European Journal of Obstetrics and Gynecology 281 (2023) 41–48

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.journals.elsevier.com/european-journal-of-obstetrics-and-gynecology-and-reproductive-biology

Long term pregnancy outcomes of women with cancer following fertility preservation: A systematic review and *meta*-analysis

Zilin Xu [a,b], Sameh Ibrahim [b], Sarah Burdett [c], Larysa Rydzewska [c], Bassel H. Al Wattar [d,*], Melanie C Davies [a,b]

[a] *Reproductive Medicine Unit, University College London Hospitals, London, United Kingdom*
[b] *UCL Institute for Women's Health, University College London, London, United Kingdom*
[c] *MRC Clinical Trials Unit, University College London, London, United Kingdom*
[d] *Beginings Assisted Conception Unit, Epsom and St Helier University Hospitals, London, United Kingdom*

ARTICLE INFO

Keywords:
Fertility preservation
Embryo cryopreservation
Oocyte cryopreservation
Ovarian tissue cryopreservation
Cancer
Systematic review

ABSTRACT

Objective: As cancer survivorship increases, there is higher uptake of fertility preservation treatments among affected women. However, there is limited evidence on the subsequent use of preserved material and pregnancy outcomes in women who underwent fertility preservation (FP) before cancer treatments. We aimed to systematically review the long-term reproductive and pregnancy outcomes in this cohort of women.

Patients: Women who underwent any type of the following FP treatments: embryo cryopreservation (EC), oocyte cryopreservation (OC) and ovarian tissue cryopreservation (OTC)) before any planned cancer treatment.

Evidence review: We searched electronic databases (MEDLINE, Embase, Cochrane CENTRAL, and HTA) from inception until May 2021 for all observational studies that met our inclusion criteria. We extracted data on reproductive and pregnancy outcomes in duplicate and assessed the risk of bias in included studies using the ROBINS-I tool. We pooled data using a random-effects model and reported using odds ratios (OR) with 95% confidence intervals (CI).

Main outcome measures: Our primary outcome was live birth rate and other important reproductive and pregnancy outcomes.

Results: Of 5405 citations, we screened 103 and included 26 observational studies (n = 7061 women). Hematologic malignancy was the commonest cause for seeking FP treatments, followed by breast and gynecology cancers. Twelve studies reported on OTC (12/26, 46 %), eight included EC (8/26, 30 %), and twelve reported on OC (12/26, 46 %). The cumulative live birth rate following any FP treatment was 0.046 (95 %CI 0.029–0.066). Only 8 % of women returned to use their frozen reproductive material (558/7037, 8.0 %), resulting in 210 live births in total, including assisted conceptions following EC/OC/OTC and natural conceptions following OTC. The odds for live birth was OR 0.38 (95 %CI 0.29–0.48 I^2 83.7 %). The odds for live birth was the highest among women who had EC (OR 0.45, 95 %CI 0.14–0.76, I^2 95.1 %), followed by the OTC group (OR 0.37, 95 %CI 0.22–0.53, I^2 88.7 %) and OC group (OR 0.31, 95 %CI 0.15–0.47, I^2 78.2 %).

Conclusions: Fertility preservation treatments offered good long-term reproductive outcomes for women with cancer with a high chance to achieve a live birth. Further research is needed to evaluate the long-term pregnancy and offspring outcomes in this cohort.

Introduction

Infertility is a common side-effect in women undergoing cancer treatments due to the associated gonadotoxic effects, reducing egg reserve and increasing the risk of early menopause[1,2]. Whilst overall cancer survivorship is rising [3], the chance of pregnancy after cancer treatment remains lower than that in the general population [4]. Early counselling on future family planning and reliable fertility preserving treatments is highlighted as a priority by most women undergoing cancer treatments [5,6].

Providing effective and reliable fertility preservation (FP) treatments to girls and young women with cancer is becoming mainstream [7] with

* Corresponding author at: Reproductive Medicine Unit, University College London Hospitals, London, United Kingdom.
E-mail address: b.wattar@nhs.net (B.H. Al Wattar).

https://doi.org/10.1016/j.ejogrb.2022.12.016
Received 8 August 2022; Received in revised form 22 November 2022; Accepted 6 December 2022
Available online 10 December 2022

a rapid increase in uptake worldwide [8,9]. The 2018 American Society of Clinical Oncology (ASCO) guidelines [10] support offering embryo cryopreservation (EC) and oocyte cryopreservation (OC) as routine established treatments for female patients with cancer. The ASCO guidelines also removed the label 'experimental' when describing ovarian tissue cryopreservation (OTC) in 2019 [11] which was also supported in the new ESHRE guideline [12].

However, the evidence on the long-term clinical effectiveness and value of FP treatments remains unclear with varied reporting on the long-term reproductive and pregnancy outcomes in this cohort [13,14]. Reports from several countries indicate an overall low utility of cryopreserved gametes and embryos [15,16], raising dilemmas on the ethical use and storage of abandoned gametes [17].

To address this knowledge gap, we aimed to evaluate long-term reproductive and pregnancy outcomes following FP treatments by systematically reviewing of the literature on women who underwent FP treatments.

Materials and methods

Study design

We conducted a systematic review and *meta*-analysis using a registered protocol (PROSPERO CRD42021269016) and reported its findings following established guidelines [18].

Literature search

We searched electronic databases (MEDLINE, Embase, Cochrane CENTRAL, and HTA) from inception until May 2021 using set keywords and subject Mesh headings (Supplementary Table 1). We included all observational studies that reported on the reproductive and pregnancy outcome of women with cancer who underwent any type of FP treatment. We excluded studies reporting on mixed patient population (e.g. male infertility) and those reporting on fundamental or animal research. We also excluded studies evaluating novel FP tools or systems, case reports, review articles, conference abstracts with insufficient information, letters, editorials, and those not published in English. Studies that evaluated non-cryopreservation FP treatment (e.g. ovarian transposition, conservative gynecologic surgery, and ovarian suppression) were excluded. Before data synthesis, the eligibility of data was checked manually in case of overlapping and duplication by comparing FP centres, the duration of the cohort, and the first/corresponding authors of every study.

Risk of bias assessment

Two independent reviewers (Z.X., S.I.) assessed the quality of included studies using the ROBINS-I tool, with disagreement solved by consensus within the whole team. In short, seven domains were evaluated, including confounding, selection, classification, deviation from intended intervention, missing data, measurement, and reporting of the outcomes [19]. Each domain was classified as low, moderate, serious or critical risk of bias according to the answers towards preset signaling questions, and then combined to get the overall risk of bias.

The quality of evidence of the included studies was then evaluated according to the GRADE principles for primary outcomes, including the risk of bias, inconsistency, indirectness, imprecision, publication bias and other considerations [20].

Data extraction and synthesis

Data were extracted by two reviewers independently (Z.X., S.I.), using pretested screening and data collection forms. The details of included studies, the outcome parameters and related details of interventions were captured precisely, including study basic information, patient information (age, cancer type, patients' childbearing intent or pregnancy attempts), intervention and reproductive outcomes.

The primary outcome was the chance of live birth, defined as the ratio of live birth (from FP treatments only) to the number of patients involved. We also reported the proportion of women who returned to use their frozen gametes, embryos and ovarian tissues, and the risk of adverse pregnancy outcomes, including miscarriage, ectopic pregnancy, stillbirth, neonatal death, Caesarean section and maternal death.

Statistical analysis

We reported on dichotomous outcome using odd ratio (OR) with 95 % confidence intervals (CI). We conducted meta-analyses using the *metan* package in STATA 16.0 (STATA Corp., College Station, TX, USA) and applied a random-effects model to pool data for each outcome across included studies [21]. Freeman-Tukey Double Arcsine Transformation was used for the proportion that was close to the margins in data transformation [22]. Heterogeneity was assessed using I^2 statistic with I^2 of 25, 50, and 75 % representing low, medium, or large heterogeneity (Cochran's Q test) [23]. For significant (I^2 >50 %) heterogeneity, sensitivity analysis was performed after exclusion of studies, and the random-effects model was used to combine study results in this condition. Publication bias was assessed using a funnel plot [24] and Egger's regression test [25].

Results

Study characteristics

Our electronic search identified 5405 citations. After removing duplicates (n = 1436) and after screening titles and abstracts, we retrieved 97 studies for full assessment against our inclusion criteria (Fig. 1). Of 56 eligible studies, 30 studies were excluded because of no data available (n = 11, 19.6 %) and potential overlapping data (n = 19, 33.9 %) (See details in Supplementary Table 2). Finally, 26 studies in total, reporting on 7061 women, met our inclusion criteria: 16 were retrospective cohort studies, seven were surveys of retrospective cohorts or FP centres, and three were prospective or ongoing cohort studies (Table 1). The median sample size was 122.5 [6,1608]. The majority of studies (n = 17) were from European countries, six were from the United States, and the other three from Brazil, Canada and Japan.

Patient characteristics

Hematologic malignancy (69.2 %, 18/26) was the commonest cause to seek FP treatments followed by breast (65.4 %, 17/26) and gynecology cancers (46.2 %, 12/26).

The median participant age at baseline was within 18–35 age range in 22 studies, over 35 (35.8 ± 4.1) in one study [26], and below 18 (14.8 ± 2.3) in another [27]. The median follow-up time was 9 [5,18] years (19studies) with three studies not reporting the exact follow-up year [26,28,29] and the rest did not specify exact time [27,30–32].

As for FP treatments, OTC was reported in twelve studies (12/26, 46 %), eight reported on EC (8/26, 30 %), and twelve reported on OC (12/26, 46 %). Majority of included studies offered one type of FP treatment (18/26, 69 %), five studies offered two options of either EC or OC (5/26, 19 %), and the other three offered EC, OC and OTC (3/26, 11.5 %). In general, FP centres tended to offer OTC to patients of a younger age, and EC or OC to adult patients. Specifically, one study focused on prepubertal and adolescent girls only offered OTC [27]. Among 11 studies including patients with median age below 30, 72.2 % (8/11) OTC was offered, and 36.4 % (4/11) offered EC/OC. In the remaining 13 studies including patients with median age over 30, 92.3 % (12/13) offered EC/OC, and 30.8 % (4/13) offered OTC.

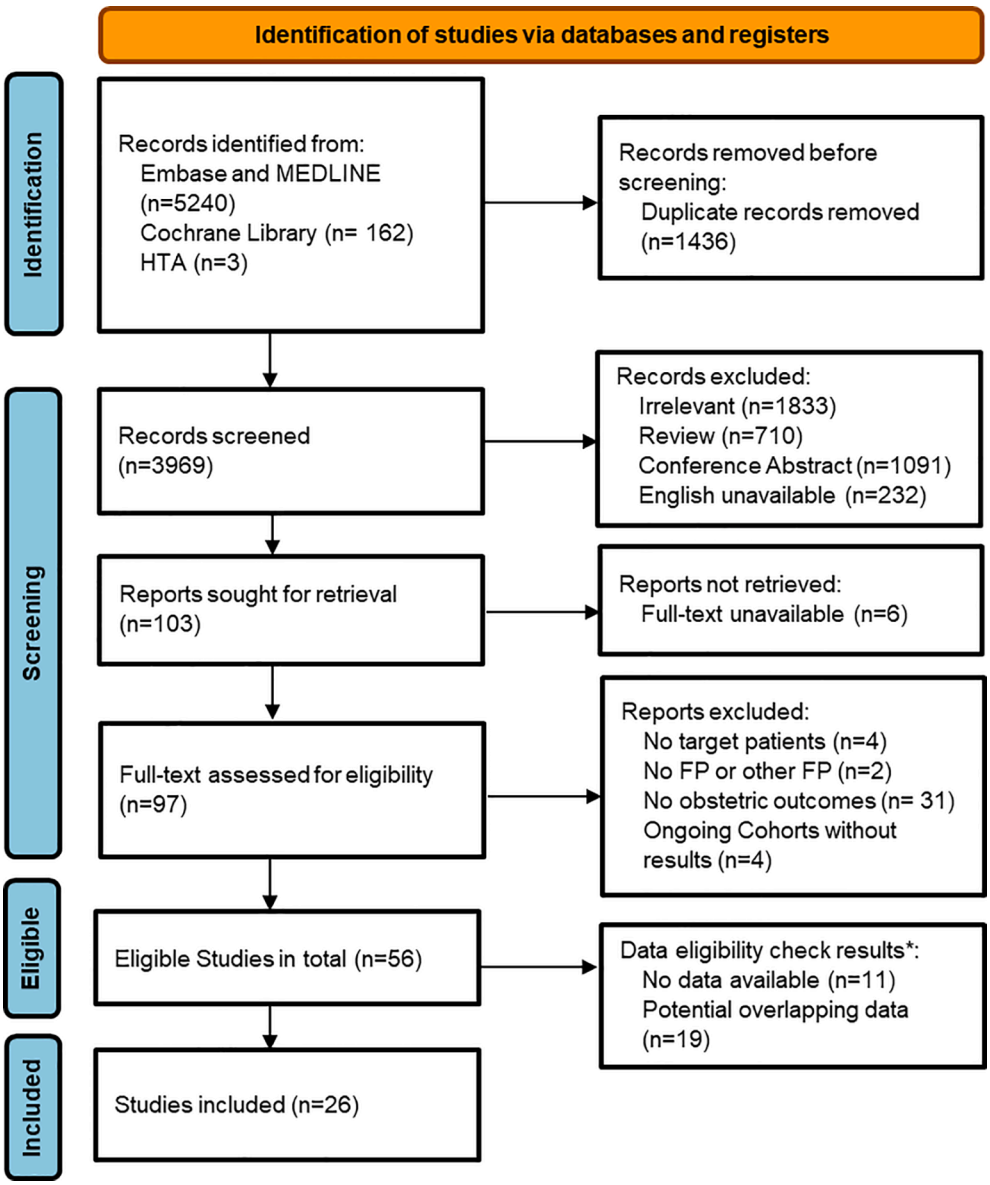

Fig. 1. Study selection and inclusion process for studies evaluating longterm reproductive outcomes on women who had fertility preservation.

Reproductive and pregnancy outcomes

We pooled data from 25 studies that reported the number of women who returned to use their frozen gametes/embryos or auto-transplantation of frozen ovarian tissue. The pooled LBR was OR 0.046 (211/7061, 95 %CI 0.029–0.066, I^2 89.0 %) across all women who had any FP treatment before cancer treatments (Fig. 2).

In total, only 8 % of these women returned to use their frozen reproductive material (558/7037, 8.0 %), resulting in 210 live births in total, including assisted conceptions following EC/OC/OTC and natural conceptions following OTC. The odds for live birth among this group of women was OR 0.38 (210/558, 95 %CI 0.29–0.48 I^2 83.7 %) (Fig. 3).

The odds for live birth was the highest among women who had EC (50/111, OR 0.45, 95 %CI 0.14–0.76, I^2 95.1 %), followed by the OTC group (114/323, OR 0.37, 95 %CI 0.22–0.53, I^2 88.7 %) and OC group (35/114, OR 0.31, 95 %CI 0.15–0.47, I^2 78.2 %) (Fig. 4). Notably, of 114 live births reported in the OTC subgroup, 67 % (76/114) came from natural conception after OTC patients had their ovarian tissues transplanted, and 33 % (38/114) were achieved by assisted reproductive technology.

About a half of all included studies (14/26, 54 %) reported on other important pregnancy outcomes. These included a total of 49 miscarriages in 14/14 studies, three biochemical pregnancies in 3/14 studies [29,33,34], one ectopic pregnancy [32] and one surgical termination for fetal anomalies [35]. There were 14 ongoing pregnancies (0.3 %, 14/4700) in 7/14 studies. In live births, six Caesarean sections (33.3 %, 6/18) [34–36] and two cases of pre-eclampsia (28.6 %, 2/7) [35] were reported.

We conducted sensitivity analyses including to explore the effect of studies with a small sample size and those with potentially high risk of bias on the overall LBR (Supplementary Fig. 3), however our findings did not suggest a significant impact of these factors on the pooled effect estimate. We also explored the risk of publication bias using a funnel plot which suggest some outliers evidence by a significant p value on Egger's test ($p < 0.05$) (Supplementary Fig. 4.).

Risk of bias assessment

More than half of the included studies (15/26, 57 %) were assessed to have a low risk of bias, with the remaining studies (11/26, 43 %)

Table 1
Characteristics of included studies evaluating longterm reproductive outcomes on women who had fertility preservation.

study ID	Study Design	Follow-up time	Country	No of Patients Involved	Age	Cancer Diagnosis	Intervention
Geoffron,2021	retrospective cohort study	7(2013,2019)	France	24	26.8 ± 6.9	GC	OTC and OC
Mayeur,2021	retrospective cohort study	9(2009,2017)	France	40	34.8 [30.0–38.0]	BC, HM, GC	EC and OC (IVM vs COS in OC)
Abel,2021	survey of a prospective cohort	10 (2010,2019)	America	181	35.0 ± 5.0	BC	EC and OC
Delattre,2020	retrospective cohort study	6(2012,2018)	Belgium	194	28.9 ± 6.1	BC, HM, GC	EC and OC (OTC + IVM in OC)
Kato,2021	follow-up inquiries of retrospective cohorts	8(2007,2015)	Japan	155	26.2 ± 0.4	HM	OC
Dueholm Hjorth,2020	retrospective cohort study	5(2012,2017)	Denmark	28	29.8 ± 5.2	BC, HM, MT	OTC
Shapira,2020	multi-centre retrospective cohort study	14 (2004,2018)	Israel, Belgium, America	1314	32.7 ± 5.6	HM, BC, MT	OTC
Lotz,2020	survey of a retrospective cohort	at least 5 years	Germany	53	14.8 ± 2.3	HM, MT	OTC
Vriens,2020	prospective cohort study	7(2008,2015)	The Netherlands	34	31 [23–40]	BC	EC and OC
Akel,2020	retrospective cohort study	10 (2007,2017)	America	90	33.0 [25.4–44.2]	GC	EC, OC and OTC
Berton,2020	retrospective cohort study	7(2011,2018)	Brazil	246	31.0 ± 5.6	BC, GC, HM	OC
Specchia,2019	retrospective cohort study	18 (2001,2019)	Italy	244	31.3 ± 6.4	BC, HM, MT	OC
Poirot,2019	retrospective cohort study	10 (2005,2015)	France	31	27.1 [16.0–37.2]	GC, HM	OTC*
Alvarez,2018	retrospective cohort study	14 (2000,2014)	UK	306	33.2 [21–43]	BC, HM, GC	EC and OC
Beckmann,2018	survey of FP centres	at least 6 months	Germany, Austria and Switzerland	1373	NA	BC, HM	OTC
Hulsbosch,2018	survey of a retrospective cohort	at least 3 years	Belgium	66	23.6 [11–37]	HM, GC, BC	OTC
Druckenmiller,2016	retrospective cohort study	9(2005,2014)	America	176	31 [24–36]	BC, GC, HM	OC
Rodriguez-Wallberg,2016	survey of FP centres	NA	Denmark, Norway, Sweden, Finland	1608	NA [18–38]	BC, HM, GC	OTC
Oktay,2015	retrospective cohort study	NA	America	131	35.8 ± 4.1	BC	EC
Martinez,2014	retrospective cohort study	5(2007,2012)	Spain	357	35.6 ± 3.4	BC, HM	OC
Imbert,2014	retrospective cohort study	12 (1999,2011)	Belgium	114	27.0 ± 6	BC, HM, GC	OTC
Courbiere,2013	survey of FP centres	NA	France	52	28.9 ± 4.3	HM, MT, GC	EC
Elizur,2009	retrospective cohort study	10 (1997,2007)	Canada	6	33.5 ± 4.5	rectal cancer	OTC
Oktay,2010	prospective longitudinal analysis	11 (1997,2008)	America	59	26.7 ± 1.2	HM, BC	OTC**
Jenninga,2008	retrospective cohort study	5(2002,2007)	The Netherlands	37	30.2 [15.1–45.2]	BC, MT, HM	OTC and EC
Pretalli,2019	ongoing cohort with result	at least 1 year	France	142	26.4 ± 4.2	HM, MT	OTC

Abbreviations: *GC, gynecology cancer. BC, breast cancer. HM, hematologic malignancies. MT, malignant tumor. IVM,* in vitro *maturation.* *: All patients had hematopoietic stem-cell transplantation (HSCT) as an additional cancer treatment. **: 57.6% patients had HSCT as an additional cancer treatment.

showing a moderate risk of bias (Supplementary Table 5). 11 studies were assessed as being at moderate risk of bias because of potential confounding in study design. Other pre-intervention and at-intervention bias in neither selection of participants into study nor classification of interventions was found in all 26 studies. In post-intervention domains, two studies were assessed as being at moderate risk of bias in selection of the reported result: one study due to missing data, and another one study due to outcomes measurement respectively.

Using the GRADE approach, we considered the quality of synthesized evidence across included studies to be 'Very low' evidence quality due to high study inconsistency and heterogeneity (Supplementary Table 6).

Discussion

Our findings suggest an overall good live birth rate among women who preserved their reproductive material before cancer treatment demonstrating the good long-term value of FP treatments in this context. While the overall reported number of women returning to use their frozen material was relatively low at 8 %, the success rate was very reassuring among all used FP treatment options compared to rates reported in older studies [13,37].

This low utilization rate could be linked to several factors. The overall follow-up period in included studies was relatively too short, ranging from 5 to 18 years, considering that many women recovering from cancer would usually delay childbearing for few years after treatment completion. A recent population-based analysis using national databases in Scotland showed the time to last pregnancy was longer after cancer, e.g., 10.7 ± 6.4 years in the overall group and 6.2 ± 2.8 years in women with breast cancer, and the longest time to last pregnancy was 17.1 ± 7.7 years in women with leukaemia [38].

Many of those women would retain their natural fertility post cancer treatment and therefore, continue to have spontaneous conception. These were not captured by our review which may have increased the denominator for the estimated live birth rate.

We were unable to synthesise high quality evidence on other important reproductive outcome as planned in our protocol, however, the reported incidence of these events is overall within the normal population range.

Strengths and limitations

The strengths of our review stem mainly from its prospective design, systematic and comprehensive literature search, and the use of quality evidence synthesis methodology.

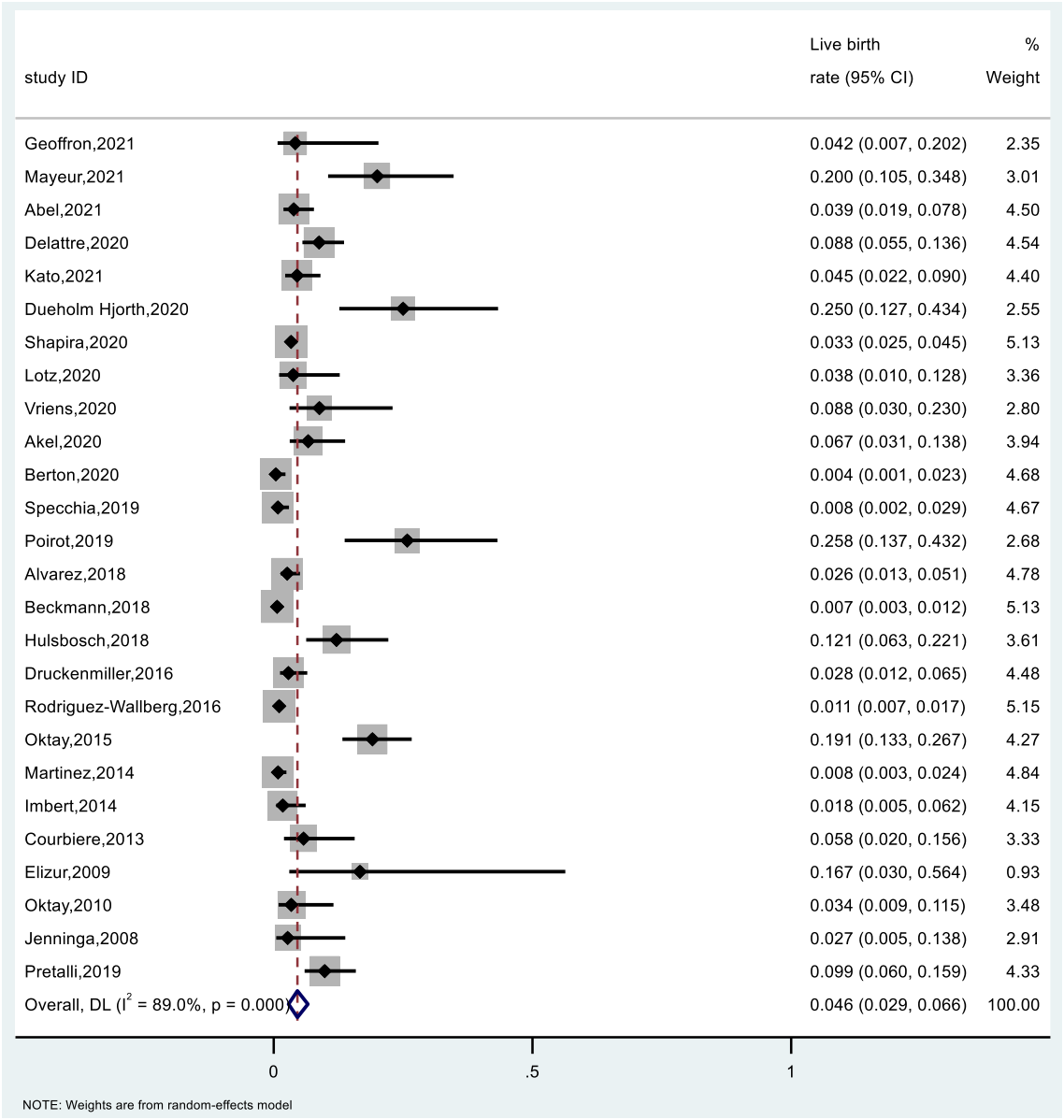

Fig. 2. Live birth rate among women who had fertility preservation.

Still, our findings were limited by several factors. First, we were unable to perform a meaningful and comprehensive synthesis on important secondary reproductive outcomes like miscarriage, fetal congenital abnormalities, due to limited reporting across included studies. We planned to perform subgroup analyses per patient characteristics, type of cancer and treatment exposure, and the type of conception (spontaneous vs assisted), however, we were unable to conduct these analyses due to limited data reporting across included studies. We detected a relatively high level of heterogeneity across included studies with varied population characteristics which limited the certainty of our synthesized effect estimate. Future work using individual patient level data is required to synthesise better quality evidence and address this uncertainty in our synthesis.

As we included observational studies with a relatively wide time range, we were unable to adjust for the potential for performance bias specifically as experience with FP treatments changed significantly overtime across centers and operators. Other potential effect modifiers should also be explored in future analysis (e.g. participant age, disease severity, co-morbidities etc.) which can be only explored using individual patient data *meta*-analyses.

Implications for clinical practice

Our results support the need to offer FP treatments to women with cancer to help them better plan and control their future fertility. This is particularly relevant given the gradual improvement in the cryopreservation technology that is enabling more reliable storage, thawing and use of reproductive material. EC has been utilised in IVF over 30 years and has led to hundreds of thousands of births [39]. Similarly, the use of OC is well established and recommended as a standard method for FP [40] with similar pregnancy outcomes compared to using fresh oocytes [37]. Patients dealing with cancer often report increased anxiety, poor self-esteem and low quality of life [49]. This psychological strain commonly affects their ability to consider and actively pursue available treatment options including those intended to preserve future fertility [49]. With many available FP treatment options, there is a need to counsel patients with cancer on the potential future value and safety of all these options. This is particularly relevant when considering other complementary treatments not covered in our review such as offering GnRH analogues or ovarian transposition.

While our results are supportive of the overall clinical value of OTC

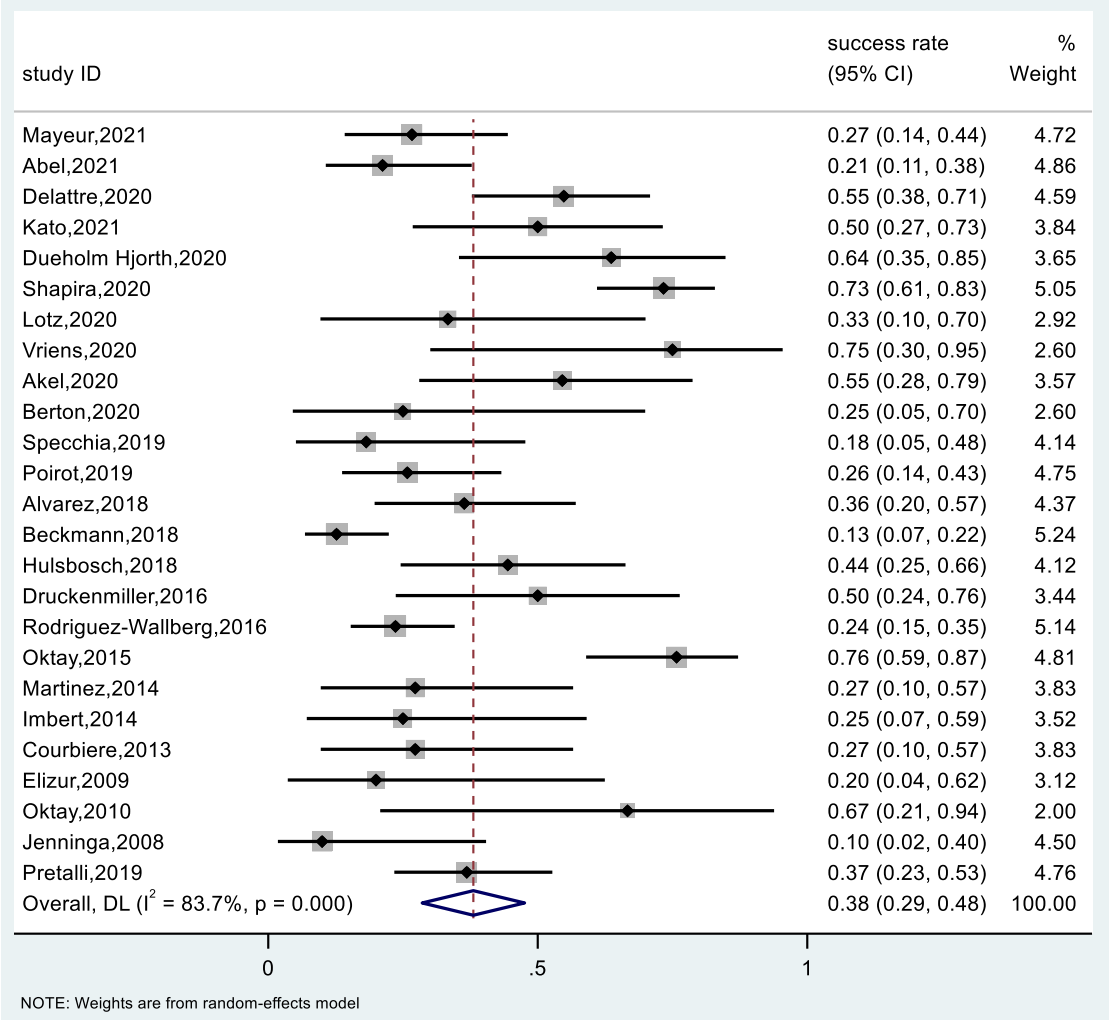

Fig. 3. Pooled odds ratio of live birth rate among women who had fertility preservation.

as an FP treatment option, there is still need to optimize the clinical experience across FP centers to facilitate its routine use. Specifically, there is a need to establish standardized patient pathways to select the patient who may best benefit from OTC over other options [51]. For example, OTC is not recommended for patients with hematologic malignancy [41], because there is a risk of re-introducing the residual neoplastic cells, despite of evidence showing even the cancer recurrence was not directly caused by OTC [42]. Some argued for the use of OTC combined with oocyte harvest and in vitro maturation with some reported success [43], however, more research is needed to clarify the safe use of this treatment option.

Considering the wide variation in treatment options and patient characteristics captured in our review, we emphasize the importance of adopting a multidisciplinary approach to caring for these women to maximize benefits and reduce the risk of immediate adverse outcomes in this cohort as recommended in recent evidence based guidelines [44].

Future research need

Giving the limitation of outcome reporting captured in our review, we emphasize the importance of establishing large, standardized national registries to prospectively capture the outcomes of patient using FP treatments. Women with ART pregnancies have a higher risk of adverse perinatal outcomes in general [45]. Considering the increased health risk among cancer survivors, prospective registries are need to evaluate the perinatal risk in women returning to use their frozen reproductive material and inform optimal antenatal and intrapartum care provision to reduce the risk of health complications in this cohort. As such, there is an apparent need to establish an evidence-based treatment pathway to enable accurate risk prediction and patient selection to the most suitable FP treatment taking into account disease severity, prognosis, and each patient co-morbidity.

Our review highlights the paucity of data on the longterm usability of cryopreserved gametes and embryos following FP treatments. While we detected a relatively low rate of use across included studies at 8 %, this rate is likely to increase in the future with increased availability, familiarity, and acceptance of the use of cryopreserved gametes and embryos. Still, there is a need to continuously monitor and re-evaluate this aspect in order to inform fertility treatment funding across different health systems as well as inform the debate on the ethical use of cryopreserved genetic materials [50].

Standardizing outcome reporting is particularly needed to enable better evidence synthesis [46] and establishing a FP core outcome set could help to address this research need. As none of the included studies involvement lay consumers in their design, conduct and reporting, there is a need for active engagement of patients and their families to help inform the future health and research need in this domain [47].

Finally, better quality qualitative research is needed to explore patient treatment wishes and satisfaction with FP treatments on the long-term. Such research is specifically needed to identify potential barriers to the uptake of FP, return to use frozen reproductive material, and optimal counselling on the use of FP treatments [48].

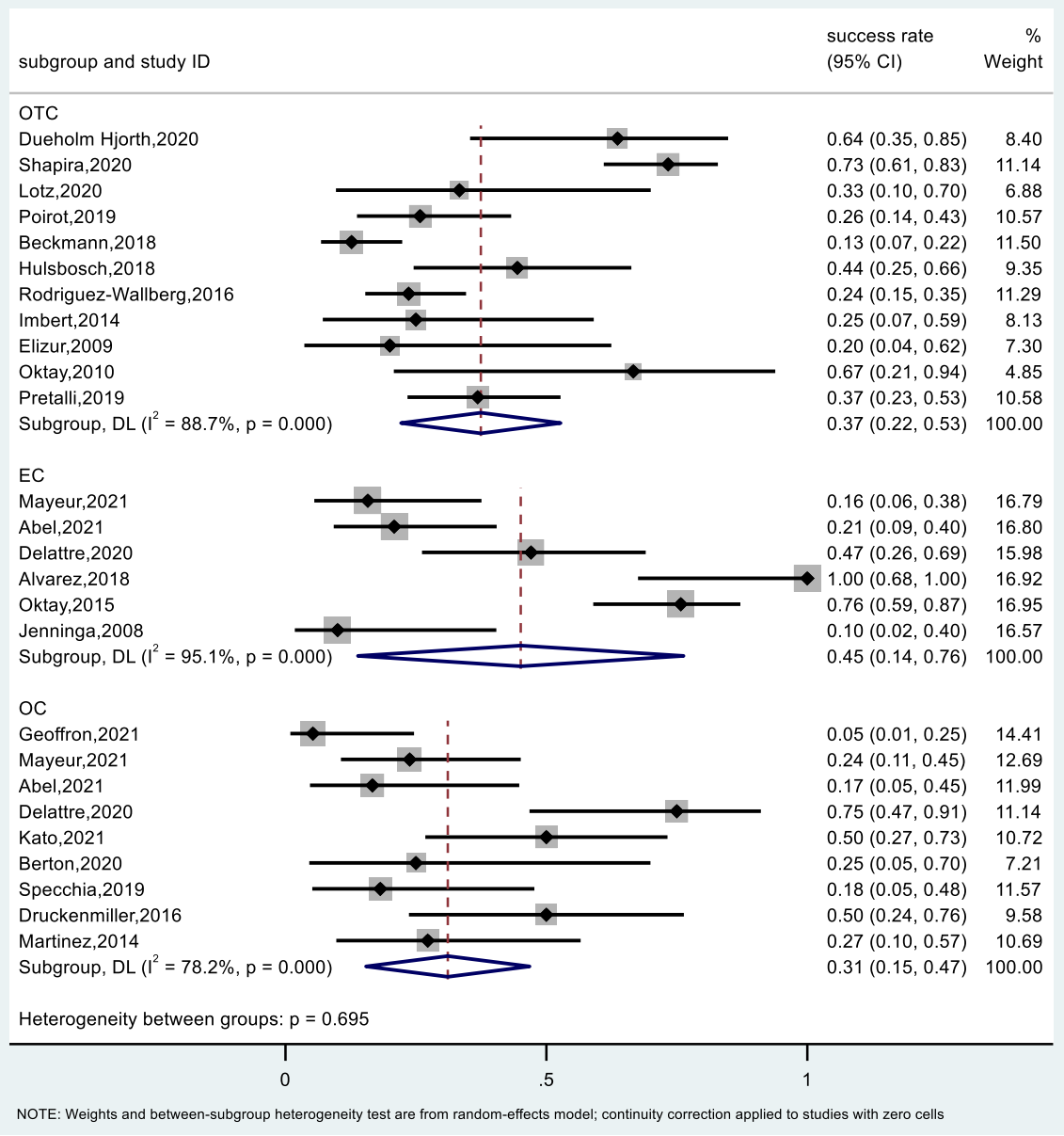

Fig. 4. Subgroup analysis evaluating the pooled odds ratio of live birth rate across different types of fertility preservation treatments.

Conclusion

Fertility preservation treatments offered good long-term reproductive outcomes for women with cancer with a high chance to achieve a live birth. Further research is needed to evaluate the long-term pregnancy and offspring outcomes in this cohort.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Funding

No funding was received towards this work directly. BHA holds a personal Lecturership from the UK National Health Institute of Research. MCD holds primary research grants from the UK National Health Institute of Research.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejogrb.2022.12.016.

References

[1] Griffiths MJ, Winship AL, Hutt KJ. Do cancer therapies damage the uterus and compromise fertility? Hum Reprod Update 2019;26(2):161–73.
[2] van Dorp W, Haupt R, Anderson RA, Mulder RL, van den Heuvel-Eibrink MM, van Dulmen-den BE, et al. Reproductive Function and Outcomes in Female Survivors of Childhood, Adolescent, and Young Adult Cancer: A Review. J Clin Oncol 2018;36(21):2169–80.
[3] Arnold M, Rutherford MJ, Bardot A, Ferlay J, Andersson TM, Myklebust T, et al. Progress in cancer survival, mortality, and incidence in seven high-income countries 1995–2014 (ICBP SURVMARK-2): a population-based study. Lancet Oncol 2019;20(11):1493–505.
[4] Anderson RA, Brewster DH, Wood R, Nowell S, Fischbacher C, Kelsey TW, et al. The impact of cancer on subsequent chance of pregnancy: a population-based analysis. Hum Reprod 2018;33(7):1281–90.
[5] Ruddy KJ, Gelber SI, Tamimi RM, Ginsburg ES, Schapira L, Come SE, et al. Prospective study of fertility concerns and preservation strategies in young women with breast cancer. J Clin Oncol 2014;32(11):1151–6.

[6] Ruggeri M, Pagan E, Bagnardi V, Bianco N, Gallerani E, Buser K, et al. Fertility concerns, preservation strategies and quality of life in young women with breast cancer: Baseline results from an ongoing prospective cohort study in selected European Centers. Breast 2019;47:85–92.
[7] Bastings L, Baysal Ö, Beerendonk CC, IntHout J, Traas MA, Verhaak CM, et al. Deciding about fertility preservation after specialist counselling. Hum Reprod 2014;29(8):1721–9.
[8] Niederberger C, Pellicer A, Cohen J, Gardner DK, Palermo GD, O'Neill CL, et al. Forty years of IVF. Fertil Steril 2018;110(2):185–324.e5.
[9] Pfeifer S. Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion. Fertil Steril 2013;100(5):1214–23.
[10] Oktay K, Harvey BE, Partridge AH, Quinn GP, Reinecke J, Taylor HS, et al. Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update. J Clin Oncol 2018;36(19):1994–2001.
[11] Kazer R, Penzias A, Bendikson K, Falcone T. Fertility preservation in patients undergoing gonadotoxic therapy or gonadectomy: a committee opinion. Fertil Steril 2019;112(6):1022–33.
[12] Anderson RA, Amant F, Braat D, D'Angelo A, de Sousa C, Lopes SM, et al. ESHRE guideline: female fertility preservation†. Hum Reprod Open 2020;2020(4).
[13] Cobo A, García-Velasco J, Domingo J, Pellicer A, Remohí J. Elective and Onco-fertility preservation: factors related to IVF outcomes. Hum Reprod 2018;33(12):2222–31.
[14] Mascarenhas M, Mehlawat H, Kirubakaran R, Bhandari H, Choudhary M. Live birth and perinatal outcomes using cryopreserved oocytes: an analysis of the Human Fertilisation and Embryology Authority database from 2000 to 2016 using three clinical models. Hum Reprod 2021;36(5):1416–26.
[15] Shenfield F, de Mouzon J, Scaravelli G, Kupka M, Ferraretti AP, Prados FJ, et al. Oocyte and ovarian tissue cryopreservation in European countries: statutory background, practice, storage and use†. Hum Reprod Open 2017;2017(1).
[16] Alikani M, Parmegiani L. Human Reproductive Cell Cryopreservation, Storage, Handling, and Transport: Risks and Risk Management. Semin Reprod Med 2018;36(5):265–72.
[17] Klipstein S, Fallat ME, Savelli S. Fertility Preservation for Pediatric and Adolescent Patients With Cancer: Medical and Ethical Considerations. Pediatrics 2020;145(3).
[18] Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. PLoS Med 2009;6(7):e1000100.
[19] Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ 2016;355:i4919.
[20] Schünemann HJ, Higgins JP, Vist GE, Glasziou P, Akl EA, Skoetz N, et al. Completing 'Summary of findings' tables and grading the certainty of the evidence. Cochrane Handbook for Systematic Reviews of Interventions 2019:375–402.
[21] Laird NM, Ware JH. Random-Effects Models for Longitudinal Data. Biometrics 1982;38(4):963–74.
[22] Miller JJ. The Inverse of the Freeman – Tukey Double Arcsine Transformation. Am Stat 1978;32(4):138-.
[23] Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. BMJ 2003;327(7414):557–60.
[24] Sterne JA, Egger M. Funnel plots for detecting bias in meta-analysis: guidelines on choice of axis. J Clin Epidemiol 2001;54(10):1046–55.
[25] Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315(7109):629–34.
[26] Oktay K, Turan V, Bedoschi G, Pacheco FS, Moy F. Fertility Preservation Success Subsequent to Concurrent Aromatase Inhibitor Treatment and Ovarian Stimulation in Women With Breast Cancer. J Clin Oncol 2015;33(22):2424–9.
[27] Lotz L, Barbosa PR, Knorr C, Hofbeck L, Hoffmann I, Beckmann MW, et al. The safety and satisfaction of ovarian tissue cryopreservation in prepubertal and adolescent girls. Reprod Biomed Online 2020;40(4):547–54.
[28] Rodriguez-Wallberg KA, Tanbo T, Tinkanen H, Thurin-Kjellberg A, Nedstrand E, Kitlinski ML, et al. Ovarian tissue cryopreservation and transplantation among alternatives for fertility preservation in the Nordic countries - compilation of 20 years of multicenter experience. Acta Obstet Gynecol Scand 2016;95(9):1015–26.
[29] Courbiere B, Decanter C, Bringer-Deutsch S, Rives N, Mirallié S, Pech JC, et al. Emergency IVF for embryo freezing to preserve female fertility: a French multicentre cohort study. Hum Reprod 2013;28(9):2381–8.
[30] Beckmann MW, Dittrich R, Lotz L, van der Ven K, van der Ven HH, Liebenthron J, et al. Fertility protection: complications of surgery and results of removal and transplantation of ovarian tissue. Reprod Biomed Online 2018;36(2):188–96.
[31] Hulsbosch S, Koskas M, Tomassetti C, De Sutter P, Wildiers H, Neven P, et al. A Real-Life Analysis of Reproductive Outcome after Fertility Preservation in Female Cancer Patients. Gynecol Obstet Invest 2018;83(2):156–63.
[32] Pretalli JB, Frontczak Franck S, Pazart L, Roux C, Amiot C. Development of Ovarian Tissue Autograft to Restore Ovarian Function: Protocol for a French Multicenter Cohort Study. JMIR Res Protoc 2019;8(9):e12944.
[33] Poirot C, Fortin A, Lacorte JM, Akakpo JP, Genestie C, Vernant JP, et al. Impact of cancer chemotherapy before ovarian cortex cryopreservation on ovarian tissue transplantation. Hum Reprod 2019;34(6):1083–94.
[34] Martinez M, Rabadan S, Domingo J, Cobo A, Pellicer A, Garcia-Velasco JA. Obstetric outcome after oocyte vitrification and warming for fertility preservation in women with cancer. Reprod Biomed Online 2014;29(6):722–8.
[35] Abel MK, Wald K, Sinha N, Letourneau JM, Simbulan R, Mok-Lin E, et al. Conception after chemotherapy: post-chemotherapy method of conception and pregnancy outcomes in breast cancer patients. J Assist Reprod Genet 2021;38(7):1755–65.
[36] Alvarez RM, Ramanathan P. Fertility preservation in female oncology patients: the influence of the type of cancer on ovarian stimulation response. Hum Reprod 2018;33(11):2051–9.
[37] Cobo A, García-Velasco JA, Coello A, Domingo J, Pellicer A, Remohí J. Oocyte vitrification as an efficient option for elective fertility preservation. Fertil Steril 2016;105(3):755.
[38] Anderson RA, Kelsey TW, Morrison DS, Wallace WHB. Family size and duration of fertility in female cancer survivors: a population-based analysis. Fertil Steril 2022;117(2):387–95.
[39] Zaat T, Zagers M, Mol F, Goddijn M, van Wely M, Mastenbroek S. Fresh versus frozen embryo transfers in assisted reproduction. Cochrane Database Syst Rev. 2021;2(2):Cd011184.
[40] Loren AW, Mangu PB, Beck LN, Brennan L, Magdalinski AJ, Partridge AH, et al. Fertility preservation for patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol 2013;31(19):2500–10.
[41] Rosendahl M, Andersen MT, Ralfkiær E, Kjeldsen L, Andersen MK, Andersen CY. Evidence of residual disease in cryopreserved ovarian cortex from female patients with leukemia. Fertil Steril 2010;94(6):2186–90.
[42] Gellert SE, Pors SE, Kristensen SG, Bay-Bjørn AM, Ernst E, Yding AC. Transplantation of frozen-thawed ovarian tissue: an update on worldwide activity published in peer-reviewed papers and on the Danish cohort. J Assist Reprod Genet 2018;35(4):561–70.
[43] Segers I, Bardhi E, Mateizel I, Van Moer E, Schots R, Verheyen G, et al. Live births following fertility preservation using in-vitro maturation of ovarian tissue oocytes. Hum Reprod 2020;35(9):2026–36.
[44] Anderson RA, Amant F, Braat D, D'Angelo A, de Sousa C, Lopes SM, et al. ESHRE guideline: female fertility preservation. Hum Reprod Open 2020;2020(4):hoaa052..
[45] Melville J, Stringer A, Black N, Quenby S, Keay SD, David AL, et al. The impact of assisted reproductive technology treatments on maternal and offspring outcomes in singleton pregnancies: a review of systematic reviews. F&S Reviews 2021;2(4):287–301.
[46] Nijagal MA, Wissig S, Stowell C, Olson E, Amer-Wahlin I, Bonsel G, et al. Standardized outcome measures for pregnancy and childbirth, an ICHOM proposal. BMC Health Serv Res 2018;18(1):953.
[47] Harrison C, Gameiro S, Boivin J. Patient willingness, preferences and decision-making about planning for three complete cycles of IVF/ICSI treatment. Hum Reprod 2021;36(5):1339–52.
[48] Daly C, Micic S, Facey M, Speller B, Yee S, Kennedy ED, et al. A review of factors affecting patient fertility preservation discussions & decision-making from the perspectives of patients and providers. Eur J Cancer Care (Engl) 2019;28(1):e12945.
[49] Lawson AK, Klock SC, Pavone ME, Hirshfeld-Cytron J, Smith KN, Kazer RR. Psychological counseling of female fertility preservation patients. J Psychosoc Oncol 2015 Jul 4;33(4):333–53.
[50] Mulder RL, Font-Gonzalez A, van Dulmen-den Broeder E, Quinn GP, Ginsberg JP, Loeffen EA, et al. Communication and ethical considerations for fertility preservation for patients with childhood, adolescent, and young adult cancer: recommendations from the PanCareLIFE Consortium and the International Late Effects of Childhood Cancer Guideline Harmonization Group. Lancet Oncol 2021;22(2):e68–80.
[51] Khattak H, Malhas R, Craciunas L, Afifi Y, Amorim CA, Fishel S, et al. Fresh and cryopreserved ovarian tissue transplantation for preserving reproductive and endocrine function: a systematic review and individual patient data meta-analysis. Hum Reprod Update 2022 May;28(3):400–16.