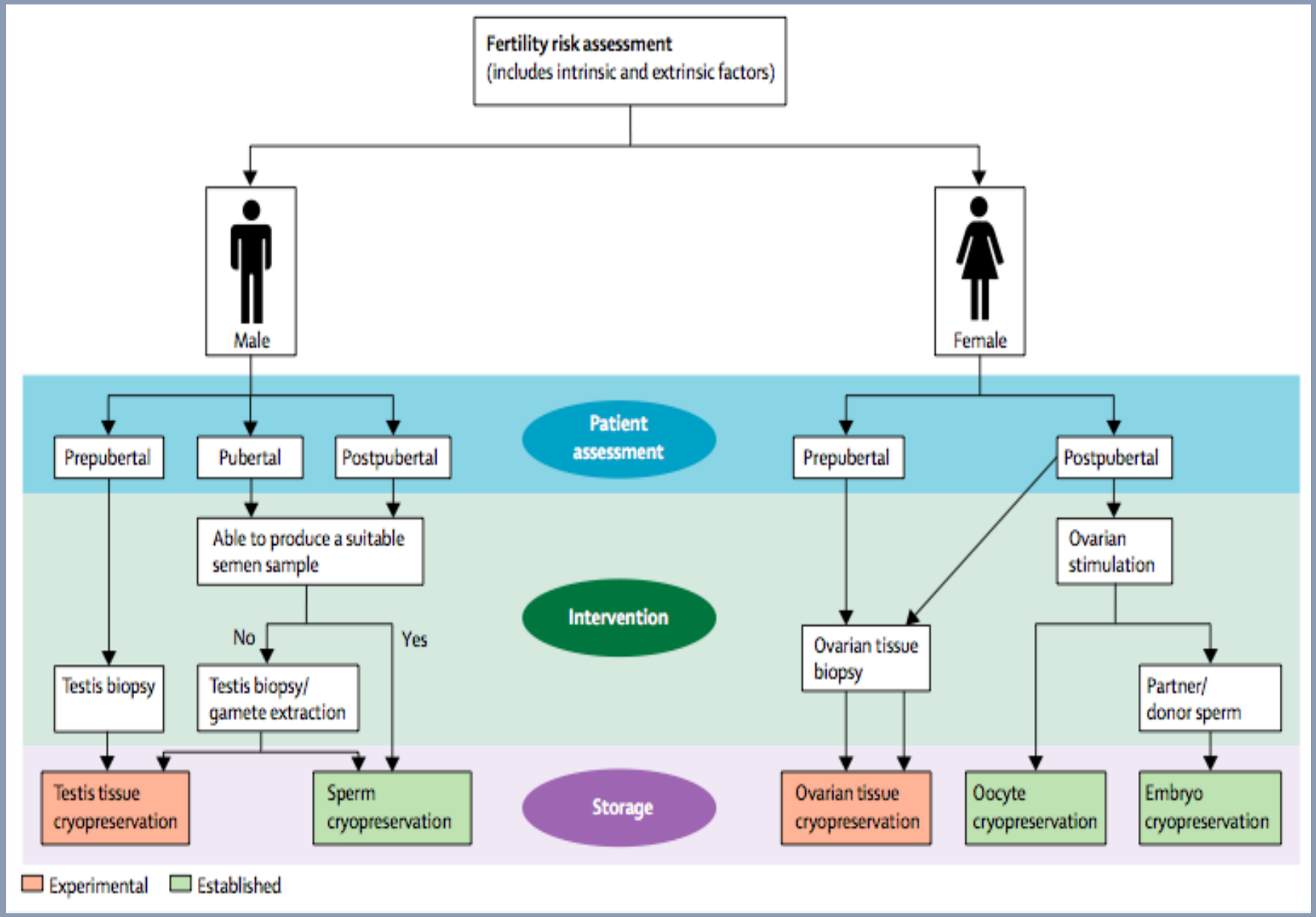
Dose received by testis P <0.05

Time Interval after radiotherapy P <0.05

Age at treatment NS



Li, Kelsey, Wallace (unpublished data)



Anderson RA…Wallace WH. Lancet Diabetes Endocrinol. 2015

Males: Fertility preservation

Young men who can produce semen should have the opportunity of sperm banking before treatment begins

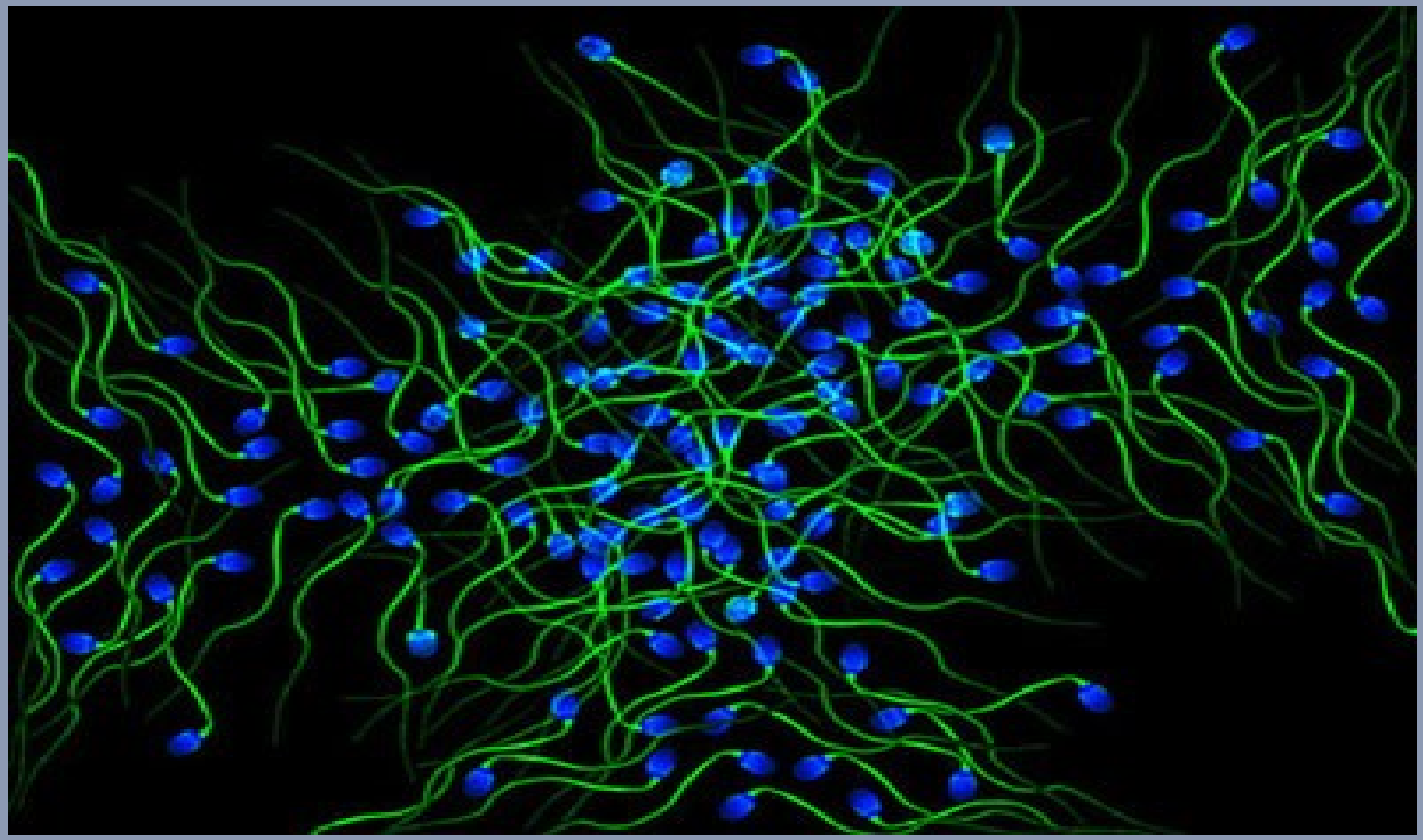
Sperm retrieval should be considered if the chances of infertility are high and the testes are >10mls

- Storage of gametes is governed by the HFE act 1990
- Written informed consent from a competent male is required

There is currently no established option to preserve fertility in the pre-pubertal boy….

Isolated human sperm cells (1500x)

Albert Tousson – Nikon Small world



Cryopreservation of pre-pubertal testis tissue prior to cancer treatment

Boys undergoing cancer treatment with >80% risk of infertility

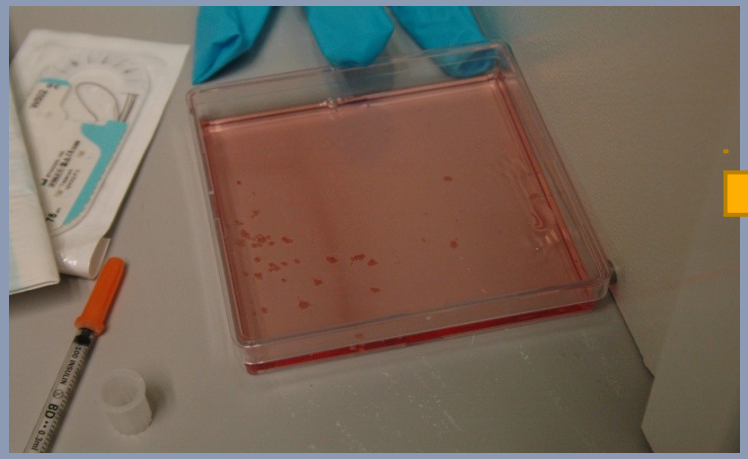
Biopsy to be taken with routine procedure

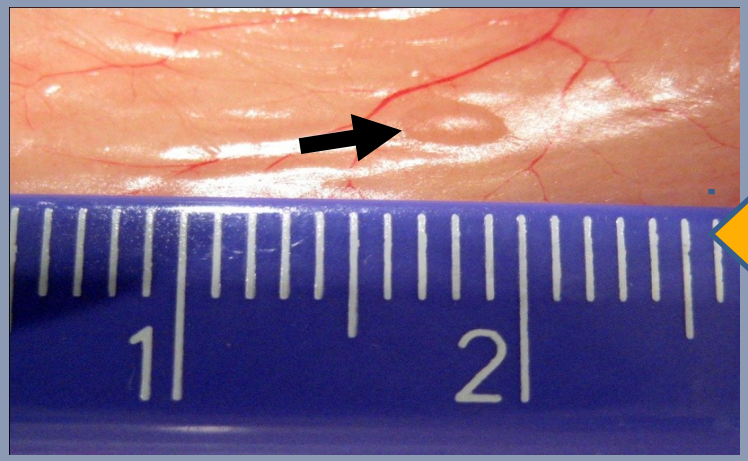
Storage by Tissue Services according to ‘mature’ or ‘immature’ protocol

Small piece of tissue to be used for research

Ethical Approval Granted – September 2013

Human Testis Xenografting





Challenges

Provide fertility counseling to all young patients with cancer

Cryopreserve ovarian tissue from the right (high risk) patients

Define the success rate of the procedures

Develop IVG/M as a safe alternative to re-implantation through basic research

Edinburgh Fertility Preservation

www.ed.ac.uk/Edinburgh-fertility-preservation

@edinfertility

Acknowledgements

Richard Anderson
David T Baird
Tom Kelsey
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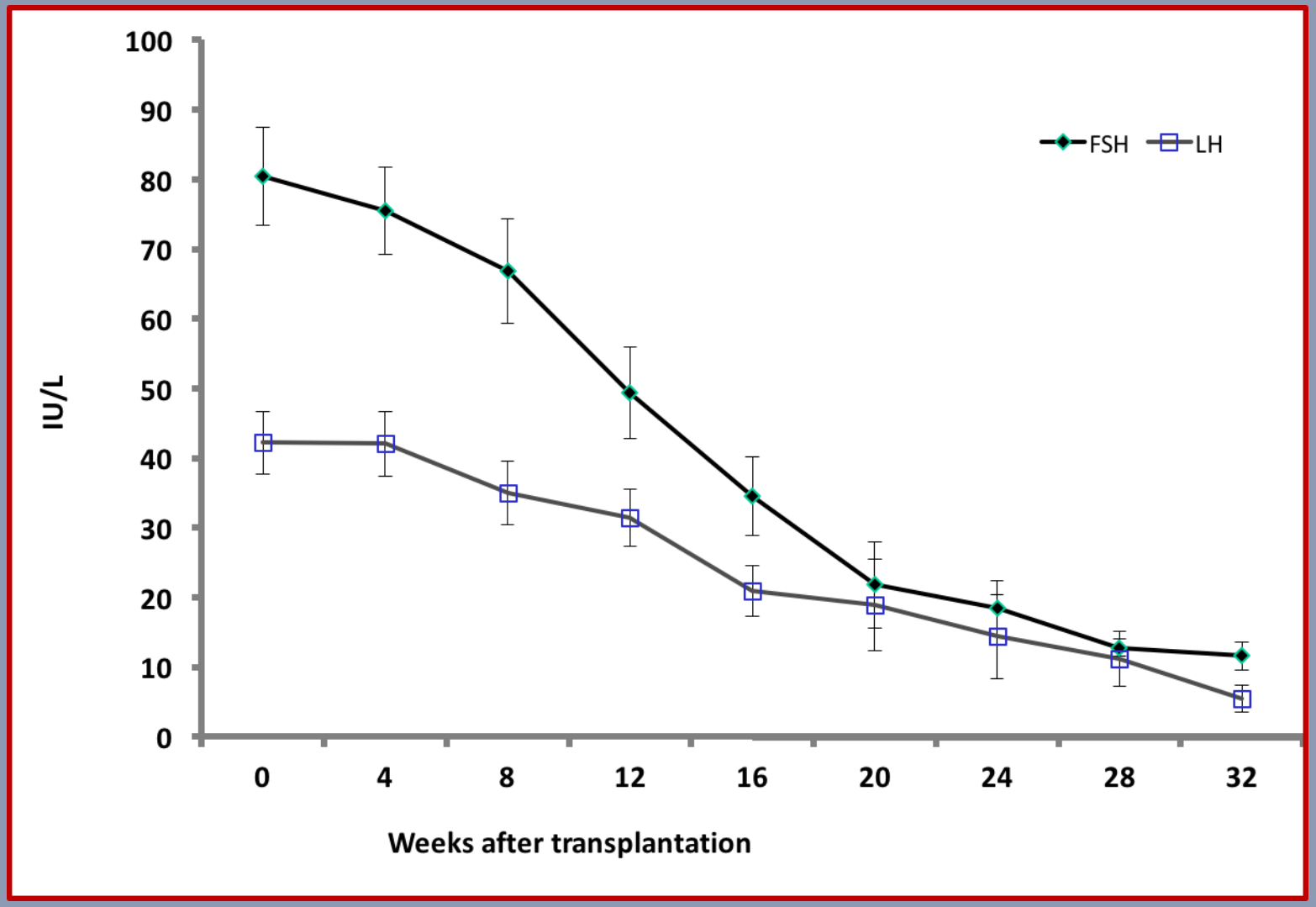
George Galea

Rod Mitchell
Louise Bath
Chris Kelnar
Angela Edgar
Mark Brougham
Fraser Munro

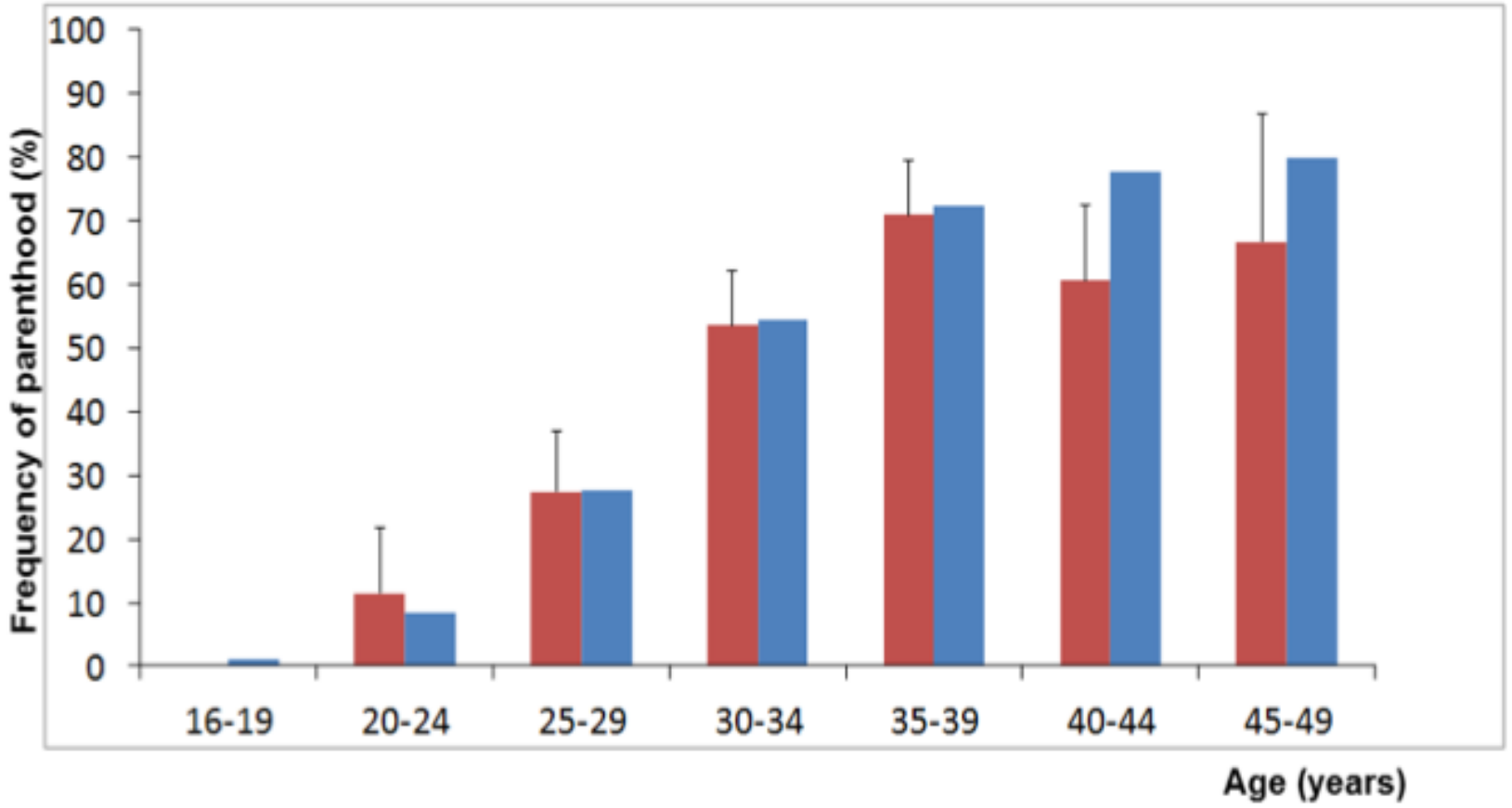
Thank You

Reduction in FSH and LH following transplantation of frozen/thawed ovarian tissue in Danish patients



Parenthood in 590 adult female survivors treated with five successive protocols for Hodgkin lymphoma during childhood and adolescence. A prospective, longitudinal and long-term study.

Professor Jürgen H. Brämswig, M.D., Marianne Riepenhausen, Ph.D. Professor Günther Schellong, M.D.

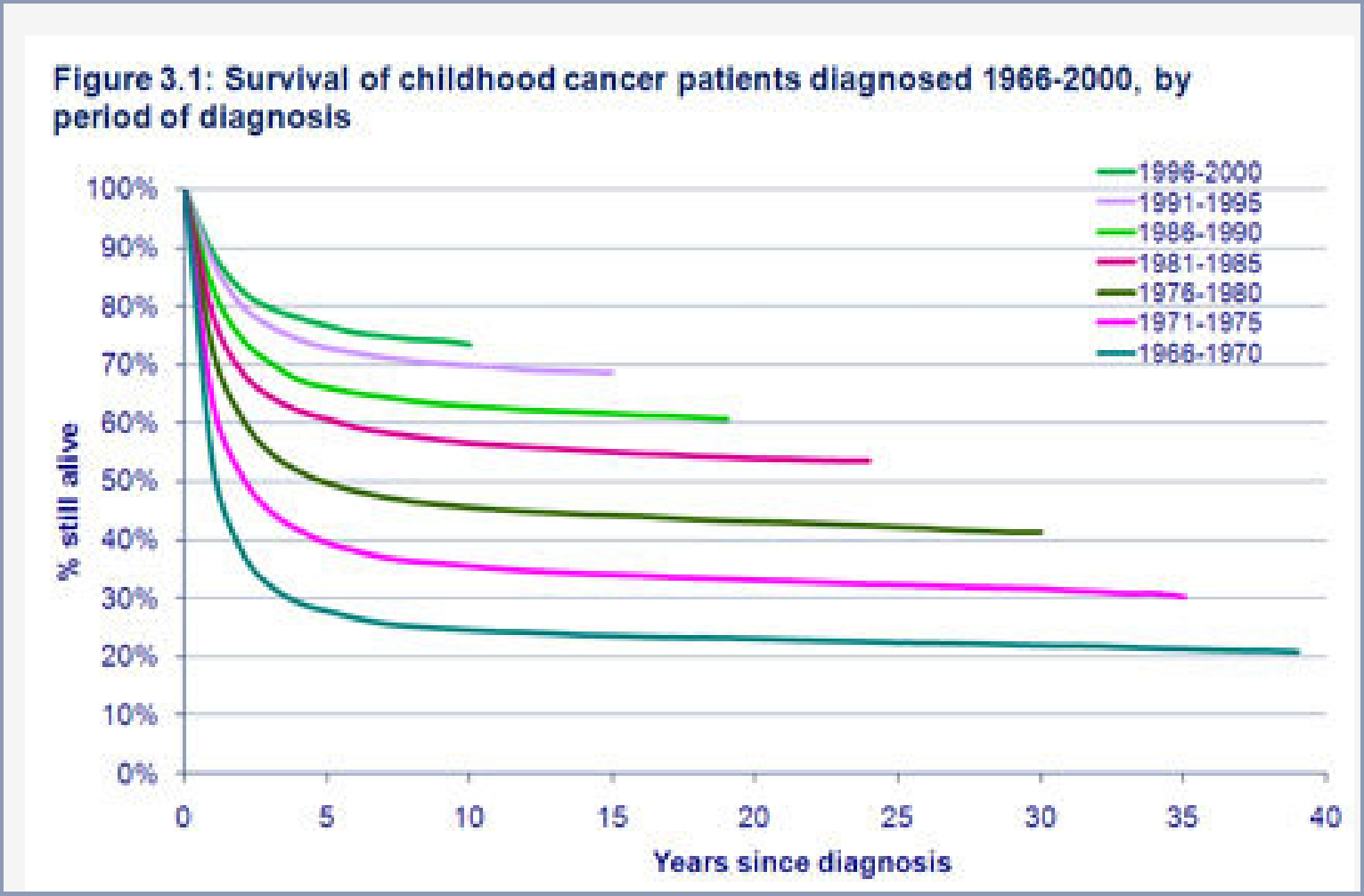


Lancet Oncology (2015)

Parenthood in female HL-survivors <18 years at diagnosis is similar to parenthood in the 16-39 year old female German population and not affected by gonadotoxic chemotherapy.

It is reduced only in women >40 years and in women who received pelvic radiation

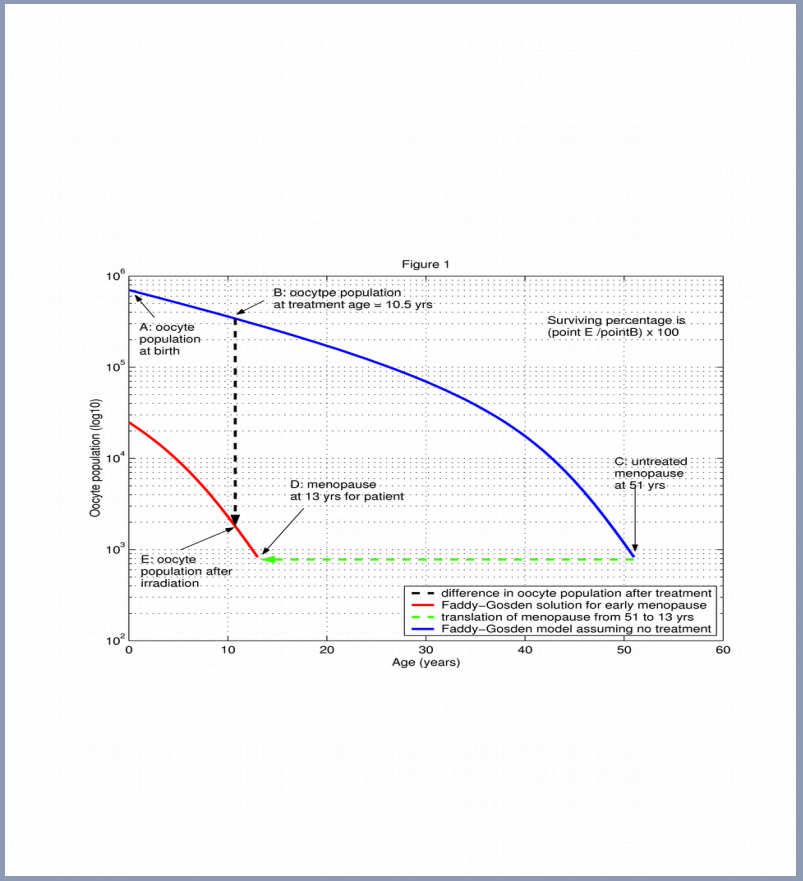
Improved Five Year Survival (1966-2000)



Radiation-induced ovarian damage

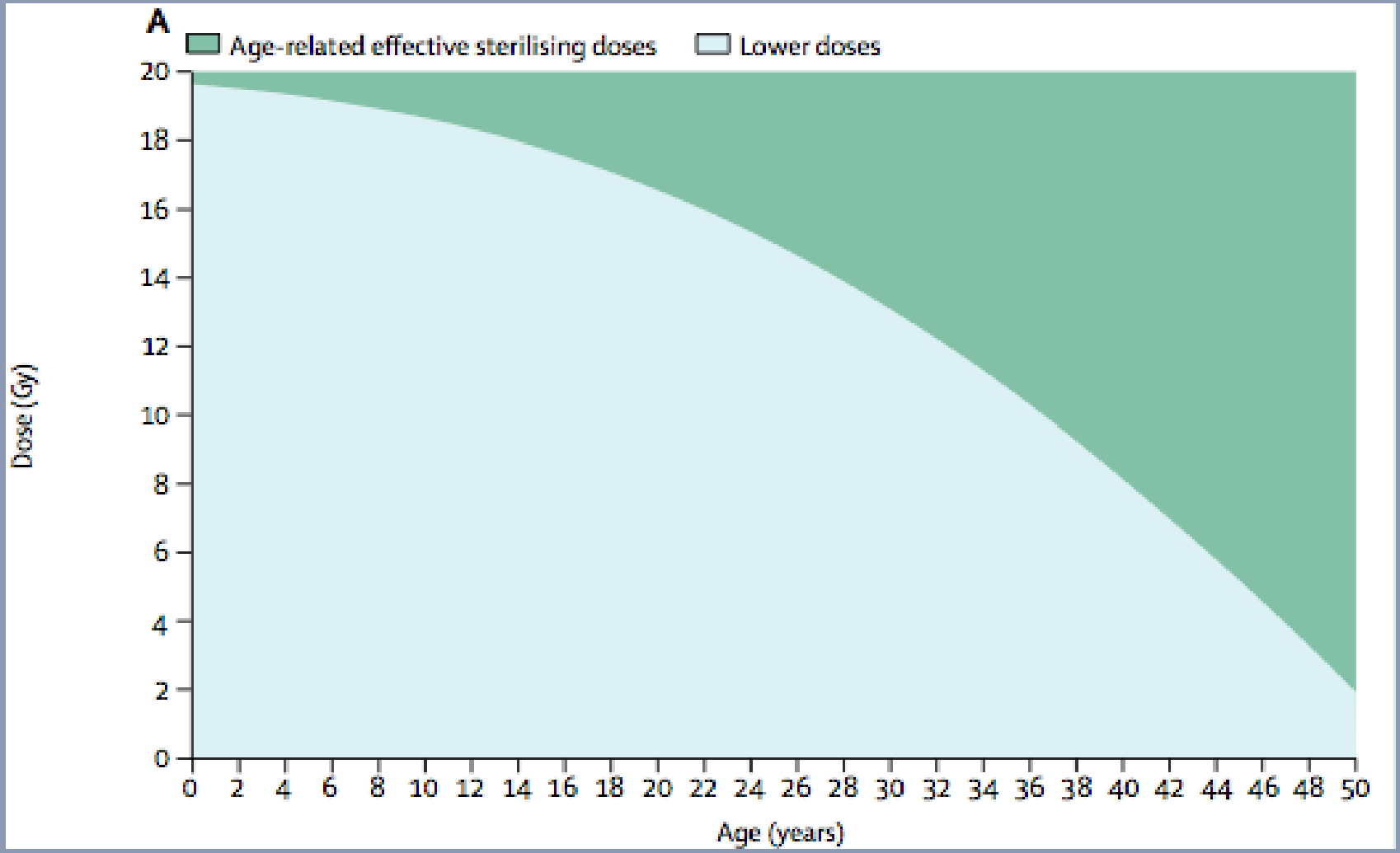
Human oocyte (Primordial follicle)

$LD_{50} < 2$ Gy

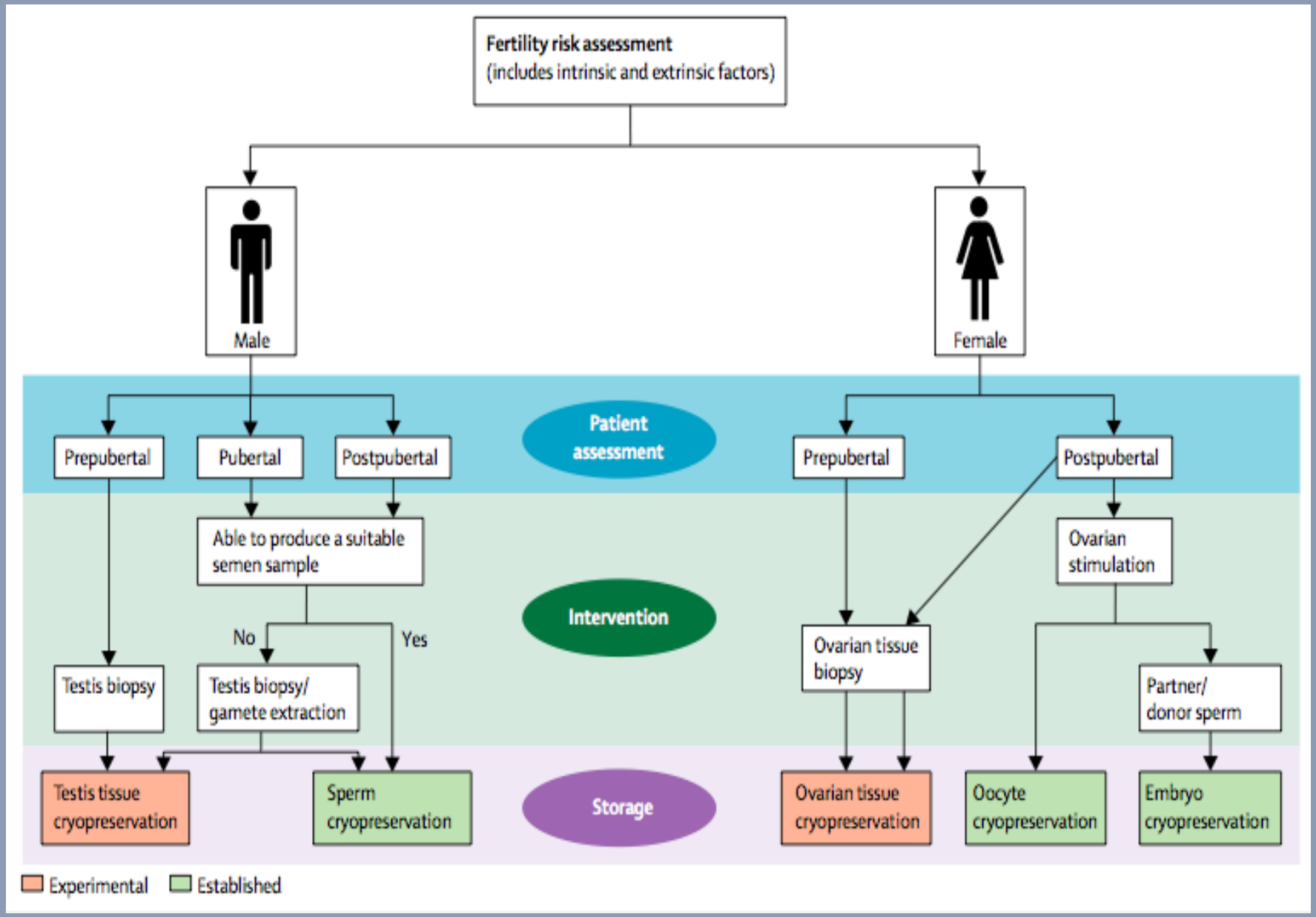


Wallace, Thomson, Kelsey. (2003) Hum Reprod.

Effective ovarian sterilizing doses of radiotherapy with increasing age

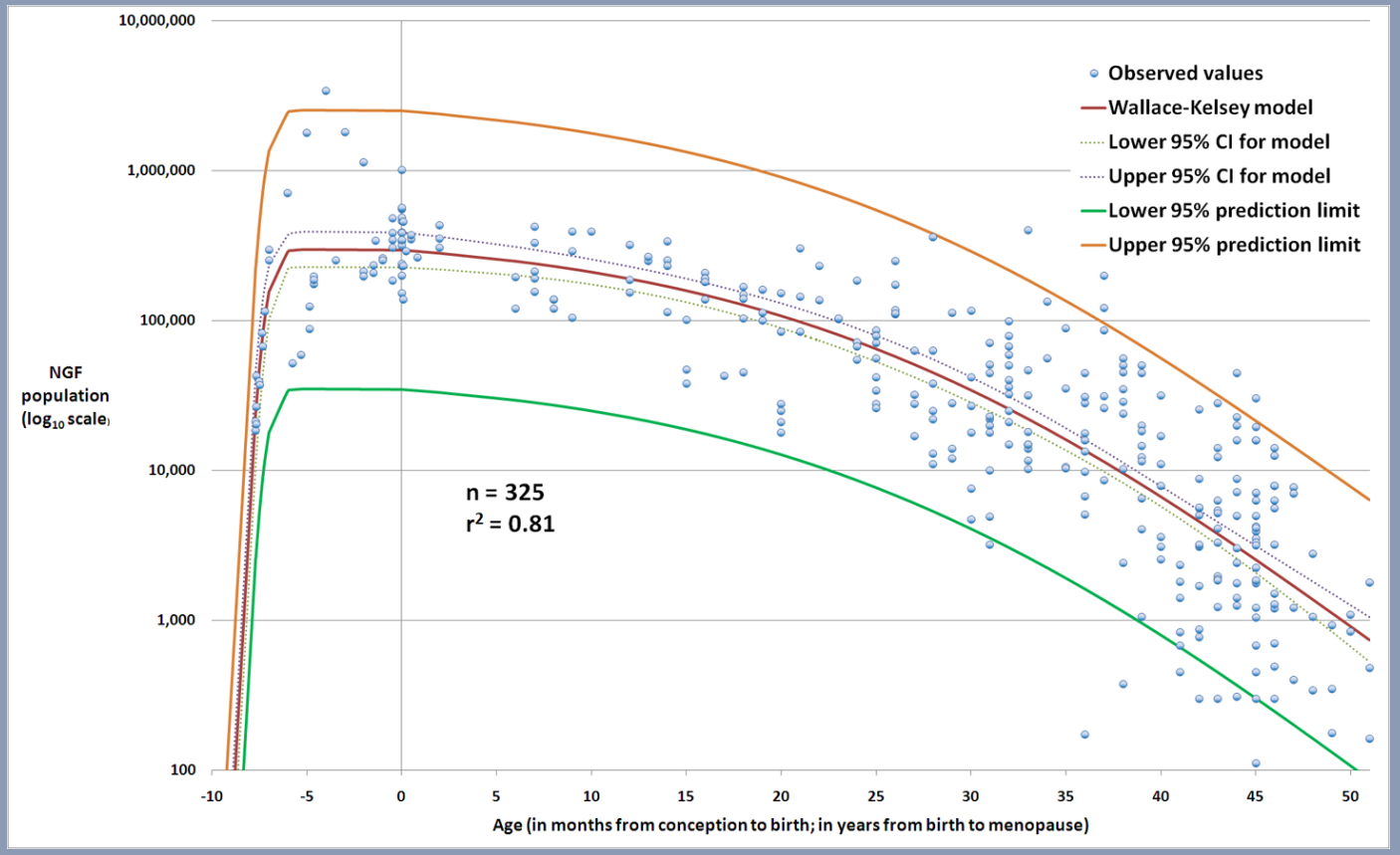


Anderson RA…Wallace WH. Lancet Diabetes Endocrinol. 2015



Anderson RA…Wallace WH. Lancet Diabetes Endocrinol. 2015

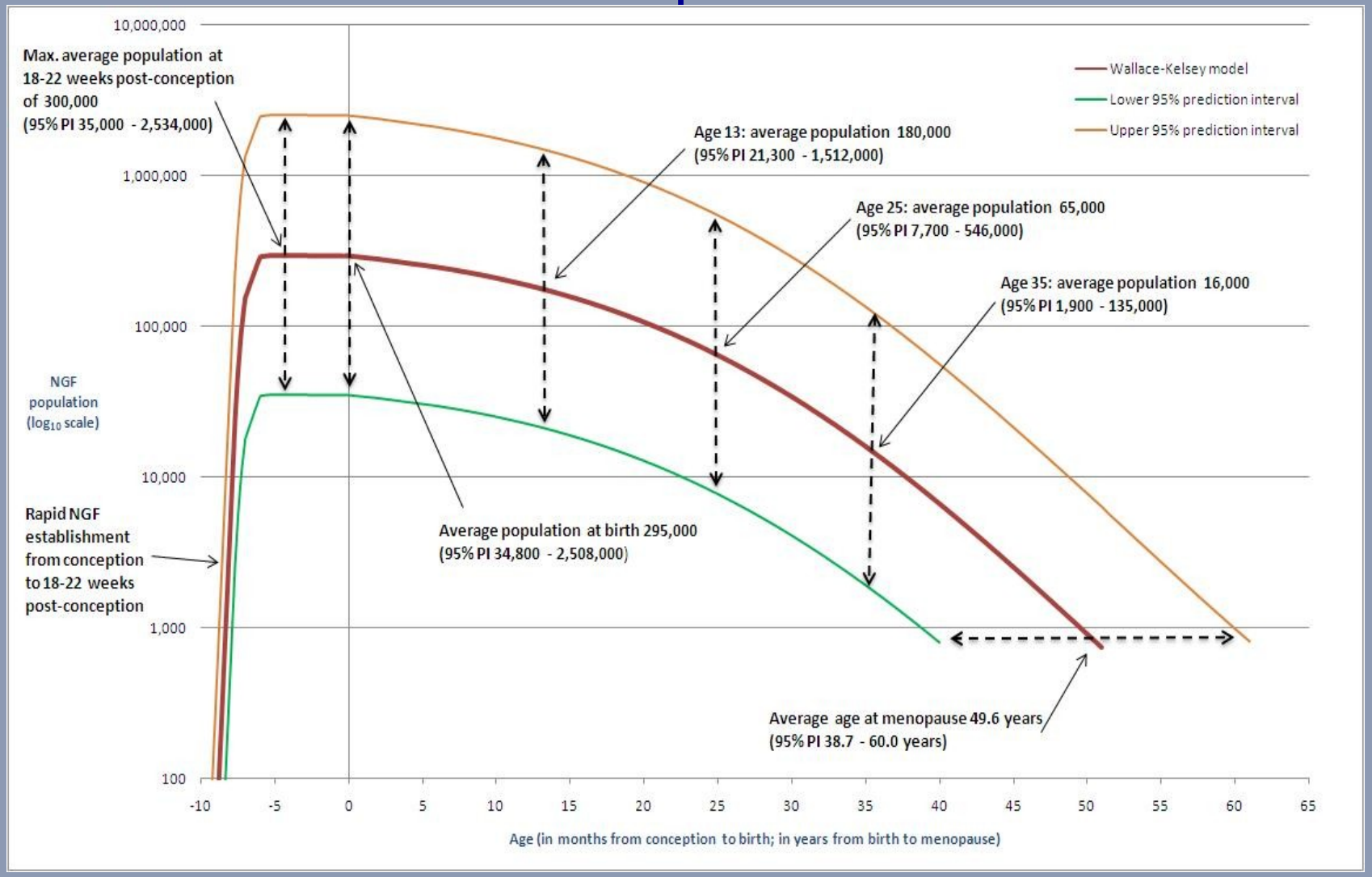
The Wallace-Kelsey Model
(Five parameter asymmetric double-Gaussian cumulative curve)



$$log_{10}(y) = \frac{a}{4}\left[1 + \mathrm{Erf}\left(\frac{x+b+\frac{c}{2}}{d\sqrt{2}}\right)\right]\left[1 - \mathrm{Erf}\left(\frac{x+b-\frac{c}{2}}{e\sqrt{2}}\right)\right]$$

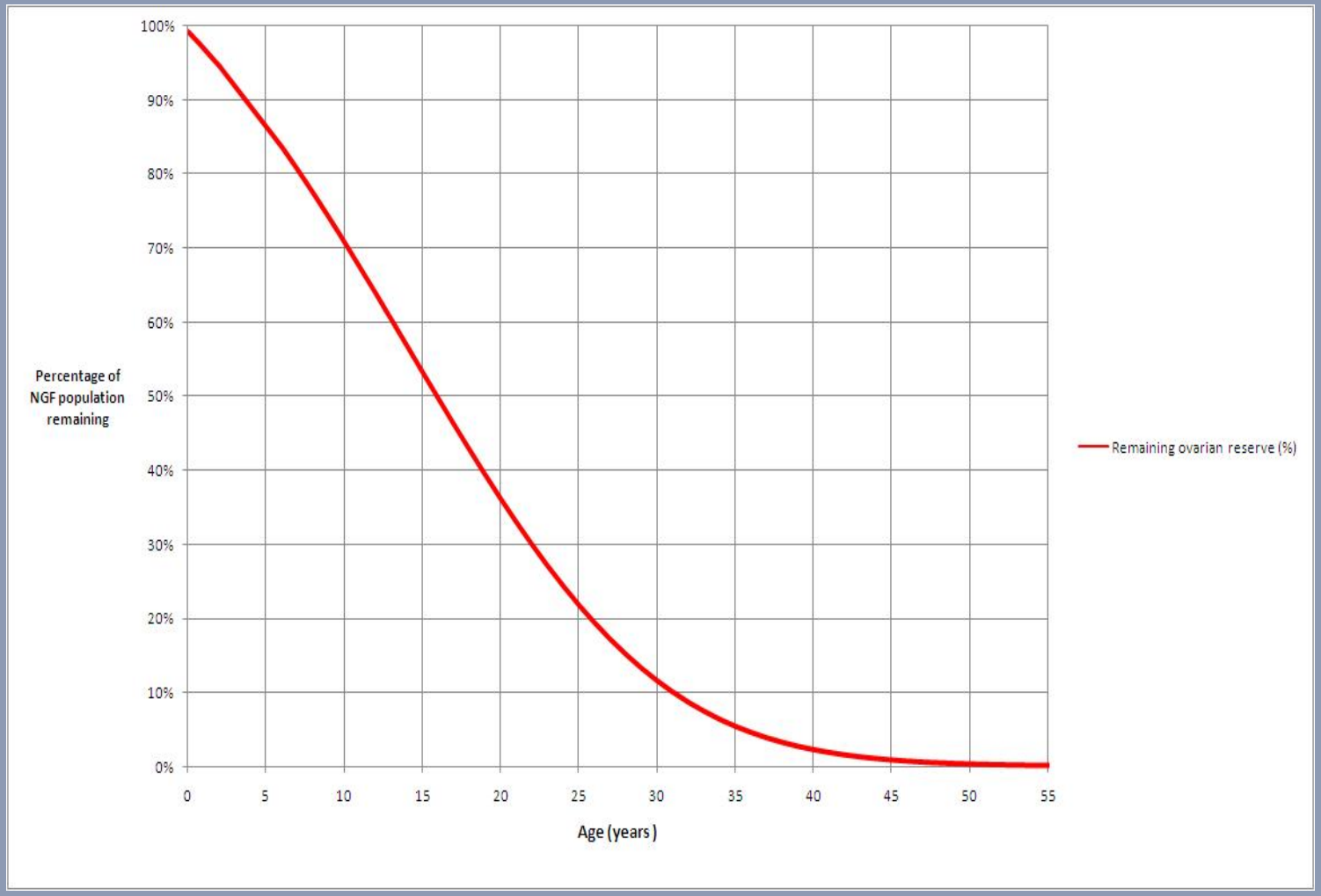
Wallace &Kelsey (2010) PloS ONE

Ovarian reserve: Conception to Menopause



Wallace &Kelsey (2010) PloS ONE

Percentage of NGF population remaining with increasing age



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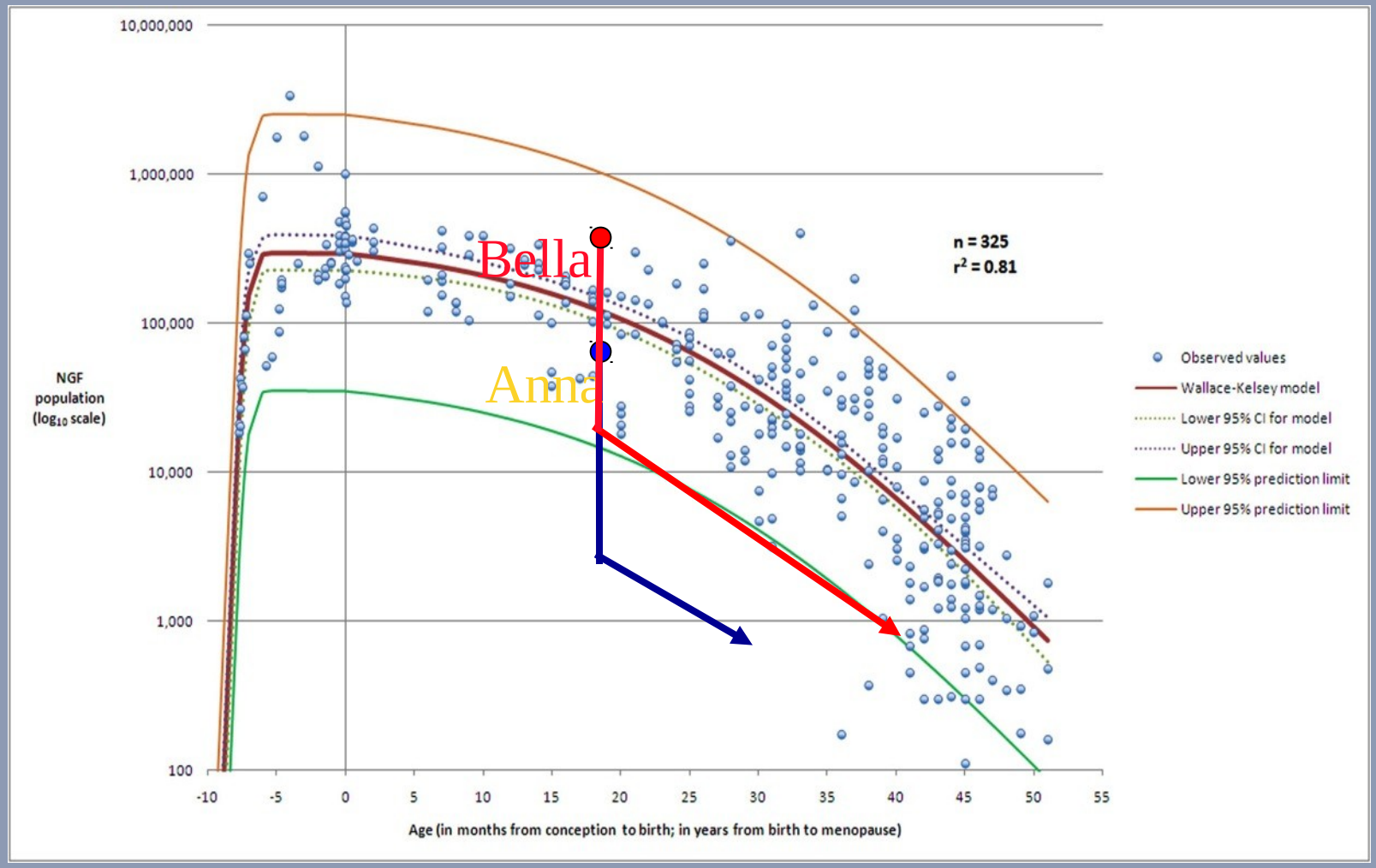


Wallace &Kelsey (2010) PloS ONE

Prediction of Ovarian Reserve (AMH)

Anti Mullerian Hormone (AMH) is an important product of the adult ovary, produced by the granulosa cells of small growing follicles

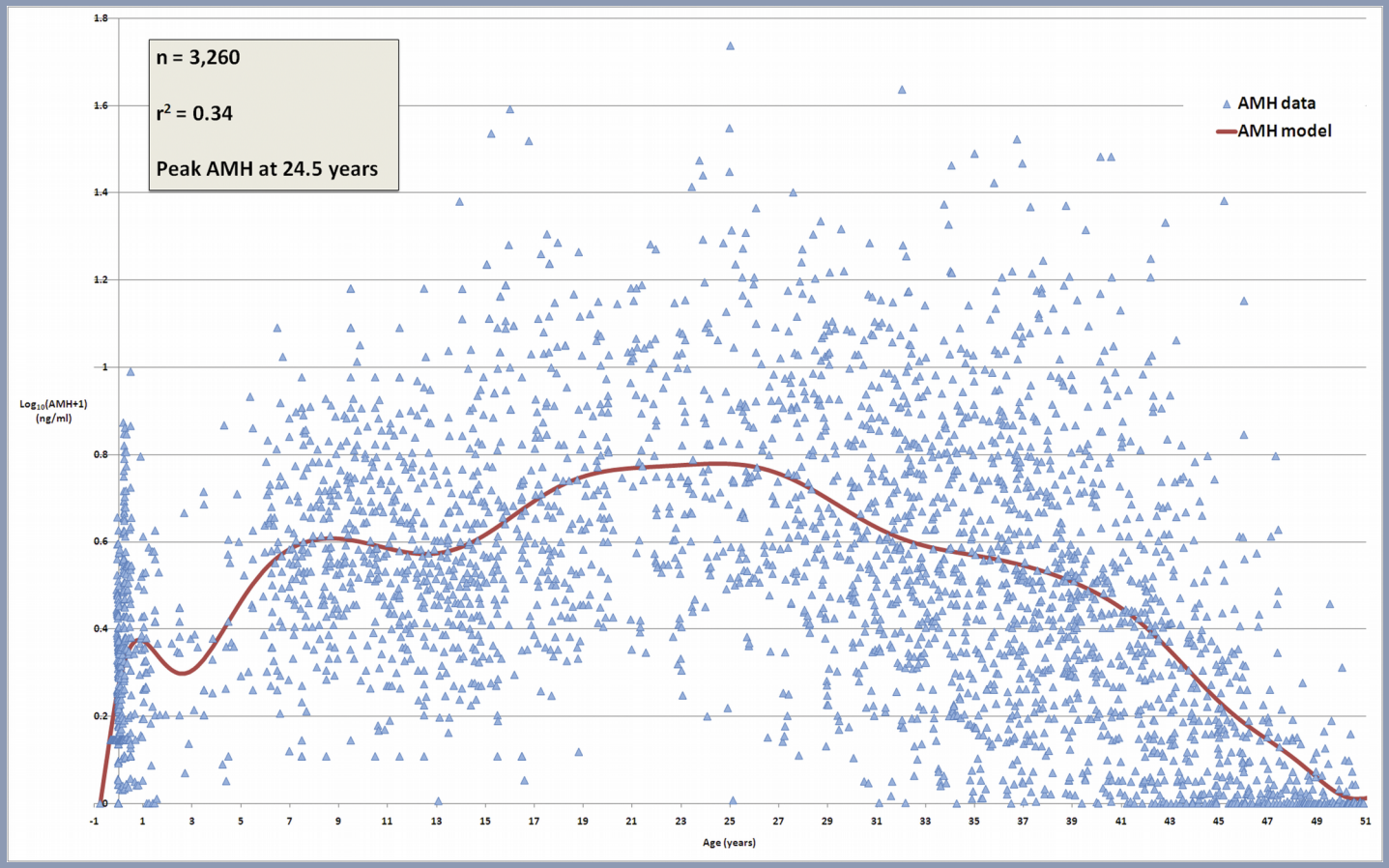
AMH has little variation across and between menstrual cycles

AMH is the best currently available marker of the number of small-growing follicles in the ovary

But there was no validated reference model for AMH available

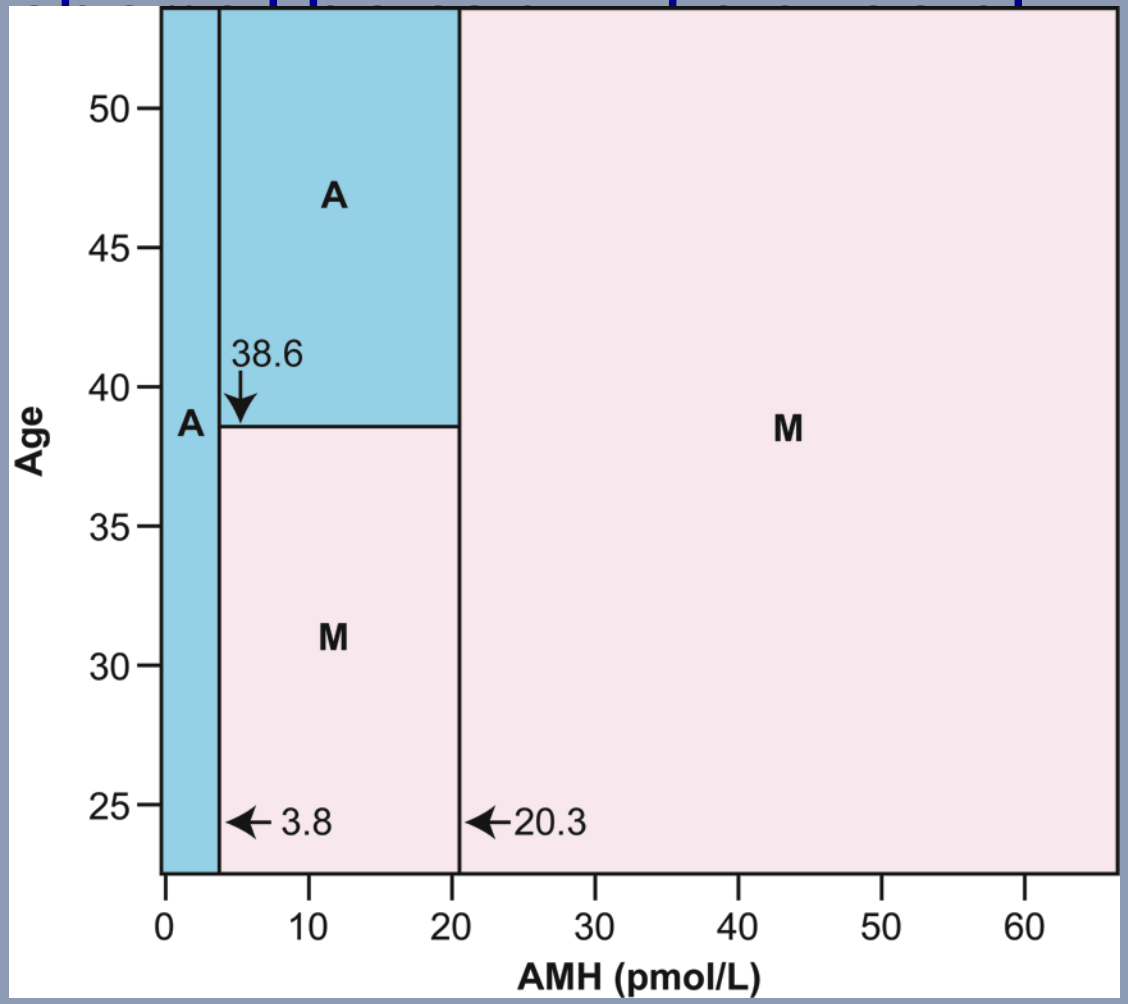
Anderson, Nelson, Wallace (2011) Maturitas

A validated model of serum anti-Mullerian hormone (AMH) from conception to menopause



Kelsey et al. PLoS ONE 2011

Pretreatment anti-Müllerian hormone predicts for loss of ovarian function after [illegible] breast



sensitivity 98.2%
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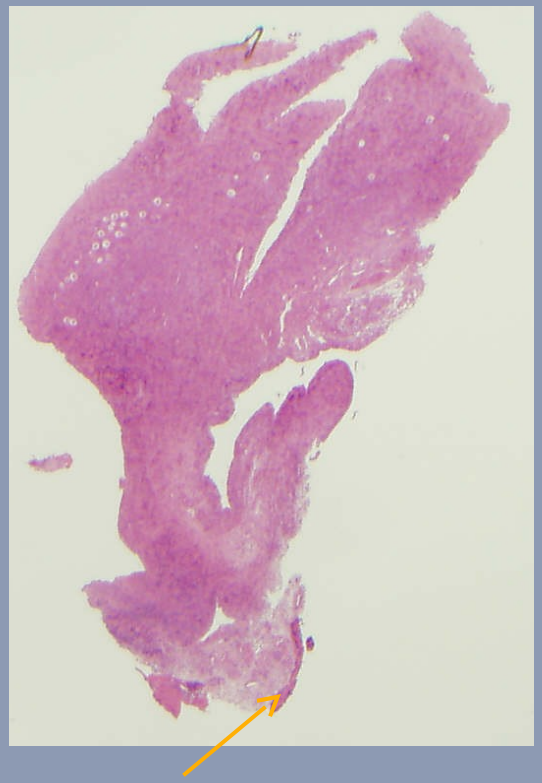
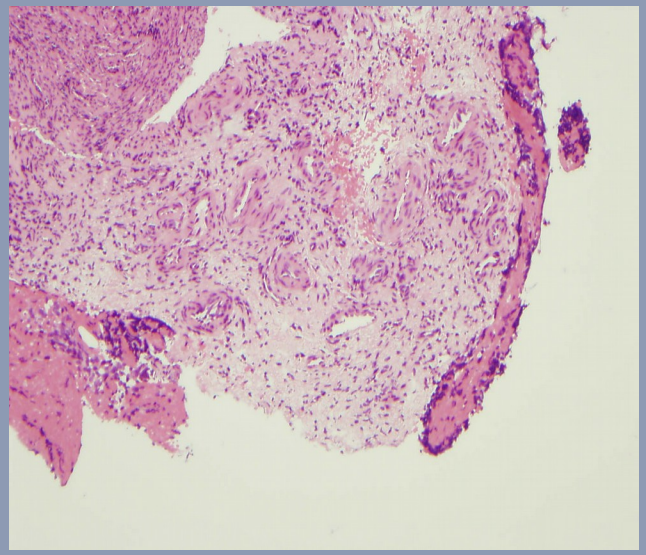
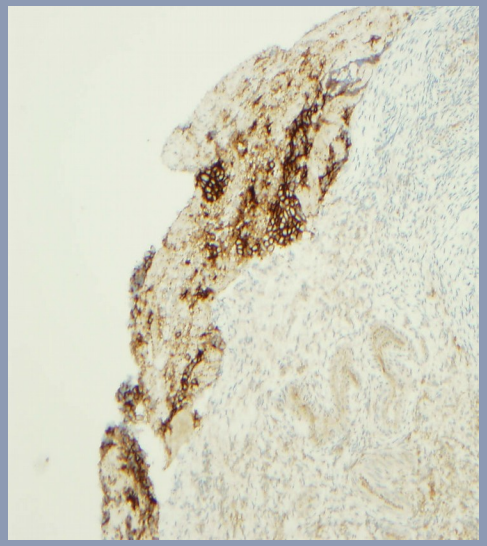
n=75

Anderson and Cameron 2011 JCE&M
Anderson et al 2013 Eur J Cancer

Ewings sarcoma localised T 7 Vertebrae (Age 12) – unexpected contamination of ovarian biopsy





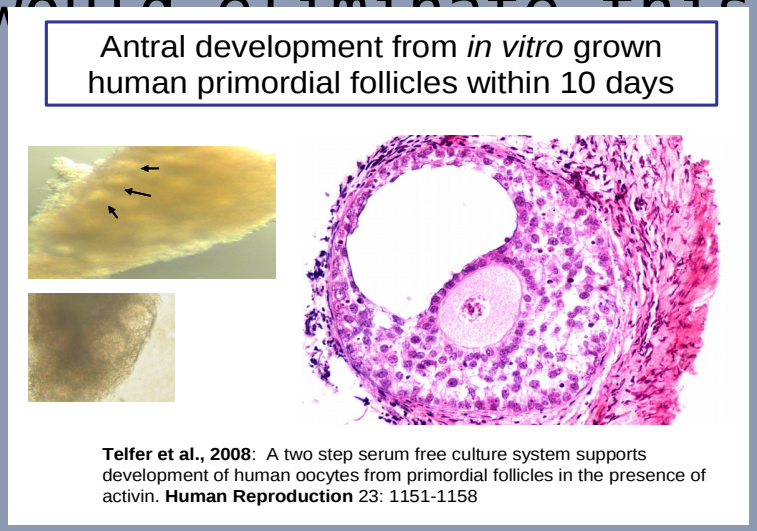


CD99

Re-implantation or IVG and maturation?

Contamination of the cryopreserved tissue with malignant cells, particularly in haematological malignant disease – shown in a rodent lymphoma model – to cause recrudescence of the original disease

Oocyte maturation in vitro, followed by IVF, would eliminate this risk



Telfer et al. (2008) Human Reproduction

Challenges

Provide fertility counseling to all young patients with cancer

Cryopreserve ovarian and pre-pubertal testicular tissue from the right (high risk) patients

Define the success rate of the procedures

Develop IVG/M as a safe alternative to re-implantation through basic research