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## Beyond treatment – Psychosocial and behavioural issues in cancer survivorship research and practice



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### ABSTRACT

The population of cancer survivors has grown steadily over the past several decades. Surviving cancer, however, is not synonymous with a life free of problems related to the disease and its treatment. In this paper we provide a brief overview of selected physical and psychosocial health problems prevalent among cancer survivors, namely pain, fatigue, psychological distress and work participation. We also address issues surrounding self-management and e-Health interventions for cancer survivors, and programmes to encourage survivors to adopt healthier lifestyles. Finally, we discuss approaches to assessing health-related quality of life in cancer survivors, and the use of cancer registries in conducting psychosocial survivorship research. We highlight research and practice priorities in each of these areas. While the priorities vary per topic, common themes that emerged included: (1) Symptoms should not be viewed in isolation, but rather as part of a cluster of interrelated symptoms. This has implications for both understanding the

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aetiology of symptoms and for their treatment; (2) Psychosocial interventions need to be evidence-based, and where possible should be tailored to the needs of the individual cancer survivor. Relatively low cost interventions with self-management and e-Health elements may be appropriate for the majority of survivors, with resource intensive interventions being reserved for those most in need; (3) More effort should be devoted to disseminating and implementing interventions in practice, and to evaluating their cost-effectiveness; and (4) Greater attention should be paid to the needs of vulnerable and high-risk populations of survivors, including the socioeconomically disadvantaged and the elderly.

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## 1. Introduction

More than half of European patients diagnosed with cancer survive 5 years or longer after their primary diagnosis [1]. A disease-free status, however, is not synonymous with a life free of physical and psychosocial health problems related to the cancer and its treatment. In this paper we provide a brief overview of selected psychosocial issues in cancer survivorship. Specifically, we focus on pain, fatigue, psychological distress and work participation. We also address issues surrounding self-management and e-Health interventions for cancer survivors, and programmes to encourage survivors to adopt healthier lifestyles. Finally, we examine approaches to assessing health-related quality of life in cancer survivors, and the use of cancer registries in conducting psychosocial survivorship research. Our intent is not to provide a comprehensive review of these topics, but rather to briefly summarise the current state of affairs and, more importantly, to highlight what we believe are some of the priorities for future research and clinical care development initiatives.

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## 2. Pain and pain management

Chronic pain is one of the most distressing and disabling symptoms experienced by cancer patients and survivors. Knowledge of pain and its effects on cancer survivors is still limited due to the small number of studies, and thus it is often left unrecognised and untreated [2].

Pain is not only caused by tissue damage produced by the cancer itself but can also be caused by treatment-related toxic or traumatic damage to peripheral and central neural structures, resulting in long-lasting or even late onset neuropathy. Pain may persist after treatment or may emerge several months or even years after treatment has been completed. This is described as post-cancer pain syndrome.

Pain rates of 30–50% have been reported in cancer survivors, varying as a function of diagnosis, stage, disease status, comorbid conditions, initial pain management, patient characteristics (e.g. sex, cultural background) and measures used to assess pain. Importantly, pain is also reported in disease-free cancer survivors. An analysis of the 2002 *National Health Interview Survey* in over 30,000 persons found that the prevalence of pain in cancer survivors was much higher (34%) than in controls without a history of cancer (18%) [3]. The highest

prevalence rates were observed in post-thoracotomy (up to 80%), post-amputation/phantom limb (50% to 80%), post-neck dissection (52%) and breast cancer (63%) patients [4].

Post-cancer pain syndromes should be viewed as part of a cluster of symptoms, including fatigue, anxiety, depression and sleep disturbance. All of these symptoms may be caused, at least in part, by a common, underlying biological mechanism. Combined, these symptoms have a negative impact on survivors' physical and psychosocial functioning [5].

Chronic pain is a persistent stressor that indirectly affects the feedback loop of the hypothalamic–pituitary–adrenal (HPA) axis through involvement of brain regions in the limbic system. The HPA axis is also activated in response to psychological stressors such as depression and anxiety [6]. Emotional distress, depression, anxiety and fear may contribute significantly to the resulting pain experience [7].

Even when the 3-step WHO pain ladder is employed, complete relief from chronic cancer pain may be an unrealistic expectation in some patients [8]. Opioid therapy is a useful tool, but in the survivorship setting its use is often discouraged due to long-term side effects, including the development of opiate-induced hyperalgesia, as well as the risk of abuse and addiction [9]. Non-opioid medication options include antidepressants, antiepileptic drugs and topical agents, in addition to non-steroidal anti-inflammatory agents and acetaminophen [10]. Intrathecal therapies with non-opioid alternatives, such as ziconotide or other drugs, should also be considered for the management of chronic pain, particularly if it is neuropathic [9]. Gene therapy represents a potentially useful, new approach. However, this requires careful selection of a therapeutic gene that properly modulates the nociceptive cascade without causing additional complications for the patient [11]. In selected patients, interventional modalities may be considered, including nerve blocks, trigger point injections, spinal cord stimulators or implanted intrathecal pumps [10].

An equally if not more useful approach may be to encourage survivors to actively participate in the plan of care for their pain management, with an emphasis on self-activation and non-pharmacologic therapies, and to help them focus on certain outcomes such as improved functional capacities, restorative sleep, social activities, mood and coping, which may help to reduce pain to a tolerable level [5,10].

Our knowledge and understanding of chronic pain in cancer survivors can be enhanced by: (1) investigations of symptom clusters and the total symptom burden experienced by

cancer survivors; (2) studies comparing cancer survivors with healthy individuals and those with other chronic diseases; (3) comparing the pain experience of short- versus long-term survivors; (4) studying a wide range of survivor populations, as much of the current evidence is based on breast cancer survivors; (5) studies of the mechanisms involved in the transition from acute pain to chronic pain syndromes; and (5) continuing studies of both pharmacologic and behavioural managements of chronic pain.

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### 3. Cancer-related fatigue

We know that the majority of patients experience cancer-related fatigue (CRF) during cancer treatment, and that it can have a profound impact on both physical and psychosocial functioning [12]. What is less clear is why some patients recover quickly from CRF while for others it develops into a chronic state. There is a need to understand the mediators of CRF including pain, mood state and inflammatory processes, in order to design suitable interventions.

Early screening and detection is an important first step, and may be initiated even before the cancer treatment begins. Screening for CRF can be done with stand alone questionnaires [13], but can also be embedded in a broader health status or quality of life assessments [14,15], and may be combined with performance indicators of functioning. Potentially, screening could also include storing serum for genetic polymorphisms or inflammatory marker measurement, as there is consistent evidence that these mediate the process of CRF [12].

There are currently many questionnaires available for assessing CRF, although most have not been developed for or specifically tested in the cancer survivorship setting [16]. Ideally, we should have at our disposal a very limited number of widely accepted measures of fatigue that would allow us to compare results across populations and studies. Such measurement uniformity, or at least comparability, may be facilitated by current efforts underway in both the United States and in Europe to develop fatigue measures based on item response theory (e.g. the PROMIS initiative in the US [17]; the Computer Adaptive Testing project of the EORTC Quality of Life Group [18]). An additional challenge is to agree upon a definition of clinically significant levels of CRF and of its reduction as the result of interventions [12].

We also need a comprehensive model, including both somatic and psychosocial factors, for understanding the multi-causal development of CRF. We know that CRF manifests itself in compromised performance and functioning, but why such problems persist and become chronic in some patients but not in others is unclear [19]. To better understand the development and course of CRF, we need longitudinal studies with long-term (e.g. 5 to 10 year) follow up after completion of primary treatment. These could be freestanding, observational studies, but we may also be able to embed CRF assessments in new or on-going cancer clinical trials. Although patients who participate in clinical trials may not be representative of the larger population of cancer patients, the clinical trial setting may offer a unique opportunity to relate changes in CRF over time to detailed disease- and treatment-related variables.

Additional opportunities are available through linkage of various data sources, including patient self-reported CRF, performance indicators (e.g. step counts) and employment data. Fatigue can be a significant factor affecting return to work, and thus such linkages could provide us with important insights into the economic costs of CRF.

We have a broad evidence base for the use of exercise and psychological therapies for treating CRF, but the effect sizes of these interventions tend to be small [20,21]. Most of the evidence is based on studies of patients under treatment, using resource intensive interventions [22,23]. Thus we need studies of practical interventions carried out during treatment with long-term follow-up, and interventions initiated after primary treatment has ended [23]. This will provide us with evidence regarding the value of early interventions to reduce peak CRF on treatment leads and to minimise chronic CRF in survivors.

While low cost, psycho-educational and self-management interventions for CRF could be developed and made available to large populations of cancer patients, more intensive forms of intervention should be reserved for those who need it the most. Thus, again, appropriate screening is necessary to target that subset of cancer patients and survivors who are suffering from or are most likely to develop chronic CRF [12]. To date, there have been only a few studies showing that early supportive strategies during treatment may prevent CRF as a late effect [24]. Therefore research on evaluation of early rehabilitation strategies for prevention of CRF in cancer survivors is also an important research task.

Understanding CRF is important for evidence-based resource allocation and for making the case for additional services. This could include subsidised gym membership or an exercise prescription initiated during treatment and monitored through the survivorship period [25]. It is also important to engage primary care physicians so that there is continuity of care from the active treatment phase through long-term survivorship. This could be incorporated into an individual survivorship care plan.

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### 4. Psychosocial and psychological distress: assessment and treatment interventions

Across all diagnoses, cancer patients are at significantly increased risk for psychological symptoms [26]. Distress is a broad construct including a wide continuum of emotions related to, among others, symptoms of depression, anxiety and adjustment disorder [27]. Overall, distress in cancer patients is often reported to be above 30% [28]. The prevalence of depressive symptoms varies between 10 and 25% [29], and a significantly increased risk for hospital admission for depression has been reported [30]. Anxiety symptoms vary between 10 and 30% [31]. High levels of comorbid symptoms of anxiety and depression have been reported and genetic risk factors for both have been shown to correlate strongly [32]. However, symptoms of anxiety and depression may also occur independently and progress quite differently after a cancer diagnosis. This process remains almost unexplored in cancer survivors.

A large number of randomised clinical trials (RCT's) have investigated whether psychological symptoms in cancer

patients can be alleviated through psychological support and interventions. Multiple reviews and meta-analyses have attempted to evaluate the evidence, but despite a somewhat overlapping pool of studies being evaluated, the conclusions are surprisingly divergent. Some reviews conclude that psychological interventions have a significant, positive effect [33], while others report a lack of convincing evidence on the efficacy of psychological interventions [34]. The observed discrepancies between these reviews may reflect varying quality of reporting in the various RCT's, which makes it challenging to compare results across studies [35].

It has been argued that the most promising and effective interventions are those targeted at high-risk cancer groups [36]. This suggests that screening for psychological distress, with appropriate referral to interventions among those at high risk, will increase the effectiveness of interventions. However, only a few RCTs have investigated the effect of screening-based interventions on psychological symptoms. Again, the conclusions drawn have been inconsistent, reflecting significant variability in the quality of reporting in the trials [37–39].

To move forward, the methodological quality of psychological intervention studies needs to be improved substantially. This includes carrying out pilot and feasibility testing prior to starting an RCT, generating protocol-based interventions and raising the standards of reporting of RCT's in this area of research. This will facilitate the interpretation of results across studies, and should result in more consistent conclusions being drawn from systematic reviews. Additional attention needs to be devoted to implementation of those programmes demonstrated to be effective.

Psychological symptoms experienced by cancer patients are not static, but rather are likely to change over time [40]. To improve the quality and efficacy of our interventions, we need to better understand the natural history of distress, depression and anxiety from pre-cancer diagnosis through to long term survivorship, the risk and protective factors involved, and the recovery process, with and without support. Such trajectories have been the subject of study in a few investigations, and have aided in identifying especially vulnerable subgroups of cancer patients and survivors [40–44].

There is accumulating evidence that psychological distress does not exist independently of social circumstances [45]. This suggests the need for conceptual and treatment models that place greater emphasis on the interplay between psychological and social factors.

Finally, given increasing health care costs and reduced budgets, we need to 'think smart and do smart' by tailoring and targeting our interventions to those at highest risk of developing psychological problems that are not self-limiting and may become chronic. Timely treatment of distress will not only benefit the psychological well-being of cancer survivors, but may also enhance compliance with maintenance adjuvant therapies, and could possibly play a role in survival as well [46].

psychosocial functionings and healthy lifestyle [47]. Although there is evidence that supportive care targeting cancer survivors and their families can be effective [48–50], referral rates are low and many survivors have unmet needs [51].

In recent years, several new models of organising supportive care have emerged. The Chronic Care Model includes the health delivery system (promoting care in an effective, efficient manner), the clinical information system (facilitating efficient and effective care), decision support (consistent with scientific evidence and patient preferences), self-management support (empowering patients to manage their health and health care) and the community (mobilising community resources to meet patients' needs) [52].

Disease management refers to a system of coordinated, comprehensive care along the continuum of cancer and across health care delivery systems, with a special focus on self-management [53]. Stepped care also has the potential to improve the efficiency of supportive care. Usually stepped care includes the following care pathway: watchful waiting, (guided) self-help, brief face-to-face therapies or counselling and specialised interventions [54]. Cancer survivors play an active role in these modern care models, and eHealth is seen as a means of facilitating innovative supportive care.

Self-management is defined as 'those tasks that individuals undertake to deal with the medical, role and emotional management of their health condition(s)' [55]. Self-management strategies are intended to empower cancer survivors and increase their self-efficacy. Empowered patients are those who are successful in managing their condition, collaborating with their health care providers and accessing appropriate and high-quality (supportive) care [55].

eHealth (or mHealth (mobile Health)) involves using information and communication technology (including mobile devices) to improve health care [56]. Beneficial effects of eHealth in cancer care have been reported for, among other outcomes, health literacy, decision making, health care participation [56], psychological well-being [57], physical activity levels [58] and quality of life [56].

There is a growing interest in self-management and eHealth among cancer survivors, health care providers, insurers and policy-makers as a means of facilitating and improving supportive care. However, despite high expectations, many cancer survivors and care providers have concerns regarding confidentiality and security, inappropriate use of (unguided) self-management and eHealth tools, cost-effectiveness and lack of reimbursement. In many cases, eHealth applications are designed by web-technologists who have little knowledge of the key stakeholders, which hinders sustainable adoption of eHealth tools in supportive care.

The development of self-management and eHealth tools should be based on relevant theoretical and applied models, such as Bandura's social learning theory, theory of planned behaviour, cognitive behavioural therapy and problem solving therapy [55–57]. In addition, (e)health literacy skills need to be taken into account to ensure usability of these tools. With the recent explosion of self-management and eHealth tools, knowing which are cost-effective, for whom, and at what point in the cancer trajectory is a challenge for both cancer survivors and health care providers. In order to embed such tools in routine supportive care, it is also important to take

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## 5. Self-management and eHealth

Supportive care for cancer survivors is multidisciplinary and aims to improve quality of life, including physical and

cancer patients' and their care providers' preferences into account, and to identify barriers, both real and perceived.

Recently, a new framework for the development of eHealth technologies has been proposed that is based on a participatory development approach, persuasive design techniques and business modelling [59]. This framework serves as an evidence-based roadmap for the development and implementation of new eHealth technologies in health care and may also be used for developing self-management interventions.

There is a clear need for more research on the development, cost-effectiveness and implementation of self-management and eHealth tools targeting cancer survivors. Three top research priorities are: (1) obtaining insight into the attitude towards and the barriers to and facilitators of self-management and eHealth tools; (2) development of self-management and eHealth tools targeting quality of life issues important to cancer survivors, based on evidence-based models and applied theories; and (3) evaluation of the cost-effectiveness and implementation strategies for self-management and eHealth tools embedded in supportive care models.

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## 6. Health behaviour and lifestyle interventions in cancer survivors

Cancer survivors are at risk for recurrence, second cancers and comorbid conditions [60]. In particular, those who are overweight, obese and/or inactive are at increased risk for cancer-related mortality [61,62]. A growing body of evidence indicates that a healthy lifestyle is associated with a reduced risk of morbidity and mortality after cancer. Recent systematic reviews and meta-analyses conclude that behavioural interventions are safe, efficacious and feasible when implemented in controlled clinical settings. Specifically, research shows that physical activity interventions are safe [63] for cancer survivors and improve physical function, strength, cardiorespiratory fitness, fatigue, mental health (e.g. depression) and health-related quality of life (HRQOL) [63–65]. Dietary interventions have been shown to improve diet quality and body weight [65]. There is also evidence that exercise and maintaining a healthy body weight influence biomarkers associated with progressive disease and overall survival (e.g. insulin levels, inflammation) [61,62].

Despite this evidence, such interventions are not widely disseminated into practice. Integrating health behaviour change interventions into standard survivorship care will take a coordinated research agenda. Future research should use a multi-level approach to elucidate the facilitators of and barriers to behaviour change at the survivor, family, provider, healthcare system and public health levels. Mechanistic research identifying the effects of health behaviour change interventions on the integrated biological system within cancer survivors, rather than isolated pathways, will provide needed information to engage physicians in prescribing these interventions and in securing their reimbursement by insurers. Research should determine the optimal types, doses and timing of interventions needed for different groups of cancer survivors, depending on survivors' individual biology, sociodemographic characteristics, outcome needs and psychosocial circumstances, recognising that one size will not

fit all. Targeted interventions aimed at specific groups, along with tailoring of interventions to individuals' needs and circumstances may increase uptake, utilisation and overall impact. Research should also focus on determining optimal methods to support survivors who need to make multiple behaviour changes (e.g. improve diet, increase physical activity and stop smoking). Additionally, most research has focused on helping survivors initiate healthy behaviour changes; research is also needed to help survivors maintain meaningful changes in health behaviour over time.

Most RCTs, to date, have focused on more highly educated, wealthier, Caucasian and younger female breast cancer survivors. Future research should include more diverse survivor populations. Studies are especially needed to understand how to overcome barriers and promote health behaviour changes in low-SES or minority communities, among men, and among adults over the age of 65 with comorbidities. This latter population is the largest segment of cancer survivors, but is typically excluded from health behaviour change research.

Many survivors report intentionally improving health through diet, exercise or smoking cessation after cancer [66], and over 50% of survivors voice an interest in pursuing healthy behaviour change interventions [67]. There is an inherent bias in current RCTs targeting behaviour change, as it is these highly motivated survivors who tend to enrol in studies. However, there is an important subgroup of survivors who report not contemplating or having no interest in making healthy behaviour changes [67]. Future research should identify strategies for engaging these survivors and motivating them to undertake health behaviour changes. This includes research addressing the underlying value of eating healthy and being physically active, as well as considering how survivors think about health behaviour change in the context of competing values and priorities (e.g. reduced time with family). Additionally, linking behaviour change to outcomes survivors see as important, such as physical and cognitive functionings, recurrence/survival and quality of life, may help them recognise the value of behaviour change interventions.

Finally, behaviour change RCTs should be designed to foster dissemination and implementation in a variety of settings. Data on costs, including intervention staff time, clinic time and patient/family costs need to be collected as part of RCTs. Trial designs should attempt to optimise post-intervention sustainability by, for example, engaging stakeholders (e.g. survivors, healthcare providers, insurers, community partners) from the beginning of the study and conducting RCTs in the settings where later adoption is likely (e.g. community settings). Clinic or other facility-based interventions should build in components transitioning the intervention to the home or community setting to facilitate sustainability and maintenance of behaviour changes.

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## 7. Work participation among cancer survivors

Research on employment and work-related issues has convincingly shown high motivation among cancer survivors to return to work after primary treatment has been completed. Approximately two-thirds of cancer patients either continue

working after their diagnosis of cancer or return to work [68]. Aside from the obvious financial benefits associated with (return to) work [69], cancer survivors also experience work as a means of maintaining their personal identity, a sense of normalcy, social relationships, self-esteem, self-worth, social roles, life satisfaction and quality of life [70–72]. However, the process of returning to work is a difficult one for many survivors due to chronic physical, emotional and occupational problems [73–76]. Cancer survivors are more likely to be unemployed than their peers in the general population [77], and they have an increased risk of early retirement [78].

Return to work after a cancer diagnosis is associated with a number of sociodemographic and clinical factors. Younger, male, well-educated survivors are more likely to resume their working life. Those with early stage disease, who undergo less invasive treatment and as a result are less fatigued, have fewer symptoms and who are in better physical condition are also more likely to be motivated to and to actually return to work [68]. Additionally, work-related factors such as the employers' willingness to allow flexible working arrangements, having supportive colleagues, being engaged in non-manual work and having a higher salaried position contribute to successful return to work.

In industrialised countries, it has been estimated that approximately 42% of cancer patients are diagnosed at a working age (between 15 and 64 years) [79]. A recent study evaluated the costs of all cancers in a population-based cost analysis including health-care costs, informal care costs and productivity losses [80]. It was estimated that, in 2009, cancer cost the European Union €126 billion; 60% of the economic burden of cancer was in non-health-care areas, with almost €43 billion in lost productivity due to early death and €9.5 billion due to lost working days.

These figures illustrate the importance of both epidemiologic and interventional research to better understand the factors that affect employment, work and work disability, and to develop initiatives that create optimal opportunities for cancer survivors to return to work, if they so desire. Towards this end, the Cancer and Work Network (CANWON) was established in 2013. CANWON's objectives include the assessment of prognostic factors and work participation in cancer patients, to identify indirect costs of cancer survivorship, to gain significant knowledge about the role of the employer in work participation and to develop innovative interventions to enhance work participation of cancer patients [77].

Future research should consider the range of individual and interpersonal factors, the short- and longer-term treatment factors and the work environment and overall legal, organisational and financial factors that may affect employment and return to work. Research should take into account different perspectives on work participation in cancer survivorship, including that of: (1) the cancer survivor; (2) the caregiver and the family; (3) the employer and coworkers; (4) the health care providers; and (5) the community or society, at large.

More research is particularly needed among those survivors with a lower socioeconomic status, difficult working conditions and occupational problems. Integrated multidisciplinary team approaches to medical and occupational rehabilitation programmes are needed that address individual and treatment-related factors, and that are tailored to the

individual's work-related needs. Interventions are needed at the workplace itself that involve employers. Finally, more efforts should be invested in programmes aimed at long-term cancer survivors where the focus is on sustaining work performance and satisfaction after the initial return to work. To use limited resources most effectively, screening procedures need to be developed that identify those cancer survivors at high risk for negative work outcomes.

## 8. Evaluating the health-related quality of life (HRQOL) of cancer survivors

The HRQOL of cancer survivors can be assessed with three classes of self-report questionnaires or patient-reported outcomes (PRO's): (1) generic measures developed for use with the widest possible range of health and clinical populations, including patients with cancer; (2) cancer-specific measures; and (3) cancer survivor-specific measures. The most well-known and widely used generic HRQOL questionnaire internationally is the Short-Form 36-Item Health Survey or SF-36 [81]. The original 1.0 version has been translated and validated in a very large number of countries, including most countries in Europe. There are also good general population norms available for the original SF-36 in many countries, although some are quite outdated [82]. The more recent, version 2.0 of the SF-36 incorporates some minor but useful changes in item wording, but most importantly it employs a norm-based scoring procedure, using U.S. normative data [83]. To date, the SF-36 version 2.0 has been normed in only a limited number of countries outside of the U.S. For this reason, many international researchers either continue to use the original version or use the newer version, but with U.S. norm-based scoring. Perhaps the most important limitation of the SF-36 for use in cancer survivorship studies is that it does not cover many of the HRQOL issues that are of specific concern to cancer survivors (e.g. fear of disease recurrence, return to work, financial problems, sexuality, etc.).

At the next level are cancer-specific HRQOL questionnaires, of which the two most widely used internationally are those of the EORTC [84] and of the FACT group in the United States [85]. Both the EORTC and the FACT employ a measurement system that includes a core questionnaire (the QLQ-C30 and the FACT-G, respectively) intended for use with all cancer patients, irrespective of diagnosis or treatment, and condition-specific, supplemental questionnaires that address HRQOL issues specific to particular patient populations (e.g. breast, colon or lung cancer). Both the EORTC and FACT suites of measures have been translated and validated in a wide range of languages and countries, and there are some general population normative data available for the core questionnaires. While both the EORTC and FACT measures can be (and are) used in cancer survivorship studies, there is a need for careful review of their content to ensure their relevance and comprehensiveness of coverage, particularly for long-term survivors. For example, some items addressing acute symptoms such as emesis may no longer be relevant, while other topics may not be covered adequately.

Finally, there are a number of questionnaires developed specifically for use among cancer survivors. Muzzatti and

Annunziata recently reviewed 8 of these survivorship-specific questionnaires, and concluded that most have not yet undergone the requisite psychometric work to verify their reliability and validity [86]. The two measures that were judged as most promising are the revised version of the Impact of Cancer questionnaire (IOCv2) [87] and the Quality of Life in Adult Cancer Survivors (QLACS) questionnaire [88]. Both questionnaires have a relatively clear subscale structure, and have been shown to be reliable and valid in a number of studies. They have been used in some international studies, but still require translation and validation in most European countries.

Thus, although there is a range of HRQOL measures that can be used in survivorship studies, there is clear need for additional methodological research in this area. This includes: (1) generating normative data for the SF-36v2 in a wider range of European countries; (2) systematically assessing the content of the EORTC and the FACT HRQOL measures to ensure their suitability for use among cancer survivor populations and, where necessary, revising or adapting them for such use; and (3) translating and validating the most promising cancer survivor-specific questionnaires for use in a broader range of European countries.

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## 9. Research methodologies and use of cancer registries

Despite the growing interest in health-related quality of life (HRQOL) and other patient-reported outcomes (PROs) as indicators of treatment efficacy in cancer clinical trials, it is not yet customary to continue collecting such data for extended periods of time after trial completion. Guidelines and standards for evaluating HRQOL in randomised clinical trials have been published (CONSORT; Consolidated Standards of Reporting Clinical Trials) [89], but long-term follow-up of clinical trial participants is expensive and labour-intensive. Researchers have had variable success in attempting to retrospectively recruit survivors who participated in earlier clinical trials in order to assess chronic or late effects of treatment [90,91]. Typical problems that arise with such a retrospective recruitment approach are difficulty in locating patients, lack of institutional commitment, lack of patient interest and ethical issues (not having an individual's informed consent for long-term follow-up) [90].

To date, most studies evaluating PRO's among cancer survivors have employed a cross-sectional, observational design. However, there are examples of successful prospective, observational cohort studies that have followed cancer survivors over longer periods of time [92,93].

Cancer registries are increasingly being used to identify and recruit cancer survivors into observational HRQOL studies. Because of the population-based nature of cancer registries, institutional referral bias can be avoided and better external validity can be obtained. Another advantage is the large number of survivors that can be included with a wide geographic reach.

A recent review of cancer registries as a resource for HRQOL research in cancer survivorship found that most studies included survivors of more common malignancies, such

as breast, colorectal and prostate cancer [94]. Surprisingly few studies have focused on the HRQOL of survivors of less common forms of cancer or of elderly cancer survivors. We would recommend that future registry-based studies focus specifically on these understudied subgroups of cancer survivors.

The recently completed EUROCOURSE ('Europe against Cancer; Optimisation of the Use of Registries for Scientific Excellence in Research': [www.eurocourse.org](http://www.eurocourse.org)) project is an example of how researchers from various countries (in this case, France, Germany, Ireland, the Netherlands and the UK) can exchange experiences and initiate cancer registry-based, collaborative HRQOL research. Privacy regulations, difficulties obtaining ethical approval and recruiting survivors and obtaining (programmatic) funding are the most common challenges facing cancer registries that wish to conduct HRQOL survivorship studies. Individual countries also have their own specific issues, and thus we recommend conducting local/national pilot projects that can help determine how best to conduct long-term survivorship studies within the context of specific registry laws and privacy regulations. Additionally, sharing such information across countries could facilitate the identification of practice variations, and ultimately achieving (inter)national standards for survivorship research [94].

To be able to interpret cancer survivors' scores on HRQOL and other PRO measures, it is useful to have normative data from the general population. Such reference data allow us to estimate the extent to which observed functional impairment and symptom burden are associated with and can be attributed to cancer and its treatment, rather than comorbid conditions or simply to the ageing process. Normative data for questionnaires that are often used in cancer survivorship studies (e.g. the SF-36, the QLQ-C30) are available for a number of, but certainly not all European countries. Additionally, normative data for such questionnaires can become dated, and thus it is important to regularly update normative databases, preferably using a common protocol (e.g. for establishing the sampling frame and procedures, for data collection) across countries. This will facilitate meaningful international comparisons of cancer survivor experiences [95].

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## 10. Summary and conclusions

In this paper we have reviewed a number of key areas of psychosocial research and practice in cancer survivorship. For each of these areas, we have identified what we believe to be important directions for future research. We are cognizant of the fact that our review does address all potential psychosocial issues relevant to cancer survivors. Separate papers in this special issue of the *European Journal of Cancer* are devoted to sexuality/fertility and to cognitive functioning in cancer survivors. Other issues, such as social relationships, spirituality and positive growth opportunities, are clearly relevant, but were beyond the scope of this paper.

We know that about one-third of cancer survivors suffer from post-cancer pain syndrome, which can have a negative and sustained impact on both physical and psychosocial

functioning. Pain should not be viewed as an isolated symptom, but rather in a cluster together with other symptoms (e.g. anxiety, depression, fatigue, sleep disturbance). Studies are needed on models of care that employ a multidisciplinary approach to pain management, combining drugs and other medical interventions with physical therapy, and psychosocial interventions aimed at patient education and self-management.

Cancer-related fatigue is an even more prevalent problem among cancer survivors, and one that also requires a comprehensive, multifactorial, approach to treatment. Longitudinal studies with long-term follow-up are needed to better understand the risk factors associated with chronic fatigue following cancer treatment. Future studies should investigate both intensive interventions targeted at those with severe fatigue, and lower intensity interventions for survivors with mild to moderate fatigue complaints. The availability of brief and diagnostically accurate screening questionnaires could facilitate triaging survivors into the most appropriate care pathway.

Overall, about one-third of cancer patients experience symptoms of psychological distress. The many controlled trials investigating the efficacy of psychosocial interventions for the treatment of distress have yielded inconsistent results. This reflects, in large part, the variable methodological quality of these trials. Future trials should investigate protocol-based interventions, use rigorous research methods and adhere to state-of-the-art reporting standards. There is particular need for tailored interventions that take into account the nature and severity of distress and the cancer survivors' background characteristics, and that are cost-effective.

One approach to providing cost-effective psychosocial care is the use of (guided) self-management strategies and eHealth tools. Such interventions need to have a strong conceptual basis, be evidence-based and target somatic and psychosocial problems that are important to cancer survivors. Additionally, effective implementation strategies need to be an integral part of any self-management, blended care, or e-Health initiative.

There is growing evidence that a healthy lifestyle reduces the risk of morbidity and mortality after cancer, and that many behavioural and lifestyle interventions (e.g. diet, exercise) are both safe and effective. Yet, such interventions are not widely available, and when available, not widely used. Future research is needed to better understand the factors that inhibit and facilitate the uptake of such programmes by cancer survivors, health care providers and health care systems. More basic research is also needed to elucidate the pathways and mechanisms through which health behaviour changes affect health risks and health outcomes in the cancer survivor population. At a practical level, research is needed to help those who require multiple behaviour changes, to facilitate maintaining behaviour change once initiated and to encourage behaviour change among those who are socioeconomically disadvantaged.

Many cancer survivors want and/or need to continue working during or to return to work as soon as possible after ending primary treatment. This is in the interest of both the cancer survivor and society at large. Future research is needed to identify individual, interpersonal and structural factors

that promote or impede return to work. Interventions targeted at work resumption should engage both the worker and the employer. There is a particular need for return-to-work programmes for vulnerable, high-risk populations, such as those with lower socioeconomic status and with difficult work conditions.

Assessment is an important element of any effort to improve the psychosocial health of cancer survivors. We already have at our disposal a range of self-report measures for assessing symptoms, functioning and well-being, some of which have been developed specifically for use in cancer survivor populations. Future research should focus on refining these measures, on making them available in a broader range of cultures and languages, and on generating normative data for various measures to facilitate our understanding of how cancer survivors feel and function in comparison to their peers.

Finally, we would advocate greater use of cancer registries to facilitate high quality, population-based investigations of the quality of life of cancer survivors. While there are examples of successful use of registry data for such purposes, most studies have focused on the more common cancer survivor populations. Future efforts should be directed towards patients with less common cancers, and at vulnerable populations of cancer survivors, including the elderly, underserved ethnic minorities and the socioeconomically disadvantaged.

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### Conflict of interest statement

None declared.

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