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DETERMINING RESEARCH PRIORITIES FOR CANCER SURVIVORSHIP: CONSULTATION AND EVIDENCE REVIEW

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EXECUTIVE SUMMARY

Aims

We aimed to identify what is known and not known about the problems faced by cancer survivors and the effectiveness of known solutions to these problems in order to identify future priorities for research investment.

The main focus was on identifying areas of research where investment could yield findings that could make a major impact on patient wellbeing within a short time frame. We also highlighted some areas for longer-term study.

Methods

Two approaches to generating the required information were used:

1. A consultation with the research community, charities and statutory bodies with an interest in survivorship research.

2. A rapid catalogue and synthesis of published research based mainly on already published systematic reviews into (a) problems with health and well-being of cancer survivors; (b) solutions for these problems.

Findings

Problems

The consultation process identified many potential problems for cancer survivors. These included long-term symptoms associated with cancer and its treatment especially psychological issues, including distress, anxiety and depression, relationships, return to work and finance The literature review found there was substantial evidence that symptoms such as, depression, anxiety, emotional distress, pain and fatigue and social issues such as employment were problems for cancer survivors. There was much less evidence on cognitive and physical impairments, finance and relationship problems. However, the evidence was almost all from short-term survivors, was only of moderate quality, and tended to be in specific cancer groups, particularly breast cancer.

Solutions

We limited our search for solutions to those which had been evaluated in randomised trials. We found there was good evidence of the effectiveness of treatments for the symptom of pain and moderate evidence for fatigue and depression but not for other symptoms. Furthermore, evidence was mostly for treatments (for example, opiates for pain) and did not address how survivors with needs could be identified and how treatments could be implemented. In general, there is a lack of research into innovations in services which would facilitate self-management and the delivery of care, information and support to survivors.

Current Situation

There has been a substantial amount of research describing many of the problems patients with cancer experience and this is strongest in the area of symptoms in the period that immediately follows treatment. For the common cancers, such as breast cancer, the problems are reasonably well described. The natural history of problems and solutions to these beyond this time remains under-addressed.

There has been promising work on the use of Information Technology systems to identify which patients have problems.

There has been progress in developing and evaluating systems of care to deliver effective treatments, especially the collaborative care model – a model of care in which a case manager (often a cancer nurse) is supervised by appropriate specialists (which may include a psychiatrist and oncologist) and the patient’s management is mainly delivered in primary care. Interventions based on rehabilitative and self-management models are in the early stage of testing.

A combination of screening using information technology and then providing treatment for problems using a collaborative care-type model has been found to be effective in many chronic illnesses

Recommendations

Best Buys

We were struck by the degree of convergence on which problems were perceived to be especially important (symptoms, functioning, employment and social well-being) and also on the relative dearth and poor quality of the evidence available. We therefore recommend that there is a need for high quality, large-scale research to systematically identify the needs of cancer survivors in both the short and especially the longer term. Appropriate approaches would be cross-sectional surveys and preferably large, prospective cohort studies. These studies should aim to characterise the scale of each problem and to identify who is most at risk. Qualitative studies, perhaps nested within the large scale surveys, would enhance understanding of the impact of problems and the ways in which people manage these.

For solutions, there is a dearth of evidence in most areas. Whilst we have potentially effective treatments for pain, depression and fatigue, there is very little evidence to tell us how to deliver these treatments. We recommend that short-term wins would involve identifying obstacles to effective delivery of already established treatments and evaluation of new methods of service organization (such as collaborative care, telephone delivered care and guided self-help) to deliver them. In the longer term, we need to develop interventions to improve the functioning of cancer survivors and the welfare of their families and carers.

It is important to note that many, if not most, of these problems are not unique to cancer survivors and evidence gathered from other medical conditions should be examined to see if adaptations for the cancer population can be piggy-backed on already substantial areas of work.

Don't Buys

We strongly recommend that funders do not invest limited research funding into small, methodologically weak studies and on researchers without a good track record of delivering high quality work. We strongly recommend that greater value for money will be achieved by funding a smaller number of well-designed large studies.

Summary

We have identified some areas where very short-term investment (less than two years) may produce useful information. These are mainly in the description of need using cross-sectional surveys and the identification of barriers to the implementation of already established treatments. In the medium term (up to five years) there is a need for prospective cohort studies to identify who develops problems and high-quality evaluations (mainly randomised trials) of methods of identifying and treating these problems. Developing effective ways of delivering treatment for pain, depression, fatigue and emotional distress are areas that could yield a good return on investment.

In the longer term (more than five years) important information will be gained from the setting up of long-term follow up studies identifying patients who have suffered cancer for ten years or more. Similarly, there is a need for large-scale programs of research to evaluate interventions and their long-term effectiveness.

OVERVIEW

Background

Following on from publication of the Cancer Reform Strategy[1] the National Cancer Survivorship Initiative (NCSI) was established to consider approaches to survivorship care and how these can be best tailored to meet individual's needs. The aim of the NCSI is, by 2012, to have taken steps to ensure that cancer survivors get the care and support necessary to enable them to lead as healthy and active a life as possible, for as long as possible. The work of NCSI is progressing in seven work streams:

1. Assessment, care planning and immediate post treatment approaches to care
2. Managing active and advanced disease
3. Late effects
4. Children and young people
5. Self-care and self-management
6. Work and finance
7. Research

There are also three cross-cutting themes of workforce, information and commissioning.

To achieve their vision the NCSI has identified a need to shift care towards personalised assessment and care planning and self-management supported with information on the consequences of cancer and its treatment. This will necessitate a shift from viewing cancer as an acute illness to a greater focus on cancer as a chronic illness and maximizing health and well being after treatment. The aspiration is to enable people who have been affected by cancer to live with and beyond cancer.

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[1] Department of Health (2007). Cancer Reform Strategy. London: Department of Health.

As part of the NCSI research was commissioned to identify what is known and not known about the health and well-being and care needs of cancer survivors and what interventions have been evaluated to improve these. This was to be achieved through a comprehensive review of evidence in the field of cancer survivorship. This information could then be used to prioritise a future research agenda. This report sets out the methods used and findings obtained from this work.

What is a research priority?

Identifying research priorities is not as simple as it might first appear. Critically it is not as straightforward as identifying important problems and corresponding ‘gaps’ in the evidence about these. The presence of ‘gaps’ in evidence may well indicate a hard to research area that would need many years of investment to address. Furthermore, even in areas where we have the information we need about a problem including possible solutions, research may be needed to work out how to implement these solutions in everyday practice. Finally, research takes more than money – although money is essential - it also requires skilled researchers with the capacity and interest in the question to deliver high quality answers. Such people are in very short supply for many of the questions posed here. Considering these facts the shrewd research investor in research might be well advised to fund topics that are considered important, where answers are reasonably close to being implementation ready and in which there are existing research groups with a track record of delivering high quality research.

Aims

We aimed to identify what is known and also what is not known about the problems faced by cancer survivors and the effectiveness of solutions to these problems in order to help to identify future priorities for research.

There were two main components to the project:

- Consultation with research community, charities and statutory bodies with an interest in survivorship research to identify unpublished and ongoing research and establish opinions on research priorities

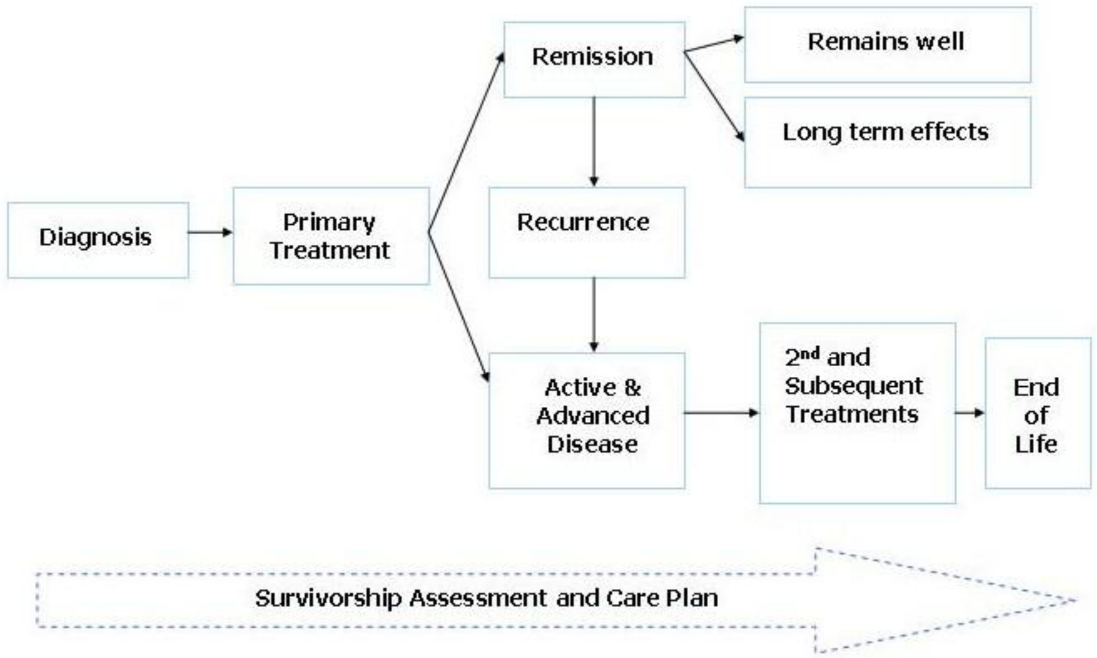
- A rapid catalogue and initial synthesis of published and unpublished research in two areas:
    - Health and well-being of cancer survivors
    - Interventions designed to improve the health and well-being of cancer survivors

These results from both these components were used to identify priority areas for future research.

Scope

There is currently no clear definition of what is meant by the term ‘cancer survivor’. The term is often defined in a vague way to refer to people who are at any point in time from the time of cancer diagnosis to the end of their life and so includes both individuals who are living with cancer and those who have had cancer in the past. The focus of the NCSI has been on the care and support given to patients and their families from the end of primary treatment onwards. The NCSI has developed a diagram to depict the “survivorship journey” and describe the experience of cancer survivors following treatment and identify problems and potential solutions at each step in this journey (see Figure 1).

Figure 1 Survivorship Journey



Source: National Cancer Survivorship Initiative Vision (2009) Department of Health, Macmillan Cancer Support and NHS Improvement.

In order to focus this review we concentrated on stages of the cancer journey covered by (a) the period immediately following treatment, (b) the short and long term consequences of cancer including recurrence (c) living with active and advanced disease. We excluded the end of life. These phases map on to what have been referred to as the acute, sub acute, long term phases of survivorship[2]. The focus of the review was confined to survivors who had been diagnosed with cancer as an adult.

Methods

Two different methods were used to address the aims of the project and arrive at a set of priorities for research: (1) a consultation and consensus exercise and (2) systematic literature scoping exercises. Detailed descriptions of the methods used are contained in three technical appendices and only a brief description will follow here.

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[2] Feuerstein M (2007) Cancer Survivorship: research, practice and policy. In M Feuerstein Handbook of Cancer Survivorship pp 483-494. Springer Science+Business Media LLC, New York, New York.

Consultation

The aim of the consultation exercise was to identify the views of researchers, those who commission research (statutory and charitable bodies) and survivors about what were considered the most pressing research questions about the health and well-being of cancer survivors. In addition, we aimed to catalogue the relevant current and planned research in the UK and also to identify the availability of any large data sets that might be suitable for secondary analysis.

The consultation was undertaken in two stages similar to those used by Shipman and colleagues[3]. First, a short structured questionnaire was developed to explore what participants perceived to be the most important and useful research required to support better care for cancer survivors. It also asked respondents to identify research that was ongoing, just completed, or planned. This was achieved through a combination of email, on-line and postal surveys. Participants were sourced on the criteria they could be considered in some way ‘expert’ in commissioning or undertaking research in this area.

A thematic analysis of participants’ responses was achieved by reviewing questionnaire responses and identifying key themes and categories. These were discussed by the research team and common categories agreed. Participants’ responses were grouped under these themes and presented back to participants to allow discussion and voting.

A consultation meeting was held at which participants discussed and debated the issues and prioritised research topics through a series of votes executed with a wireless digital voting system. There was an opportunity to hear about early results from the literature reviews. Participants were selected on a

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[3] Shipman, C Gysels, M White, P et al Improving generalist end of life care: national consultation with practitioners, commissioners, academics, and service user groups. BMJ 2008;337:a1720

purposeful basis to gain wide representation from among different stakeholder groups. The final outcome of the day was suggested priorities for research

Scoping reviews

The aim of conducting the scoping reviews was to determine what is known and remains unknown about the problems faced by cancer survivors and the effectiveness of interventions to address these problems. The first review systematically scoped and collated research evidence regarding the health and well being of cancer survivors and the second addressed possible solutions to these problems.

The reviews took the form of rapid scoping reviews as oppose to comprehensive systematic reviews. Literature scoping is a preliminary assessment of potentially relevant literature and its size, and an essential preparatory step before conducting a systematic review[4]. The scoping reviews were conducted as rigorously as possible in the time scale and used multiple data bases with carefully formulated search terms, explicit inclusion and exclusion criteria, and independent assessment of abstracts.

In order to address the large literature we aimed to identify systematic reviews rather than all the original publications. We then supplemented these reviews with more recently published individual studies.

The search strategies for both reviews were developed with the assistance of specialist librarians. The most common electronic databases were searched to include evidence from a wide range of academic disciplines including: Medline, EMBASE, Psychlit and PsychINFO, Cochrane Library, CINAHL (Cumulative Index to Nursing & Allied Health Literature), Web of Science, BNI (British Nursing Index).

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[4] Centre for Reviews and Dissemination (2001) Systematic Reviews: CRD's guidance for undertaking systematic reviews of research on effectiveness. CRD report No. 4 (2nd edition).NHS Centre for Reviews and Dissemination, University of York.

Review one

The first scoping review focused on 'health and well-being' of cancer survivors including, physical, psychological, social and practical aspects.

Inclusion and exclusion criteria for health and well being review

The following inclusion/exclusion criteria were used for the database searches in order to conduct the scoping review and future literature searches:

Inclusion criteria

- English language
- Papers published between 2000 and 2009
- Research focussed on health and well-being in the acute, sub acute, long term and disease free phases
- All cancers
- Patients diagnosed ≥18 years
- Literature review articles (included systematic, comprehensive or other types of literature reviews of research evidence and included reviews of both qualitative and/or quantitative studies)

Exclusion criteria

- Childhood and adolescent cancer
- Biomedical data (e.g., drug trials, clinical trials)
- Review articles other than research literature reviews
    e.g. retrospective data review; overview; review of treatment outcome; review of an individual patient case

Review two

The second scoping review was targeted at scoping and collating research evidence regarding solutions to the problems of cancer survivors. Therefore the focus of this review was on retrieving systematic reviews and randomised controlled trials (RCTs) of interventions

We focused on studies of interventions for the following common problems

Symptoms of:	Depression
	Anxiety and fear of recurrence
	Emotional distress
	Fatigue
	Pain
Impairment in:	Physical functioning
	Social functioning, including relationships,
	Work and employment
	Cognitive functioning

Inclusion and exclusion criteria for solutions review

The following inclusion/exclusion criteria were used for the database searches:

Inclusion criteria

- English language
- Publications since 1990
- Any intervention that had relief of one of the above as its primary aim.
- Drug and non drug and professional delivered and self-help.
- Systematic reviews

Exclusion criteria

- Childhood and adolescent cancer
- Review articles other than those of randomised controlled trials

Procedures

Abstracts and titles of review articles considered potentially relevant were selected for further examination. The bibliographic details, keywords, abstracts, website address (where available) of all identified reports were imported into bibliographic databases. Relevant reviews were selected for synthesis using the inclusion/exclusion criteria.

Data were extracted and summarised using data extraction sheets suitable to the different types of reviews. Each review identified for possible inclusion in the problems in health and well being element of the scoping review was awarded a quality score (out of 7) as a broad indication of quality. A review was included if it achieved a score of 2 or greater. Most reviews in the solutions scoping review were high quality Cochrane type reviews and quality screening was not undertaken.

To supplement the search for reviews additional searches to identify primary research papers published beyond the timeframe of the included reviews were done. As a simple method of focussing on high quality publications we only included those studies published in journals with an impact factor of more than 3 for studies of health and well being and 5 for studies of interventions. We included 25 reviews and 61 primary research papers in relation to problems of health and well-being and 49 reviews and 21 primary research papers with respect to solutions.

DISCUSSION

Main findings

The findings from both elements of the project, the consultation and scoping reviews, have been combined. Detailed findings can be found in the accompanying technical appendices. Results of the scoping reviews have been drawn together into a series of tables (see Tables 1, 2 and 3). These summarise the current state of evidence in the field in relation to the amount, scope and quality of research. An indication as to the amount and quality of research has been made where possible. Judgments have made by the research team about the time frame necessary to obtain clear answers in relation to the particular topic and to have reached a point where research-based solutions are implementation-ready. These represent the 'best buys' for investment in terms of having an impact on the care of cancer survivors. We have used the periods of less than two years (very short term), between two-five years (medium term) and greater than five years (long term) to qualify these recommendations. These take into account the stage the research has reached in relation to each topic and the relative complexity, scale and length of time it might take to undertake the necessary research.

This detailed analysis has only been undertaken in relation to specific topics i.e. where data were available from both review teams (for full details of findings on all topics reviewed see the technical appendices). The specific topics that have been addressed in detail are: fatigue and physical functioning, pain, sexual functioning, cognitive functioning, general distress, depression, anxiety, social needs and employment, finance and employment/return to work.

In addition, a short commentary is offered on aspects research funders might take into account when considering which research they fund in future. Some recurrent themes surfaced during the review and research funders should remain mindful of these when considering the nature, focus and type of research they might commission in future.

Fatigue and physical functioning

Problem

Impairment in physical function has been commonly researched in relation to fatigue or other symptoms whereupon physical function is studied as a secondary outcome. There is strong evidence that cancer survivors experience fatigue soon after treatment but only modest evidence in the longer term and unclear how or if it this differs from the general population. There is modest evidence to demonstrate fatigue is associated with other symptoms such as pain and sleep disturbance and that it has impact on quality of life. Most evidence relates to disease free women with breast and ovarian cancer and survivors of Hodgkin's Lymphoma.

Solutions

There is a modest amount of research testing interventions for fatigue and physical functioning, mainly patient education, rehabilitative approaches such as exercise and achieving behavioral change through Cognitive Behavioural Therapy (CBT) based treatment approaches. Results are inconsistent but the best evidence is for exercise. There is conflicting evidence on the efficacy of pharmacological approaches to fatigue management. No clear overall recommendations for treatment can be made at present.

Current research

There is research underway in relation to physical functioning including the value and barriers to implementing rehabilitation interventions. Research is also ongoing to better describe its natural course and biological pathogenesis once treatment has finished, and testing interventions such as Complementary and Alterative Medicine (CAM) and exercise.

Best buys

Less than 2 years: (a) pilot studies of simple, feasible methods of identifying fatigue in survivors (b) studies of barriers to implementing treatments such as guided self-help, telephone delivered treatment based on CBT principles and exercise.

2-5 years: Large, multi-centre studies of fatigue management with adequate follow up period that integrate screening and treatment.

5 years plus: Prospective cohort studies with age-matched comparisons to study course of fatigue and physical function in relation to factors such as cancer site, treatment history and stage.

Table 1: Physical and practical

ISSUES	PROBLEMS				SOLUTIONS			
	Amount of research[†]	Quality of research[‡]	Scope	Conclusion and opportunity[¥]	Amount of research	Quality of research	Scope	Conclusion and opportunity
Fatigue	High	Moderate	Ovarian, Hodgkin's disease, breast & mixed cancers	There is strong evidence that cancer survivors experience fatigue soon after treatment, but there is a need to explore its prevalence among the long term survivors and its association with other physical symptom (i.e. pain and sleep). Ovarian, Hodgkin's & breast < 2 years if good quality research. Other cancers 2-5 years.	Moderate	Moderate	Mainly mixed cancer samples and early stages of survivorship	Some evidence for the benefit of exercise during treatment, but inconclusive after treatment. Lack of long term follow-up. Evidence for drugs reducing fatigue for patients with anaemia. Weak evidence for CBT in treating fatigue.
Physical functioning/ Functional impairment	Moderate	Unclear	Mixed cancers, mainly in relation to older cancer survivors	Moderate evidence of the side effect of treatments on patients' physical performance. Older cancer survivors have poorer physical functioning than non-cancer. More information is needed from younger survivors. 2-5 years for all cancers.	Low	Low	Mixed samples	Possible benefit of practising tai-chi but weak evidence base.
Pain	Moderate	High	Mixed cancers, mainly in relation to fatigue	Moderate amount of evidence that cancer survivors experience pain, mainly as a result of the treatment – but evidence is mainly related to fatigue. 2-5 years for all cancers.	High	Moderate	Mainly mixed cancer samples and mixed stages of survivorship	Analgesics given by various routes effective in reducing pain. Limited evidence for the use of massage (short term benefits) and the evidence for complementary therapies, CBT and TENS are inconclusive.
Sexual functioning	High	Moderate	Ovarian, testicular & mixed cancers	Strong evidence of the consequences of cancer treatment for survivors' sexual function. However more evidence is needed on how survivors cope with these difficulties. Ovarian & testicular cancers < 2 years if good quality research. Other cancers 2-5 years.	Low	Low	Gynae and urological cancer samples at various survivorship stages	Limited evidence for the use of drug treatment and mechanical devices. The evidence for psychological treatment is inconclusive.

ISSUES	PROBLEMS				SOLUTIONS			
	Amount of research	**Quality of research**	**Scope**	**Conclusion and opportunity**	**Amount of research**	**Quality of research**	**Scope**	**Conclusion and opportunity**
Cognitive functioning	Low	Unclear	Ovarian cancer only	There is some evidence that some treatment for ovarian cancer might affect cognitive function, more information is needed about this problem amongst other cancer survivors and more understanding of the incidence and course of this problem. Ovarian cancer 2-5 years. Other cancers > 5 years.	-	-	-	No reviews or RCTs found.
Work/ employment	Moderate	High	Mixed cancers	There is evidence of substantial survivors need, but little evidence of assessment of risk, and little separation of personal (e.g. early retirement) versus medical (disability, body image) factors in predicting unemployment. There is an (unquantified) need for support for employers. < 2 years for all cancers.	Low	Low	Breast cancer	No RCTs found in recent review.
Finance	Low	Moderate	Mixed cancers	Very little evidence of the financial consequences of cancer. There is a need for more understanding how cancer and its treatment affect the financial situation of the survivor and his family. > 5 years for all cancers.	-	-	-	No reviews or RCTs found.

Key: † A scale ranging from Low- Moderate -High has been used to provide a broad indication of the amount of research described in the reviews. ‡ Terms such as Low, Moderate, High and Unclear have been applied to give a broad indication of the quality of research inferred from the comments made in original reviews.¥ This column summarises findings from reviews and an indication of time frame necessary to achieve clear answers about a particular topic.

Pain

Problem

There is a very large literature on pain. The systematic reviews and more recent publications indicate that pain is a problem for many cancer survivors and specifically that chronic pain is more prevalent in breast cancer survivors than it is in the general population. Radiotherapy and younger age are predictors. Some cancer treatments may cause pain

Solutions

There is very strong evidence that Non Steroidal Anti Inflammatory drugs (NSAIDS) and opiates are effective for pain in the general population. There is moderate evidence that these are effective for pain in cancer survivors. There is less evidence on the effective methods to ensure these treatments are given to those who need them.

Current research

There is one ongoing trial of methods of improving pain recognition and treatment in cancer inpatients

Best buys

Less than 2 years: (a) secondary analysis of existing data on prevalence of pain and risk factors in survivors (b) pilot studies of simple and feasible methods of identifying pain in survivors (c) studies of the barriers to implementing pain management models such as collaborative care.

2-5 years: Large trials of interventions based on feasible models of delivery that integrate screening and treatment systems such as collaborative care

5 years plus: Cohort study to identify risk factors for long term pain

Sexual function

Problem

There is strong evidence that cancer and its different forms of treatment can have consequences for a person’s sexual function. This issue has been most studied in ovarian, testicular prostate cancer, bladder and cervical cancer. There is modest evidence to suggest symptoms that accompany treatment-induced menopause are distressing. We need better understanding of those most at risk, how best to assess patients and the impact of experiencing a disruption in sexual function.

Solutions

There is limited evidence for the use of drug treatments and mechanical devices to improve sexual function in patients with gynaecological and urological cancers. The evidence for psychological treatment is inconclusive. There would be merit in studying the best ways to detect and assess those experiencing difficulties with sexual function and ways of helping those experiencing difficulties.

Current research

There is work just about to start exploring systems of assessment for female sexual problems and other exploratory work underway focussed on fertility in Black and Minority Ethnic (BME) communities and intimacy in head and neck cancer.

Best Buys

Less than 2 years: Surveys of prevalence and psychological and social associations.

2-5 years: Feasibility studies of integrated systems of assessment and management

More than 5 years: Large trials of interventions

Cognitive functioning

Problem

There is some evidence that cognitive dysfunction occurs as a consequence of cancer treatment (‘chemobrain’) and affects quality of life, but much of the evidence is limited to women with breast cancer. We need more understanding of the incidence, course and effect of alterations in cognitive function in cancer survivors.

Solutions

We did not find any reviews of RCTs of interventions specifically intended to address cognitive impairment.

Current research

There was no ongoing major research revealed through the consultation on the topic of cognitive impairment

Best buys

Less than 2 years: Prevalence and risk factor studies of cognitive impairment and its association with functional and psychosocial ability.

2-5 years: Pilot studies of methods to identify and intervene with those who are suffering from cognitive impairment.

5 years plus: Large trials of preventative and treatment interventions (if these are identified).

Employment, finance and return to work

Problem

This important problem emerged strongly from the consultation exercise but has received little attention from researchers. We have a reasonable understanding of the issues and problems people confront as they try to return to work and there is good evidence that those who have survived cancer are more likely to be unemployed than the general population. There is also good evidence that those who have head and neck cancer, do a job that involves manual labour and perceive their work environment to be unsupportive are less likely to return to work. More understanding is needed of the effect of different types of cancer treatment, different types of cancer and other factors on return to work.

Solutions

No evidence on the effectiveness of interventions was located. The application of vocational rehabilitation in other fields could be explored to identify potential approaches.

Current research

There is ongoing research in this field examining attitudes and experiences of employers and occupational physicians and exploring the impact of cancer on employment.

Best buys

Less than 2 years: (a) theoretical and modelling work to establish the transferability of vocational rehabilitation approaches used in other contexts to cancer survivorship (b) in-depth studies to understand the financial effects of cancer (c) studies to evaluate the best way to educate and support employers to support cancer survivors whilst returning to work.

2-5 years: Well designed pilot trials of feasible methods of intervention.

5 years plus: Large, prospective cohort studies to identify factors that impact on return to work and vulnerable sub-groups and large scale intervention studies.

Emotional distress

Problem

There is moderately strong evidence that cancer survivors suffer from increased distress during and soon after active treatment but less evidence for the presence of substantially increased distress in long term survivors. However, within the group of long term survivors there are individuals (for example those with actual and fear of recurrence) who have high levels of distress meriting help. Those most at risk include women, those with lower social economic status (SES) and those with disabling and disfiguring cancers such as head and neck cancers. Most of the evidence is limited to women with breast cancer.

Solutions

There has been a large amount of poor quality research evaluating a range of psychological interventions such as counselling and group therapy. The best evidence is for CBT. There is evidence of temporary benefit only from CAM. Much of the research has been flawed by attempts to treat all patients rather than confining the intervention to those with distress. No clear overall recommendations for treatment can be made at present.

Current research

We are not aware of any major ongoing UK studies

Best buys

Less than 2 years: (a) secondary analysis of existing data on long term outcome (b) well designed pilot trials of feasible methods of intervention.

2-5 years: Large trials of interventions based on patient education including guided self-help and telephone delivered treatment based on CBT principles.

5 years plus: (a) large, prospective cohort studies of mixed cancer groups. (b) studies to improve understanding, identification and management of distress in men and BME groups.

Table 2: Psychological

ISSUES	PROBLEMS				SOLUTIONS			
	Amount of research[†]	**Quality of research[‡]**	**Scope**	**Conclusion and opportunity[¥]**	**Amount of research**	**Quality of research**	**Scope**	**Conclusion and opportunity**
Depression	Moderate	Mixed, Low-High	Mostly women - mostly breast and ovarian cancer; men - prostate cancer	Moderate amount of evidence that cancer survivors experience depression - particularly those who are younger, have more advanced disease, more physical symptoms - but evidence is mainly focused on women with breast cancer. Breast cancer < 2 years if good quality research. 2-5 years ovarian & prostate cancer. Other cancers > 5 years.	Moderate	Moderate	Mainly mixed samples but some focused on breast cancer	There is evidence for the effectiveness of antidepressants and CBT in reducing depression. There is modest evidence for group interventions, but the evidence for non-CBT treatments is weak or inconclusive.
Anxiety	Moderate	Mixed, Low-High	Mostly women - mostly breast and ovarian cancer	Overall similar levels of anxiety to general population- moderate evidence that some cancer survivors (up to 30%) experience high levels of anxiety. Moderate evidence for a relationship between younger age, being diagnosed with more advanced disease, more physical symptoms and shorter time since diagnosis with increased levels of anxiety. Inconclusive results on the role of anxiety in recurrence and survival outcome. Evidence is mainly focused on women with breast cancer. Breast cancer < 2 years if good quality research. 2-5 years ovarian cancer. Other cancers > 5 years.	Low	Low	Mainly mixed samples but some focused on breast cancer	There is modest evidence for treating anxiety with music therapy and CBT. The evidence for exercise was inconsistent. Participating in support groups can also reduce anxiety.

ISSUES	PROBLEMS				SOLUTIONS			
	Amount of research[†]	Quality of research[‡]	Scope	Conclusion and opportunity[¥]	Amount of research	Quality of research	Scope	Conclusion and opportunity
General distress	Moderate	Mixed, Low-High	Mostly women - mostly breast and ovarian cancer	Low to moderate amount of evidence that cancer survivors have similar levels of general distress to healthy controls. Distress is associated with poorer QoL, lower SES, and head and neck cancer survivors may be more vulnerable to distress. Evidence mostly based on women with breast cancer. Breast cancer < 2 years if good quality research. 2-5 years ovarian cancer. Other cancers > 5 years.	Moderate	Low	Mainly mixed samples but some focused on breast cancer	There is a moderate body of evidence for a range of psychological interventions (e.g. CBT and counselling) although strong recommendations cannot be made. The evidence supporting group interventions is inconsistent. Patient education looks to be a promising area of research.
Fear of recurrence	High	Mixed, Low – High	Mostly women - mostly breast and ovarian cancer	High amount of evidence that fear of recurrence is a concern for cancer survivors and their families. Evidence mostly based on women with breast cancer. Breast cancer < 2 years if good quality research. 2-5 years ovarian cancer. Other cancers > 5 years.	-	-	-	No reviews or RCTs found.

Key: † A scale ranging from Low- Moderate -High has been used to provide a broad indication of the quantity of research described in the reviews. ‡ Terms such as Low, Moderate, High and Unclear have been applied to give a broad indication of the quality of research inferred in the reviews.¥ This column summarises findings from reviews and an indication of time frame necessary to achieve clear answers about a particular topic.

Depression

Problem

This is an important problem and there is good evidence for a significantly increased rate of depression in cancer survivors during and soon after active treatment. However, there is less evidence concerning long term survivors; persistent and recurrent depression is likely to be a problem for an important minority. Those most at risk are people who are younger, female and who have more advanced disease. Much of the evidence is limited to women with breast cancer.

Solutions

There is good evidence that antidepressant drugs and CBT and complex treatment models such as collaborative care are effective for depression in the general population. However, there is only moderately good evidence that antidepressants and CBT and collaborative care are effective in reducing depression specifically in cancer survivors. We do not know how to identify depression in long term survivors.

Current research

There are major ongoing studies of the effectiveness of collaborative care in short term survivors.

Best buys

Less than 2 years: (a) secondary analysis of existing data on prevalence and risk factors in long-term survivors (b) pilot studies of simple feasible methods of identifying depression in survivors in hospital and primary care (c) studies of the barriers to implementing established treatment models such as collaborative care.

2-5 years: Large trials of interventions based on feasible models of delivery that integrate screening and treatment systems and have an emphasis on primary care provision such as collaborative care.

5 years plus: Studies to improve understanding of how we can identify and manage depression in men and BME.

Anxiety

Problem

There is modest evidence for increased levels of anxiety after treatment and this is connected with anxiety over check-ups and medical follow up appointments. There is little evidence concerning long term survivors but anxiety is likely to be a problem for a small proportion. Those most at risk are younger, have more physical symptoms are closer to point of diagnosis and have more advanced disease. Most of the evidence is limited to women, particularly those with breast and ovarian cancer. Fear of recurrence is an increasingly well documented problem that persists in the long-term in patients and family members and contributes to the anxiety experienced by a substantial proportion of survivors.

Solution

There is a moderate amount of low to moderate quality research that has tested interventions for anxiety. The findings are largely inconclusive. Forms of CBT are likely to help but have not been adequately evaluated. A recent RCT suggests aromatherapy massage may bring some short-term relief. Exercise may also have a role.

Current research

No ongoing research specific to anxiety was identified through the consultation, but there is research underway on fear of recurrence.

Best buys

Less than 2 years: Secondary analysis of existing data to determine prevalence of anxiety in the long term and associations with fear of recurrence.

2-5 years: Well designed pilot trials of feasible methods that combine detection and intervention suitable to address minor, modest and severe anxiety and interventions for fear of recurrence.

5 years plus: (a) large scale, multi centre trials of simple feasible interventions
(b) cohort study to identify risk factors for persistent anxiety

Social needs

Problem

The social impact of cancer and the influence of social support on outcomes such as emotional well being and quality of life have been studied in mixed (but mainly breast cancer) populations. There is a small amount of evidence to suggest social functioning does not differ in cancer survivors from the general population. There is modest evidence that level of perceived social support is positively associated with factors such as mental well-being and quality of life. Studies of the nature of needs of family members and informal caregivers and best ways to meet these were a priority identified through consultation. The psychosocial implications of cancer survivorship for family members have not been well studied. The evidence we have suggests distress in family members persists in the five years following diagnosis. Much of the evidence is limited to women with breast cancer.

Solutions

There is modest evidence that support groups have a positive effect on marital satisfaction and sexual relationships and some evidence that interventions targeted at spouses might improve marital relationships.
No other clear recommendations can be made about approaches that might prove effective with respect to meeting social need.

Current research

There are studies just completed, ongoing and in set-up phase concerned with social difficulties and testing ways in which to best resolve these. Studies underway include families and informal carers as their population of interest and are testing family-based interventions.

Best buys

Less than 2 years: (a) exploratory studies to identify forms of social support that might prove effective and factors that dictate whether families do or do not seek support (b) secondary analysis of existing data on long term outcome and moderating factors.

2-5 years: (a) pilot trials of feasible methods of intervention to minimise or manage the effect of cancer on relationships (b) studies of the effect of a diagnose if cancer on relationships.

5 years plus: Cohort studies of mixed cancer groups that include family members. More understanding of how to identify and manage those who perceive they have unmet need, especially in those with cancers other than breast cancer and in BME and other disadvantaged groups.

Table 3: Social

ISSUES	PROBLEMS				SOLUTIONS			
	Amount of research[†]	Quality of research[‡]	Scope	Conclusion and opportunity[¥]	Amount of research	Quality of research	Scope	Conclusion and opportunity
Social needs (function)	Low	Unclear	Mixed, mainly breast cancer	Low evidence that levels of social functioning similar in cancer survivors to control groups. Evidence mainly based on women with breast cancer. Breast cancer 2-5 years if good quality research. Other cancers > 5 years.	Moderate	Moderate	Marital relationships	Modest evidence for the effectiveness of support groups.
Social support	Moderate	Unclear	Mixed, mainly breast cancer	Moderate evidence that perceived social support is positively associated with mental well-being, less distress and, higher levels of QOL. Inconclusive evidence that social support is linked to survival from breast cancer. Evidence mainly based on women with breast cancer. Breast cancer 2-5 years if good quality research. Other cancers > 5 years.				No reviews or RCTs found

Key: † A scale ranging from Low- Moderate -High has been used to provide a broad indication of the quantity of research described in the reviews. ‡ Terms such as Low, Moderate, High and Unclear have been applied to give a broad indication of the quality of research inferred in the reviews.¥ This column summarises findings from reviews and an indication of time frame necessary to achieve clear answers about a particular topic

Methodological issues

In reviewing the published literature, we were struck by a number of recurrent methodological problems that were frequently highlighted by those conducting systematic reviews. These included:

1. Problems with the samples studied

The origin of samples is sometimes poorly described and they may not be representative. Much research has been done on women with breast cancer and other cancers been neglected. There has been little research into the needs of minority groups and certain cancers, such as lung cancer and the less common cancers. Mostly samples have been simply too small to yield robust results.

2. Measures

A wide variety of measures have been used, with little consistency between studies, making the combination of the data across studies problematic. A standard set of measures would be highly desirable.

3. Design

A common criticism is that studies are not of generally high quality and are subject to multiple sources of bias which may make the result unreliable. Another major problem of design is the lack of long-term follow up, both in studies of need and of interventions.

4. Interventions

There are many problems with the interventions evaluated. They are often not well characterised and may not be in a form in which they can be implemented in practice.

5. General Issues

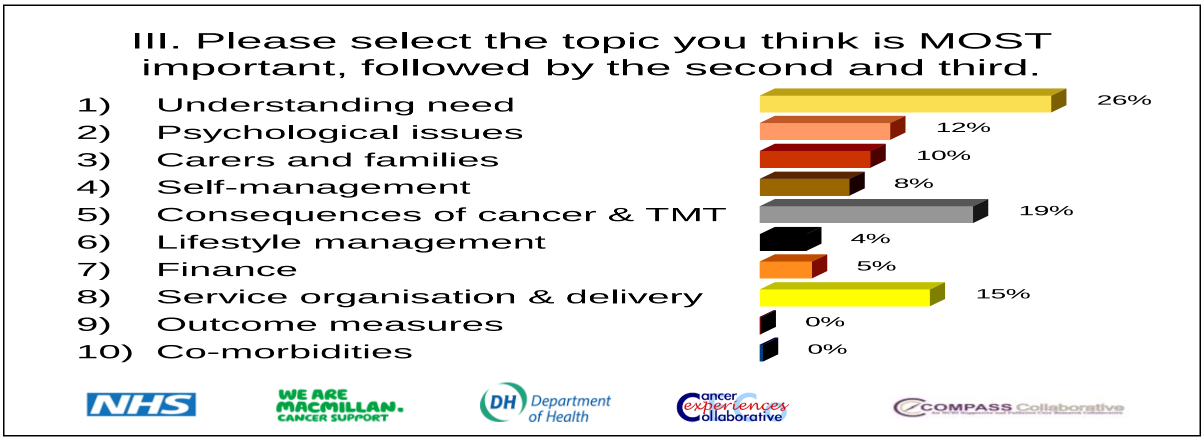
A key problem is the lack of precision in the research questions that have been asked (for example, the effect of a rather vaguely specified intervention on a wide range of rather vaguely specified outcomes). Such studies, not surprisingly, produce only vague answers.

Major areas of need and priority areas for investment

Alongside the lack of knowledge about how to address the issues of cancer survivors there was a strong feeling expressed at the consensus meeting that the creation of new knowledge frequently does not lead to implementation in practice. Where evidence does exist, within or outside the UK, or from other conditions (e.g. cardiac and diabetes care) this needs to be evaluated and modified for the purposes of a particular context and steps taken to ensure translation into practice. Likewise, the barriers to implementation of new research findings need to be explored. It was also felt success will only be achieved through well-funded, co-ordinated research efforts executed by those with the relevant expertise who work in partnership with clinicians and cancer survivors. The survey revealed there are a small number of researchers with the necessary expertise.

Funders should cease funding numerous, small scale research studies, which on occasion has been of dubious quality. Rather they might work collaboratively to generate sufficient funds for (a) large scale, prospective cohort studies that will sufficiently describe needs of this population and help us better understand the mechanism underlying long term consequences of cancer and its treatment (including physical, psychological and behavioural effects) and predict those most at risk. (b) large trials of delivery ready interventions. As research into models and approaches to care is at an early stage we need research to determine the most effective and efficient ways to organise care and to evaluate alternatives. There is also room for high quality, theoretically situated qualitative enquiry that illuminates patient experiences and underpins the theoretical and modelling phases of research.

Figure 2 Results of final vote at consensus meeting



Key: TMT= treatment

The consensus meeting identified a broad range of topics (see Figure 2), but because of methods used it was not possible to prioritise any particular aspect of a research topic further. However, in addition to the specific topic areas some overarching themes have emerged from both the reviews and consensus exercise. These are:

1. Considering needs and best means of support for families and caregivers as well as the needs of the patient
2. Considering the needs of specific populations and underserved groups
3. Considering need at different points of the survivorship pathway
4. Studies that explore different models of care for problems (including prevention, identification, surveillance and management) and incorporate evaluation of economic benefits and costs as well as barriers to implementation

Limitations

Whilst this report sets out future priorities for research into problems associated with survivorship it is important to acknowledge that recommendations are based on conclusions by the review team and these in themselves influenced by the results of the searches, extraction and synthesis. The lack of a previously agreed pathway in terms of what the concept of survivorship extends to e.g. from the point of diagnosis or some later point in a patient's pathway, meant we faced having to search across all stages from diagnosis through to death, clearly an unmanageable task.

Decisions had to be made and processes adopted in order to make the task realistic and these will have influenced our findings.

- The search terms employed, in particular not including terms to reflect different stages of survivorship journey e.g. advanced cancer, recurrence. Rather the term 'survivor' was used hence we may have failed to locate all the reviews and/or primary studies that pertain to these sub-populations. But we did extract information on whether the reviews were concerned with a particular stage of the pathway. We found most reviews did not specify stage of survivorship and most collated primary research studies that included populations at different stages of the survivorship journey.
- Searches were targeted at issues and concerns rather than populations e.g. did not explicitly search for reviews focussed on carers nor specific interventions e.g. CBT or exercise. Furthermore, the way researchers had defined the nature of the problem at which an intervention might be targeted at was inconsistent and the interventions themselves often multi-faceted Trying to distil the effect of the interventions on different problem and issues thus proved difficult.
- The consultation and the reviews were conducted simultaneously, hence there were some areas identified through consultation e.g. carers, sleep, weight loss and breathlessness which we were not able to pursue in the reviews.
- Focusing on 'impact factor' as a marker of quality to locate the health and well being and intervention primary research papers will have meant some relevant papers may have been excluded. For example, small scale, negative trials, exploratory trials and relevant qualitative studies may have been excluded
- There was a lack of specific descriptions of what was included under the topic labels used at the consensus meeting. But as no consensus

currently exists over what might be included under the term 'survivorship' it would most likely have proved a time consuming exercise and one where it might prove impossible to arrive at mutually exclusive labels in all cases.

- The methods employed (e.g. lack of hand searching and reference to grey literature) and the focus on topics previously subject to systematic review will have limited the information obtained to some degree. We have attempted to address this as far as possible. Furthermore, we were asked to focus on locating interventions close to implementation. It is extremely unlikely any intervention ready for implementation (or close to this position) would not have been the focus of a published systematic review. There is a chance however that important ongoing research was not captured through the consultation. Funders should therefore check their current portfolios to validate our findings.

CONCLUDING REMARKS

The reviews and consultation have confirmed that amongst researchers, health professionals, organisations and cancer survivors themselves there is growing interest in, and commitment to, building an evidence base that will inform cancer survivorship. This exercise was intended to assist those involved in developing the vision for the NCSI. The findings from this comprehensive review will be combined with the findings from the National Cancer Research Institute rapid review of cancer survivorship and other work undertaken by the NCSI research work stream to arrive at a final set of research priorities. It is clear that there are gaps in our knowledge that will, if left unfilled, have an impact on achieving the collective vision. It is also clear that there are opportunities for research that may inform what we do in a reasonable time scale. Survivorship is an important but under-researched aspect of the cancer trajectory. In order to make timely and effective progress difficult choices will need to be made by research funders about those topics and research groups mostly likely to give a good return on investment of increasingly scarce research funds and subsequently make the most difference to the lives of people living with and beyond cancer.

There are three separate technical appendices that accompany this report. These are:

1. Foster, C Amir, Z Jarrett, N Stamataki Z. Brearley, S Scott, I (2009). Scoping of research evidence regarding the health and well-being of cancer survivors: Psychological and social problems faced by cancer survivors, and their physical and practical well-being: Technical report. University of Southampton and University of Manchester.

2. Armes, J Richardson, A Addington-Hall, J (2009). Report on National Cancer Survivorship Consultation on research priorities: Technical report. King's College London and University of Southampton.

3. Ziegler, L, Hook, J Stark, D Neilly, L Hodges, L Walker, J Sharpe, M (2009) Systematic scope and collation of research evidence regarding interventions: Technical report. University of Leeds and University of Edinburgh

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