# Oocyte freezing: reproductive panacea or false hope of family?


## ABSTRACT

Advanced technology now allows young women to freeze and store oocytes with a realistic chance of future pregnancy. Vitrification has revolutionized oocyte preservation, with comparable pregnancy rates to fresh oocyte use. Traditionally used for women who were about to undergo sterilizing oncology treatment, now the opportunity has been extended for 'social freezing'. A steady rise in all women accessing freezing continues. Despite this, there is a lack of understanding of natural fertility and the impact of age on pregnancy outcomes. The optimum time for freezing is before a woman reaches her late 30s, which unfortunately is not reflected in those accessing egg freezing. The underlying message prevails that planning for fertility is best done early, whether that be by physical completion of family size or storing oocytes before the passage of time and age prevents it.


The first birth from a frozen oocyte occurred in Australia over 30 years ago (Chen, 1986). This scientific breakthrough heralded the beginnings of the current day opportunity for women to circumvent medical illness and more recently the passage of time with postponement of starting a family. Advanced technology now allows young women to freeze and store oocytes with a realistic chance of future pregnancy.

## Cryopreservation technique and outcome

Early techniques for oocyte cryopreservation revolved around slow freezing which, as the name suggests, involves a slow step-wise reduction in temperature of the oocyte before immersing in liquid nitrogen (Argyle et al, 2016). While there have been many successes with slow freezing (Boldt et al, 2006; Borini et al, 2010) the overall outcome has repeatedly been inferior to those with fresh treatment cycles. Italian law limiting surplus embryo creation has supplemented the research field surrounding oocyte cryopreservation. There is a significant reduction in fertilization rates of frozen-thawed oocytes compared with fresh sibling oocytes (73% *vs* 83%, *P*<0.001) (Magli et al, 2010). Significant differences were also seen in top quality day 2 and 3 embryos, with a higher proportion of transferred cycles occurring with fresh oocytes (93% *vs* 79%, *P*<0.001). A corresponding reduction in clinical outcome (Borini et al, 2010) reflects the reduced laboratory findings with slow freeze-thawed oocytes. Deliveries per transfer were significantly reduced in thawed *vs* fresh oocyte transfer cycles (11.6% *vs* 21.6%, *P*<0.001).


**Dr Susie Jacob**, Subspecialty Trainee in Reproductive Medicine, Leeds Fertility, Seacroft Hospital, Leeds LS14 6UH

**Professor Adam Balen**, Professor, Leeds Fertility, Seacroft Hospital, Leeds

Correspondence to: Dr S Jacob (Susie.jacob@nhs.net)


Vitrification of oocytes, the process of ultra-rapid cooling, has seemingly revolutionized the process of oocyte preservation. In short, oocytes are cooled at rates of 100–10 000°C per minute with the addition of high concentrations of cryo-protective additives to reduce the risk of ice nucleation and crystallization, before submersing in liquid nitrogen (Argyle et al, 2016). There are two main methods: open (direct contact between oocyte and liquid nitrogen) or closed (indirect contact through tubing systems) (Glujovsky et al, 2014). The latter is favoured because of concerns regarding bacterial contamination when using open systems (Criado et al, 2011). A survey of UK clinics suggests that three-quarters of them chose to use closed systems for vitrification (Brison et al, 2012).

Although there have been conflicting reports on the efficacy and outcome of the closed method because of slower cooling rates (Bonetti et al, 2011), excellent clinical outcomes have nonetheless been documented (Stoop et al, 2012; Papatheodorou et al, 2013). Comparisons between slow freezing and vitrification demonstrate improved survival, fertilization and pregnancy rates with vitrification techniques (Fadini et al, 2009; Edgar and Gook, 2012). This superiority has been acknowledged within the most recent National Institute for Health and Care Excellence (2013) guideline, which states that 'In cryopreservation of oocytes and embryos, use vitrification instead of controlled-rate freezing if the necessary equipment and expertise is available'. It is now suggested that oocyte vitrification can achieve comparable results to fresh oocyte treatment cycles. A meta-analysis of five trials demonstrated no difference in ongoing pregnancy rates, top quality embryos or fertilization between fresh or vitrified oocyte groups (Cobo and Diaz, 2011). This has been confirmed more recently (Rienzi et al, 2017).

With any developing technology, it is imperative that long-term health data are collected. Cobo et al (2014) compared the obstetric and perinatal outcomes of vitrified *vs* fresh oocyte pregnancies (804 *vs* 996). There was no difference in obstetric problems (including diabetes, hypertension or prematurity), birth weight or congenital abnormalities. A French cohort of 50 children born after autologous oocyte vitrification show no difference in newborn health parameters including birth weight and congenital abnormalities (Anzola et al, 2015).

Traditionally women in a relationship who are about to undergo sterilizing chemotherapy have been advised to cryopreserve oocytes fertilized with their partner's sperm, as the survival of cryopreserved embryos has been significantly higher than that of oocytes. With modern techniques, however, the option for freezing oocytes has to be discussed because of the potential risks that a relationship may not survive, in which case embryos would not be able to be used in the future unless there is the consent of both parties.

## Uptake of freezing

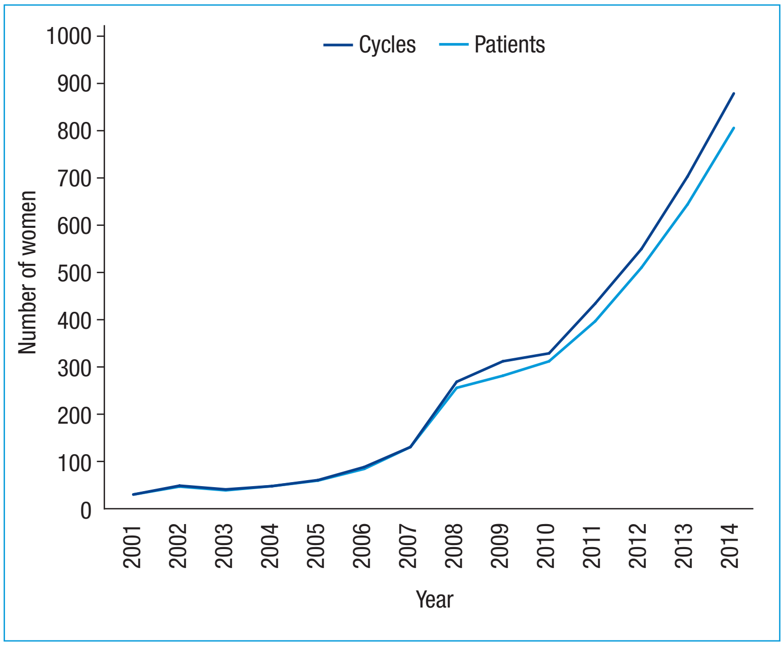
The Human Fertilisation and Embryology Authority (2016) Trends and Figures report, detailing data held up to and including 2014, documents a steady rise in women undergoing freezing including those doing so for medical or 'social' reasons (*Figure 1*). Sixty-five clinics in the UK offer the treatment with eight of these performing over half of the storage cycles. Although the exact reason for storage is unclear, >30% are recorded to have no male partner at the time of oocyte retrieval. While the numbers opting to store eggs are rapidly increasing, these remain only a small proportion of the women having fertility treatment (890 out of approximately 60 000 cycles in 2014) with an even smaller proportion having subsequently thawed stored oocytes. The report suggests that the steeper increase in uptake since 2010 correlates with the widespread introduction of vitrification into UK clinics (Human Fertilisation and Embryology Authority, 2016).

The spike in those seeking oocyte preservation is not just isolated to the UK. A group of 13 Spanish clinics has seen a 5-fold increase in those undergoing elective oocyte cryopreservation between 2007 and 2015 (Cobo et al, 2016). More than 90% of those choosing to freeze their oocytes do so for age-related reasons with the remainder doing so for non-oncology medical conditions such as endometriosis which may impact on their ovarian reserve.

## Who is storing?

Until recent years, oocyte freezing was concentrated under the umbrella of fertility preservation for those with cancer or other medical conditions who required gonadotoxic therapies. For these women, the ability to store oocytes was considered a lifeline for their future genetic offspring regardless of the lower success rates seen with the older slow freeze techniques and potential side effects of treatment (Shenfield et al, 2004). This stance has been modified, mainly because of the introduction of vitrification and improved success rates, to incorporate all women of reproductive years regardless of reasoning for the process (ESHRE Task Force on Ethics and Law et al, 2012; Martinez, 2017). Emphasis is placed on detailed individualized counselling with realistic assessments of the probability of offspring from the stored oocytes. With improved efficacy of oocyte cryopreservation the experimental medicine label has also been lifted (The Practice Committees of the American Society for Reproductive Medicine and the Society for Assisted Reproductive Technology, 2013).

Figure 1. Egg freezing cycles completed and patients undertaking procedure by year. From Human Fertilisation and Embryology Authority (2016).




With improving long-term survival rates from cancer, the focus on future fertility is increasing. There are now over 30 000 childhood cancer survivors living in the UK (Wallace et al, 2013), many of whom will wish to have a family. Reduced reproductive health is detrimental to the quality of life of breast cancer survivors (Howard-Anderson et al, 2012). With improved efficacy of oocyte cryopreservation it is imperative that the option of gamete storage is raised with these patients. Uptake of gamete storage is >50% when offered to those faced with cancer treatment (Alvarez and Ramanathan, 2016) with the majority of cases being in breast cancer.

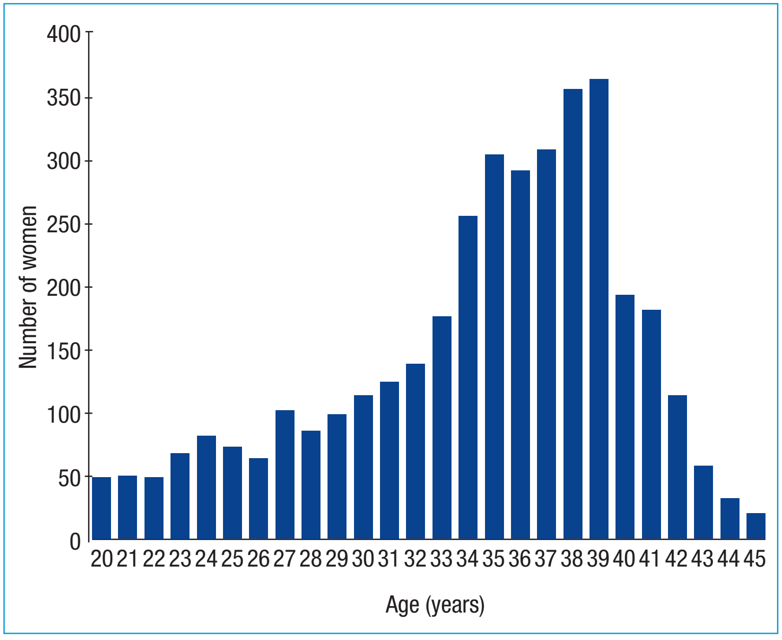
The delay in starting oncology treatment is often seen as a detractor for storing gametes. A comparison in time taken to start neoadjuvant chemotherapy has revealed no increase in time to treatment when using a random start protocol (which roughly requires 2 weeks to complete) for oocyte collection (Letourneau et al, 2017). Furthermore, there was no detriment to the number of oocytes stored using such a protocol. Using random start protocols also gives the option to consider back-to-back stimulation cycles which may be particularly useful in women with low ovarian reserve or for added reassurance with more oocytes stored. No decrease in 5-year survival has been shown in those who began neoadjuvant chemotherapy up to 6 weeks post-diagnosis (Smith et al, 2013), strengthening the argument that it is safe to undergo oocyte cryopreservation during this highly stressful time. A retrospective study (Druckenmiller et al, 2016) of women who stored oocytes because they had cancer and who returned to use them showed a live birth rate similar to those who were undergoing non-cancer-related fertility treatment (44% (confidence interval 12–77%) *vs* 33% (confidence interval 22–44%)). Within this cohort the average time from referral to oocyte collection was 12 days.

> "The option to freeze eggs is not solely for those undergoing cancer treatment or those opting to delay motherhood ... conditions such as endometriosis and rheumatological conditions can impact on ovarian reserve."

As the rate of oocyte preservation increases, the number of women doing so for elective social reasons increases accordingly. *Figure 2* shows the number of women who choose to freeze oocytes is highest in the 38–39-year-old group overall. It can be presumed that the larger proportion of these are doing so for elective reasons. A UK study suggested that the average woman electively storing her oocytes was 37 years of age, university educated and without a partner at the time of storage (Baldwin et al, 2015). It has been suggested that women place more emphasis now on finding the 'right' life partner rather than entering motherhood as a single woman or in a compromised relationship, which in part is an explanation for delayed parenthood (Cobo et al, 2016).

An interesting cross-sectional study of American women revealed that 87.2% were aware of elective oocyte freezing, of whom 25% would consider undergoing it. Yet of this cross-section only 29% knew what the process actually involved (Milman et al, 2017). A further survey in a medically educated cohort revealed knowledge of the effect of age on fertility was limited, with 89.4% delaying child bearing for their career and education (Anspach et al, 2017). These findings are alarming in the modern age when media coverage is widespread regarding the impact of delayed child bearing, and indicate that more needs to be done to educate the population as a whole about the decline in natural fertility with age. These figures also suggest that although social freezing has gained momentum, there may still be large numbers of the population who would freeze oocytes if they were aware of it and could afford to freeze for social reasons.

Figure 2. Age at storage of oocytes from 2001–2014. From Human Fertilisation and Embryology Authority (2016).




Advocates of ovarian reserve screening argue that having knowledge of one's own individual assessment (Tremellen and Savulescu, 2014) may alter the reproductive choices made. For example, this may allow informed earlier recourse to oocyte vitrification allowing reproductive autonomy. The counter argument to this is that storage may actually stifle reproductive autonomy by placing a 'pressure' on women to produce genetic offspring and therefore denormalising alternative family methods. In the same vein, corporate offers from giants such as Facebook and Apple to fund egg freezing for their employees (Mertes, 2015) may be seen as well meaning by some but may also be seen as a cynical way of jeopardising family life to maximize workplace efficiency. Women who place more importance on their career are more likely to be optimistic about delayed child bearing and also more amenable to the use of donor eggs if required (Simoni et al, 2017). Despite optimism, it is recognized that with delay in child bearing comes the occurrence of childless families who ultimately would not have chosen that outcome (Kneale and Joshi, 2008).

The option to freeze eggs is not solely for those undergoing cancer treatment or those opting to delay motherhood. Other conditions such as endometriosis and rheumatological conditions can impact on ovarian reserve, with patients benefiting from oocyte freezing (Cobo et al, 2016). For those wishing to undergo gender reassignment, oocyte and tissue cryopreservation may serve to allow genetic parenthood in the future (De Roo et al, 2016), although this raises concern of where the gametes will ultimately be used.

In the UK, there is an additional consideration based upon the legal framework of the Human Fertilisation and Embryology Authority which allows for the freezing of oocytes for no more than 10 years unless there is a risk of premature infertility – in other words storing for social reasons has a legal restriction of 10 years.

## Reality and outcomes?

The age at storage is crucial for the success of oocyte cryopreservation. While there is no doubt that the technology available for storage and use of frozen oocytes has radically improved, the overall success of treatment is reliant on the quality of the oocyte. This is especially true for those in the social freezing category. While data from an oocyte donation programme cites a 6.5% oocyte-to-baby rate with an increasing live birth rate with increasing number of oocytes used (Cobo et al, 2015), it is clear from the Human Fertilisation and Embryology Authority data that the peak age of those freezing is among 38–39-year-olds who are unlikely to achieve optimum egg storage numbers and as such live birth outcomes. Initial estimates of 100 cryopreserved oocytes being required for one pregnancy (Argyle et al, 2016) have now radically reduced to 8–10 oocytes (Cobo et al, 2016) for those under 36 years of age. In the latter study, if more than 10 oocytes were used the success rate continued to increase in those ≤35 years but no improvement in clinical pregnancy rate was seen in those older than this.

Without question there is a higher chance of success the younger the age at which oocytes are frozen. One of the largest data sets to look at outcomes for women electively choosing to cryopreserve (Cobo et al, 2016) shows a significant reduction in oocyte survival, clinical pregnancy and live birth rate when comparing those ≤35 years with those ≥36 years. The survival rate was shown to be 94.6% *vs* 82.4%, with a live birth rate over 50% lower in the older age group (50% *vs* 22.9%). These data were based on a 9.3% return rate to use the frozen oocytes after a relatively short mean storage period of 2.1 years. Given that the primary objective of storage is to postpone the time until attempted pregnancy, it is highly likely that with extended review more women would return for treatment and presumably similar if not widened differences in success rates would be seen (as more of the younger frozen oocytes are used). These differences in success rates are no surprise and clearly mirror the decline in fertility seen with advancing age, largely in response to declining oocyte quality and aneuploidy rates.

It is imperative that women who request oocyte freezing are given realistic expectations by counselling before treatment. The vast majority of results for oocyte freezing are generated from donor populations who are in general a younger population, with a better prognosis. As the most common consultation (Human Fertilisation and Embryology Authority, 2014; Cobo et al, 2016) is in the older woman when fertility is already in decline the truth is that these women may already have left it too late for optimum outcome. Despite this knowledge, there is speculation that patients may benefit psychologically from attempting to preserve the ability to have their own genetic offspring (Hodes-Wertz et al, 2013).

The financial implication of freezing is also an important consideration. For those storing for oncological reasons the initial storage of gametes is usually covered by the clinical commissioning group in the UK, if all other funding criteria are met. For those women who wish to store otherwise the cost of storage is upwards of £3000 per cycle plus medication costs. The future thaw and fertilization of the stored oocytes costs a further £3000 minimum per cycle. A rudimentary search of the internet for egg freezing in the UK reveals a plethora of clinics offering the service. An interesting modelling study looked at the cost effectiveness of oocyte freezing at 35 years of age to enable a pregnancy at the age of 40 years. Their Markov model showed that oocyte freezing provides more value for money than standard in-vitro fertilization at the age of 40 years (van Loendersloot et al, 2011). It is recognized that although oocyte freezing is always more costly, whether that be for the patient or funding body, it is more effective at producing live births than no storage in oncology situations. This is especially true for older women undergoing low risk chemotherapy regimens or younger women undergoing high risk regimens (Lyttle Schumacher et al, 2017).



## KEY POINTS

- There has been a rapid increase in the number of women choosing to freeze oocytes.
- Vitrification of oocytes can achieve comparable results to fresh oocyte treatment cycles.
- The clinical pregnancy rate is inversely related to the woman's age at freezing.
- Freezing 8–10 oocytes for women aged <36 years gives a reasonable chance of pregnancy.
- Knowledge about the impact of age on fertility is still limited.

## Conclusions

Improved technology and public education has allowed oocyte cryopreservation to become a feasible option for many women wishing to preserve their fertility. With clinical success rates equalling that of fresh embryo transfer cycles, the viability of the technique has been proven. Caution is necessary when counselling older women regarding their individual outcomes. As with all fertility treatments, there is not a 'one-size-fits-all' policy. With the peak number of women accessing egg freezing being in their late 30s, the reality persists that the chance of a baby is slim from treatment. For those who have no other option such as those undergoing sterilizing oncological regimens, the balance shifts further in favour of storage. The underlying message remains that planning for fertility is best done early, whether that be by physical completion of family size or storing oocytes before the passage of time and age prevents it. **BJHM**

*Conflict of interest: none.*


Alvarez RM, Ramanathan P (2016) Fertility preservation in female oncology patients: the influence of the type of cancer on ovarian stimulation response. *Hum Reprod* pii: dew158. https://doi.org/10.1093/humrep/dew158

Anspach Will E, Maslow BS, Kaye L, Nulsen J (2017) Increasing awareness of age-related fertility and elective fertility preservation among medical students and house staff: a pre- and post-intervention analysis. *Fertil Steril* **107**(5): 1200–1205.e1. https://doi.org/10.1016/j.fertnstert.2017.03.008

Anzola AB, Pauly V, Geoffroy-Siraudin C, Gervoise-Boyer MJ, Montjean D, Boyer P (2015) The first 50 live births after autologous oocyte vitrification in France. *J Assist Reprod Genet* **32**(12): 1781–1787. https://doi.org/10.1007/s10815-015-0603-2

Argyle CE, Harper JC, Davies MC (2016) Oocyte cryopreservation: where are we now? *Hum Reprod Update* **22**(4): 440–449. https://doi.org/10.1093/humupd/dmw007

Baldwin K, Culley L, Hudson N, Mitchell H, Lavery S (2015) Oocyte cryopreservation for social reasons: demographic profile and disposal intentions of UK users. *Reprod Biomed Online* **31**(2): 239–245. https://doi.org/10.1016/j.rbmo.2015.04.010

Boldt J, Tidswell N, Sayers A, Kilani R, Cline D (2006) Human oocyte cryopreservation: 5-year experience with a sodium-depleted

slow freezing method. *Reprod Biomed Online* **13**(1): 96–100. https://doi.org/10.1016/S1472-6483(10)62021-4
Bonetti A, Cervi M, Tomei F, Marchini M, Ortolani F, Manno M (2011) Ultrastructural evaluation of human metaphase II oocytes after vitrification: closed versus open devices. *Fertil Steril* **95**(3): 928–935. https://doi.org/10.1016/j.fertnstert.2010.08.027
Borini A, Levi Setti PE, Anserini P et al (2010) Multicenter observational study on slow-cooling oocyte cryopreservation: clinical outcome. *Fertil Steril* **94**(5): 1662–1668. https://doi.org/10.1016/j.fertnstert.2009.10.029
Brison D, Cutting R, Clarke H, Wood M (2012) ACE consensus meeting report: oocyte and embryo cryopreservation Sheffield 17.05.11. *Hum Fertil* **15**(2): 69–74. https://doi.org/10.3109/14647273.2012.687124
Chen C (1986) Pregnancy after human oocyte cryopreservation. *Lancet* **327**(8486): 884–886. https://doi.org/10.1016/S0140-6736(86)90989-X
Cobo A, Diaz C (2011) Clinical application of oocyte vitrification: a systematic review and meta-analysis of randomized controlled trials. *Fertil Steril* **96**(2): 277–285. https://doi.org/10.1016/j.fertnstert.2011.06.030
Cobo A, Serra V, Garrido N, Olmo I, Pellicer A, Remohi J (2014) Obstetric and perinatal outcomes of babies born from vitrified oocytes. *Fertil Steril* **102**(4): 1006–1015.e4. https://doi.org/10.1016/j.fertnstert.2014.06.019
Cobo A, Garrido N, Pellicer A, Remohí J (2015) Six years experience in ovum donation using vitrified oocytes: report of cumulative outcomes, impact of storage time, and development of a predictive model for oocyte survival rate. *Fertil Steril* **104**(6): 1426–1434.e8, 8. https://doi.org/10.1016/j.fertnstert.2015.08.020
Cobo A, García-Velasco JA, Coello A, Domingo J, Pellicer A, Remohí J (2016) Oocyte vitrification as an efficient option for elective fertility preservation. *Fertil Steril* **105**(3): 755–764.e8. https://doi.org/10.1016/j.fertnstert.2015.11.027
Criado E, Moalli F, Polentarutti N, Albani E, Morreale G, Menduni F, Levi-Setti PE (2011) Experimental contamination assessment of a novel closed ultravitrification device. *Fertil Steril* **95**(5): 1777–1779. https://doi.org/10.1016/j.fertnstert.2010.12.044
De Roo C, Tilleman K, TSjoen G, De Sutter P (2016) Fertility options in transgender people. *Int Rev Psychiatry* **28**(1): 112–119. https://doi.org/10.3109/09540261.2015.1084275
Druckenmiller S, Goldman KN, Labella PA, Fino ME, Bazzocchi A, Noyes N (2016) Successful oocyte cryopreservation in reproductive-aged cancer survivors. *Obstet Gynecol* **127**(3): 474–480. https://doi.org/10.1097/AOG.0000000000001248
Edgar DH, Gook DA (2012) A critical appraisal of cryopreservation (slow cooling versus vitrification) of human oocytes and embryos. *Hum Reprod Update* **18**(5): 536–554. https://doi.org/10.1093/humupd/dms016
ESHRE Task Force on Ethics and Law; Dondorp W, de Wert G, Pennings G et al (2012) Oocyte cryopreservation for age-related fertility loss. *Hum Reprod* **27**(5): 1231–1237. https://doi.org/10.1093/humrep/des029
Fadini R, Brambillasca F, Renzini MM, Merola M, Comi R, De Ponti E, Dal Canto MB (2009) Human oocyte cryopreservation: comparison between slow and ultrarapid methods. *Reprod Biomed Online* **19**(2): 171–180. https://doi.org/10.1016/S1472-6483(10)60069-7
Glujovsky D, Riestra B, Sueldo C et al (2014) Vitrification versus slow freezing for women undergoing oocyte cryopreservation. *Cochrane Database Syst Rev* **9**: CD010047. https://doi.org/10.1002/14651858.CD010047.pub2
Hodes-Wertz B, Druckenmiller S, Smith M, Noyes N (2013) What do reproductive-age women who undergo oocyte cryopreservation think about the process as a means to preserve fertility? *Fertil Steril* **100**(5): 1343–1349.e2. https://doi.org/10.1016/j.fertnstert.2013.07.201
Howard-Anderson J, Ganz PA, Bower JE, Stanton AL (2012) Quality of life, fertility concerns, and behavioral health outcomes in younger breast cancer survivors: a systematic review. *J Natl Cancer Inst* **104**(5): 386–405. https://doi.org/10.1093/jnci/djr541
Human Fertilisation and Embryology Authority (2016) Fertility Treatment 2014 trends and figures. www.hfea.gov.uk/media/1783/fertility-treatment-2014-trends-and-figures.pdf (accessed 28 March 2018)
Kneale D, Joshi H (2008) Postponement and childlessness - Evidence from two British cohorts. *Demogr Res* **19**: 1935–1968. https://doi.org/10.4054/DemRes.2008.19.58
Letourneau JM, Sinha N, Wald K et al (2017) Random start ovarian stimulation for fertility preservation appears unlikely to delay initiation of neoadjuvant chemotherapy for breast cancer. *Hum Reprod* **32**(10): 2123–2129. https://doi.org/10.1093/humrep/dex276
Lyttle Schumacher B, Grover N, Mesen T, Steiner A, Mersereau J (2017) Modeling of live-birth rates and cost-effectiveness of oocyte cryopreservation for cancer patients prior to high- and low-risk gonadotoxic chemotherapy. *Hum Reprod* **32**(10): 2049–2055. https://doi.org/10.1093/humrep/dex257
Magli MC, Lappi M, Ferraretti AP, Capoti A, Ruberti A, Gianaroli L (2010) Impact of oocyte cryopreservation on embryo development. *Fertil Steril* **93**(2): 510–516. https://doi.org/10.1016/j.fertnstert.2009.01.148
Martinez F (2017) Update on fertility preservation from the Barcelona International Society for Fertility Preservation–ESHRE–ASRM 2015 expert meeting: indications, results and future perspectives. *Hum Reprod* **32**(9): 1802–1811. https://doi.org/10.1093/humrep/dex218
Mertes H (2015) Does company-sponsored egg freezing promote or confine womens reproductive autonomy? *J Assist Reprod Genet* **32**(8): 1205–1209. https://doi.org/10.1007/s10815-015-0500-8
Milman LW, Senapati S, Sammel MD, Cameron KD, Gracia C (2017) Assessing reproductive choices of women and the likelihood of oocyte cryopreservation in the era of elective oocyte freezing. *Fertil Steril* **107**(5): 1214–1222.e3. https://doi.org/10.1016/j.fertnstert.2017.03.010
National Institute for Health and Clinical Excellence (2013) *Fertility: Assessment and treatment for people with fertility problems.* CG156. National Institute for Health and Clinical Excellence, London
Papatheodorou A, Vanderzwalmen P, Panagiotidis Y, Prapas N, Zikopoulos K, Georgiou I, Prapas Y (2013) Open versus closed oocyte vitrification system: a prospective randomized sibling-oocyte study. *Reprod Biomed Online* **26**(6): 595–602. https://doi.org/10.1016/j.rbmo.2013.02.014
Practice Committees of American Society for Reproductive Medicine; Society for Assisted Reproductive Technology (2013) Mature oocyte cryopreservation: a guideline. *Fertil Steril* **99**(1): 37–43. https://doi.org/10.1016/j.fertnstert.2012.09.028
Rienzi L, Gracia C, Maggiulli R et al (2017) Oocyte, embryo and blastocyst cryopreservation in ART: systematic review and meta-analysis comparing slow-freezing versus vitrification to produce evidence for the development of global guidance. *Hum Reprod Update* **23**(2): 139–155. https://doi.org/10.1093/humupd/dmw038
Shenfield F, Pennings G, Cohen J, Devroey P, Sureau C, Tarlatzis B; ESHRE Task Force on Ethics and Law (2004) Taskforce 7: ethical considerations for the cryopreservation of gametes and reproductive tissues for self use. *Hum Reprod* **19**(2): 460–462. https://doi.org/10.1093/humrep/deh051
Simoni MK, Mu L, Collins SC (2017) Womens career priority is associated with attitudes towards family planning and ethical acceptance of reproductive technologies. *Hum Reprod* **32**(10): 2069–2075. https://doi.org/10.1093/humrep/dex275
Smith EC, Ziogas A, Anton-Culver H (2013) Delay in surgical treatment and survival after breast cancer diagnosis in young women by race/ethnicity. *JAMA Surg* **148**(6): 516–523. https://doi.org/10.1001/jamasurg.2013.1680
Stoop D, De Munck N, Jansen E, Platteau P, Van den Abbeel E, Verheyen G, Devroey P (2012) Clinical validation of a closed vitrification system in an oocyte-donation programme. *Reprod Biomed Online* **24**(2): 180–185. https://doi.org/10.1016/j.rbmo.2011.10.015
Tremellen K, Savulescu J (2014) Ovarian reserve screening: a scientific and ethical analysis. *Hum Reprod* **29**(12): 2606–2614. https://doi.org/10.1093/humrep/deu265
van Loendersloot LL, Moolenaar LM, Mol BWJ, Repping S, van der Veen F, Goddijn M (2011) Expanding reproductive lifespan: a cost-effectiveness study on oocyte freezing. *Hum Reprod* **26**(11): 3054–3060. https://doi.org/10.1093/humrep/der284
Wallace WHB, Thompson L, Anderson RA; Guideline Development Group (2013) Long term follow-up of survivors of childhood cancer: summary of updated SIGN guidance. *BMJ* **346**: f1190. https://doi.org/10.1136/bmj.f1190