

Maintaining Fertility in Younger Breast Cancer patients

Dr Alison Jones

May 2014

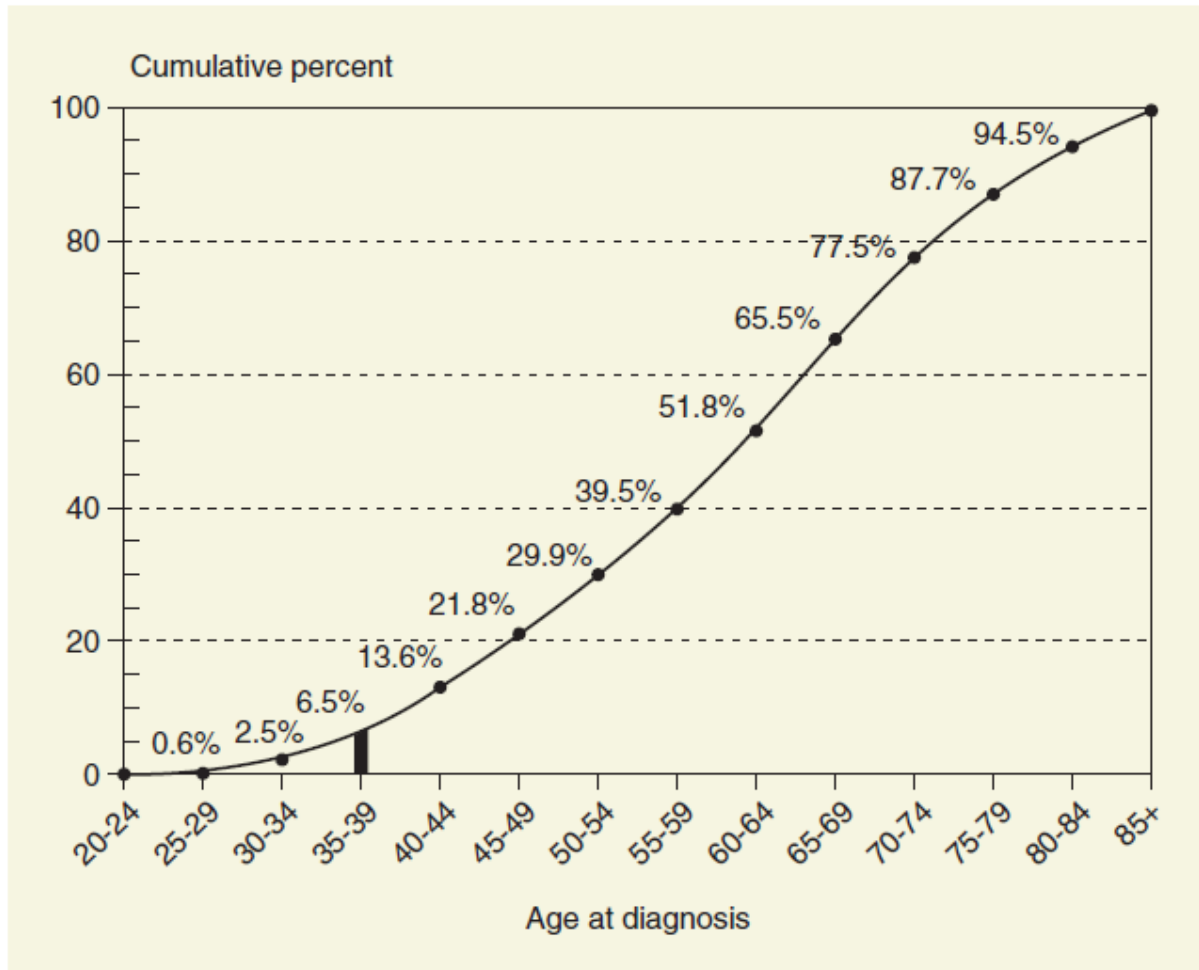


Breast Cancer and Pregnancy

- Who are the 'younger' patients?
- How many woman does this affect?
- Impact of treatment on fertility?
- Can we protect fertility?
- When can women consider having a baby after breast cancer treatment?
- Are there any other options?



Breast cancer in young women is a relatively rare disease



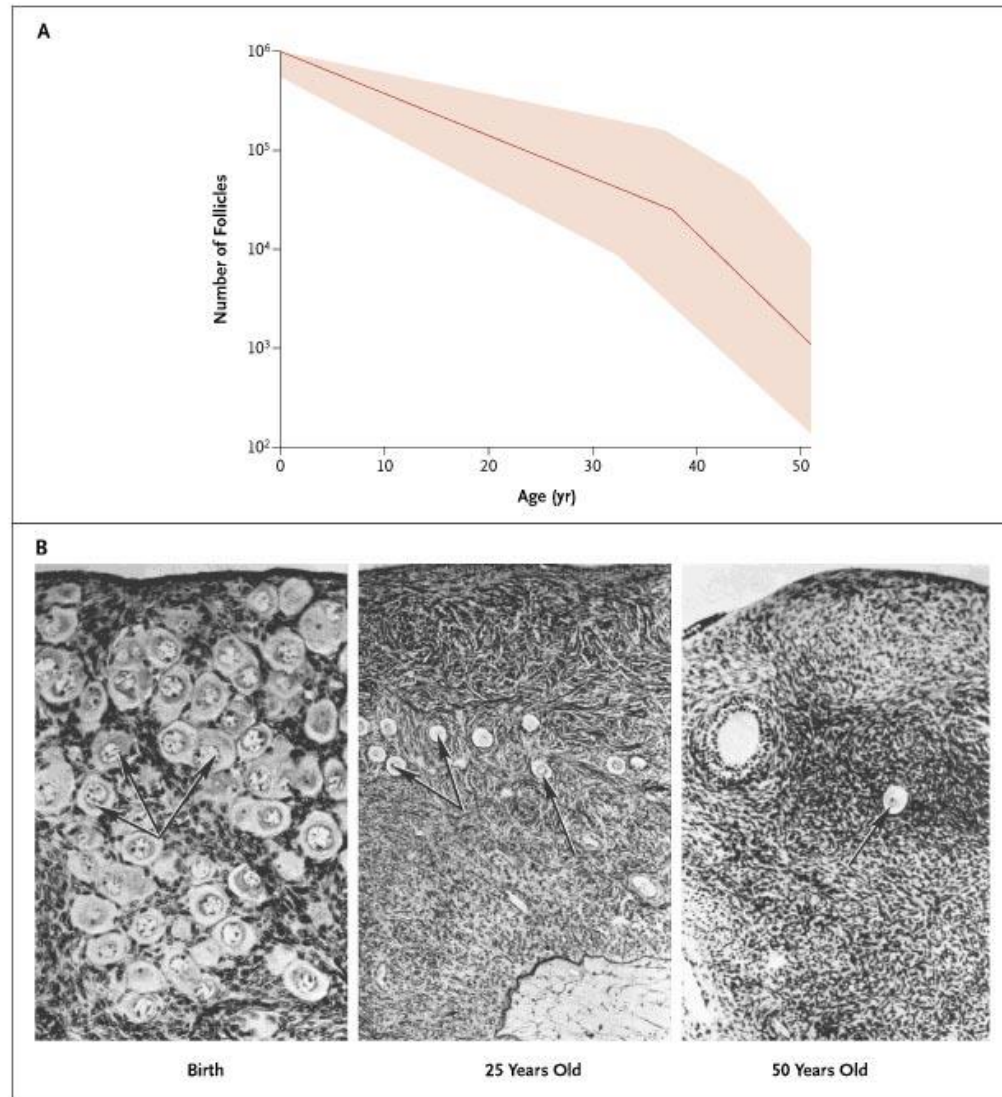


Age and Pregnancy in the UK 2012

- Average age of first time mothers is 28.1 years
- Average age for second baby is 30.1 years
- 50% babies born to women over 30 years
- 28000 mothers each year are over 40 years of age
- 141 babies are born born to mothers over 50 years of age

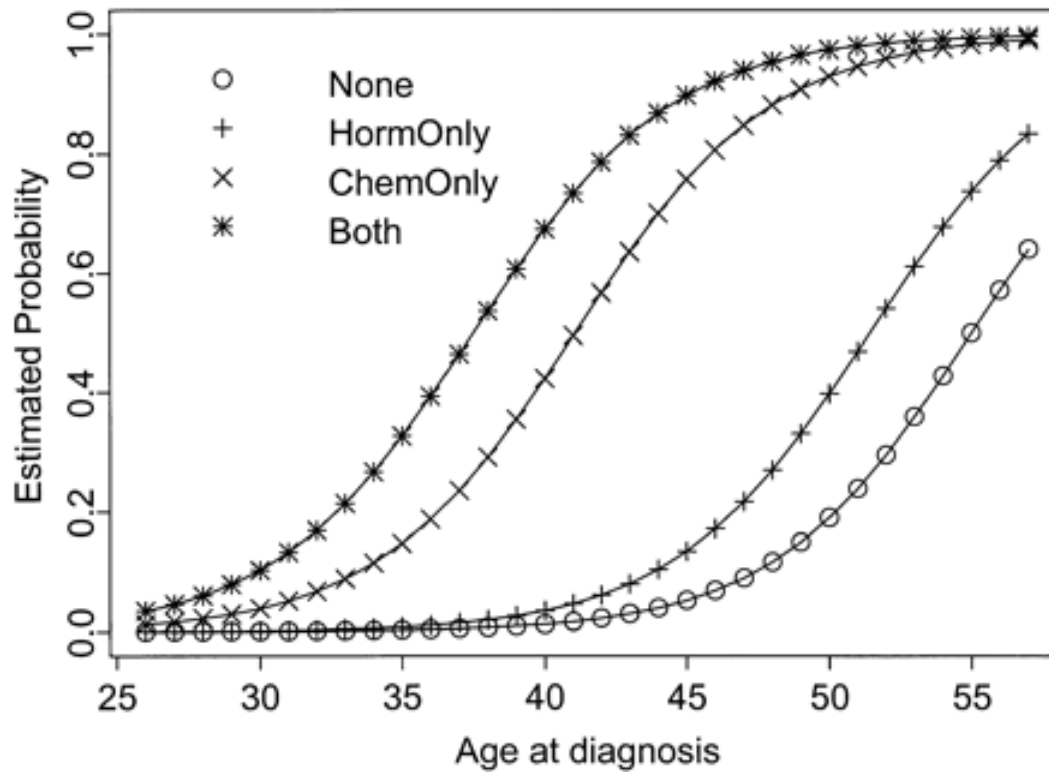


Natural Decline of Oocytes with Age





Probability of menopause during the first year after diagnosis of breast cancer and effect of systemic treatment



Effects of Endocrine Therapy

- Adjuvant endocrine therapy for breast cancer (tamoxifen or ovarian suppression) does not appear to cause permanent amenorrhea or infertility
- BUT... endocrine therapy usually entails years of treatment when pregnancy contraindicated, and aging during that time compromises fertility



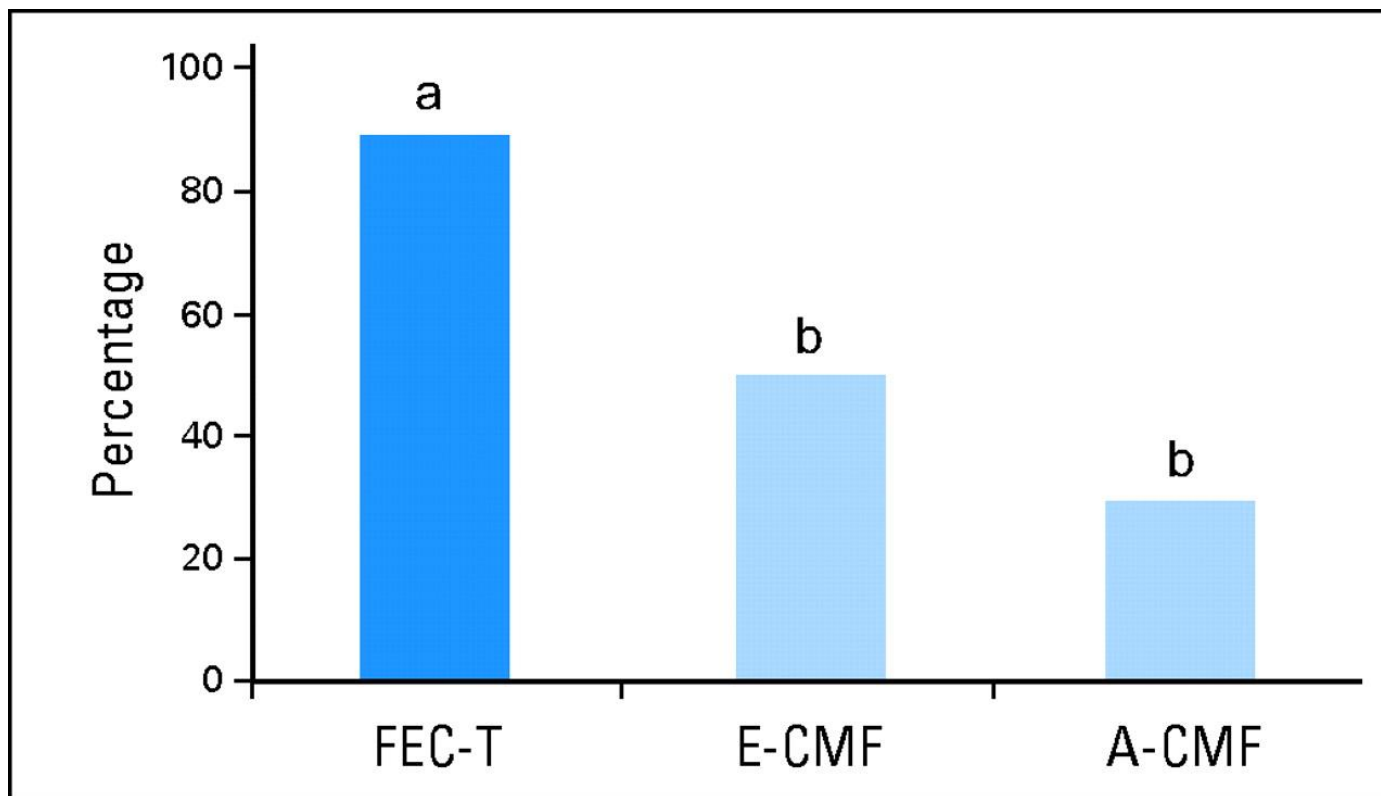
PREGNANCY AND BREAST CANCER ISSUES TO DISCUSS BEFORE FERTILITY TREATMENT

- A woman's personal chance of 5 and 10 year survival from her diagnosis of breast cancer
- Impact of a future pregnancy on risk of breast cancer recurrence;
 - ER +ve vs. ER -ve breast cancer
 - Duration of endocrine treatment (Up to 10 years for tamoxifen)
- ? Any risk to baby from mothers diagnosis and treatment
- Support for woman and family





The percentage of women becoming amenorrheic within 6 months of initiation of chemotherapy by treatment regimen





Issues for Women Who Remain Premenopausal

- Will a woman be less fertile, even if she continues to menstruate?
- Will a woman go through menopause earlier (“delayed, premature menopause”)



Providers May Neglect to Discuss Fertility

- Only 68% of women age 50 or younger at diagnosis of breast cancer recalled physician discussion of early menopause
- 34% of women recalled discussion of infertility risk

(Duffy et al., JCO 2005)



BREAST CANCER & FERTILITY PROTECTION OF OVARIAN FUNCTION

- GnRH analogues (e.g. Zoladex)
- Embryo cryopreservation (only if she has a partner or donor sperm)
- Oocyte cryopreservation
- Ovarian tissue banking (still experimental)



Cryopreservation of Embryos

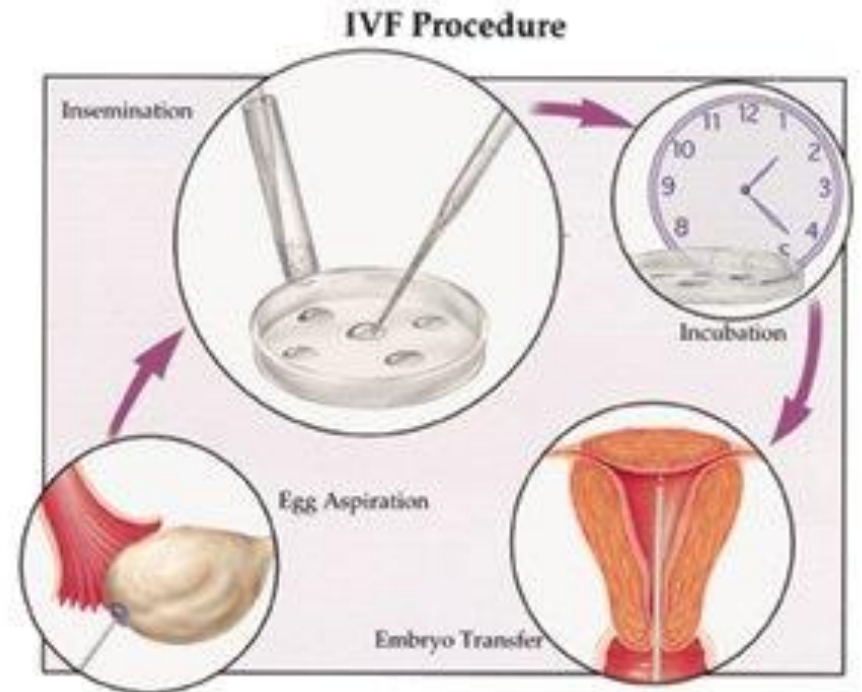
- Standardly available: 20-30% pregnancy rate per transfer of 2-3 embryos
- Requires medical stability, time, and partner/sperm, adequate ovarian reserve
- Expensive, ethically problematic if patient dies
- Requires ovarian stimulation prior to systemic breast cancer treatment- concerning in patients with hormone-sensitive cancer
- Natural cycle IVF has low yield

(Oktay et al, JCO, 2005; Partridge & Winer, JCO 2005)



Process of IVF

1. Hyper ovulation
2. Egg Retrieval
3. Artificial Insemination
4. Embryo Transfer



In IVF, eggs are harvested from the woman's ovary and fertilized in the laboratory with sperm. The embryos are then transferred into the uterus.



Breast cancer risk & infertility treatment (IVF)

Prospective cohort study using self administered questionnaires (follow up 10 year)			
	Total	Infertility treatment	No infertility treatment
Fertility & treatment	92555	6602	85953
Breast cancer	2571	183 (2.7%)	2388 (2.7%)

RR = 0.95 (0.82 – 1.11)

Borderline significance for women with a family history of breast cancer



Fertility Preservation in breast cancer patients

Ovarian stimulation: Tamoxifen vs Letrozole

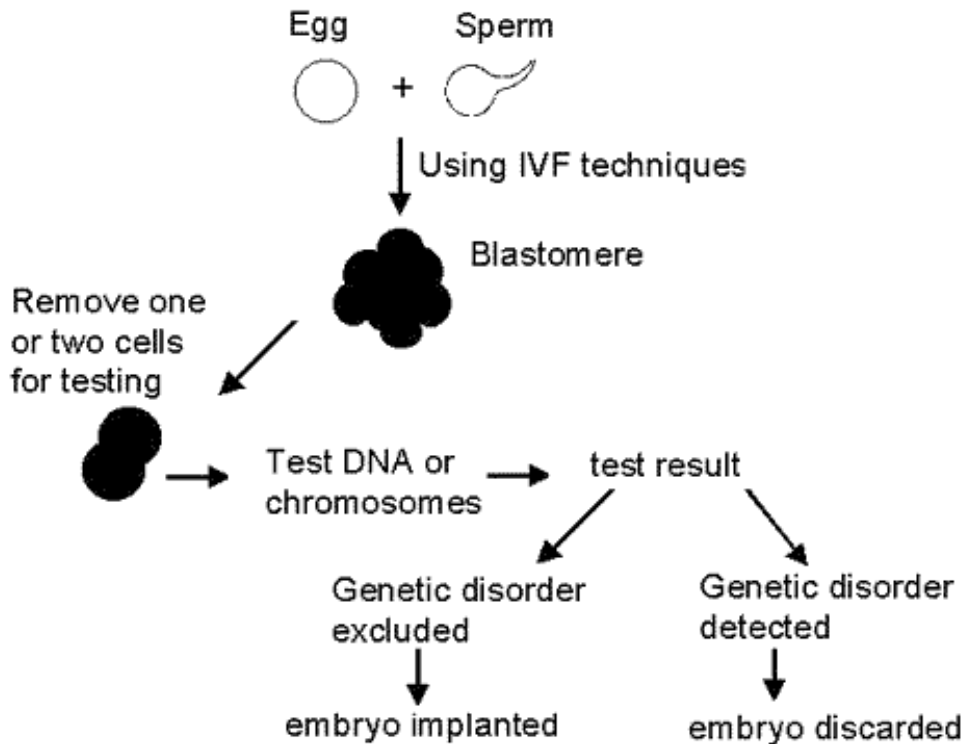
60 women (age 24-43) 33 ovarian stimulation cycles				
	Tamoxifen (60mg/day	Tamoxifen + FSH	Letrozole + FSH	P
No follicles	2 \pm 0.3	6 \pm 1	7.8 \pm 0.9	<0.001
Mature oocytes	1.5 \pm 0.3	5.1 \pm 1.1	8.5 \pm 1.6	<0.001
Embryos	1.3 \pm 0.2	3.8 \pm 0.8	5.3 \pm 0.8	<0.001

After 554 \pm 31 days follow up cancer recurrence similar IVF vs control (HR = 1.5: 95% (I 0.29-74)



Preimplantation Genetic Diagnosis (PGD)

genetic testing performed prior to embryo transfer



“The debate [around PGD] has been building since the late 1980s, when doctors at London's Hammersmith Hospital learned how to tease a cell from a 3-day-old embryo and study its chromosomes for gender.”

(Zitner 2002)

- Adds \$2000 to IVF
- Reduces rate of miscarriages from 23% to 10%
- Does not increase chance of pregnancy



Oocyte Cryopreservation

- Requires time and stimulation prior to treatment
- No requirement for sperm, less ethical concern
- *Experimental- approximately 2% pregnancy rate per thawed oocyte*



Cryopreservation of Ovarian Tissue

- Requires surgical procedure to remove ovary or piece of ovary
- May increase risk of infertility in low risk situation
- Potential for reintroduction of malignant cells at reimplantation
- *Highly experimental- few babies born to date*



Ovarian Cryopreservation

- Heterotopic transplantation technique:
 - Optimal site unknown
 - Most have been to arm or forearm (or suprapubic area)
- **No need for abdominal surgery**
- **Easy monitoring of follicular development**
- **Easy removal if necessary**



(Oktay K, et al, JAMA, 2001;286:1490-3)



Other options

- Egg donation
- Embryo donation
- Surrogacy
- Adoption



PREGNANCY AFTER BREAST CANCER

No. of patients	Maternal Outcome	Author
47	No adverse effect on survival	Ariel and Kempner 1989
23	No adverse effect on survival	Sutton et al 1990
91	No adverse effect on survival	Sankila et al 1994
50	No adverse effect on survival	Von Schoultz et al 1995
21	No adverse effect on survival	Malamos et al 1996
173	Decreased risk in pregnant women	Kroman et al 1997
53	No adverse effect on survival	Kelentgas et al 1991
137	Decreased risk in pregnant women	Gelber et al 2001
383	No adverse effect on survival	Blakely et al 2003
62	No adverse effect on survival	Ives et al 2007

No evidence for adverse effect on survival



Safety and Timing of Pregnancy after Cancer

- Conventional wisdom is to wait until patient gets through the period of highest risk recurrence
 - Receive optimal therapy (endocrine therapy may be prolonged)
- No data to suggest harm in pregnancy sooner
- No evidence for increased risk of disease recurrence associated with most fertility preservation methods and pregnancy- little data!
- Aside from hereditary genetic syndromes and in-utero exposure to chemotherapy, no evidence for increased risk of cancer or abnormality in progeny



American Society of Clinical Oncology Recommendations on Fertility Preservation in People Treated for Cancer

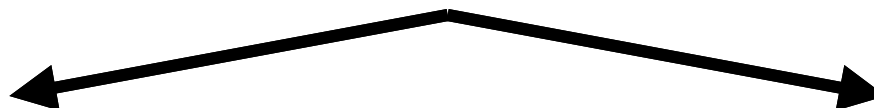
- **Assessment of risk for infertility**
- **Communication with patient**



- Patient at risk for treatment-induced infertility
- Patient interested in fertility preservation options



Refer to specialist with expertise in fertility preservation methods



Eligible for proven fertility preservation method

Male:
sperm cryopreservation

Female:
embryo cryopreservation
conservative gynecologic surgery
oophoropexy

Investigational fertility preservation technique*

- Cryopreservation of testicular or ovarian tissue
- Cryopreservation of oocytes
- Ovarian suppression

*Clinical trial participation encouraged



Conclusions: Fertility Concerns in Cancer Survivors

- Very complex and difficult issues
- Limited available data
- Patient preferences critical in some settings
- Managing expectations often necessary