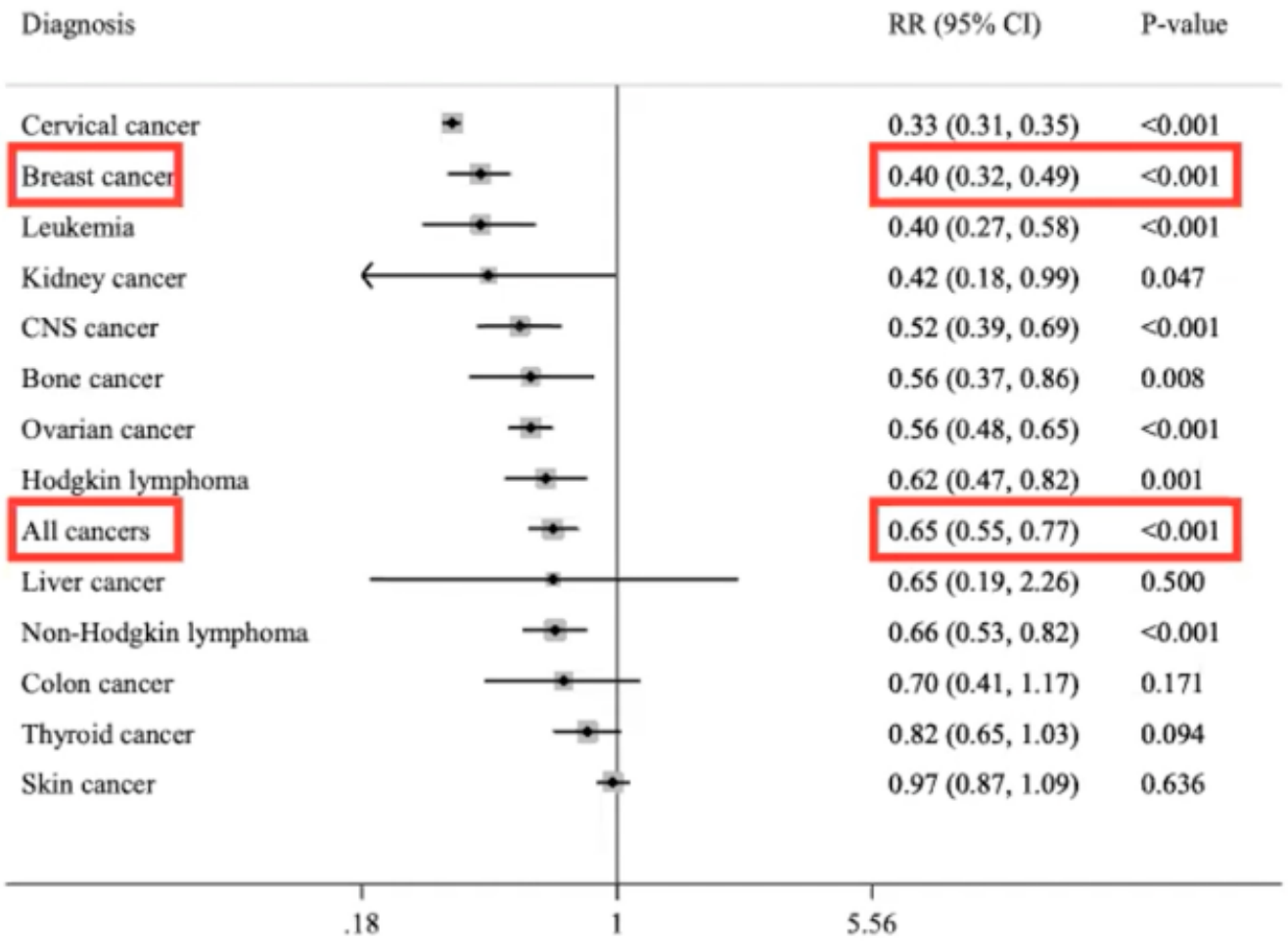
Parenthood after cancer: clinical evidence and outcomes

Michel De Vos, MD PhD

The probability of pregnancy after cancer is reduced



Breast cancer, leukaemia and cervical cancer survivors have the **lowest** likelihood to have a subsequent **pregnancy** among cancer survivors.

PREDICT AYA

Project duration: 1 June 2025 – 30 May 2030

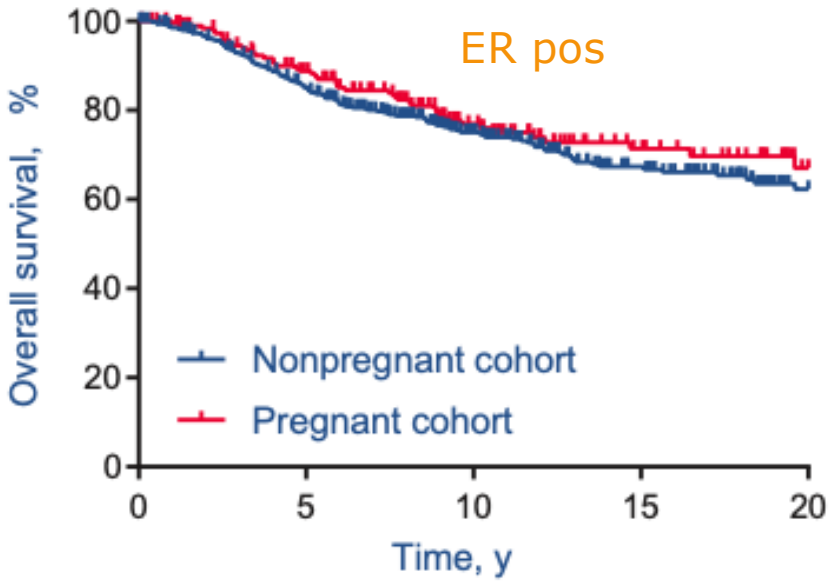
PredictAYA is a multidisciplinary research project funded by Horizon Europe to **better understand the late effects of cancer treatments on adolescents and young adults (AYAs) aged 15-39.**

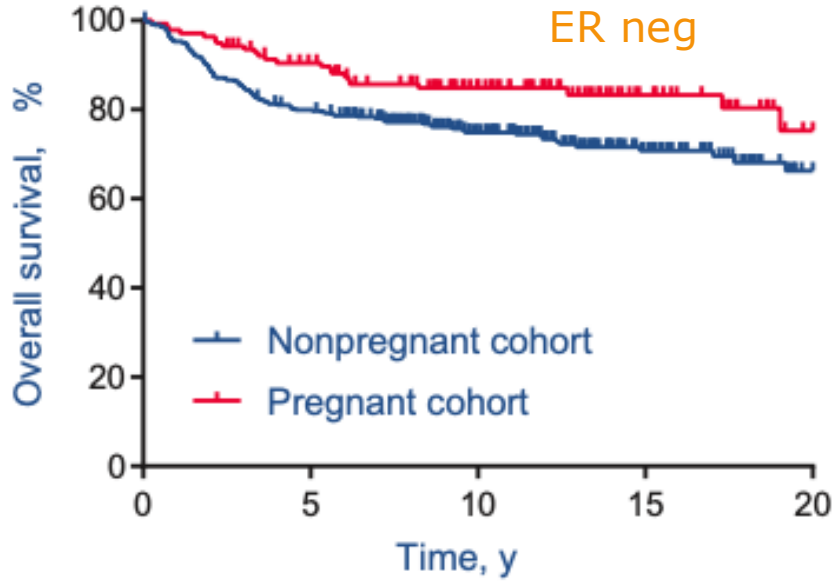
Lambertini et al., J Clin Oncol 2021;
Garg et al., Fertil Steril Rep 2021

Young breast cancer survivors

Pregnancy after breast cancer is safe

333 patients with pregnancy after breast cancer were matched (1:3) to 874 non-pregnant patients with similar characteristics





- Increased risk of obstetric and birth complications in female cancer survivors
- Interval of at least 1 year following completion of ChT is recommended in cancer survivors
- Specific wash-out period should be considered before conception (TAM: 3mnths; anti-HER2: 7mnths)
- If hormone receptor positive: 5-10 years of tamoxifen

Pregnancy Outcome and Safety of Interrupting Therapy for women with endocrine responsIVE breast cancer (POSITIVE)

N= 516
median age 37y
62% chemo

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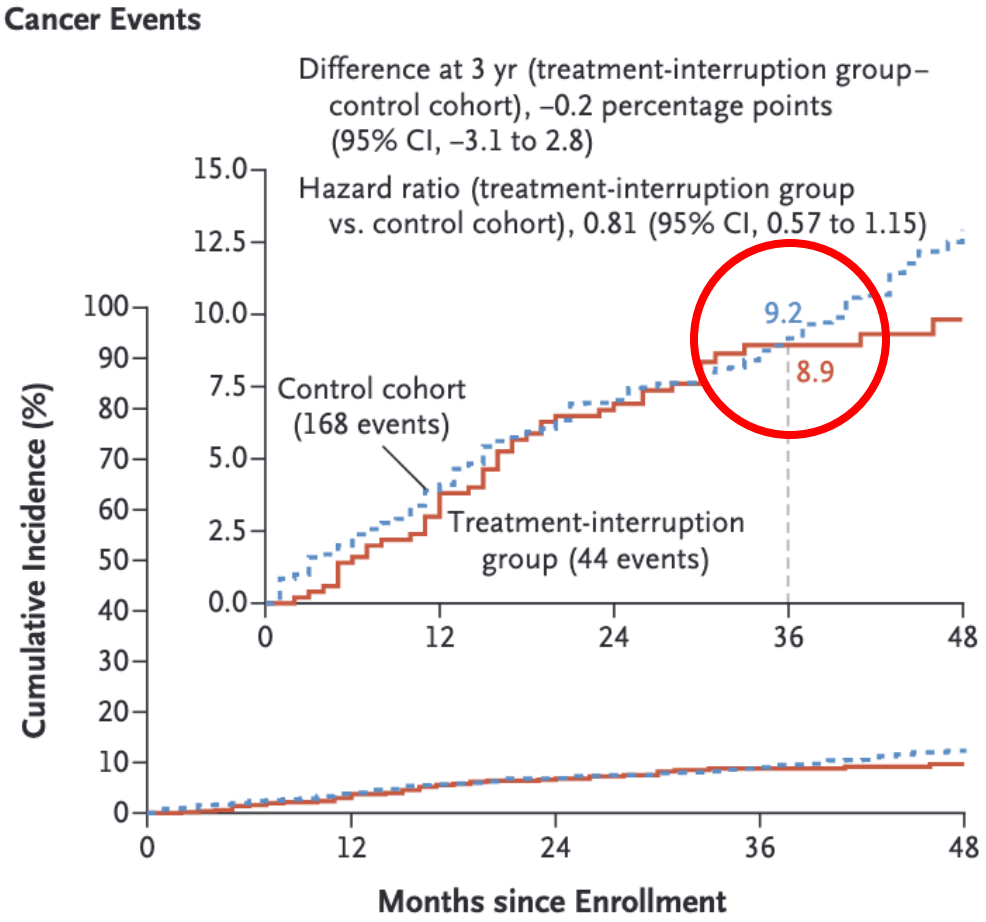
Interrupting Endocrine Therapy to Attempt Pregnancy after Breast Cancer

A.H. Partridge, S.M. Niman, M. Ruggeri, F.A. Peccatori, H.A. Azim, Jr., M. Colleoni, C. Saura, C. Shimizu, A.B. Sætersdal, J.R. Kroep, A. Mailliez, E. Warner, V.F. Borges, F. Amant, A. Gombos, A. Kataoka, C. Rousset-Jablonski, S. Borstnar, J. Takei, J.E. Lee, J.M. Walshe, M. Ruíz-Borrego, H.C.F. Moore, C. Saunders, V. Bjelic-Radisic, S. Susnjar, F. Cardoso, K.L. Smith, T. Ferreiro, K. Ribi, K. Ruddy, R. Kammler, S. El-Abed, G. Viale, M. Piccart, L.A. Korde, A. Goldhirsch,* R.D. Gelber, and O. Pagani, for the International Breast Cancer Study Group and the POSITIVE Trial Collaborators†

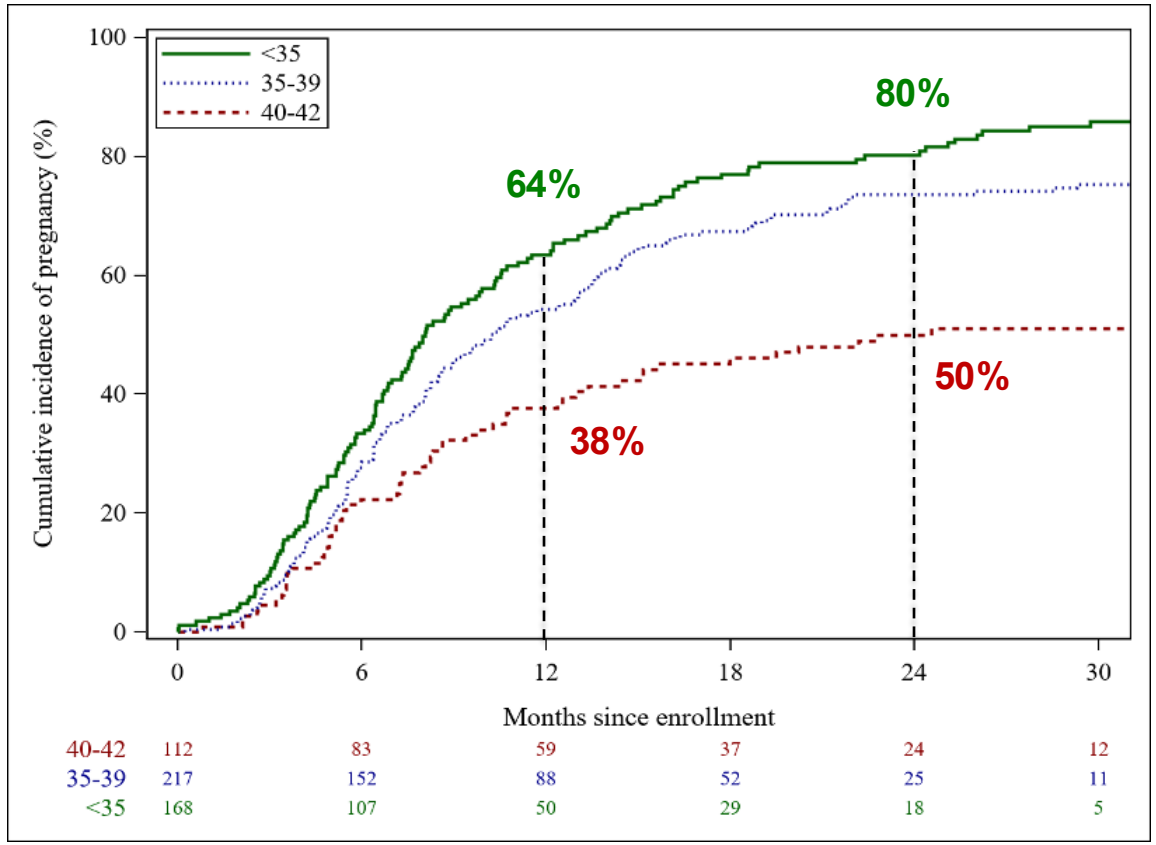


Among select women with previous hormone receptor-positive early breast cancer, **temporary interruption of endocrine therapy** to attempt pregnancy did not confer a greater short-term risk of breast cancer recurrence

Partridge et al., NEJM 2023

Pregnancy Outcome and Safety of Interrupting Therapy for women with endocrine responsIVE breast cancer (POSITIVE)

368 patients (74%) reported at least one pregnancy



Time to pregnancy

Multivariable Fine and Gray competing risk model	HR (95% CI)
Chemo + GnRHa vs Chemo alone	1.29 (0.94 – 1.79)
None vs Chemo alone	1.05 (0.85 – 1.32)
35-39 vs <35	0.74 (0.59 – 0.93)
40-42 vs <35	0.40 (0.29 – 0.56)
SERM+OFS vs SERM only	0.94 (0.71 – 1.24)
AI+OFS vs SERM only	0.94 (0.67 – 1.33)
Prior birth: Yes vs No	0.94 (0.72 – 1.23)
Irregular vs Persistent amenorrhea	1.17 (0.85 – 1.63)
Normal vs Persistent amenorrhea	1.01 (0.78 – 1.32)

Young age was the main factor associated with shorter time to pregnancy

Azim et al., J Clin Oncol. 2024

Pregnancy Outcome and Safety of Interrupting Therapy for women with endocrine responsIVE breast cancer (POSITIVE)

Chance of pregnancy

Multivariate logistic regression model	OR (95% CI)
35-39 vs <35	0.50 (0.29 - 0.86)
40-42 vs <35	0.16 (0.08 - 0.29)
Ovarian stimulation for IVF after enrollment vs No ART	0.85 (0.48 - 1.50)
Cryopreserved embryo transfer * vs No ART	2.41 (1.17 - 4.95)
Other ART vs No ART	1.80 (0.92 - 3.57)
Chemotherapy + GnRHa vs Chemotherapy no GnRHa	1.41 (0.70 - 2.82)
None vs Chemotherapy without GnRHa	1.10 (0.70 - 1.75)

Use of cryopreserved embryos was the main factor associated with pregnancy

Azim et al., J Clin Oncol. 2024

Follow-up of breast cancer survivors who previously had FP

Fertility outcomes several years after urgent fertility preservation for patients with breast cancer

Maëliss Peigné, M.D., Ph.D.,[a] Pauline Mur, M.D.,[b] Laëtitia Laup, M.D.,[a] Anne-Sophie Hamy, M.D., Ph.D.,[c] Christophe Sifer, M.D.,[d] Anne Mayeur, M.D., Ph.D.,[e] Florence Eustache, M.D., Ph.D.,[f] Solmaz Sarandi, M.D.,[d] Claire Vinolas, M.D.,[a] Sophia Rakrouki, M.W.,[a] Alexandra Benoit, M.W., Ph.D.,[b] Michaël Grynberg, M.D., Ph.D.,[a,b] and Charlotte Sonigo, M.D., Ph.D.[b,g]

- Retrospective study in 844 breast cancer patients who had FP at age 33.1 (30.0–36.0) years between January 2013 and July 2019
- FP consisted of ovarian stim (45.7%), IVM (43.4%) and/or OTC (10.9%)
- Follow-up of reproductive outcome in 255 survivors who tried to conceive, duration of follow-up was 6.5 (4.7–7.6) years

38.8% of the patients who attempted pregnancy became pregnant

79.3% of pregnancies were obtained without medical assistance

1.2%

Only 3 patients asked for transplantation of frozen ovarian tissue, and none led to pregnancy.

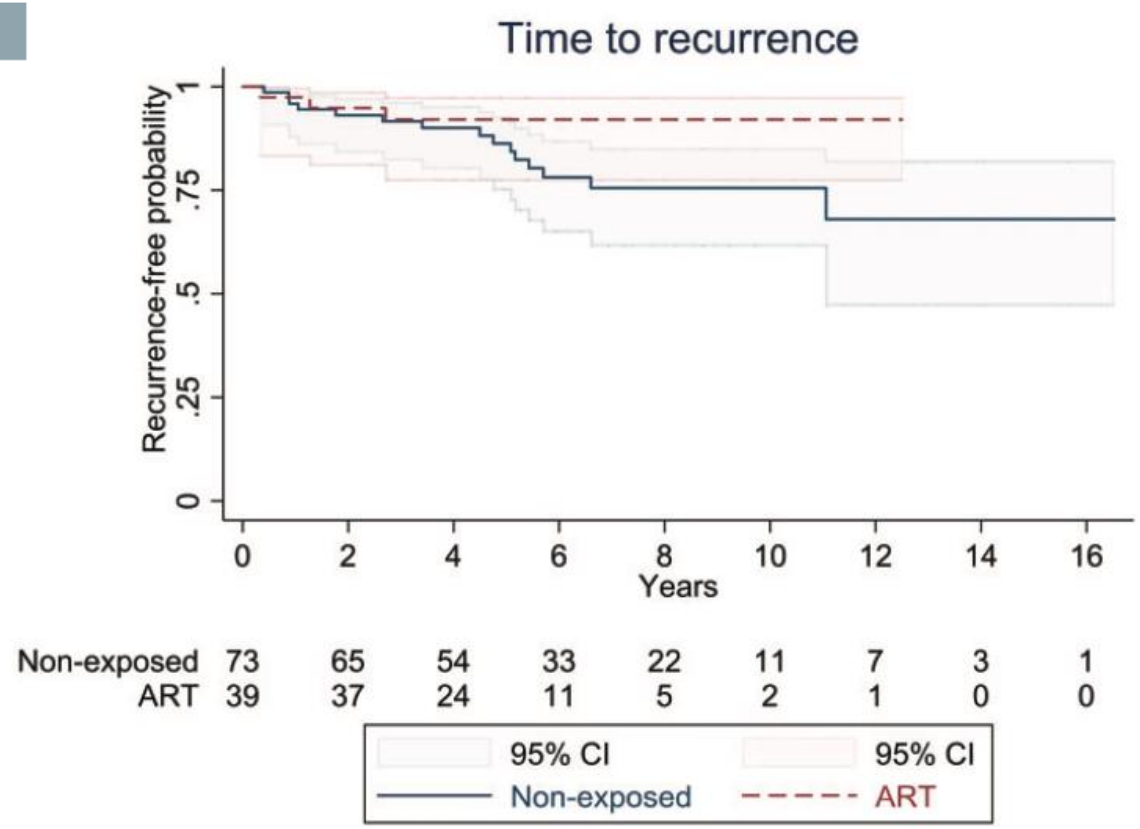
Safety of ART after breast cancer – Belgian data

Human Reproduction, pp. 1–9, 2020
doi:10.1093/humrep/deaa319

human reproduction ORIGINAL ARTICLE *Infertility*

Impact of ARTs on oncological outcomes in young breast cancer survivors

- Retrospective multicentric matched cohort study
- 39 breast CA patients who had ART, matched with 73 breast cancer patients who did not
- When natural conception fails, ART can be used safely in women with good oncologic prognosis
- Short exposure to high estradiol level does not seem to have negative impact on onco outcome, but long term follow-up is needed



Condorelli et al., Hum Reprod 2020 (cohort study)
Arecco et al., Hum Reprod 2022 (systematic review + meta-analysis)

Assisted reproductive technology in young BRCA carriers with a pregnancy after breast cancer: an international cohort study

International retrospective cohort study including BRCA1/2 carriers with a pregnancy after prior breast cancer diagnosis at ≤ 40 years of age between 2000 and 2020.

Disease-free survival (DFS) in BRCA carriers who became pregnant: no negative impact from ART use	ART at diagnosis n=45	ART after anticancer treatments n=33	Oocyte donation n=21	No-ART group n=436
Median follow-up from conception, years (IQR)	2.9 (1.4-5.2)	2.8 (1.5-6.7)	2.8 (1.7-7.9)	5.7 (2.7-9.8)
DFS event/100*person-years	**5.47**	**2.60**	**1.29**	**5.35**
Death due to breast cancer (BCSS)/ 100*person-years	0.30	0	0	0.48
Death to any cause (OS)/100*person-years	0.30	0	0	0.53

At a median follow-up of 5.2 years after conception, **no apparent detrimental effect of ART** on DFS was observed (adjusted HR=0.72, 95 % CI 0.39–1.34).

Magaton et al., EJC 2025

In the ART group, 42.1% of pregnancies were achieved with oocytes/embryos cryopreserved at diagnosis.

Reproductive outcomes in cancer survivors who returned to the fertility clinic

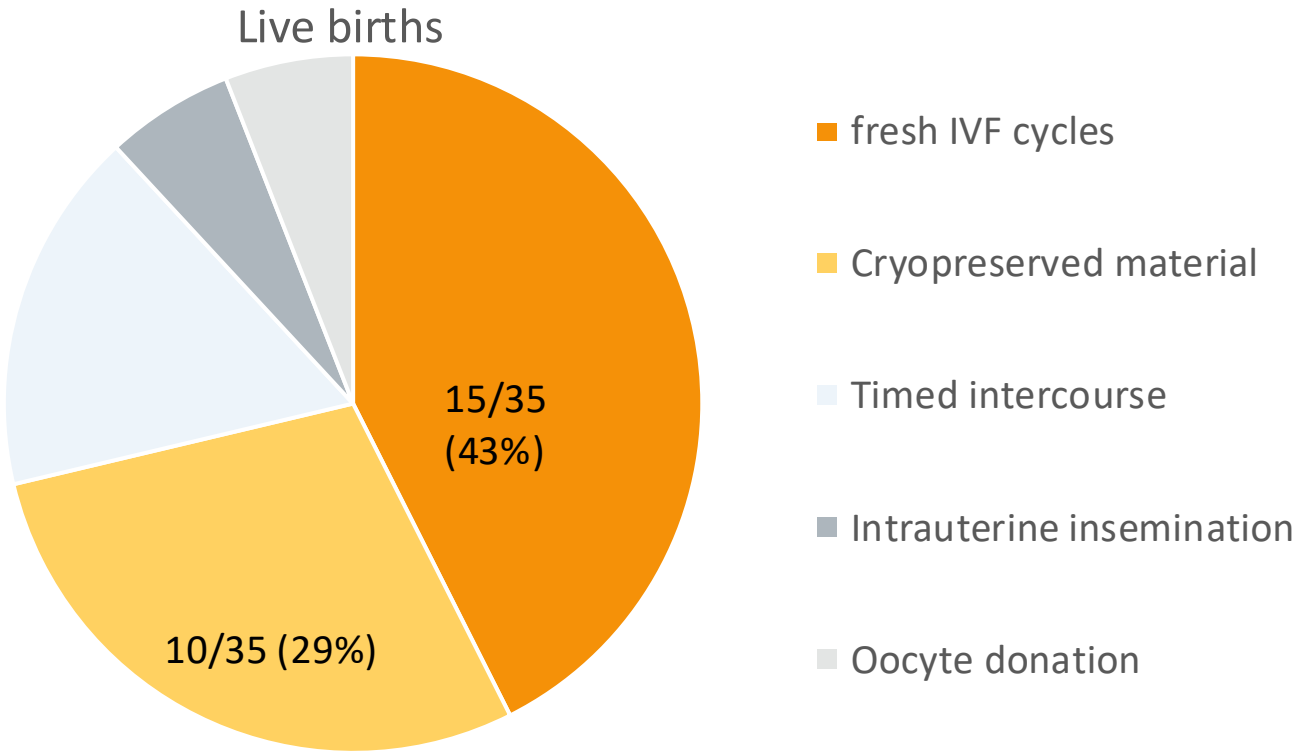
Clinical outcomes in cancer survivors who returned to use their cryopreserved oocytes or ovarian tissue - Spain

	[1,2]Oocyte warming		[3]Ovarian tissue autotransplantation
Patients who had their material warmed	80/1073 (7.4%)		70/1314 (5.3%)
Mean age at cryopreservation (Y)	34.8 +/- 2.1		26.3 +/- 6.3
Mean age at warming (Y)	38.8 +/- 3.5		32.7 +/- 5.6
Warmed oocytes/patient	7.5 +/- 2.8		N/A
Age at vitrification	<36 Y	≥36 Y	N/A
Oocyte survival rate	81.2%	82.7%	N/A
CLBR/patient	**42.1%**	**29.0%**	**41.7%**

[2]Oocytes harvested after conventional ovarian stimulation (cOS)

[1]Cobo et al., Hum Reprod 2018; [3]Shapira et al., Fertil Steril 2020

Reproductive outcomes in cancer survivors returning for infertility treatment after fertility preservation (FP) – own data



- 33% of pregnancies resulted in early pregnancy loss.
- **Cumulative live birth per patient was 49% (35/71*)**

Human Reproduction Open, pp. 1–9, 2020
doi:10.1093/hropen/hoaa045

human reproduction open
ORIGINAL ARTICLE

Pelvic irradiation and the uterus

Clinical summary guide: reproduction in women with previous abdominopelvic radiotherapy or total body irradiation

G. Rozen [1,2,3,*], P. Rogers[2], S. Chander[4], R. Anderson[5], O. McNally[6], M. Umstad[7,8], A. Winship [9,10], K. Hutt [9], W.T. Teh[1,2,3], A. Dobrotwir[11], R. Hart[12], W. Ledger[13], and K. Stern[1,3]

- Radiotherapy to the adult uterus with TBI (12 Gy) is associated with increased risks of miscarriage, premature birth, and LBW.
- The prepubertal uterus is much more vulnerable to the effects of radiation – pregnancy is contraindicated beyond >25 Gy.
- If the uterus is irradiated in adulthood, tumour treatment doses alone cannot at present be used to accurately predict uterine damage.

Human Reproduction Open, pp. 1–9, 2020
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human reproduction open ORIGINAL ARTICLE

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Post radiotherapy management

Evaluation of suitability

- Medically suitable for pregnancy
- Liaison with radiation oncologist regarding uterine dose
- Pregnancy management clinic
- Frozen gametes

If medically suitable and possible uterine functionality

Assessment of uterus

- Ultrasound to assess uterine volume, doppler, endometrial thickness
- MRI
- Hormonal stimulation and mid luteal biopsy

Can attempt pregnancy

- High risk pregnancy, managed in a multidisciplinary team with MFM subspecialist
- Tertiary level ultrasound
- Increased incidence of
  - miscarriage
  - preterm birth
  - IUGR
  - possibly uterine rupture

Reproductive outcomes in cancer survivors - conclusion

- It is vital to provide accurate **counselling** on expected (centre-specific) success rates
- A substantial proportion of LB in cancer survivors were achieved **without** using cryopreserved materials
- Increased risk of **obstetric** (including miscarriage) **complications** in female cancer survivors
- Women with **hormone receptor positive breast cancer** may interrupt hormonal treatment at no increased risk of relapse – and have good chances of pregnancy
- Pregnancy in **BRCA1/2 carriers** after breast cancer is safe – with or without ART
- The **utilisation** of cryopreserved oocytes and ovarian tissue is **low**. Large longitudinal follow-up studies are required to identify which patients will most likely need their frozen materials.

Thank you

Brussels IVF

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