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Pregnancy and Breast Cancer

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This title was first published as RCOG advice in 1997 and subsequently as a Green-top Guideline in January 2004. This document is the second edition of the guideline and updates the previous 2004 edition.

1. Purpose and scope

This document aims to provide clinical guidance to health professionals caring for women of childbearing age with a diagnosis or history of breast cancer. The management of pregnancy in relation to breast cancer is multidisciplinary. The guideline will be of value to obstetricians and gynaecologists, fertility specialists and midwives as well as oncologists and breast care nurses.

2. Background

Breast cancer is the most common cancer in females, with a lifetime risk of one in nine in the UK, and is the leading cause of death in women aged 35–54 years. Fifteen percent of cases are diagnosed before the age of 45 years, thus breast cancer affects almost 5000 women of reproductive age in the UK annually. Between 1991 and 1997 there were 1.3–2.4 cases of breast cancer in women per 10 000 live births,[1,2] although when breast cancer is diagnosed in women aged 30 years or less, 10–20% of cases may be associated with pregnancy or occur within 1 year postpartum.

The prognosis of breast cancer is improving, with 5-year survival around 80% for the under 50s age group; however, the survival rate may be lower in very young women.[3] Treatment of pregnancy-associated cancer should be in a multidisciplinary team according to standard UK guidelines[4] with inclusion of the obstetric team as core members.

Fewer than 10% of women diagnosed with breast cancer subsequently become pregnant,[5,6] but increasing numbers of women are seeking pregnancy following treatment. Young women presenting with breast cancer often have fertility-related concerns[7–9] and need well-informed discussions on fertility, pregnancy and lactation after breast cancer and the availability of fertility preservation procedures.

3. Identification and assessment of evidence

This guideline was developed in accordance with standard methodology for producing RCOG Green-top Guidelines. Medline, Pubmed, all EBM reviews (Cochrane CRCT, Cochrane Database of Systematic Reviews, Methodology register, ACP journal club, DARE, HTA, Maternity and Infant Care), EMBASE and TRIP were searched for relevant randomised controlled trials, systematic reviews and meta-analyses, cohort studies and case studies. The search was restricted to articles published between 2002 and December 2009, updated from the original search for the previous edition. The search terms included were: 'breast neoplasms', 'breast cancer', 'pregnancy', 'pregnancy complications', 'breast cancer and fertility', 'mastectomy', 'breast-feeding', 'lactation', 'contraception', 'fertility' and 'infertility'. Abstracts were used to identify key articles. The National Library for Health and the National Guidelines Clearing House were searched for relevant guidelines.

In contrast to the extensive literature on treatment of breast cancer, there is no level 1 evidence on pregnancy and breast cancer. There are some well-designed observational studies. Thus, recommendations for practice are limited to grade C/D but, where possible, recommendations are based on, and explicitly linked to, the evidence that supports them. Areas lacking evidence are highlighted and annotated as 'good practice points'.

4. What is the optimal management of breast cancer diagnosed during pregnancy?

4.1 Prognosis

Pregnancy itself does not appear to worsen the prognosis for women diagnosed in pregnancy compared with non-pregnant controls matched for age and stage[10] (provided that standard treatment guidelines for the breast cancer are adhered to).

Evidence level 2–

However, as pregnancy-associated breast cancer occurs in a younger population who may have features that carry a higher risk of metastases such as high-grade tumours and estrogen receptor negative tumours, these younger women may be expected to have an inferior prognosis.[11,12]

Evidence level 2+/3

4.2 Diagnosis

Women presenting with a breast lump during pregnancy should be referred to a breast specialist team and any imaging or further tests should be conducted in conjunction with the multidisciplinary team.

Diagnosis may be difficult in women who are pregnant or lactating. Women presenting with a breast lump during pregnancy should be referred to a breast specialist team and any imaging or further tests should be conducted within the breast multidisciplinary team. Women should have a designated key worker, usually a breast care nurse. Ultrasound is used first to assess a discrete lump, but if cancer is confirmed, mammography is necessary (with fetal shielding) to assess the extent of disease and the contralateral breast. Tissue diagnosis is with ultrasound-guided biopsy for histology rather than cytology, as proliferative change during pregnancy renders cytology inconclusive in many women. Histology is similar to that in age-matched non-pregnant counterparts: histological grade, receptor status and human epidermal growth factor receptor 2 (HER2) inform treatment planning. Staging for metastases is conducted only if there is high clinical suspicion and should comprise chest X-ray and liver ultrasound if possible. Gadolinium-enhanced magnetic resonance imaging is not recommended unless there is a specific need for it to investigate a clinical problem; there are limited data for the use of this imaging method in pregnancy, although no adverse effects of gadolinium on the fetus have been reported.[13] Tumour markers such as CA15-3, CEA and CA125 are not used in early breast cancer and may be misleading in pregnancy, and are not recommended.

Bone scanning and pelvic X-ray computed tomography are not recommended because of the possible effect of irradiation on the fetus.

In women who are not pregnant, X-ray computed tomography (CT) and isotope bone scan are the preferred methods of investigation to establish or exclude metastases. These methods are not appropriate in women who are pregnant, in whom chest X-ray and liver ultrasound are preferred. If there is concern about bone involvement, a plain film of the relevant area and/or magnetic resonance imaging to minimise radiation exposure to the fetus is suggested.

4.3 Consideration of termination of pregnancy

The decision to continue the pregnancy should be based on careful discussion of the cancer prognosis, treatment and future fertility with the woman and her partner and multidisciplinary team.

4.4 Treatment during pregnancy

The multidisciplinary team review outcome should be forwarded to the obstetric team and family doctor.

Surgical treatment including loco-regional clearance can be undertaken in all trimesters. Breast-conserving surgery or mastectomy can be considered, based on tumour characteristics and breast size, following multidisciplinary team discussion. Reconstruction should be delayed to avoid prolonged anaesthesia and to allow optimal symmetrisation of the breasts after delivery. Sentinel node assessment using radioisotope scintigraphy does not cause significant uterine radiation,[14] but blue dye is not recommended as the effect upon the fetus is unknown. Sentinel node biopsy is indicated in women who have a negative result from a preoperative axillary ultrasound and needle biopsy. If the axilla is positive, axillary clearance is indicated.

Evidence level 4

Radiotherapy is contraindicated until delivery unless it is life saving or to preserve organ function (e.g. spinal cord compression). If necessary, radiotherapy can be considered with fetal shielding or, depending on gestational age, early elective delivery could be discussed. Routine breast/chest wall radiotherapy can be deferred until after delivery.

Systemic chemotherapy is contraindicated in the first trimester because of a high rate of fetal abnormality, but is safe from the second trimester and should be offered according to protocols defined by the risk of breast cancer relapse and mortality. Anthracyline regimens are safe; there are fewer data on taxanes, which should be reserved for high-risk (node-positive) or metastatic disease.[15–17] Standard antiemetics including 5HT3 serotonin antagonists and dexamethasone should be used. There are no data on a neurokinin recptor antagonist with very high efficacy in chemotherapy-induced emesis. There is no evidence for an increased rate of second-trimester miscarriage or fetal growth restriction, organ dysfunction or long-term adverse outcome with the use of chemotherapy.[17,18]

Evidence level 3

For women in whom tumour characteristics, defined by imaging and core biopsy, mean that chemotherapy is indicated, a decision may be made to offer neoadjuvant chemotherapy before surgery to allow tumour downstaging and to facilitate surgery. Occasionally, with a low-risk tumour in which chemotherapy is not indicated, there may be an indication for mastectomy. In this situation radiotherapy would be deferred.

Tamoxifen and trastuzumab are contraindicated in pregnancy and should not be used.

D

Tamoxifen is not used until after delivery. Trastuzumab, a monoclonal antibody targeted against the HER2/neu receptor, is contraindicated during pregnancy because of reported adverse fetal outcome.[19,20] There are no data on other targeted therapies such as vascular endothelial growth factor antagonists, including bevacizumab. However, there are no compelling oncological reasons for use of targeted therapies including monoclonal antibodies or small-molecule tyrosine kinase inhibitors during pregnancy as conventional chemotherapy can be used, allowing these drugs to be reserved for postpartum. Haemopoietic growth factors (granulocyte colony-stimulating factor) may be employed to ameliorate chemotherapy-induced neutropenia and have been used extensively in haematological malignancy; their use is recommended to minimise potential maternal and fetal problems associated with neutropenia.[21] Use of these and other drugs should be discussed with the obstetrician.

Evidence level 3

4.5 Timing of delivery of the baby

The birth of the baby should be timed after discussion with the woman and the multidisciplinary team.

✓

Most women can go to full term of pregnancy and have a normal or induced delivery. If early delivery of the baby is necessary, consideration of corticosteroids for fetal lung maturation is appropriate. However, birth should be more than 2–3 weeks after the last chemotherapy session to allow maternal bone marrow recovery and to minimise problems with neutropenia.

4.6 Lactation

Women should not breastfeed when taking trastuzumab (Herceptin®, Roche) or tamoxifen, as it is unknown whether these drugs are transmitted in breast milk. ✓

The ability to breastfeed may depend on surgery and whether major ducts have been excised. Breastfeeding while on chemotherapy is not advised, as the drugs cross into breast milk and may cause neonatal leucopenia with a risk of infection. There should be a time interval of 14 days or more from the last chemotherapy session to start of breastfeeding to allow drug clearance from breast milk.[22]

Evidence level 3

If chemotherapy is restarted, breastfeeding must cease. A short period of lactation may be psychologically beneficial after a stressful pregnancy and be beneficial to the baby.[23] Women taking tamoxifen should not breastfeed.

Evidence level 4

Women should not breastfeed when taking trastuzumab as it is unknown whether this drug is transmitted in breast milk.

5. What are the contraceptive choices for women wishing to avoid pregnancy after treatment of breast cancer?

Non-hormonal contraceptive methods are recommended. ✓

Women with a history of breast cancer should seek specialist contraceptive advice. Hormonal contraception is contraindicated in women with current or recent breast cancer (World Health Organization/UK medical eligibility category 4).[24] This advice does not differentiate between hormone-sensitive and hormone-insensitive tumours. Although hormonal contraception may be considered after at least 5 years free of recurrence (World Health Organization/UK category 3)[24] and current evidence allays concerns that long-term oral contraceptive use affects breast cancer risk,[25,26] there is insufficient evidence to support the use of combined or progestogen-only hormonal contraceptives when alternative non-hormonal methods are suitable and acceptable.

Evidence level 4

The levonorgestrel intrauterine system (LNG-IUS: Mirena®, Bayer Healthcare Pharmaceuticals) may reduce the risk of endometrial abnormalities during tamoxifen therapy,[27] but further evidence is required on its safety in breast cancer survivors. No overall increase in recurrence risk was found in a retrospective controlled cohort study of LNG-IUS users compared with non-users (adjusted hazard ratio 1.86, 95% CI 0.86–4.00),[28] although subgroup analysis suggested a higher recurrence risk, which was of borderline significance, in women who developed breast cancer while using LNG-IUS and continued its use (adjusted hazard ratio 3.39, 95% CI 1.01–11.35).[28]

Evidence level 2+

6. What advice should be given to women planning pregnancy following breast cancer?

Women planning a pregnancy after treatment for breast cancer should consult their clinical oncologist, breast surgeon and obstetrician. ✓

Women on tamoxifen are advised to stop this treatment 3 months before trying to conceive because of the long half-life of the drug, and to have any routine imaging before trying to conceive to avoid the need for imaging during pregnancy. Women with metastatic disease should be advised against a further pregnancy as life expectancy is limited and treatment of metastatic disease would be compromised. The remainder of this section concerns women treated for early-stage disease.

6.1 Impact of pregnancy on risk of recurrence

Women can be reassured that long-term survival after breast cancer is not adversely affected by pregnancy. C

Since many breast cancers are estrogen receptor positive and endocrine responsive, women used to be advised against pregnancy because of concerns that it would worsen prognosis. However, the evidence from the published studies is reassuring, showing either no impact on survival or improved survival. Despite the limitations of the studies, which are mainly retrospective case–control series with limited numbers, they at least demonstrate that outcome after treatment for breast cancer is not adversely affected by pregnancy.[29,30]

The prognosis is good for women with a subsequent pregnancy after early-stage breast cancer.[31–33] The published series reflect an improvement in treatment over recent decades. A recent population-based study in Western Australia from 1982 to 2003 reported survival rates of 92% at 5 years and 86% at 10 years.[6]

Evidence level 2+

Several studies show better survival outcome in women who conceive after treatment for breast cancer.[5,6,32,34,35] In the largest series, women who had a full-term pregnancy (n = 199) had a relative risk of death of 0.73 (95% CI 0.54–0.99).[5] These findings may be explained by selection bias and the 'healthy mother effect' described by Sankila:[36] healthy women are more likely to conceive, and women with poor prognosis or early relapse do not embark upon pregnancy.

Evidence level 2+

However, some authors postulate an actual protective effect of pregnancy.[6,37]

The impact of pregnancy does not seem to be modified by tumour characteristics (e.g. size, hormone receptor status),[5] but there are insufficient data to draw firm conclusions. In women with *BRCA* gene mutations, the risks associated with subsequent pregnancy are uncertain.[38]

Evidence level 2+

6.2 Time interval before pregnancy

Advice on postponement of pregnancy should be individualised and based on treatment needs and prognosis over time. Most women should wait at least 2 years after treatment, which is when the risk of cancer recurrence is highest. ✓

Women are generally advised to wait for at least 2 years after treatment for breast cancer before conception[37,39–41] because of the risk of early relapse. The rate of disease recurrence is highest in the first 3 years after diagnosis and then declines,[42] although late relapses do occur up to 10 years and more from diagnosis.[3]

Evidence level 3

Women with estrogen receptor positive disease should be advised that the recommended duration of tamoxifen treatment is 5 years.

This advice has been challenged because of the lack of published data showing that postponing pregnancy has an impact on outcome;[6] the literature on recurrent disease also needs to be reviewed in the light of changing treatment regimens and improved understanding of cancer subtypes. It has been suggested that women with a good prognosis need not wait 2 years to become pregnant.[6]

Evidence level 2+

An understanding of the prognostic factors affecting the individual woman – tumour size, grade, nodal status, estrogen and progesterone receptor and HER2 status – should enable the oncologist to give appropriate advice.[43,44] This is of great importance to the woman desiring pregnancy, who may need to weigh up the benefit of postponing conception, for example to complete prolonged adjuvant therapy with tamoxifen, against the risk of infertility as a result of delay.

Evidence level 4

6.3 Outcome of pregnancy

The majority of pregnancies after breast cancer proceed to live birth. There may be an increased miscarriage rate following breast cancer,[45] but the published series are small and not all report maternal age (a major risk factor for miscarriage) or distinguish between spontaneous miscarriage and induced termination.[31,46,47] A recently reported series of 465 pregnant women who were breast cancer survivors resulted in 236 full-term births (51%), 36 spontaneous miscarriages (8%) and 193 induced terminations (41%).[5] Women are more likely to terminate a pregnancy when it occurs soon after treatment or during adjuvant therapy.[5,6]

Evidence level 3

Women can be reassured concerning the risk of malformation in children conceived after treatment for breast cancer.

D

Most of the available data do not show any increase in congenital malformations or stillbirth among the offspring of women who have completed treatment for breast cancer.[6,48,49] A large study derived from the Danish registries identified 216 births to women with a prior diagnosis of breast cancer and found no stillbirths, no increase in congenital anomalies no increase in low birth weight and no substantial risk of preterm birth (OR 1.3, 95% CI 0.7–2.2).[49] The Swedish data on 331 births, however, showed a tendency towards an increased risk of malformations (OR 2.1, 95% CI 1.2–3.7), birth before 32 weeks of gestation (OR 3.2, 95% CI 1.7–6.0) and birth weight below 1500 g (OR 2.9, 95% CI 1.4–5.8);[50] nevertheless, adverse outcomes are uncommon.

Evidence level 2+/3

The heritability of breast cancer is a source of anxiety but does not affect childhood health. Women who are known to be breast cancer gene (*BRCA*) carriers may wish to consider preimplantation genetic diagnosis, which is now available in the UK. However, some young women with a family history indicative of genetic risk may not wish to undergo testing so as not to compromise their decisions regarding having a family.

7. What is the optimal management of pregnancy following treatment for breast cancer?

Pregnancy following breast cancer should be jointly supervised by the obstetrician, oncologist and breast surgeon.

✓

Echocardiography should be performed during pregnancy in women at risk to detect cardiomyopathy through resting left ventricular ejection fraction or echocardiographic fractional shortening.

D

During pregnancy, a breast treated by surgery/radiotherapy may not undergo hormonal change and the woman may require a temporary prosthesis. If breast imaging is needed, ultrasound (performed through the breast multidisciplinary team) is preferred. Metastatic relapse may be harder to detect and common complaints in pregnancy such as backache can be difficult to assess.

These women may have received adjuvant chemotherapy with anthracyclines (doxorubicin, epirubicin), which can cause cumulative dose-dependent left ventricular dysfunction and, rarely, cardiomyopathy.[51,52] Although cardiac complications during pregnancy are rare in cancer survivors,[53] echocardiography should be performed during pregnancy in women at risk to detect cardiomyopathy through resting left ventricular ejection fraction or echocardiographic fractional shortening.

A slightly increased risk of delivery complications (OR 1.5, 95% CI 1.2–1.9) and caesarean section (OR 1.3, 95% CI 1.0–1.7) has been reported in breast cancer survivors.[50]

Evidence level 2+

The supervision of pregnancy after breast cancer should be consultant led, but midwifery involvement will help to normalise care.

8. What advice should be given to women wishing to breastfeed following treatment for breast cancer?

Women can be reassured that they can breastfeed from the unaffected breast. ✓

There is no evidence that breastfeeding increases the risk of recurrence in women who have completed treatment for breast cancer. Only one study has reported on survival in relation to lactation,[32] and suggested that breastfeeding was associated with better survival than bottle-feeding.

Evidence level 2+

Breast-conserving surgery may not inhibit lactation in the affected breast, but radiotherapy causes fibrosis, making lactation unlikely.[54–57] There is no evidence that previous chemotherapy affects the safety of breastfeeding.

Evidence level 3

In view of the well-recognised benefits of breastfeeding to the baby,[23] women who wish to breastfeed should be encouraged to do so.[39,58] Midwifery support helps to establish successful lactation.[59]

9. What is the effect of breast cancer treatment on the woman's fertility?

The effect of treatment on fertility should be discussed with all women of reproductive age diagnosed with breast cancer, and written information should be provided. Referral to a fertility specialist should be available. Specialist counselling should be available. ✓

Infertility after treatment is a major concern for young women with breast cancer.[60–63] In an American survey of 657 women diagnosed with breast cancer under the age of 40 years, 57% reported 'substantial concern' about becoming infertile and 29% stated that it influenced their treatment decisions.[63] In this sample, only 51% felt that their concerns had been adequately addressed, and several other authors have noted women's frustration with the paucity of information available.[64–66] Women's preferred source of information on fertility is consultation with a fertility specialist backed up by an information booklet.[64,67]

Evidence level 3

A recent joint working party of the Royal Colleges of Physicians, Radiologists and Obstetricians and Gynaecologists in the UK recommended that people with cancer should be fully informed of potential gonadotoxicity before treatment, and that specialist psychological support and counselling should be available.[68]

Evidence level 4

9.1 What is the effect of adjuvant chemotherapy on fertility?

Chemotherapy-induced gonadotoxicity may cause permanent amenorrhoea with complete loss of germ cells, transient amenorrhoea, menstrual irregularity and subfertility. The degree of gonadotoxicity is dependent on the specific agents used, the cumulative dose administered and the woman's age. Amenorrhoea is reported in 20–70% of premenopausal women with breast cancer,[69] but the rate ranges from less than 5% in women under 30 years of age to 50% in women aged 36–40 years.[70] Alkylating agents such as cyclophosphamide have well-recognised gonadotoxicity,

Evidence level 3

and the classic CMF regimen (cyclophosphamide, methotrexate, 5-fluorouracil) causes a higher incidence of amenorrhoea than anthracycline-based regimens such as FEC (5-fluorouracil, epirubicin, cyclophosphamide).[71] The newer taxanes appear to be less gonadotoxic.[72]

Evidence level 3

9.2 What is the effect of adjuvant hormonal therapy on fertility?

The agents used for adjuvant hormonal therapy do not in themselves cause long-term effects on fertility. Tamoxifen (a selective estrogen receptor modulator) often causes menstrual irregularity and there is an increased risk of endometrial pathology; conception during tamoxifen therapy should be avoided because of potential teratogenicity, and a 'washout period' of 2–3 months is advised. Gonadotrophin-releasing hormone (GnRH) analogues cause amenorrhoea and profound estrogen deficiency; women may find the menopausal symptoms worrying, but the effect is entirely reversible. Trastuzumab is a monoclonal antibody that binds selectively to the HER2 protein expressed by some breast cancers; there is no evidence that it impairs fertility, but pregnancy is not advised during treatment.

9.3 What advice should be given to the woman about postponement of pregnancy before embarking on further pregnancy?

Women are generally advised to postpone pregnancy for at least 2 years after treatment and may be advised to continue tamoxifen for 5 years. However, age is a major determinant of fertility and delay with already poor ovarian function owing to chemotherapy is likely to lead to infertility. Women in their 30s desiring pregnancy may wish to discuss the value of prolonged treatment with tamoxifen and consider discontinuation after 2–3 years. Resuming treatment with tamoxifen after childbearing has not been studied, but it is a reasonable strategy.

9.4 Can fertility be preserved before treatment?

There is a rapidly growing literature on preservation of fertility potential before chemotherapy. At present, only a minority of women of reproductive age undertake fertility-preservation procedures and there are scarcely any data on long-term outcome.

9.4.1 GnRH analogues

There are insufficient level 1 data to support the routine use of GnRH analogues for ovarian protection in estrogen receptor positive breast cancer. ✓

GnRH analogues have therapeutic use in hormone-sensitive breast cancer, as they induce profound ovarian suppression and create a low-estrogen state. Trials are in progress to examine the effect on fertility potential, although there are concerns that concomitant GnRH analogues may lessen tumour response to chemotherapy in estrogen receptor positive breast cancer. There are several observational and phase II studies of the use of GnRH analogues during chemotherapy with the intention of protecting the oocyte pool from depletion.[73] Non-randomised studies in women with breast cancer (total n = 222) are suggestive of benefit.[74–76]

Evidence level 3

A recently reported randomised controlled trial in premenopausal women with breast cancer found that co-treatment with GnRH analogues during chemotherapy lessened the risk of ovarian damage (35/39 resumed menses versus 13/39, $P < 0.001$).[77] The uncertainties can be discussed with the woman by the treating oncologist.

Evidence level 1+

9.4.2 Cryopreservation

Ovarian stimulation for egg or embryo freezing requires careful discussion in light of unknown long-term risks. Modified stimulation regimes should be considered for women with estrogen-sensitive breast cancer. ✓

Embryo cryopreservation is a well established technique with success rates of at least 20% per cycle,[78] although it is possible that success rates may be lower when oocytes are retrieved from women with cancer. The time required for ovarian stimulation and egg harvest may postpone chemotherapy, and there is a small risk of procedural complications such as ovarian hyperstimulation. There is concern that elevated estrogen levels may be deleterious in estrogen receptor positive breast cancer; to minimise this risk, stimulation regimens with tamoxifen or letrozole, usually combined with gonadotrophins, are proposed.[79,80]

Evidence level 2+

Oocyte storage may be offered to women without a partner. Freeze–thaw techniques are rapidly improving, but there have been only a few hundred births worldwide after use of this technique and there are no long-term safety data. Harvesting immature oocytes without requiring a hormone-stimulated cycle is an attractive proposition, but is not an established technique.[81]

Evidence level 3

There are insufficient data to support ovarian tissue storage for fertility preservation in women with breast cancer; this should be offered only in the context of a research trial.

D

Cryopreservation of ovarian cortex or the whole ovary has resulted in a small number of pregnancies after regrafting.[82] This remains an experimental technique and tissue storage regulations in the UK have restricted its use. The need for a surgical procedure is a disadvantage, but this technique does not delay chemotherapy.

Evidence level 3

Every breast oncology service should have a designated pathway for prompt referral to a fertility specialist able to offer assisted conception; service provision should not be dependent on local in vitro fertilistion funding arrangements.

✓

The organisational aspects of the expanding breast oncology service need to be addressed. Prompt referral is essential; preparations for egg retrieval can be instigated during breast cancer diagnostic procedures and surgery to minimise delays in starting systemic treatment. The National Institute for Health and Clinical Excellence[83] recommended universal access to sperm, egg and embryo storage for people undergoing gonadotoxic treatment. However, NHS funding is not available in all areas, and is dependent upon the primary care trust and the local infertility budget. The oncology referral pathway in the cancer network does not necessarily coincide with local in vitro fertilisation arrangements. The joint Royal Colleges working party recommended that adequate funding should be made available.[68]

9.5 Assisted reproduction after treatment for breast cancer

Fertility treatment after chemotherapy is limited by loss of ovarian reserve.[84,85] The stimulation aspect of in vitro fertilisation carries a theoretical risk as it is a hyperestrogenic state, although of shorter duration than pregnancy. Women who have chemotherapy-induced menopause can become pregnant with donated eggs; this requires short-term hormone replacement therapy, which again carries a theoretical risk. Replacement of cryopreserved embryos is also performed in a medicated hormone replacement therapy cycle. Women for whom pregnancy is contraindicated may wish to consider surrogacy.

10. Suggested audit topics

Relatively few women present with pregnancy during or after treatment for breast cancer.

Oncologists may wish to audit:

- what percentage of young women treated for breast cancer have been given information on contraception and future pregnancy
- outcome of referrals to a fertility specialist.

Gynaecologists may wish to audit:

- outcome of referrals for fertility preservation.

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Appendix

Classification of evidence levels

1++ High-quality meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a very low risk of bias

1+ Well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias

1– Meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a high risk of bias

2++ High-quality systematic reviews of case–control or cohort studies or high-quality case–control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal

2+ Well-conducted case–control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal

2- Case–control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal

3 Non-analytical studies, e.g. case reports, case series

4 Expert opinion

Grades of recommendations

A At least one meta-analysis, systematic review or randomised controlled trial rated as 1++ and directly applicable to the target population; or

A systematic review of randomised controlled trials or a body of evidence consisting principally of studies rated as 1+ directly applicable to the target population and demonstrating overall consistency of results

B A body of evidence including studies rated as 2++ directly applicable to the target population, and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 1++ or 1+

C A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results; or

Extrapolated evidence from studies rated as 2++

D Evidence level 3 or 4; or

Extrapolated evidence from studies rated as 2+

Good practice point

✓ Recommended best practice based on the clinical experience of the guideline development group

This guideline was produced on behalf of the Guidelines Committee of the Royal College of Obstetricians and Gynaecologists by:

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The final version is the responsibility of the Guidelines Committee of the RCOG.

The guidelines review process will commence in 2014, unless evidence requires earlier review

