Oncofertilità:
L'esempio del carcinoma mammario

carcinoma mammario in gravidanza e gravidanza dopo carcinoma mammario

Fedro A Peccatori, MD PhD

Istituto Europeo di Oncologia & European School of Oncology

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European School of Oncology
Learning to care

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Oncofertility

- ✓ **Oncofertility** is a subfield of medicine that bridges oncology and reproductive research to explore and expand options for the reproductive future of cancer survivors.
- ✓ In a broader dimension it also includes cancer occurring during pregnancy.

Theresa K Woodruff, Northwestern University

the Oncofertility® Consortium

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Lecture outline

- ✓ Breast cancer during pregnancy
- ✓ Adjuvant treatments during pregnancy
- ✓ Short and long term effects on pregnancy and babies

- ✓ Fertility issues in breast cancer patients
- ✓ Pregnancy after breast cancer
- ✓ Fertility preservation in breast cancer

Lecture outline

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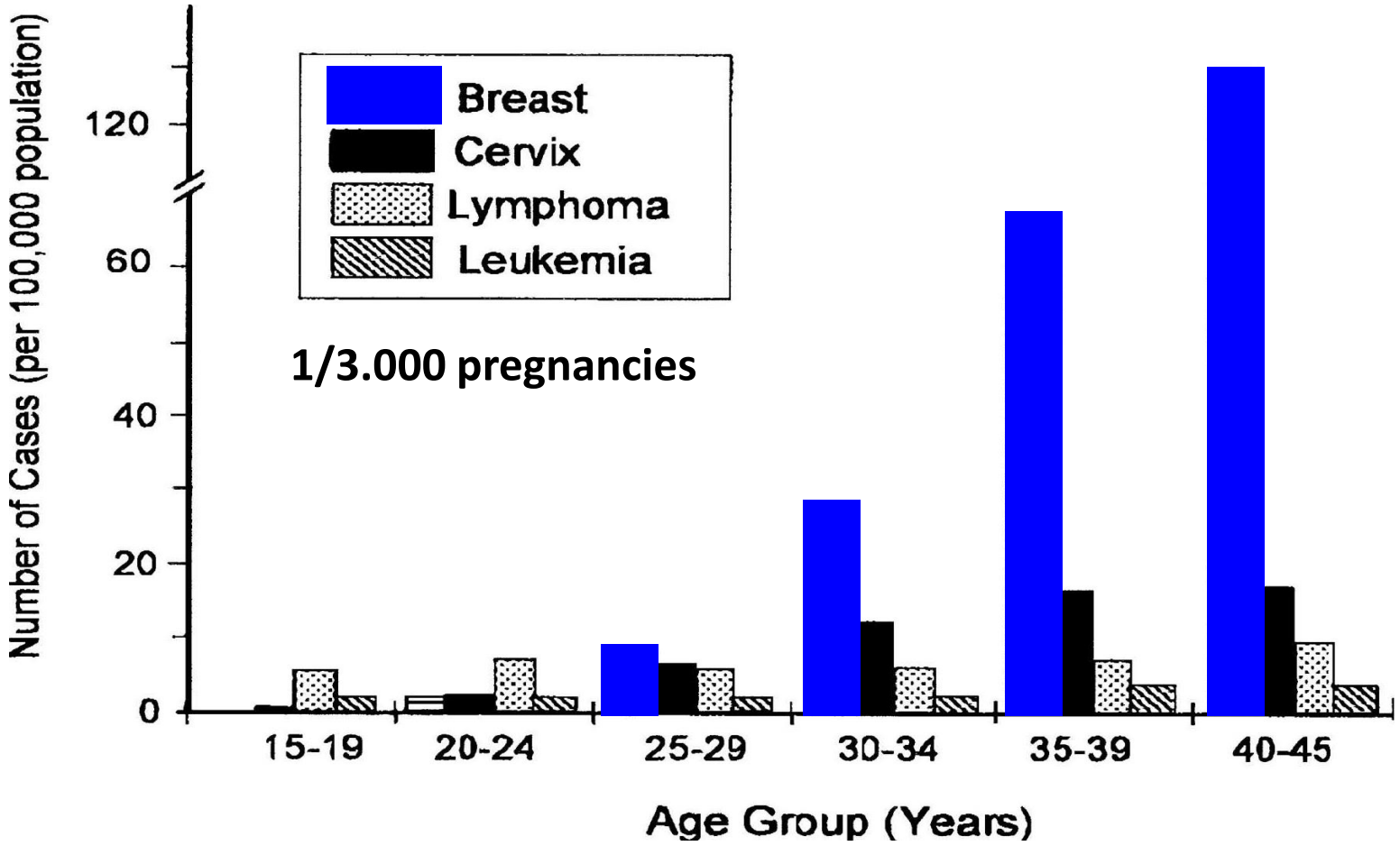
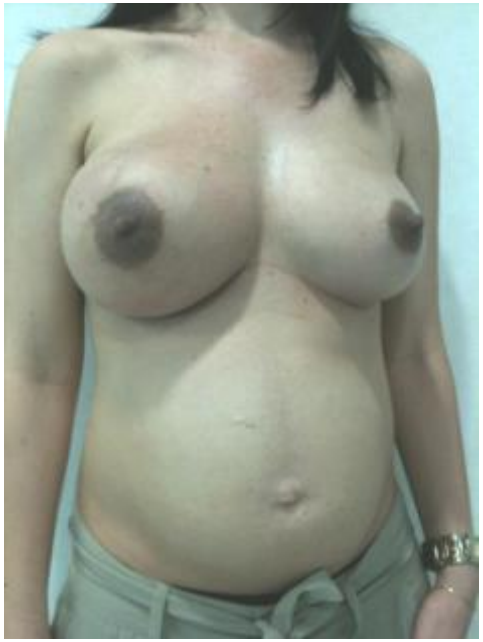
Epidemiology of gestational breast cancer (GBC)



Berry DL et al; JCO 1999

Impact on practice

- 137.000.000 deliveries every year worldwide
- Around 46.000 new cases of GBC worldwide
- Around 200 new cases of GBC in Italy



WHO facts and figures www.who/whr/2005

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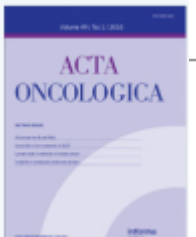
Clinical characteristics of GBC

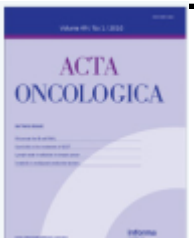
		Pregnant Cases N = 65	Controls N = 130
Age (years)	< 35	20 (30.8)	41 (31.5)
	35-39	33 (50.8)	61 (46.9)
	≥ 40	12 (18.5)	28 (21.5)
	Median	36 (28-47)	36 (28-47)
Year of Surgery	1996 - 2003	16 (24.6)	37 (28.5)
	2004 - 2005	20 (30.8)	35 (26.9)
	2006 - 2008	16 (24.6)	36 (27.7)
	2009 - 2010	13 (20.0)	22 (16.9)
	Median	2005	2005
pT	1a-b	5 (7.6)	10 (7.6)
	1c	21 (32.3)	42 (32.3)
	2	31 (47.7)	62 (47.7)
	3	6 (9.2)	12 (9.2)
	X	2 (3.1)	4 (3.1)
pN	pN0	28 (43.1)	56 (43.1)
	pN1	19 (29.2)	38 (29.2)
	pN2	10 (15.4)	20 (15.4)
	pN3	6 (9.2)	12 (9.2)
	pNx	2 (3.1)	4 (3.1)



Azim HA Jr et al; Acta Oncol 2012

Biological characteristics of GBC

		Pregnant Cases N = 65	Controls N = 130	p
Estrogen Receptor	Present Absent	43 (66.1) 22 (33.9)	98 (75.4) 32 (24.6)	0.175
Progesteron Receptor	Present Absent	42 (64.6) 23 (35.4)	87 (66.9) 43 (33.1)	0.748
Grade	1 2 3	4 (7.5) 18 (34.0) 31 (58.5)	4 (3.6) 43 (39.1) 63 (57.3)	0.503
Ki-67 %	< 20 ≥ 20	18 (28.6) 45 (71.4)	30 (23.4) 98 (76.6)	0.442
Her2/neu	Negative Positive	54 (83.1) 11 (16.9)	103 (81.1) 24 (18.9)	0.737
Perivascular Invasion	Absent Present	31 (47.7) 34 (52.3)	70 (55.1) 57 (44.9)	0.330
Molecular subtypes	Luminal A Luminal B Her2/Neu Triple Negative	8 (12.3) 37 (56.9) 6 (9.2) 14 (21.5)	13 (10.3) 82 (65.1) 4 (3.2) 27 (21.4)	0.306



Azim HA Jr et al; Acta Oncol 2012

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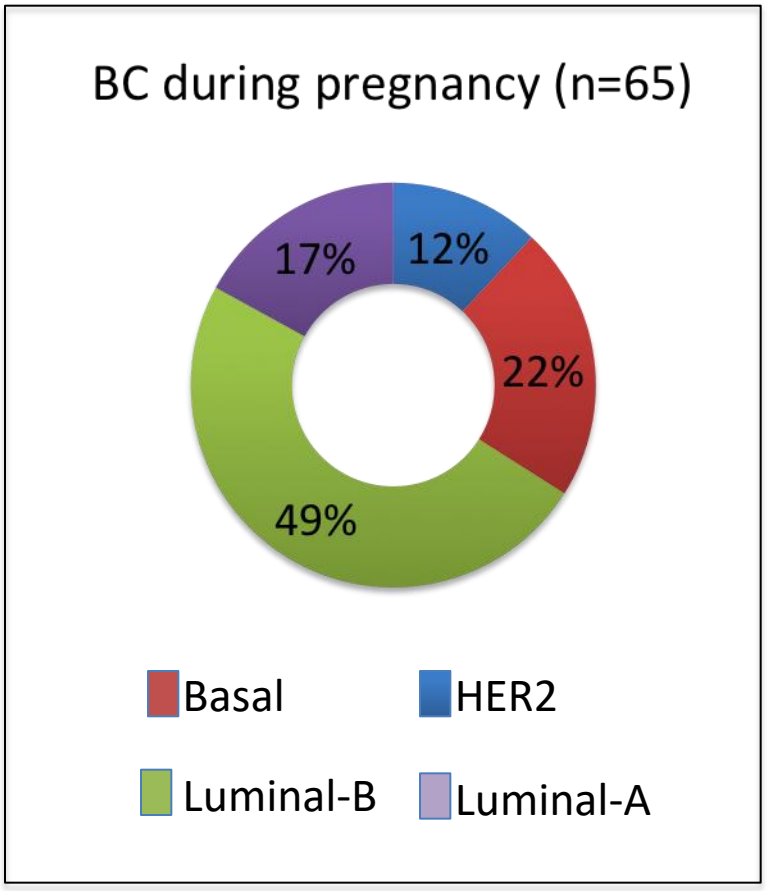
Biological and Clinical features of GBC

Aggressive biology
Advanced stages
=
MANY PATIENTS NEED CHEMOTHERAPY !



Biological and Clinical features of GBC

Aggressive biology
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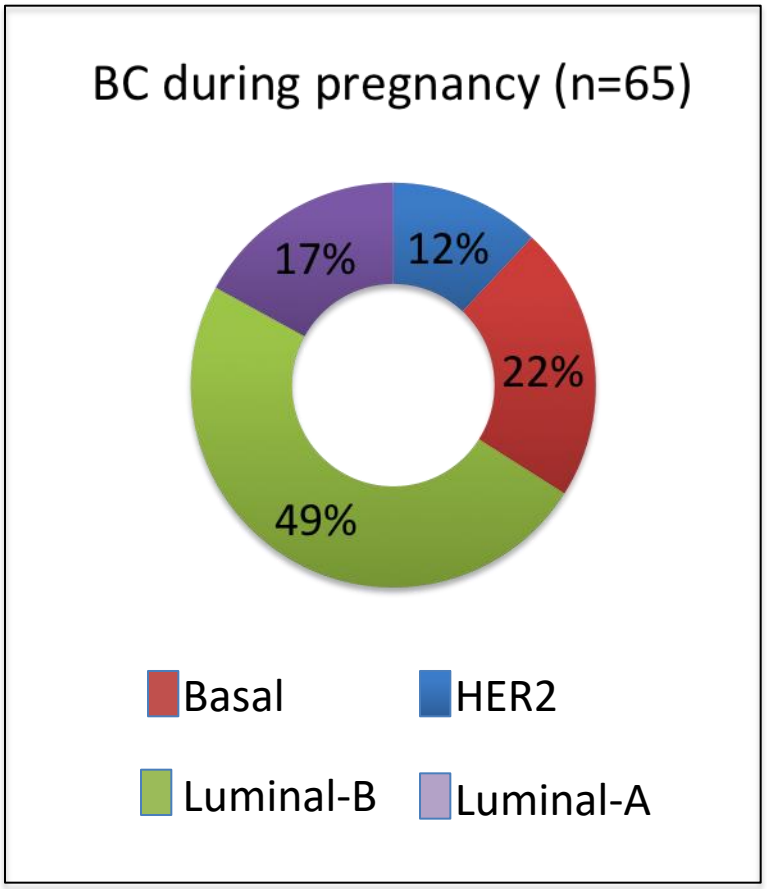
MANY PATIENTS NEED CHEMOTHERAPY !

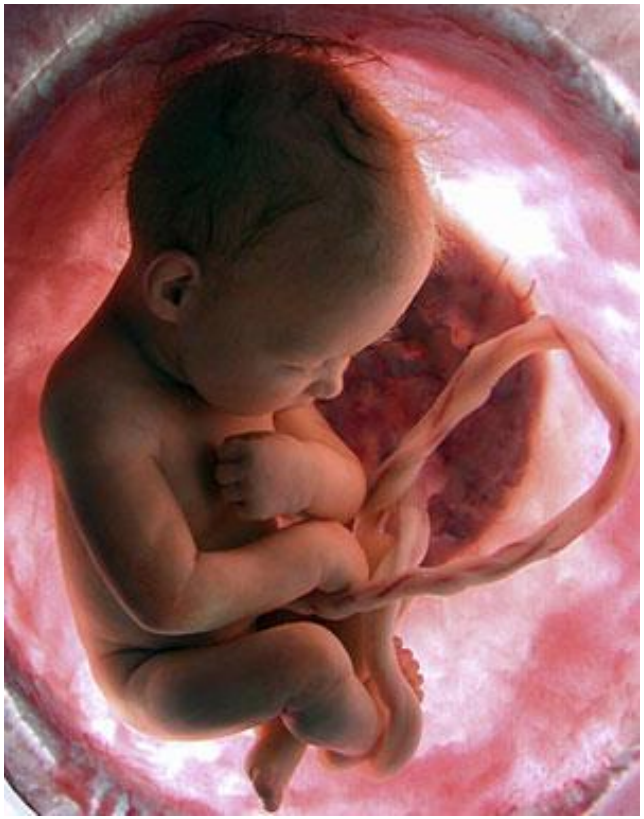
~~HORMONAL TREATMENT~~
~~TRASTUZUMAB~~



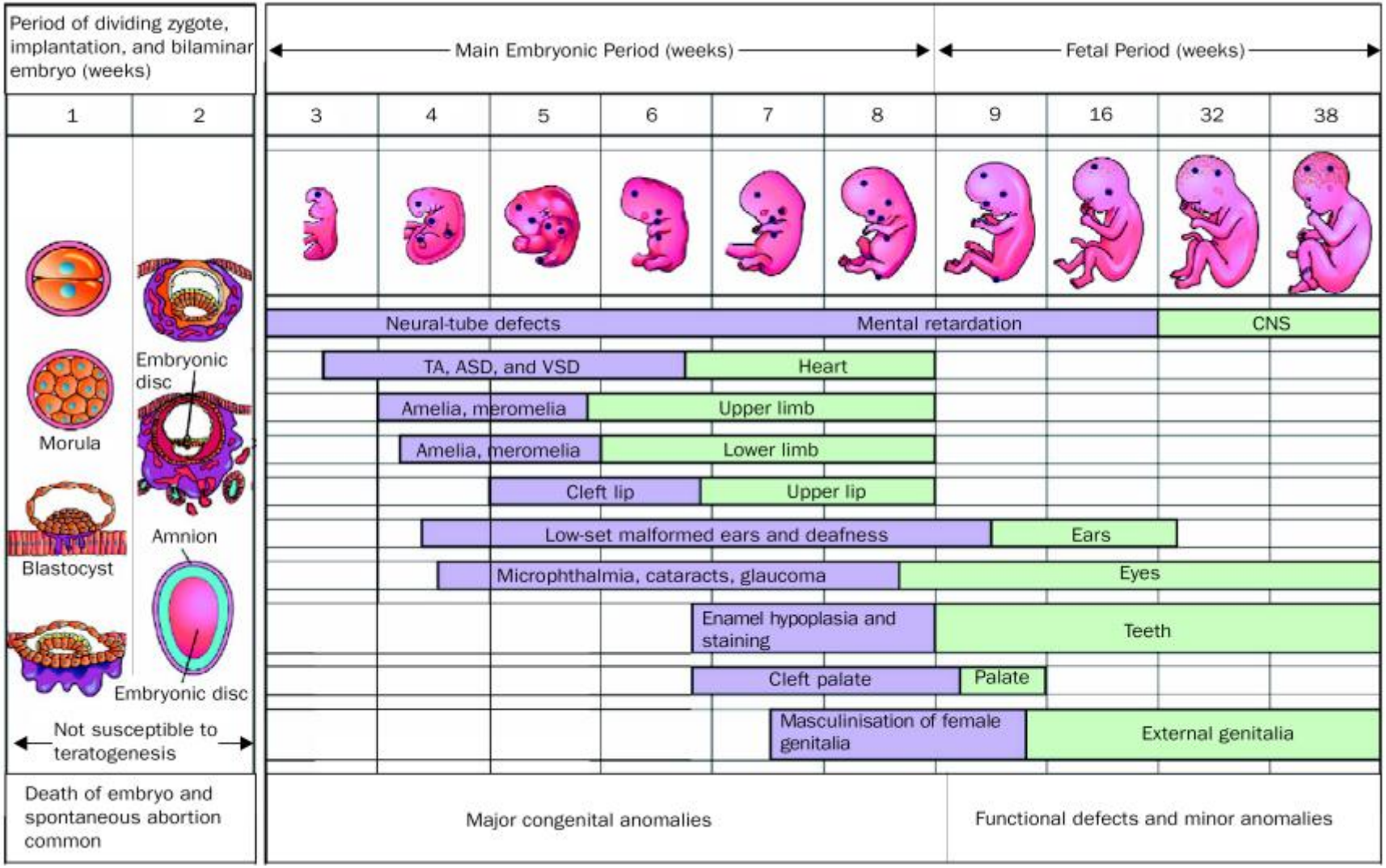
Gestational chemotherapy

CRITICAL FACTORS

- ✓ Gestational age
- ✓ Drugs administered
- ✓ Effects on pregnancy & fetus
- ✓ Effects on newborn & children

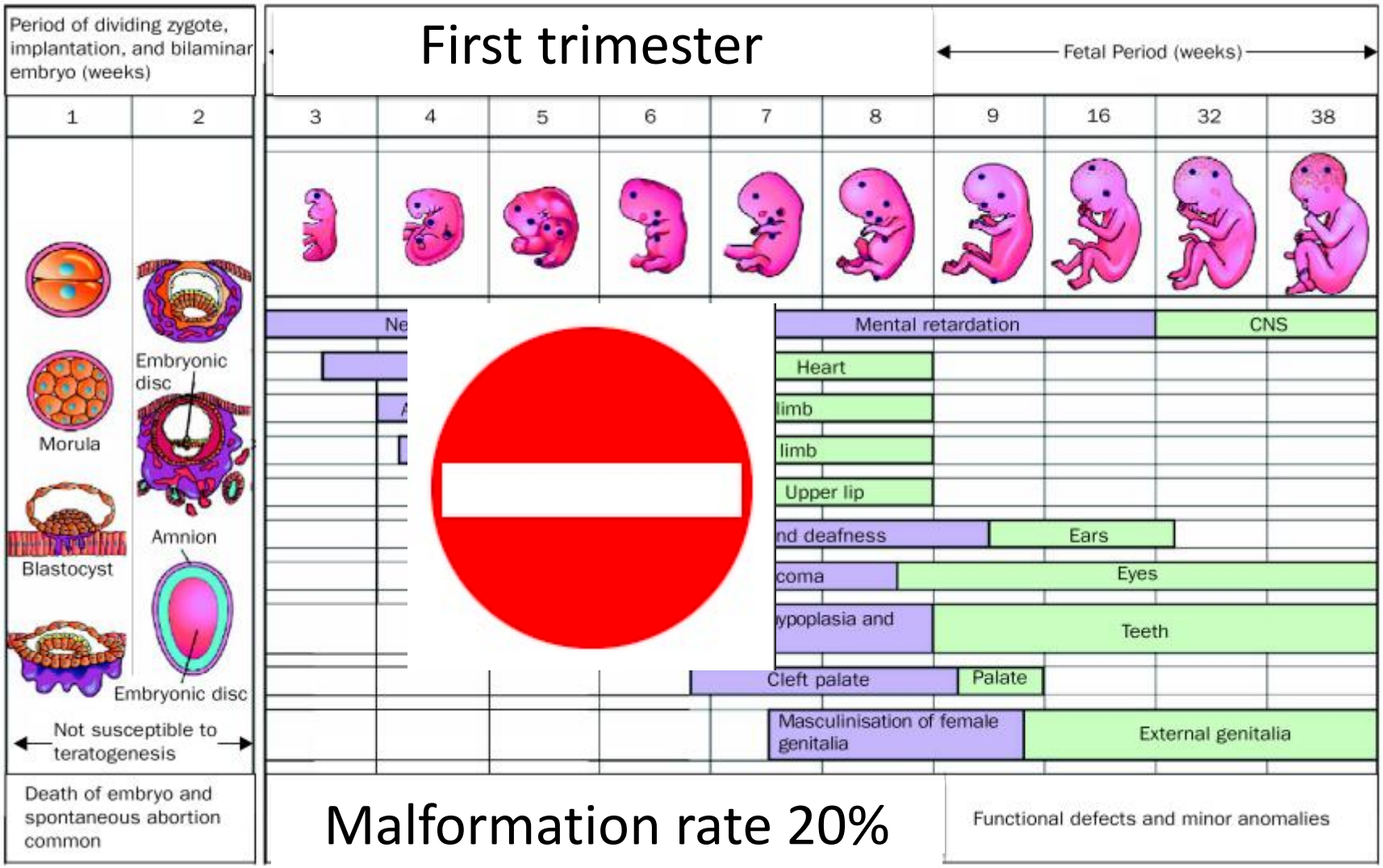


Gestational age



Cardonick E & Iacobucci; Lancet Oncol 2004

Gestational age



Cardonick E & Iacobucci; Lancet Oncol 2004

Drugs administered: anthraciclines

	Ring, 2005	Hahn, 2006	Peccatori, 2009	Loibl, 2012
Study type	Retrospective	Prospective	Prospective	Prospective
	Multicentric	Monocentric	Monocentric	Registry
N.	28	57	20	197
Regimen	**A(E)C=16** CMF=12	**FAC (100%)**	**Weekly E (100%)**	**A-based=178** **A(E)C (n=55)** Taxane=14 CMF=15
Median gestational W at chemo	W20 (15 – 33)	W23 (11 – 34)	W19 (16 – 30)	W24 (NR)
Median gestational W at delivery	W37 (30 – 40)	W37 (29 – 42)	W35 (28 – 40)	W37 (32 – 42)
Congenital malformations	0	3/57 (5%)	1/20 (5%)	8/179 (4.5%)

Ring A et al; JCO 2005, Hahn et al; Cancer 2006
Peccatori F et al; BCRT 2009, Loibl S et al; Lancet Oncol 2012

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Drugs administered: taxanes

Number	55
- Breast cancer	39
- Other	16
- Paclitaxel	**33**
- Docetaxel	19
- Both	3
Neonatal outcome	
- Mean Gestational age at delivery	W 36
- Foetal weight	2400 g
- Early preterm delivery	1 (2%)
- Foetal complications	Anaemia (n=1), neutropenia (n=1)
- Foetal malformations	Pyloric stenosis (n=1)

Mir O et al; Ann Oncol 2010
Cardonick E et al; Ann Oncol 2012

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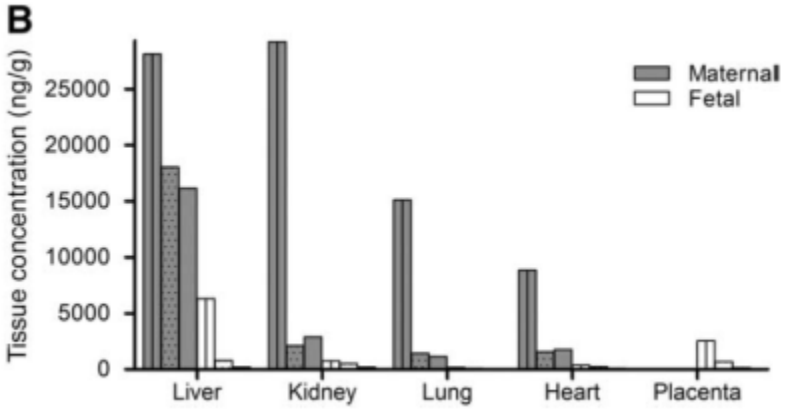
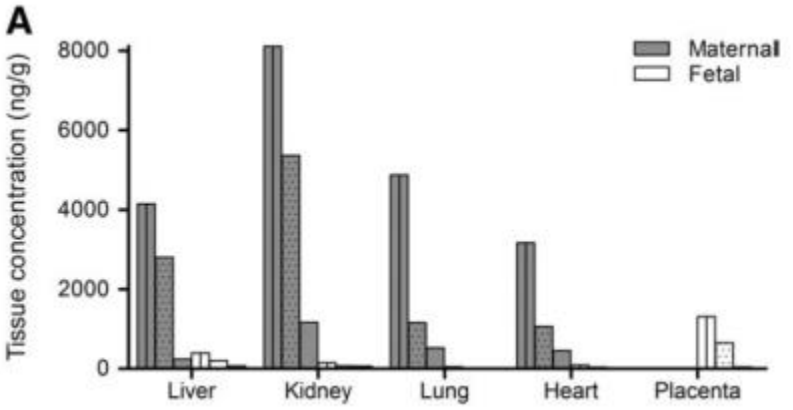
	Number	Drug detected in fetus (n)	% drug detected in fetus
Doxorubicin	15	6	7.5 ± 3.2
Epirubicin	11	8	4.0 ± 1.6
Paclitaxel	11	7	1.4 ± 0.8
Docetaxel	9	0	0
Cyclophosphamide	4	3	25.1 ± 6.3
Carboplatin	7	7	57.5 ± 14.2

EPIRUBICIN



PACLITAXEL



van Calsteren et al; Acta Obstet Gynecol 2011
van Calsteren et al; Gynecol Oncol 2011

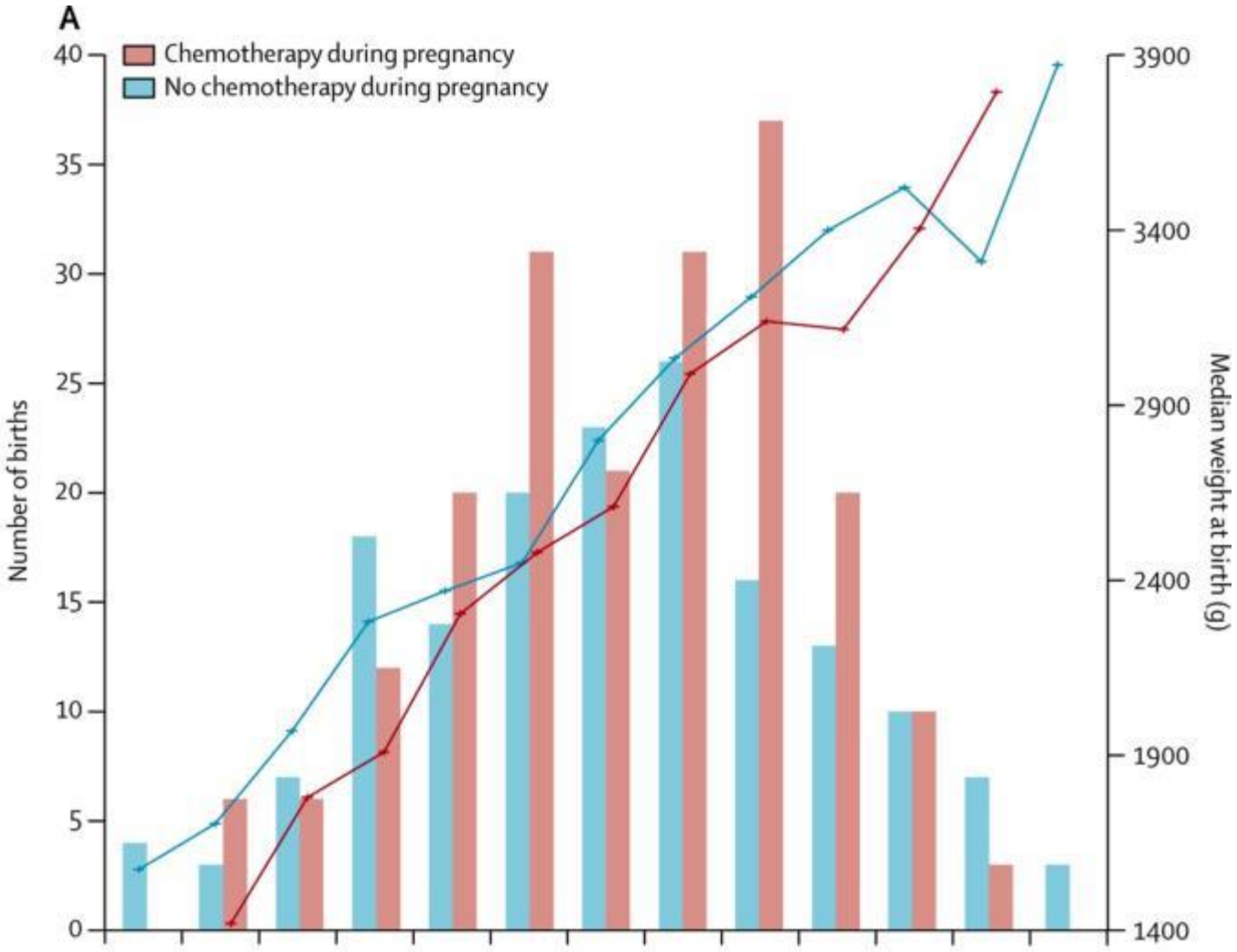
Effects of gestational chemotherapy on pregnancy and fetus

	No chemotherapy during pregnancy (N=164)	Chemotherapy during pregnancy (N=179)	p value
Any obstetrical complication			
No	149 (91%)	148 (83%)	0·027
Yes	15 (9%)	31 (17%)	
Premature labour			
No	161 (98%)	169 (94%)	0·090
Yes	3 (2%)	10 (6%)	
Premature rupture of the membrane			
No	164 (100%)	174 (97%)	0·062
Yes	0 (··)	5 (3%)	
Intrauterine growth restriction			
No	163 (99%)	172 (96%)	0·069
Yes	1 (1%)	7 (4%)	

Table 4: Obstetrical complications in women with early breast cancer with and without chemotherapy during pregnancy (n=343)*

Loibl et al; Lancet Oncol 2012

Effects of gestational chemotherapy on newborn



Loibl et al; Lancet Oncol 2012

Long term effects of gestational chemotherapy on children

Long-term cognitive and cardiac outcomes after prenatal exposure to chemotherapy in children aged 18 months or older: an observational study

Frédéric Amant, Kristel Van Calsteren, Michael J Halaska, Mina Mhallem Gziri, Wei Hui, Lieven Lagae, Michèl A Willemsen, Livia Kapusta, Ben Van Calster, Heidi Wouters, Liesbeth Heyns, Sileny N Han, Viktor Tomek, Luc Mertens, Petronella B Ottevanger

Lancet Oncology 2012

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Long term effects of gestational chemotherapy on children

- ✓ Child's behavior, general health, hearing and growth was reported as in a general population
- ✓ Most of the children have an age-adequate neurological development (intelligence, attention, memory) and cardiac function
- ✓ Prematurity was frequently encountered, and was associated with impairment in cognitive development

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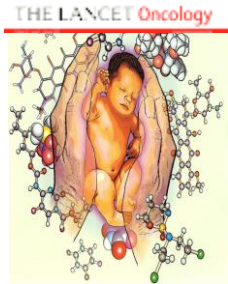
Published Online
February 10, 2012
DOI:10.1016/S1470-2045(11)70363-1



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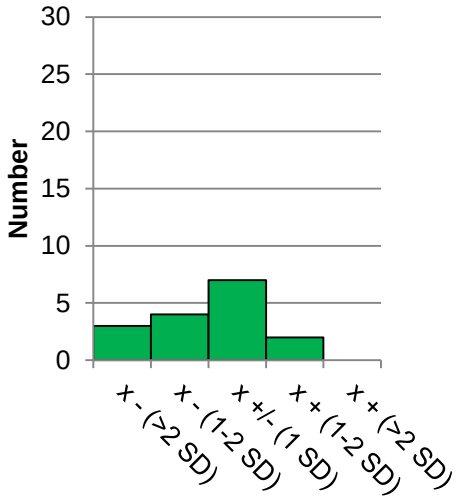
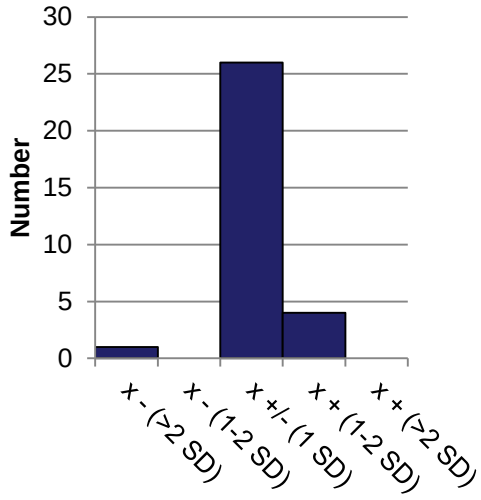
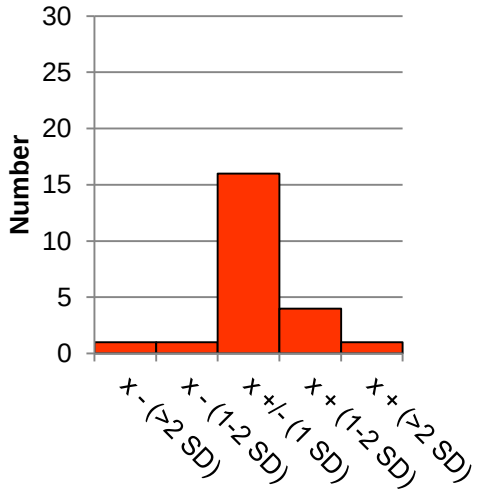


<34 weeks

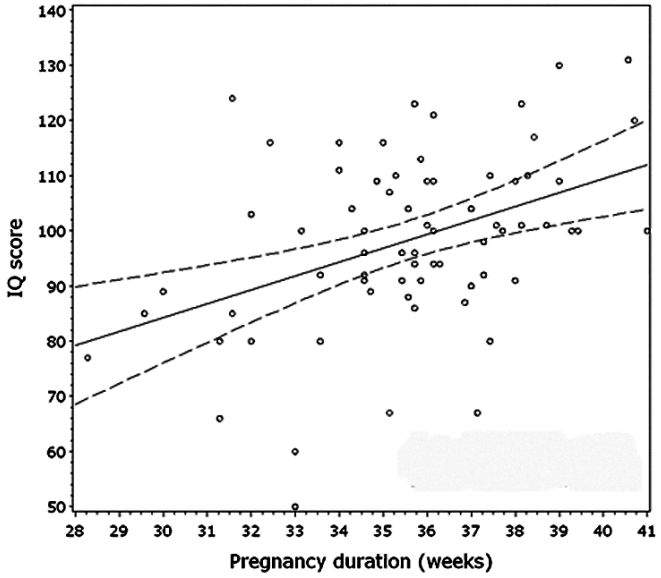


34-37 weeks



>37 weeks

IQ score increases with 2.5 (95% CI:1.2-3.9) for each week increase in pregnancy duration (p= 0.0003).



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Case control study on pediatric outcome after gestational cancer

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Pediatric Outcome after Maternal Cancer Diagnosed during Pregnancy

F. Amant, T. Vandenbroucke, M. Verheecke, M. Fumagalli, M.J. Halaska, I. Boere, S. Han, M.M. Gziri, F. Peccatori, L. Rob, C. Lok, P. Witteveen, J.-U. Voigt, G. Naulaers, L. Vallaeys, F. Van den Heuvel, L. Lagae, L. Mertens, L. Claes, and K. Van Calsteren, for the International Network on Cancer, Infertility, and Pregnancy (INCIP)

N Engl J Med 2015;373:1824-34.
DOI: 10.1056/NEJMoa1508913

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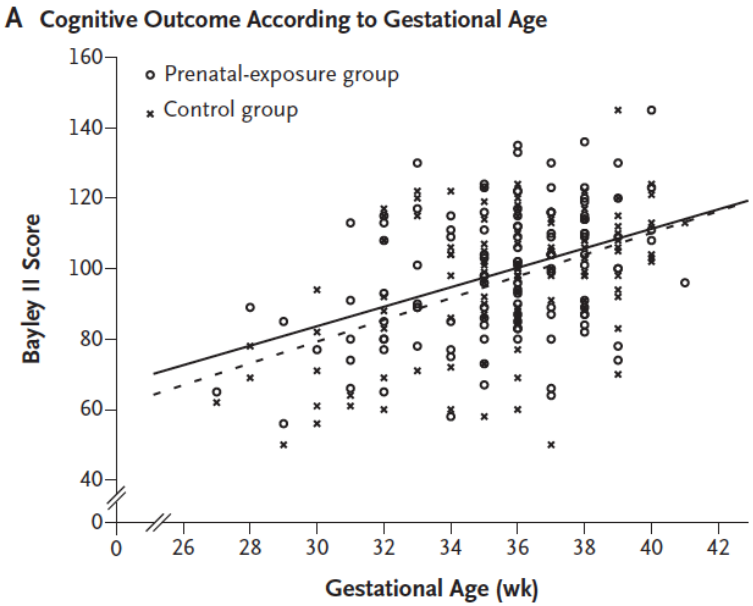
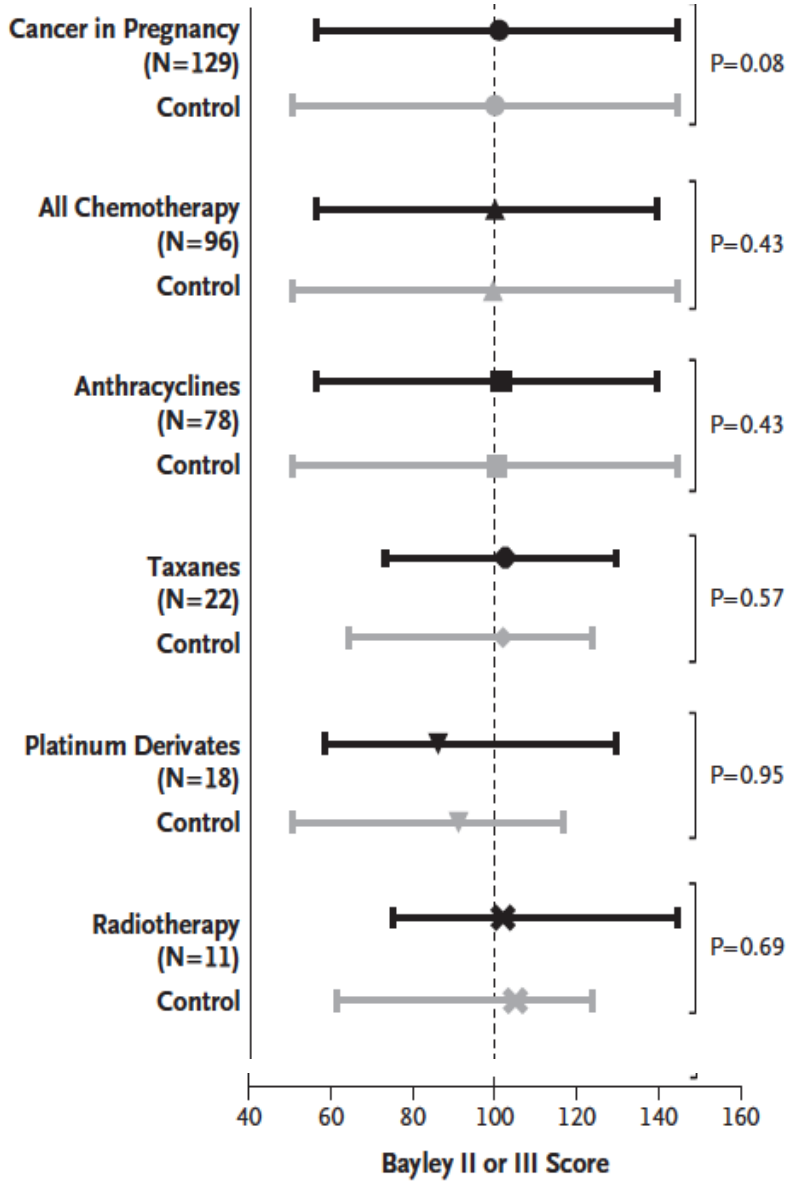




RISK FACTORS

After gestational chemotherapy, the kids are all right

Fedro A. Peccatori, Giacomo Corrado and Monica Fumagalli

Refers to Cardonick, E. H. *et al.* *Am. J. Obstet. Gynecol.* http://dx.doi.org/10.1016/j.ajog.2014.11.032 (2014) | Murthy, R. K. *et al.* *Breast Cancer Res.* **16**, 3414 (2014) | Amant, F. *et al.* *Lancet Oncol.* **13**, 256 (2012)

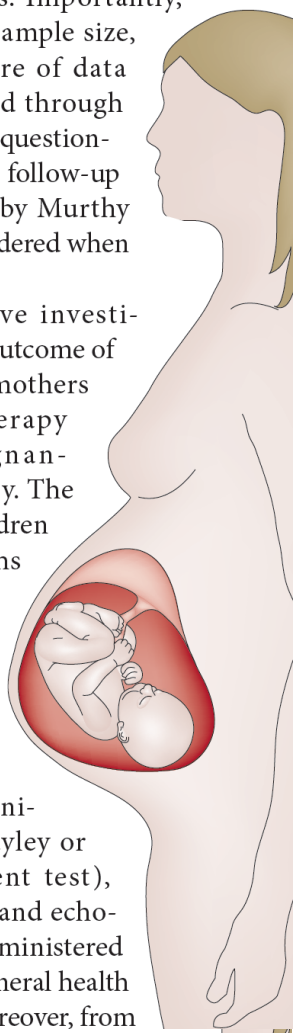
When a pregnant woman is diagnosed with cancer, clinical management is complicated by concerns about the possible detrimental effects of cancer treatments on pregnancy outcome and the health of the baby. Evidence about the outcomes of children after maternal chemotherapy for cancer during pregnancy is growing and we can say 'the kids are all right'.

The clinical management of a pregnant woman who is diagnosed with cancer is complicated by concerns about the possible detrimental effects of oncological treatments on pregnancy outcome and the short-term and long-term health of the baby. Recent data have clarified that anthracyclines, taxanes, and platinum compounds have limited transplacental passage,[1] and when chemotherapy is administered to the pregnant woman after the first trimester, no increased risk of neonatal malformations has been described.[2] Nonetheless, concerns remain regarding the long-term health outcomes of children exposed to chemotherapy during pregnancy.

> "...treating pregnant women with chemotherapy during the second or third trimester is safe..."

Recently published papers have shed light on some of these issues. Teams of researchers from the USA[6,7] and Belgium[8] have investigated the outcomes of children whose mothers had been treated with chemotherapy during pregnancy. In the study of Cardonick *et al.*,[6] 35 children who were exposed to chemotherapy during pregnancy not jeopardize the health outcomes of the developing fetus. Importantly, however, the small sample size, the subjective nature of data acquisition (obtained through parent-administered questionnaires), and the short follow-up period in the study by Murthy *et al.*[7] should be considered when interpreting results.

Amant *et al.*[8] have investigated the long-term outcome of 70 children whose mothers received chemotherapy for various malignancies during pregnancy. The authors assessed children at birth, at 18 months of age, and at age 5–6, 8–9, 11–12, 14–15, or 18 years. They performed clinical neurological examinations, tests of the general level of cognitive functioning (Bayley or intelligence-quotient test), electrocardiography and echocardiography, and administered a questionnaire on general health and development. Moreover, from

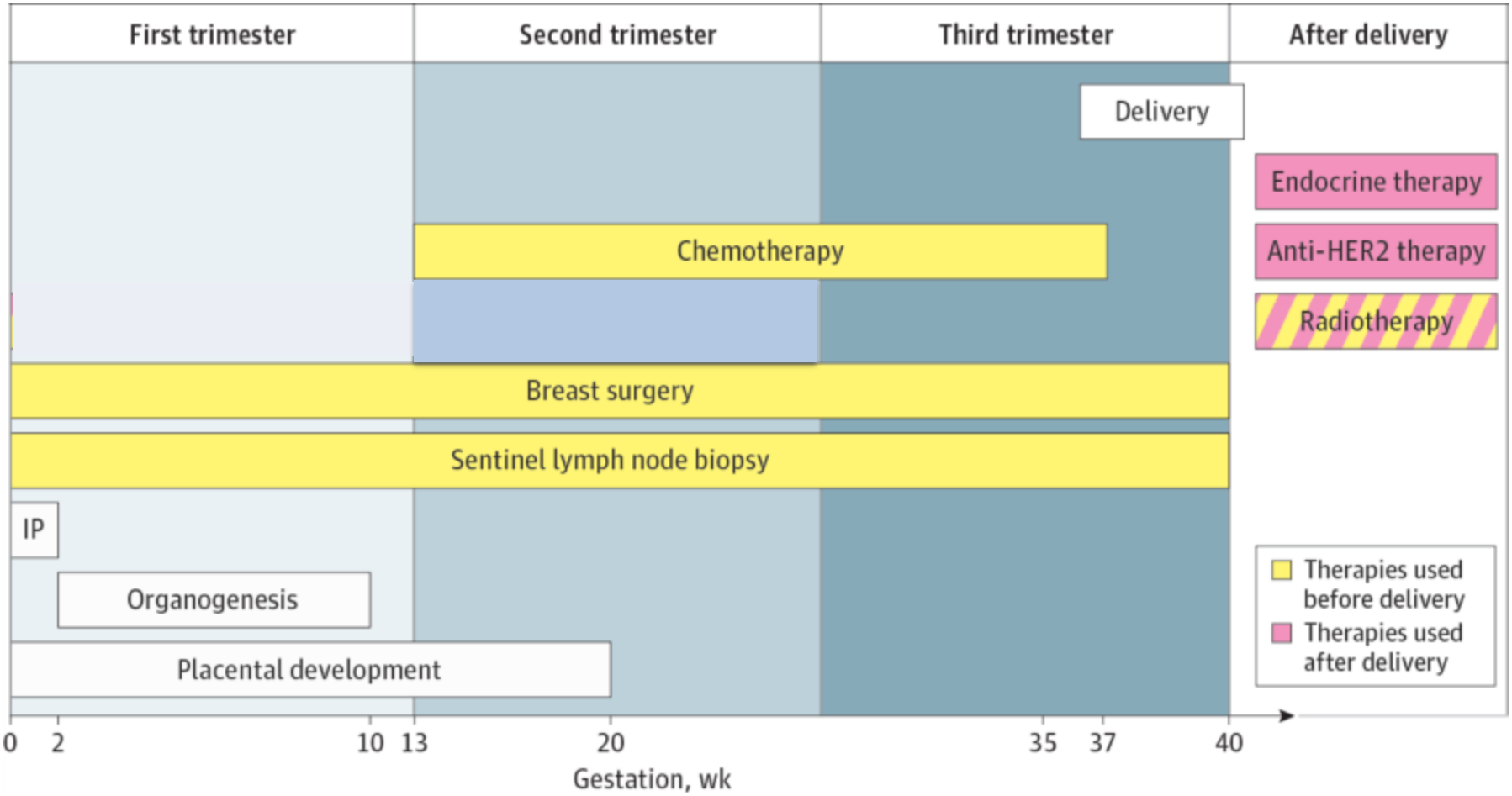


Peccatori FA, Corrado G, Fumagalli M. Nat Rev Clin Oncol 2015

Take home messages

- ✓ Gestational breast cancer is not so rare and shares clinical and biological characteristics of breast cancer in young women
- ✓ Anthracycline and taxane-containing chemotherapy can be safely administered after the first trimester
- ✓ Gestational chemotherapy should be administered where true multidisciplinarity is available
- ✓ The kids are all right (after gestational chemotherapy)

Conclusions



Lecture outline

- ✓ Breast cancer during pregnancy
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- ✓ Fertility preservation in breast cancer

Fertility concerns of breast cancer patients

Racial, Socioeconomic, and Demographic Disparities in Access to Fertility Preservation in Young Women Diagnosed With Cancer

Joseph M. Letourneau, MD[1]; James F. Smith, MD, MS[2]; Erin E. Ebbel, BA[1]; Amaranta Craig, BA[1]; Patricia P. Katz, PhD[3]; Marcelle I. Cedars, MD[1]; and Mitchell P. Rosen, MD, HCLD[1]

Characteristic	Total Sample, n=918	Type of Cancer				
		Leukemia, n=121	Hodgkin Disease, n=286[a]	Non-Hodgkin Lymphoma, n=169[a]	Breast Cancer, n=223	Gastrointestinal Cancer, n=108
Age at diagnosis, y, mean (SD)	31.5 (6.7)	28.3 (7.2)	27.9 (6.2)	31.6 (6.0)	36.3 (4.0)	34.9 (4.6)
Age at survey, y, mean (SD)	40.9 (8.4)	37.0 (8.3)	36.5 (8.0)	40.5 (7.1)	47.1 (5.9)	44.6 (6.2)
Years since diagnosis, mean (SD)	9.6 (4.4)	8.7 (4.3)	8.6 (4.4)	8.9 (3.9)	10.8 (4.5)	9.7 (4.0)
Children before treatment, No. (%)	476 (52%)	46 (38%)	105 (37%)	88 (52%)	163 (73%)	76 (70%)
Desiring children after treatment, No. (%)	504 (54%)	71 (59%)	181 (63%)	82 (49%)	104 (47%)	61 (56%)

47% of young patients with breast cancer want a baby

Cancer 2012;118:4579-88. © 2012 .

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Fertility concerns of breast cancer patients

ARTICLE

Impact of Fertility Concerns on Tamoxifen Initiation and Persistence

Natalia C. Llarena, Samantha L. Estevez, Susan L. Tucker, Jacqueline S. Jeruss

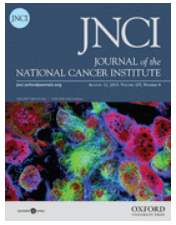
515 ER+ patients <45 y/o in whom TAM was indicated

149 (28.9%) did not start or discontinued TAM

Fertility concerns associated with:

Non initiation (OR 5.04, 95%CI=2.29-11.07)

Early discontinuation (HR 1.78, 95%CI=1.09-3.38)



JNCI J Natl Cancer Inst (2015) 107(10): djv202

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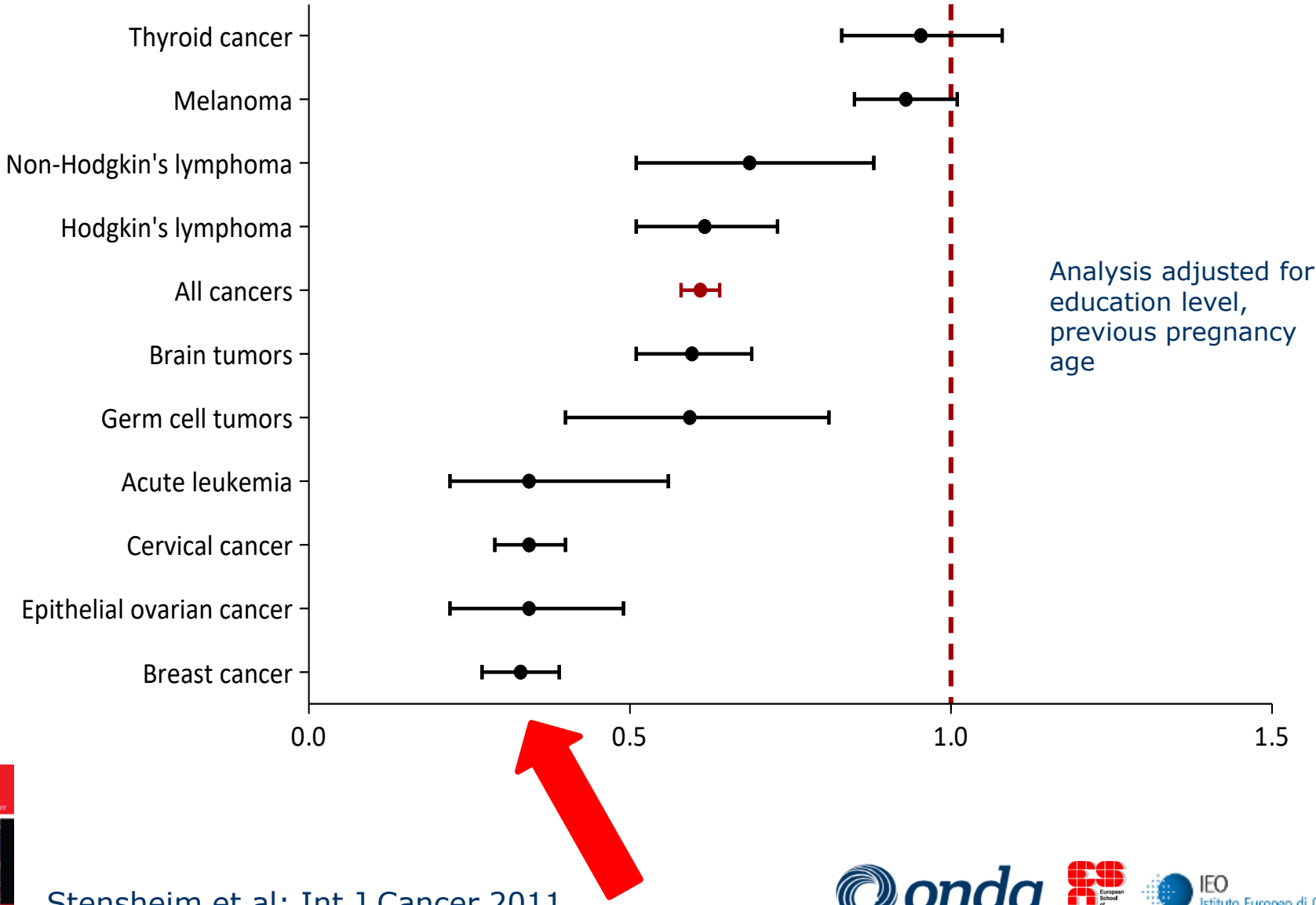
Pregnancy rate after cancer: not all alike



Stensheim et al; Int J Cancer 2011

Low pregnancy rate

- ✓ Fear of pregnancy
- ✓ Relatively “old” premenopausal
- ✓ Gonadotoxicity of chemotherapy
- ✓ Prolonged endocrine treatment
- ✓ Low rate of fertility preservation

GYNECOLOGICAL ENDOCRINOLOGY

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Gynecol Endocrinol, 2015; 31(6): 458–464
 DOI: 10.3109/09513590.2014.1003293

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BREAST CANCER AND FERTILITY

Attitudes on fertility issues in breast cancer patients: an Italian survey

Nicoletta Biglia[1]*, Rosalba Torrisi[2]*, Marta D'Alonzo[1]*, Giovanni Codacci Pisanelli[3], Selene Rota[2], and Fedro Alessandro Peccatori[3]

[1]Department of Gynaecology and Obstetrics, University of Turin, Turin, Italy, [2]Department of Hematology and Oncology, Humanitas Cancer Center, Milan, Italy, and [3]Fertility and Procreation Unit, Division of Gynecologic Oncology, European Institute of Oncology (IEO), Milan, Italy

Attitudes on fertility issues in breast cancer patients: an Italian survey

Nicoletta Biglia[1]*, Rosalba Torrisi[2]*, Marta D'Alonzo[1]*, Giovanni Codacci Pisanelli[3], Selene Rota[2], and Fedro Alessandro Peccatori[3]

10. May a pregnancy in women previously affected by BCa increase the risk of recurrence?

Only 51% of oncologists believed that pregnancy does not affect the prognosis of BCa patients, while 49% of them supports that an increase in estrogen levels during pregnancy could stimulate the growth of hidden tumor cells (Statement 10).

GYNECOLOGICAL ENDOCRINOLOGY

Safety: meta-analysis

Safety of pregnancy following breast cancer diagnosis: A meta-analysis of 14 studies

Hatem A. Azim Jr. [a,b], *Luigi Santoro* [c], *Nicholas Pavlidis* [d], *Shari Gelber* [e], *Niels Kroman* [f], *Hamdy Azim* [g], *Fedro A. Peccatori* [h,*]

EUROPEAN JOURNAL OF CANCER 47 (2011) 74–83

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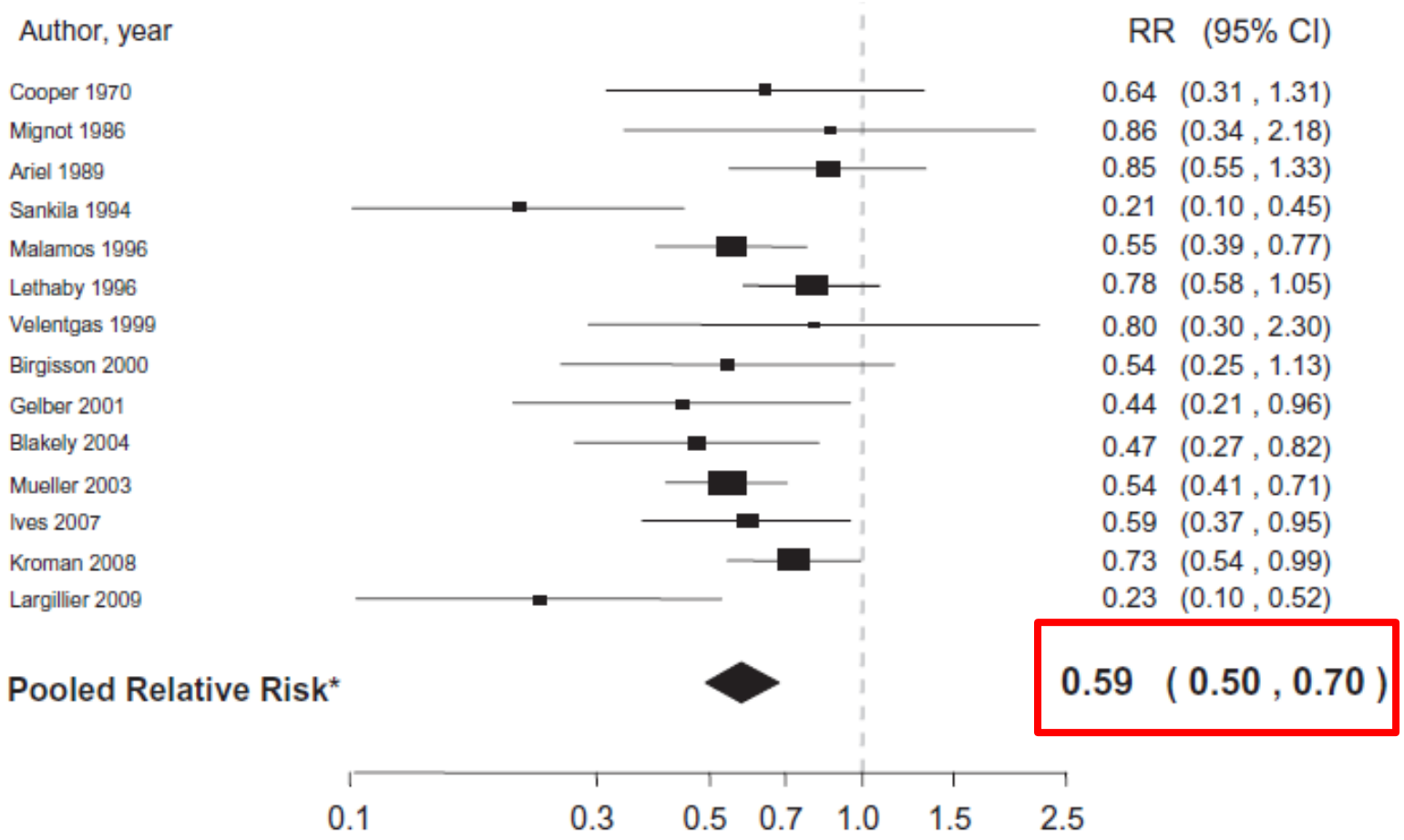
Safety: meta-analysis

All studies, 41% risk reduction



Safety of pregnancy following breast cancer diagnosis: A meta-analysis of 14 studies

Hatem A. Azim Jr. [a,b], *Luigi Santoro* [c], *Nicholas Pavlidis* [d], *Shari Gelber* [e], *Niels Kroman* [f], *Hamdy Azim* [g], *Fedro A. Peccatori* [h,*]

Safety: multicenter study in ER+/ER-

Prognostic Impact of Pregnancy After Breast Cancer According to Estrogen Receptor Status: A Multicenter Retrospective Study

Hatem A. Azim Jr, Niels Kroman, Marianne Paesmans, Shari Gelber, Nicole Rotmensz, Lieveke Ameye, Leticia De Mattos-Arruda, Barbara Pistilli, Alvaro Pinto, Maj-Britt Jensen, Octavi Cordoba, Evandro de Azambuja, Aron Goldhirsch, Martine J. Piccart, and Fedro A. Peccatori

Published Ahead of Print on November 19, 2012 as 10.1200/JCO.2012.44.2285
The latest version is at http://jco.ascopubs.org/cgi/doi/10.1200/JCO.2012.44.2285

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Safety: multicenter study in ER+/ER-

Retrospective, multicenter cohort study (7 Institutions)

Primary endpoint: DFS ER+ pts.
(Two sided test a= 5% , b=20%, 226 events 645 pts for HR 0.65)

Secondary endpoints: DFS in ER- pts., OS

Subgroup analysis: DFS according to time of preg
DFS according to breastfeeding

Prognostic Impact of Pregnancy After Breast Cancer According to Estrogen Receptor Status: A Multicenter Retrospective Study

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Safety: multicenter study in ER+/ER-

333 cases with pregnancy after breast cancer

874 non pregnant controls
matched for ER, stage, adjuvant treatment, age, year at diagnosis

Median follow-up from date of conception: 4.7y

35% of patients were histological grade III

40% of patients were node-positive

80% of patients received adjuvant chemo

Prognostic Impact of Pregnancy After Breast Cancer According to Estrogen Receptor Status: A Multicenter Retrospective Study

Hatem A. Azim Jr, Niels Kroman, Marianne Paesmans, Shari Gelber, Nicole Rotmensz, Lieveke Ameye, Leticia De Mattos-Arruda, Barbara Pistilli, Alvaro Pinto, Maj-Britt Jensen, Octavi Cordoba, Evandro de Azambuja, Aron Goldhirsch, Martine J. Piccart, and Fedro A. Peccatori

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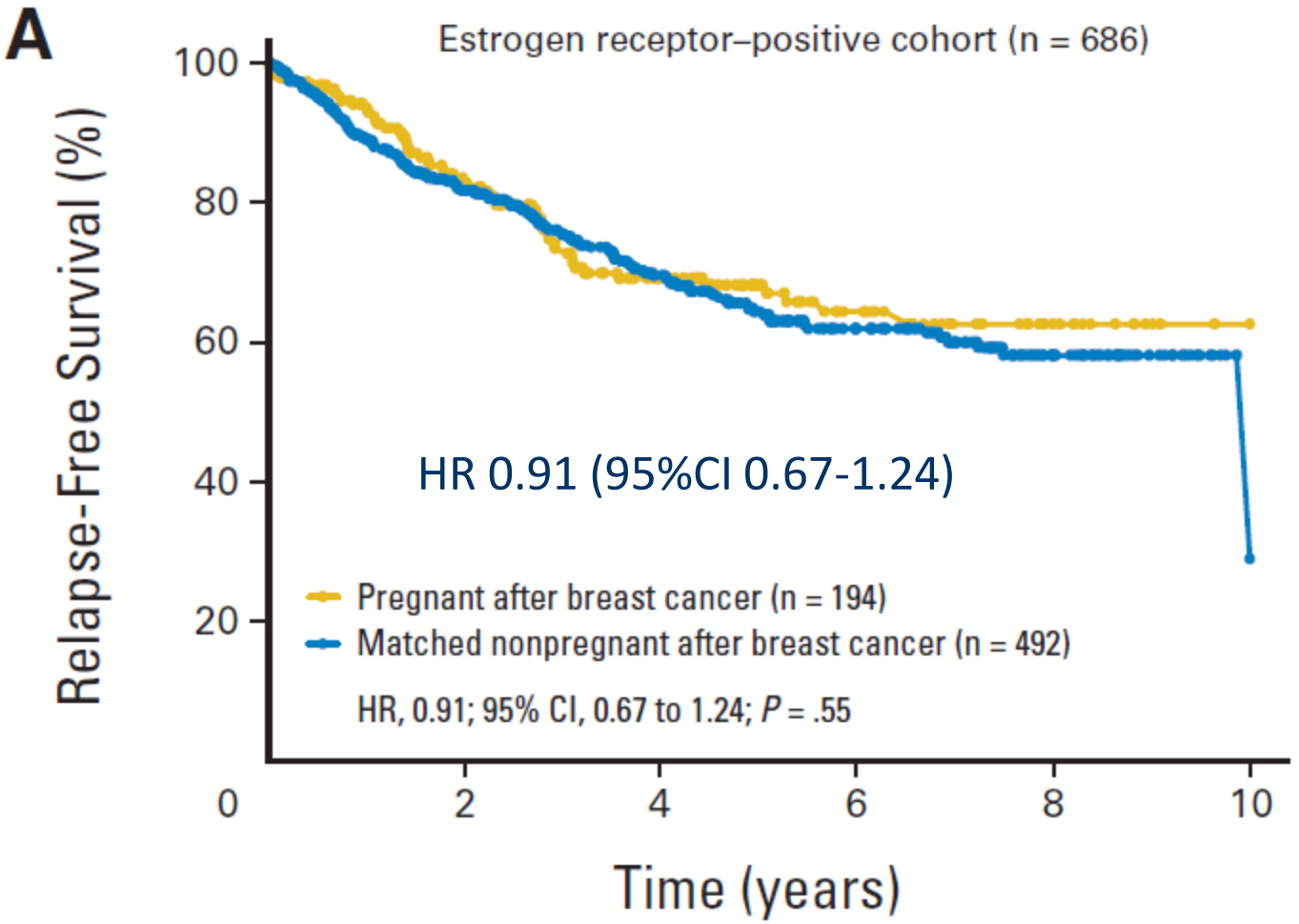
Safety: relapse free survival in ER+



Prognostic Impact of Pregnancy After Breast Cancer According to Estrogen Receptor Status: A Multicenter Retrospective Study

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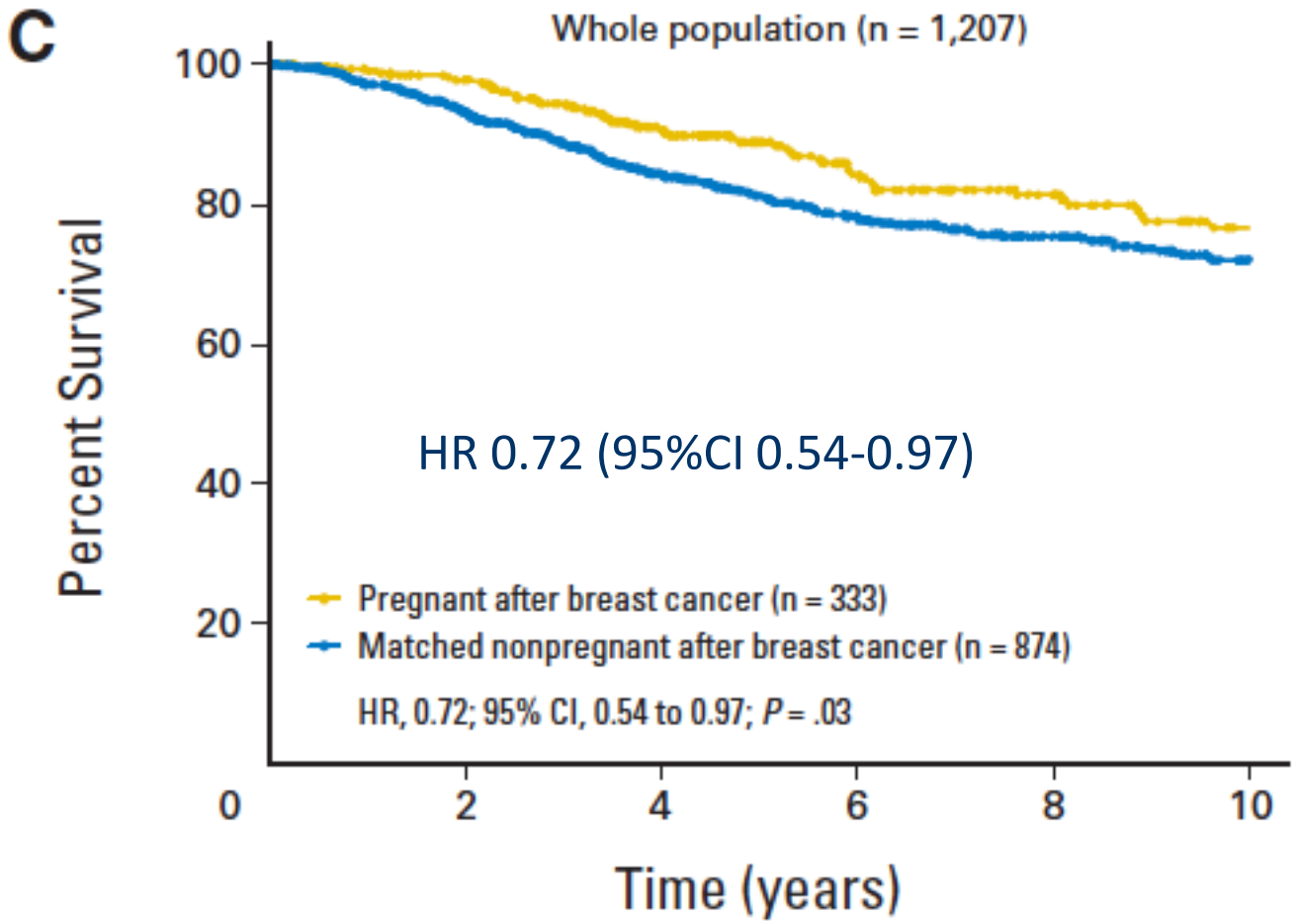
Safety: overall survival in ER+ and ER-



Prognostic Impact of Pregnancy After Breast Cancer According to Estrogen Receptor Status: A Multicenter Retrospective Study

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Frequently asked questions

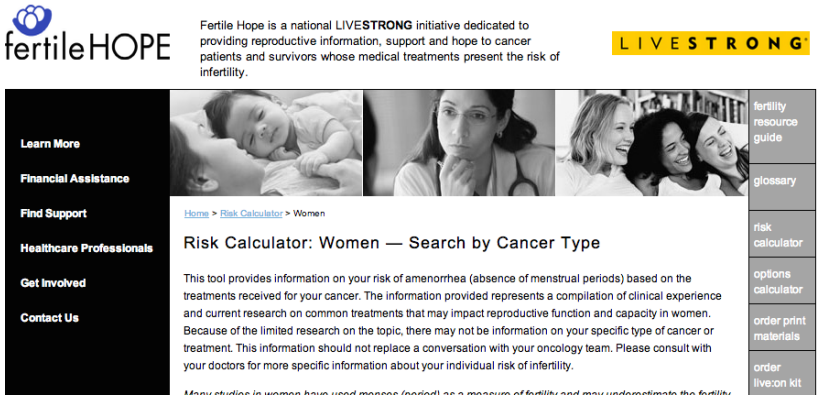
What is the risk of chemotherapy-induced infertility ?

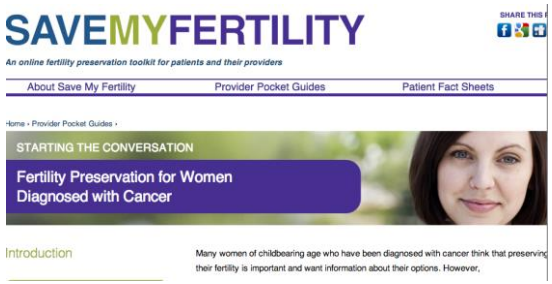
Is there anything we can do to reduced it?

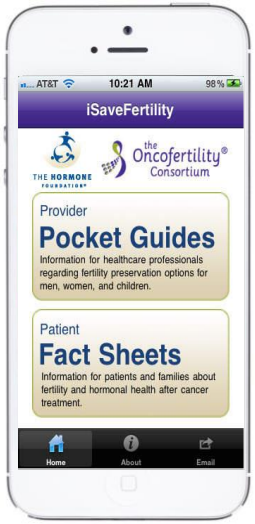
Assessing the risk of infertility

CRITICAL FACTORS:

- ✓ Drugs administered (schedule and dosage)
- ✓ Age at diagnosis (oocyte quantity and quality)
- ✓ Age at pregnancy (treatment duration)







the Oncofertility® Consortium
AT NORTHWESTERN UNIVERSITY

http://oncofertility.northwestern.edu/about-us

http://www.savemyfertility.org/pocket-guides

http://www.fertilehope.org/tool-bar/risk-calculator-women-type.cfm

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Assessing the risk of infertility

36 y/o N+ Luminal B tumor
ECx4 ->wPTX x12 -> LHRHa+Exemestane x 5y

Intermediate Risk
Approximately 30-70% of women develop amenorrhea post-treatment.

- CMF x 6 cycles in women ages 30-39 (cyclophosphamide, methotrexate, 5-fluorouracil)
- CEF x 6 cycles in women ages 30-39 (cyclophosphamide, epirubicin, 5-FU)
- CAF x 6 cycles in women ages 30-39 (cyclophosphamide, doxorubicin, 5-FU)
- AC x 4 cycles in women ages 40 and older (doxorubicin, cyclophosphamide)

http://www.fertilehope.org/tool-bar/risk-calculator-women-type.cfm

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Ovarian toxicity: drugs

Panel 1: Estimated risk of gonadal dysfunction with cytotoxic drugs[29]

High risk	Medium risk	Low risk
Cyclophosphamide	Cisplatin	Vincristine
Ifosfamide	Carboplatin	Methotrexate
Chlormethine	Doxorubicin	Dactinomycin
Busulfan		Bleomycin
Melphalan		Mercaptopurine
Procarbazine		Vinblastine
Chlorambucil		

THE LANCET (Wallace et al, Lancet Oncol 2005)

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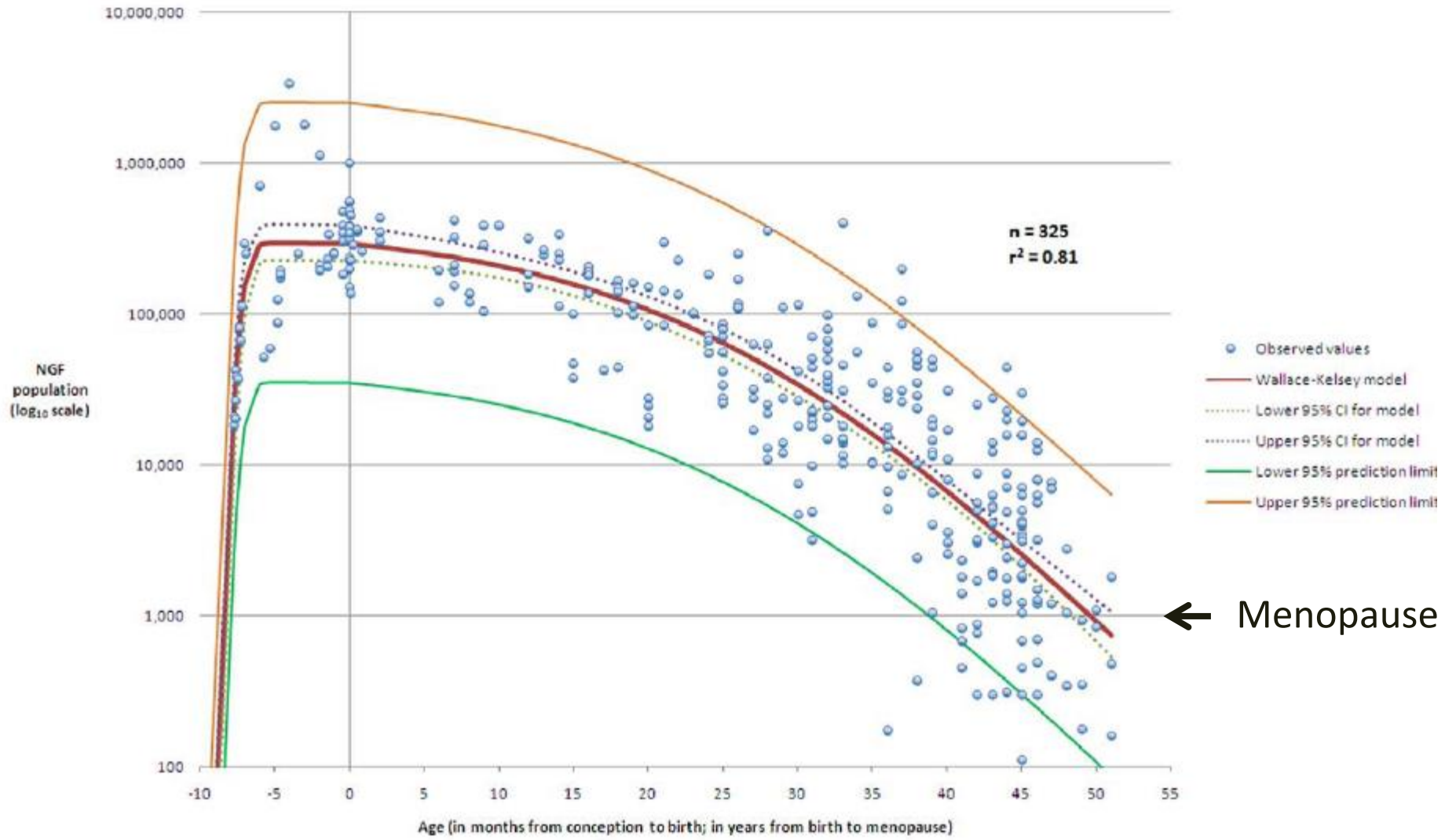
Ovarian reserve



← Menopause

Human Ovarian Reserve from Conception to the Menopause

W. Hamish B. Wallace[1]*, Thomas W. Kelsey[2]

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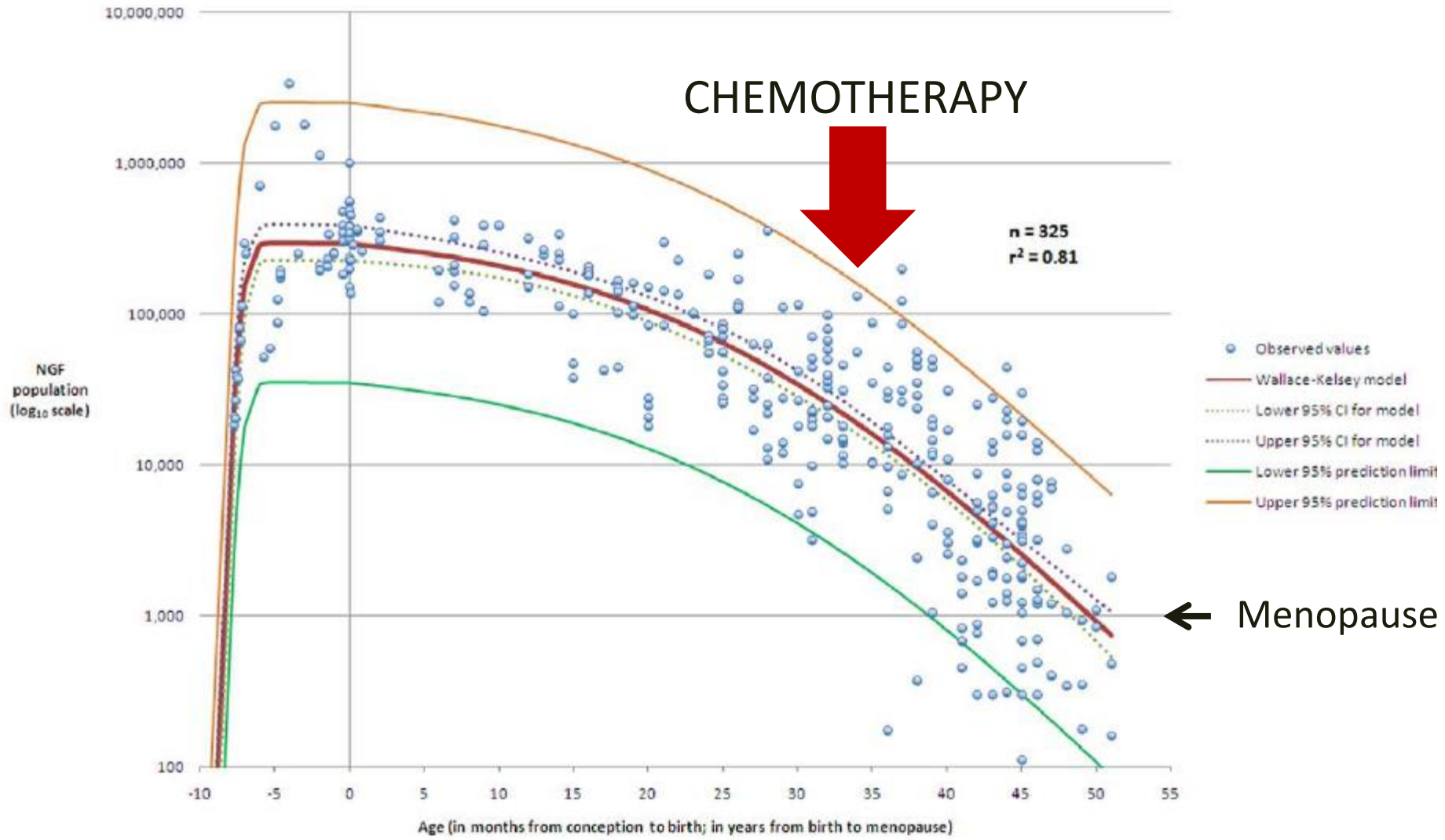
Ovarian reserve at chemotherapy



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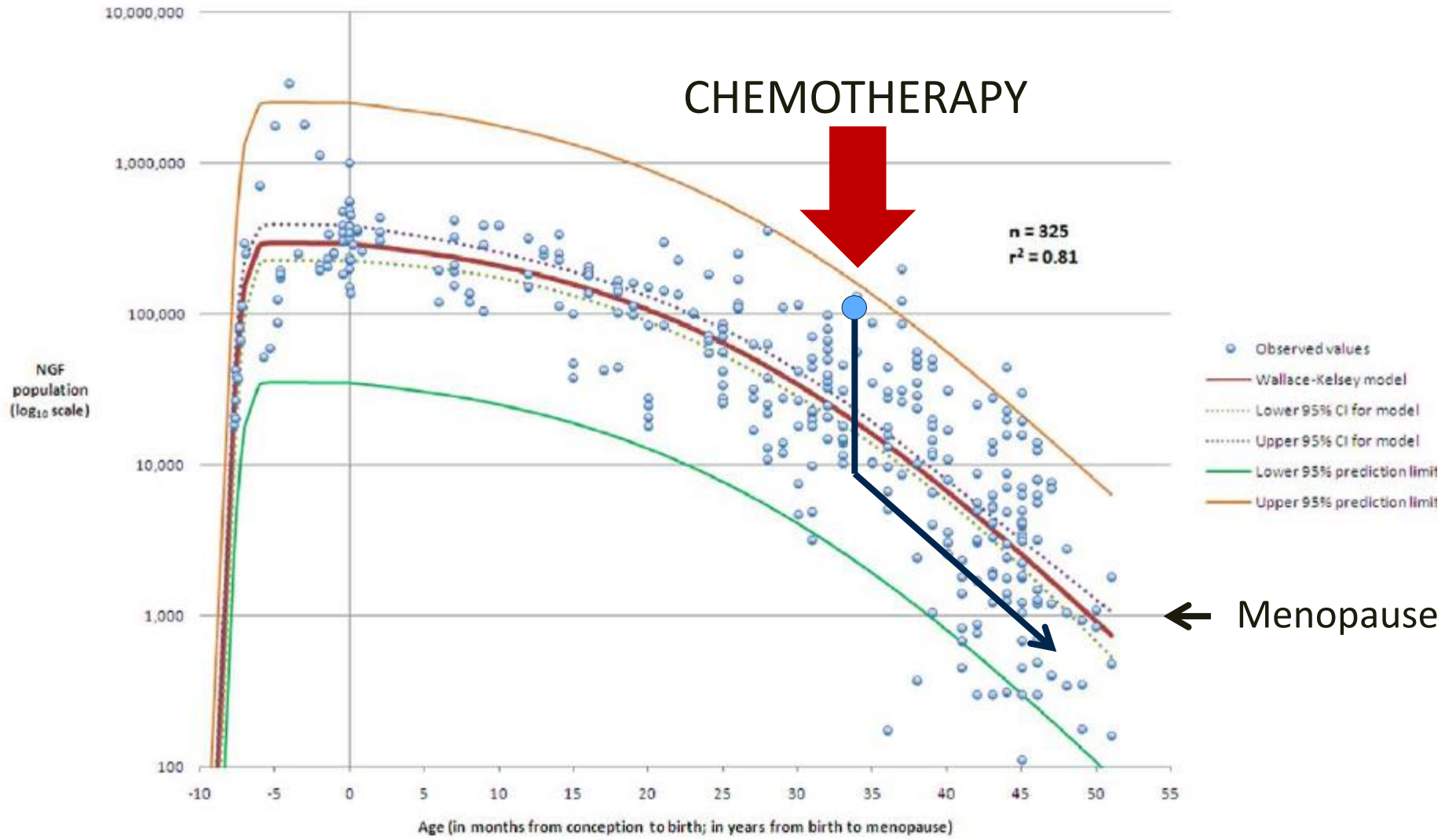

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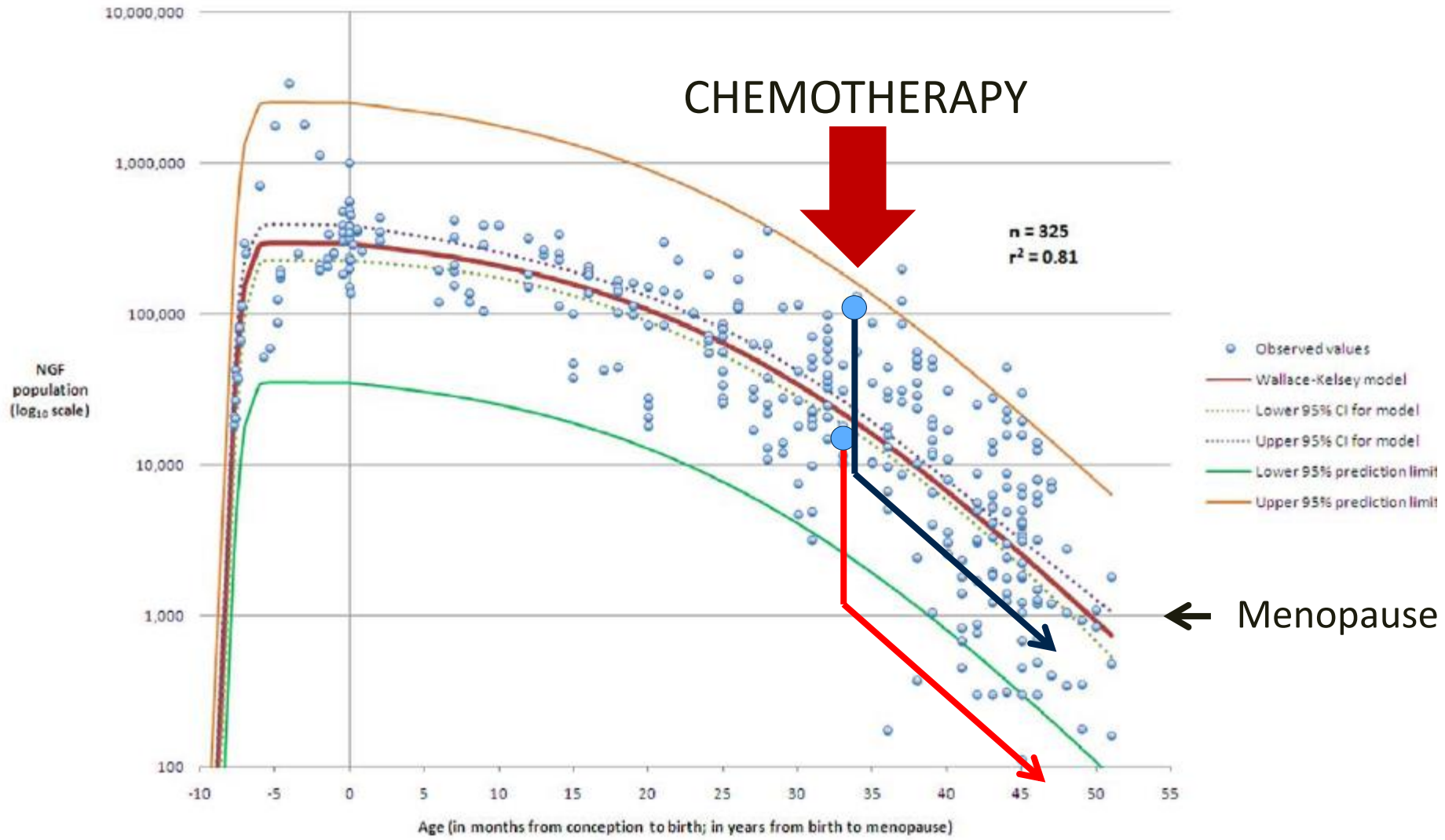
Ovarian reserve at chemotherapy



Human Ovarian Reserve from Conception to the Menopause

W. Hamish B. Wallace[1]*, Thomas W. Kelsey[2]

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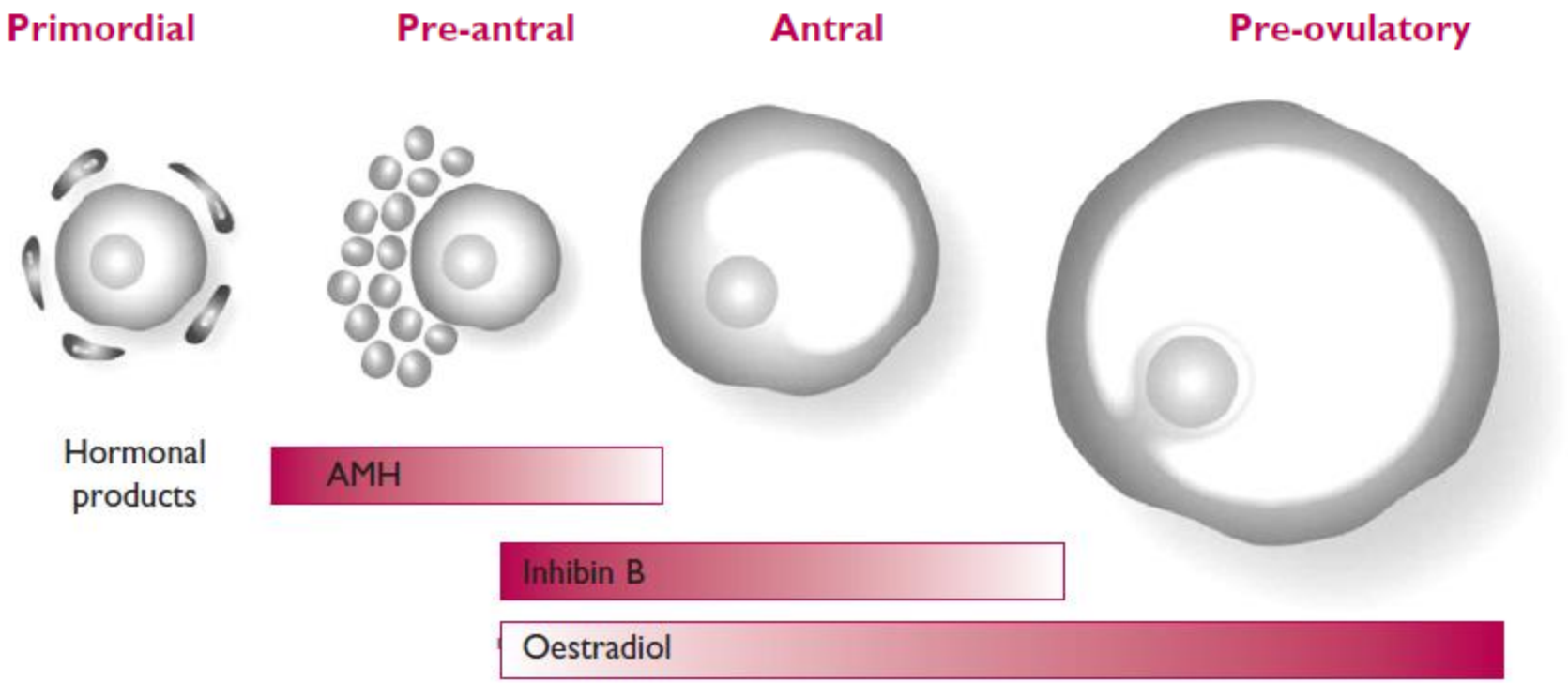
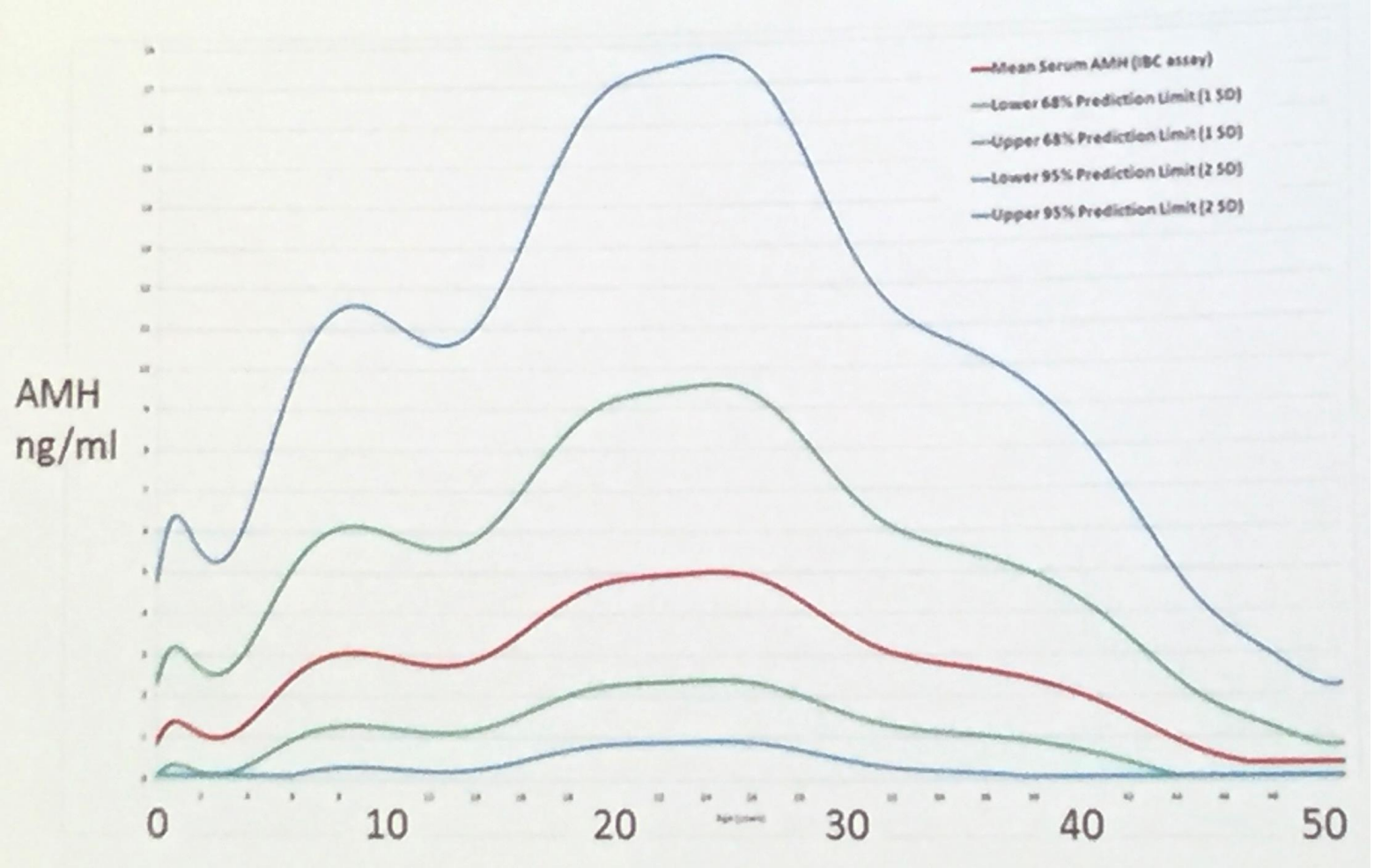
Ovarian reserve: AMH



Ovarian reserve: AMH

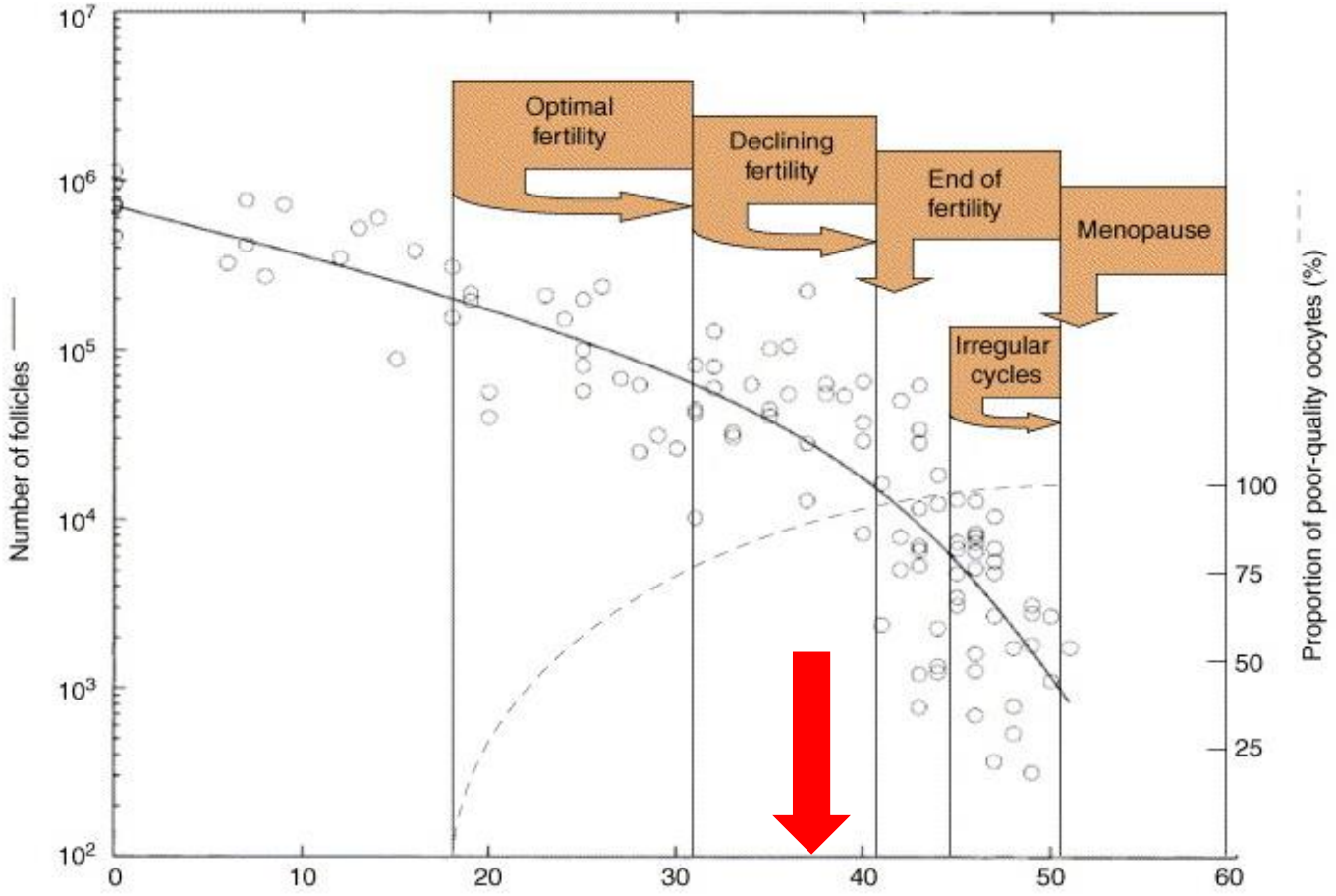


Kelsey et al, 2011 PLOS

Treatment duration and ovarian ageing

36 y/o N+ Luminal B tumor

ECx4 ->wPTX x12 -> LHRHa+Exemestane x 5y



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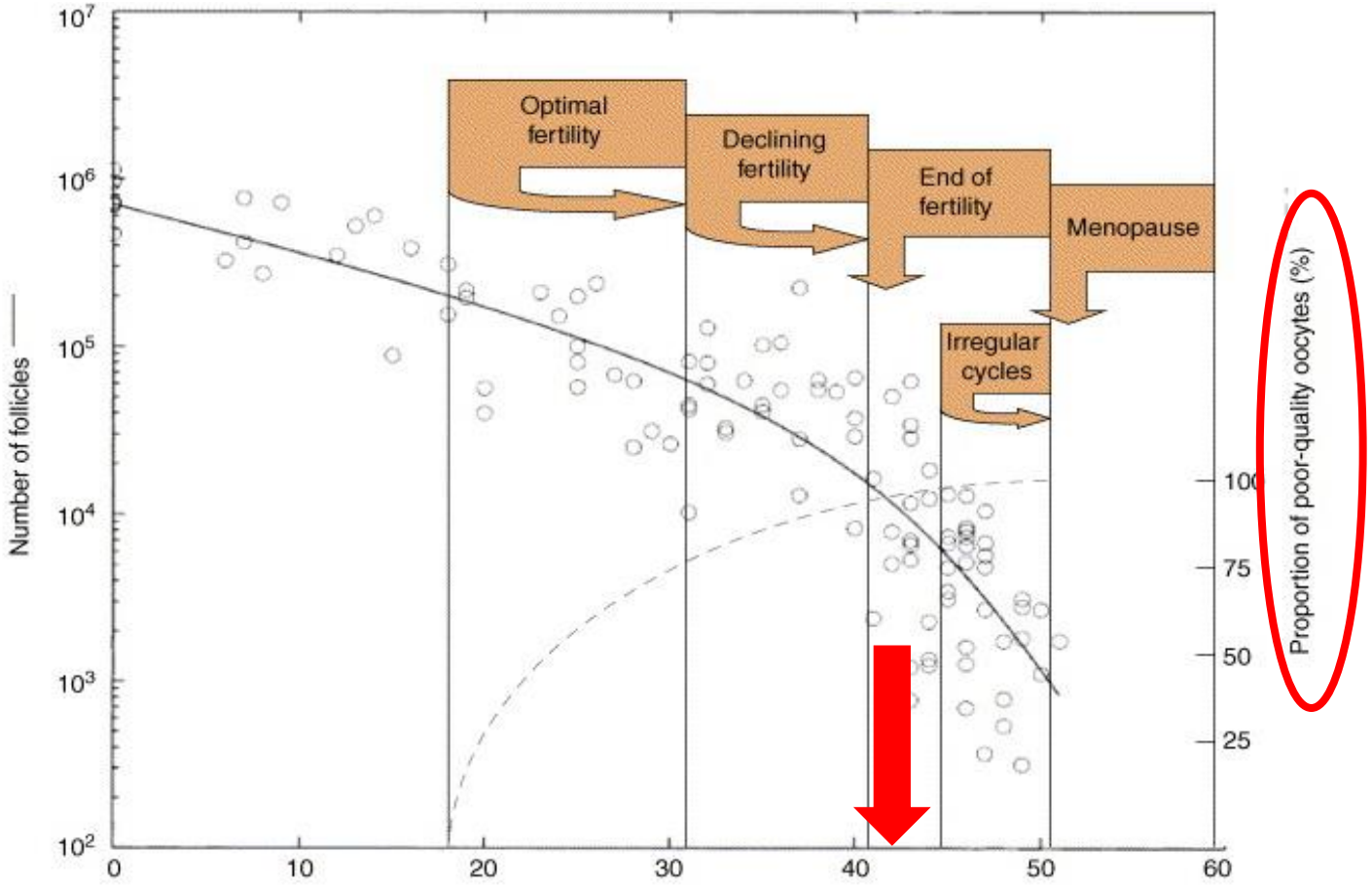


What can be done

- ✓ Inform the patient about the risk of infertility
- ✓ Consider egg/embryo freezing before chemotherapy
- ✓ Consider LHRHa during chemotherapy

Inform the patient about the risk of infertility

Young women desiring future fertility should be counselled on available fertility preserving options before starting anticancer treatments. Counselling should be implemented soon after diagnosis, to allow prompt referral to fertility specialists [IV, B]. Age is the most important determinant of chemotherapy or radiotherapy-induced ovarian dysfunction

clinical practice guidelines

Annals of Oncology 24 (Supplement 6): vi160–vi170, 2013
doi:10.1093/annonc/mdt199
Published online 27 June 2013

Cancer, pregnancy and fertility: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†

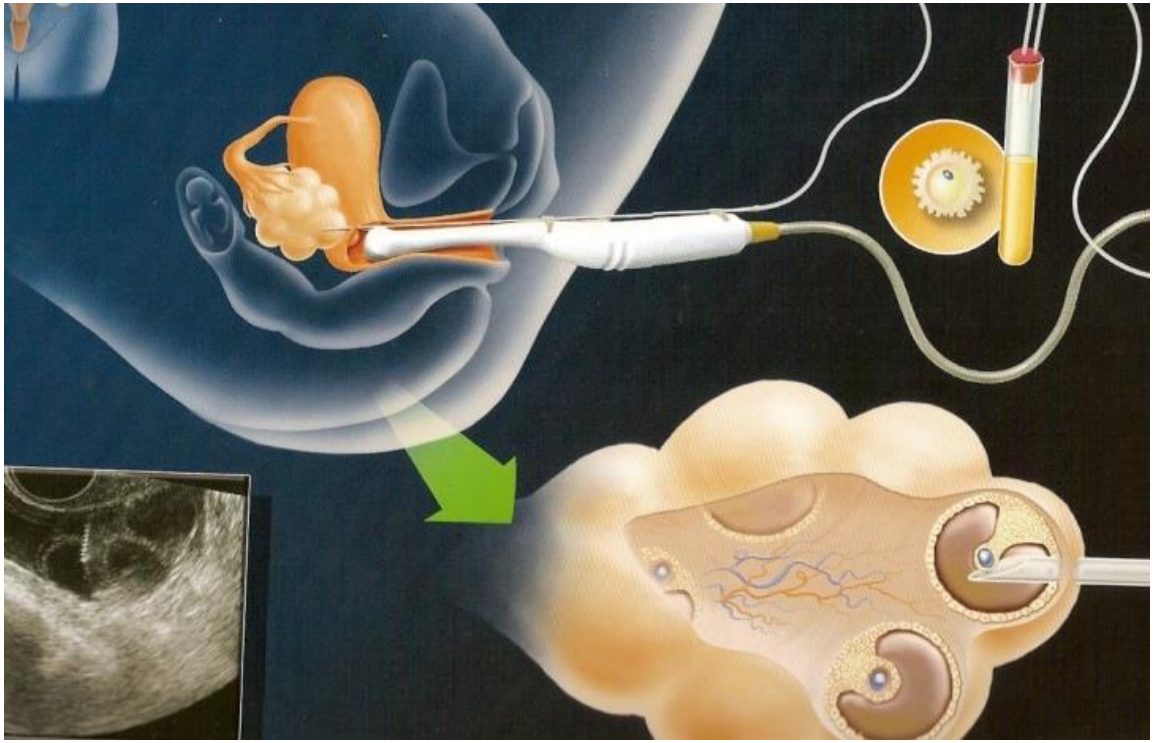
F. A. Peccatori[1], H. A. Azim Jr[2], R. Orecchia[3], H. J. Hoekstra[4], N. Pavlidis[5], V. Kesic[6] & G. Pentheroudakis[5], on behalf of the ESMO Guidelines Working Group*

[1]Fertility and Procreation Unit, Division of Gynaecologic Oncology, European Institute of Oncology, Milan, Italy; [2]Department of Medicine, BrEAST Data Centre, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium; [3]Department of Radiotherapy, European Institute of Oncology, Milan, Italy; [4]Department of Surgical Oncology, University Medical Centre Groningen, Groningen, The Netherlands; [5]Department of Medical Oncology, University of Ioannina, Ioannina, Greece; [6]Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Belgrade, Belgrade, Serbia;

These Clinical Practice Guidelines are endorsed by the Japanese Society of Medical Oncology (JSMO)

2013

Consider egg/embryo freezing before chemo

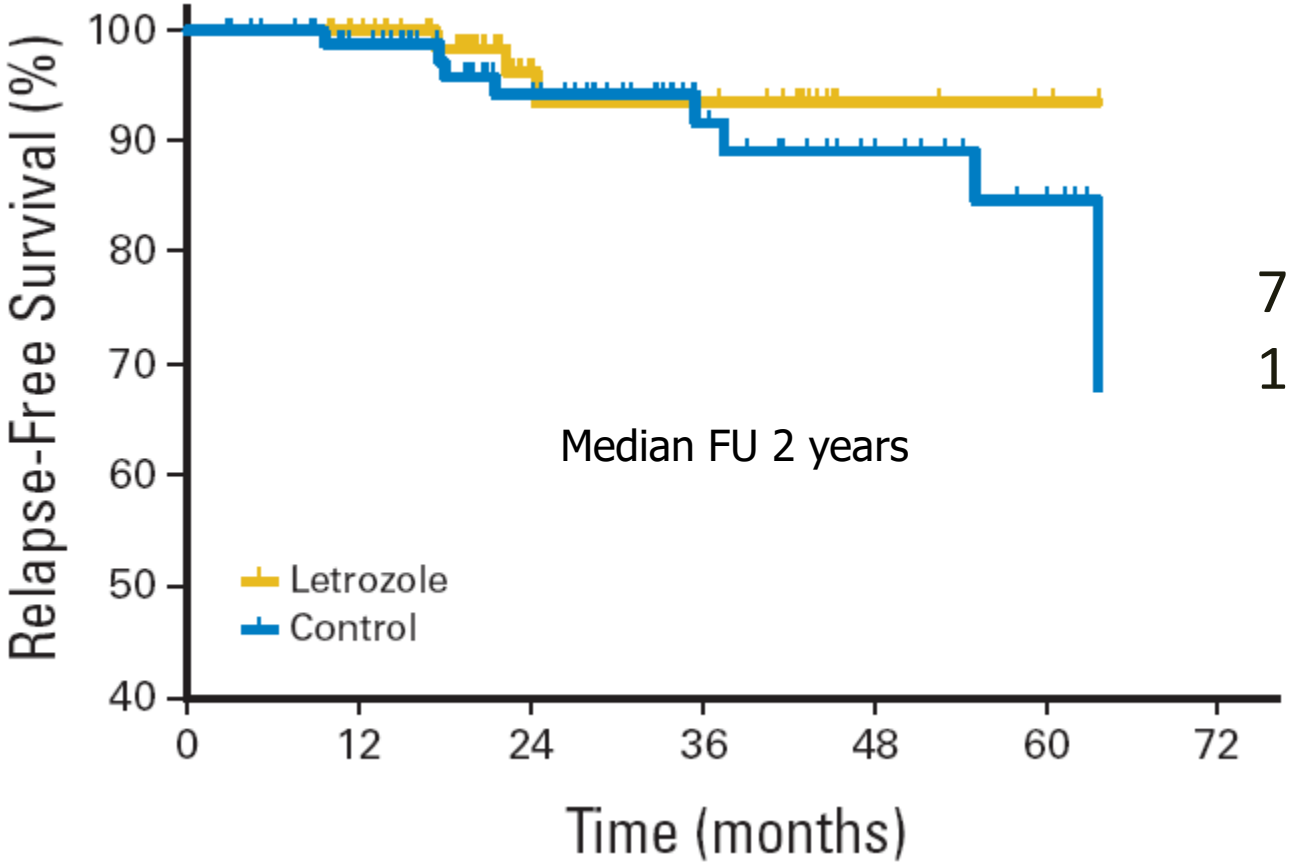


Gonadotrophin administration
Oocytes pick up

Oocytes freezing

IVF/ICSI and embryo freezing

Controlled ovarian stimulation: safety



79 letrozole
136 controls

Median FU 2 years

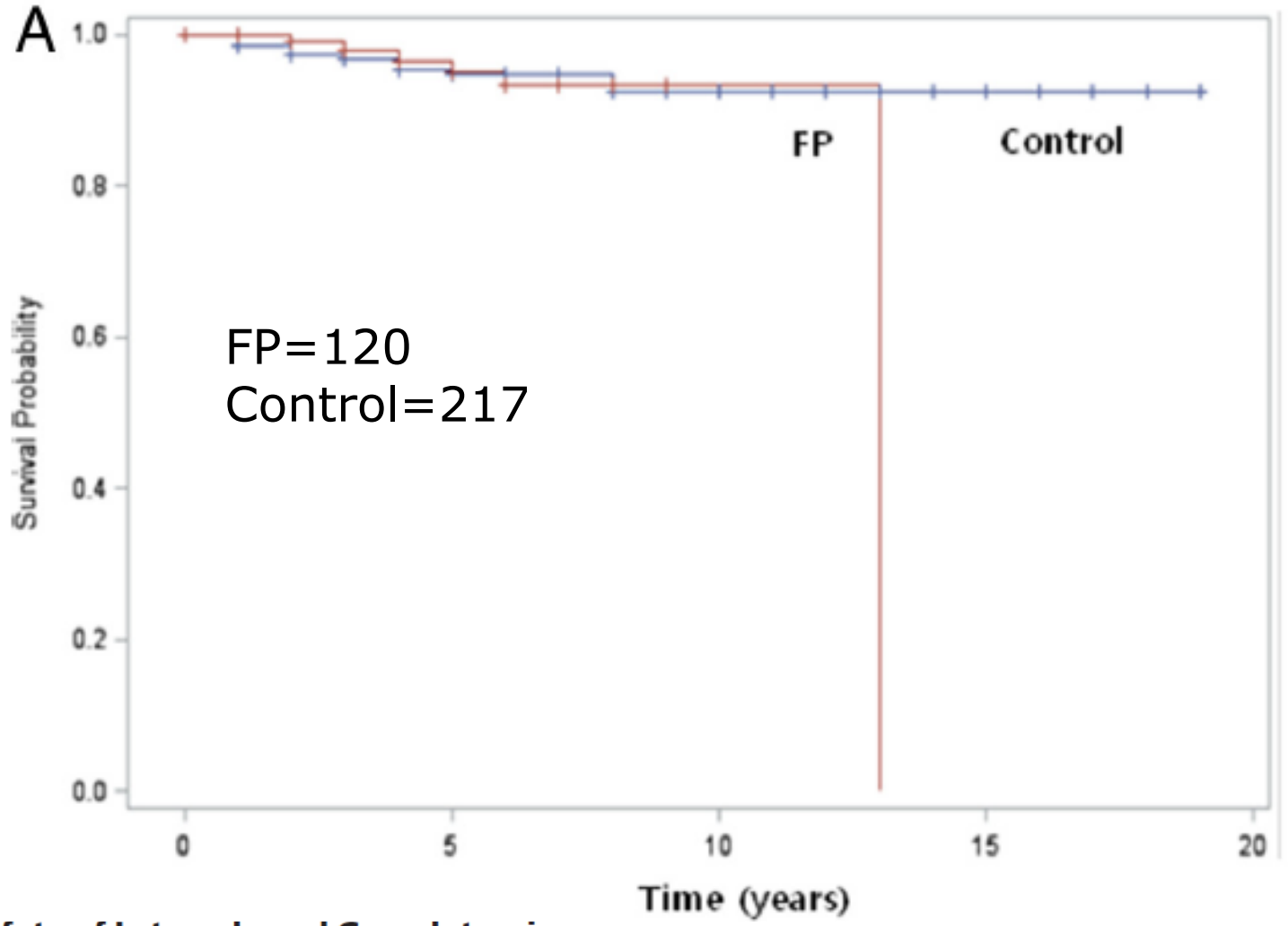
No. of patients at risk						
Letrozole	79	74	37	18	7	5
Control	136	81	56	38	26	19

Safety of Fertility Preservation by Ovarian Stimulation With Letrozole and Gonadotropins in Patients With Breast Cancer: A Prospective Controlled Study

Amr A. Azim, Maria Costantini-Ferrando, and Kutluk Oktay

VOLUME 26 · NUMBER 16 · JUNE 1 2008

Controlled ovarian stimulation: safety



Long-Term Safety of Letrozole and Gonadotropin Stimulation for Fertility Preservation in Women With Breast Cancer

Jayeon Kim, Volkan Turan, and Kutluk Oktay

DOI: http://dx.doi.org/10.1210/jc.2015-3878

JCEM THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

2016, JCEMonline ahead of print

Consider LHRHa during chemotherapy

Ovarian suppression using luteinizing hormone-releasing hormone agonists during chemotherapy to preserve ovarian function and fertility of breast cancer patients: a meta-analysis of randomized studies

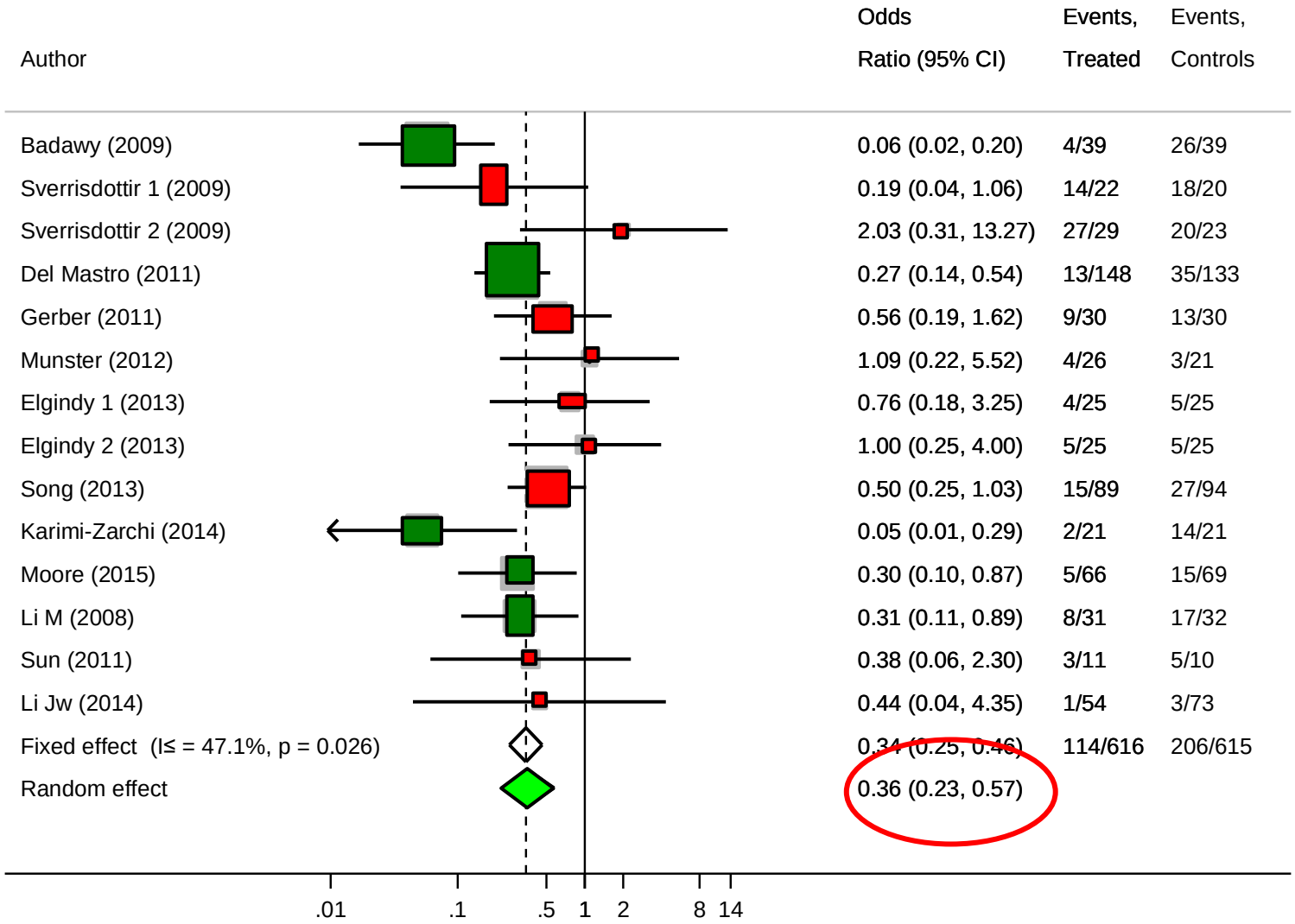
M. Lambertini[1], M. Ceppi[2], F. Poggio[1], F. A. Peccatori[3], H. A. Azim Jr[4], D. Ugolini[5], P. Pronzato[1], S. Loibl[6,7], H. C. F. Moore[8], A. H. Partridge[9], P. Bruzzi[2] & L. Del Mastro[10*]

[1]Department of Medical Oncology, U.O. Oncologia Medica 2, IRCCS AOU San Martino-IST, Genova; [2]Unit of Clinical Epidemiology, IRCCS AOU San Martino-IST, Genova; [3]Fertility and Procreation Unit, Gynecologic Oncology Department, European Institute of Oncology, Milan, Italy; [4]BrEAST Data Centre, Department of Medicine, Institut Jules Bordet, Université Libre de Bruxelles, Brussels, Belgium; [5]Department of Internal Medicine, University of Genoa, Unit of Clinical Epidemiology, IRCCS AOU San Martino-IST, Genova, Italy; [6]German Breast Group (GBG), Neu-Isenburg; [7]Sana-Klinikum Offenbach, Offenbach am Main, Germany; [8]Cleveland Clinic Foundation, Taussig Cancer Institute, Cleveland; [9]Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, USA; [10]Department of Medical Oncology, U.O. Sviluppo Terapie Innovative, IRCCS AOU San Martino-IST, Genova, Italy

Received 7 July 2015; revised 12 August 2015; accepted 1 September 2015

Lambertini et 2015, Annals of Oncology

Consider LHRHa during chemotherapy



Lambertini et 2015, Annals of Oncology

Take home messages

- ✓ Chemotherapy may impair ovarian function.
  Age, drug type and dosage are the critical factors

- ✓ Early oncofertility counseling is essential for effective fertility preservation

- ✓ Egg freezing before chemotherapy +LHRHa during chemotherapy can be used to improve results

- ✓ Dedicated research protocols for young women with cancer are warranted

Conclusions

VIEWPOINT

Oncologists' Role in Patient Fertility Care
A Call to Action

Teresa K. Woodruff, PhD
Northwestern University Feinberg School of Medicine, Chicago, Illinois.

Kristin Smith, BS
Northwestern University Feinberg School of Medicine, Chicago, Illinois.

William Gradishar, MD
Northwestern University Feinberg School of Medicine, Chicago, Illinois.

Related article

Oncofertility is a term coined just a few years ago to address the urgent, unmet needs of young cancer patients who were offered life-preserving but fertility-threatening treatments. The issue for many oncologists was not that they did not want to provide options to their patients; rather, the option list and the physician groups on the fertility side were limited. This issue has largely been addressed and the remaining barriers are few. Here are answers to the questions most frequently asked of oncologists by patients.

1. **Do patients care about fertility in the face of a cancer diagnosis?** Yes, many studies conducted over the past 5 years have shown that young women and men are concerned about their endocrine health and the fertility consequences of cancer treatment. Patients who are not told about later fertility concerns at the time of diagnosis have stress levels in the range of posttraumatic stress disorder during survivorship.[1,2] Thus, oncologists are urged to provide a fertility consultation to mitigate the long-term health consequence associated with treatment.

2. **What amount of time is necessary for women**

4. **Is fertility care affordable?** There is a great deal of work toward affordability of fertility care options by oncofertility clinics. Some insurance companies will cover fertility options as long as they are coded appropriately, using the cancer diagnosis. Certain advocacy organizations provide discounted services at specific clinics, free stimulation medications, and/or grants for patients undergoing fertility preservation. In today's social media-fueled world, many patients find ways to cover the fertility costs through crowd funding and from friends and family. The bottom line is that all young males and females should be advised of the fertility threat of their cancer care to enable the financial decisions to be made by the patient, not by the clinician before any irreversible damage to the gonads is done.[6]

5. **What fertility preservation options are available?** The number of options for males and females, from birth upwards, continues to increase as experimental options of ovarian and testicular tissue freezing come to fruition in centers around the globe. A detailed list of options is available on Northwestern's oncofertility web-

Woodruff et al, JAMA Onc 2016; 2(2):171

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Grazie!

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