Living With and Beyond Cancer James Lind Alliance Priority Setting Partnership Evidence (all 26 questions)

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Details of resources searched

Systematic reviews
- Joanna Briggs Institute EBP Database. Access via OVID Platform
- The Campbell Collaboration Online Library. https://www.campbellcollaboration.org/library.html
- Database of Promoting Health Effectiveness Reviews (DoPHER) is a specialised register of health promotion reviews. Available from the Evidence for Policy and Practice Information and Co-ordinating Centre (EPPI Centre) http://eppi.ioe.ac.uk/webdatabases4/Intro.aspx?ID=9
- EPPI-Centre systematic reviews which contains a chronological list of EPPI C-Centre reviews. http://eppi.ioe.ac.uk/cms/Default.aspx?tabid=62

Other types of high quality evidence synthesis
- NIHR Journals library. https://www.journalslibrary.nihr.ac.uk/#/
- International prospective register of systematic reviews (PROSPERO). https://www.crd.york.ac.uk/PROSPERO/
- Database of Abstracts of Reviews of Effects (DARE) archives (records up until 31 March 2015). https://www.crd.york.ac.uk/CRDWeb/
- Health Technology Assessment (HTA) database (CRD will maintain and continue to add records until 31 March 2018). https://www.crd.york.ac.uk/CRDWeb/
- Guidance sought on which filters to use to identify systematic reviews by using The InterTASC Information Specialists’ Sub-Group (ISSG) Search Filter Resource for Medline, EMBASE, CINAHL, PsycINFO and AMED
  - https://sites.google.com/a/york.ac.uk/issg-search-filters-resource/filters-to-identify-systematic-reviews
    - Allied & Complementary Medicine (AMED). Access via the OVID platform
    - The Excerpta Medica database (EMBASE). Access via the OVID platform
    - The Cumulative Index to Nursing & Allied Health Literature (CINAHL). Access via the EBSCO platform
    - PsycINFO. Access via the OVID platform
- Hand searching Journals
Guidelines

- NICE Evidence (Search engine for evidence in Health & Social Care). https://www.evidence.nhs.uk/
- Relevant Royal Colleges’ guidance: Royal College of Nursing https://www.rcn.org.uk/
  - Royal College of Physicians https://www.rcplondon.ac.uk/
  - Royal College of General Practitioners http://www.rcgp.org.uk/
  - Royal College of Psychiatrists http://www.rcpsych.ac.uk/
  - Royal College of Radiologists https://rcr.ac.uk/
  - Royal College of Paediatrics and Child Health (RCPCH) http://www.rcpch.ac.uk/rcpch-guidelines-and-standards-clinical-practice
1. What are the best models for delivering long-term cancer care including screening, diagnosing and managing long-term side effects and late-effects of cancer and its treatment (e.g. primary and secondary care, voluntary organisations, self-management, carer involvement, use of digital technology, etc)?

<table>
<thead>
<tr>
<th><strong>H2:</strong> What are the best models for delivering long-term cancer care for people living with and beyond cancer (including primary and secondary care, voluntary organisations, self-management, carer involvement and use of digital technology)?</th>
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<tbody>
<tr>
<td><strong>Keywords:</strong> cancer, support, long-term care, self-management, digital technology, web-based</td>
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<tr>
<td><strong>Exclusions:</strong> Specific areas already answered in previous questions for primary and secondary care models, e.g. exercise, CBT, behavioural interventions, diet, educational interventions, employment</td>
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<tr>
<td><strong>Guidelines</strong> None</td>
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<tr>
<td><strong>Summary of reviews (6 SRs)</strong></td>
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| | **Web-based self-management support interventions:** We searched for web-based interventions designed to help cancer survivors manage their symptoms and the side effects of cancer treatments, which yielded 37 studies that were systematically reviewed. For the meta-analyses, five articles were selected for fatigue, seven for depression, five for anxiety, and five for overall quality of life. The most popular mode of intervention delivery was "peer-to-peer access" in the communicative functions category, followed by "the use of an enriched information environment" in the automated functions category. The effects across all outcome measures were small to moderate compared to standard care. Healthcare providers could use information technologies to support self-management among cancer survivors based on their needs across the cancer care continuum (Kim and Park 2015). **Telehealth:** Across 22 included papers, 3 analytical themes emerged, each with 3 descriptive subthemes: (1) influence of telehealth on the disrupted lives of cancer survivors (convenience, independence, and burden); (2) personalized care across physical distance (time, space, and the human factor); and (3) remote reassurance-a safety net of health care professional connection (active connection, passive connection, and slipping through the net). Telehealth interventions represent a convenient approach, which can potentially minimize treatment burden and disruption to cancer survivors' lives. Telehealth interventions can facilitate an experience of personalized care and...
reassurance for those living with and beyond cancer; however, it is important to consider individual factors when tailoring interventions to ensure engagement promotes benefit rather than burden. Telehealth interventions can provide cancer survivors with independence and reassurance. Future telehealth interventions need to be developed iteratively in collaboration with a broad range of cancer survivors to maximize engagement and benefit (Cox et al 2017).

Health coaching
The authors reviewed 2210 references and selected 12 studies (6 randomized trials and 6 pre-post). These studies included 1038 cancer survivors, mean age 57.2 years, with various type of cancers: breast, colorectal, prostate, and lung. Health coaching was associated with improved quality of life, mood, and physical activity but not self-efficacy. In cancer survivors, health coaching improved quality of life and supported patient capacity by several mechanisms, suggesting an important role for "Capacity Coaching." Future interventions that improve self-efficacy and patients' environments of care are needed. Capacity Coaching may improve health and quality of life of cancer survivors (Barakat et al 2018).

Summary of other reviews (2 NRs)
Though there is no evidence supporting a single model of cancer survivorship care, studies have shown that cancer survivors receiving care from a primary care provider and an oncologist are more likely to be up-to-date on cancer-related and non-cancer related preventive services (Garcia-Jimenez et al 2017).

Digital interventions
Social media for breast cancer survivors: Online groups and communities may improve the well-being of breast cancer survivors by providing opportunities to engage with wider social networks, connect with others navigating similar cancer experiences, and obtain cancer-related information. Researchers should consider the potential role of social media in addressing the unmet needs of breast cancer survivors, and particularly the implications for clinical and public health practice (Falisi et al 2017).

Summary of primary research
Digital interventions
Online communities: A theory developed explaining how individuals 'navigated' the experience of cancer using online cancer communities. Online advice and information led participants on a 'journey to become informed'. Online friendships normalised survivorship and cast participants on a 'journey to recreate identity'. Participants navigated a 'journey through different worlds' as they discovered relevant and hidden communities. This theory highlights virtual paths people affected by cancer can take to self-manage their experience of the disease. Online community experiences can be improved by promoting online evaluation skills and signposting visitors to bereavement support. Cancer survivors can benefit through both lurking and posting in online communities. However, individuals risk becoming distressed when they befriend individuals who may soon die. Additionally, people affected by rarer cancers can struggle to find shared experiences online and may need to look elsewhere for support (Harkin et al 2017).

Conclusions
Partially answered: self-management intervention, online communities, health coaching, employment, telehealth

From H1
Fully answered: Home-based multidimensional survivorship programmes for breast cancer survivors
Partially answered: Macmillan cancer recovery package, Survivorship care plans (Breast cancer)
<table>
<thead>
<tr>
<th>Authors / Year</th>
<th>Study</th>
<th>Systematic Reviews</th>
<th>Primary Research</th>
<th>Guidelines</th>
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<tr>
<td>Garcia-Jimenez et al. 2017</td>
<td>Cancer Survivors – Who are they, what are their needs, and how can medical providers meet these needs? <a href="https://www.clinicalcorrelations.org/?p=13623">https://www.clinicalcorrelations.org/?p=13623</a></td>
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**SELF-MANAGEMENT INTERVENTIONS**

**DIGITAL INTERVENTIONS**

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<th>Authors</th>
<th>Title</th>
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<th>References</th>
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**Further comments**
Carer involvement in survivorship not searched  
Role of voluntary organisations in survivorship not searched

**Suggestions for additional searches**
Carer involvement in survivorship  
Role of voluntary organisations in survivorship
2. How can patients and carers be appropriately informed of cancer diagnosis, treatment, prognosis, long-term side-effects and late effects of treatments, and how does this affect their treatment choices?

**T1: How can patients and carers be appropriately informed of the long-term side-effects and late effects of treatments, and how does this affect their treatment choices?**

**Keywords:** Cancer OR chemotherapy or radiotherapy OR radiation AND Inform* AND effects OR long OR late OR delay* (AND decision making OR decisions OR choice*)

**Exclusions:** Late effects of childhood cancer

**Generic guidelines on late effects**

Macmillan Cancer Support 2013:

Excessive information on consequences of cancer and its treatment at the point of cancer diagnosis or treatment choice can be a burden to some patients, so a proactive approach to personalised assessment of information needs and provision at multiple time points should be used.

- The provision of high-quality timely personalised information is a fundamental element of cancer care (including follow up in primary and community care) and one that can be improved at little or no cost, resulting in a better patient experience, fewer symptoms, fewer crises and better quality of life.
- There is an urgent need for more research on the best strategies for communication about the risk of consequences of cancer and its treatment and their management, within an overall approach that prepares and supports people when living with and beyond cancer.

**Summary of other types of review (x 1 NR)**

**Head and neck cancer patients: Information on side effects of radiation treatment**

The review of literature revealed that that patients’ and relatives’ desire for information was centered on practical issues, such as the implications of the different forms of treatment, their side effects and how they could be managed. Tools such as the Satisfaction with Cancer Information Profile (SCIP) were developed to measure patient satisfaction of information. However, it was found that these tools did not focus much on radiation-related side effects. For the studies that did focus on radiation-related side effects, it was found that data collection was done several months after the end of treatment, making it possible that the patients’ ability to recall experiences was compromised (Sivanrupan 2016)

**Summary of primary research (x1)**

**Long-term and late effects of pelvic radiotherapy**

As more patients survive cancer for longer term, the long-term and late effects of treatments become increasingly important issues for cancer survivors and providing information to enable survivors to recognise and manage them becomes an increasingly pressing challenge for health care professionals. The aim of this study was to explore the experiences of cancer survivors regarding information given on potential long-term and late effects of pelvic radiotherapy. Semi-structured interviews were conducted with 28 cancer survivors who had had radiotherapy to the pelvic area for a range of cancers 1-11 years previously. Participants were recruited using maximum variation sampling from a larger questionnaire survey of patients treated at one hospital. Interviews were recorded, transcribed and analysed using Framework. Participants recognised the value of information to reassure and to inform action but also its potentially undesirable effects to frighten or raise anxieties about future problems and its inherent limitations in meeting their wider needs. They identified the timing, amount of information and context in which it was given as...
of particular importance. Information based on personal experience was also valued. These findings highlight the importance of appropriate, individualised information during treatment, at hospital discharge and subsequently in primary care (Boulton et al 2015)

Conclusions
Not answered

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<tr>
<th>Authors / Year</th>
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SR – Systematic review, N= narrative review

Further comments
(see comments on P1_P7 for list of late; long term side effects)

Suggestions for additional searches
Search by specific side effects and cancers listed in P1_P7 AND Inform*

Out of date

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A randomized clinical trial with 152 patients was conducted to examine the effects of an informational intervention on the severity of side effects resulting from radiation therapy for prostate cancer. We also examined negative affect both as a predictor and as an outcome variable. The informational intervention, given to patients at the first and fifth treatments, was based upon self-regulation theory and provided patients with specific, objective information about what to expect during their radiation treatments. Patients in the comparison group received general information at the same point in time. Negative affect was measured using the Profile of Mood States (POMS) prior to the intervention and at the last treatment. The severity of side effects for each individual was assessed at their last treatment. The results showed that patients in the informational intervention group reported significantly fewer problems with sleep and less fatigue (marginally significant) than those in the comparison group. Negative affect was not influenced by group assignment. Baseline negative affect was not related to symptom development, although the development of side effects was associated with an increase in negative mood. The results suggest that patients could benefit from increased knowledge about what to expect during their radiation treatments.

**H10: What are the most effective ways to give people information about their diagnosis, treatment, prognosis and living with and beyond cancer?**

**Keywords:** Cancer AND inform* OR communication AND diagnosis OR treat* or manage* or prognosis / Cancer AND inform* AND effect* OR effic*

**Exclusions:** None

**Guidelines**

Macmillan cancer support. 2015

We want to see national resources and guidance in place that support local approaches to improving the quality, format and accessibility of holistic information for people affected by cancer

Our recommended ways to achieve this are:

a) NHS England should explore the extent to which the Information Standard's benefits are recognised by health professionals and people affected by cancer, and promote its use more.

b) NHS England should issue a framework detailing what information should be produced nationally and locally. – We believe there may be merit in NHS England building on the model of the information prescriptions service by commissioning an online central repository of high-quality national information resources on NHS Choices. – This should then be promoted to people affected by cancer and professionals. – The repository should be accompanied by guidance about its use.

c) CCGs and hospital trusts should ensure health professionals have access to, and utilise, up-to-date local information directories about the local services and support options available. – Macmillan suggests CCGs commission, and hospital trusts appoint, an information lead to collate and maintain a directory of local services for people with cancer and their carers.

**Summary of reviews** (x2 SR)

**Treatment decisions for prostate cancer patients**

Although each prostate cancer patient is unique, studies suggest that most patients seek extensive information to help inform their treatment decisions. This may happen before, during, and after the treatment choice is made. Given the amount of information patients may access, it is important that they also establish the trustworthiness of the various types and sources of information. When information conflicts, patients may be unsure about how to proceed. Open collaboration between patients and their health care providers can help patients manage and navigate their concerns so that their values and perspectives are captured in their treatment choices (Kandasamy et al. 2017)
**Internet and computer-based patient education programmes for prostate cancer patients**
The Internet or computer-based programmes had a positive impact on prostate cancer patient education. Most papers reported that the programmes were beneficial, but few presented data from studies with rigorous research methodologies to support these claims (Salonen et al 2014).

**Summary of other types of review (x1 Discussion article/review)**

**Educational tools for radiation therapy patients**
With increasing rates of cancer patients undergoing radiation therapy, the treatment itself can cause patients significant amounts of anxiety and distress. This can be attributed to the diagnosis of the disease, lack of knowledge of what radiation therapy is, expectations and management of side effects, and the lack of knowledge of supportive care for patients and their families. Providing patients with effective educational tools to meet the informational needs of cancer patients undergoing radiation therapy can empower patients and allow them to participate in treatment decision-making and their own healthcare. This discussion paper will evaluate several studies on the psychological impact of cancer patients undergoing radiation therapy and how video material can effectively meet the informational and educational needs of this patient population group. The authors concluded that educational videos have established a positive impact on increasing knowledge, understanding and making informed treatment decisions, reducing stress, coping, and enhancing self-care practices optimizing psychological well-being (Nathoo 2017).

**Summary of primary research (x2)**

**Treatment decision-making information for localized prostate cancer patients**
The current study reports findings from evaluation research conducted to identify how online prostate cancer treatment decision-making information can be both improved and more effectively disseminated to those who need it most. A multi-method, multi-target approach was used and guided by McGuire’s Communication Matrix Model. Focus groups (n = 31) with prostate cancer patients and their family members, and in-depth interviews with physicians (n = 8), helped inform a web survey (n = 89). Results indicated that physicians remain a key information source for medical advice and the Internet is a primary channel used to help make informed prostate cancer treatment decisions. Participants reported a need for more accessible information related to treatment options and treatment side effects. Additionally, physicians indicated that the best way for agencies to reach them with new information to deliver to patients is by contacting them directly and meeting with them one-on-one. Advice for organizations to improve their current prostate cancer web offerings and further ways to improve information dissemination are discussed (Silk et al 2013).

**Information about the screening process for colorectal cancer patients**
Detailed information about the invasive follow-up test has a negative effect on individuals' screening participation decisions in non-invasive colorectal cancer screening campaigns. This result poses new challenges for policymakers who aim not only to increase uptake but also to provide full disclosure to potential screening participants (Benning et al 2014).

**Treatment process videos for radiation therapy patients**
Statistical analysis found 98% of patients reported that the video was useful in meeting one or more of the learning objectives. Forty-nine percent of patients also reported a reduction in fear and anxiety as a result of watching the video. Patients reported subsequent review of videos at home (39%), primarily to explain treatment processes to loved ones (46%). Conclusion: The combination of real footage and 3D visualisation software assisted in meeting learning objectives regarding the
treatment process. Standardised videos provided consistency of information provision to patients and facilitated multiple viewings of the video if desired (Williams et al. 2017)

Conclusions
Not met between 2013 and 2018 but answered partially in 2007 SR and other older SRs (see below for full details)

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<thead>
<tr>
<th>Authors / Year</th>
<th>Study</th>
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<td>Author(s)</td>
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<tr>
<td>Williams et al. 2017</td>
<td>Meeting radiation therapy patients informational needs through educational videos augmented by 3D visualisation software.</td>
<td>X</td>
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<tr>
<td>Salonen et al. 2014</td>
<td>Educational benefits of Internet and computer-based programmes for prostate cancer patients: a systematic review.</td>
<td>X</td>
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Further comments
Older research

Prouse 2010. The impact of methods of information on chemotherapy-related side effects. Clinical Journal of Oncology Nursing (CLIN J ONCOL NURS), Apr2010; 14(2): 206-211. A systematic review of the literature regarding the effectiveness of various methods of information given to patients with cancer receiving chemotherapy education revealed that psycho-educational interventions minimized the intensity and impact of treatment-related fatigue on daily life in the short term for patients undergoing chemotherapy. Studies that investigated efficacy of interactive multimedia devices revealed no statistical improvement in information recall, quantity of self-care activities, and fatigue levels between groups. Three of the multimedia studies focused on anxiety and depression trends before and during treatment, with mixed results. Several studies revealed no significant difference in either anxiety or depression. Others concluded that patients who viewed video information in conjunction with standard care were less anxious and depressed. Combined, these studies revealed that multimedia devices did not improve recall of information and that psycho-educational interventions were able to improve the impact of treatment-related side effects, namely fatigue, in the short term. This suggests that the educational needs of patients with cancer require a complex series of factors that impact the individual's ability to understand how and when to initiate recommended self-care strategies.

The interventions used were described as interactive computer or multimedia programs and use of the Internet. The methodological solutions of the studies varied. The effects of the studies were diverse except for knowledge-related issues. Internet or interactive computer-based patient education programs in the care of breast cancer patients may have positive effect increasing breast cancer knowledge. Conclusion; The results suggest a positive relationship between the Internet or computer-based patient education program use and the knowledge level of patients with breast cancer but a diverse relationship between patient's participation and other outcome measures.

Coulter 2007. Evidence on the effectiveness of strategies to improve patients' experience of cancer care. Cancer reform strategy patients experience working group
The Patient Experience Working Group has made a number of recommendations for improving patients' experience of cancer care, including the following:
• Providing information at key points along the care pathway
Research points to the importance of tailoring information to patients’ needs and characteristics. In comparison to general information, personalised materials tend to produce better health and service-related outcomes and are more highly valued by patients themselves. Computer-based systems are one means by which a tailored approach to consumer health information provision may be achieved, ideally using the patient’s medical record as a prompt to deliver the right information at the right time. Written health information (leaflets, booklets) can be helpful to reinforce oral communication in medical consultations, as can material in other formats, including audiotope and videotape. Mass media communications can be used to reach groups unobtainable by other means and, if carefully targeted, can have a beneficial effect. Strategies for reducing inequalities by targeting information to people with low levels of health literacy have not been well studied, but there is some evidence of potential benefit.

The research indicates that many patients want more information than they currently receive and that health professionals tend to overestimate the amount of information they supply. Leaflets on their own have not been shown to improve health behaviour or health status, but written information used as an adjunct to professional consultation and advice has been shown to improve patients’ health knowledge and outcomes, particularly when it is personalised to the individual. Alternative format resources, such as websites, can also improve knowledge and studies have demonstrated high user satisfaction and beneficial effects on self-efficacy and health behaviour. The internet is a valuable source of health information, but the quality and reliability of health websites is variable. Harm arising from unreliable websites may be under-reported. Although the digital divide remains a problem, there is some evidence of greater health benefit for disadvantaged groups when access barriers are overcome, for example by providing free computers. Initiatives designed to specifically target low literacy groups have had mixed results, with some studies showing beneficial effects on knowledge and behaviour, but there have been relatively few attempts to test the effect of these initiatives on reducing health inequalities. Targeted mass media campaigns have been shown to increase awareness, but the effects may be short-lived. There is some evidence of impact on utilisation of services, e.g. uptake of cervical cancer screening, but little evidence of beneficial effect on health behaviour apart from smoking, where studies have shown that the mass media may be effective in reducing smoking rates among young people.

Based on the following evidence
There is increasing evidence to suggest that patients with cancer require more information about their disease and its consequences than they receive. In an attempt to address these needs, a variety of methods have been used to facilitate the passage of information from health professionals and other cancer information sources to cancer patients and their families. These include written material, telephone help-lines, teaching and audiovisual aids. Although these efforts have been well received, little attention has been given to the effectiveness of the methods employed. The aims of this paper were to systematically review randomized controlled trials that have evaluated methods of information-giving to cancer patients and their families. Relevant literature was identified through computerized databases, Internet cancer sites and bibliography searches. Multiple reviewers independently analysed the methodological quality of the papers according to agreed criteria. From this process, 10 studies were identified. Interventions ranged from written information to audiotapes, audiovisual aids and interactive medium. Individually tailored methods such as patient care records and patient educational programmes were also reviewed. The evidence indicated that the interventions had positive effects on a number of patient outcomes, such as knowledge and recall, symptom management, satisfaction, preferences, health care utilization and affective states. This was above and beyond the usual care provision. In the majority of studies the interventions had no effect on psychological indices. Furthermore, the review highlighted that certain methods should be based on individual preferences for information rather than uniformly administered.


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Sowden and Arblaster (2000) conducted a Cochrane systematic review of mass media interventions for preventing the uptake of smoking in young people. Six studies met the inclusion criteria, all using a controlled trial design. Two of the studies concluded that mass media was effective in influencing smoking behaviour. Both campaigns described in these studies had a solid theoretical basis, used formative research in designing campaign messages, and were relatively intensive over longer periods of time.


Black and colleagues (2002) conducted a systematic review of the literature on the effectiveness of community-based strategies to increase women’s participation in cervical cancer screening. Nineteen studies were included in the review; mass media campaigns were most commonly evaluated, either alone or in combination with other interventions. Seventeen of the 19 studies measured outcomes in terms of smear rates and, of these, 12 reported statistically significant improvements compared to controls (although in some studies the actual difference was small). Of the four studies of mass media campaigns alone, the only one that was effective targeted a definite sub-population with tailored material. All five studies that combined mass media campaigns with other interventions were effective at increasing smear rates or early cancer detection.


Eysenbach (2003) conducted a systematic review of literature on cancer patients’ use of the internet and its impact on health outcomes. Twenty four surveys were identified, which included responses from a total of 8,679 patients with cancer. These covered four types of internet use: communication (email), community (virtual support groups), content (health information) and ecommerce. From the available evidence, the effect of electronic support groups is unclear, although recent studies suggest they can increase perceived social support and decrease loneliness. Internet information has positive effects on self-efficacy and task behaviour, empowers patients to make health-related decisions and improves confidence in the doctor-patient encounter. However, patients reported feeling overwhelmed by the sheer volume of internet output and confused by conflicting medical information about cancer treatments.


Gaston and Mitchell (2005) carried out a systematic review of studies evaluating approaches to providing information to patients with advanced cancer. They concluded that consultation tapes have a small but significant effect on patients’ knowledge and satisfaction. Summary letters can also be effective, but patients tend to prefer the audiotape format. There is some evidence that written information can decrease levels of anxiety. Take home materials can also be shared with friends and family, thereby increasing levels of practical and emotional support. The added effect of videotape information is uncertain.


Jones and colleagues (2006) compared various different approaches to delivering information to cancer patients. They were particularly interested in the impact of information on psychological well being. Four hundred patients were recruited, and were randomised into eight groups defined by binary factors (personalised versus general information; patient interactively selecting information versus automatic production; and receive versus not receive anxiety management advice). The quantity of information that was automatically produced was much higher than the amount that patients chose for themselves. Participants who received automatically produced booklets were more likely to find the information useful and more satisfied with what they had received, but some found the booklets overwhelming. More of the patients who received personalised materials felt these told them something new and of relevance to their situation. They were also more likely to show the information to others and to say that it helped them in discussions about their illness and treatment. There was no significant difference between the three groups in relation to changes in anxiety or depression.

Suggestions for additional searches
Search for specific information strategies – leaflets, websites, written material, telephone helplines, audio visual aids, educational videos, internet
3. How can care be better co-ordinated for people living with and beyond cancer who have complex needs (with more than one health problem or receiving care from more than one specialty)?

H7: How can care be better co-ordinated for people living with cancer and beyond with complex needs (with more than health problem or receiving care from more than one specialty)?

Keywords: complex need* or comorbid* or coexisting condition*/illness* AND treat* or manage* OR care AND cancer or carcinoma

Exclusions: Prevalence, diagnosis, screening, paediatrics, impact of comorbidities on treatment

Guidelines
None

Summary of reviews (x1 SR)
Comorbidity is very common among patients with cancer. Multidisciplinary team meetings (MDTs) are increasingly the context within which cancer treatment decisions are made internationally. Little is known about how comorbidity is considered, or impacts decisions, in MDTs. A systematic literature review was conducted to evaluate previous evidence on consideration, and impact, of comorbidity in cancer MDT treatment decision making. Twenty-one original studies were included. Lack of information on comorbidity in MDTs impedes the ability of MDT members to make treatment recommendations, and for those recommendations to be implemented among patients with comorbidity. Where treatment is different from that recommended due to comorbidity, it is more conservative, despite evidence that such treatment may be tolerated and effective. MDT members are likely to be unaware of the extent to which issues such as comorbidity are ignored. MDTs should systematically consider treatment of patients with comorbidity. Further research is needed to assist clinicians to undertake MDT decision making that appropriately addresses comorbidity. If this were to occur, it would likely contribute to improved outcomes for cancer patients with comorbidities (Stairmand et al. 2015).

Summary of primary research (x3)
Service targets that focus resources solely on the presenting disease can disadvantage older patients with complex health and social care needs that extend beyond this primary diagnosis. Care should be taken to ensure time-based targets do not disincentivise thorough and timely assessment that can lead to the formulation of treatment plans tailored to individual needs and circumstances (Bridges et al. 2015)

The purpose of this study is to investigate provider specialty, care coordination, and cancer survivors' comorbid condition care.

Methods: This retrospective cross-sectional Surveillance, Epidemiology, and End Results (SEER)-Medicare study included cancer survivors diagnosed in 2004, 2-3 years post-cancer diagnosis, in fee-for-service Medicare. We examined (1) provider specialties (primary care providers (PCPs), oncology specialists, other specialists) visited post-hospitalization, (2) role of provider specialties in chronic and acute condition management, and (3) an ambulatory care coordination measure. Outcome measures covered (1) visits post-hospitalization for nine conditions, (2) chronic disease management (lipid profile, diabetic eye exam, diabetic monitoring), and (3) acute condition management (electrocardiogram (EKG) for congestive heart failure (CHF), imaging for CHF, EKG for transient ischemic attack, cholecystectomy, hip fracture repair). Results: Among 8661 cancer survivors, patients were more likely to visit PCPs than oncologists or other specialists following hospitalizations for 8/9 conditions. Patients visiting a PCP (vs. not) were more likely to receive recommended care for 3/3 chronic and 1/5 acute condition indicators. Patients visiting another specialist...
(vs. not) were more likely to receive recommended care for 3/3 chronic and 2/5 acute condition indicators. Patients visiting an oncology specialist (vs. not) were more likely to receive recommended care on 2/3 chronic indicators and less likely to receive recommended care on 1/5 acute indicators. Patients at greatest risk for poor coordination were more likely to receive appropriate care on 4/6 indicators. Conclusions: PCPs are central to cancer survivors’ non-cancer comorbid condition care quality. Implications for Cancer Survivors PCP involvement in cancer survivors’ care should be promoted (Snyder et al. 2015)

**Diabetes:** Patients with diabetes and cancer have higher mortality and morbidity rates, and are more likely to be hospitalized during treatment. In addition, they often prioritize cancer treatment over self-management of diabetes. Objectives: This research aims to identify the issues regarding the management of diabetes in patients with cancer by examining the perspectives of oncology providers, nurses, and patients. Methods: This study used six focus groups of oncology providers, nurses, and patients with preexisting diabetes who received chemotherapy for a solid tumor or lymphoma. Participants were recruited from two outpatient cancer centers in Michigan. All focus group discussions were audio recorded and transcribed, and thematic analysis was conducted to identify common themes. Findings: Three overarching themes were identified by patients, nurses, and oncologists: prioritization and responsibility, care coordination, and health/self-management. This study highlighted areas for improvement in the management of patients with preexisting diabetes being treated with chemotherapy. Additional research is needed to test interventions that improve care coordination and self-management in this population (Goebel et al. 2016)

**Conclusions**
Not answered

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<th>Authors / Year</th>
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<th>Systematic Reviews</th>
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<tr>
<td>Bridges et al. 2015</td>
<td><strong>Cancer treatment decision-making processes</strong> for older patients with <strong>complex needs:</strong> a qualitative study. BMJ Open. 14;5(12):e009674 <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4679903/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4679903/</a></td>
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<td>Snyder et al. 2015</td>
<td><strong>Comorbid condition care</strong> quality in <strong>cancer survivors:</strong> role of primary care and specialty providers and care coordination. <em>Journal Of Cancer Survivorship: Research And Practice</em>: Vol. 9 (4), pp. 641-649 <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4550556/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4550556/</a></td>
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SR – Systematic review, N= narrative review

**Further comments**
We did a search on diabetes and cancer to see what we would get

**Suggestions for additional searches**
Specific complex needs – dementia, depression, diabetes, heart disease etc

4. What causes **fatigue** in people living with and beyond cancer and what are the best ways to manage it?

<table>
<thead>
<tr>
<th>S1a: What causes fatigue in people living with and beyond cancer</th>
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<tr>
<td><strong>Keywords</strong> Cancer AND fatigue AND Cause(s) OR Risk OR mechanism OR aetiology OR pathophysiology OR factor(s)</td>
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<td><strong>Exclusions:</strong> None</td>
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<td><strong>Guidelines</strong> None</td>
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<tr>
<td><strong>Summary of reviews</strong> (x1 meta-analysis)</td>
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<td><strong>Breast cancer:</strong> Risk factors of severe fatigue were higher disease stages, chemotherapy and receiving the combination of surgery, radiotherapy, and chemotherapy, both with and without hormone therapy. Having a partner, receiving only surgery, and surgery plus radiotherapy decreased the risk (Abrahams et al. 2016)</td>
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<td><strong>Summary of other types of review</strong> (x1 NR across 2 publications)</td>
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<td>A growing number of longitudinal studies have identified risk factors for fatigue during and after cancer treatment. These include genetic risk factors (SNPs in inflammation-related genes), psychosocial factors (pre-treatment fatigue, depression, and sleep disturbance, dysfunctional coping and appraisal processes, loneliness, early life stress) and biobehavioral factors (physical inactivity, elevated body mass index). Many of these factors are associated with inflammatory processes, including depression, sleep disturbance, physical inactivity, body mass index, early life stress, and loneliness. Individuals with these risk factors may already have elevated inflammatory activity at the time of diagnosis, increasing risk for pre-treatment fatigue. In addition, these factors may increase the inflammatory response to diagnosis and treatment. The mechanisms through which these and other risk factors influence fatigue are an important topic for future research (Bower 2014)</td>
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<td>It may also be useful to distinguish between factors that increase risk for fatigue during treatment (precipitating factors) and those that lead to its persistence in the post-treatment period (perpetuating factors). To date, studies have primarily focused on the period during and immediately after treatment, or in the years after treatment completion. Longitudinal studies that follow patients from pre-treatment into the survivorship period will illuminate which factors are most important for acute and more persistent fatigue. This will help to identify appropriate targets for intervention at different stages of the cancer trajectory (Bower 2014)</td>
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<td>The evolving literature on cancer-related fatigue increasingly supports the hypothesis that inflammation is associated with fatigue symptoms in cancer populations. The evidence linking inflammation and fatigue in cancer survivors is particularly strong, with consistent findings emerging from large, well-controlled studies of breast cancer survivors. This review also highlighted several new frontiers in research on cancer-related fatigue. There is growing interest in neural mechanisms underlying inflammation-related fatigue, with a focus on dopaminergic pathways. However, there has been minimal examination of these processes in cancer patients and survivors. At the methodological level, we have found stronger links between cancer-related fatigue and downstream markers of inflammatory activity (e.g., sTNF-RII, IL-1RA, CRP) as compared to noisier instantaneous plasma cytokine levels (e.g., IL-1β, IL-6). These downstream markers may provide a more robust, stable, and sensitive marker of systemic inflammation, facilitating the detection of relationships with fatigue. Thus, we recommend their incorporation in future research, particularly studies with post-treatment survivors (Bower and Lamkin 2013)</td>
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Summary of primary research

Breast cancer

Approximately one in four breast cancer sufferers suffer from severe fatigue. Depressive symptoms and inflammation were independent risk factors for cancer-related fatigue at 1-year post-radiotherapy, and thus represent independent treatment targets for this debilitating symptom (Xiao et al 2017).

Conclusions

Fully answered for all cancers
Partially answered for breast cancer

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Further comments

Current understanding of the aetiology of cancer-related fatigue is poor. It is likely that it is a result of a complex interaction of multiple factors related to both the disease process itself and side effects of treatment, but it is also likely to be influenced by a range of other factors such as medications, nutrition, sleep disturbance, pain, anxiety, and depression (Purcell et al 2009).


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Suggestions for additional searches
Search using the specific factors that are listed in the study above

S1b: What are the best ways to manage it (fatigue)?

Keywords: Cancer AND fatigue

Exclusions: None

Guidelines (x2)
Recommendations focused on patients who have completed active treatment or are considered in clinical remission. Treat underlying causes, moderate physical activity after cancer treatment with PT and lymphedema referrals as needed (meta-analysis, systematic review, [randomized controlled trial [RCT]; 10 cited), cognitive behavioural therapy (meta-analysis, RCT, systematic reviews; 6 cited), psychoeducational therapies (systematic, RCT; 3 cited), psychosocial services, mindfulness-based interventions (RCT; 3 cited), yoga (RCT; 2 cited), acupuncture (RCT; 2 cited), psychostimulants/wakefulness agents (limited evidence in patients who are post-treatment disease-free). Additional areas in which research needed include biofield therapies, massage, music therapy, relaxation, Reiki, Qigong, ginseng, and vitamin D (Bower et al 2014).

NCCN guidelines (2016) recommendations include: Energy conservation, Physical activity, Cognitive behavioural therapy (CBT) for sleep shown to be effective and counselling.

Summary of reviews (x3 Cochrane SRs, x 2 other SRs)

Exercise
Exercise interventions included aerobic, resistance, flexibility, and combinations of these. Interventions included supervised, unsupervised, home-based, hospital- or other setting–based, and group or individual exercise sessions. Moderate quality evidence that exercise had a positive effect on fatigue compared to usual care existed (standard mean deviation = 0.32, 95% confidence interval [0.13, 0.52]). A combination of aerobic and resistance provided the largest treatment effect. Aerobic intensity was negatively related to treatment effect. No relationships existed between resistance exercise and treatment effect (Dennett et al 2016).
Findings show a moderate effect of exercise on fatigue among women receiving adjuvant treatment for breast cancer (Furmanak et al. 2016: Cochrane SR)
Structured exercise can have a positive effect on cancer related fatigue. The effect may be greater when activity is professionally led and after active treatment (Tian et al 2016).

Educational interventions
Educational interventions may have a small effect on reducing fatigue intensity, fatigue’s interference with daily life, and general fatigue, and could have a moderate effect on reducing fatigue distress. Educational interventions focused on fatigue may also help reduce anxiety and improve global quality of life, but it is unclear what effect they might have on capacity for activities of daily living or depressive symptoms. Additional studies undertaken in the future are likely to impact on our confidence in the conclusions (Bennet et al 2016: Cochrane SR).

Psychosocial interventions
We found little evidence around the benefits of psychosocial interventions provided to reduce fatigue in adult patients with incurable cancer receiving cancer treatment with palliative intent. Additional studies with larger samples are required to assess whether psychosocial interventions are beneficial for addressing fatigue in patients with incurable cancer (Poort et al 2017: Cochrane SR).

**Conclusions**

Fully answered for exercise

Partially answered for educational and psychosocial interventions

For further info also see https://www.ons.org/practice-resources/pep/fatigue

This resource last updated 2017 and includes recommendations for practice, likely to be effective, benefits balanced with harm and effectiveness not established for all management strategies for fatigue

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<td>Oncology Nurses Society. 2017</td>
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<td>Evidence based synopses</td>
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5. What are the short-term and long-term psychological impacts of cancer and its treatment and what are the most effective ways of supporting the psychological wellbeing of all people living with and beyond cancer, their carers and families?

Y6a: What are the short and long-term psychological impacts of cancer and its treatment at all points on the cancer journey?

Keywords: psychological (distress, outcomes, functioning, adjustment, health, burden, wellbeing) OR emotional AND cancer

Exclusions: None

Guidelines (x1) / Impact Brief (x1)

Psychological distress: in cancer patients is a significant and ongoing problem. Emotional and psychological long-term side effects of cancer and its treatment include depression, anxiety, memory problems, difficulty concentrating, sexual problems and reduced social skills (Macmillan Cancer Support, 2014?)

The benefits of effective psychological support include reduced depression, anxiety and pain, improved self management and coping skills, helping patients feel more in control and improving their quality of life (Macmillan Cancer Support, 2018; last reference dated 2014).

Possible long-term consequences of cancer and its treatment: Psychological and social consequences (Figure 1, page 18)

Fear of cancer recurrence; Fear of future HPV infection; Body image issues; Lack of confidence; Memory/concentration problems; Impact on family/friends

Financial problems; Isolation Anxiety; Stress; Depression; Change of outlook on life; Unable to work or continue education

Embarrassment or difficulty coping, which can affect relationships, work and day to-day life in many ways (Macmillan Cancer Support, 2013).

Psychosocial consequences (more information the full document)

Psychological morbidity, such as anxiety and depression, is a major problem that arises from the many significant changes experienced by individuals and the people around them resulting from a diagnosis of cancer and the effects of treatment. These psychosocial impacts can often be seen as ‘adjustment disorders’ as they represent a difficulty in adjusting to the functional and existential crisis that cancer represents. Psychosocial consequences are not just about emotions, but arise from the challenge of adapting to the physical and functional problems associated with cancer and its treatment. People with a pre-existing mental health diagnosis are at higher risk of psychosocial problems (Macmillan Cancer Support, 2013).

Estimated prevalence of common psychosocial consequences: Table 4B: Estimated prevalence of common psychosocial consequences of cancer and its treatment (Macmillan Cancer Support, 2013).

Summary of reviews (x1 SR)

Testicular cancer survivors

Testicular cancer survivors’ mean anxiety levels were higher than in the general population, while mean depression and distress were no different. Clinically significant anxiety (=1 in 5) and to a lesser extent distress (=1 in 7), but not depression, were more prevalent in Testicular cancer survivors than the general population. Approximately 1 in 3 TC survivors experienced elevated fear of cancer returning. Poorer psychological outcomes were more common among TC survivors who were single, unemployed/low socio-economic status, suffering from co-morbidities, experiencing worse symptoms/side effects, and using passive coping strategies. Authors conclusions: many TC survivors do not experience significant psychological morbidity, but anxiety and FCR are prevalent. Inadequate coping resources (eg, low socio-
economic status and social support) and strategies (eg, avoidance) and greater symptoms/side effects were associated with poorer outcomes. Theoretically driven prospective studies would aid understanding of how outcomes change over time and how to screen for risk. Age and gender appropriate interventions that prevent and manage issues specific to TC survivors are also needed (Smith et al 2017)

Summary of other reviews (x1 rapid review, x1 NR)

Adult cancer survivors
To establish what is known regarding the psychological and social problems faced by adult cancer survivors (people who are living with and beyond a diagnosis of cancer) and identify areas future research should address. A rapid search of published literature reviews held in electronic data bases was under taken. Inclusion and exclusion criteria, and removal of duplicated papers, reduced the initial number of papers from 4051 to 38. Twenty-two review papers were excluded on grounds of quality and 16 review papers were selected for appraisal. The psychological and social problems for cancer survivors are identified as depression, anxiety, distress, fear of recurrence, social support/function, relationships and impact on family, and quality of life. A substantial minority of people surviving cancer experience depression, anxiety, and distress or fear associated with recurrence or follow up. There is some indication that social support is positively associated with better outcomes. Quality of life for survivors of cancer appears generally good for most people, but an important minority experience a reduction in quality of life, especially those with more advanced disease and reduced social and economic resources. The majority of research knowledge is based on women with breast cancer. The longer term implications of cancer survival have not been adequately explored. Focussing well designed research in the identified areas where less is already known about the psychological and social impact of cancer survival is likely to have the greatest impact on the wellbeing of people surviving cancer (Jarret et al 2013)

Ovarian cancer survivors
Physical complications and side effects have significant impact on Ovarian Cancer (OvCa) survivors' psychosocial health. Access to social support services and relational support is critical, as feelings of isolation are common. Survivors report low levels of sexual activity and satisfaction, potentially causing strain on personal relationships, and survivors experience high levels of distress, depression, and anxiety. However, QoL can improve after diagnosis for some OvCa survivors, many of whom report spiritual growth and strengthened personal relationships. Younger survivors are likely to have greater distress and lower QoL compared with older survivors. Authors conclusions: OvCa is the deadliest of all gynecologic cancers, greatly impacting the psychosocial health of survivors. Increased awareness of psychosocial health among OvCa survivors themselves, their social support system, and their health care providers is necessary to adequately address their unique needs (Roland et al 2013)

Conclusions
Fully Met

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<tr>
<td>Jarret et al. 2013</td>
<td>Informing future research priorities into the psychological and social problems faced by cancer survivors: a rapid review and synthesis of the literature.</td>
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<td>HTA</td>
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<td>Smith et al. 2017</td>
<td>A systematic review of quantitative observational studies investigating psychological distress in testicular cancer survivors</td>
<td>Psychooncology.</td>
<td>2017 Nov 23</td>
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<td>Psychological and emotional support. Impact briefs</td>
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**Further comments**
There is a body of work around screening and psychological distress/impact but not sure if you are interested in this.

**Suggestions for additional searches**
Psychological (distress, outcomes, functioning, adjustment, health, burden, wellbeing) OR emotional AND cancer AND screening
Post traumatic stress disorder AND cancer

**Y5: What psychological support would most benefit people living with and beyond cancer at the point at which treatment stops?**

**Y7: What are the most effective ways to meet the individual psychological support needs of people living with and beyond cancer?**

**Keywords:** psychological support OR emotional support AND cancer
psychological OR Psychosocial OR emotional AND intervention* OR therap* AND cancer

**Exclusions:** None
Guidelines (x1)
To minimise psychosocial consequences, the concept of preparing people during treatment with simple strategies of how to proactively manage their physical, psychological and social recovery, and any long-term problems after cancer treatment ('prehabilitation') is recognised as an area that needs much more consideration. The Department of Health survivorship survey suggests that very few people are suitably prepared for what to expect when treatment finishes.

Summary of reviews (x6 SR, x6 Cochrane SR)
Psychosocial interventions for men with Prostate cancer
Although some findings of this review are encouraging, they do not provide sufficiently strong evidence to permit meaningful conclusions about the effects of these interventions in men with prostate cancer. Additional well-done and transparently reported research studies are necessary to establish the role of psychosocial interventions in men with prostate cancer (Parahoo et al 2013: Cochrane SR)

Music interventions
The results suggest that music interventions may have a beneficial effect on anxiety in people with cancer. Results also suggested a moderately strong, positive impact on depression, but because of the very low quality of the evidence for this outcome, this result needs to be interpreted with caution. We found no support for an effect of music interventions on mood or distress (Bradt et al 2016: Cochrane SR)

Dance/movement therapy
The authors found no evidence for an effect of dance/movement therapy on depression, stress or anxiety (Bradt et al 2015: Cochrane SR)

Psychological interventions for breast cancer
To assess the effects of psychological interventions on psychosocial and survival outcomes for women with metastatic breast cancer. Three RCTs were on cognitive behavioural therapy and four were on supportive-expressive group therapy. The remaining three studies were individual based and the types of psychological interventions were not common to either cognitive behavioural or supportive-expressive therapy. Psychological interventions appear to be effective in improving survival at 12 months but not at longer-term follow-up, and they are effective in reducing psychological symptoms only in some of the outcomes assessed in women with metastatic breast cancer. However, findings of the review should be interpreted with caution as there is a relative lack of data in this field, and the included trials had reporting or methodological weaknesses and were heterogeneous in terms of interventions and outcome measures (Mustafa et al 2013: Cochrane SR)

Cognitive behavioral therapy: Twenty four trials investigating a cognitive behavioural therapy in women with non metastatic breast cancer. Pooled standardised mean differences (SMD) from baseline indicated less depression, anxiety and mood disturbance for the cognitive behavioural therapy group than the control group. Authors conclusions: A psychological intervention, namely cognitive behavioural therapy, produced favourable effects on some psychological outcomes, in particular anxiety, depression and mood disturbance (Jassim et al 2015: Cochrane SR)

Psychotherapy: Four studies compared psychotherapy to control with one to two studies reporting on each outcome. The four studies were assessed as high risk of bias and provided limited evidence of the efficacy of psychotherapy (Jassim et al 2015; Cochrane SR).

Cognitive behavioral therapy: CBT is an effective therapy for psychological symptoms of cancer survivors and patients, with meaningfully clinical effect sizes. These findings suggested that CBT should be used as the intervention for breast cancer survivors and patients when possible (Ye et al 2018)
**Psychological interventions for all cancers**

*Psychotherapy:* Significant small-to-medium effects were observed for individual and group psychotherapy and psychoeducation. These effects were sustained, in part, in the medium term (≤ 6 months) and long term (> 6 months). These results should be interpreted with caution, however, because of the low quality of reporting in many of the trials (Faller et al 2013).

*Relaxation training:* Short-term effects were evident or relaxation training. These results should be interpreted with caution, however, because of the low quality of reporting in many of the trials (Faller et al 2013).

*Expressive writing*  
Our results do not support the general effectiveness of EWI in cancer patients and survivors (Zachariae and O'Toole 2015).

*Self-management education / Self guided interventions*  
Self-management education interventions improve symptoms of fatigue, pain, depression, anxiety, emotional distress and quality of life. Results for specific combinations of core elements were inconclusive. Very few studies used the same combinations of core elements, and among those that did, results were conflicting. Thus, conclusions as to the components or elements of self-management education interventions associated with the strength of the effects could not be assessed by this review (Howell et al 2017).  
Of the interventions, three studies comprised hard-copy workbooks, six studies used resource packs, four were online resources and one was a brief multimedia resource. One study was adequately powered and demonstrated a positive effect. Almost all interventions required some level of facilitation. Distressed participants may benefit more from interventions. Authors conclusions: Self-guided interventions represent a potentially efficient way of delivering support for people affected by cancer, however evidence supporting them is lacking (Ugalde et al 2016).

*Psychoeducational interventions*  
*Telecommunication technologies:* Interventions used a variety of delivery resources, such as telephone, e-mail and websites, but all were aiming to respond to information needs and develop stress control skills. A trend toward reducing distress and improving QoL was found, but estimated effect sizes were typically small (d<0.5). Telephonically delivered psycho-educational interventions presented the highest between-group effects on these outcomes during survival, but were limited by sample size (Bartolo et al 2017).  
*Nurse delivered interventions:* 30 trials were included in the review. It can be tentatively concluded that nurse-delivered interventions comprising information combined with supportive attention may have a beneficial impact on mood in an undifferentiated population of newly diagnosed cancer patients (Galway et al 2012: Cochrane SR).

**Conclusions**  
*In Progress:* Psychological interventions for cancer survivors and cancer patients in the palliative phase  
*Partially met:* Expressive writing, relaxation therapy, individual and group psychotherapy, self-management education / self-guided interventions, telecommunication technologies, music intervention, dance/movement therapy for all cancer patients, nurse led interventions for newly diagnosed cancer patients  
*Partially met:* Psychosocial interventions for patients with prostate cancer, Psychotherapy for breast cancer patients, Psychological interventions for metastatic breast cancer
**Fully met:** CBT for breast cancer patients and survivors
This question also links to the following questions:
Y1: What are the best ways to support people with depression, anxiety or other mental health problem following cancer treatment? Fully answered
Y2: What are the best ways to cope with the fear and anxiety about cancer returning (combining self-management approaches, treatments and psychological support)? Not answered
S11: Do complementary therapies benefit people living with and beyond cancer? Answered in full for massage and symptom relief, yoga and health-related quality of life, mental health and cancer-related symptoms and acupuncture and pain relief (searches have not been conducted for other complementary therapies or other benefits)

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**Further comments**

The majority of reviews just talk about cancer patients and a more in depth read is needed to determine at what stage of treatment the psychological support has been studied.

**Out of date**


**Reviews not included in table**

Quality of psychological treatment for emotional distress

Temple et al 2018

The methodological quality of psychological treatment trials for emotional distress in BCa is improving. However, if relevant health policies are to be adequately empirically informed, trials of greater methodological rigour are essential. Trials should include participants with clinical levels of distress, control for concomitant treatments and report the clinical significance of findings. Trialists must also consider the specific requirements of psychotherapy trials (Temple et al 2018).

Suggestions for additional searches
prehabilitation

Y8a What are the psychological and social impacts on partners, family members and carers of people living with and beyond cancer
Y8b and what are the best ways to support partners, family members and carers?

Keywords: Impact AND partner* OR famil* OR care* OR caregiver* OR spouse AND Cancer
Psychological OR social or psychosocial AND partner* OR famil* OR carer* OR caregiver* OR spouse AND Cancer

Exclusions: Palliative care patients

Guidelines
None

Summary of reviews (x6 SR)

Psychological impacts
Most family members report favourable psychological well-being; however, up to 40% experience clinically evident psychological distress, including elevated anxiety and depression. Approximately 11% lack social support, with negative consequences on their relationships. More than half struggle with intimacy and sexual dysfunction post-treatment. Ongoing financial difficulties are experienced by approximately 25% of family members. The total economic burden for families can range from 12 500-19 500. Approximately two thirds report unmet needs post-treatment, specifically the need for accessible, tailored support addressing their psychosocial, financial and informational concerns. Authors conclusion: Cancer has a long-term impact on patients and families. Family members have unique issues and needs within survivorship but are often overlooked. Their needs should be considered when developing support services, focusing on those at increased risk of psychological distress (Moffat et al. 2016).

Fifty-two articles were included in this review. Analysis identified four overarching attributes: "gender," "personal resources," "finding meaning" and "social context." Despite the challenges associated with caring, this combination of internal and external factors enabled some carers to report positive experiences related to caring (Young and Snowden 2017).

Informal caregivers (ICs) are relatives, friends, and partners who have a significant relationship with and provide assistance (i.e., physical, emotional) to a patient with a life-threatening, incurable illness. The multidimensional burden that results from providing care to a patient with cancer is well documented, and as a result, a growing number of psychosocial interventions have been developed specifically to address this burden. (Applebaum and Breibart 2013)

Cachexia: The complexity of caring for a cancer patient with cachexia translates into a range of problems and experiences for informal carers. By addressing the impact of caring for a patient with cancer cachexia on carers, both caregiver and patient quality of life may improve (Wheelwright et al 2016).
Relationship issues for colorectal cancer
A synthesis of the studies revealed that (1) relationship factors (eg, support, communication, dyadic coping, and relationship satisfaction) affect adjustment to cancer; (2) cancer-related distress impacts each partner’s adjustment or the relationship; and (3) gender, role (patient/caregiver), and clinical characteristics (treatment, mental health) can mediate adjustment to cancer. Authors conclusions: The quality of the relationship can influence patients’ and their partners’ adjustment to colorectal cancer. Psychosocial interventions that address relationship issues may be beneficial to couples facing the challenges of colorectal cancer (Kayser et al. 2018).

Relationship issues for prostate cancer
The construct accepting change vs seeking continuity reflects the range of ways individuals within the dyad and couples adjust to the diagnosis. Cultivating connection vs disengaging illustrates how couples seek to manage the impact of (Prostate cancer) PCa and its treatment on their relationship, which may lead to a threatened identity, including sexual insecurities. Shielding me, you and us reflects the ways in which couples strive to protect themselves as individuals and/or each other from the impact of PCa. Being a partner and its challenges highlights the responsibilities partners assume and the impact of their supporting role. Yet, partners sometimes report feeling unsupported and side-lined both by the man they are caring for and by healthcare professionals. Couples often recognise the value of facing PCa together.
Conclusions: PCa affects both members of the dyad as individuals, as well as the couple’s relationship. How best to support couples and how to overcome difficulties in expressing their concerns to one another requires further consideration. Healthcare professionals should endeavour to employ a couple-focused approach where (Collaço et al. 2018)

Relationship issues for breast cancer
Thematic analysis was employed to determine key themes arising from the dyadic accounts of women and their partners' experiences during early breast cancer survivorship. Results: Women and their partners experienced many changes to their previous roles, responsibilities and relationships during early breast cancer survivorship. Couples also reported a range of communication, intimacy and sexuality concerns which greatly impacted their interactions with each other, adding further demands on the relationship. Three significant themes were determined: (1) a disconnection within the relationship - this was expressed as the woman survivor of breast cancer needing to prioritise her own needs, sometimes at the expense of her partner and the relationship; (2) reformulating the relationship - this reflects the strategies used by couples to negotiate changes within the relationship; and (3) support is needed to negotiate the future of the relationship - couples emphasised the need for additional support and resources to assist them in maintaining their relationship during early survivorship. Conclusion: It can be concluded that the early survivorship period represents a crucial time for both women and their partners and there are currently limited options available to meet their shared needs and preferences for support. Findings indicate that a suitable model of care underpinned by a biopsychosocial framework, access to comprehensive assessment, timely support and the provision of targeted resources are urgently needed to assist women and their partners during this critical time.

Psychosocial interventions (x7 SR, x1 NIHR SR)
Caregivers: Interventions targeting problem-solving and communication skills may ease the burdens related to patient care and role changes associated with care while improving caregiver's overall QoL. Further research is needed to establish efficacy of interventions across all stages of the cancer caregiving experience, especially focusing on issues of caregiver retention, caregiver relationships to the cancer patient, and individual differences in caregiver experiences with different types of cancer (Waldron et al. 2013)
The interventions, which varied in terms of modality and patient population, fell into the following eight categories: psychoeducation, problem-solving/skills building interventions, supportive therapy, family/couples therapy, cognitive-behavioral therapy, interpersonal therapy, complementary and alternative medicine interventions,
and existential therapy. Benefits and disadvantages of each of the categories are discussed, with special attention given to studies that produced null findings. Beyond specific techniques, structured, goal-oriented, and time-limited interventions that are integrative appear to be the most feasible and offer the greatest benefits for ICs of cancer patients. Future studies are needed to examine the specific benefits and challenges of delivering interventions in alternative modalities (Internet, Skype) so that the needs of a greater number of ICs may be addressed (Applebaum and Breibart 2013)

There is no ‘one size fits all’ intervention to support carers. Potential exists for effective support in specific groups of carers. This includes shared learning, cognitive reframing, meditation and computer-delivered psychosocial support for carers of people with dementia, and psychosocial interventions, art therapy and counselling for carers of people with cancer. Counselling may also help carers of people with stroke. The effectiveness of respite care remains a paradox, given the apparent conflict between the empirical evidence and the views of carers (Thomas et al 2017: NIHR SR)

The intervention modes fell into the following nine categories: family connect intervention, self-determination theory-based intervention (SDT), cognitive behavioral therapy (CBT), emotion-focused therapy (EFT), comprehensive health enhancement support system (CHESS), FOCUS programme, existential behavioral therapy (EBT), telephone interpersonal counseling (TIP-C), problem-solving intervention (COPE). Conclusion: paired-intervention targeting self-care and interpersonal connections of caregivers and symptom management of patients is effective in improving quality of life and alleviating depression of cancer caregivers while music therapy is helpful for reducing anxiety of cancer caregivers (Fu et al. 2017)

Couples: Couple-based interventions had small but beneficial effects in terms of improving multiple aspects of QOL for both patients and their partners. Questions remain regarding when such interventions should be delivered and for how long. Identifying theoretically based mediators and key features that distinguish couple-based from patient-only interventions may help to strengthen their effects on patient and partner QOL (Badr and Krebs 2013).

A total of 17 articles were identified and included in this review. These interventions focused mainly on patient caregiving and caregiver self care, and usually lasted for 6 weeks using a face-to-face group mode, with follow-up at around 3 months. The outcome measures can be grouped into three main dimensions: dyadic appraisal, dyadic coping, and dyadic adjustments. Positive outcomes were reported for these interventions, including improvements in communication, dyadic coping, the quality of life of both the patients and their partners, psychosocial distress, sexual functioning, and marital satisfaction. Authors conclusions: These findings highlighted the positive outcomes of couple-based interventions that focus on couples coping with cancer. Future studies on couple-based interventions should be conducted in different cultures, such as in Asian countries. Collaboration between researchers and clinicians is crucial to ensure the development of effective and accessible supportive interventions targeting couples coping with cancer (Li and Loke 2014)

Partners of men with prostate cancer: Despite strong evidence that partners of men with prostate cancer experience difficulties associated with the impact of prostate cancer, there is limited research that has investigated the efficacy of psychosocial interventions for partners. Of the reviewed studies, it is evident that interventions targeting the reduction of emotional distress, improved communication and sexual intimacy between the couple and utilisation of strategies that enable partners to express their distress, learn new strategies and implement behavioural change show the most promising results in enhancing partner well-being (Wooten et al 2014)

The evidence is less clear for the female partners of these men and couples as a dyadic unit. Couple-focused interventions were the least acceptable approach and almost half of the couple interventions produced poorer outcomes for partners. When couple interventions were effective, they improved relationship outcomes for the partner but not the man; had a positive effect on the partner’s mental health but conversely; improved sexuality outcomes for the man but not the partner. No interventions improved sexuality outcomes for female partners. Based on these results, effective and acceptable interventions for female partners and couples remain an area of uncertainty. It may be that couples interventions have been primarily focused on the PCa survivor’s needs, leaving the partner’s concerns poorly managed. This is an area where significant further work is required to understand the needs and preferences of couples, and to determine approaches to improve sexual and relationship satisfaction for both partners (Chambers et al. 2017)
**Art therapy:** Art therapy was effective in reducing anxiety, stress and negative emotionality in family caregivers of patients with cancer. Further research using randomized controlled trials or qualitative research studies on the impact of art therapy in coping among family caregivers of cancer patients will add further insight to this field of research. (Lang and Cheng Lim 2014)

**Conclusions**
Psychological impact: Fully answered (see reference list for Applebaum and Breitbart (2013).
Psychosocial interventions: Partially answered (but further specific searching needs to be conducted see comments below table)
Art therapy: partially answered

https://www.ons.org/practice-resources/pep/caregiver-strain-and-burden

Provide a range of interventions that are recommended for practice, likely to be effective and effectiveness not established

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<tr>
<th>Authors / Year</th>
<th>Study</th>
<th>Systematic Reviews</th>
<th>Primary Research</th>
<th>Guidelines</th>
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<td><strong>Fu et al. 2017</strong></td>
<td><strong>A systematic review of psychosocial interventions to cancer caregivers.</strong> Front Psychol. 2017 May 23;8:834</td>
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<td><strong>Thomas et al. 2017</strong></td>
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<td><strong>Applebaum and Breibart. 2013</strong></td>
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<td>Wooten et al. 2014</td>
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<td>Psychosocial interventions to support partners of men with prostate cancer: a systematic and critical review of the literature. Cancer Surviv. 2014 Sep;8(3):472-84. <a href="https://link.springer.com/article/10.1007%2Fs11764-014-0361-7">link</a> <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5535006/">PMC5535006</a></td>
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SR – Systematic review, N= narrative review

**Further comments**

This is a massive topic area the reviews above are a just a small section of the work that has been conducted

**Out of date guidance**

NICE 2004

Improving Supportive and Palliative Care for Adults with Cancer


**Out of date primary research**


This tool (Siminoff et al 2008) was validated ten years ago but still appears valid: The [Cancer Communication Assessment Tool for Patients and Families (CCAT-PF)] is an instrument that assesses congruence in patient-caregiver communication. The tool can be used on patients, caregivers, or both and identifies specific areas of conflict that may be amenable to [intervention]. In the initial validation study, higher CCAT-PF scores were significantly correlated with the following:

- Higher perceived family conflict.

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[ncri.org.uk](http://ncri.org.uk)
• Lower patient and caregiver well-being.
• Less expressiveness.
• Lower perceived family cohesion.

The CCAT-PF can be administered by any member of the oncology team.

Further examples of primary research
Lim and Shon (2018). The Dyadic Effects of Family Cohesion and Communication on Health-Related Quality of Life: The Moderating Role of Sex
Enhancing family cohesion and communication within the family can improve the spouses’ HRQOL. Findings regarding sex differences serve as a rationale for gender-based approaches to improving HRQOL in survivorship care in the family context. Couple- and/or family-based interventions should be designed to enhance family cohesion and improve family communication skills for effective adjustments within couples and families. Supportive care within the family context can be promoted to address the diverse challenges of survivorship care (Lim and Shon 2018).

Lime et al (2014). The dyadic effects of coping and resilience on psychological distress for cancer survivor couples
Findings from Lime et al (2014) provide insight into the relationships between coping, resilience characteristics, and psychological distress at the individual and dyadic levels. Enhancing cancer survivors’ and their spouses’ positive thoughts and available external resources can improve resilience and, in turn, reduce their psychological distress of couples coping with cancer.

Compared to the standard care group, the intervention group receiving a psychoeducational intervention the Caring for the Caregiver Programme (CCP)reported significantly higher QOL, social support satisfaction and number of supported people, closeness with the patient, self-efficacy in self-care, rewards of caregiving, and knowledge, and lower stress and depression (Leow et al 2015).

Song et al (2016). Appraisals, perceived dyadic communication, and quality of life over time among couples coping with prostate cancer.
Patients’ and spouses’ appraisals of the illness and their dyadic communication were associated with their long-term QOL. Interventions that reduce negative appraisals of illness and promote dyadic communication may improve QOL for both patients with prostate cancer and their spouses (Song et al 2016).

Chambers et al (2014). A Randomized Trial Comparing Two Low-Intensity Psychological Interventions for Distressed Patients With Cancer and Their Caregivers
Many distressed patients with cancer and their caregivers may benefit significantly from a single session of a nurse psychoeducation intervention that can be delivered remotely by telephone and supported by self-management materials. Research is needed to develop an algorithm that moves beyond the use of distress as the only indicator for referral to specialist psychological services. Survivors and caregivers with low education and low literacy may require more in-depth and targeted support (Chambers et al 2014).
Suggestions for additional searches
Instead of Impact – burden OR distress as search terms

By specific interventions eg cognitive behavioural therapy, couples based interventions and those mentioned in the reviews above (Wooten et al. 2014 and Applebaum and Breibart. 2013)


Based on the negligible effect of CBTs across outcomes, future studies should consider moving beyond traditional CBT methods as these do not appear efficacious. It is suggested that future interventions orient towards advances in the basic affective sciences and derived therapies in order to better understand and treat the emotional struggles experienced by informal caregivers (O’Toole et al 2016)

Relationship issues/ functioning /quality / intimate relationships
Couples AND coping

Marital adjustment

Results evidenced that psychosocial variables play an important role on marital adjustment. Specifically, open and constructive communication, more social support, and supportive dyadic coping were found to be associated with higher levels of marital adjustment. Other variables such as self-efficacy, sexual functioning, and psychological adjustment were also positively associated with marital adjustment. Authors conclusions: Most studies evidenced an association between psychosocial variables and marital adjustment for both women and their partners. Some important dimensions such as communication patterns, coping strategies, and social support dynamics were identified as potential targets for psychological interventions. Some variables, however, were explored only in a few studies, which limit our conclusions. Future studies should explore the role these variables and other relational and emotional variables play in promoting marital adjustment after BC
6. How can the **short-term, long-term and late effects** of cancer treatments be (a) prevented, and/or (b) best treated/managed?

**S2a: How can the short-term, long term and late effects of cancer treatments be prevented**

**Keywords:** Cancer OR therapy OR treatment OR chemo* OR radio* AND side effects OR effect* AND prevent* / Cancer AND chemotherapy OR radiotherapy OR treatment OR therapy AND prophylaxis OR prophylactic*

**Exclusions:** Not prevention of cancer, Hepatitis B reactivation

**Generic guidelines on late effects**

Macmillan (2013) ‘Gradual changes, sometimes termed ‘late effects’, mean that some people do not experience symptoms until many months, years or even decades after treatment. Examples include heart failure after anthracyline chemotherapy for a range of cancers 35, and bone fractures due to osteoporosis caused by the effect of hormonal treatment on bone cells in breast or prostate cancer patients 36. There is a growing body of evidence implicating cancer treatments in increased risk of second primary cancers later in life, again due to a lengthy sequence of sub-cellular changes that currently cannot necessarily be prevented’. ‘It is not the intention of this document to provide detailed information on all the methods currently in use or being researched for the prevention and clinical management of the consequences of cancer treatment. This section briefly outlines how strategies for cancer treatment continually develop and that future significant progress is possible on preventing consequences of treatment by modifying cancer treatment techniques. The goal of research into any new cancer treatment is to find the most effective cancer-killing regime with the minimal level of toxicity during and after treatment. Scientists are constantly seeking treatments that target cancer cells as precisely as possible, e.g. robotic surgery, intensity modulated radiotherapy (IMRT), stereotactic ablative radiotherapy (SABR), PBT, IR and biological therapies, which damage normal tissue to a lesser extent than older treatments. However, each patient is likely to have a different response to the same treatment, and none of these methods can avoid causing any consequences. While researchers aim to develop new treatments that improve survival and minimise consequences of treatment, there is evidence that some new therapies may not achieve any reduction in the incidence or severity of consequences, or risk rare but serious complications 7,37,38. Hence, monitoring for consequences will always be necessary’.

The Macmillan guidance (2013) is based upon the following references, which are all before 2013:


38 Lo et al. Serious complications associated with stereotactic ablative radiotherapy and strategies to mitigate the risk. 2013, Clin Oncol 25:378-387

**Guidelines (x5)**
Venous thromboembolism

Venous thromboembolism (VTE) is the second leading cause of death in patients with cancer. These patients are at an increased risk of developing VTE and are more likely to have a recurrence of VTE and bleeding while taking anticoagulants. Management of VTE in patients with cancer is a major therapeutic challenge and remains suboptimal worldwide. In 2013, the International Initiative on Thrombosis and Cancer (ITAC-CME), established to reduce the global burden of VTE in patients with cancer, published international guidelines for the treatment and prophylaxis of VTE and central venous catheter-associated thrombosis. The rapid global adoption of direct oral anticoagulants for management of VTE in patients with cancer is an emerging treatment trend that needs to be addressed based on the current level of evidence. In this Review, we provide an update of the ITAC-CME consensus recommendations based on a systematic review of the literature ranked according to the Grading of Recommendations Assessment, Development, and Evaluation scale. These guidelines aim to address in-hospital and outpatient cancer-associated VTE in specific subgroups of patients with cancer. (Farge et al 2016)

American Society of Clinical Oncology Guidelines (2014) Most hospitalized patients with active cancer require thromboprophylaxis throughout hospitalization. Routine thromboprophylaxis is not recommended for patients with cancer in the outpatient setting. It may be considered for selected high-risk patients. Patients with multiple myeloma receiving antiangiogenesis agents with chemotherapy and/or dexamethasone should receive prophylaxis with either low–molecular weight heparin (LMWH) or low-dose aspirin. Patients undergoing major surgery should receive prophylaxis starting before surgery and continuing for at least 7 to 10 days. Extending prophylaxis up to 4 weeks should be considered in those undergoing major abdominal or pelvic surgery with high-risk features. LMWH is recommended for the initial 5 to 10 days of treatment for deep vein thrombosis and pulmonary embolism as well as for long-term secondary prophylaxis (at least 6 months). Use of novel oral anticoagulants is not currently recommended for patients with malignancy and VTE because of limited data in patients with cancer. Anticoagulation should not be used to extend survival of patients with cancer in the absence of other indications. Patients with cancer should be periodically assessed for VTE risk. Oncology professionals should educate patients about the signs and symptoms of VTE.

Nausea and vomiting
Netupitant/palonosetron for the prevention of chemotherapy induced nausea and vomiting is not appropriate for referral for a NICE technology appraisal and it is not currently planned into any work programme. There is no published NICE guidance on the treatment of chemotherapy induced nausea and vomiting (NICE 2016). Different guidance applies in Scotland and Wales (see Scottish Medicines Consortium, 2016, 2017, All Wales Medicine Strategy Group 2016)
Netupitant/palonosetron (Akynzeo®) is recommended as an option for restricted use within NHS Wales for the prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin based cancer chemotherapy (All Wales Medicine Strategy Group 2016).

Summary of reviews (x7 Cochrane SRs, x4 SRs)
Venous thromboembolism
Low molecular weight heparin: Primary thromboprophylaxis with low molecular weight heparin (LMWH) significantly reduced the incidence of symptomatic VTE in ambulatory cancer patients treated with chemotherapy. In addition, the ultra LMWH semuloparin, which is not commercially available, significantly reduced the incidence of symptomatic VTE. The risk of major bleeding associated with LMWH, while not reaching statistical significance, suggest caution and mandate additional studies to determine the risk-to-benefit ratio of LMWH in this setting. Despite the encouraging results of this review, routine prophylaxis in ambulatory cancer patients cannot be recommended before safety issues are adequately addressed. We need additional studies investigating targeted primary prophylaxis in people with specific types or stages of cancer associated with a higher risk of VTE. : (Di Niso et al, 2016: Cochrane SR)
Infections

**Prophylactic antibiotics or G(M)-CSF:** The authors only found two small trials with 195 patients altogether, no conclusion for clinical practice is possible. More trials are necessary to assess the benefits and harms of G(M)-CSF compared to antibiotics for infection prevention in cancer patients receiving chemotherapy. (Skoetz et al. 2015; Cochrane SR)

**Low bacterial diet:** At the moment, no evidence from individual RCTs in children and adults with different malignancies underscores use of an LBD for prevention of infection and related outcomes. All studies differed with regard to co-interventions, outcome definitions and intervention and control diets. As pooling of results was not possible, and as all studies had serious methodological limitations, we could reach no definitive conclusions. It should be noted that 'no evidence of effect', as identified in this review, is not the same as 'evidence of no effect'. On the basis of currently available evidence, we are not able to provide recommendations for clinical practice. Additional high-quality research is needed (Van Dalen et al 2016: Cochrane SR)

Febrile Neutropenia

**Colony-stimulating factors (CSF) to prevent chemotherapy-related febrile neutropenia (FN):**
Based on the findings from this review of real-world comparative effectiveness studies, risks of FN and FN-related complications were generally lower for prophylaxis with pegfilgrastim versus prophylaxis with short-acting G-CSFs (Mitchell et al 2016)

Pegfilgrastim reduced the incidence of FN and CIN compared with no prophylaxis. Most studies showed better efficacy and effectiveness for pegfilgrastim than filgrastim. Efficacy and safety profiles of lipegfilgrastim and balugrastim were similar to pegfilgrastim (Pfeil et al. 2015)

**Colony-stimulating factors (CSF) to prevent chemotherapy-related febrile neutropenia (FN) in breast cancer:**
In patients with breast cancer receiving chemotherapy, CSFs have shown evidence of benefit in the prevention of FN. There is evidence, though less reliable, of a decrease of all-cause mortality during chemotherapy and a reduced need for hospital care. No reliable evidence was found for a reduction of infection-related mortality, a higher dose intensity of chemotherapy with CSFs or diminished rates of severe neutropenia and infections. The majority of adverse events reported from CSF use were bone pain and injection-site reactions but no conclusions could be drawn regarding late-term side effects (Renner et al. 2012: Cochrane SR).

Moderate-quality evidence from six trials including around 200 women supports the prophylactic use of colony-stimulating factors to prevent chemotherapy-related febrile neutropenia in women with either localized, locally advanced or metastatic breast cancer (57 vs. 153 per 1000 participants had neutropenia). There was a high degree of between-study statistical heterogeneity. In addition, low-quality evidence suggested that, in people receiving the planned dose of chemotherapy, rates of infection-related mortality did not differ between groups, whereas rates of all-cause mortality over 4 months to 10 years were lower in patients receiving colony-stimulating factors. Finally, no information was available regarding long-term effects of administering colony-stimulating factors to these patients. (Cochrane clinical answers)

Primary FN prophylaxis reduces the incidence of FN. Despite considerable cost and toxicity differences between G-CSF and antibiotics, there is insufficient data to make a recommendation of one strategy over another (Fernandes et al. 2017)

**Dry mouth and salivary gland dysfunction following radiotherapy**

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Amifostine: There is some low-quality evidence to suggest that amifostine prevents the feeling of dry mouth in people receiving radiotherapy to the head and neck (with or without chemotherapy) in the short- (end of radiotherapy) to medium-term (three months postradiotherapy). However, it is less clear whether or not this effect is sustained to 12 months postradiotherapy. The benefits of amifostine should be weighed against its high cost and side effects. There was insufficient evidence to show that any other intervention is beneficial (Riley et al 2017a: Cochrane SR).

Oral mucositis
Keratinocyte growth factor: We are confident that keratinocyte growth factor (KGF) is beneficial in the prevention of oral mucositis in adults who are receiving: a) radiotherapy to the head and neck with cisplatin or fluorouracil; or b) chemotherapy alone for mixed solid and haematological cancers. We are less confident about a benefit for KGF in adults receiving bone marrow/stem cell transplant after conditioning therapy for haematological cancers because of multiple factors involved in that population, such as whether or not they received total body irradiation (TBI) and whether the transplant was autologous (the patients’ own cells) or allogeneic (cells from a donor). KGF appears to be a relatively safe intervention. Due to limited research, we are not confident that there are any beneficial effects of other cytokines and growth factors. (Riley et al 2017b: Cochrane SR)

Radiodermatitis
Topical agents could not prevent or treat RD effectively. New type of agents should be developed to improve the efficiency based on the pathophysiology of RD (Zhang et al. 2013).

Thrombocytopenia
Thrombopoietin receptor agonists for prevention and treatment of chemotherapy-induced thrombocytopenia in patients with solid tumours. No certain conclusions can be drawn due to the lack of strong evidence in the review. The available weak evidence did not support the use of TPO-RAs for preventing CIT or preventing recurrence of CIT in patients with solid tumours. There was no evidence to support the use of TPO-RAs for treating CIT in patients with solid tumours (Zhang et al 2017b: Cochrane SR).

Conclusions
Venous thromboembolism:
Fully answered: Low molecular weight heparin: hospitalized patients
Partially answered: Low molecular weight heparin: for ambulatory cancer patients

Radiodermatitis
Not answered: Topical agents

Oral mucositis
Partially answered: keratinocyte growth factor

Thrombocytopenia
Not answered: Thrombopoietin receptor agonists
Febrile Neutropenia
Partially answered: Colony-stimulating factors (CSF) to prevent chemotherapy-related febrile neutropenia (FN) – all patients or breast cancer patients

Dry mouth and salivary gland dysfunction following radiotherapy
Partially answered: Amifostine

Nausea and Vomiting
Not answered: Netupitant/palonosetron

Infections
Not answered: Prophylactic antibiotics or G(M)-CSF, Low bacterial diet

<table>
<thead>
<tr>
<th>Authors / Year</th>
<th>Study</th>
<th>Systematic Reviews</th>
<th>Primary Research</th>
<th>Guidelines</th>
<th>Other</th>
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VENOUS THROMBOEMBOLISM
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<tr>
<th>Reference</th>
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<tr>
<td>Di Niso et al. 2016</td>
<td>Primary prophylaxis for venous thromboembolism in ambulatory cancer patients receiving chemotherapy (Update)</td>
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<td>Pfeil et al 2015</td>
<td>Efficacy, effectiveness and safety of long-acting granulocyte colony-stimulating factors for prophylaxis of chemotherapy-</td>
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<td><strong>NAUSEA AND VOMITING</strong></td>
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<td>All Wales Medicine Strategy Group. 2016</td>
<td>Netupitant/palonosetron (Akynzeo) - for the prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin-based cancer chemotherapy</td>
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<td>All Wales Medicine Strategy Group. 2016</td>
<td>Aprepitant (EMEND) - for the prevention of nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy</td>
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<tr>
<td>Scottish Medicines Consortium. 2016</td>
<td>Netupitant palonosetron (Akynzeo) - in adults for the prevention of acute and delayed nausea and vomiting associated with chemotherapy</td>
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<td>NICE 2016</td>
<td>Prevention of chemotherapy induced nausea and vomiting in adults: netupitant/palonosetron</td>
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<tr>
<td>Scottish Medicines Consortium. 2017</td>
<td>Aprepitant (Emend) - for the prevention of nausea and vomiting associated with moderately emetogenic cancer chemotherapy Rolapitant (Varuby) - Prevention of delayed nausea and vomiting associated with highly and moderately emetogenic cancer chemotherapy in adults</td>
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**Further comments**

A massive search area
The literature doesn’t distinguish between short, long and late effects we would have to search for the side effects individually

**Suggestions for additional searches**

Specific cancers and specific therapies
Specific side effects for specific cancers
Use the term intervention as opposed to treat or manage

**Examples of primary research titles**

- Optimizing expectations to prevent side effects and enhance quality of life in breast cancer patients undergoing endocrine therapy: study protocol of a randomized controlled trial.
- Preventing the acute skin side effects in patients treated with radiotherapy for breast cancer: the use of corneometry in order to evaluate the protective effect of moisturizing creams.
Abiraterone With Different Steroid Regimens for Side Effect Related to Mineralocorticoid Excess Prevention in Prostate Cancer Prior to Chemotherapy

Probiotic LGG for Prevention of Side Effects in Patients Undergoing Chemoradiation for Gastrointestinal Cancer

Exercise to Prevent Aromatase Inhibitor Side Effects in Breast Cancer Patients

Angiotensin II-Receptor Inhibition With Candesartan to Prevent Trastuzumab-Related Cardiotoxic Effects in Patients With Early Breast Cancer: a Randomized Clinical Trial


Prophylactically applied Hydrofilm polyurethane film dressings reduce radiation dermatitis in adjuvant radiation therapy of breast cancer patients.

A Randomized Phase 2 Trial of Prophylactic Manuka Honey for the Reduction of Chemoradiation Therapy-Induced Esophagitis During the Treatment of Lung Cancer: Results of NRG Oncology RTOG 1012.

Prophylactic use of antidiarrheal agents to control diarrhea associated with lapatinib therapy in breast cancer patients.

Efficacy of ginger for prophylaxis of chemotherapy-induced nausea and vomiting in breast cancer patients receiving Adriamycin-cyclophosphamide regimen: a randomized, double-blind, placebo-controlled, crossover study.

Use of trolamine to prevent and treat acute radiation dermatitis in cancer patients undergoing radiotherapy: a systematic review

S2b: How can the short-term, long-term and late effects of cancer treatments be best treated/managed?

Keywords: Cancer AND side effects AND treat* OR manage*

Exclusions: None

Generic guidelines on late effects

Macmillan Cancer Support 2013:

To minimise psychosocial consequences, the concept of preparing people during treatment with simple strategies of how to proactively manage their physical, psychological and social recovery, and any long-term problems after cancer treatment (‘prehabilitation’) is recognised as an area that needs much more consideration.

The Macmillan guidance (2013) is based upon the following references, which are all before 2013:


There is a growing acknowledgement that healthy lifestyle choices can help to protect against some short- and long-term consequences of cancer and its treatment. A recent report by Cancer Research UK highlights the acceptability to patients, family and friends of professionals offering lifestyle advice to cancer patients.

The Macmillan guidance (2013) is based upon the following references, which are all before 2013:
Appendix 4 provides some links to information on the clinical management of consequences once they occur. Pg 111 for the following side effects

**Guidance for Gastrointestinal problems** by Macmillan, BMJ, NCSI, British Society of Gastroenterology, NICE

**Urinary problems** by Macmillan

**Sexual difficulties** by Macmillan, Prostate cancer UK, British society for sexual medicine, MCSI

**Fertility** by Macmillan, royal college of physicians

**Lymphoedema** by Macmillan, Lymphoedema support network, International lymphoedema framework, RCN

**Stoma Care** by colostomy association, ursosotomy association, RCN

**Body image changes** by Macmillan

**Head, neck and mouth changes** by Macmillan, NICE

**Psychosocial problems** by Macmillan

**Fatigue** by Macmillan

**Pain** by Macmillan, British pain society

**Bone** by Macmillan

**Conclusions**

Fully answered

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<td>Macmillan Cancer Support. 2013</td>
<td>Throwing light on the consequences of cancer and its treatment.</td>
<td>C</td>
<td>HTA</td>
<td>JBI</td>
<td>Other</td>
</tr>
<tr>
<td></td>
<td>Macmillan Cancer Support 2013</td>
<td></td>
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SR – Systematic review, N= narrative review
Further comments
We could see if there are any updated information since 2013 form the list of consequences provided in the Macmillan document. This document covers all side effects. To answer this question separately for short-term, long-term and late effects would involve an extensive search for all types of cancers, all types of treatments (radiotherapy, chemotherapy, surgery etc...) and all types of side effects?
(see comments on P1_P7 for list of late; long term side effects)

The following reviews we came across when looking for other things

Suggestions for additional searches
Prehabilitation
Intervention* AND late NS effect* AND cancer*
7. What are the **biological bases of side-effects** of cancer treatment and how can a better understanding lead to improved ways to manage side-effects?

<table>
<thead>
<tr>
<th>599.1 &amp; 937.3 Would a greater understanding of the biological basis of the side-effects of cancer treatment, lead to better ways to manage them?</th>
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<tbody>
<tr>
<td><strong>Keywords</strong> Biolog* OR mechanism* AND cancer OR tum?r OR carcinoma<em>OR neoplasm</em> OR chemotherapy OR radiotherapy AND side effect*</td>
</tr>
<tr>
<td><strong>Exclusions:</strong> None</td>
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</table>

**Generic guidelines on late effects**
Macmillan Cancer Support 2013:
Research into the mechanisms by which cancer treatments cause symptoms to arise is needed so that preventative or protective measures against healthy-tissue damage can start to be uncovered. Mechanisms of radiation damage are better understood than other therapies.

The Macmillan guidance (2013) is based upon the following references, which are all before 2013:
33 ICRP Statement on Tissue Reactions/Early and Late Effects of Radiation in Normal Tissues and Organs — Threshold Doses for Tissue Reactions in a Radiation Protection Context (ICRP, 2012)

**Summary of other types of review (x 1 NR)**

**Mucositis**
This article examined potential therapeutic agents that have been investigated for the prevention and/or inhibition of mucositis induced by conventional chemotherapy and radiotherapy. They can be classified according to their mechanisms of action: scavenging reactive oxygen species, inhibition of specific cytokine production or inflammation, and inhibition of apoptosis. These early events may be good target pathways for preventing the pathogenesis of mucositis. Considering that both cancer therapy and therapeutic agents for mucositis act on both normal and cancer cells, agents that inhibit mucositis should act through mechanisms that selectively protect normal cells without compromising cancer treatment. Therefore, mechanism-based guidance for the treatment of mucositis is critical to prevent risky treatments for cancer patients and to relieve detrimental side effects effectively from cancer therapy (Youngjoo 2016).

**Conclusions**
Not met

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<th>Guidelines</th>
<th>Other</th>
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MECHANISMS


Further comments
Use specific side effects may produce more hits

Suggestions for additional searches
Radiosensitivity
Radiation sensitivity
Chemosensitivity
Molecular basis
Cellular basis


8. What are the best ways to manage persistent pain caused by cancer or cancer treatments?

### S6: What are the best ways to manage chronic cancer/treatment related pain?

**Keywords** Cancer AND Pain  
**Exclusions:** None

**Guidelines (x1)**

**SIGN 2013**

2.1 assessment and planning of care: A concise history, examination and biopsychosocial assessment, identifying pain type (neuropathic/ nociceptive/mixed), severity, functional impact and context should be conducted in all patients with chronic pain. This will inform the selection of treatment options most likely to be effective

2.2 supported self management: Healthcare professionals should signpost patients to self help resources, identified and recommended by local pain services, as a useful aide at any point throughout the patient journey. Self management may be used from an early stage of a pain condition through to use as part of a long term management strategy.

2.3 pharmacological management:

- Patients using analgesics to manage chronic pain should be reviewed at least annually, and more frequently if medication is being changed, or the pain syndrome and/or underlying comorbidities alter
- Strong opioids should be considered as an option for pain relief for patients with chronic low back pain or osteoarthritis, and only continued if there is ongoing pain relief. Regular review is required. (GRADE B)
- Specialist referral or advice should be considered if there are concerns about rapid-dose escalation with continued unacceptable pain relief, or if >180 mg/day morphine equivalent dose is required. (GRADE D)

2.4 psychologically based interventions

- C Referral to a pain management programme should be considered for patients with chronic pain. (GRADE C)

Clinicians should be aware of the possibility that their own behaviour, and the clinical environment, can impact on reinforcement of unhelpful responses.

2.5 physical therapies

- Exercise and exercise therapies, regardless of their form, are recommended in the management of patients with chronic pain. (GRADE B)
- Advice to stay active should be given in addition to exercise therapy for patients with chronic low back pain to improve disability in the long term. Advice alone is insufficient. (GRADE A)

**Summary of reviews** (x 7 Cochrane reviews, x1 Cochrane Review of Reviews)

**Codeine, alone and with paracetamol (acetaminophen)**

We identified only a small amount of data in studies that were both randomised and double-blind. Studies were small, of short duration, and most had significant shortcomings in reporting. The available evidence indicates that codeine is more effective against cancer pain than placebo, but with increased risk of nausea, vomiting, and constipation. Uncertainty remains as to the magnitude and time-course of the analgesic effect and the safety and tolerability in longer-term use (Straube et al. 2014)
Opoids
The amount and quality of evidence around the use of opioids for treating cancer pain is disappointingly low, although the evidence we have indicates that around 19 out of 20 people with moderate or severe pain who are given opioids and can tolerate them should have that pain reduced to mild or no pain within 14 days. This accords with the clinical experience in treating many people with cancer pain, but overstates to some extent the effectiveness found for the WHO pain ladder. Most people will experience adverse events, and help may be needed to manage the more common undesirable adverse effects such as constipation and nausea. Perhaps between 1 in 10 and 2 in 10 people treated with opioids will find these adverse events intolerable, leading to a change in treatment (Wiffen et al. 2017).

This review demonstrates that it is possible to titrate with oral morphine of any formulation, and to be confident that most patients will achieve a high level of pain relief within two weeks. There is likely to be a small number of patients who do not benefit from morphine, or who may develop intolerable adverse events, so other opioids need to be included in formularies. Oral morphine remains the gold standard for treating moderate to severe pain. The WHO ladder has strong opioids as the top rung of the ladder, and the evidence we have, such as it is, supports that position. Opioids are tried and tested for the treatment of cancer pain. Morphine remains the first line treatment in guidelines and textbooks, although oxycodone is the major opioid in the USA. Fentanyl as a transdermal patch is widely used in higher income countries and may cause less constipation than oral opioids. Codeine has no proven role from clinical trial data in treating cancer pain (Wiffen et al. 2017).

Corticosteroids
The evidence for the efficacy of corticosteroids for pain control in cancer patients is weak. Significant pain relief was noted in some studies, albeit only for a short period of time. This could be important for patients with poor clinical status. Further trials, with increased numbers of participants, are needed to evaluate the safety and effectiveness of corticosteroids for the management cancer pain in adults, and to establish an ideal dose, duration of therapy and route of administration (Haywood et al. 2015).

Ketamine
Current evidence is insufficient to assess the benefits and harms of ketamine as an adjuvant to opioids for the relief of refractory cancer pain. The evidence was of very low quality, meaning that it does not provide a reliable indication of the likely effect, and the likelihood that the effect will be substantially different is high. Rapid dose escalation of ketamine to high dose (500 mg) does not appear to have clinical benefit and may be associated with serious adverse events. More randomised controlled trials (RCTs) examining specific low-dose ketamine clinical regimens in current use are needed (Bell et al. 2017).

NSAIDs
There is no high-quality evidence to support or refute the use of NSAIDs alone or in combination with opioids for the three steps of the three-step WHO cancer pain ladder. There is very low-quality evidence that some people with moderate or severe cancer pain can obtain substantial levels of benefit within one or two weeks (Derry et al. 2017).

Paracetamol alone or in combination with opioids
There is no high-quality evidence to support or refute the use of paracetamol alone or in combination with opioids for the first two steps of the three-step WHO cancer pain ladder. It is not clear whether any additional analgesic benefit of paracetamol could be detected in the available studies, in view of the doses of opioids used (Wiffen et al. 2017).

Spinal cord stimulation
Since the first publication of this review, no new studies were identified. Current evidence is insufficient to establish the role of Spinal cord stimulation (SCS) in treating refractory cancer-related pain. Future randomised studies should focus on the implantation of SCS in participants with cancer-related pain (Wiffen et al. 2017).

**Acupuncture**
There is insufficient evidence to judge whether acupuncture is effective in treating cancer pain in adults (Paley et al. 2015).

**Conclusions**
- Fully answered-opoids
- Partially answered-corticosteroids, codeine
- Not answered-ketamine, NSAIDS, paracetamol alone or in combination with opioids, spinal cord stimulation, acupuncture.

For further info also see
https://www.ons.org/practice-resources/pep/breakthrough-pain
https://www.ons.org/practice-resources/pep/chronic-pain
https://www.ons.org/practice-resources/pep/pain/refractoryintracta

This resource last updated 2017 and includes recommendations for practice, likely to be effective, benefits balanced with harm and effectiveness not established for all of the above areas.

<table>
<thead>
<tr>
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<th>Guidelines</th>
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<tr>
<td>Oncology Nursing Society</td>
<td><a href="https://www.ons.org/practice-resources/pep/acute-pain">https://www.ons.org/practice-resources/pep/acute-pain</a></td>
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<td><a href="https://www.ons.org/practice-resources/pep/breakthrough-pain">https://www.ons.org/practice-resources/pep/breakthrough-pain</a></td>
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<td>Scottish Intercollegiate</td>
<td>Management of chronic pain. A national clinical guideline, Scottish</td>
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<td></td>
<td>X Evidenced based synopsis</td>
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### Cochrane Reviews

### Cochrane reviews withdrawn from publication

<table>
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<tr>
<th>Authors</th>
<th>Title</th>
<th>Publication Details</th>
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<tbody>
<tr>
<td>Ballantyne et al. 2013</td>
<td>Comparative efficacy of epidural, subarachnoid, and intracerebroventricular opioids in patients with pain due to cancer.</td>
<td>Cochrane Database of Systematic Reviews 2013, Issue 10. Art. No.: CD005178</td>
</tr>
<tr>
<td></td>
<td>October 2015: after discussion with the authors and PaPaS editors, the decision was made to halt the development of the protocol that was being planned to replace and update this review. It was felt that the review question was no longer a priority.</td>
<td></td>
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<tr>
<td>McNicol et al. 2015</td>
<td>NSAIDS or paracetamol, alone or combined with opioids, for cancer pain.</td>
<td>Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD005180</td>
</tr>
<tr>
<td></td>
<td>This review is out of date, although it is correct at the date of publication. The review may be misleading as new studies could alter the original conclusions. All previous versions of the review can be found in the ‘Other versions’ tab. A new author team intends to develop four new reviews on this topic, which will serve to update and supersede this review. The new reviews will cover paracetamol, paracetamol plus opioids, NSAIDs, and NSAIDs plus opioids, for cancer pain. For more information, contact the PaPaS Review Group.</td>
<td></td>
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<tr>
<td></td>
<td>At August 2015, this review has been withdrawn. It is correct at the date of publication, and previous versions can be accessed in the ‘Other versions’ tab on the Cochrane Library. The Cochrane Editorial Unit (CEU) agreed with the authors of the feedback that the review was misleading, and because the original author team was unavailable to update the review, the CEU advised that it should be withdrawn. See below for full details. PaPaS is seeking a new author team to develop a new review which will serve to update the original.</td>
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### Further comments


Cochrane Pain, Palliative and Supoprtive Care Review Group (PAPAS)

http://papas.cochrane.org/our-reviews

### Other outdated reviews

- Transcutaneous electric nerve stimulation (TENS) for cancer pain in adults Hurlow et al 2012

### Suggestions for additional searches

None
9. What specific **lifestyle changes** (e.g. diet, exercise and stress reduction) help with recovery from treatment, restore health and improve quality of life?

**R4a: What specific lifestyle changes (e.g. exercise) help with recovery from treatment, restore health and improve quality of life?**

**Keywords:** Cancer AND Exercise OR Physical activity

**Exclusions:** None

**Guidelines** (x1 Macmillan)

**Relevant for all cancers**

Low quality evidence that exercise training is feasible in the weeks prior to surgery and during neo-adjuvant treatment and leads to improvements in physical function. Low quality evidence that exercise programmes undertaken during chemotherapy helped prevent declines in cardiorespiratory and muscular fitness, and even led to small improvements in a systematic review of 14 RCTs. Similarly, increases in muscular strength were reported from a systematic review of 16 RCTs of patients performing aerobic and/or resistance exercise during chemotherapy or radiotherapy. Moderate evidence of small reductions in fatigue from a meta-analysis of 25 RCTs involving exercise programmes during chemotherapy or radiotherapy. Moderate evidence of improved outcomes for cardiorespiratory and muscular fitness after aerobic and resistance training post-treatment (Stevinson et al 2017).

**Summary of SRs** (2x Cochrane SR, 1 x other SR)

**Quality of life** (Relevant for all cancers): Mishra et al (2012), Cochrane systematic review, indicates that exercise may have beneficial effects at varying follow-up periods on HRQoL and certain HRQoL domains including physical functioning, role function, social functioning, and fatigue. Positive effects of exercise interventions are more pronounced with moderate- or vigorous-intensity versus mild-intensity exercise programs.

**Cancer related fatigue and lymphedema** (Relevant for all cancers): Strong evidence supports the use of exercise for cancer-related fatigue and indicates that lymphedema is not exacerbated by exercise (Hunter et al 2017).

**Breast cancer**

Physical activity interventions may have small-to-moderate beneficial effects on HRQoL, and on emotional or perceived physical and social function, anxiety, cardiorespiratory fitness, and self-reported and objectively measured physical activity. The positive results reported in the current review must be interpreted cautiously owing to very low-to-moderate quality of evidence, heterogeneity of interventions and outcome measures, imprecision of some estimates, and risk of bias in many trials (Lahart et al 2018).

**Summary of other types of review** (Evidence review x1)

**Side effects** (Relevant for all cancers): Thomas et al (2014) Emerging evidence suggests physical activity improves several common side-effects of cancer treatments.

**Conclusions**

Fully answered for exercise – all cancers

Partially answered - essential attributes of exercise (mode, intensity, frequency, duration, timing) – all cancers, breast cancer

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www.ncri.org.uk
For further info on exercise for specific cancers see https://www.macmillan.org.uk/_images/the-importance-physical-activity-for-people-living-with-and-beyond-cancer_tcm9-290123.pdf

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<tr>
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</table>

SR – Systematic review, N= narrative review

Further comments
None

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Suggestions for additional searches
Searching specifically for quality of life AND exercise and Cancer as the Cochrane review that covered all cancers was published in 2012

R4b: What specific lifestyle changes (e.g. diet) help with recovery from treatment, restore health and improve quality of life?

Keywords: Cancer AND diet* OR nutrition

Exclusions: Adolescents and children

Guidelines
None

Summary of SRs (4 x SRs)

High quality diet (Relevant for all cancers)
Adherence to a high-quality diet and a prudent/healthy dietary pattern is inversely associated with overall mortality among cancer survivors, whereas a Western dietary pattern is positively associated with overall mortality in this population (Schwedhelm et al 2016)

Vitamin B supplementation does not have an effect on cancer incidence, death due to cancer, or total mortality. It is associated with a lower risk of skin melanoma, but has no effect on other cancers (Zhang et al 2016)

Dietary intervention and exercise (specific to prostate cancer)
Targeted physiological pathways suggest dietary intervention may alleviate cancer-related fatigue and improve quality of life, however the efficacy of nutrition management with or without exercise prescription requires further exploration (Baguley et al 2017)

Healthy eating (specific to breast cancer)
To investigate the relationship between the Healthy Eating Index (HEI)/the Alternative Healthy Eating Index (AHEI) and risk of breast cancer mortality or survival rates
No association between the Healthy Eating Index (HEI)/the Alternative Healthy Eating Index (AHEI) and risk of mortality or survival from breast cancer in women with breast cancer. The HEI and AHEI are useful for evaluating changes in diet quality over the time and relationship between nutrient and dietary pattern with disease or health. Evidence in this field is limited and inconsistent, further studies are needed (Pourmasoumi et al 2016).

Conclusions
Partially answered for diet and vitamin B supplementation – all cancers
Partially answered for dietary intervention and exercise - prostate cancer
Partially answered for healthy eating - breast cancer

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<tr>
<td>Schwedhelm et al. 2016</td>
<td>Effect of diet on mortality and cancer recurrence among cancer</td>
<td>X</td>
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<tr>
<td>survivors: a systematic review and meta-analysis of cohort studies</td>
<td>Nutr Rev. 2016 Dec;74(12):737-748</td>
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<tr>
<td>Zhang et al. 2016</td>
<td>Effect of vitamin B supplementation on cancer incidence, death</td>
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<td>meta-analysis of randomized controlled trials</td>
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<td>Pourmasoumi et al. 2016</td>
<td>Healthy Eating Index/Alternative Healthy Eating Index and Breast</td>
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<td>Fatigue and Quality of Life in Men with Prostate Cancer: A Systematic</td>
<td>Nutrients. 2017 Sep 12;9(9). pii: E1003</td>
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SR – Systematic review, N= narrative review

Further comments

Of potential interest

Canadian Agency for Drugs and Technologies in Health (2014) Nutritional Supplementation for Patients with Cancer: A Review of the Clinical Effectiveness and Guidelines

Rapid Response Report: Summary with Critical Appraisal


Suggestions for additional searches:

Nutritional supplementation AND cancer

Nutritional interventions AND cancer
R4c: What specific lifestyle changes (e.g. stress reduction) help with recovery from treatment, restore health and improve quality of life?

Keywords: Cancer AND stress (management/reduction)

Exclusions: None

Guidelines
None

Summary of SRs (x 4 SRs, x1 Cochrane SR)

Mindfulness-based stress reduction (MBSR)

All cancers

Out of 13 quantitative articles involving mindfulness-based stress reduction interventions targeting cancer patients, 9 demonstrated positive changes in either psychological or physiological outcomes related to anxiety and/or stress, with 4 describing mixed results. Despite the limitations, mindfulness-based stress reduction appears to be promising for stress management among cancer patients (Rush and Sharma 2016).

Breast cancer

MBSR shows a positive effect on psychological function and QOL of breast cancer survivors. This approach can be recommended to breast cancer patients as a part of their rehabilitation (Huang et al 2016).

Haller et al (2017) meta-analysis revealed evidence for the short-term effectiveness and safety of mindfulness-based interventions in women with breast cancer. However, their clinical relevance remains unclear. Further research is needed.

MBSR shows a moderate to large positive effect size on the mental health of breast cancer patients and warrants further systematic investigation because it has a potential to make a significant improvement on mental health for women in this group (Zainal et al 2013).

Home-based multidimensional survivorship programmes

Breast cancer

The results of this Cochrane systematic review and meta-analysis revealed that HBMS programmes in breast cancer survivors appear to have a short-term beneficial effect of improving breast cancer-specific quality of life and global quality of life as measured by FACT-B and EORTC-C30, respectively. In addition, HBMS programmes are associated with a reduction in anxiety, fatigue and insomnia immediately after the intervention (Cheng et al 2017: Cochrane SR).

Conclusions

Fully answered for mindfulness-based stress reduction for all cancers and home-based multidimensional survivorship programmes for breast cancer

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<tr>
<th>Authors / Year</th>
<th>Study</th>
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**Further comments**

None

**Suggestions for additional searching**


Cancer AND Lifestyle AND interventions OR change AND quality of life


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10. How can we predict which people living with and beyond cancer will experience long-term side-effects (side-effects which last for years after treatment) and which people will experience late effects (side-effects which do not appear until years after treatment)?

P1: How can we predict which people living with and beyond cancer will experience long-term side-effects (side-effects which last for years after treatment)?

P7: How can we predict which people living with cancer and beyond will experience late effects (side-effects which do not appear until years after treatment)?

Keywords: Predict* OR toxicity AND cancer OR tum?r OR carcinoma* OR neoplasm* OR chemotherapy OR radiotherapy AND (late or long AND side effect*)

Exclusions: Short term side effects

Generic guidelines on late effects

Macmillan Cancer Support 2013:

An additional goal of cancer research is to find ways to assess patients to predict their responses to treatment, thus allowing modification of the regime to improve the chances of destroying the cancer with a lessened risk of damage to healthy tissue. For example, a pharmacogenomic approach aims to identify individuals with a high risk of toxicity from conventional doses of a chemotherapy drug, thus indicating reduced doses and a decreased risk of toxicity. Biomarkers have the potential to predict the occurrence of consequences, such as anthracycline-induced cardiotoxicity, before the patient becomes symptomatic, thus allowing for early and potentially life-saving interventions. Biomarkers may also help to improve preoperative cancer staging, better inform treatment options, and improve the referral patterns of patients with urgently treatable cancers towards more appropriate modes of therapy.

Research is also being undertaken into whether there are agents that can protect against or reduce the severity of certain consequences, without affecting the cancer-killing properties of the cancer treatment. These agents may have to be taken in advance, or alongside and after treatment. For example, several novel agents are being tested as drugs to prevent or reduce gastrointestinal radiation injury. These drugs may also reduce injury after radiation exposure has occurred, but much more research is needed to confirm this.

The Macmillan guidance (2013) is based upon the following references, which are all before 2013:


Oon et al. The identification and internal validation of a preoperative serum biomarker panel to determine extracapsular extension in patients with prostate cancer. 2012, Prostate 72:1523-1531

The Macmillan guidance (2013) is based upon the following references, which are all before 2013:

There is limited research into ways to predict, avoid, minimise and treat consequences of cancer and its treatment (from the summary)

**Summary of primary research**
The project is aiming to identify multi-parametric predictors of late RT-induced rectal bleeding by developing novel machine learning techniques that fully integrate clinical, dosimetric, and genetic data from the CHHiP prostate RT-fractionation trial. (Somaiah et al 2017)

**Conclusions**
Not answered

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<th>Other</th>
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SR – Systematic review, N= narrative review, LR = literature review
Further comments
Several articles about predicting side effects in general or rare side effects

Long-term effects begin during or shortly after treatment and don’t go away in the six months after treatment. They may go away eventually on their own, with symptoms gradually reducing for up to a year or two after treatment ends. Sometimes, long-term effects are permanent.
Late effects are a delayed reaction to treatment. They don’t appear during treatment, but can happen months or even years later.

Late side effects and long term side effects often just referred to as long term effects

Cancer Research. Updated November 2017. Late side effects of chemotherapy
http://www.cancerresearchuk.org/about-cancer/cancer-in-general/treatment/chemotherapy/side-effects
- Problems with different organs
- Second cancers
- Chemo brain, chemo fog – memory, concentration, mild cognitive impairment, cognitive dysfunction

- Fatigue
- Sexual difficulties
- Mental health problems
- Pain
- Urinary and gastrointestinal problems
- Lymphoedema
- Hot flushes
- Swallowing and speech problems
- Body image problems
- Second cancers
- Increased risk of other serious conditions

Macmillan Cancer Support. Summary of potential consequences of cancer and its treatment
Fatigue, weight gain, lymphoedema, neuropathic pain, heart damage leading to an increased risk of cardiovascular disease, lung damage, bowel, bladder and sexual problems, and increased risk of osteoporosis, anxiety and depression
Other consequences:
- Lymphoedema in the arms, leg or neck
• Metabolic and hormonal consequences (e.g. pituitary hormone deficiencies after whole brain irradiation, adrenal insufficiency resulting from prolonged use of steroids, thyroid dysfunction following radiotherapy to neck)
• Adverse lipid profile and metabolic syndrome (for example insulin resistance, dyslipidaemias, hypertension and abdominal obesity after bone marrow transplantation) • Fertility consequences
• Skin problems
• Neuro-psychological effects
• Chronic pain
• Eating and speaking difficulties
• Neuropathy

Suggestions for additional searches
Searching by specific side effects listed above and the keywords related to prediction
11. What are the most effective ways to stop cancer coming back (combining treatments and life-style changes)?

R1: What are the most effective ways to stop cancer coming back (combining treatments and life-style changes)?

Keywords: Cancer OR carcinoma OR neoplasm* OR Lymphoma* AND recurren* AND prevent* / Cancer AND recurrence AND lifestyle OR diet* OR alcohol* OR smok* OR nutrition OR supplement*

Exclusions: treatment for recurrent cancer

Guidelines (x1)

Adjuvant bisphosphonates

NICE (2017) evidence summary discusses a meta-analysis of individual participant data from 26 randomised controlled trials (RCTs) including 18,766 women with early breast cancer (the Early Breast Cancer Trialists’ Collaborative Group [EBCTCG] meta-analysis 2015). The meta-analysis found that, at 10 years compared with control, adjuvant bisphosphonates (in addition to standard breast cancer treatments) produced small, borderline statistically significant reductions in distant recurrence (recurrence in the bone or elsewhere, not in the breasts or regional lymph nodes), bone recurrence and breast cancer mortality (absolute reductions 1.4%, 1.1% and 1.7% respectively), but not breast cancer recurrence or all-cause mortality. No benefits were seen in premenopausal women, but the benefits in postmenopausal women were found to be greater than in the general study population. At 10 years compared with control, the absolute reductions in the risk of breast cancer mortality, bone recurrence and all-cause mortality in postmenopausal women were 3.3%, 2.2% and 2.3%, respectively. The results of the meta-analysis suggest that bisphosphonates may be beneficial in postmenopausal women and provide an estimate of the average effects of bisphosphonates across the whole subgroup. However, evidence is insufficient to determine precise subgroups of postmenopausal women who would or would not benefit.

Summary of reviews (x6 SRs. x2 Cochrane SR)

Helicobacter pylori eradication (Gastric cancer)

Controversies persist regarding the effect of Helicobacter pylori eradication on the development of metachronous gastric cancer after endoscopic resection of early gastric cancer (EGC). The aim of this study was to assess the efficacy of Helicobacter pylori eradication after endoscopic resection of EGC for the prevention of metachronous gastric cancer. A systematic literature review and meta-analysis were conducted using the core databases PubMed, EMBASE, and the Cochrane Library. The rates of development of metachronous gastric cancer between the Helicobacter pylori eradication group vs. the non-eradication group were extracted and analyzed using risk ratios (RRs). A random effect model was applied. The methodological quality of the enrolled studies was assessed by the Risk of Bias table and by the Newcastle-Ottawa Scale. Publication bias was evaluated through the funnel plot with trim and fill method, Egger’s test, and by the rank correlation test. Ten studies (2 randomized and 8 non-randomized/5,914 patients with EGC or dysplasia) were identified and analyzed. Overall, the Helicobacter pylori eradication group showed a RR of 0.467 (95% CI: 0.362-0.602, P < 0.001) for the development of metachronous gastric cancer after endoscopic resection of EGC. Subgroup analyses showed consistent results. Publication bias was not detected. Helicobacter pylori eradication after endoscopic resection of EGC reduces the occurrence of metachronous gastric cancer (Bang et al. 2015).
**Dietary fibre (Colorectal cancer)**: There is a lack of evidence from existing RCTs to suggest that increased dietary fibre intake will reduce the recurrence of adenomatous polyps in those with a history of adenomatous polyps within a two to eight year period. However, these results may be unreliable and should be interpreted cautiously, not only because of the high rate of loss to follow-up, but also because adenomatous polyp is a surrogate outcome for the unobserved true endpoint colorectal cancer. Longer-term trials with higher dietary fibre levels are needed to enable confident conclusion (Yao et al 2017: Cochrane SR).

**Weight loss interventions (Endometrial cancer)**
There is currently insufficient high-quality evidence to determine the effect of combined lifestyle and behavioural interventions on survival, quality of life, or significant weight loss in women with a history of endometrial cancer compared to those receiving usual care. The limited evidence suggests that there is little or no serious or life-threatening adverse effects due to these interventions, although musculoskeletal problems were increased, presumably due to increased activity levels. Our conclusion is based on low- and very low-quality evidence from a small number of trials and very few patients. We therefore have very little confidence in the evidence: the true effect of weight-loss interventions in obese women with endometrial cancer is currently not known. Further methodologically-rigorous, adequately-powered RCTs are required with follow-up of 5 to 10 years duration. These should focus on the effects of varying dietary modification regimens, pharmacological treatments associated with weight loss and bariatric surgery on survival, quality of life, weight loss and adverse events (Kitson et al. 2018: Cochrane SR).

**Nutrition Interventions (Colorectal cancer)**
Eight completed RCTs, all in colorectal adenoma survivors, were identified, with four investigating the effect of folic acid. A meta-analysis of the four folic acid RCTs showed no statistically significant effect of folic acid on colorectal adenoma recurrence (relative risks=0.93; 95% confidence interval: 0.69, 1.25). The impact of the remaining completed RCTs, investigating antioxidant supplementation, green tea extract, prebiotic fibre and phytooestrogens/insoluble fibre, could not be reliably estimated because of the limited number and heterogeneity of the interventions. In addition, three heterogeneous ongoing RCTs were identified, investigating green tea (n=1) and eicosapentaenoic acid (n=1) in colorectal adenoma survivors and dietary modifications (n=1) in CRC survivors in remission. Authors conclusions: Overall, this systematic review highlights the need for further research, especially in colorectal cancer survivors, as we identified no completed and only one ongoing RCT in this population (Van Dijk and Pot. 2016).

**Smoking (Prostate and Head and neck cancer)**
There is consistent evidence that survival rates are lower and recurrence rates are higher for patients who continue to smoke after being diagnosed with head and neck (van Imhoff et al 2016)

Smoking is associated with aggressive tumor features and worse cancer-related prognosis; as this negative impact seems to be maintained for 10yr after smoking cessation, urologists should advise men to quit smoking latest at prostate cancer diagnosis to improve their prognosis. As several studies indicate a positive impact of exercise on tumor development, progression, and treatment outcome, it is certainly reasonable to advocate an active lifestyle. Least convincing evidence is available for the interaction of sexual activity and prostate cancer and well-conducted and longitudinal studies are clearly necessary to evaluate whether the suggested associations between prostate cancer risk and sexual behavior are real or spurious (Brookman-May et al. 2018).

**Alcohol (Breast cancer)**
There is some evidence that alcohol consumption increases the risk of breast cancer recurrence, particularly in postmenopausal women. The association between alcohol and development of a second primary breast cancer is less clear. Inconsistencies in methodology and results across studies complicate attempts to develop a cohesive interpretation of findings (Simapivapan et al 2016)
Physical activity (Breast cancer)
Twenty-two prospective cohort studies were eligible in this meta-analysis. During average follow-up periods ranging from 4.3 to 12.7 years there were 123,574 participants, 6,898 all-cause deaths and 5,462 breast cancer outcomes (i.e. breast cancer-related deaths or recurrences). The average Newcastle-Ottawa score was six stars (range 4-8). Compared to those who reported low/no lifetime recreational pre-diagnosis physical activity, participants who reported high lifetime recreational pre-diagnosis physical activity levels had a significantly lower risk of all-cause (HR = 0.82, 95% CI 0.70-0.96, p < 0.05) and breast cancer-related death (HR = 0.73, 95% CI 0.54-0.98, p < 0.05). Significant risk reductions for all-cause and breast cancer-related death was also demonstrated for more recent pre-diagnosis recreational physical activity (HR = 0.73, 95% CI 0.65-0.82, p < 0.001; and HR = 0.84, 95% CI 0.73-0.97, p < 0.05, respectively), post-diagnosis physical activity (HR = 0.52, 95% CI 0.43-0.64, p < 0.01; and HR = 0.59, 95% CI 0.45-0.78, p < 0.05, respectively) and meeting recommended physical activity guidelines (i.e. ≥ 8 MET-h/wk) post-diagnosis (HR = 0.54, 95% CI 0.38-0.76, p < 0.01; and HR = 0.67, 95% CI 0.50-0.90, p < 0.01, respectively). However, there was evidence of heterogeneity across lifetime recreational pre- and post-diagnosis physical activity analyses. Both pre-diagnosis (lifetime and more recent combined) and post-diagnosis physical activity were also associated with reduced risk of breast cancer events (breast cancer progression, new primaries and recurrence combined) (HR = 0.72 95% CI 0.56-0.91, p < 0.01; and HR = 0.79, 95% CI 0.63-0.98, p < 0.05, respectively). Authors conclusions: There is an inverse relationship between physical activity and all-cause, breast cancer-related death and breast cancer events. The current meta-analysis supports the notion that appropriate physical activity may be an important intervention for reducing death and breast cancer events among breast cancer survivors (Lahart et al 2015)

Summary of other reviews (x6 NR)
Lifestyle
There is increasing evidence that lifestyle after the diagnosis of cancer may affect prognosis. Several studies have shown that a Western dietary pattern, obesity, weight gain, a sedentary lifestyle, metabolic syndrome, high serum levels of insulin, growth factors, and inflammatory cytokines after the diagnosis of cancer are associated with an increased incidence of recurrences. Most studies have been on breast and colon cancer. However, in the clinical management of cancer, little attention is presently paid to improving lifestyle and controlling body weight. Lifestyle intervention trials are needed to corroborate or confute the observational results on cancer recurrences, but, even now, there is no contraindication to promoting moderate physical exercise, moderate calorie restriction (CR), and a Mediterranean dietary pattern. In fact, the AICR/WCRF 2007 systematic literature review recommends cancer patients to adopt the lifestyle recommended for the prevention of cancer. Interestingly, the evidence-based AICR/WCRF recommendations coincide with traditional rules, based on far Eastern philosophy, of avoiding extremely yin food, such as sugared beverages and calorie-dense foods, and extremely yang food, such as processed meat, and relying on the equilibrium of slightly yang food, such as whole-grain unprocessed cereals, eaten with slightly yin food, such as legumes and vegetables (Berrino 2014)

Diet
Higher intakes of vegetables and fish were inversely associated with overall mortality, and higher alcohol consumption was positively associated with overall mortality (RR, 1.08; 95%CI, 1.02–1.16). Adherence to the highest category of diet quality was inversely associated with overall mortality (RR, 0.78; 95%CI, 0.72–0.85; postdiagnosis RR, 0.79; 95%CI, 0.71–0.89), as was adherence to the highest category of a prudent/healthy dietary pattern (RR, 0.81; 95%CI, 0.67–0.98; postdiagnosis RR, 0.77; 95%CI, 0.60–0.99). The Western dietary pattern was associated with increased risk of overall mortality (RR, 1.46; 95%CI, 1.27–1.68; postdiagnosis RR, 1.51; 95%CI, 1.24–1.85). Authors conclusions: Adherence to a high-quality diet and a prudent/healthy dietary pattern is inversely associated with overall mortality among cancer survivors, whereas a Western dietary pattern is positively associated with overall mortality in this population (Schwedhelm et al 2016)
Vaccines
Cancer vaccines have the potential to provide a nontoxic treatment for the prevention of cancer recurrence in the adjuvant setting. Many cancer vaccines have been tested in multiple phase III trials with minimal success. However, through these failed clinical trials, we have learned that the ideal setting for vaccine therapy is the adjuvant setting. Also, we have learned important lessons about patient selection to maximize the probability of success. This article will highlight some of the successes, our trial results in the adjuvant setting, and future directions (Hale et al 2016)

Human vaccines against infectious agents are often effective in a prophylactic setting. However, they are usually not effective when used post-exposure. Rabies vaccine is one of the exceptions, which can be used post-exposure, but is effective only when used in combination with other treatments. Similar results have been obtained with cancer vaccines and immunotherapies. Cancer immunotherapies generally prolong patients’ survival when they are used during advanced stage disease. The potential of immunotherapy to cure cancer could be revealed when it is applied in a prophylactic setting. This article provides a brief overview of cancer immunotherapeutics and suggests that immunotherapy can cure cancer if used at the right time against the right target; we suggest that targeting cancer during dormancy in order to prevent tumor recurrence as advanced stage disease is potentially curative (Manjili and Payne 2015)

Helicobacter pylori eradication (Gastric cancer)
Helicobacter pylori (H. pylori) plays an important role in gastric carcinogenesis, as the majority of gastric cancers develop from H. pylori-infected gastric mucosa. The rate of early gastric cancer diagnosis has increased in Japan and Korea, where H. pylori infection and gastric cancer are highly prevalent. Early intestinal-type gastric cancer without concomitant lymph node metastasis is usually treated by endoscopic resection. Secondary metachronous gastric cancers often develop because atrophic mucosa left untreated after endoscopic treatment confers a high risk of gastric cancer. The efficacy of H. pylori eradication for the prevention of metachronous gastric cancer remains controversial. However, in patients who undergo endoscopic resection of early gastric cancer, H. pylori eradication is recommended to suppress or delay metachronous gastric cancer. Careful and regularly scheduled endoscopy should be performed to detect minute metachronous gastric cancer after endoscopic resection (Jang and Chun 2014)

miRNA THERAPY
Cancer stem cells (CSCs) are a small subpopulation of cells within tumors that retain the properties of self-renewal and tumorigenicity in vivo. Although CSCs have been reported in multiple cancers, the regulation of CSCs has not been described at the molecular level. miRNAs are endogenous small noncoding RNAs that post-transcriptionally regulate the expression of their target genes via RNA interference and are involved in almost all cellular processes. Since aberrant miRNA expression occurs in CSCs, such dysregulated miRNAs may be promising therapeutic targets. In this review, we summarize the current knowledge regarding miRNAs that regulate CSC properties and discuss an in vivo delivery system for synthetic miRNA mimics and miRNA inhibitors for the development of innovative miRNA therapy against CSCs (Osaki et al 2015)

Summary of primary research
Dietary fat: Dietary fat in dairy is a source of estrogenic hormones and may be related to worse breast cancer survival. We evaluated associations between high- and low-fat dairy intake, recurrence, and mortality after breast cancer diagnosis. We included 1893 women from the Life After Cancer Epidemiology study diagnosed with early-stage invasive breast cancer from 1997 to 2000, who completed the Fred Hutchinson Cancer Research Center Food Frequency Questionnaire after diagnosis. A total of 349 women had a recurrence and 372 died during a median follow-up of 11.8 years, with 189 deaths from breast cancer. We used delayed entry Cox proportional hazards regression to evaluate associations between categories of the cumulative average of dairy fat at baseline and at follow-up 5 to 6 years later and...
subsequent outcomes. Tests of statistical significance were two-sided. In multivariable-adjusted analyses, overall dairy intake was unrelated to breast cancer-specific outcomes, although it was positively related to overall mortality. Low-fat dairy intake was unrelated to recurrence or survival. However, high-fat dairy intake was positively associated with outcomes. Compared with the reference (0 to <0.5 servings/day), those consuming larger amounts of high-fat dairy had higher breast cancer mortality (0.5 to <1.0 servings/day: hazard ratio [HR] = 1.20, 95% confidence interval [CI] = 0.82 to 1.77; and ≥1.0 servings/day: HR = 1.49, 95% CI = 1.00 to 2.24, P trend = .05), higher all-cause mortality (P trend < .001), and higher non-breast cancer mortality (P trend = .007); the relationship with breast cancer recurrence was positive but not statistically significant. The higher risk appeared consistent across different types of high-fat dairy products. Intake of high-fat dairy, but not low-fat dairy, was related to a higher risk of mortality after breast cancer diagnosis (Kroenke et al. 2013)

**Weight loss (Breast cancer)**
A behavioral weight loss intervention can lead to clinically meaningful weight loss in overweight/obese survivors of breast cancer. These findings support the need to conduct additional studies to test methods that support sustained weight loss and to examine the potential benefit of intentional weight loss on breast cancer recurrence and survival (Rock et al. 2015)

**Conclusions**
Partially answered: Diet (all cancers)
Partially answered: Smoking (Prostate and Head and neck cancer)
Partially answered: Helicobacter pylori eradication (gastric cancers)
Partially answered: Alcohol (Breast cancers)
Not answered: Vaccines and miRNA therapy (all cancers)
Not answered: Nutritional interventions and dietary fibre (colorectal cancers, adenoma), physical activity (breast cancer), dietary fat (breast cancer)
Not answered: Weight loss interventions (Endometrial cancer, breast cancer)

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<th>Primary Research</th>
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VACCINES
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<td></td>
<td>Rock et al. 2015</td>
<td>Results of the Exercise and Nutrition to Enhance Recovery and Good Health for You (ENERGY) Trial: A Behavioral Weight Loss</td>
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## Intervention in Overweight or Obese Breast Cancer Survivors

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**Further comments**

Using the term survival as opposed to recurrence as lots of the studies use mortality as an outcome

**Suggestions for additional searches**

Specific interventions for specific cancers
Survival AND cancer AND interventions
Weight loss AND recurrence

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12. What are the social, financial and economic impacts of living with and beyond cancer – how does it affect families, relationships, finances, work and use of NHS services?

O2: What are the social, financial and economic impacts of living with and beyond cancer – how does it affect families, relationships, finances, work and use of NHS services?

Keywords: Financ* or economic or social AND Cancer AND impact* or burden*

Exclusions:

Guidelines
None

Summary of reviews (x 8SR)

Social difficulties
There were few reports concerned with impacts on patients’ roles/responsibilities in everyday life although practical and emotional struggles with parenting were identified. Social difficulties were common and associated with multiple factors including being a caregiver. Many studies were single time-point surveys and used non-validated measures. Exceptions were employment of the COST and Social Difficulties Inventory (SDI), validated measures of financial and social distress respectively.

Conclusions: Impact on some important parts of patients’ everyday lives is insufficiently and inconsistently captured. Further PROM development focussing on roles and responsibilities, including work and caring for dependents, is warranted. Implications for Cancer Survivors: Factors such as finances, employment and responsibility for caring for dependants (e.g. children and elderly relatives) can affect the well-being of cancer survivors. There is a need to ensure that any instruments used to assess patients’ social well-being are broad enough to include these areas so that any difficulties arising can be better understood and appropriately supported (Catt et al. 2017).

Financial burden
Among 676 studies identified, 45 met the inclusion criteria and were incorporated in the review. The majority of the studies (82%, n=37) reported financial hardship as a material condition measure; others reported psychological (7%, n=3) and behavioral measures (16%, n=7). Financial hardship measures were heterogeneous within each broad category, and the prevalence of financial hardship varied by the measure used and population studied. Mean annual productivity loss ranged from $380 to $8236, 12% to 62% of survivors reported being in debt because of their treatment, 47% to 49% of survivors reported experiencing some form of financial distress, and 4% to 45% of survivors did not adhere to recommended prescription medication because of cost. CONCLUSIONS: Financial hardship is common among cancer survivors, although we found substantial heterogeneity in its prevalence. Our findings highlight the need for consistent use of definitions, terms, and measures to determine the best intervention targets and inform intervention development in order to prevent and minimize the impact of financial hardship experienced by cancer survivors (Altice et al. 2016).

From 417 citations, a total of 25 studies were included in this review. Seventy outcomes of FT were reported with 47 covering monetary, objective and subjective indicators of FT. A total of 28-48% of patients reported FT using monetary measures and 16-73% using subjective measures. The most commonly reported factors associated with FT were: being female, younger age, low income at baseline, adjuvant therapies and more recent diagnosis. Relative to non-cancer comparison groups,
cancer survivors experienced significantly higher FT. Most studies were cross-sectional and causal inferences between FT and determinants were not possible. Measures of FT were varied and most were not validated, while monetary values of out-of-pocket expenses included different cost components across studies. **CONCLUSIONS:** A substantial proportion of cancer survivors experience financial hardship irrespective of how it is measured. Using standardised outcomes and longitudinal designs to measure FT would improve determination of the extent of FT. Further research is recommended on reduced work participation and income losses occurring concurrently with FT and on the impacts on treatment non-adherence (Gordon et al. 2017).

Ten studies were included in this review and with a majority originating from high-income countries. The prevalence of the financial burden perception was reported between 14.8 and 78.8 %. The most frequent and significant risk factor reported associated with the perception of financial difficulty was the households with low income. Discontinuation of treatment and poverty were conversely the important consequence of financial burden in cancer patients and their families. **CONCLUSION:** Evidently, cancer is a long-term illness that requires a high financial cost, and a significant number of cancer patients and families struggle with financial difficulty. Identifying such groups with a high risk of facing financial difficulty is a crucial measure to ensure safety nets are readily available for these targeted population (Azzani et al. 2015).

**Economic Burden**
This systematic review examines the excess cost of chronic conditions on the economic burden of cancer survivorship among adults in the US. Areas covered: Twelve published studies were identified. Although studies varied substantially in populations, comorbidities examined, methods, and types of cost reported, costs for cancer survivors with comorbidities generally increased with greater numbers of comorbidities or an increase in comorbidity index score. Survivors with comorbidities incurred significantly more in total medical costs, out-of-pocket costs, and costs by service type compared to cancer survivors without additional comorbidities. **Expert commentary:** Cancer survivors with comorbidities bear significant excess out-of-pocket costs and their care is also more expensive to the healthcare system. On-going evaluation of different payment models, care coordination, and disease management programs for cancer survivors with comorbidities will be important in monitoring impact on healthcare costs (Rim et al. 2016).

**Small Cell Lung Cancer** (SCLC): The majority of publications provided data on limited and extensive disease of SCLC. The reported burden was categorised as direct costs and indirect costs, with the majority of the publications (n = 16) reporting on direct costs and one reporting on both direct and indirect costs. The only indirect costs reported for SCLC were lost productivity (premature mortality costs) and caregiver burden. Chemotherapy, diagnostic costs and treatment costs were identified as significant costs when managing SCLC patients, including the associated treatment costs such as hospitalisation, nurse visits, emergency room visits, follow-up appointments and outpatient care. Conclusions: SCLC and its treatment have a substantial impact on costs. The scarcity and heterogeneity of economic cost data negated meaningful cost comparison, highlighting the need for further research. Capturing the economic burden of SCLC may help patients and clinicians make informed treatment choices and improve SCLC management (Enstone et al. 2017).

**Chemotherapy-induced febrile neutropenia:** The primary objective of this review was to identify the cost components that were most frequently associated with the economic burden of febrile neutropenia (FN) among patients with lymphoma. The secondary objective was to identify any parameter associated with higher FN cost. Ten cost of illness (COI) studies were identified. General characteristics on study design, country, perspective, and patient population were extracted and systematically reported. It was observed that majority (70%) of the studies employed the perspective of healthcare provider. 20% of the studies considered long-term costs. Estimated costs were adjusted to 2013 US dollars and ranged from US$5819 to US$34,756. The cost components that were most frequently associated with economic

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burden were ward and medication costs. Inpatient management, male gender, discharged dead, and comorbidity were positively associated with higher FN costs. Future COI studies on FN should focus on the accurate estimation on ward and medication costs (Wang et al. 2015)

**Cancer-related venous thromboembolism:** The objective of this study was to present evidence on the epidemiology, health outcomes and economic burden of cancer-related venous thromboembolism (VTE). The annual average total cost for cancer patients with VTE was found to be almost 50% higher than that of cancer patients without VTE. Inpatient care costs accounted for more than 60% of total cost. The existing evidence assessed in the present review demonstrated the significant health and economic consequences of cancer-related VTE, which make a strong case for the importance of its proper and efficient prevention and management (Kourlaba et al. 2015)

**Summary of other reviews (x4 NR)**

**Financial burden**
The substantial economic burden of cancer is increasingly being shifted to patients. Financial burden experienced by patients as a result of medical treatment has an impact on their lifestyle choices, health behaviors, and quality of life. Variation in treatment recommendations based on the patients’ economic status or affordability may be against the basic tenet of social justice and is a growing challenge for policy makers. This review summarizes the multifaceted constructs and current trends associated with financial hardship within the context of cancer care and healthcare economics focusing mainly on hematological malignancies but supplemented by nonhematological cancer and general medical literature. We also highlight the patient and physician perspectives about this issue and identify important areas for future research. We discuss the need for more proactive solutions so that patients can achieve good clinical outcomes, without catastrophic financial consequences for themselves and their families (McNuty and Khera. 2015).

**Financial costs**
Four themes were identified: measuring costs; sources of costs; the impact of costs and reducing costs. The wide variety of measures for ascertaining hidden costs makes comparison of findings difficult; some articles cover a very narrow range of costs. Qualitative research is useful for elucidating a wide range of costs. Costs pertaining to hospital visits, nutrition and clothing are widely mentioned. Low additional expenditure may indicate that needs/wants are going unmet. Financial capacity to cope and subjective perception of impact are important. Low income, younger age, chemotherapy and living ruraly are associated with greater impact. Extra expense can exert long-term effects on family finances. Primary care follow-up, telemedicine and treatments that entail fewer visits may serve to reduce patient costs. Conclusions: The key question is how to organise/deliver cancer care in order to reduce additional expenses to patients and families. Future research could identify critical time-points and demographic groups susceptible to significant additional costs, in order to target support at those most in need (Brooks et al. 2011)

**Economic Burden**
*Head and Neck Cancer:* Of 606 studies initially identified, 77 met the inclusion criteria and were evaluated in the assessment. Most included studies were conducted in the USA. The vast majority of studies assessed direct costs of HNC, such as those associated with diagnosis and screening, radiotherapy, chemotherapy, surgery, side effects of treatment, and follow-up care. The costs of treatment far exceeded those for other aspects of care. There was considerable heterogeneity in the reporting of economic outcomes in the included studies; truly comparable cost data were sparse in the literature. Based on these limited data, in the US costs associated with systemic therapy were greater than costs for surgery or radiotherapy. However, this trend was not seen in Europe, where surgery incurred a higher cost than radiotherapy with or without chemotherapy. Conclusions: Most studies investigating the direct healthcare costs of HNC have utilized US databases of claims to public
and private payers. Data from these studies suggested that costs generally are higher for HNC patients with recurrent and/or metastatic disease, for patients undergoing surgery, and for those patients insured by private payers. Further work is needed, particularly in Europe and other regions outside the USA; prospective studies assessing the cost associated with HNC would allow for more systematic comparison of costs, and would provide valuable economic information to payers, providers, and patients (Wissinger et al. 2014)

**Economic burden**

**Toxicities associated with cancer treatment:** Side effects or toxicities are frequent, undesirable companions of almost all forms of non-surgical cancer therapy. It is unusual for patients to complete treatment with radiation or chemotherapy without experiencing at least one form of therapy-associated tissue injury or systemic side effect. Often, toxicities do not occur as solitary events; rather, they result in clusters of symptoms that share a common biological aetiology. Like any disease, cancer treatment-related toxicities (CTRTs) vary in their severity. But, in contrast to most diseases in which incidence is described as being present or absent, the current approach to CTRT typically limits reporting to severe cases only. Not only does this dilute the frequency with which CTRTs occur, but it also undermines our ability to determine the full burden of their impact and to accurately assess the cost effectiveness of potential toxicity interventions. In this article, we report the results of a directed literature review for the years 2000–2012, in which we studied and compared three tissue-based toxicities (nausea and vomiting, diarrhoea, and oral mucositis) and one systemic toxicity (fatigue). Our results confirm the heavy burden of resource use and cost associated with CTRTs. The inclusion of fatigue in our analysis provided an opportunity to compare and contrast a toxicity in which there are both acute and chronic consequences. Our findings also demonstrate a number of challenges to, and opportunities for, future study. Among the most obvious are the lack of provider consistency in diagnosis and grading, especially when there is no global agreement on severity scales. Compounding this inconsistency is the disconnect between healthcare providers and patients that exists when describing toxicity severity and impact. In many cases, cancer can be thought of as a chronic disease that requires prolonged but episodic treatment once the acute disease is eradicated. This change reflects increasing treatment successes, but it also implies that the burden of CTRTs will be expanded and prolonged. Creation of hierarchical attribution of costs in the presence of simultaneous CTRTs, accurate coding, and consistent tracking tools for toxicities will be imperative for effective appraisal of the costs associated with cancer treatment regimen toxicities (Carlotto et al. 2013)

**Conclusions**

Impact – Fully answered
How does it affect families, relationships – see QY8 What are the psychological and social impacts on partners, family members and carers of people living with and beyond cancer and what are the best ways to support partners, family members and carers?; Fully answered
How does it affect finances, work and use of NHS services? - fully answered

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SR – Systematic review, NR= narrative review

**Further comments**
None

**Suggestions for additional searches**
None
13. What are the best ways to cope with the fear and anxiety about cancer returning (combining self-management approaches, treatments and psychological support)?

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**Guidelines**
None

**Summary of other types of review** (1 NR)
This literature review provided current evidence of published interventions to manage uncertainty in the female breast cancer survivor population, as well as future research recommendations. Interventions surrounding being mindful, managing uncertainty, having more effective patient–provider communication, and handling stress through counselling are options for managing fear of cancer recurrence (Dawson et al. 2016).

**Summary of primary research**

**Conquer Fear: Attention training, metacognitions, acceptance/mindfulness, screening behaviour, and values-based goal setting.** This randomized trial demonstrated efficacy of ConquerFear compared with attention control (Taking-it-Easy relaxation therapy) in reduction of fear of cancer recurrence inventory total scores immediately post-therapy and 3 and 6 months later and in many secondary outcomes immediately post-therapy. Cancer-specific distress (total) remained more improved at 3– and 6-month follow-up (Butow et al. 2017)

**Blended cognitive behaviour therapy:** has a statistically and clinically significant effect on the severity of fear of cancer recurrence in cancer survivors and is a promising new treatment approach (van de Wal et al. 2017)

**Psychoeducational intervention:** This newly developed evidence-based psychoeducational intervention was effective in reducing fear of cancer recurrence and stress and increasing melanoma-related knowledge in people at high risk for another melanoma (Dieng et al. 2016)

**Cognitive bias modification:**: The results of the current pilot study suggest the promise of Attention and Interpretation Modification for Fear of Breast Cancer Recurrence in reducing fear of cancer recurrence in survivors of breast cancer. Future research should attempt to replicate these findings in a larger-scale trial using a more sophisticated, user-friendly program and additional measures of improvement in more diverse samples (Lichtenthal 2017).

**Conclusions**
Not answered
One ongoing SR listed in Prospero

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<td>Recurrence in Breast, Prostate, and Colorectal Cancer Survivors: The SWORD Study, a Randomized Controlled Trial. <em>J Clin Oncol.</em> 2017 Jul 1;35(19):2173-2183</td>
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<td><em>Psychoeducational Intervention</em> to <em>Reduce Fear of Cancer Recurrence</em> in People at High Risk of Developing Another Primary Melanoma: Results of a Randomized Controlled Trial. <em>J Clin Oncol.</em> 2016 Dec 20;34(36):4405-4414</td>
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**Further comments**

SR – Systematic review, N= narrative review

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None

**Suggestions for additional searches**
None
14. How can we predict who is at risk of developing mental health conditions in people living with and beyond cancer (e.g. depression) and what are the best ways of supporting those with mental health conditions?

Y6b How can we predict who is at risk of developing a mental health problem?

**Keywords:** Predict AND mental OR emotional OR psychological AND cancer

**Exclusions:** caregivers

**Guidelines** (x1)

Some groups of cancer patients experience higher levels of distress especially those suffering from lung, pancreatic, Hodgkin’s lymphoma, brain, head and neck, leukaemia and lymphoma cancers. Women, those with young children, those with co-morbidities and those from poorer backgrounds are also more likely to suffer psychological and emotional problems as a result of a cancer diagnosis (Macmillan Cancer Support. 2013).

Mental health problems such as anxiety and depression are common conditions that can be triggered by difficult events, such as a cancer diagnosis or having treatment for cancer. Around a third of people diagnosed with breast, colorectal or prostate cancer or non-Hodgkin lymphoma five years previously experience anxiety or depression. More than one in eight of those diagnosed up to five years previously report moderate to extreme anxiety and depression54. (Macmillan Cancer Support. 2013)

Some psychosocial consequences may be particularly severe, resulting in persistent mental health difficulties. People living with and beyond cancer are considered to be at risk for post-traumatic stress disorder due to the shock and trauma of being diagnosed with a life-threatening disease and receiving treatment that can be both physically and mentally gruelling165 (Macmillan Cancer Support. 2013)

The Macmillan guidance (2013) is based upon the following references, which are all before 2013:


**Summary of reviews** (x2 SR)

**Longer term emotional distress**

**Demographic, clinical, or social factors:** There was no consistent evidence that demographic, clinical, or social factors reliably predicted longer-term distress. Of the psychological factors examined, only baseline distress (significant in 26 of 30 relevant papers; 24 of 28 studies) and neuroticism (significant in all 5 papers/studies that examined it) consistently predicted longer-term distress. The heterogeneity of included studies, particularly in populations studied and methodology, precluded meta-
analytic techniques. Authors conclusions: This review supports current clinical guidance advising early assessment of distress as a marker of vulnerability to persistent problems. Additionally, neuroticism is also indicated as a useful marker of vulnerability. However, the review also highlights that more sophisticated research designs, capable of identifying the psychological processes that underlie the association between these marker variables and persistent distress, are needed before more effective early interventions can be developed (Cook et al 2018).

**Psychological adjustment**

*Sociodemographic, disease-related, and psychosocial factors:* Consistent sociodemographic and disease-related variable predictors of adjustment were income, fatigue, cancer stage, and physical functioning. Psychosocial factors, particularly optimism and trait anxiety, as well as perceived social support, coping strategies, and initial levels of psychological functioning, were found to be predictive of later depressive and anxiety symptoms, psychological distress, and quality of life for women with BC, in predictable ways. Other psychosocial variables, such as cognitive and body image factors, predicted psychological adjustment but were explored only by a few studies. Authors conclusions: The majority of studies showed a significant relationship between psychosocial factors and psychological adjustment. These results point to specific sociodemographic, disease-related, and psychosocial factors that can help to identify women at the time of diagnosis who are at risk for long-term psychological challenges so they can be referred for psychological support that targets their specific needs and can improve their quality of life and mood and decrease indicators of anxiety, depression, and psychological distress (Brandão et al 2017).

**Summary of primary research**

Identifying risk factors for psychological distress in patients with cancer may help providers more efficiently screen, identify, and manage distress. This article presents predictors of psychological distress in a large heterogeneous sample of cancer patients. In total, 836 patients were enrolled in a large randomized control trial and completed computerized psychosocial assessments Mental Health Assessment and Dynamic Referral for Oncology. Multivariate regressions examined predictors of distress and interest in mental health services. Final models suggest that psychological distress was related to six variables, and interest in mental health services was related to previous history of mental health counseling, total number of cancer-related symptoms, and race/ethnicity. Results may be used to identify high-risk patients who may benefit from proactive psychosocial interventions (O’Hea et al. 2016).

**Conclusions**

Partially answered

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| **O’Hea et al. 2016** |
| *Predictors of psychological distress and interest in mental health services in individuals with cancer.* |
| X |

**Further comments**

Came across these primary papers

**Cook et al 2015. The Association of Metacognitive Beliefs With Emotional Distress After Diagnosis of Cancer**


*Objective:* Emotional distress after a diagnosis of cancer is normal and, for most people, will diminish over time. However, a significant minority of patients with cancer experience persistent or recurrent symptoms of emotional distress for which they need help. A model developed in mental health, the self-regulatory executive function model (S-REF), specifies that maladaptive metacognitive beliefs and processes, including persistent worry, are key to understanding why such emotional problems persist. This cross-sectional study explored, for the first time, whether metacognitive beliefs were associated with emotional distress in a cancer population, and whether this relationship was mediated by worry, as predicted by the S-REF model. *Method:* Two hundred twenty-nine participants within 3 months of diagnosis of cancer were included. Participants completed a self-report questionnaire that measured anxiety, depression, posttraumatic stress disorder (PTSD) symptoms, metacognitive beliefs, worry, and illness perceptions. *Results:* Regression analysis showed that metacognitive beliefs were associated with symptoms of anxiety, depression, and PTSD, and explained additional variance in these outcomes after controlling for age, gender, and illness perceptions. Structural equation modeling was consistent with the cross-sectional hypotheses derived from the theory that metacognitive beliefs cause and maintain distress both directly and indirectly by driving worry. *Conclusions:* The findings provide promising first evidence that the S-REF model may be widely applied in cancer. Further study is required to establish the predictive and clinical utility of these findings.
Quattropani et al. 2015. The Role of Metacognitions in Predicting Anxiety and Depression Levels in Cancer Patients Ongoing Chemotherapy. Procedia - Social and Behavioral Sciences, Volume 2015, 9 October 2015, Pages 463-473

Cancer patients often have to deal with numerous side effects and psychological distress during chemotherapy. Research has shown that dysfunctional metacognitive beliefs are the basis for the development and maintenance of emotional disorders. The present research is a first attempt to explore how metacognitions influence anxiety and depression in cancer patients undergoing chemotherapy. A sample of 175 cancer patients undergoing chemotherapy completed a demographic questionnaire, the Metacognitions Questionnaire-30 (MCQ-30) and the Hospital Anxiety and Depression Scale (HADS). Medical information about the stage of disease and the history of treatment was obtained. Linguistic analysis (Stansfield et al., 1992) was employed to ensure that the form had been correctly translated because the Italian form of the MCQ-30 was utilized (Quattropani, et.al, 2014) Negative beliefs, the need to control thoughts, and positive beliefs explained up to 89% of variance of anxiety in cancer patients during chemotherapy. The negative beliefs about worry and the gender explained up to 81% of variance of depression in cancer patients during chemotherapy. In fact, female gender was positively correlated with depression level of patients. The negative beliefs about worry and the need to control thoughts explained the 81% variance for the overall distress of patients during chemotherapy. In conclusion, some metacognitive factors have a crucial role both for anxiety and depression in cancer patients undergoing chemotherapy. It is suggested that the psychological intervention for cancer patients should assess such factors and try to address them in clinical practice.

Reviews not in table

Studies examining the pathophysiological mechanisms between PC and psychological distress were included for analysis. Results Eight studies were identified that fulfilled inclusion criteria. Four mechanisms were identified accounting for the possible relationship between psychological distress and PC, including (1) stress-induced β-adrenergic signaling, (2) interleukin-6-mediated effects, (3) kynurenine pathway upregulation, and (4) altered cerebral glucose metabolism. Conclusions The relationship between psychological distress and PC is complex, and our understanding of these mechanisms may have implications for holistic clinical management and oncological outcome. The evidence exploring the pathophysiology of this interaction is sparse, but most well established with regard to the stress-induced β-adrenergic signaling mechanism. Further studies in larger cohorts are required to elucidate the relationship between PC and psychological distress to be able to identify therapeutic targets for both conditions (Bettison et al 2018)


Testicular cancer survivors’ mean anxiety levels were higher than in the general population, while mean depression and distress were no different. Clinically significant anxiety (=1 in 5) and to a lesser extent distress (=1 in 7), but not depression, were more prevalent in TC survivors than the general population. Approximately 1 in 3 TC survivors experienced elevated FCR. Poorer psychological outcomes were more common among TC survivors who were single, unemployed/low socio-economic status, suffering from co-morbidities, experiencing worse symptoms/side effects, and using passive coping strategies. Authors conclusions: many TC survivors do not experience significant psychological morbidity, but anxiety and FCR are prevalent. Inadequate coping resources (eg, low socio-economic status and social support) and strategies (eg, avoidance) and greater symptoms/side effects were associated with poorer outcomes. Theoretically driven prospective studies would aid understanding of how outcomes change over time and how to screen for risk. Age and gender appropriate interventions that prevent and manage issues specific to TC survivors are also needed (Smith et al 2017)

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Suggestions for additional searches
Post traumatic stress disorder/ PTSD and cancer AND predict*
Individual psychological symptoms addressed in Y6a AND predict*
Metacongnitions AND predict and Cancer

Y1a: What are the best ways to support people with anxiety or mental health following cancer treatment?
**Keywords** Cancer AND Anxiety OR Mental Health
**Exclusions:** None

**Guidelines**
None

**Summary of SRs** (x3 Cochrane review, x 1 other SR)

**Yoga**
Moderate-quality evidence supports the recommendation of yoga as a supportive intervention for improving health-related quality of life and reducing fatigue and sleep disturbances when compared with no therapy, as well as for reducing depression, anxiety and fatigue, when compared with psychosocial/educational interventions (Cramer et al. 2017)

**Mindfulness**
Zhang et al (2015) meta-analysis supported the efficacy of mindfulness-based therapies in the improvement of anxiety and depression levels for people with cancer. The authors note that previous meta-analysis of MBSR studies included only 2 of 9 studies that were RCTs. All seven studies included in this analysis were RCTs. MBSR and mindfulness-based art therapy were the most frequently used mindfulness therapies (5 of 7), and all studies reported anxiety and depression scores. Subgroup analysis of the data further supported the effectiveness of mindfulness-based intervention in relieving anxiety and depression across cancer type and stage

**Psychoeducation/psychoeducational interventions**
Educational interventions appear to play some role in reducing overall fatigue, fatigue intensity, and fatigue interference, and might provide some benefit for anxiety. No effect on depression was found in this study, but baseline levels of depression were not generally clinically relevant (Bennett et al 2016).

**CBT for Breast cancer**
A psychological intervention, namely cognitive behavioural therapy, produced favourable effects on some psychological outcomes, in particular anxiety, depression and mood disturbance. However, the evidence for survival improvement is still lacking. These findings are open to criticism because of the notable heterogeneity across the included studies and the shortcomings of the included studies (Jassim et al 2015).

**Conclusions**
Fully answered by ONS and Cochrane SRs for CBT, Mindfulness-Based stress reduction and psychoeducation/psychoeducational interventions
For further info see [https://www.ons.org/practice-resources/pep/anxiety](https://www.ons.org/practice-resources/pep/anxiety)
This resource last updated 2017 includes recommendations for practice, likely to be effective, benefits balanced with harm and effectiveness not established for all management strategies for anxiety. ONS note that anxiety is highest shortly after diagnosis and decreases over time. Recommended for practice are CBT, Mindfulness-Based stress reduction and psychoeducation/psychoeducational interventions.

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**Further comments**
Interventions are for those who are suffering as opposed to those who support them.

**Suggestions for additional searches**
None

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Y2: What are the best ways to cope with the fear and anxiety about cancer returning (combining self-management approaches, treatments and psychological support)?

Keywords: Cancer OR Cancer-related AND Fear OR Anxiety AND recurrence OR return* AND intervention* OR Cope OR help OR trial*

Exclusions: Prevalence or factors influencing fear or anxiety

Guidelines
None

Summary of other types of review (1 NR)
This literature review provided current evidence of published interventions to manage uncertainty in the female breast cancer survivor population, as well as future research recommendations. Interventions surrounding being mindful, managing uncertainty, having more effective patient–provider communication, and handling stress through counselling are options for managing fear of cancer recurrence (Dawson et al. 2016).

Summary of primary research

Conquer Fear: Attention training, metacognitions, acceptance/mindfulness, screening behaviour, and values-based goal setting. This randomized trial demonstrated efficacy of ConquerFear compared with attention control (Taking-it-Easy relaxation therapy) in reduction of fear of cancer recurrence inventory total scores immediately post-therapy and 3 and 6 months later and in many secondary outcomes immediately post-therapy. Cancer-specific distress (total) remained more improved at 3- and 6-month follow-up (Butow et al. 2017)

Blended cognitive behaviour therapy: has a statistically and clinically significant effect on the severity of fear of cancer recurrence in cancer survivors and is a promising new treatment approach (van de Wal et al. 2017)

Psychoeducational intervention: This newly developed evidence-based psychoeducational intervention was effective in reducing fear of cancer recurrence and stress and increasing melanoma-related knowledge in people at high risk for another melanoma (Dieng et al. 2016)

Cognitive bias modification: The results of the current pilot study suggest the promise of Attention and Interpretation Modification for Fear of Breast Cancer Recurrence in reducing fear of cancer recurrence in survivors of breast cancer. Future research should attempt to replicate these findings in a larger-scale trial using a more sophisticated, user-friendly program and additional measures of improvement in more diverse samples (Lichtenthal 2017).

Conclusions
Not answered
One ongoing SR listed in Prospero

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<tr>
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<th>FEAR OF REOCURRENCE</th>
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<td><strong>Dawson et al. 2016</strong></td>
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<td><strong>Dieng et al. 2016</strong></td>
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<td><strong>Lichtenthal. 2017</strong></td>
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<td><strong>Randell and Gillanders 2017.</strong></td>
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<tr>
<td>Psychological interventions targeting fears of cancer recurrence among cancer survivors: a systematic review. PROSPERO <a href="http://www.crd.york.ac.uk.abc.cardiff.ac.uk/prospero/display_record.php?ID=CRD42017057998">http://www.crd.york.ac.uk.abc.cardiff.ac.uk/prospero/display_record.php?ID=CRD42017057998</a></td>
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SR – Systematic review, N= narrative review

Further comments
None

Suggestions for additional searches
None
15. What are the best ways to support people living with and beyond cancer to make lifestyle changes to improve their health?

R2: What are the best ways to support people living with and beyond cancer to make lifestyle changes to improve their health?

Keywords: Cancer AND lifestyle OR exercise OR physical activity OR nutrition OR diet

Exclusions: Return to Work (answered by R2), children, paediatric, pediatric, and adolescents.

Guidelines
None

Summary of reviews (x2 Cochrane SR, SRs x4)

Physical activity and exercise

Motivational interviewing and other types of behavioural counselling, referral to supervised gym-based exercise, walking including pedometer programmes.

Macmillan guidance (Campbell et al 2012) includes a 2010 commissioned systematic review of randomised controlled trials to promote physical activity among cancer patient. This evidence is likely to still be relevant. Effective strategies include: oncologist-recommended exercise programme, Motivational interviewing and other types of behavioural counselling, referral to supervised gym-based exercise, walking including pedometer programmes.

Exercise prescriptions Certain exercise prescriptions for patients with cancer may improve self-reported quality of life (QoL) and self-reported physical function (PF). We investigated the effects of exercise on QoL and PF in patients with cancer and studied differences in effects between different intervention-related and exercise-related characteristics. Exercise interventions, especially when supervised, have statistically significant and small clinical benefit on self-reported QoL and PF in patients with cancer. Unsupervised exercise intervention effects on PF were larger when prescribed at a higher weekly energy expenditure (Sweegers et al. 2017)

Setting programme goals, prompting practise and self-monitoring: Interventions to promote exercise in cancer survivors who report better levels of adherence share some common behaviour change techniques. These involve setting programme goals, prompting practise and self-monitoring and encouraging participants to attempt to generalise behaviours learned in supervised exercise environments to other, non-supervised contexts. However, expecting most sedentary survivors to achieve current guideline recommendations of at least 150 minutes per week of aerobic exercise is likely to be unrealistic. As with all well-designed exercise programmes in any context, prescriptions should be designed around individual capabilities, and frequency, duration and intensity or sets, repetitions, intensity or resistance training should be generated on this basis (Bourke et al 2013: Cochrane SR).

Barriers and facilitators for lung cancer patients: Barriers and enablers to physical activity in lung cancer are multidimensional and span diverse factors. These include patient-level factors, such as symptoms, comorbidities, sedentary lifestyle, mood and fear, and environmental factors. These factors should be considered to identify and develop suitable interventions and clinical services in attempt to increase physical activity in patients with lung cancer (Granger et al 2016).

Multi-dimensional rehabilitation programmes (MDRPs)

Patients who survive cancer may experience a range of physical and emotional symptoms which impact on their health and quality of life. Physical symptoms may include fatigue, reduced muscle strength and weight gain, while emotional symptoms may include, for example, anxiety and depression. It has been proposed that multidimensional rehabilitation programmes (MDRPs) which include physical and psychosocial components provide people with the skills to manage their own care and lead to improvements in knowledge, coping behaviour, self efficacy and enhanced quality of life (QoL). Rehabilitation programmes have been developed to address
These symptoms and problems and to help survivors have a better quality of life. MDRPs which looked at one specific behaviour area, such as diet, physical activity or stress, appeared to be more helpful for patients than programmes which attempted to address several different behaviours (Scott et al 2013: Cochrane SR).

**Digital health behaviour change interventions**

Digital technologies offer a promising approach to encourage health behaviour change among cancer survivors. Random effects meta-analyses showed significant improvements in moderate-vigorous physical activity and body mass index. Narrative synthesis revealed mixed evidence for effects on diet, generic QoL measures and self-efficacy and no evidence of an effect on mental health (Roberts et al 2017).

**Summary of primary research (x1)**

A dietary and physical activity intervention framed as helping men to regain fitness and aid post-treatment recovery aimed at men with elevated PSA may be appealing and acceptable to African Caribbean prostate cancer survivors (Er et al 2017).

**Conclusions**

- Fully answered-physical activity/exercise
- Partially answered-MDRPs (more trials required)
- Partially answered-digital health behaviour change interventions

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**PHYSICAL ACTIVITY AND EXERCISE**

- **Campbell et al. 2012**
  - Interventions to promote physical activity: a review Macmillan Cancer Support
  - [https://www.macmillan.org.uk/documents/aboutus/health_professionals/physicalactivityevidencebasedguidance.pdf](https://www.macmillan.org.uk/documents/aboutus/health_professionals/physicalactivityevidencebasedguidance.pdf)
  - X SR

- **Bourke et al. 2013**
  - X

- **Sweegers et al. 2017**
  - X SR
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<th>Reference</th>
<th>Title</th>
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<tr>
<td>Scott et al. 201</td>
<td>Multidimensional rehabilitation programmes for adult cancer survivors</td>
<td>X</td>
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SR – Systematic review, N= narrative review

**Further comments**

None

**Suggestions for additional searches**

Cancer AND healthy eating OR smoking cessation OR alcohol
16. If people with cancer are involved in their own healthcare decisions (including participating in multi-disciplinary team meetings with health professionals), does this lead to better outcomes?

<table>
<thead>
<tr>
<th>1245.4 &amp; 1293.1 If people with cancer are involved in their own healthcare decisions (including participating in multi-disciplinary team meetings with health professionals), does this lead to better outcomes?</th>
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<tr>
<td><strong>Keywords</strong>: Involv* AND decision* AND cancer / shared decision making AND cancer (AND outcomes)</td>
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<td><strong>Exclusions</strong>: Information to aid decision making, HCP perspectives, (perceptions, experiences, satisfaction) of involvement, decision aids, update of shared decision making for healthcare professionals</td>
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<td><strong>Guidelines</strong>: None</td>
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<tr>
<td><strong>Summary of reviews</strong></td>
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<td><strong>Quality of Life</strong></td>
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<td>The growing consensus espousing the use of shared decision making (SDM) in cancer treatment has coincided with the rise of health care evaluation paradigms that emphasize quality of life (QOL) as a central outcome measure. This review systematically examines the association between treatment SDM and QOL outcomes in cancer. METHODS: A range of bibliographic databases and gray literature sources was searched. The search retrieved 16,726 records, which were screened by title, abstract, and full text to identify relevant studies. The review included 17 studies with a range of study designs and populations. Data were extracted on study methods, participants, setting, study or intervention description, outcomes, main findings, secondary findings, and limitations. Quality appraisal was used, in conjunction with a narrative approach, to synthesize the evidence. RESULTS: The review found weak, but suggestive, evidence for a positive association between perceived patient involvement in decision making, a central dimension of SDM, and QOL outcomes in cancer. The review did not find evidence for an inverse association between SDM and QOL. The poor methodological quality and heterogeneity of the extant literature constrained the derived conclusions. In addition, the literature commonly treated various subscales of QOL instruments as separate outcomes, increasing the probability of spurious findings. CONCLUSIONS: There is weak evidence that aspects of shared decision-making approaches are positively associated with QOL outcomes and very little evidence of a negative association. The extant literature largely assessed patient involvement, only capturing one aspect of the shared decision-making construct, and is of poor quality, necessitating robust studies examining the association (Kashaf and McGill 2015).</td>
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<td><strong>Prostate cancer</strong></td>
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<td>Men facing prostate cancer screening and treatment need to make critical and highly preference-sensitive decisions that involve a variety of potential benefits and risks. Shared decision-making (SDM) is considered fundamental for &quot;preference-sensitive&quot; medical decisions and it is guideline-recommended. There is no single definition of SDM however. We systematically reviewed the extent of SDM implementation in interventions to facilitate SDM for prostate cancer screening and treatment. Thirty-six RCTs including 19 196 randomised patients met the eligibility criteria; they were mainly conducted in North America (n = 28). The median year of publication was 2008 (1997-2015). Twenty-three RCTs addressed decision-making for screening, twelve for treatment and one for both screening and treatment for prostate cancer. Bi-directional interactions between healthcare providers and patients were verified in 31 RCTs, but only 14 fulfilled the three key SDM features, 14 had at least &quot;deliberation&quot;, one had &quot;unclear deliberation&quot; and two had no signs of deliberation. CONCLUSIONS: There is significant variation in the extent of SDM...</td>
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Implementation among studies addressing SDM for prostate cancer screening and treatment. **Further evaluation of these results on patient outcomes, a standardised SDM definition and guidance for an effective implementation in several clinical settings are needed** (Martinez-Gonzalez et al. 2018)

**Summary of other primary research**

**Quality of life**

The aim of this study was to understand the shared surgical decision-making process from the patients’ perspective by implementing qualitative methods. Nineteen patients were included in the analysis. The mean age was 58.3 (+ 12.2) years, 52.9% were married, 84.2% were Caucasian, 68.4% were currently employed and 31.6% had a family history of breast cancer, 10.4% diagnosed with Stage 0, 52.6% stage I and 36.8% stage II breast cancer. Factors contributing to decision-making were dichotomized into satisfied (n=11) or dissatisfied (n=8). Satisfied patients were further categorized as either (i) positive outlook n= 2; (ii) acceptance of choice n= 9; Dissatisfied patients were further categorized as (i) experiencing regret n=4; (ii) fear of recurrence n=4. Authors conclusions: As decision-making needs vary by individual women, a personalized decision-making approach is an essential factor to improve HR-QOL among women with early stage breast cancer. Additional prospective quantitative studies of the preoperative decision-making and post-operative HR-QOL are necessary, as these findings may compliment existing outcomes research (Scott et al. 2014).

**Conclusions**

Partially answered

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<tr>
<th>Authors / Year</th>
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<tr>
<td>Scott et al. 2014</td>
<td>Shared Decision-Making in Women with Early Stage Breast Cancer and Implications for Long-Term Health-Related Quality of Life <a href="https://linkinghub.elsevier.com/retrieve/pii/S1098-3015(14)04300-9">https://linkinghub.elsevier.com/retrieve/pii/S1098-3015(14)04300-9</a></td>
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SR – Systematic review, N= narrative review

**Further comments**

**Suggestions for additional searches**

Need to know what the outcomes of interest are so that a specific search can be conducted
17. What are the psychological and social impacts on children who have a parent (or parents) with cancer, and what are the best ways to support those children?

Y4: What are the psychological and social impacts on children of having a parent with cancer, and what are the best ways to support those children?

Keywords: Parent* AND Cancer
Exclusions: parents of children with cancer

Guidelines
None

Summary of reviews (x6 SR)
Impact
Five themes were identified: being informed of parental cancer, emotional concerns, changes in daily life, seeking factual information and seeking emotional support. As indicated in the results, most children had been informed of the parent’s diagnosis of cancer. They suffered from a wide range of concerns when facing the situation, and their lives had been interrupted to different degrees. In order to cope with the event, children adopted various strategies. Their information and support needs were reported to have been poorly met. Authors conclusions: This systematic review provides insight into the scenario of children living with a parent with non-terminal cancer and indicates some suggestions for future studies. The experience of children when the father has cancer should be further explored. Short-term and long-term impacts of parental cancer on children, especially young children within different cultural contexts, should be investigated to help health care professionals provide individualised assistance to those children (Huang and O’Connor 2014)

Most studies analysed the mother’s perceptions about the experience of having BC in parenting and in the parent-child relationship. The majority of studies explored experiences and perspectives on the parent-child relationship in mothers with minor children, although a minority of studies included adult children. Additionally, a few studies (17%) addressed perceptions and experiences of women with advanced stage cancer. Three main themes were found: priorities and concerns of patients, decision-making processes about sharing the diagnosis with their children, and mother-child relationship and parenting after mother’s diagnosis. Authors conclusions: Findings indicated that the diagnosis of BC is accompanied by an array of challenges that affect parental roles and parenting. Further studies are needed to explore these issues more sensitively. For now, however, the evidence suggests that the families of women with BC, and particularly the women themselves, may benefit from informal and formal support aimed at helping them cope effectively with this challenging life event (Tavares et al. 2018)

Twenty-nine studies reported negative impacts related to parental cancer, while eight identified positive outcomes related to post-traumatic growth. Five returned null or mixed findings. Unmet needs were frequently explored and a new validated measure developed. Communication and information were particularly important for offspring, though these needs were often unmet and parents wanted guidance regarding discussions with their children. Offspring may adopt a variety of coping strategies, some of which appear maladaptive, and may cycle between different approaches. Few evaluations of interventions were identified, and further work in this area is needed. Further evidence has emerged that poorer family functioning and other family and illness-related factors predict worse psychosocial outcomes for offspring, however evidence for other predictors such as age and gender remain mixed. Authors conclusions: Additional evidence for the negative psychosocial impact of parental cancer on adolescent and young adult offspring, their needs, and factors predicting psychosocial outcomes has emerged in the last decade. However,
substantial gaps and methodological issues remain and evidence for the development, efficacy or implementation of interventions for this population is very limited. There is also a clear need for greater focus on bereaved and young adult offspring and those from non-western cultural groups, who remain under-represented in research conducted to date (Walczak et al. 2018)

This study reviewed the literature regarding the psychological, social, and behavioural impact of parental cancer on offspring aged 10–24 years, at the time of the parent’s first diagnosis. A systematic literature review was conducted following 2015 PRISMA guidelines. Seven studies met inclusion criteria. Offspring were impacted by their parent’s cancer and experienced psychological and behavioural problems. Daughters and offspring who experienced more problems at their parent’s diagnosis appeared to be most impacted. Offspring refrained from communicating their disease-related concerns, but expected their parents to communicate openly. Turning to oneself and peer-support were coping strategies used by offspring. The majority of offspring were significantly impacted by their parent’s cancer. The paucity of literature focusing on offspring aged 10–24 years at the time of their parent’s incident cancer diagnosis indicates that research has overlooked offspring age at their parent’s cancer onset as a factor that may influence their future outcomes (Morris et al. 2018)

Support
Interventions focused on children, parents or several family members and analyses revealed a broad picture of theoretical background and primary aims. Several studies focused on developmental or implementation phases or descriptions of interventions. Other included studies reported results of evaluations using qualitative and quantitative methods. Results suggest that interventions are helpful and that participants improved in various outcomes. The thematic analyses indicate that barriers for use of support services refer to aspects concerning the patients and families, such as practical difficulties, perceived need for support or fear of stigma. Cancer patients who understood the need and benefit of support services may have used them more often. Additionally, intervention characteristics such as a flexible structure and accessibility were important to reach families affected by parental cancer. Disease characteristics and complications in collaborations were identified as potential barriers. The provision of information about interventions by clinicians and understanding the support as part of routine care seem to be key issues for implementation and use of psychosocial support. Authors conclusions: This review identified a broad number of intervention concepts for families with minor children affected by parental cancer. Findings provide a basis for existing or future psychosocial interventions to anticipate potential barriers and facilitators to implementation and use and can help to reach a wider range of families in need for support (Inhestern et al. 2016)

Three factors emerged as critical to consider in future intervention development: (1) Children need age-appropriate information about their parent’s cancer; (2) Children require support communicating with parents, family members and health professionals and (3) Children need an environment where they feel comfortable sharing positive/negative emotions and can have their experiences normalised among peers. All intervention studies reported at least one positive outcome, however, only five reported significant improvements in child/family functioning based on validated quantitative measure/s. Variability in study design and quality, combined with considerable heterogeneity in intervention characteristics and outcome variables limited the conclusions, which could be drawn. Therefore, further carefully designed and scientifically evaluated interventions for children facing a parent’s cancer diagnosis are clearly warranted (Ellis et al. 2017)

Summary of other reviews
Impact
In the majority of studies, children were significantly impacted by the parent’s cancer diagnosis and exhibited distress. Daughters appeared to experience worsened mental health, and sons experienced a greater totality of internalizing and externalizing problems. Children of all ages were impacted by their parent’s cancer diagnosis and initiated a number of coping strategies in response. Despite this, a significant number of studies revealed that parents underestimated the impact that their cancer
had on their children. Family functioning, as well as the ill parents' gender, coping strategies, cancer severity, and mental and physical health mediated their children's well-being. Parent-child communication was a key element in supporting children. Authors conclusions: Parental cancer may impact children's long-term well-being. Further investigations are needed in this area. Additionally, review of support programs and interventions are warranted in terms of their uptake and impact on families affected by a parent's cancer (Morris et al. 2016)

Conclusions
Impact – partially answered
Support – partially answered

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<td>Morris et al.</td>
<td>The psychological, social, and behavioural impact of a parent's cancer on adolescent and young adult offspring aged 10–24 at time of diagnosis: A systematic review</td>
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<td>2018</td>
<td>Journal of Adolescence 65(June 2018), 67-71</td>
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<td>2016</td>
<td>Support Care Cancer. 2016 Jul;24(7):3235-51</td>
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<td>Huang and O'Connor 2014</td>
<td>School-aged and adolescent children's experience when a parent has non-terminal cancer: a systematic review and meta-synthesis of qualitative studies.</td>
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<td>Psychooncology. 2014 May;23(5):493-506</td>
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<tr>
<td>Tavares et al.</td>
<td>Mothers with breast cancer: A mixed-method systematic review on the impact on the parent-child relationship.</td>
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SR – Systematic review, N= narrative review

**Further comments**

None

**Suggestions for additional searches**

None
18. What is the best form of rehabilitation and other support to help people living with and beyond cancer return to or maintain their usual activities (e.g. work)?

**H4: What is the best form of rehabilitation for people living with and beyond cancer?**

**Keywords:** cancer and rehabilitation

**Exclusions:** None

**Guidelines**

None

**Summary of reviews (x1 Cochrane review)**

**Multidimensional rehabilitation programmes**

Multidimensional rehabilitation programmes (MDRPs) have developed in response to the growing number of people living with and surviving cancer. MDRPs comprise a physical component and a psychosocial component. The findings from the narrative analysis suggested that Multidimensional rehabilitation programmes (MDRPs) with a single domain or outcome focus appeared to be more successful than programmes with multiple aims. In addition, programmes that comprised participants with different types of cancer compared to cancer site-specific programmes were more likely to show positive improvements in physical outcomes. The most effective mode of service delivery appeared to be face-to-face contact supplemented with at least one follow-up telephone call. There was no evidence to indicate that MDRPs which lasted longer than six months improved outcomes beyond the level attained at six months. In addition, there was no evidence to suggest that services were more effective if they were delivered by a particular type of health professional. Authors’ conclusions: There is some evidence to support the effectiveness of brief, focused MDRPs for cancer survivors. Rigorous and methodologically sound clinical trials that include an economic analysis are required (Scott et al. 2013)

This article focuses on the use of multidisciplinary rehabilitation and interventions that address psychosocial outcomes, sexuality, and return to work. Strong evidence indicates that multidisciplinary rehabilitation benefits cancer survivors and that psychosocial strategies can reduce anxiety and depression. Moderate evidence indicates that interventions can support survivors in returning to the level of sexuality desired and help with return to work (Hunter et al. 2017)

**Psychoeducational interventions**

Evidence regarding the effectiveness of potential rehabilitation interventions was reviewed for physical functioning, fatigue, pain, sexual functioning, cognitive functioning, depression, employment, nutrition and participation. With the exception of physical rehabilitation interventions following breast cancer, this literature tends to focus on psychoeducational interventions, which have demonstrated limited effectiveness for rehabilitation outcomes. Authors conclusions: Most of the knowledge available regarding potential rehabilitation interventions comes from psychosocial oncology literature. While there are limitations, this literature provides an excellent starting point to examine the potential effectiveness of rehabilitation interventions within cancer survivorship programs. Implications for rehabilitation: Good evidence exists for the use of exercise/physical rehabilitation in reducing fatigue after treatment for most cancers, and improving upper extremity functioning following treatment for breast cancer. Preliminary evidence exists in a number of areas that may be improved by rehabilitation interventions, such as pain, sexual functioning, cognitive functioning and return to work, but further research is needed. No intervention studies addressing participation limitations were identified.
Rehabilitation professionals are encouraged to take the lead in exploring participation limitations among cancer survivors and developing suitable interventions (Egan et al. 2013).

**Psychosocial interventions**

Two RCTs and one non-randomized psychosocial study comprising 317 bladder cancer patients were included. Timing of the intervention was preoperative (n = 2), postoperative (n = 2) or both pre- and postoperative (n = 2). Psychosocial interventions showed positive effects on anxiety (n = 1), fatigue (n = 1), depression (n = 1), HRQoL (n = 1) and posttraumatic growth (n = 1). Quality assessment showed most shortcomings with sample sizes and strong heterogeneity was observed between studies. Authors conclusions: The evidence relating to the for psychosocial interventions is very limited (Rammant et al. 2017)

**Exercise interventions**

Three RCTs were included. Timing of the intervention was preoperative (n = 2), postoperative (n = 2) or both pre- and postoperative (n = 2). Positive effects of exercise were found for physical fitness (n = 3), some health-related quality-of-life (HRQoL) domains (n = 2), personal activities in daily living (n = 1) and muscle strength (n = 1). Authors conclusions: The evidence relating to the effects of exercise in bladder cancer is very limited (Rammant et al. 2017).

Rehabilitation had positive effects on fatigue, general condition, mood, and coping with cancer. Authors conclusions: Rehabilitation is needed also among patients with advanced disease and in palliative care. Exercise improves physical performance and has positive effects on several other quality of life domains. More data and RCTs are needed, but current evidence gives an indication that rehabilitation is suitable and can be recommended for patients living with advanced cancer. (Salakari et al. 2015)

**Conclusions (for the effectiveness of individual interventions only)**

Multidimensional rehabilitation programs – partially answered

Domains for rehabilitation taking from “Improving Supportive and Palliative Care for Adults with Cancer” (2004) NICE (see further comments below)

- Physical rehabilitation – see R4
- Psychological rehabilitation – see Y1a, Y1b, Y2, Y3, Y5/Y7
- Spiritual rehabilitation – see Y9
- Informational – see H10, S11
- Practical – H2b
- Social – Y8c
- Financial – not searched

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**MULTIDIMENSIONAL REHABILITATION PROGRAMS**
**Scott et al. 2013**  
Multidimensional rehabilitation programs for adult cancer survivors  
Cochrane Database of Systematic Reviews 2013, Issue 3. Art. No.: CD007730.  

**Hunter et al. 2017**  
https://ajot.aota.org/article.aspx?articleid=2599874

**Egan et al. 2013**  
Rehabilitation following cancer treatment.  

**Rammant et al. 2017**  
A systematic review of exercise and psychosocial rehabilitation interventions to improve health-related outcomes in patients with bladder cancer undergoing radical cystectomy.  
*Clin Rehabil.* 2017 Dec 1:269215517746472  
http://journals.sagepub.com/doi/pdf/10.1177/0269215517746472

**Salakari et al. 2015**  
Effects of rehabilitation among patients with advanced cancer: a systematic review.  

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<th>SR – Systematic review, N= narrative review</th>
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**Further comments**  
The majority of studies are focus on a single rehabilitation intervention and its effect on a number of outcomes as opposed to looked at the best form of rehabilitation  
For example  
**Sommer et al. 2018**  
Effect of postsurgical rehabilitation programmes in patients operated for lung cancer: A systematic review and meta-analysis.  
*J Rehabil Med.* 2018 Feb 28;50(3):236-245
To review the evidence concerning the effects of postoperative exercise interventions on exercise capacity and health-related quality of life following resection for non-small cell lung cancer, and to review whether different initiation times of exercise produce different effects on exercise capacity.

National Standards for Rehabilitation of Adult Cancer Patients

Welsh assembly government. 2010
Regional Cancer Networks to develop a Cancer Network Rehabilitation Advisory Group (CNRAG) such that they bring together those planning and providing cancer rehabilitation with an open and transparent management structure, to ensure that all aspects of cancer rehabilitation are developed, coordinated and delivered to an agreed uniform standard of care in line with best practice.

To formalise and identify existing service provision of cancer rehabilitation, gaining approval that it is an essential component throughout the continuum of cancer care. To ensure that all cancer rehabilitation interventions delivered throughout the Network will be assessed as relevant to the person receiving the intervention using an initial screening and ongoing assessment process of need, to be delivered by the most appropriate team members to achieve optimum results.

Cancer rehabilitation should be delivered by competent, capable practitioners supported by well informed support agencies and carers. Patients with rehabilitation needs should be identified, referred, assessed and treated promptly in line with best practice guidelines.

Improving Supportive and Palliative Care for Adults with Cancer (2004) NICE
NICE have described the domains of care in cancer rehabilitation
Each assessment of a patient’s rehabilitation needs should consider each of these domains as and when they progress through their cancer journey. The domains are as follows;
Physical - such as optimising functional ability and management of symptoms such as breathlessness or fatigue
Nutritional - optimising nutritional status to ensure maximum benefit from physical programmes; management of nutrition related symptoms
Psychological - from recognising signs of psychological distress to accruing knowledge and skills to deal with certain levels of distress
Informational - written, audio and visual information
Practical - activities to enhance daily living; returning to work
Spiritual - finding personal value; identifying personal meaning; seeking, finding and maintaining hope; being able to express emotions
Social - relationships; socialising hobbies and pastimes
Financial - paying the rent or mortgage; loss of earnings; travel and other insurance

Out of date findings
Two RCTs, including 262 participants, met the inclusion criteria. Both trials scored poorly for methodological quality. There was 'low level' evidence that multidisciplinary rehabilitation produced short-term gains at the levels of impairment (that is range of shoulder movement), psychosocial adjustment and quality of life after breast cancer treatment (up to 12 months). No evidence was available for the longer-term functional outcomes for caregivers or the cost effectiveness of these programmes. It was not possible to suggest the most appropriate frequency and duration of therapy or choice of one type of intervention over another. Authors' conclusions: There was 'low level' evidence that multidisciplinary rehabilitation can improve the outcomes of people with breast cancer in terms of functional ability, psychosocial adjustment and participation.
in social activities. There was no evidence available on functional gain at the level of activity. This review highlights the limitations of RCTs in rehabilitation settings and the need for high-quality trial-based research in this area. Regular evaluation and assessment of breast cancer survivors for rehabilitation is recommended.

Experiences
Midtgarrd et al. 2015
Dheensa et al. 2013

Suggestions for additional searches
None

<table>
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<tr>
<th>H3: What is the best form of support to help people living with and beyond cancer return to their usual activities (e.g. work)?</th>
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<tbody>
<tr>
<td><strong>Keywords:</strong> Cancer AND work OR employment</td>
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<td><strong>Exclusions:</strong> None</td>
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**SRs (x1 Cochrane SR, 1 Campbell SR x1 SR)**
Two studies involved psycho-educational interventions including patient education and teaching self-care behaviours. Results indicated low quality evidence. Seven RCTs assessed the effects of a medical intervention on return to work (RTW). In all studies a less radical or functioning conserving medical intervention was compared with a more radical treatment. We found low quality evidence that less radical, functioning conserving approaches had similar RTW rates as more radical treatments and moderate quality evidence of no differences in quality of life (De Boer et al 2015: Cochrane SR)

Five RCTs involved multidisciplinary interventions in which vocational counselling, patient counselling, biofeedback-assisted behavioral training and/or physical exercises were combined. Moderate quality evidence showed that multidisciplinary interventions involving physical, psycho-educational and/or vocational components led to higher RTW rates than care as usual. We found no differences in the effect of multidisciplinary interventions compared to care as usual on quality of life outcome.’ (De Boer et al 2015: Cochrane SR)

‘Strong evidence indicates that rehabilitation programs benefit survivors with many types of cancer. Multidisciplinary rehabilitation programs resulted in improved function and participation regardless of type of cancer, stage of cancer, or age of survivor. Moderate evidence indicates that high-intensity exercise (strength, interval, and home based) helped patients minimize the decrease in work ability after cancer and treatment and that multidisciplinary interventions that include physical and psychological aspects in addition to vocational support provided return-to-work benefits’ (Hunter et al 2017).

Our results provide promising evidence that the included interventions may improve employment status (OR = 1.71, 95% confidence interval (CI) = 1.26 to 2.32) for cancer survivors. For RCTs (k = 6), the weighted mean effect size for employment status was OR = 1.44 (CI = 0.99 to 2.09), favoring the intervention groups.
This review highlights the positive effect psychosocial interventions may have on employment outcomes for cancer survivors. However, the methodological shortcomings of the included studies overall makes it likely that there is bias in the results and too few studies to provide sufficiently strong evidence to recommend particular practices. This review brings attention to the need for additional rigorous studies in this area, in particular, randomized controlled trials with more detailed reporting of data and study design and methodology (Fong et al 2015: Campbell SR).

Conclusions:
Fully answered-multiprofessional interventions enhance improved function, participation, and the RTW rates of patients with cancer.

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<th>Authors / Year</th>
<th>Study</th>
<th>Systematic Reviews</th>
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<tr>
<td>Fong et al. 2015</td>
<td>Behavioral, Psychological, Educational, and Vocational Interventions to Facilitate Employment Outcomes for Cancer Survivors: A Systematic Review. Campbell Systematic Reviews 2015:5 <a href="https://www.campbellcollaboration.org/media/k2/attachments/Fong_Cancer_Review.pdf">https://www.campbellcollaboration.org/media/k2/attachments/Fong_Cancer_Review.pdf</a></td>
<td>X</td>
<td></td>
<td>SR</td>
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SR – Systematic review, N= narrative review

Further comments
All other lifestyle activities have already been covered in previous questions

Suggestions for additional searches
Cancer AND Normal activities OR usual activities or daily activities AND return or resume
19. What are the best ways to manage the consequences of nerve damage caused by cancer treatments?

**S9: What are the best ways to manage the consequences of nerve damage caused by cancer treatments**

**Keywords:** Neuropathic Pain OR nerve damage OR peripheral neuropath* AND cancer AND manage

**Exclusions:** Non cancer

**Guidelines**

**Management: Antidepressants, anticonvulsants, topical analgesics:** support a moderate recommendation for treatment with duloxetine. Although the CIPN trials are inconclusive regarding tricyclic antidepressants (such as nortriptyline), gabapentin, and a compounded topical gel containing baclofen, amitriptyline HCL, and ketamine, these agents may be offered on the basis of data supporting their utility in other neuropathic pain conditions given the limited other CIPN treatment options. Further research on these agents is warranted (Hershman et al.2014)

**Summary of reviews** (x1 Cochrane SR, x5 SR)

**Psychological interventions**

Participants included adult patients with cancer related neuropathy but no included papers were retrieved. Two studies retrieved (spinal cord injury and burning mouth syndrome). There is insufficient evidence of the efficacy and safety of psychological interventions for chronic neuropathic pain. The two available studies show no benefit of treatment over either waiting list or placebo control groups (Eccleston et al. 2015)

**Drug treatment: Anticonvulsants: Pregabalin**

There were limited published data reporting efficacy and safety outcomes for pregabalin in the treatment of neuropathic pain in adult patients with cancer. Due to limitations within the studies included in this review, it is not possible to draw any conclusions on the descriptive summary of pregabalin for the treatment of cancer-related neuropathic pain, and further studies are required (Bennett et al. 2013)

**Antidepressants and anticonvulsants:** Antidepressants were used in six studies and anticonvulsants in four studies. We found positive results for amitriptyline (topical), venlafaxine, and oxcarbazepine in one study each, but the results were not sufficient to draw definite conclusions. One trial with duloxetine showed a moderate effect (effect size, 0.513, P = .003) on CIPN pain relief. However, none of the results has yet been duplicated in an RCT with a large sample size. Authors conclusions: insufficient RCTs exist to confirm the efficacy of CNS agents to reduce CIPN. This study highlighted the need for and the importance of conducting well-designed RCTs to generate evidence on CIPN symptom management. Additional RCTs are warranted to accelerate the potential use of CNS drugs for CIPN in cancer patients (Chu et al 2015)

**Drug treatment, topical analgesics and complementary therapy:** The preliminary data for using lafutidine, acupuncture and sweet bee venom pharmacopuncture indicate that they may be useful in CIPN management. The use of duloxetine was effective and supported as a management of CIPN; likewise the use of scrambler therapy significantly decreased CIPN pain. However, the use of electroacupuncture and topical amitriptyline and ketamine was not supported. Authors conclusions: the use of duloxetine was effective in CIPN management. Further studies with larger sample size are needed (Al-Atiyyat and Obaid 2017)
**Lifestyle Related factors**
Significant improvements were detected on postural control. Additionally, patients’ quality of life and independence were found ameliorated after exercise sessions. Combined exercise protocols including endurance, strength and sensorimotor training showed larger improvements. Authors conclusions: This systematic review comes from a highly selected but small source of data. Nevertheless, specific exercise for cancer patients undergoing chemotherapy with CIPN symptoms should be recommended since these interventions appeared as feasible and have been demonstrated as useful tools to counteract some of the limitations due to chemotherapy (Duregon et al 2018)

**Colorectal cancers**: In total, 22 articles were included, which suggested that dietary supplements, such as antioxidants and herbal extracts, as well as physical exercise and complementary therapies, such as acupuncture, may have beneficial effects on preventing or reducing CIPN symptoms. However, many of the reviewed articles presented various limitations, including small sample sizes and heterogeneity in study design and measurements of CIPN. **Authors conclusions**: No strong conclusions can be drawn regarding the role of lifestyle-related factors in the management of CIPN in CRC patients. Certain dietary supplements and physical exercise may be beneficial for the management of CIPN, but further research is warranted (Derksen et al. 2017)

**Conclusions**
Cochrane protocol published review in progress for antipsychotics
Not answered – anticonvulsants (pregabalin, gabapentin) tricyclic antidepressants (nortriptyline), topical gel (containing baclofen, amitriptyline HCL, and ketamine), lutfidine, acupuncture and sweet bee venom pharmacopuncture, psychological therapies
Partially answered – duloxetine, exercise, dietary supplements

For further info also see [https://www.ons.org/practice-resources/pep/](https://www.ons.org/practice-resources/pep/) peripheral-neuropathy
This resource last updated 2017 and includes recommendations for practice, likely to be effective, benefits balanced with harm and effectiveness not established for all treatments associated with peripheral-neuropathy

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<td>Oncology Nursing</td>
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<td>C</td>
<td>HTA</td>
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<td>Society 2017</td>
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<td>X Evidence-based synopsis</td>
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<td><strong>DRUG TREATMENT</strong></td>
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**Further comments**

Cochrane have conducted reviews neuropathic pain in general but they are not specific to cancer patients but have included participants who are adult patients with cancer related neuropathy and have found the studies listed in some of the non Cochrane reviews for cancer related neuropathy

**Out of date**


Multiple, good-quality studies demonstrate superior efficacy of two-drug combinations. However, the number of available studies for any one specific combination, as well as other study factors (e.g. limited trial size and duration), preclude the recommendation of any one specific drug combination for neuropathic pain. Demonstration of combination benefits by several studies together with reports of widespread clinical polypharmacy for neuropathic pain surely provide a rationale for additional future rigorous evaluations. In order to properly identify specific drug combinations which provide superior efficacy and/or safety, we recommend that future neuropathic pain studies of two-drug combinations include comparisons with placebo and both single-agent components. Given the apparent adverse impact of combining agents with similar adverse effect profiles (e.g. CNS depression), the anticipated development and availability of non-sedating neuropathic pain agents could lead to the identification of more favourable analgesic drug combinations in which side effects are not compounded.

**Suggestions for additional searches**

Search by specific management strategies/ treatments AND peripheral neuropathy (e.g acupuncture, herbal medicines, nutraceuticals, taxines, platinum derivatives, drugs)
20. How do the support needs of people with rare and less common cancers differ from people with more common cancers, and how are those needs best met?

93.1 & 417.3. How do the support needs of people with rare cancers differ from people with more common cancers, and how are those needs best met?

Keywords: Rare* AND cancer* OR carcinoma* OR tumour OR tumor OR neoplasm OR oncology OR lymphoma* OR adenoma* AND support OR need* or care

Exclusions: None

Guidelines
None

Summary of reviews
None

Summary of other reviews (x5 NRs)

Rare adult cancer (RAC) is characterised by an incidence of less than six cases per 100,000 people per annum; 4,300,000 patients in the European Union are living with rare cancer (22% of all new human cancers). These cancers are linked with worse survival rates than ‘frequent’ tumours (5-year survival: 47% for RAC against 65% for ‘common’ cancers), mainly because of: (1) delays in obtaining an accurate diagnosis, (2) inadequate treatments given in curative phases and (3) restricted opportunities for patients to participate in clinical trials because of the lack of support for dedicated trials for this disease group from both academic and industrial sponsors.

Although quantitative studies to measure the socioeconomic burden of RACs as a whole are still lacking, the increasing fragmentation of all cancers into molecular subgroups implies a substantial increase in the number of RACs and their associated socioeconomic burden. To answer this urgent and growing need, some countries, cooperative groups, and cancer institutes delineated national and/or regional organisations to promote quality management for RACs. Currently, the European Union (EU) is supporting an official EU call to organise a European network dedicated to RACs. The goals will be to pool the vast knowledge and expertise of the 67 EU clinical reference centres and to cover ten rare adult solid cancer domains across more than 18 countries in order to deploy an integrated, EU-wide capacity towards accelerated innovative treatments and care for RACs while empowering patients. This article will summarise these experiences and the potential benefit for patients (Ray-Coquard et al. 2017)

Rare cancers are at the crossroads of two worlds - the world of cancers and the world of rare diseases. Many issues faced in the organisation of care for rare cancer patients are also identified in the organisation of care for patients with rare diseases: small number of patients, scarcity of expertise, few resources, delay in diagnosis, lack of scientific research and information, insufficient access to care and challenges to develop innovative therapies (Stordeur et al. 2014)

Rare cancers account for about 22 per cent of all cancers diagnosed worldwide, disproportionately affecting some demographic groups, with an occurrence of less than 6 per 100,000 individuals annually. Many rare cancers in adults, adolescents and children are not curable, and patients and care providers have little option to take therapeutic decisions. The epidemiology of rare cancers is a challenging area of study but is inadequately addressed. Despite efforts mainly in some European nations, a few improvements have been observed in the management of rare cancers. Reasons for this obvious stagnation are multifactorial and are mainly inherent to logistical difficulties in carrying out clinical trials in very small patient populations, hesitation of the pharmaceutical industry to spend in small markets and complexity in
Creating adequate information for the development of cost-effective drugs. Rare cancers also face specific challenges that include late and incorrect diagnosis, lack of clinical expertise and lack of research interest and development of new therapies. The utilization of nationally representative study findings for the patients’ evaluation may possibly offer chances to find out pathogenesis and prevalence, and this will eventually lead to control and prevention. Currently, advancing targeted therapies offer a great opportunity for the better management of rare cancers. Conducting clinical trials with small patient population, innovative clinical trial approach, prevailing controlling obstacles for international cooperation and financial support for research are the present challenges for rare cancers. The International Rare Cancers Initiative functions as a main platform for achieving new international clinical trials in rare tumours. This review delineates the current challenges and issues in the interpretation, management and research scenarios of rare cancers (Raveendran and Jayasree, 2017).

Rare cancers, as a collective, account for around a quarter of all cancer diagnoses and deaths. Historically, they have been divided into two groups: cancers defined by their unusual histogenesis (cell of origin or differentiation state)—including chordomas or adult granulosa cell tumours—and histologically defined subtypes of common cancers. Most tumour types in the first group are still clinically and biologically relevant, and have been disproportionately important as sources of insight into cancer biology. By contrast, most of those in the second group have been shown to have neither defining molecular features nor clinical utility. Omics-based analyses have splintered common cancers into a myriad of molecularly, rather than histologically, defined subsets of common cancers, many of which have immediate clinical relevance. Now, almost all rare cancers are either histomolecular entities, which often have pathognomonic mutations, or molecularly defined subsets of more common cancers. The presence of specific genetic variants provides rationale for the testing of targeted drugs in rare cancers. However, in addition to molecular alterations, it is crucial to consider the contributions of both mutation and cell context in the development, biology, and behaviour of these cancers. Patients with rare cancers are disadvantaged because of the challenge of leading clinical trials in this setting due to poor accrual. However, the number of patients with rare cancers will only increase as more molecular subsets of common cancers are identified, necessitating a shift in the focus of clinical trials and research into these cancer types, which, by epidemiological definitions, will become rare tumours (Boyd et al. 2016).

Rare cancers are defined by an incidence of less than six per 100 000 people per year. They represent roughly 20% of all human cancers and are associated with worse survival than are so-called frequent tumours, because of delays to accurate diagnosis, inadequate treatments, and fewer opportunities to participate in clinical trials (because of a paucity of dedicated trials from both academic and industrial sponsors). In this Series paper, we discuss how these challenges can be addressed by research consortia and suggest the integration of these consortia with reference networks, which gather multidisciplinary expert centres, for management of rare tumours (Blay et al. 2016).

Summary of primary research
With more treatment options for people with cancer long-term survivorship is increasing. Physical and psycho-social needs have been identified in survivors of common cancers but very little has been written about the needs of patients with rarer cancers. Patients treated for rarer cancer are discharged to the primary health care team (PHCT), yet little is known about the assessment, management and support of these patients. Thirty-nine semi-structured interviews were conducted with (1) survivors of and (2) people living with rarer cancer (i.e. <5% of cancer burden). Participants were asked about physical and psycho-social needs and service provision. Data were analysed thematically using Atlas ti. Contrary to expectation, disease-free survivors of rarer cancer were indistinguishable from those living with disease in their ability to cope, and range of symptoms and needs. Participants with a clinical nurse specialist (CNS) reported that they were well supported on their return home and their needs were met. Participants without a CNS were referred to the PHCT who were unsure how to assess or support them. These participants felt abandoned. There is a need for the rehabilitation of patients with rarer cancer to strengthen individual coping mechanisms, and family and social support. Although
there are resource and training implications, this is a potential role for the PHCT, district nursing in particular, and may lead to more focused and targeted provision of services (Griffiths et al. 2007)

Medullary thyroid carcinoma (MTC) is a rare disease, and specific experience with the condition is not commonly found outside of major cancer centers. Because of the rarity and slow-growing natural history of the disease, patients with MTC frequently have many questions concerning prognosis, treatment, and follow-up care. Many of these patients have joined an e-mail group on the Internet through which they share information and concerns. The author has joined this group and shares her expert clinical knowledge about the disease. When individuals are armed with accurate and expert information, they can make informed decisions. The source of this information can be diverse. Nurses with expert knowledge can use opportunities such as e-mail groups to answer questions and respond openly about subjects about which they have unique perspectives (Schultz 2002)

Conclusions
Not met

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<th>Authors / Year</th>
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<td>Schultz 2002</td>
<td>Providing information to patients with a rare cancer: using internet discussion forums to address the needs of patients with medullary thyroid carcinoma.</td>
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<td>Boyd et al. 2016</td>
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<td>Blay et al. 2016</td>
<td>The value of research collaborations and consortia in rare cancers.</td>
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SR – Systematic review, N= narrative review

Further comments
Not a lot of research in this area

http://www.cancerresearchuk.org/about-cancer/rare-cancers/living-with

Only 122 articles from 2013-2018 with the word rare cancer in the title

Suggestions for additional searches
Specific types of rare cancer although Macmillan state that there are 198 different types of rare cancer!
21. What can be done to reduce and manage the impact of cancer treatments on people’s sex lives?

<table>
<thead>
<tr>
<th>S8: What can be done to reduce and manage the impact of cancer treatments on people’s sex lives (managing loss of libido, pain during sex, orgasmic changes and impotence, and psychological impacts)?</th>
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</table>

**Keywords:** Cancer AND sexual (function/dysfunction/problems/rehabilitation/life/issues/satisfaction/health/quality of life/concerns) AND intervention(s) AND manage(ment)

Exclusions: Young adults and adolescents

**Guidelines (Relevant for all cancers)**

**American Society of Clinical Oncology Guidelines, 2017:** It is recommended that there be a discussion with the patient, initiated by a member of the health care team, regarding sexual health and dysfunction resulting from cancer or its treatment. Psychosocial and/or psychosexual counseling should be offered to all patients with cancer, aiming to improve sexual response, body image, intimacy and relationship issues, and overall sexual functioning and satisfaction. Medical and treatable contributing factors should be identified and addressed first. In women with symptoms of vaginal and/or vulvar atrophy, lubricants in addition to vaginal moisturizers may be tried as a first option. Low-dose vaginal estrogen, lidocaine, and dehydroepiandrosterone may also be considered in some cases. In men, medication such as phosphodiesterase type 5 inhibitors may be beneficial, and surgery remains an option for those with symptoms or treatment complications refractory to medical management. Both women and men experiencing vasomotor symptoms should be offered interventions for symptomatic improvement, including behavioral options such as cognitive behavioral therapy, slow breathing and hypnosis, and medications such as venlafaxine and gabapentin.

**NICE guidelines. 2008 and updated in 2014 (Specific for Prostate Cancer)**

Sexual dysfunction Ensure that men have early and ongoing access to specialist erectile dysfunction services. [2008, amended 2014]

Offer men with prostate cancer who experience loss of erectile function phosphodiesterase type 5 (PDE5) inhibitors to improve their chance of spontaneous erections. [2008] 1.3.33 If PDE5 inhibitors fail to restore erectile function or are contraindicated, offer men vacuum devices, intraurethral inserts or penile injections, or penile prostheses as an alternative. [2008]

**Summary of SRs (4 SRs, x1Cochrane, x3 other)**

**Occupational therapy interventions** (Relevant to all cancer patients)

Limited research has been conducted on interventions related to sexuality. This area of rehabilitation is relevant for occupational therapists, and more high-quality studies should be conducted in this area in the future. Moderate evidence supports interventions to address sexuality in cancer patients and survivors. The strongest evidence related to sexuality supports physical exercise for survivors, an important area to address for numerous types of cancer (Hunter et al. 2017: SR)

**Interventions conducted with women**

The trials varied not only in intervention content but in outcome measurements, thereby restricting combined analysis. In the trials evaluating a psychotherapeutic intervention the effect on sexual dysfunction was mixed; in three trials benefit was found for some measures of sexual function and in five trials no benefit was found.
Evidence from the other three trials, two on different pharmaceutical applications and one on exercise, differed and was limited by small sample sizes. Only the trial of a pH-balanced vaginal gel found significant improvements in sexual function (Candy et al 2016: Cochrane SR)

**Couple-based interventions**

**Breast cancer:**

There was no clear consensus about how couple-based interventions are best structured. The results provide tentative evidence for how the quality of future research studies can be improved and how knowledge can be used in clinical practice (Jonsdottir et al. 2017: SR)

Couple-based sex therapy appears to be an effective and highly accepted treatment for addressing sexual problems in breast cancer patients. These interventions were associated with improvements in sexual physiology, sexual functioning, sexual self-image, and sexual relationships, as well as improved psychological well-being of both breast cancer patients and their partners. (Carroll et al 2016: SR)

**Summary of other types of review** (x 1 NR)

**Prostate cancer**

‘While several preventive and treatment strategies for the preservation and recovery of sexual function are available, no specific recommendation or consensus guidelines exist regarding the optimal rehabilitation or treatment protocol. While medical and surgical therapies are effective in erectile function recovery and/or preservation, psychological and sexual counseling are equally important in sexual rehabilitation’. (Chung and Brock 2013)

**Conclusions:**


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**Comments:**

**Out of date guidance:**
Prostate cancer and sexual function (there is a massive literature on this area)

**Suggestions for additional searches**
- Interventions AND sexual AND radiotherapy OR chemotherapy
- Psychological interventions AND Sex AND Cancer
- Oestrogen creams and pessaries
- Benzydamine douches
- Moisturising creams and lubricants
- Vaginal stent/ dilator
- vaginal lubricants
- AND radiotherapy

**Examples of the types of papers that would be retrieved from the above:**
22. What are the best ways to support people living with and beyond cancer who live alone?

<table>
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<tr>
<th>Y3: What are the best ways to support people living with and beyond cancer who live alone?</th>
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<tbody>
<tr>
<td><strong>Exclusions:</strong> Palliative care, end of life care</td>
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**Guidelines**
None

**Summary of primary research (x6)**

**Lived experience**
This study describes the lived experiences of older people coping with terminal cancer and living alone, focusing on how they face challenges of the biographical life changes from their disease progression. Face-to-face semi-structured interviews were conducted in two phases with palliative care clients of a community-based service in Western Australia (2009-2011): Brief interviews with 43 cancer patients who live alone and then in-depth interviews with 8 of them. Using biographical disruption as the analytical framework for interpreting the qualitative data, four main themes emerged: Biographical disruption: adjusting to change; Biographical continuity: preserving normality; Biographical reconstruction: redefining normality; and Biographical closure: facing the end. Biographical disruption was a suitable framework for analysis, permitting identification of the biographical disruptions of the individual's world and the reframing that is undertaken by the individual to maintain autonomy and independence while acknowledging and accepting their closeness to death. Understanding the factors associated with the individual's need to maintain their own identity will enable nurses working with this population to tailor support plans that meet the individuals' needs while maintaining or restoring the person's sense of self. Interventions that directly address end-of-life suffering and bolster sense of dignity and personhood need to be considered (Aoun et al. 2016)

Many experiences were common to all participants, but had broader consequences for people who lived alone. Five themes are presented from the data: a perception that it is a disadvantage to live alone as a patient, the importance of relational continuity with health professionals, informal appraisal of care, place of care and future plans. People who lived alone perceived emotional and practical barriers to accessing care, and many shared an anxiety that they would have to move into a care home. Participants were concerned with remaining life, and all who lived alone had made plans for death but not for dying. Uncertainty of timescales and a desire to wait until they knew that death was imminent were some of the reasons given for not planning for future care needs. Authors conclusions: Older people who live alone with cancer have emotional and practical concerns that are overlooked by their professional carers. Discussion and planning for the future, along with continuity in primary care may hold the key to enhancing end-of-life care for this group of patients (Hanratty et al. 2013)

This paper seeks to understand the experiences of single colorectal cancer patients. This study consisted of 12 semi-structured interviews that were digitally voice-recorded, transcribed, and analyzed. Six main themes emerged: (a) gradual shift in view of cancer diagnosis from fatalistic to normalized, (b) perception of cancer as a nadir experience, (c) concerns of singlehood, (d) factors influencing cancer experiences, (e) factors influencing coping with cancer, and (f) range of responses towards cancer diagnosis. Singles with colorectal cancer require short- to long-term individualized care plans, and psycho-emotional support. This may help enhance their individual coping and adjustment to the diagnosis (Tan et al. 2015)
Cancer patients who live alone place specific importance on acting independently during treatment. We want to describe what it means to act independently and which strategies patients use to continue to act independently. We used a qualitative design, based on grounded theory. We interviewed 32 patients, 17 of them a second time. Patients who live alone defined acting independently in two different ways: It meant not only doing things alone but also using the help of others in a controlled way. These two meanings lead to two types of strategies. As treatment evolves, patients needed to change their preferred type of strategies to continue acting independently. Succeeding to change led to a feeling of mastery and success. However, failing to change led to struggling, whereby patients' needs became invisible. Health care providers should anticipate patients' inability to change strategies during cancer treatment, thereby preventing the patient's struggle from only becoming visible during crisis (Benoot et al. 2015b).

Social isolation intervention
The primary objective of the PREDOMOS study is to evaluate the impact of establishing a Program of Social intervention associated with techniques of Domotic and Remote assistance (PS-DR) on the improvement of QoL of elderly isolated patients, treated for locally advanced or metastatic cancer. The secondary objectives include treatment failure, tolerance, survival, and autonomy (Crétel-Durand et al. 2017).

Informal support
Objective: Staying independent is an important need for cancer patients living alone. Such patients might have specific informal support needs in order to stay independent. We want to explore which informal support patients living alone perceive as helpful along the cancer care continuum. Methods: A purposeful sample of 32 patients living alone and undergoing cancer treatment were interviewed, using a semi-structured interview guide. Seventeen of them were interviewed a second time, 8 months to 1 year later. Analysis was conducted using grounded theory techniques. Results: The informal support patients received was not experienced unconditionally positive. We found that an equilibrium was necessary between reducing the disadvantages of living alone while not endangering the advantages of living alone, resulting in a need for an equilibrium between distance and proximity with their informal network. The needed equilibrium was influenced by the patients' history of living alone, the perception of helpfulness of the informal network, the acuteness of side-effects and prognosis of the disease. We found that, as treatment progressed, patients tended to favor proximity and needed a greater share of the support to be provided by professionals. Conclusions: Cancer patients living alone experience informal support as an ambiguous blessing. Such support has to be given in a fine balance in order to be perceived as helpful. Health care providers should educate the informal network of the patient about which support is helpful, and under what circumstances (Benoot et al. 2015).

Conclusions
Not answered
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SR – Systematic review, N= narrative review

**Further comments**
None

**Suggestions for additional searches**
None

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23. How is cancer perceived across multiple black and minority ethnic groups – what are the similarities and differences?

241.3. How is cancer conceptualised across multiple black and minority ethnic groups - comparison on similarities and differences.

**Keywords:** cancer conceptualised AND minorit* cancer AND minorit* AND review

**Exclusions:** Screening, EOL care, surveillance, genetic testing, research participation

**Guidelines**
None

**Summary of reviews** (x2 SRs)

**Cancer beliefs**
People from ethnic minorities often experience poorer cancer outcomes, possibly due to later presentation to healthcare and later diagnosis. We aimed to identify common cancer beliefs in minority populations in developed countries, which can affect symptom appraisal and help seeking for symptomatic cancer. Our systematic review found 15 relevant qualitative studies, located in the United Kingdom (six), United States (five), Australia (two) and Canada (two) of African, African-American, Asian, Arabic, Hispanic and Latino minority groups. We conducted a meta-synthesis that found specific emotional reactions to cancer, knowledge and beliefs and interactions with healthcare services as contributing factors in help seeking for a cancer diagnosis. These findings may be useful to inform the development of interventions to facilitate cancer diagnosis in minority populations. We found that fatalism, fear, stigma, poor knowledge about cancer causation, symptoms, treatment and prognosis, and attitudes about cancer influence symptom appraisal and help seeking and could potentially affect timely cancer diagnosis in people from ethnic minority backgrounds (Licurish et al. 2017).

**Shared decision making**
To assess decision-making for cancer treatment among racial/ethnic minority patients, we systematically reviewed and synthesized evidence from studies of "shared decision-making," "cancer," and "minority groups," using PubMed, PsycInfo, CINAHL, and EMBASE. We identified significant themes that we compared across studies, refined, and organized into a conceptual model. Five major themes emerged: treatment decision-making, patient factors, family and important others, community, and provider factors. Thematic data overlapped categories, indicating that individuals' preferences for medical decision-making cannot be authentically examined outside the context of family and community. The shared decision-making model should be expanded beyond the traditional patient-physician dyad to include other important stakeholders in the cancer treatment decision process, such as family or community leaders (Mead et al. 2013).

**Conclusions**
Partially answered

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Further comments
Cancer conceptualised (0) hits in database searches
This question needs unpacking so that it can be searched

Suggestions for additional searches
Specific minority groups

356.1 & 356.3 What is the biological mechanism causing hot flushes in breast cancer living with and beyond breast cancer and is this different to women without breast cancer?

S10 What are the safest and most effective ways of managing early menopause caused by cancer treatments?

Keywords: Breast Cancer AND hot flushes OR hot flashes / Cancer AND menopause AND manage*

Exclusions: Men with prostate cancer

Guidelines (x2, X1 quality statement)
Managing early menopause-Breast cancer
NICE 2017a: Discontinue hormone replacement therapy (HRT) in women who are diagnosed with breast cancer.
- 1.13.9 Do not offer HRT (including oestrogen/progestogen combination) routinely to women with menopausal symptoms and a history of breast cancer. HRT may, in exceptional cases, be offered to women with severe menopausal symptoms and with whom the associated risks have been discussed.
- 1.13.10 Offer information and counselling for all women about the possibility of early menopause and menopausal symptoms associated with breast cancer treatment.
• 1.13.11 Tibolone or progestogens are not recommended for women with menopausal symptoms who have breast cancer.

• 1.13.12 The selective serotonin re-uptake inhibitor antidepressants paroxetine and fluoxetine may be offered to women with breast cancer for relieving menopausal symptoms, particularly hot flushes, but not to those taking tamoxifen.

• 1.13.13 Clonidine, venlafaxine and gabapentin should only be offered to treat hot flushes in women with breast cancer after they have been fully informed of the significant side effects.

• 1.13.14 Soy (isoflavone), red clover, black cohosh, vitamin E and magnetic devices are not recommended for the treatment of menopausal symptoms in women with breast cancer.

Managing early menopause-Other cancer treatments

NICE 2017b: Treatments that are likely to cause menopause include: radiotherapy and chemotherapy for cancer and gynaecological surgery that involves the ovaries.

NICE 2015. Offer women who are likely to go through menopause as a result of medical or surgical treatment (including women with cancer, at high risk of hormone-sensitive cancer or having gynaecological surgery) support and information about menopause and fertility before they have their treatment and referral to a healthcare professional with expertise in menopause

Summary of other types of review (x1)

Biological mechanism- Breast cancer-

A review by Kaplon and Mahon (2014) notes ‘Hot flashes are reported to be significantly more frequent and severe in women treated for breast cancer than in women undergoing natural menopause (Carpenter, 2005; Kadakia et al., 2012). Hot flashes are believed to be precipitated by the abrupt suppression of ovarian function caused by chemotherapy-induced premature menopause and/or the use of estrogen withdrawal therapies, including tamoxifen and aromatase inhibitors (Baber, Hickey, & Kwik, 2005; Howell et al., 2005; Morrow, Mattair, & Hortobagyi, 2011). Tamoxifen has been shown to produce more frequent and severe hot flashes than the aromatase inhibitors anastrozole and letrozole (Howell et al., 2005; Morrow et al., 2011).’

Conclusions

Fully answered- Biological mechanism
Fully answered -menopausal symptoms caused by breast cancer treatment
Fully answered-management of early menopause caused by cancer treatments

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SR – Systematic review, N= narrative review

Further comments
https://www.ons.org/practice-resources/pep/hot-flashes provides evidence on treatment "likely to be effective", "benefits balanced with harm" and "effectiveness not established".

Suggestions for additional searches
None
24. Can lymphoedema be prevented? If not, how is it best treated/managed?

**Can lymphoedema be prevented?**

**Keywords searched:** Lymph(o)edema AND prevent*

**Exclusions:** None

**Guidelines**
None

**Summary of SRs (3 SRs, x1 Cochrane, x2 others)**

**Manual lymph drainage**
Based on the current available evidence, Stuiver et al (2015; Cochrane SR) state that they cannot draw firm conclusions about the effectiveness of interventions containing manual lymph drainage. The evidence does not indicate a higher risk of lymphoedema when starting shoulder-mobilising exercises early after surgery compared to a delayed start (i.e. seven days after surgery). Shoulder mobility (lateral arm movements and forward flexion) is better in the short term when starting shoulder exercises earlier compared to later. The evidence suggests that progressive resistance exercise therapy does not increase the risk of developing lymphoedema, provided that symptoms are closely monitored and adequately treated if they occur.

**Microsurgery**
Hayes Inc (2013) suggest that when conservative measures (massage, exercise, compression bandages or garments) fail surgery may be considered. Resection or debulking involves removal of the swollen tissue whereas microsurgery aims to create a way for the lymph fluid to drain from the arm; possibly into areas above the lymphedema or into the venous circulation. Primary prevention of lymphedema would be advantageous in patients undergoing breast cancer surgery.

**Lymphovenous anastomosis (LVA)**
Jørgensen et al. (2017) found from a meta analysis that patients treated with prophylactic LVA had a significant reduction in lymphedema incidence. The authors conclude that prophylactic LVA in relation to lymphadenectomy shows promising results, however because of the low number of eligible studies and method heterogeneity between studies, there is an urgent need for uniformly high quality studies, before the treatment can be concluded effective.

**Conclusions**
Partially answered:
Some promising results for microsurgery but more trials needed.

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**PREVENTION**

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SSb? If not, how is it (lymphedema) best treated/managed?

Keywords searched: Lympho(o)dema AND treat* OR manage OR prevent*

Guidelines

NICE (2017) Liposuction for chronic lymphoedema. Recommendations:

1.1 Current evidence on the safety and efficacy of liposuction for chronic lymphoedema is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit.

1.2 Patient selection should only be done by a multidisciplinary team as part of a lymphoedema service.

Summary of SRs (5 SRs x1 Cochrane, x1 JBI, 3 others)

Manual lymphatic drainage

Manual lymphatic drainage is safe and may offer additional benefit to compression bandaging for swelling reduction. Compared to individuals with moderate-to-severe BCRL, those with mild-to-moderate BCRL may be the ones who benefit from adding MLD to an intensive course of treatment with compression bandaging. This finding, however, needs to be confirmed by randomized data. In trials where MLD and sleeve were compared with a non MLD treatment and sleeve, volumetric outcomes were inconsistent within the same trial. Research is needed to identify the most clinically meaningful volumetric measurement, to incorporate newer technologies in LE assessment, and to assess other clinically relevant outcomes such as fibrotic tissue formation. Findings were contradictory for function (range of motion), and inconclusive for quality of life. For symptoms such as pain and heaviness, 60% to 80% of participants reported feeling better regardless of which treatment they
received. One-year follow-up suggests that once swelling had been reduced, participants were likely to keep their swelling down if they continued to use a custom-made sleeve (Ezzo et al 2015: Cochrane Review)

**Exercise; Intermittent pneumatic compression and compression sleeves**
Rogan et al (2016) Exercise seems beneficial in reducing oedema volume in BCRL. Intermittent pneumatic compression (IPC) seems beneficial in helping to reduce the oedema volume in the acute phase of treatment. Compression sleeves do not aid in the volume reduction in the acute phase; however, they do prevent additional swelling. All conclusions should be taken with precautions because of the insufficient quality of the selected papers.

**Decongestive treatments**
Jeffs et al (2018) Weak evidence (grade B) for the impact of decongestive lymphedema treatment on women with early lymphedema (i.e. less than 12 months duration of BCRL symptoms) did not allow any conclusions to be drawn about the most effective treatment to be offered when these women first present for treatment. Findings provided no justification to support change to current practice (Jeffs et al 2018: JBI review)

**Current treatments**
Li et al (2016) Although many treatments for BCRL might reduce lymphoedema volume, their effects were not well established. The quality of many of the original studies in the included reviews was not optimal, so that in future randomized control trials are a high priority. Combined physical therapy (CPT) with different combinations of surgery, oral pharmaceuticals, low-level laser therapy, weight reduction, mesenchymal stem cell therapy, kinesio tex taping, and acupuncture might be effective in reducing lymphoedema, but exercise demonstrated no obvious benefit. The results of direct comparisons showed CPT might be more effective than standard physiotherapy (ST). Manual lymphatic drainage (MLD) may not offer additional benefits to ST for swelling reduction, but could facilitate compression bandaging. MLD seemed to have similar effects with self-administered simple lymphatic drainage (SLD) or using an intermittent pneumatic compression pump (IPC). IPC might also not be associated with additional effectiveness for CPT. Efficacy of stem cell therapy vs. compression sleeve or CPT, as well as the effects of daflon and coumarin could not be established.

Leung et al (2015) Few studies have evaluated the clinical effectiveness and potential side effects of treatments for lower limb lymphoedema. Moreover, symptoms and quality-of-life assessments were inconsistently reported. All included studies report lower limb volume reduction after treatment, which includes complex decongestion therapy, graded compression stockings and lymphovenous microsurgical shunts. Adequately powered randomised controlled trials of these interventions are recommended. Effort should be made to establish standardised outcomes, to minimise bias and to improve reporting quality in future trials of treatment for lower limb lymphoedema.

**Summary of other types of review article**
Leung et al (2015) Liposuction reduces the volume and symptoms of lymphedema, but requires continual compressive therapy to avoid recurrence. Lymphatic reconstruction or bypass techniques including lymph node transfer (inguinal nodes are transferred to the affected limb), lymphatico-lymphatic bypass (lymphatics bypass the axilla using a lymph vessel graft reconstructing lymphatic flow from arm to neck) and lymphaticovenous anastomoses (lymphatics in the arm are joined to the venous system aiding lymph drainage) show promise in reducing lymphedema significantly. Further research is required, including into the role of primary lymphaticovenous anastomoses in the prevention of lymphedema at the time of axillary dissection.
### Conclusions
- Fully answered: Liposuction (NICE 2017) and manual lymphatic drainage (Ezzo et al 2015).

For further info also see https://www.ons.org/practice-resources/pep/lymphedema

This resource last updated 2017 and includes recommendations for practice, likely to be effective, benefits balanced with harm and effectiveness not established for all treatments associated with lymphoedema.

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**Further comments**

**Out of date guidance**

RCN 2011 – Reducing the risk of upper limb lymphoedema

**Suggested additional search terms**

None covered by Oncology Nursing Society 2017
25. What is the optimal follow-up approach to detect whether a cancer has come back?

**T3: What is the optimal approach to follow-up to detect whether a cancer has come back?**

**Keywords:** Detect OR monitor* OR screen* OR surveillance AND cancer AND recur*

**Exclusions:** risk of recurrence, incidence of recurrence, treatments for recurrent cancer, accuracy of diagnostic tests

**Guidelines** (x 7 NICE, x1 Royal College of Radiologists, x1 other)

**Follow up strategies**

**Colorectal cancer:**

NICE. 2014 See: 1.4.1 Follow-up after apparently curative resection

1.4.1.1 Offer follow-up to all patients with primary colorectal cancer undergoing treatment with curative intent. Start follow-up at a clinic visit 4–6 weeks after potentially curative treatment.

1.4.1.2 Offer patients regular surveillance with:

- a minimum of two CTs of the chest, abdomen, and pelvis in the first 3 years and
- regular serum carcinoembryonic antigen tests (at least every 6 months in the first 3 years).

1.4.1.3 Offer a surveillance colonoscopy at 1 year after initial treatment. If this investigation is normal consider further colonoscopic follow-up after 5 years, and thereafter as determined by cancer networks. The timing of surveillance for patients with subsequent adenomas should be determined by the risk status of the adenoma.

1.4.1.4 Start reinvestigation if there is any clinical, radiological or biochemical suspicion of recurrent disease.

1.4.1.5 Stop regular follow-up:

- when the patient and the healthcare professional have discussed and agreed that the likely benefits no longer outweigh the risks of further tests or
- when the patient cannot tolerate further treatments.

**Bladder cancer**

NICE 2015: See 1.6 Follow-up after treatment for muscle-invasive bladder cancer

Offer follow-up after radical cystectomy or radical radiotherapy.

1.6.2 After radical cystectomy consider using a follow-up protocol that consists of:

- monitoring of the upper tracts for hydronephrosis, stones and cancer using imaging and glomerular filtration rate (GFR) estimation at least annually and
- monitoring for local and distant recurrence using CT of the abdomen, pelvis and chest, carried out together with other planned CT imaging if possible, 6, 12 and 24 months after radical cystectomy and
- monitoring for metabolic acidosis and B12 and folate deficiency at least annually and
- for men with a defunctioned urethra, urethral washing for cytology and/or urethroscopy annually for 5 years to detect urethral recurrence.

1.6.3 After radical radiotherapy consider using a follow-up protocol that includes all of the following:

- rigid cystoscopy 3 months after radiotherapy has been completed, followed by either rigid or flexible cystoscopy:
  - every 3 months for the first 2 years then
• every 6 months for the next 2 years then
• every year thereafter, according to clinical judgement and the person’s preference
• upper-tract imaging every year for 5 years
• monitoring for local and distant recurrence using CT of the abdomen, pelvis and chest, carried out with other planned CT imaging if possible, 6, 12 and 24 months after radical radiotherapy has finished.

**Early breast cancer**
NICE 2017: See 1.14 Follow Up

*Follow-up imaging*

1.14.1 Offer annual mammography to all patients with early breast cancer, including DCIS, until they enter the NHSBSP/BTWSP. Patients diagnosed with early breast cancer who are already eligible for screening should have annual mammography for 5 years.

1.14.2 On reaching the NHSBSP/BTWSP screening age or after 5 years of annual mammography follow-up we recommend the NHSBSP/BTWSP stratify screening frequency in line with patient risk category.

1.14.3 Do not offer mammography of the ipsilateral soft tissues after mastectomy.

1.14.4 Do not offer ultrasound or MRI for routine post-treatment surveillance in patients who have been treated for early invasive breast cancer or DCIS

*Clinical follow-up*

1.14.5 After completion of adjuvant treatment (including chemotherapy, and/or radiotherapy where indicated) for early breast cancer, discuss with patients where they would like follow-up to be undertaken. They may choose to receive follow-up care in primary, secondary, or shared care.

1.14.6 Patients treated for breast cancer should have an agreed, written care plan, which should be recorded by a named healthcare professional (or professionals), a copy sent to the GP and a personal copy given to the patient. This plan should include:

- designated named healthcare professionals
- dates for review of any adjuvant therapy
- details of surveillance mammography
- signs and symptoms to look for and seek advice on
- contact details for immediate referral to specialist care, and
- contact details for support services, for example support for patients with lymphoedema.

**Oesophageal cancer**
NICE 2018: see 1.7 Follow-up

1.7.1 For people who have no symptoms or evidence of residual disease after treatment for oesophago-gastric cancer with curative intent:

- provide information about the symptoms of recurrent disease, and what to do if they develop these symptoms
- offer rapid access to the oesophago-gastric multidisciplinary team for review, if symptoms develop.

1.7.2 For people who have no symptoms or evidence of residual disease after treatment for oesophago-gastric cancer with curative intent, do not offer:

- routine clinical follow-up solely for the detection of recurrent disease
- routine radiological surveillance solely for the detection of recurrent disease.
Skin Cancer
NICE see 1.9 Follow-up after treatment for melanoma
1.9 Follow-up after treatment for melanoma
Follow-up for all people who have had melanoma
1.9.1 Perform a full examination of the skin and regional lymph nodes at all follow-up appointments.
1.9.2 Consider personalised follow-up for people who are at increased risk of further primary melanomas (for example people with atypical mole syndrome, previous melanoma, or a history of melanoma in first-degree relatives or other relevant familial cancer syndromes).
1.9.3 Consider including the brain for people having imaging as part of follow-up after treatment for melanoma.
1.9.4 Consider imaging the brain if metastatic disease outside the central nervous system is suspected.
1.9.5 Consider CT rather than MRI of the brain for adults having imaging as part of follow-up or if metastatic disease is suspected.
1.9.6 Consider MRI rather than CT of the brain for children and young people (from birth to 24 years) having imaging as part of follow-up or if metastatic disease is suspected.
1.9.7 Provide psychosocial support for the person with melanoma and their family or carers at all follow-up appointments.
1.9.8 All local follow-up policies should include reinforcing advice about self-examination (in line with recommendation 1.1.2), and health promotion for people with melanoma and their families, including sun awareness, avoiding vitamin D depletion (in line with recommendation 1.1.3), and NICE guidance on smoking cessation.
1.9.9 Continue to manage drug treatment for other conditions in line with recommendations 1.4.1 and 1.4.2 after treatment for melanoma.
See also
Follow-up after stage 0 melanoma
Follow-up after stage IA melanoma
Follow-up after stages IB–II melanoma or stage IIC melanoma (fully staged using sentinel lymph node biopsy)
Follow-up after stage IIC melanoma with no sentinel lymph node biopsy or stage III melanoma
Follow-up after stage IV melanoma

Oesophago-gastric cancer
NICE 2018: see 1.7 Follow-up
1.7.1 For people who have no symptoms or evidence of residual disease after treatment for oesophago-gastric cancer with curative intent: provide information about the symptoms of recurrent disease, and what to do if they develop these symptoms
offer rapid access to the oesophago-gastric multidisciplinary team for review, if symptoms develop.
1.7.2 For people who have no symptoms or evidence of residual disease after treatment for oesophago-gastric cancer with curative intent, do not offer: routine clinical follow-up solely for the detection of recurrent disease routine radiological surveillance solely for the detection of recurrent disease.

Cancer of the upper aerodigestive tract
NICE see 1.8 Follow-up of people with cancer of the upper aerodigestive tract and management of osteoradionecrosis
Follow-up
1.8.1 Ensure people with cancer of the upper aerodigestive tract and their carers have tailored information about the symptoms of recurrence and late effects of treatment at the end of curative therapy.

1.8.2 Consider structured, risk-adapted follow-up using locally-agreed protocols for people who have had curative treatment for cancer of the upper aerodigestive tract. Use the follow-up protocols to:

- help improve quality of life, including discussing psychosocial issues
- detect disease recurrence or second primary cancer, possibly including narrow-band imaging to improve detection.

**Laryngeal cancer**

European Laryngological Society 2014: See statement 9

“...The risk of developing an SPT and its early detection should be part of the follow-up of patients treated with LC and, therefore, appropriate and adequate screening strategies should be employed routinely — Grade B.

**Cross-sectional imaging** (Royal College of Radiologists): see full text in other comments below

**Colon, rectum and anal canal cancer**

**Lung cancer:**

**Oesophagus and stomach cancers**

**Testicular cancer**

**Summary of reviews** (x6 Cochrane SR, 2 HTA review, x6 SR)

**Diagnostic tests**

**Blood Carcino-Embryonic Antigen (CEA) levels for colorectal cancer**

CEA is insufficiently sensitive to be used alone, even with a low threshold. It is therefore essential to augment CEA monitoring with another diagnostic modality in order to avoid missed cases. Trying to improve sensitivity by adopting a low threshold is a poor strategy because of the high numbers of false alarms generated. We therefore recommend monitoring for colorectal cancer recurrence with more than one diagnostic modality but applying the highest CEA cut-off assessed (10 µg/L) (Nicholson et al. 2015: Cochrane SR)

Results point toward a sensitivity of CEA ranging between 50 % and 80 %, and a specificity and negative predictive value above 80 %. Results on positive predictive value showed low reliability. Overall, CEA did not effectively detect treatable recurrences at an early stage, and a clinically relevant effect on patient mortality remains to be proven. (Sorenson et al. 2016, Shrinkins et al. 2017: HTA SR)

The results suggest that (1) CEA testing should not be used alone as a triage test; (2) in year 1, testing frequency should be increased (to monthly for 3 months and then every 2 months); (3) the threshold for investigating a single test result should be raised to 10 µg/l; (4) after the second CEA test, decisions to investigate further should be made on the basis of the trend in CEA levels; (5) the optimal threshold for investigating the CEA trend falls over time; and (6) continuing smokers should not be monitored with CEA testing. Further research is needed to explore the operational feasibility of monitoring the trend in CEA levels and to externally validate the proposed thresholds for further investigation (Sorenson et al. 2016)
Serum CA125 levels: Limited evidence from a single trial suggests that routine surveillance with CA125 in asymptomatic patients with ovarian cancer and treatment at CA125 relapse does not seem to offer survival advantage when compared to treatment at symptomatic relapse. RCTs are needed to compare different types of follow-up, looking at survival, QoL, cost and psychological effects as outcomes (Clarke et al 2014: Cochrane SR)

Cross sectional imaging

Positron emission tomography (PET) and positron emission tomography–computed tomography (PET-CT)

This SR focused on the use of positron emission tomography (PET) and PET with computed tomography for the surveillance of patients after treatment for lymphoma, colorectal cancer, or cancers of the head and neck. The authors concluded that there was insufficient evidence for surveillance with these technologies because of factors such as poor study quality, lack of standard definitions for surveillance, scanning protocol differences, and inconsistent test accuracy reporting (Patel et al 2013).

The combined sensitivity and specificity for conventional PET were both found to be 84%; for PET-CT, they were 93% and 81%, respectively. The overall accuracies were 91% and 93%, respectively. Authors conclusions: (18) Fluorodeoxyglucose (FDG)-PET and PET-CT are highly accurate diagnostics tools for DTC recurrence in patients who present a negative whole-body scintigraphy and could impact the clinical and therapeutic management of DTC (Caetano et al. 2016)

The sensitivity, specificity, positive likelihood ratio and negative likelihood ratio of (18)FDG PET-CT were 0.86 (95% confidence interval [CI] = 0.71-0.94), 0.88 (95% CI = 0.75-0.94), 17.0 (95% CI = 3.5-14.0), and 0.16 (95% CI = 0.07-0.34), respectively. Overall weighted area under the curve was 0.93 (95% CI = 0.91-0.95). Authors conclusions: (18)FDG PET-CT has moderate sensitivity and specificity for detection of gastric cancer recurrence after surgical resection (Zou and Zhao 2013).

MRI

Patients with a history of breast cancer are at increased risk for developing a second breast cancer as well as recurrence of the primary tumor in the ipsilateral breast; however, there is little information about whether follow-up imaging improves outcomes in patients who undergo mastectomy and breast reconstruction. With the increasing popularity of breast reconstruction after mastectomy, there is a need to identify reliable tests for early diagnosis of potentially treatable recurrences (HTA 2014)

To carry out a meta-analysis to assess the effectiveness of magnetic resonance imaging (MRI) during the follow-up of patients with prostate cancer after undergoing external beam radiotherapy (EBRT) or radical prostatectomy. A limited number of small studies suggest that MRI can accurately detect local recurrences after EBRT or radical prostatectomy. dynamic contrast-enhanced (DCE) MRI is particularly accurate. The addition of MRSI to DCE MRI can significantly improve the diagnostic accuracy of local prostate cancer recurrence. The eventual role of 1H-MRSI alone remains controversial and needs to be defined further (Wu et al. 2013)

CT colonography:

CT colonography compares favourably to colonoscopy for detection of anastomotic recurrence and metachronous colorectal cancer, and appears financially beneficial. These findings should be considered alongside limitations of small patient numbers and high clinical heterogeneity between studies (Porte et al. 2017)

Biomarkers

Human epididymis 4 (HE4): The search identified seven papers in line with eligibility criteria for this systematic review; all of them demonstrated a good performance of HE4 in OC recurrence. The challenge to anticipate the diagnosis of OC recurrence and to translate this early diagnosis of relapse in a survival and quality of life
Improvement is still open, and as reported in this review, HE4 may play a key role in this scenario. More studies are needed to validate and reinforce the role of HE4 in ovarian cancer recurrence and in its early detection (Capriglione et al. 2017)

### Follow up strategies

**Early breast cancer:** This updated review of RCTs conducted almost 20 years ago suggests that follow-up programs based on regular physical examinations and yearly mammography alone are as effective as more intensive approaches based on regular performance of laboratory and instrumental tests in terms of timeliness of recurrence detection, overall survival and quality of life. In two RCTs, follow-up care performed by trained and not trained general practitioners working in an organised practice setting had comparable effectiveness to that delivered by hospital-based specialists in terms of overall survival, recurrence detection, and quality of life (Moschetti et al 2016: Cochrane SR)

**Non-metastatic colorectal cancer:** The results of our review suggest that there is no overall survival benefit for intensifying the follow-up of patients after curative surgery for colorectal cancer. Although more participants were treated with salvage surgery with curative intent in the intensive follow-up group, this was not associated with improved survival. Harms related to intensive follow-up and salvage therapy were not well reported (Jeffrey et al 2016; Cochrane SR)

**Cervical cancer:** We found no evidence to inform decisions about different follow-up protocols after primary treatment for women with cervical cancer. Ideally, a large RCT or, at the very least, well-designed non-randomised studies (NRSs) that use multi-variate analysis to adjust for baseline imbalances are needed to compare these follow-up protocols. Such studies could include prospective trials conducted to determine the benefits and harms of different follow-up protocols upon completion of primary treatment for cervical cancer, along with an RCT undertaken to compare predefined follow-up protocols versus participant-initiated follow-up versus no follow-up until a participant is referred to a gynaecological oncology service after signs or symptoms of recurrence have been identified in the primary care or community setting (Lanceley et al 2013: Cochrane SR)

### Conclusions

**Follow up strategies by type of cancer**

- Fully answered: Follow up strategies for Colorectal cancer, Bladder cancer, Early breast cancer, Oesophageal cancer, Skin Cancer, Oesophago-gastric cancer, Cancer of the upper aerodigestive tract and Laryngeal cancer
- Not answered: Follow up strategies for Cervical cancer (a Cochrane review is underway)

**Diagnostic blood tests and biomarkers**

- Fully answered: Blood Carcino-Embryonic Antigen (CEA) levels for colorectal cancer, cross sectional imaging for colon, rectum and anal canal cancer
- Partially answered: Human epididymis 4 (HE4):
- Not answered: Serum CA125 levels

**Cross sectional imaging**

- Fully answered: cross sectional imaging for colon, rectum and anal canal cancer, oesophagus and stomach cancers, testicular cancer; prostate cancer, cancer of the larynx, paranasal sinuses, hypopharynx / salivary glands, oral cavity and oropharynx and thyroid cancer, pancreatic cancer, renal cell carcinoma, adrenocortical cancer, liver cancer and spinal cord tumours, breast cancer
Partially answered: cross sectional imaging for cancer of the nasopharynx, Positron emission tomography (PET) and positron emission tomography–computed for lymphoma, colorectal cancer, or cancers of the head and neck and gastric cancer. CT tomography (PET-CT); MRI for prostate cancer and breast cancer, CT colography for colorectal cancer.

<table>
<thead>
<tr>
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<th>Study</th>
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<th>Primary Research</th>
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www.ncri.org.uk
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<td><strong>Oesophagus and stomach cancers</strong></td>
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<td>Olliff et al. 2014</td>
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<td>Chua et al. 2014</td>
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<td>Patel et al. 2013</td>
<td>The Lack of Evidence for PET or PET-CT Surveillance of Patients with Treated Lymphoma, Colorectal Cancer, and Head and Neck</td>
<td></td>
<td>SR</td>
<td>X</td>
</tr>
</tbody>
</table>
### CT

**Caetano et al. 2016**  
Accuracy of positron emission tomography and positron emission tomography-CT in the detection of differentiated thyroid cancer recurrence with negative (131) I whole-body scan results: A meta-analysis.  

**Zou and Zhao 2013**  
18FDG PET-CT for detecting gastric cancer recurrence after surgical resection: a meta-analysis.  

### MRI

**HTA 2014**  
Magnetic resonance imaging (MRI) for surveillance for breast cancer recurrence following mastectomy and breast reconstruction. Lansdale: HAYES, Inc.. Healthcare Technology Brief Publication.  
[http://www.hayesinc.com/hayes/crd/?crd=16955](http://www.hayesinc.com/hayes/crd/?crd=16955)

**Wu et al. 2013**  
Role of magnetic resonance imaging in the detection of local prostate cancer recurrence after external beam radiotherapy and radical prostatectomy.  
*Clin Oncol (R Coll Radiol)*. 2013 Apr;25(4):252-64.  

### CT COLONOGRAPHY

**Porte et al. 2017**  
CT colonography for surveillance of patients with colorectal cancer: Systematic review and meta-analysis of diagnostic efficacy.  

### FOLLOW UP STRATEGIES
| NICE. 2014 | **Colorectal cancer**: the diagnosis and management of colorectal cancer (NICE clinical guideline 131)  
http://www.nice.org.uk/guidance/cg131 | | x |
| NICE 2015 | **Bladder cancer**: diagnosis and management (NICE guideline NG2)  
https://www.nice.org.uk/guidance/ng2 | | x |
| NICE 2017 | **Early and locally advanced breast cancer**: diagnosis and treatment  
(NICE clinical guideline CG80)  
https://www.nice.org.uk/guidance/cg80 | | x |
| NICE 2018 | **Oesophago-gastric cancer**: assessment and management in adults  
(NICE guideline NG83)  
https://www.nice.org.uk/guidance/ng83 | | x |
| NICE 2015 | **Melanoma**: assessment and management (NICE guideline NG14)  
https://www.nice.org.uk/guidance/ng14 | | x |
(NICE guideline NG83)  
https://www.nice.org.uk/guidance/ng83 | | x |
| NICE 2016 | **Cancer of the upper aerodigestive tract**: assessment and management in people aged 16 and over. (NICE guideline NG36)  
https://www.nice.org.uk/guidance/ng36 | | x |
https://link.springer.com/article/10.1007%2Fs00405-014-2966-x | | X |
| Moschetti et al. 2016 | **Follow-up strategies for women treated for early breast cancer.**  
| Jeffrey et al. 2016 | **Follow-up strategies for patients treated for non-metastatic colorectal cancer.**  
<table>
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<tr>
<th>Author(s)</th>
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<th>Year</th>
<th>Link</th>
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<th>Cochrane Protocol</th>
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</table>

SR – Systematic review, N= narrative review

Further comments
The Royal College of Radiologist guidance is due to be updated section by section in 2018. Also sections on ovarian cancer, cancer of the cervix, vagina and vulva, endometrial cancer, melanoma which has not been extracted due to time

### Oesophageal Cancer
CT is the primary imaging modality for follow-up with the same protocol, dictated by the type of treatment (combination chemotherapy, chemoradiotherapy, surgery); although there is growing evidence supporting the use of FDG PET-CT for reassessment of patients following neoadjuvant treatment as this is more accurate than CT alone. Following surgery, a CT at three months is recommended as a baseline for further assessment. Subsequent imaging will depend on disease status and patient symptoms.

### Lung Cancer
At present, the evidence supporting follow-up imaging is poor after curative therapy, surgery or radiotherapy, and local practice may be followed. Either MDCT or PET-CT should be performed after neoadjuvant therapy before resection. MDCT is routinely performed after chemotherapy to assess disease response.

### Colon Cancer
- Intensive follow-up that incorporates carcinoembryonic antigen (CEA) monitoring and six-monthly CT scanning of chest, abdomen and pelvis in the first two years contributes to the earlier detection of asymptomatic disease recurrence in patients with colorectal cancer who are then more likely to proceed to potentially curative resection of metastatic disease.
**Testicular cancer**

**Follow-up for metastatic disease**

**Non-seminomatous germ cell tumours**
CT should be performed using the same protocol as for staging, using intravenous contrast medium.

All sites of disease should be assessed according to response criteria and residual masses following completion of treatment and should be assessed for possible surgical excision in terms of size, precise location and relationship to adjacent structures, including major vessels.

**Paranasal sinuses**
Routine follow-up three to four months after completion of treatment is useful for establishing a baseline for future comparison. MRI is more helpful than CT, and evaluating radiologists should be familiar with the expected post-surgical changes.

**Nasopharynx**

Reassessment imaging should be performed 3–6 months following completion of radiotherapy. It is advisable to use the same technique employed for initial staging at follow-up, although there is growing evidence that FDG PET-CT may be the most accurate method of response assessment when performed three to six months post-chemoradiotherapy in patients with residual masses following treatment. Further imaging follow-up usually depends on disease status and clinical symptoms.

**Larynx**

Imaging three to four months after completion of radiotherapy is useful in documenting tumour response and serves as a baseline for future comparisons. The same imaging technique should be used as for the pretreatment evaluation.

**Prostate cancer**

Follow-up for prostate cancer will depend on the type of treatment used. Routine imaging follow-up is not indicated following radical treatment (either surgery or radiotherapy).

**Hypopharynx / Salivary glands**

Follow-up imaging two to three months after treatment is useful to establish a baseline for future comparison.
<table>
<thead>
<tr>
<th>Oral cavity and oropharynx</th>
<th>Thyroid cancer</th>
<th>Upper urinary tract tumours</th>
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<tbody>
<tr>
<td>Follow-up imaging maybe performed 3–6 months after completion of treatment to establish a baseline for future comparison. This is particularly relevant following complex soft tissue reconstructions and following radiotherapy for larger tumours. There is no consensus for the role of surveillance imaging, and subsequent imaging follow-up depends on disease status and clinical suspicion. Radiologists should be aware of expected post-treatment appearances.</td>
<td>Follow-up MRI is useful two to three months after completion of treatment to establish a baseline for future comparison.</td>
<td>CT is the primary imaging modality for follow-up after nephroureterectomy for upper tract TCC or where there is evidence of metastatic disease. In patients receiving systemic treatment for metastatic disease, the timing and frequency of reassessment is usually determined by chemotherapy schedules and planned surgery. For early-stage disease treated with primary surgery, there is no clear evidence base for timing and frequency of follow-up, which is therefore often dictated by patient symptoms.</td>
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<tr>
<th>Bladder cancer</th>
<th>Renal cell carcinoma</th>
<th>Adrenocortical cancer</th>
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<tr>
<td>CT is the primary imaging modality for follow-up with the same protocol as above. Where combination therapy is used, timing of follow-up will be dictated by chemotherapy cycles and planned surgery. With primary surgical management, there is no clear evidence base to dictate frequency and duration of follow-up. Reassessment at six months and one year is often undertaken; subsequent imaging depends on disease status and patient symptoms.</td>
<td>The frequency of follow-up depends on stage and histology at presentation at surgery. In principle, larger tumours with lymph node infiltration or venous tumour extension are reviewed more frequently. Data suggest that no follow-up is needed for T1 N0 M0 tumours. T2 and T3 tumours not receiving adjuvant therapy are scanned at 24 and 60 months or when symptomatic. Patients with T3a tumours are rescreened at three to six months following surgery, as a baseline for future follow-up. CT is the optimal technique. Only post-contrast scans to include chest and abdomen are required, unless there is a specific indication to include the pelvis.</td>
<td>CT of the abdomen as a baseline following surgery and if relapse is suspected.</td>
</tr>
</tbody>
</table>
Pancreatic cancer

Routine imaging after surgery is not warranted as palliative chemotherapy is generally only considered when there is symptomatic disease. Follow-up imaging is conducted when there is clinical evidence of recurrence. Follow-up is performed to assess response to chemotherapy (+/-radiotherapy) and is, therefore, performed at a frequency to correspond with the chemotherapy regimens.

Liver cancer

Imaging follow-up is conducted:
- After surgery or ablative therapy to identify small volume recurrent disease which may be amenable to further resection/ablation
- To assess response to chemoembolisation
- To assess the significance of indeterminate hypervascular lesions.

Spinal cord tumours

A post-treatment baseline scan three months after surgery or radiotherapy is useful and further imaging may be obtained as determined by symptoms or as protocolled by the local oncology multidisciplinary team (MDT).

Breast Cancer

It is recommended by the National Institute for Health and Care Excellence (NICE)³ that routine surveillance following treatment for breast cancer should be by annual mammography until the patient enters a national screening programme. Patients diagnosed with early breast cancer who are already eligible for screening should have annual mammography for five years.

The rationale for early detection of local recurrence is that treatment may be more effective and there may be a survival benefit, since mammography may detect recurrence with better prognostic factors than clinical examination.

Stomach cancer

CT is the primary imaging modality for follow-up with the same protocol, dictated by the type of treatment. Following surgery, a CT at three months is recommended as a baseline for further assessment. Subsequent imaging will depend on disease status and patient symptoms.

Lymphoma

No clear evidence-based consensus exists on the optimal imaging modality, interval or duration of routine follow-up in lymphoma, either following treatment or in the ‘watch and wait’ scenario often employed in early-stage low-grade NHL. An important general principle in follow-up imaging is that the benefits must be perceived to outweigh the costs and the risks of increased radiation exposure. Review of retrospective series suggests that whatever the imaging schedule employed, most relapses are still detected clinically. Routine imaging with CT or ¹⁸FDG PET-CT is not advised given the lack of evidence supporting its role. Either CT or ¹⁸FDG PET-CT may be used to investigate suspected relapse, dependent upon the level of clinical concern, local availability and the known FDG avidity of the individual’s tumour. The need for histological confirmation of positive findings should be discussed at a multidisciplinary team (MDT) meeting.
This is a massive area and there is a lot of US and Canadian guidance which we haven’t summarized but pre 2015 can be found in the rapid response report cited below


American Society of Colon and Rectal Surgeons. 2015
*Practice guideline for the surveillance of patients after curative treatment of colon and rectal cancer*

**American College of Radiology** 2016
*ACR appropriateness criteria: Stage I Breast Cancer: Initial Workup and Surveillance for Local Recurrence and Distant Metastases in Asymptomatic Women*

Canadian Urological Association 2013
*Canadian guidelines for postoperative surveillance of upper urinary tract urothelial carcinoma*

**American College of Radiology** 2016
*ACR appropriateness criteria: Post-Treatment Surveillance of Bladder Cancer*

**American College of Gastroenterology** 2016
*Colonoscopy Surveillance after Colorectal Cancer Resection: Recommendations of the US Multi-Society Task Force on Colorectal Cancer*

**American College of Radiology** 2016
*ACR appropriateness criteria: Prostate Cancer—Pretreatment Detection, Surveillance, and Staging*

**Suggestions for additional searches**
Follow up strategies for specific cancers where there isn’t a Cochrane review or NICE guidance
Search by specific biomarkers e.g HE4
CT, MRI or other imaging techniques AND cancer and surveillance
Survivorship AND surveillance
26. What are the spiritual care needs of people living with and beyond cancer?

Y9: What are the spiritual care needs of people living with and beyond cancer?

Keywords: Spirit* AND cancer OR oncology

Exclusions: interventions to address spiritual needs, family carers, nursing perspectives,

Guidelines
None

Summary of reviews (x1 SR)
Advanced cancer
Spirituality is among the resources that many turn to as they deal with a diagnosis of advanced cancer. Researchers have made much progress in exploring and understanding spirituality's complex and multifaceted role in the midst of metastatic disease. As a result, spirituality is seen as an important aspect of a holistic and respectful approach to clinical care for patients and their loved ones. In this article, we provide a systematic review of the literature related to the interface between spirituality and metastatic cancer. We included articles published from January 2013 to June 2014. Twenty-two articles were reviewed, consisting of clinical intervention trials, association studies, surveys, qualitative studies, and review articles. The articles discussed efforts to improve patients' spiritual well-being, with relevant measurement scales; the associations of spirituality and end of life treatment practices; and efforts to better understand and meet the spiritual needs of patients and caregivers (Piderman et al. 2015).

Summary of primary research (x2)
Spain
Although it is widely recognised that people turn to spirituality in times of crises, the interest in exploring the spiritual needs of cancer patients is just beginning to grow. The purpose of this study was to conduct a spiritual needs assessment with cancer patients living in a Northern European metropolitan region in order to (a) examine the relevance and nature of spiritual needs; (b) to clarify the role of demographic and clinical characteristics in spiritual needs; and (c) to identify their associations with dimensions of psychological distress. N = 285 outpatients with mixed cancer sites and of all tumour stages were surveyed cross-sectionally. Instruments included the Spiritual Needs Questionnaire (SpNQ) and measures of anxiety, distress, hopelessness and meaning-related life attitudes. Almost all patients (94%) reported at least one spiritual need. The needs for Inner Peace and Actively Giving emerged to be of greatest importance. Significant, but weak differences were found for age, gender and being in a partnership. No associations for medical characteristics were observed. Regression analyses revealed anxiety as the strongest predictor for the subscales Existential Needs, Inner Peace and Actively Giving. The results emphasise the relevance of spiritual needs in cancer patients. The call for spiritual assessment and interventions to meet spiritual needs in cancer patients is strengthened (Höcker et al 2014)

India
Diagnosis of cancer can cause huge spiritual crisis in a person and affect different aspects of life. At this stage, patients have certain spiritual needs. Aim: This study was conducted to explain spiritual needs of cancer patients in Iran. Materials and Methods: In this qualitative study, 18 cancer patients, referred to the Cancer Institute of Imam Khomeini Hospital in Tehran were selected using purposive sampling method, and their spiritual needs emerged out of conventional content analysis of
Interviews conducted with them. Results: From 1850 initial codes, 4 themes (connection, peace, meaning and purpose, and transcendence) were identified that contained categories of social support, normal behavior, inner peace, seeking forgiveness, hope, acceptance of reality, seeking meaning, ending well, change of life meaning, strengthening spiritual belief, communication with God, and prayer. Conclusions: Spiritual needs of cancer patients should be recognized, realized, and considered in care of patients by the medical team. An all-out support of health system policy makers to meet patients' spiritual needs is particularly important.

Conclusions
Not answered

<table>
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<tr>
<th>Authors / Year</th>
<th>Study</th>
<th>Systematic Reviews</th>
<th>Primary Research</th>
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SR – Systematic review, N= narrative review

Further comments
The majority of other reviews were for interventions to address spiritual care needs

One JBI review and one other systematic review for palliative care/advanced cancer
There were 16 primary studies included. A total of 1469 patients have been evaluated, whereas eight groups of spiritual needs have been identified: finding the meaning and purpose of life; finding the meaning in experiencing the disease; being connected to other people, God and nature; having access to religious/spiritual practices; physical, psychological, social and spiritual wellbeing; talking about death and the experience of dying; making the best out of their time; being independent and being treated like a normal person (Mesquita, 2017).
A systematic review evaluated the effectiveness of spiritual and religious interventions for adults in the terminal phase of a disease. The review reported that meditation and multi-disciplinary palliative care interventions that involved a chaplain or spiritual counselor as a member of the intervention team had comparable effects for quality of life or wellbeing.4 (Level 1)

A systematic review evaluated the individual perspective regarding the role of the doctor in the discussion of spirituality. The proportion of people who thought it was appropriate for doctors to inquire about spiritual needs in at least some circumstances ranged from 2.1% to 100% across studies (median 70.5%). The reviewers concluded that although the majority of people expressed an interest in the discussion of spirituality in medical consultations, there was a mismatch in perception of what constitutes this discussion.6 (Level 1)

A systematic review of qualitative research explored the understanding of spirituality and its role in palliative care. The review reported that spirituality principally focused on relationships and was a broad term that may or may not encompass religion. People wanted meaningful relationships with their healthcare providers to help fulfil their spiritual care needs, with family caregivers also identified as an important source for spiritual care.7 (Level 1)

Suggestions for additional searches
None