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Multimorbidty in older adults living with and beyond cancer

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Corresponding Author:	Teresa Corbett UNITED KINGDOM
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Corresponding Author's Secondary Institution:	
First Author:	Teresa Corbett
First Author Secondary Information:	
Order of Authors:	Teresa Corbett
	Jackie Bridges
Order of Authors Secondary Information:	

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and beyond cancer.

Corresponding author:

Dr Teresa Corbett

Building 67 Room 3031, School of Health Sciences, University of Southampton, Highfield, Southampton SO17 1BJ

Phone: +442380598292

Email: t.k.corbett@soton.ac.uk

Co-author:

Professor Jackie Bridges, School of Health Sciences, University of Southampton. Email: Jackie.Bridges@soton.ac.uk

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Structured Abstract:

Purpose of review: This review draws attention to the need for longer-term management of multiple conditions in older adults with cancer.

Recent findings: Older people living with and beyond cancer (LWBC) are more likely than younger people to have higher prevalence of multimorbidity leading to an overall increase in illness and treatment burdens, and limiting health-related quality of life and capacity to self-manage. Older age presents a higher risk of cancer treatment side-effects and development or progression of other conditions, leading to worsening health, long-lasting functional problems and social isolation. While many prioritise functional independence and continuance of valued activities over survival, older people living with multimorbidity are more likely to experience poor physical functioning during and beyond cancer treatment.

Summary: Cancer treatment decisions and survivorship plans should be developed in the context of other conditions and in line with the individual's priorities for continued quality of life. More research is needed to guide service development and clinical practice in this important area.

Keywords: Aged, cancer, multimorbidity, survivorship, aging

Introduction:

Approximately 50% of those diagnosed with cancer live 10 years beyond their diagnosis, and two- thirds have lived beyond 5 years[1-3]. Those living with and beyond cancer (LWBC) report long-lasting physical and psychological symptoms after (or on continuous) treatment[4, 5]. Moreover, a diagnosis of cancer is associated with a significantly lower health-related QoL (HRQOL) compared to those who have never had cancer—particularly in relation to physical symptom burden, activities of daily living, social activities and psychological well-being[6]. Commonly experienced persistent symptoms and side effects include functional limitations, pain, fatigue, insomnia, peripheral neuropathy, lymphoedema, gastrointestinal problems, bladder dysfunction, and early menopause[6].

Increased age has been established as a predictive factor for cancer [7], and approximately 70% of those LWBC are aged 65 and older[2, 8]. By 2040, older people will account for 77% of all people living with a cancer diagnosis [3]. Follow-up care and psychosocial support after cancer is further complicated by the presence of multiple conditions in older age [8, 9]. Older people are more likely to have two or more long-term conditions (used in this paper as a definition of multimorbidity (MM)) and those LWBC have been shown to have higher prevalence of MM than an age-matched control group without cancer [10]. Frequently reported chronic conditions co-occurring with cancer include cardiovascular disease, obesity, metabolic illness, mental health problems chronic renal insufficiency, and musculoskeletal conditions [7, 11]. In addition to MM, many older adults also have sensory impairment and incontinence issues [12]. MM co-occurring with cancer is associated with reduced physical health and psychological well-being, increased levels of frailty, poor mental health decreased QoL, and poorer survival compared to those who have no history of cancer [6-15]. Unsurprisingly, these complex needs require multifaceted care and also lead to increased use of health services. Associated costs increase with each additional condition[8], and some studies highlight an increased risk of polypharmacy, hospital admission, length of stay and readmission[12]. An ageing population, means that managing multiple complex conditions in older adults with cancer will become a routine challenge for oncologists and other health professionals [5, 14, 16].

While oncologists and patients are predominantly focused on cancer and its treatment, attention to longer-term management of multiple conditions will become increasingly important[14]. A recent review by Kenzik et al[17] identified no studies that addressed the

potential impact of cancer on long- term care needs of the aging population. Further, a recent qualitative review concluded that qualitative research to date has not focused on multi-morbidity in cancer survivors [9]. Therefore, in this paper we review one of the complex and significant challenges to health care services: the long-term impact of cancer in older adults with multiple conditions.

Cancer in the context of older age.

Older adults with cancer are a diverse population with complex needs [3], and focusing on chronological age alone can lead to both under and overtreatment, and poor health outcomes[11, 16]. Nevertheless, there is some evidence to suggest that cancer and its treatment might impact older adults differently than younger counterparts[18]. For example, evidence suggests that older adults LWBC are more likely to have MM and to experience poorer physical functioning than younger people with cancer[6, 19].

In addition to the impact of MM on cancer and it's treatment, older adults are at increased risk of the side-effects of some cancer-related drugs [10, 11]. These patients often lack the physiologic reserve required to adequately recover from acute toxicities, leading to long-lasting functional problems and diminished QoL[10]. Cancer patients are often prescribed a substantial number of medicines, both for cancer management and for supportive care and so the risk of polypharmacy is higher for cancer patients [1, 13]. Polypharmacy can result in increased risk of drug interactions, morbidity and adverse events, especially for older people [1, 11, 13, 15].

Some common features of aging may be exacerbated by cancer treatment[20]. Mild cognitive impairment, dementia, and delirium increases with age and can lead to reduced understanding of treatment instructions and delayed reporting of poor health outcomes[11]. Further, malnutrition and weight loss are associated with treatment difficulties and increased mortality in older people with cancer[11]. In addition, ageing is often associated with poverty and social isolation which may cause challenges in seeking care, transportation, and accessing resources [2, 15]. Older people LWBC report a greater need for social support during and after treatment, as well as decreased social activity due to health-related or emotional problems [7, 15]. Further, many older people with cancer live alone [11]. Social isolation and minimal social support has been linked to increased cancer mortality[11, 21]. Conversely, high levels of social support are related to perceived improved HRQOL for those living with MM[8].

Self-management of multiple health conditions alongside cancer

With the growing number of people LWBC, there is an increasing emphasis on self-management and lifestyle changes to optimise health [5], yet older adults often report needing long-term support for health monitoring and management of complex health conditions after cancer treatment [4, 17]. The type of cancer that an older person is diagnosed with may influence the impact of the disease and treatment on other health conditions [3]. For example, even in older age groups, individuals with breast and prostate cancer report lower comorbidity burden compared to those with other cancers including colorectal, oral, bladder, and leukaemia cancer [3] Additionally, the type of cancer diagnosis may impact the *management* of other conditions. Those with colorectal cancer are less likely to manage their other conditions in accordance with recommendations compared with those who have not had cancer[17]. Conversely, those with breast and prostate cancer display patterns of MM management that are akin to those without cancer[17]. This includes adherence to recommended appointments, screening, and receiving appropriate care after an acute event[17].

The type of co-occurring conditions may also impact self-management, with evidence indicating that conditions that increase burden or are considered limiting are associated with lower HRQOL, and the number of conditions that interfere with activities is more strongly associated with increased mortality than the presence of co-existing conditions alone[10, 19]. For instance, a recent study reported that a diagnosis of diabetes, arthritis, and depression/anxiety was significantly associated with low HRQOL in a study of older cancer survivors[10]. Significantly, those who reported having diabetes with no limitations reported higher physical HRQOL than those who did not have diabetes[10]. Conversely, patients who stated that the diabetes limits their activity reported significantly decreased HRQOL[10]. Limitations associated with having a diagnosis of depression and/or anxiety were also significantly associated with poor HRQOL. In comparison, those with arthritis that limited their activity, reported reduced scores on a measure of mental health[10].

The long-term impact of cancer and its treatment

The effect of the interaction between cancer and MM on functional status should be a key consideration when planning cancer treatment[11]. Roughly 70% of those who have cancer have preexisting conditions which can be exacerbated by long-lasting or late effects of cancer [1, 3]. Further conditions are also likely to develop after- and perhaps as a consequence of-

cancer and its treatment, including diabetes, cardiovascular disease, neuropathy, or renal impairment [9, 14]. One study reported that older adults had an average of five comorbid conditions, two of which appeared to have developed after a cancer diagnosis[3]. It is key to establish the baseline status of existing conditions because if they are not managed well, they may negatively impact cancer recovery, hinder longevity, and reduce QoL[20]. The long-term and late effects of cancer treatment- combined with the management of other chronic conditions- also makes older adults LWBC particularly vulnerable to the adverse effects of polypharmacy [1]. The use of inappropriate medications can contribute to the an increase in ongoing negative symptoms, frailty, and poor physical function [13]. However, the long-term effects of new cancer drugs are not yet known[22].

Most older adults value the maintenance of their HRQOL higher than their overall survival, often prioritising functional independence and continuing to engage in valued activities [10, 11, 16, 21, 23]. A sense of control and of personal identity is important to those LWBC[9]. In considering treatment, the benefits of life-prolonging treatments should be weighed against the risk of increased treatment toxicities and the impact on HRQOL and independence[11]. While complex information regarding chemotherapy for advanced cancer is discussed with older patients and their families, age-related concerns and outcomes are not usually addressed in clinical consultations [15]. One reason for this may be that clinicians have little evidence to help treat this age group[11, 20, 24]. Clinical trials have traditionally excluded older people, and people living with frailty or multimorbidity despite the large proportion of patients that fall into this category [9, 10, 16, 19, 20]. Less than a quarter of patients enrolled in National Cancer Institute (NCI) Cooperative Group Clinical Trials are aged 65 to 74 years, and less than 10% are aged over 75 years [15]. Evidence-based treatment guidelines are scarce for this group and it is difficult to extrapolate study findings into real-world practice [7, 11, 14, 15]. This exclusion of older adults limits our ability to understand the impact of treatments into long-term survivorship[3]. For example, relatively little is known about the toxicity of chemotherapy and other cancer treatments for older adults with cancer [20]. Chemotherapy can lead to problematic long-lasting side effects, including pain and cognitive impairment. Most clinical trials in oncology include survival endpoints as their primary measure of success, rather than patient-centred outcomes [11]. A recent review of geriatric oncology trials by Burdentt et al. reported that only half the studies analysed included formal measures of QoL, despite the importance of this outcome for older adults[16]. Less than half the studies included made any baseline assessment of comorbidity or frailty in order to assess the impact

of treatment on the exacerbation or initiation of other health problems[16]. Further, there is limited information relating to how polypharmacy affects outcomes of older patients with cancer[15].

Conclusion:

This paper illustrates that older adults frequently report long-lasting or late effects associated with cancer and its treatment. However, recovery and self-management is likely to be compromised as a result of conditions aggravated by (or that may have arisen as a consequence of) the disease and its treatment. Further complications arise due polypharmacy and socio-economic factors associated with of aging, frailty, social isolation and poor health. In some cases, the presence of multiple conditions leads to confusion about the source of symptoms, which can exacerbate fears of the cancer returning [9].

However, we currently know relatively little about people's everyday experiences of managing long-term conditions alongside cancer, and to date, no studies have explored the long- term care needs of older adults LWBC[17].Care should be guided by patient's functional rather than chronological age and taking into account their values and preferences [2, 11, 15]. Incorporating geriatric assessments (GA) when making decisions about the treatment of older people with cancer may help to clarify the goals of treatment (to maintain QoL and/or to prolong survival) and identify age-related health concerns [3, 11, 15, 16]. Assessments of a patient's history of falls, comorbidity, cognition, social support, psychological status, nutrition, and activities of daily living (ADL) enable the clinician to develop a comprehensive understanding of the older adult [10, 11, 15, 16]. Crucially, GA can also help to predict risk for chemotherapy toxicity, functional decline, and other adverse outcomes [15].While there are currently no completed RCTs that demonstrate that GA-based care improves outcomes of older adults LWBC, GA has been shown to improve outcomes in older noncancer populations and is likely to be transferable to older patients with cancer[11, 15].

Given global policy shifts towards self-management of long-term conditions, a significant portion of follow-up care will be delivered in the community[4] . Primary care has an important role in addressing post-cancer treatment concerns and barriers to health behaviours, such as symptom burden (e.g., fatigue, lymphedema), psychological distress, functional limitations [2, 4] . Nevertheless, some research suggests that primary care practitioners have suboptimal knowledge of cancer survivorship care [2] and that oncology providers provide

suboptimal non-oncology care [22]. Healthcare delivery in the UK and many other countries remains centred on the treatment of single diseases[12], meaning inadequate support for those with MM[12, 14]. Health-care professionals often lack knowledge and skills to support older people with complex conditions [11]. Using single-disease guidelines for the management of complex conditions can lead to increased levels of polypharmacy and unnecessary healthcare visits. Kingston et al [12] note that the application of National Institute for Health and Care Excellence (NICE) guidelines for an older adult with five conditions could potentially result in the prescription of at least 11 medications, 8–10 routine primary care appointments and 4–6 GP appointments, as well as several self-care/lifestyle modifications. These findings highlight a need for integrated teams, care coordination, and cross-specialty collaboration between oncologists, geriatricians, and other practitioners, in order to optimize HRQOL [7, 17, 18, 22].

There is a clear need for further research on interventions to enhance the health of older adults LWBC[15]. Older adults represent a diverse cohort in their physical and psychological health, often living with complexity that influences not only HRQOL, but also recovery from (or ability to live with) cancer [9, 14, 16, 23]. Research into expressed physical, emotional, psychological, social, practical, and financial concerns of people LWBC indicates that 'one size does not fit all' with regard to rehabilitative and supportive care needs [6, 25]. Gaps in knowledge relating to older adults who are under-represented because of race, ethnicity, socioeconomic status, or disability can lead to care disparities [15]. In particular, there is a dearth of studies focusing on those with gynaecologic, head and neck, pancreatic cancers and adult- onset hematologic cancers. As these conditions are associated with significant morbidity, evidence is needed on long- term health and outcomes in order to inform follow-up [17].

We must address the challenge of growing numbers of patients LWBC, increasing age and complexity of cancer care, in the context of an uncertain political climate [3, 7, 14]. Recent NICE guidelines for management of MM promote the incorporation of patients' goals and preferences in clinical decision-making. However, concerns have been raised that this new model of care will require training and longer consultations in an already over-stretched healthcare service [12]. Creative solutions are needed to help to develop economically sustainable, patient- centred follow-up care that focuses on the individual needs and priorities of older adults living with and beyond cancer.

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Conflicts of interest

The authors have no conflicts of interest.

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    In this paper, the authors discuss the use of a geriatric assessment-based approach to cancer care, and provide clinicians with tools to better assess the risks and benefits of treatment to

engage in shared decision making and provide better personalised care for older people with cancer. The authors highlight that there is substantial heterogeneity in the physiological and functional characteristics of older people, and life expectancy and tolerance to stress vary greatly among individuals of the same chronological age.

12. Kingston, A., et al., *Projections of multi-morbidity in the older population in England to 2035: estimates from the Population Ageing and Care Simulation (PACSim) model.* Age and ageing, 2018. **47**(3): p. 374-380.*

This study used a dynamic microsimulation model, the Population Ageing and Care Simulation (PACSim) model, to provide projections of a range of fatal and non-fatal chronic diseases and geriatric conditions conditional on the sociodemographic characteristics, health behaviours and existing morbidities of a real population aged 35 years and over as they age. The authors highlight that over the next 20 years, there will be greater numbers of older people aged 65 years and over, both with individual diseases and with multi-morbidity, particularly with four or more diseases for which numbers will double, as will numbers with cancer, respiratory disease and diabetes.

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The authors conducted a systematic review of phase II and III oncology trials for systemic therapy in older patients with solid organ malignancy. Overall survival remained a common end point. Only 12.2% used disease-specific survival measures as end points, and only 24.4% specifically reported on deaths unrelated to cancer. Less than half the studies included made any formal assessment of comorbidity or frailty. For the geriatric population, quality of life and maintenance of independence become much more important factors, especially in the context of therapy for incurable malignancy. The authors promote the incorporation of EORTC and SIOG recommendations into the methodology for all clinical trials designed for older adults with cancer.

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Key points

1. Older people living with and beyond cancer (LWBC) are more likely than younger people to have higher prevalence of multimorbidity leading to an overall increase in illness and treatment burdens, and limiting health-related quality of life and capacity to self-manage.
2. Older age presents a higher risk of cancer treatment side-effects and development or progression of other conditions, leading to worsening health, long-lasting functional problems and social isolation.
3. It can be difficult for people living with multiple complex conditions to manage their health needs. First, the type of cancer may influence the impact of the disease and treatment on MM burden. Additionally, the type of cancer diagnosis may impact the management of other conditions. The number of conditions that interfere with activities is more strongly associated with increased mortality than the presence of co-existing conditions alone
4. While many prioritise functional independence and continuance of valued activities over survival, older people living with multimorbidity are more likely to experience poor physical functioning during and beyond cancer treatment. MM co-occurring with cancer is associated with frailty and decreased QoL.