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Review Article

Multimorbidity in people living with and beyond cancer: a scoping review

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Abstract: Globally, both cancer incidence and survival are increasing. Early cancer detection and improved treatment means many people with cancer will survive for ten or more years following diagnosis. Multimorbidity, defined as two or more chronic conditions, is up to three times higher in people living with and beyond cancer (LWBC) compared to the general population. This scoping review summarises the research evidence on the association between cancer and multimorbidity in people LWBC. It explores five key domains in people LWBC: 1) prevalence of multimorbidity, 2) association between ethnicity and socio-economic status (SES) and multimorbidity, 3) association between health status and multimorbidity, 4) adverse health consequences of cancer and related treatments, and 5) whether being a cancer survivor impacts treatment received for multimorbidity. It focuses on ten common cancers with high survival rates: prostate, breast, non-Hodgkin lymphoma, bowel/colorectal, kidney, head and neck, bladder, leukaemia, uterine and myeloma. A search of Medline, CINAHL, Embase, PsychINFO and Web of Science databases identified 9,460 articles, 115 of which met the inclusion criteria. Articles were included in the review that involved multimorbidity in adult cancer patients. An evaluation of the evidence was performed, and a summary of findings was generated according to Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) Extension for Scoping Reviews guidelines. This review included work from 20 countries, most studies were from the US (44%). The results showed that the most common long-term conditions in people LWBC were: hypertension, heart conditions, depression, COPD, and diabetes. The most reported incident comorbidities *after* a cancer diagnosis were congestive heart failure, chronic pain, and chronic fatigue. Multimorbidity tended to be higher amongst people LWBC from ethnic minority groups and those with lower SES. Quality of life was poorer in people LWBC with multimorbidity. The review identified the need for a uniform approach to measure multimorbidity in cancer patients across the world. Further research is required to compare multimorbidity before and after a cancer diagnosis, to explore the association of multimorbidity with ethnicity and socio-economic status and to determine whether a cancer diagnosis impacts care received for multimorbidity in people LWBC.

Keywords: Cancer survivor, living with and beyond cancer, cancer survivorship, cancer survivors, multimorbidity, comorbidity, scoping review, quantitative study, quality of life, cancer treatment, cancer care

Introduction

Multimorbidity is defined as the co-occurrence of two or more long term conditions (LTC) [1]. Prevalence of one comorbid condition in people with a cancer diagnosis ranges from 40 to 69% and prevalence of more than two comorbid conditions ranges from 12 to 32% [2, 3]. Patterns of multimorbidity vary according to cancer site and stage, as well as other factors such as ethnicity, deprivation, and health status [4-7]. There is a social gradient in multimorbidity, with multimorbidity onset 10-15 years earlier amongst people living in more deprived areas [6]. Moreover, members of some ethnic groups have an increased prevalence of multimorbidity, and cancer survivors experience inferior quality of life [8-10]. Multimorbidity potentially affects every aspect of cancer, from prevention through detection to end-of-life care, as well as the development, stage at diagnosis, therapy, and prognosis.

The number of people living with and beyond cancer (people LWBC) (also known as "cancer survivors") is expanding at a pace of around 2%

each year worldwide due to rising cancer incidence, early detection, and better treatments [11]. Improvements in cancer survival over the last few decades have resulted in a rising number of long-term survivors; over half of people LWBC in high-income countries may now expect to live for 10 years or more [12]. Although a great advancement, this poses a challenge for healthcare systems to manage multimorbidity alongside cancer in an ageing population.

The presence of multimorbidity potentially affects the diagnosis of cancer, the treatment received, and a person's healthcare needs. The detection of cancer may be influenced by multimorbidity, with some people having their cancer diagnosed sooner due to frequent interactions with healthcare providers, and others being diagnosed later if their cancer shares the same symptoms as a comorbid disease, as in the case of COPD and lung cancer [13]. Cancer treatment may also be associated with several long-term sequelae such as chronic pain and fatigue, sexual dysfunction, anxiety, depression, and lymphedema [14, 15]. People with multimorbidity are less likely to receive cancer treatment with curative intent [13]. The presence of multimorbidity leads to the increased complexity of health needs for people LWBC, which cannot be catered for by a single-disease model. Hence, a call has been made to enhance the long-term quality of life for those living with and beyond cancer, as well as to better understand the needs and experiences of those who have completed primary cancer treatment [16].

As more and more people are experiencing cancer as a chronic and life-changing condition, research on living with and beyond cancer is becoming a priority at governmental level in high income countries such as Australia, Canada, UK and USA [17, 18]. The UK Department of Health made it a policy priority to meet the needs of people living with and beyond cancer leading to the formation of National Cancer Survivorship Initiative in England and Wales and Scotland's Better Cancer Care [19]. In addition, the National Cancer Research Institute (NCRI) and James Lind Alliance (JLA) have published "the top 10 research priorities for people living with and beyond cancer", their third most important research priority is to address "how can care be better co-ordinated for people living with and beyond cancer who have complex needs (with more than one health problem or receiving care from more than one specialty)" [16]. Understanding the association between multimorbidity and living with and beyond cancer also indirectly lends itself to other research priorities such as the short-term and long-term psychological impacts of cancer and its treatment (JLA priority five) and how the short-term, long-term, and late effects of cancer treatments should be (a) prevented, and/or (b) best treated/managed (JLA priority six) [16].

Multimorbidity impacts people LWBC regardless of age, cancer site, stage of cancer and type of treatment. Previous reviews have focused on multimorbidity in older people LWBC (age 65+) [20], the related impact on cancer treatment [13] or on specific cancers [21]. No previously published review to date has comprehensively examined ethnicity, deprivation, quality of life, the effects of cancer treatment and access to care in relation to multimorbidity among cancer survivors. To address this gap, this scoping review was undertaken. This scoping review focuses on adults who have completed their cancer treatment and summarises previously published research on the prevalence and nature of multimorbidity. The review also explores how multimorbidity interacts with: ethnicity, social deprivation, quality of life, cancer treatment, and access to care in this patient group.

Methods

A scoping review was conducted to fully capture the diversity of studies since multimorbidity in people LWBC including a myriad of conditions and measurements. Scoping reviews map existing heterogeneous literature, typically on topics that are complex in nature, and are used to identify knowledge gaps [22]. To guide our review, we used an *a priori* protocol that has already been published [23]. Methods for this scoping review were based on Arksey & O'Malley [24] and Joanna Briggs Institute (JBI) Guidelines and further enhanced by methodological guidelines updated by the JBI in 2021 [25-27]. Preferred Reporting Items for Systematic Reviews and Meta-Analyses-ScR extension for scoping reviews were followed to report the results of this scoping review [26, 28]. The methodology includes identifying the research question, identifying relevant studies, study

Table 1. Inclusion and exclusion criteria based on population-concept-context structure

	Inclusion criteria	Exclusion criteria
Population	• Cancer survivors • Adult population (age ≥18) • Participants assessed for the presence of multimorbidity • People LWBC diagnosed with at least one of the ten cancer: prostrate, breast, non-Hodgkin lymphoma, bowel/colorectal, kidney, head and neck, bladder, leukaemia, uterine and myeloma [30]	• Childhood cancer survivors
Concept	Studies assessing: • Multimorbidity burden • Quality of life in relation to multimorbidity • Multimorbidity arising from cancer treatment • Healthcare use in relation to multimorbidity	• Cancer related drugs/drug trials • Being a person LWBC was not an inclusion criterion of the study • Primary outcome is mortality • Focuses on health behaviour
Context	• Any geographical setting • Any care setting	• Paediatric setting or childhood cancer centres
Type of evidence	• Published between January 1990 and December 2021 • Published in English • Peer reviewed articles • Primary research, quantitative or mixed-methods study design	• Reviews, commentaries, and editorials • Qualitative study design • Grey literature [113]

selection, charting the data collating, summarising, and reporting the results [29].

Identifying the research question

Research questions were derived using Population-Concept-Context structure (PCC) recommended by the Joanna Briggs Institute [25]. For the purpose of this review, the *population* is adult cancer survivors aged over 18. We limited the study to ten common cancers with good survival since the focus is on cancer survivors (using the ten most common cancers with the highest survival rate in the UK as a guidance [30]). The *concept* was multimorbidity; the *context* was any geographical setting and any care setting excluding paediatrics or childhood cancer centres.

The following research questions were explored in relation to people LWBC:

1) What is the reported overall prevalence of multimorbidity?

2) Is there any association between multimorbidity, and ethnicity or social deprivation?

3) What is the health status (as defined by the authors of the included studies) of cancer survivors; and how does this compare in those with, or without, multimorbidity?

4) What are the reported risks for survivors experiencing adverse health consequences and multimorbidity arising from their cancer diagnosis or cancer treatment?

5) Does being a cancer survivor affect the care received for multimorbidity, and, if so, in what way?

Identifying relevant studies

Initially, a research librarian facilitated the generation of search terms, which were subsequently reviewed and refined by all authors. Preliminary searches were conducted in MedLine and adapted for EMBASE, PsychINFO, Web of Science and Cumulative Index of Nursing and Allied Health Literature (CINAHL). The search terms used were pre-defined and exhaustive and are available in the published protocol [23]. Titles, abstracts, Medical Subject Headings (MeSH) terms, and keywords were queried. Searches were restricted to English language articles with a quantitative/mixed-methods study design and carried out in January 2022, including articles from 1990-January 2022. Only publications after 1990 were considered for inclusion, because "comorbidity" was introduced as a MeSH term in 1990.

Inclusion and exclusion criteria

Studies were considered for inclusion if they included multimorbidity in cancer survivors. As the focus of this review is survivorship, we excluded studies with mortality as a primary outcome. The inclusion and exclusion criteria are given in **Table 1**.

Data synthesis

To facilitate the research selection process, literature search results were uploaded to Ray-

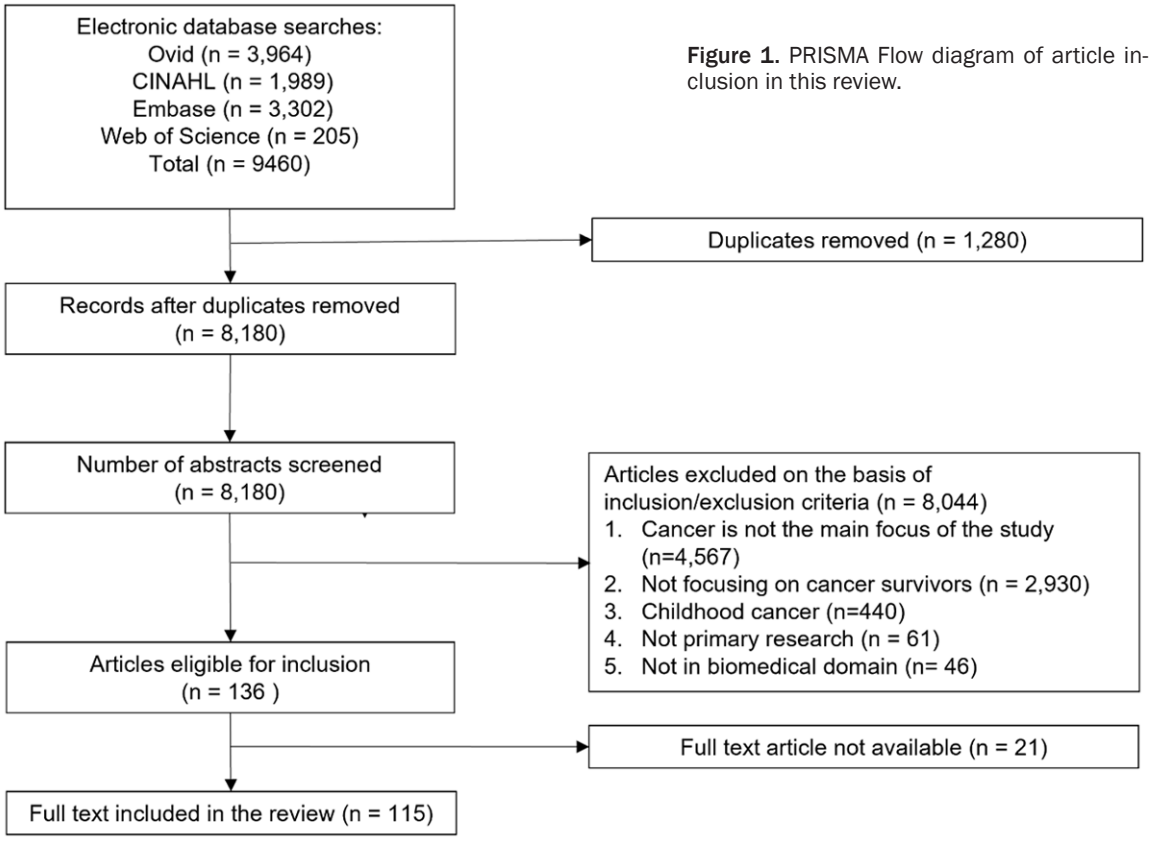

Figure 1. PRISMA Flow diagram of article inclusion in this review.

yan Systematic Review software [31]. Two authors (TAA and DPG) reviewed each abstract independently for inclusion. TAA and DPG then independently reviewed all full texts and determined whether they should be in the final sample for extraction. In the event of disagreement, any reason for exclusion was documented by the authors and was resolved through discussion with senior author SJCT. TAA developed the data extraction form and extracted data from all the included studies. SJCT checked the data extraction tables for completeness and accuracy in a randomly selected 10% sample of the papers (97% agreement was reached, disagreements were resolved through discussion). A formal quality assessment was not conducted as it is not part of scoping review methodology [24]. The PRISMA flowchart [32] of included studies is presented in **Figure 1**.

Summarizing and reporting the results

Study findings were narratively synthesised, structured according to the research questions identified for this review.

Results

The search of the electronic databases identified 9,460 articles, 1,280 of which were duplicates. 8,180 articles were screened using titles and abstracts by TAA and DPG, which resulted in 8,044 articles being excluded. 115 studies were eligible for inclusion in the final review (reasons for exclusion are given in **Figure 1**). Of the included studies, 63 were cross-sectional studies, 28 were retrospective cohort studies, 22 were prospective cohort studies and 2 were case-control studies. Forty-three studies (37%) focused on several types of cancers, whereas the remainder focused on specific cancers (**Figure 2**). Study settings varied: 44 (38%) studies used a cancer registry as the data source for analysis to identify people LWBC; 31 (27%) studies used population-based databases and 21 studies (18%) collected data from specialised cancer centre (**Figure 3**). Population-based databases included primary care data linked to cancer registry, electronic healthcare data and population surveys. The characteristics of the included studies are summarised in **Figure 2**.

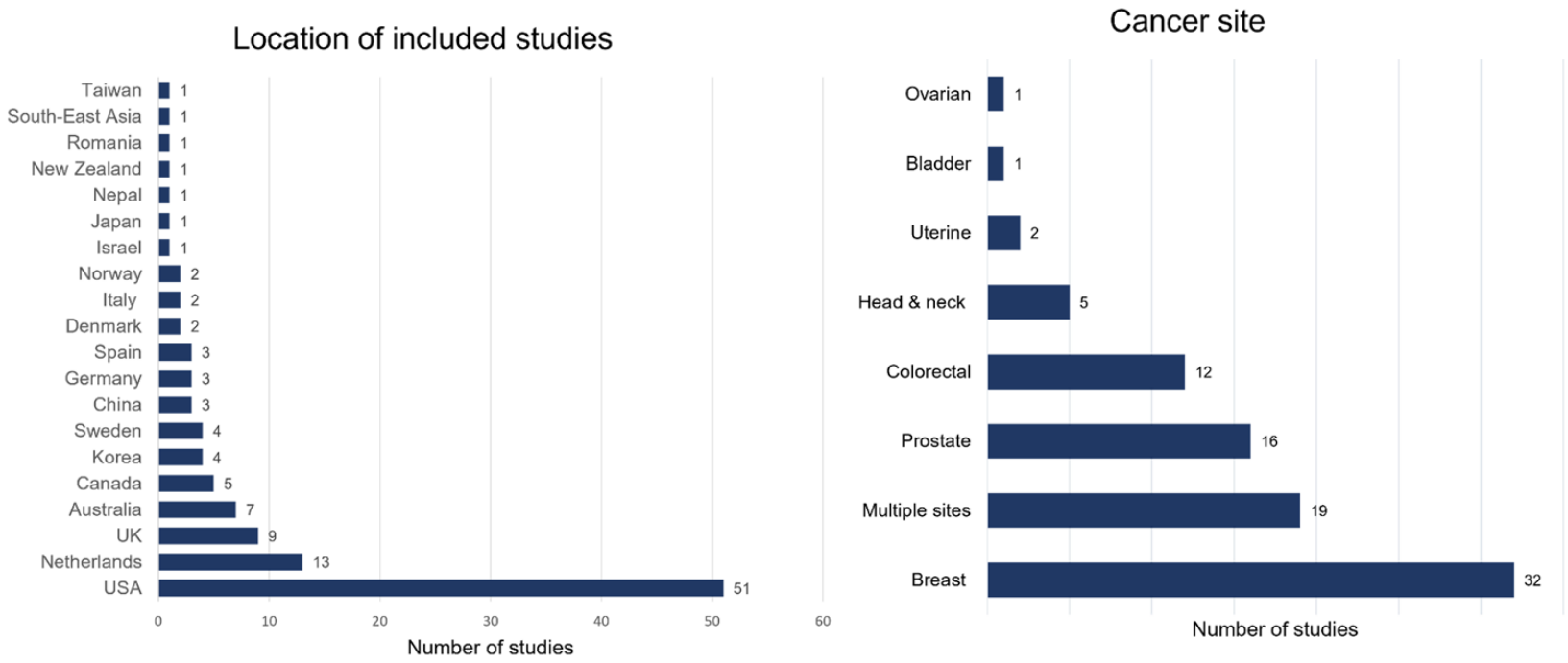

Figure 2. Characteristics of included studies (location of included studies and cancer site).

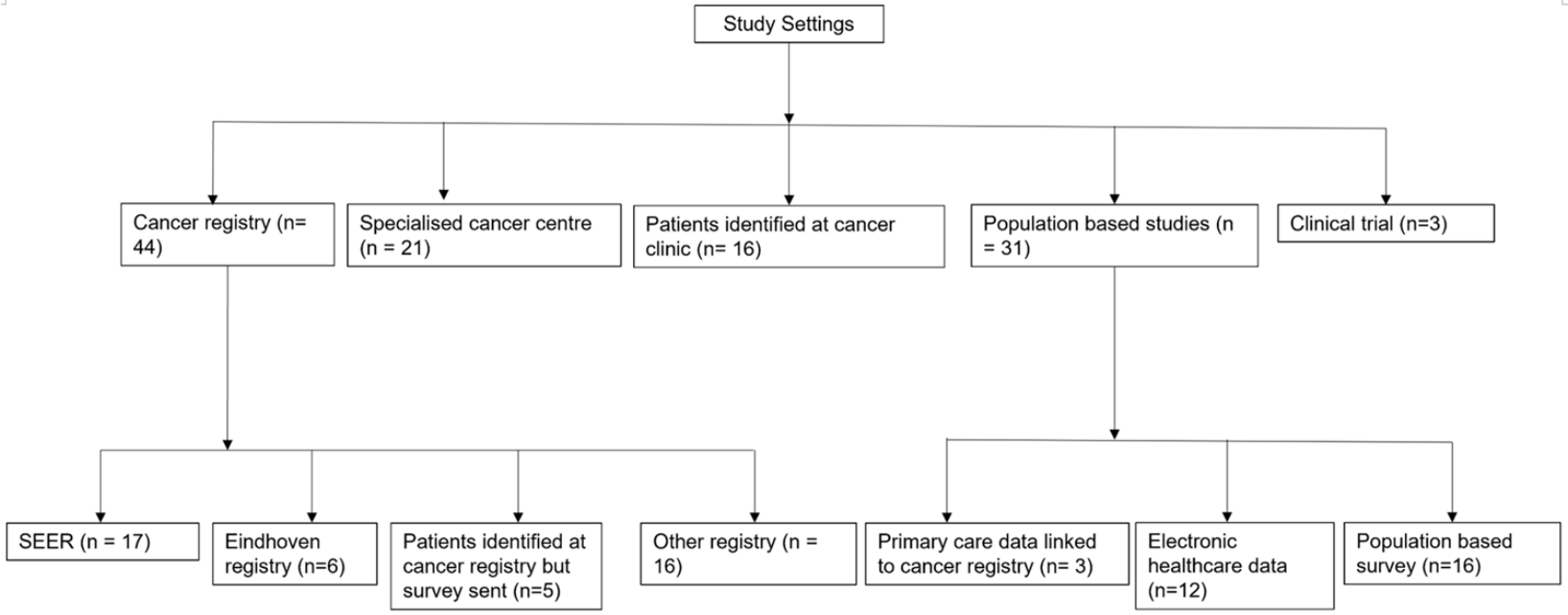

Figure 3. Breakdown of study setting.

Table 2. Number of comorbidities in people living with and beyond cancer compared to general population

Author	Type of cancer	Sample size	Prevalence of comorbidity (in addition to cancer) in cancer survivors (brackets = non-cancer controls)
Mao J (2007)	Any cancer except Melanoma	1,904 cancer survivors and 29,092 controls	1 LTC: 39.1% (18.1%) 2 LTCs: 12.2% (3.9%) 3 or more LTCs: 9.5% (1.6%)
Ng H (2018)	Any cancer	5,829 cancer survivors and 34,385 controls	1-2 LTCs: 46% (50.5%) 3-4 LTCs: 31% (19.3%) 5+ LTCs: 11% (4.3%)

The studies included in this review were geographically diverse. Almost half of the studies were conducted in the United States (n = 51), whereas one-third was conducted in Europe (n = 38) and rest were in Asia (n = 12), Australia/New Zealand (n = 8) and Canada (n = 5) (**Figure 2**). Multimorbidity in cancer survivors is multifaceted, and most studies examined more than one theme. The key characteristics of all included studies are presented in detail in Supplementary Table 1.

Prevalence of multimorbidity in cancer survivors

Forty-two studies (37%) reported the prevalence of comorbidities in people LWBC (various cancer sites), with 28 studies using no comparison group and 14 studies using the general population as a comparator. The number of LTCs explored in the included studies ranged from 1 to 50. Sixteen of these studies used self-reported questionnaires or forms to collect data, whereas twenty-six studies used data from electronic health records. The two largest studies comparing the number of comorbidities in people LWBC vs the general population are described in **Table 2**.

The prevalence of multimorbidity among cancer survivors varied based on the population studied, the type of cancer, and the methodologies used. Overall, the most commonly reported comorbidity was hypertension (mean prevalence 41.3% (range 12.6-63.6%); n = 19 studies), depression (mean 17.9%), heart conditions (mean 17.3%), COPD, diabetes, psychological and cerebrovascular conditions (**Table 3**). The prevalence of multimorbidity varied by cancer sites. The most common LTC in breast cancer patients was hypertension (mean prevalence 36.3%) and chronic pain (18.3%), followed by hypertension (44%) in prostate cancer patients and hypertension (43%) and arthritis (32%) in colorectal cancer patients.

The three largest studies exploring prevalence of multimorbidity were those by Ng, Sarfati and Strongman [33, 34]. Ng et al's study involving 40,214 Australian participants found the prevalence of 1-2 LTCs was similar amongst cancer survivors and the general population (46% vs 50%), but survivors had a higher prevalence of 3-4 LTCs (31% vs 19%) and of 5 or more LTCs (11% vs 4.3%) when compared to the general population [35]. This was consistent with other large studies conducted in the USA, UK, and New Zealand [33, 34, 36, 37].

Sarfati et al's study with 14,096 people LWBC from New Zealand found that the most common LTCs were hypertension (prevalence 8.0-20.9%), cardiac conditions (2.1-13.5%) and diabetes with and without complications (2.3-13.3% and 2.9-12.9%), respectively from a list of 50 different LTCs in cancer survivors [33]. Strongman and colleagues' study including 108,215 British cancer survivors (from 20 most common cancers) found a substantially increased risk of venous thromboembolism for most cancers (18 out of 20), increased risk of heart failure or cardiomyopathy in survivors of non-Hodgkin lymphoma, leukaemia, multiple myeloma, breast, bladder and kidney cancer compared to 523,541 controls without a history of cancer matched for age, gender and general practice (GP). The authors found a >50% increase in risk of heart failure after a diagnosis of haematological, oesophageal, lung, kidney, and ovarian cancer. Venous thromboembolism risk remained elevated for at least 5 years after cancer diagnosis, even among people with no record of receiving chemotherapy, suggesting long-term effects of the underlying

Table 3. Average prevalence of the most reported comorbidities (in order of prevalence)

Name of comorbidity	Mean reported prevalence (range)	Number of studies reporting
Hypertension	41.26% (12.6-63.6%)	19 studies [33, 34, 36, 41, 47, 53, 100, 101, 114-124]
Depression	17.86% (4.1-48.2%)	14 studies [41-43, 47, 48, 51, 53, 114, 115, 118-121, 125]
Heart conditions (Myocardial infarction, heart attack, coronary bypass, angioplasty, or stent)	16.30% (3.3-57.2%)	20 studies [40, 41, 53, 102, 115-118, 120, 121, 125-128]
COPD	13.73% (5-26.4%)	9 studies [41, 53, 103, 116, 118, 120, 121, 123, 125]
Diabetes	13.43% (4.3-27%)	23 studies [33, 34, 36, 41, 47, 52, 53, 100, 101, 103, 115-119, 121-128]
Psychological conditions (Anxiety, depression, dementia & bipolar disorder)	9.73% (2.85-14.70%)	15 studies [42-47, 49-52, 55, 122, 124, 129]
Cerebrovascular conditions (Stroke, TIA, or requiring carotid surgery)	7.04% (1.64-18%)	14 studies [36, 40, 41, 47, 52, 53, 103, 116-118, 120, 126-128]

malignancy and/or endocrine therapies or confounding by shared risk factors [34]. In contrast other studies have found that venous thromboembolism risk was only elevated immediately after diagnosis [38, 39]. The incidence of heart failure increased with time from cancer diagnosis [34]. Incidence of arrhythmia, coronary artery disease, and heart failure at 5 years after cancer diagnosis was found to be much higher compared to matched controls, a finding not seen in previous studies [34]. A Canadian study with 81,418 survivors that explored new onset of cardiovascular disease after cancer diagnosis reported that colorectal cancer survivors were mostly predisposed to arrhythmias (15.4% incidence proportion) and chronic heart failure (7.2%) whereas prostate cancer survivors were most at-risk for myocardial infarction (6.3%) and cerebrovascular accidents (8.2%) when compared to other cancer survivors [40]. An American study involving 51,950 breast cancer survivors aged ≥66 years reported hypertension as the most common new condition following cancer diagnosis [41].

Of the studies reporting psychological conditions (n = 15), one third (5) made comparison to the general population [42-45]. Eight studies included survivors from multiple cancer sites [42-47] and seven were single cancer studies. In general, cancer survivors experienced worse mental health compared to controls, in particular experiencing higher prevalence of anxiety and depression. The largest study included in this review describing psychiatric comorbidities involving 87,843 South Korean people with a breast cancer diagnosis [48] found that in the year preceding cancer diagnosis, 9.5% (n = 8430) were diagnosed with a mental health condition, most of which were depression (38.6%) or anxiety (32.5%). The overall frequency of a mental health disorders being reported peaked within one month after cancer diagnosis, but gradually attenuated over the following six years. Depression was highest in younger people, and anxiety was higher in older people. However, another study found no significant difference in prevalence of common mental disorders (CMD-included anxiety, mood and substance misuse disorders) amongst cancer survivors compared to cancer-free individuals six year after cancer diagnosis (Adjusted odds ratio (AOR) = 0.95, 95% CI 0.82-1.11), suggesting that the initial increase in CMD after diagnosis may represent an adjustment problem to cancer rather than a consequence of cancer [49]. However, in long-term cancer survivors, the prevalence for anxiety and depression were above 30% and further exacerbated by the presence of multimorbidity [50-53]. Similar patterns of CMD were characterised in high-income and low-middle-income countries [50].

Association between multimorbidity and ethnicity or social deprivation

From the 115 identified studies included in this scoping review, 11 studies (10%) explored the association between multimorbidity, ethnicity and/or social deprivation in cancer survivors. Although the prevalence of comorbidity and distribution of socioeconomic status (SES) varied greatly across the studies of different cancer types, the gradient of increasing comorbidity with lower SES was apparent [5, 7, 54, 55]. The comorbidities included physical and men-

tal health conditions. Andrykowski et al.'s study with 1,300 Dutch colorectal cancer survivors found that high SES survivors were around 50% less likely than low SES survivors to report clinically important levels of anxiety and depression symptoms [54]. However, the authors also found that relative to high SES survivors, lower SES survivors reported greater positive mental health outcomes on 2 of 5 mental health indices examined (Positive Self-Evaluation & Meaning of Cancer) [54]. Aart et al.'s study argued that comorbidity was strongly associated with low health-related quality of life (HRQOL) rather than SES [5]. Pinheiro et al.'s study reported spiritual HRQOL was significantly better for Black cancer survivors and not attenuated by SES [10], a similar finding to Andrykowski et al.'s study [54].

All included studies (n = 6) exploring the association between ethnicity and comorbidity in cancer survivors were conducted in the USA or Australia. Comparisons were made between White, African American, Hispanic, and Latin American cancer survivors (majority white population). All studies found that membership of a non-white ethnic group was associated with higher prevalence of comorbidity [4, 8-10, 46, 56]. Penedo et al.'s study from the USA found that 37% of the variance in QOL scores was explained by three factors: medical comorbidity, physical activity, and social functioning [4]. The association between ethnicity (African, American, and Hispanic) and lower QOL appeared to be partially explained by health behaviour components such as physical activity, food, sleep, and alcohol intake, with each factor adding significant incremental variance (5%, 5% and 17% of variance, respectively). Therefore, rather than ethnicity and SES, variations in sleep functioning and physical activity may be some of the confounding factors that contribute to differences in QOL. An Australian study found that migrant cancer survivors also experienced increased anxiety, depression and low QOL compared to white Australians [46].

Health status and quality of life

26 studies (23%) explored the health status of cancer survivors. The terms health status, health-related quality of life (HRQOL) and quality of life (QOL) are used interchangeably in the literature. Thus, here we report health status as defined by the authors of the studies. A summary of the various instruments used in studies reporting on "Quality of Life" is available on request from the authors.

Most of the studies suggested that the presence of comorbidity was associated with poorer QOL and lower HRQOL scores among cancer survivors. In haematological cancers, such as leukaemia, survivors with two or more comorbidities were twice as likely to have worse HRQOL scores compared to survivors without any comorbidity [57, 58]. Comorbidity explained more variance in physical and emotional function, pain, and fatigue in cancer survivors than sociodemographic and cancer characteristics, regardless of cancer type [59-63].

In contrast, a study led in eight low- or medium-income Southeast Asian countries reported that cancer stage at diagnosis, rather than comorbidities, was the most important predictor of poor HRQOL and psychological distress [50]. Eakin's study conducted in Australia found that long-term cancer survivors reported substantial decline in health status, days out of role, and mental well-being (all $P<0.02$), but not in quality of life when compared with matched cancer-free controls [64].

Overall, most studies found that cancer survivors reported poorer QOL compared to people without a cancer diagnosis, even after matching for common characteristics such as age, gender, and comorbidities at diagnosis. Due to the wide range of measures reported in the included studies, it was not possible to provide an aggregate summary of the impact of cancer on QOL. Cardiovascular diseases were found to have the greater negative impact on QOL than other diseases [65-67]. According to Poll-Franse et al.'s study of prostate cancer survivors from Netherlands [65], men with cardiovascular disease had worse baseline physical HRQOL and showed worse scores over time in this domain compared to matched controls ($P = 0.003$). The negative effect of cardiovascular disease on physical HRQOL over time appeared to be stronger for those with worse baseline scores ($P = 0.07$). Another study of breast cancer survivors found that cardiovascular diseases and depression had the strongest association with lower HRQOL [66]. Colorectal cancer survivors with cardiovascular illnesses had a

worse QOL than those with other comorbidities, according to a Chinese study [62]. One study involving prostate cancer survivors found that men with existing diabetes had the poorest score on general and cancer specific HRQOL and non-diabetic men had the best scores, regardless of type of treatment for cancer [67].

Adverse health consequences and multimorbidity arising from cancer/cancer treatment

Thirty-three (29%) studies explored adverse health consequences and morbidity arising from cancer or cancer treatment, almost half of which (n = 16) involved breast cancer survivors. Eight of the studies explored the impact of chemotherapy, either alone or in comparison to radiotherapy. All studies except one reported higher symptom burden, such as hot flushes, night sweats, numbness/tingling, fatigue and poorer QOL using chemotherapy treatment [68-74]. Battaglini et al.'s study [75] conducted in Australia reported that survivors with severe chemotherapy induced peripheral neurotoxicity (CIPN) (76.5%) had a worse QOL, more comorbidities, a higher BMI, and were more likely to report being treated with several neurotoxic chemotherapies than those with moderate CIPN. When comparing respondents who completed chemotherapy >6 years ago to those who completed chemotherapy <1 year ago, there was no difference in reported CIPN or pain levels. Ganz's study [76] focusing on long term survivors of breast cancer revealed that past chemotherapy was a significant predictor of a poorer QOL. The only study contradicting this trend was Bloom et al.'s study [77] conducted in the USA with 185 survivors (5 years post diagnosis), which found that women who were treated with chemotherapy had better physical QOL compared to those that did not have chemotherapy.

Two studies compared radiotherapy and chemotherapy treatment for people with breast cancer. Hooning et al.'s study with 4,410 survivors of 10+ years reported a higher risk of congestive heart failure in those who underwent radiotherapy in addition to adjuvant chemotherapy (cyclophosphamide, methotrexate, and fluorouracil after 1979) when compared to people treated with radiotherapy alone (Hazard Ratio (HR) = 1.85, 95% CI = 1.25 to 2.73; P = 0.002) [70]. Schmidt et al.'s study found that among people who received both chemotherapy and radiotherapy, 61.4% reported higher, 30.0% reported the same, and 8.6% reported lower fatigue levels during chemotherapy compared to radiotherapy [74].

The effects of treatment differed depending on the cancer site. Eight studies explored the impact of colorectal cancer and its treatment. Negative associations with treatment included increased risk of pelvic fractures [72], dementia [78], sexual inactivity, dysfunction and dyspareunia [79], increased bowel problems and faecal incontinence [80] and fatigue [80] for colorectal cancer survivors. For prostate cancer survivors, adverse treatment effects included subsequent risk of rectal cancer (HR = 1.14, 95% CI = 1.02 to 1.27) [81], urinary problems after prostatectomy and bowel problems after radiotherapy, urinary incontinence (23-48%), bowel leakage (5-14%) and erection problems (40-74%) [82]. Survivors of prostate cancer with Androgen Deprivation Therapy (ADT) had a higher risk of any fracture, hip fracture and major osteoporotic fracture (MOF) but not of non-skeletal fall injury [83] and a significantly higher risk of developing cardiovascular conditions, depression, diabetes, gastric acid disorders, hyperlipidaemia, osteoporosis and pain/pain-inflammation compared to those without ADT treatment [44]. For genitourinary cancer survivors the most frequently reported associations with treatment were lower urinary tract symptoms, genital organ disorder and long-term comorbidities such as renal failure, urinary tract infections, and non-malignant breast conditions, persisting 5-10 years after cancer treatment [84-87]. For head and neck cancer survivors, the most commonly reported associated conditions were late effect lymphedema, hearing loss and tinnitus [88, 89].

Care received by cancer survivors for multimorbidity

Only three studies explored whether being a cancer survivor affected the care received for multimorbidity [45, 90, 91]. The largest of these studies looking at 21,366 British people diagnosed with breast, colorectal or prostate cancer, found that history of cancer was not associated with poorer management of chronic diseases such as hypertension, diabetes and cerebrovascular diseases, or coronary artery

diseases [91]. In this study, chronic disease management was measured by number of Quality and Outcomes Framework (QOF) financially incentivised clinical indicators present for blood pressure, cholesterol and haemoglobin A1C (HbA1c) levels. There were some disparities in monitoring received by cancer survivors towards the end of life, but the numbers were too small for a formal multivariate subgroup analysis to explore this further. A similar study including 8,661 US cancer survivors (breast, colorectal and prostate) reported that only breast cancer survivors received equivalent care on both chronic (odds ratio [OR] = 1.06, 95% CI = 0.96 to 1.17) and acute (OR = 0.92, 95% CI = 0.76 to 1.13) indicators compared to 17,332 controls [45]. Colorectal cancer survivors were less likely to receive adequate treatment on both chronic (OR = 0.88, 95% CI = 0.81 to 0.95) and acute (OR = 0.72, 95% CI = 0.61 to 0.85) indicators. Prostate cancer survivors were more likely to receive appropriate chronic care (OR = 1.28, 95% CI = 1.19 to 1.38) but less likely to receive quality acute care (OR = 0.75, 95% CI = 0.65 to 0.87) [45]. Appropriate chronic care was measured by the number of visits to a GP and the frequency of tests, such as being tested for cholesterol, haemoglobin or fructosamine every 6 months. Arora et al.'s study [90] looking at perceptions of cancer follow-up care found that the perception of the quality of care was positive in all aspects except two: discussion about health promotion and physician's knowledge of people LWBC. In adjusted analyses, individuals without private health insurance (P<0.02) and Hispanic and Asian survivors reported lower timeliness of care than white survivors (P<0.001). Survivors with various comorbidities scored higher on timeliness of care (P<0.01) and medical knowledge (P<0.05) than survivors without comorbidities.

Discussion

The findings of this scoping review of 115 primary research articles highlight the significant burden of multimorbidity among people LWBC. The five domains explored in this review are interrelated. For instance, a high prevalence of multimorbidity is associated with a lower quality of life and higher prevalence of multimorbidity is associated with lower socio-economic status and ethnic group. Access to care may be influenced by ethnicity, language barriers and socioeconomic status. Additionally, cancer or the adverse effects of cancer treatment, might cause or exacerbate multimorbidity, further degrading the quality of life. Although the studies that explored relationships between ethnicity, socio-economic condition, access to care and quality of life support an interplay of these elements with multimorbidity, the review failed to identify any mediator analyses in the cancer survivorship literature to date examining these relationships.

This is the first study to systematically explore and synthesise the existing literature on associations between cancer survivorship and multimorbidity. The survivors presented in this review varied in age at cancer diagnosis from 18 through 65 years of age or older and as well as in time since diagnosis, both of which affect multimorbidity. The findings suggest prevalence of multimorbidity in people LWBC are consistently up to three times higher compared to people who were not people LWBC [33, 35, 36]. There are several plausible explanations for this. The first of these is age: older age is associated with an increased risk of cancer [92] and other long-term conditions [93]. Secondly, comorbidity-related biological pathways may predispose to cancer. For example, hypertension is linked with a higher incidence of breast [94, 95] and renal cancers [96]; diabetes is associated with an increased risk of several cancers, including breast, colorectal, endometrial, pancreatic and liver cancers [97, 98]. Thirdly, cancer and comorbid conditions share common risk factors. Although shared risk factors for diabetes and cancer (such as obesity) may play a role in these correlations, there are distinct molecular mechanisms that link diabetes and cancer. High circulating levels of insulin and other insulin-like growth factors increase cellular proliferation and alter programmed cell death (apoptosis), raising the risk of cancer [97]. It is also possible that increased incidence of LTCs reported in people after cancer diagnosis was due to the greater interaction with healthcare system rather than LTCs being a consequence of cancer [41].

The most frequent multi-morbidities in people LWBC, in order of prevalence, were hypertension, heart conditions, depression, diabetes and COPD. However, hypertension is very prev-

alent in the general population [99] and these diagnoses may not necessarily be due to the underlying malignancy/complications. This may be explained by increased incidental detection due to increased healthcare contact. Haematological, colorectal, and prostate cancer survivors reported increased heart conditions compared to the cancer free controls [34, 40]. In prostate cancer patients, the most common comorbidity after cancer diagnosis was myocardial infraction and cerebrovascular accidents [44, 65, 100, 101]. In colorectal cancer survivors, it was arrythmia, chronic heart failure and sexual dysfunction [60, 79, 101-103]. There was >50% increase in risk of heart failure after diagnosis of haematological, oesophageal, kidney, and ovarian cancer survivors compared to non-cancer controls [34, 101]. People LWBC also had higher prevalence of depression and anxiety, which was further intensified by the presence of comorbidity [49-53]. It was difficult to ascertain whether these conditions are a precursor to cancer as most of the included articles focused on overall prevalence or incidence after diagnosis only. There is a gap in the literature comparing comorbidities before and after cancer diagnosis.

The prevalence of multimorbidity tends to be higher amongst people LWBC from minor ethnic groups compared to majority white populations and those with lower socio-economic status (SES) compared to those with higher SES [5, 104]. This trend was independent of other sociodemographic characteristics such as age, gender, marital status, and education. These patterns are also seen in the general population [105, 106]. However, two studies reported Black cancer survivors scored higher in scales of spiritual HRQOL compared to whites [10, 54]. Only eleven studies were found exploring the impact of multimorbidity and ethnicity or socio-economic status in cancer survivors, indicating there is a need for more research.

The impact of multimorbidity on the quality of life of people LWBC is extensively documented in the literature and described in 26/115 studies. Most studies included in this review used various validated instruments of “Quality of life” or “Health related quality of life” to measure health status. Almost all studies reported that the presence of comorbidity leads to lower quality of life in people LWBC regardless of cancer type [57, 59, 76, 107]. Pre-existing cardiovascular disease and diabetes in particular were associated with poorer QOL in breast, prostate, and colorectal cancer survivors [62, 65, 66]. Two studies suggested that other factors such as stage at diagnosis of cancer, days out of work and mental well-being had a greater impact on quality of life than the presence of comorbidities [50, 64]. This might be because the relative contribution of cancer and its treatment to a person’s overall impression of quality of life is so large that it “overrides” the influence of comorbidities for many people. Nonetheless, a greater disease burden is linked to higher healthcare needs and associated costs, higher risk of disability, higher risk of financial strain, and resulting socioeconomic disadvantage. All of these are linked to a lower quality of life.

Adverse health consequences from cancer itself and its treatment were reported from almost all studies examining this phenomena, although the magnitude of the effects differed depending on the type of cancer and the length of time since diagnosis. In studies including cancer survivors across a wide range of cancers, the most commonly reported health consequences were pain, depression and chronic fatigue [68, 71, 74, 108]. The treatment related consequences remained even years after diagnosis. People living with and beyond breast cancer who were undergoing chemotherapy reported hot flushes, night sweats, numbness/tingling, fatigue and poorer QOL [75, 76]. There were higher levels of fatigue [74] and a higher risk of congestive heart failure in people with breast cancer who underwent radiotherapy in addition to chemotherapy [70]. For those with colorectal cancer, long-term side-effects of chemotherapy were associated with an increased risk of dementia, osteoporosis, erectile dysfunction [78] and female sexual problems [79]. Treatment with radiotherapy has been associated with increased bowel problems and faecal incontinence [80], increased risk of pelvic fractures, and odds of sexual dysfunction and dyspareunia [79]. Similarly, for people with prostate cancer, urinary problems were common after prostatectomy and bowel problems were mostly common after radiotherapy [82]. The amount to which treatment are tolerated will, of course, be determined by a variety of complicated interrelated factors, such as the cancer

treatment, stage at diagnosis, pre-existing comorbidities, baseline health condition and age.

Little difference was found in terms of care received for multimorbidity between those who were and were not LWBC in studies included in this review, however only three studies addressed this topic. This suggests more research is required in this area to fully understand whether comorbidity impacts on care delivery for people LWBC. The presence of comorbidity in addition to cancer poses a substantial challenge to health care systems focused on increased specialisation in secondary care [109]. The delivery of care to people LWBC with multimorbidity necessitates extensive coordination both inside the cancer setting and throughout the wider health-care system, including community-based care [110]. While there are well-established models of care for managing chronic illnesses, many of them exclude cancer, thus little is known about how well they apply to people LWBC [109].

The scoping review found various indices were used to measure multimorbidity in cancer survivors, the most common being Charlson comorbidity index (CCI). Although it is very useful in measuring comorbidity, there are a few disadvantages in using CCI for cancer survivors. This index does not measure some of most prevalent conditions in this group such as chronic pain, chronic fatigue, depression, anaemia, and constipation, hence it cannot detect the burdens of these comorbidities. CCI was developed by only including conditions that are associated with poorer survivals in general population [111], these conditions may not be the same for cancer survivors. For example, some conditions comprised in the CCI have been found to poorly influence survival among colorectal cancer patients (i.e., peptic ulcer disease), while others having an impact (i.e., weight loss) were not included in this index [112]. As CCI focuses on conditions that impact survival, it might not be appropriate for studies that focus on other impacts such as quality of life, which is far more important area of research for cancer survivors. Hence, there is a need for developing a comorbidity index to measure comorbidities that impact cancer survivors only.

One key strength of this review is that is it the first to systematically identify, explore and map five key domains relating to multimorbidity in cancer survivors. Although some reviews previously summarised findings from one aspect of multimorbidity in cancer survivors or focused on cancer survivors from one type of cancer, no studies to date have combined all these aspects in one review.

There are some limitations to this review. First, as this review included ten types of cancer, it was impossible to summarise the impact of each type of cancer on each of the areas explored due to the heterogeneity of the included studies. The literature reflects a wide range of indices or methods to measure multimorbidity, making it difficult to draw conclusions about the breadth and depth of multimorbidity in this population. Secondly, some terms such as “health status”, “comorbidity” and “multimorbidity” are very broad. Although an attempt was made to include all synonyms of these terms in the search strategy, it is possible it may have missed some relevant studies if alternative terms were used by the authors. Since this review focused specifically on ten types of cancer the findings from this review are not necessarily generalisable to survivors of rarer cancers.

Another limitation of this review is that the searches were restricted to peer-reviewed, English-language studies. By excluding grey literature and non-English language publications the search may have missed out relevant studies and reports, such as work by Macmillan, a British cancer charity who take part in commissioning cancer care. The scoping review also did not differentiate between multimorbidity incidence in cancer survivors before or after cancer diagnosis as only a few primary research articles made this distinction in their reporting. Finally, and in line with the JBI’s guidance for the conduct of scoping reviews [27], we did not attempt to provide an assessment of the quality of the evidence and assessment for important potential biases such as selection, case ascertainment and measurement biases, and potential confounders were not considered in this review, hence, the findings should not be considered absolutely conclusive.

This scoping review could inform guidelines which would assist clinicians to make cancer treatment decisions for those with multimorbidity. The review found that there was no uniform

way of measuring comorbidity in cancer patients across the studies. An agreed, standard way of measuring comorbidity in cancer patients across the world should be introduced to assist future cancer research and would enable the assessment of any changing trends in cancer and comorbidity in future. Clinicians need to be aware of the impact of multimorbidity in people LWBC and provide integrated care as it is fundamental to effective delivery of cancer care. Better tools for clinicians need to be developed by policymakers, e.g., clinical guidelines that explicitly address managing coexisting conditions with cancer needs.

In this scoping review, three areas that need further research were identified. Firstly, more studies are needed to compare comorbidities in people LWBC before and after cancer diagnosis. Secondly, there were limited studies that explored multimorbidity in relation to socioeconomic status and ethnicity in people LWBC. Thirdly, more research is needed to explore whether the presence of multimorbidity in people LWBC impacts the care they receive for their conditions, and, if it does, the reasons for this.

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None.

Abbreviations

ADT, Androgen deprivation theory; BCS, Breast cancer survivors; CIPN, Chemotherapy-induced peripheral neurotoxicity; CMD, Common mental health disorders; CVD, Cardiovascular disease; EORTC, European Organisation for Research and Treatment of Cancer; FACT-G, Functional Assessment of Cancer Therapy-General; HRQOL, Health-Related Quality of Life; LTC, Long term condition; LWBC, Living with and beyond cancer; NCCS, National Coalition for Cancer Survivorship; NCI, National cancer institute; NCRI, National Cancer Research Institute; PROMIS®, National Institutes of Health's Patient-Reported Outcomes Measurement Information System®; SES, Socioeconomic status; SF-36, 36 items Short form health survey; QQF, Quality and Outcomes Framework; QOL, Quality of life.

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Supplementary Table 1. Key characteristics of all included studies

First author (Year)	Country	Study design	Participants			Definition of survivorship	Dependent variable/s explored	Outcome(s) explored
			No.	Age range	Cancer			
Aarts J.M. (2010)	Netherlands	Cross-sectional	585	18-75	Prostate	Alive after 5 years of diagnosis	Socioeconomic status	Health related quality of life (HRQOL)
Anderson (2010)	USA	Cross-sectional	Multiple cancer survivors (N = 1003) to single primary survivors (N = 12,849) and participants without cancer (N = 63,578)	≥18	Multiple sites excluding skin	1 year after diagnosis	Medical condition	Medical conditions and its impact on physical function
ACTION Study group (2017)	In eight LMICs in Southeast Asia - Laos, Indonesia, Vietnam, Philippines, Malaysia, Thailand, Cambodia and Myanmar	Cross-sectional	5249	≥18	Multiple	1 year after diagnosis	Psychological distress	Health related quality of life (HRQOL)
Andrykowski M. (2013)	Netherlands	Cross-sectional	1300	≥18	Colorectal	2 years post diagnosis	Socioeconomic status	Mental health (MH)
Arora N.K. (2011)	USA	Cross-sectional	623	≥18	Leukaemia, bladder, and colorectal	2-5 years post diagnosis	Survivor's perception	Cancer related follow up care
Ashing K. (2020)	USA	Cross-sectional	137	≥18	Breast	Not defined	Type 2 diabetes	Physical functioning
Ashing K. (2014)	USA	Cross-sectional	320	≥18	Breast	Not defined	Ethnicity - African American and Latina	Prevalence of comorbidity
Atere-Roberts J. (2021)	USA	Cross-sectional study	317	≥50	Prostate	Ever had a prostate cancer diagosis	Racial and ethnic differences	Self-reported health status, chronic conditions, and selected behavioural risk factors
Battaglini E. (2021)	Australia	Cross-sectional	986	≥20	Breast & Colorectal	Comparison made between patients currently on chemotherapy and those who completed ≥6 years	Chemotherapy-induced peripheral neurotoxicity (CIPN)	CIPN symptoms, pain, neuropathic pain, Quality of life (QoL), physical activity
Bloom J.R. (2012)	USA	Prospective cohort study	312	≤50	Breast	Alive after 5 years of diagnosis	Number of comorbidities, social network	Quality of life (QoL)
Bloom J.R. (2004)	USA	Prospective cohort	185 women who were under 50 at diagnosis and were cancer-free 5 years later	≤50	Breast	5 years post diagnosis	Comorbidity	Quality of life (QoL)
Bohn H. (2019)	Norway	Cross-sectional	1088	19-39	Breast cancer, colorectal cancer, non-Hodgkin lymphoma, acute lymphoblastic leukemia, or non-metastatic malignant melanoma	5 years post diagnosis	Radiotherapy, comorbidity, pain	Chronic fatigue

Butow P. (2013)	Australia	Cross-sectional	596	18-80	Breast, Prostate, Colorectal, Bladder, Kidney, Leukemia, Head & Neck, Other	1 year post diagnosis	Anxiety and depression	Quality of life (QoL)
Cordoso C.R. (2018)	USA	Cross-sectional	906	≥18	Head & Neck	1 year post diagnosis	Prevalence of oral morbidities	Quality of life
Cox-Martin (2020)	USA	Cross-sectional	1,702	25-64	All	Completed cancer treatment	Cancer related pain	Health related quality of life (HRQOL)
Cummings A. (2018)	UK	Prospective cohort study	872	≥18	Colorectal	Questionnaires administered at 3, 9, 15, 24 months and annually up to 5 years	Comorbidities	Quality of life (QoL)
Cuthbert C. (2018)	Canada	Prospective Cohort	12,265	≥18	Colorectal (stage I-III)	Not defined	Comorbidities	Treatment received for cancer
Danese M.D. (2012)	USA	Prospective cohort study	51,950	≥66	Breast	3 months and 12 months post-diagnosis	Comorbidities before and after cancer diagnosis	Incidence and prevalence of comorbidity
Desai R. (2019)	USA	Retrospective cohort study	10,452	≥18	Breast	1+ years since diagnosis	Mental health comorbidities (anxiety/depression)	Opoid use & survival
Deimling G.T. (2005)	USA	Cross-sectional	321	≥60	Breast, prostate, and colorectal	5+ years post diagnosis	Comorbidities, current symptoms, social demographics	Quality of life
Deng J. (2012)	USA	Cross-sectional	81	≥18	Head & Neck	3 months post treatment	Incidence of lymphedema	Secondary lymphedema
Desautels D. (2016)	Canada	Cross-sectional, survivor matched with up to 5 controls	14,164 cancer survivors 69,051 men without cancer	≥18	Prostate	3 years after diagnosis	Treatment modality - radiation therapy	Risk of colorectal cancer/other invasive cancer after diagnosis of prostate cancer
Deshpande A. (2011)	USA	Cross-sectional	1089	≥18	Breast	1 year post diagnosis	Comorbidity burden	Quality of Life
Downing A. (2019)	UK	Retrospective cohort study	35,823	≥18	Prostate	18-42 months post diagnosis	Stage of cancer	Health related quality of life
Downing A. (2015)	UK	Retrospective cohort study	21,802	≥18	Colorectal	12-36 months post diagnosis	Long-term conditions, treatment, disease status, stoma status	Health related quality of life (using the EuroQol-5D domains)
Eakin E. (2006)	Australia	Cross sectional	968 cancer survivors, 5,808 cancer-free	≥18	Colorectal, female breast, prostate, and cancers of the female reproductive organs, including cancer of the cervix, cancer of the uterus, and cancer of the ovaries	Excludes those with current cancer	Chronic comorbidity	Quality of life & self-reported health status
Efficace F. (2018)	Italy	Prospective Cohort study	174	≥60	Chronic myeloid leukemia	11+ years post diagnosis	Presence of comorbidity, symptom burden	Health related quality of life
Efficace F. (2016)	Italy	Cross-sectional	307	60-87	Acute promyelocytic leukemia	3+ years post diagnosis	Presence of comorbidity	Health related quality of life

Eytan (2019)	USA	Cross-sectional	10,524	≥66	Head & Neck	1+ year post diagnosis	Presence of comorbidity	30 comorbid conditions
Foster M. (2021)	UK	Retrospective cohort	8,438	40-70	Breast	0-5+ years	Multimorbidity and cancer	Depression
Fu M.R. (2015)	USA	Prospective cohort study	134	≥18	Breast	Before and 12 months after surgery	Presence of comorbidity	Quality of life
Ganz P.A. (2008)	USA	Retrospective cohort study	180	34-85	Breast	Comparison of 5-8 years vs 10-13 years post diagnosis	Adjuvant anthracycline therapy	Cardiac effects - Left ventricular ejection fraction (LVEF)
Ganz P.A. (2002)	USA	Prospective cohort study	817 survivors, 763 cancer free	≥18	Breast	1-5 years post diagnosis	Adjuvant therapy	Quality of life
Girones R. (2010)	Spain	Retrospective cohort	91	≥70	Breast	1-12 years post diagnosis	Presence of comorbidities and disability	Comprehensive geriatric assessment
Green C.R. (2011)	USA	Cross-sectional	199	18-80	Breast, colorectal, lung, and prostate cancer and multiple myeloma	2+ years post diagnosis	Chronic pain	Quality of life
Greenfield D.M. (2010)	UK	Case-control	Men only; 176 cancer survivors and 213 controls	25-45	Nonhormone-dependent cancers (lymphoma, 40.9%; germ cell, 38.6%); other [eg, leukaemia, gastrointestinal, brain, sarcoma, and skin], 20.5%	2+ years post treatment	Cancer	QOL, self-esteem, fatigue, and sexual function
Greer J.A. (2011)	USA	Cross-sectional	225 survivors and 5337 cancer-free	≥18	Breast (24.0%), melanoma (18.7%), cervical (10.0%), prostate (8.0%), uterine (7.2%), colon (7.0%), ovarian (1.8%), lymphoma/leukaemia (1.8%), lung (0.7%), and others (25.6%)	5+ years post diagnosis/cured or in remission	Cancer	Anxiety disorder
Haque R. (2014)	USA	Retrospective cohort study	2722 women (1361 matched pairs)	≥65	Cervical (10.0%), prostate (8.0%), uterine (7.2%), colon	5+ years post diagnosis	Smoking, diabetes, and hypertension	Cardiovascular disease risk
Hawkins M. (2020)	USA	Prospective cohort	7114 survivors 25,979 cancer-free		Breast (stage I and II)	1+ years after diagnosis	Cancer	Risk of endocrine and metabolic disease
Heo J. (2017)	Korea	Retrospective cohort study	87,843	≥18	Breast	6+ months post diagnosis	Cancer, time since diagnosis, age	Mental disorders
Hiyoshi A. (2017)	Sweden	Cross-sectional with survivors compared to non-cancer patients	Men; 878 survivors 4340 cancer-free	≥18	Colorectal, male genitourinary system (including kidney and urinary tract), skin and lung cancers (including bronchus) as well as leukaemia, and thyroid	1+ years after diagnosis, followed for 5 years	Comorbidities, Socioeconomic characteristics, physical, cognitive and psychological function	Comorbidities trajectories
Hooning M.J. (2007)	Netherlands	Retrospective cohort study	4,414	18-71	Breast	10+ years post diagnosis	Treatment modalities - Breast irradiation, Radiation only, Radiation with adjuvant chemotherapy	Incidence of cardiovascular disease

Hoopes M. (2019)	USA	Retrospective Cohort	42,359	≥19	All except Melanoma	Identifying cancer survivors and understanding their patterns of utilization and physical and mental comorbidities	Cancer	Charles Comorbidity Index, Chronic pain and Opoid use
Houterman S. (2006)	Netherlands	Retrospective cohort study	6,340	≥18	Prostate	0-5 years since diagnosis	Comorbidity, age	Treatment and survival
Hovaldt H.B. (2015)	Denmark	Cross-sectional	227,704	≥18	All	Median 6 years post diagnosis	Cancer	Prevalence of comorbidity, Social position
Husson O. (2015)	Netherlands	Cross-sectional with comparison between cases and controls	6011 survivors, 2040 normal population	≥18	Endometrial, colorectal, thyroid, Hodgkin or non-Hodgkin lymphoma and multiple myeloma	Comparison of: >2 years 2-5 years >5 years since diagnosis	Cancer, time since diagnosis, age, treatment, comorbidity, educational level and partnership	Fatigue severity
Ilie G. (2021)	Canada	Cross-sectional	6,585 male	49-69	Prostate	Ever diagnosed with cancer	Cancer, socioeconomic status, age, household income, ethnicity and number of comorbidities	Depression
Jansana A. (2021)	Spain	Cross-sectional	6512	≥18	Breast	5+ years since diagnosis	Clusters of multimorbidity	Health service use, mortality
Jefferson M. (2020)	USA	Retrospective cohort study	316 prostate cancer patients treated with radical prostatectomy	≥18	Prostate	5+ years since diagnosis	Cancer in past 4 years vs >5 years, age, race, ethnicity	Comorbidity
Jordan J. (2014)	USA	Prospective cohort	1,361 Survivors, 1,361 non-cancer patients	≥65	Breast (Stage I and II)	5+ years since diagnosis	Cancer	Incident comorbidity, mortality
Joshy G. (2020)	Australia	Cross-sectional	22,505 cancer survivors and 244,000 people without cancer	≥45	Breast, prostate, lung, melanoma, colorectal, non-hodgkin lymphoma, kidney, oesophagus, uterus, thyroid, bladder, leukaemia and multiple myeloma	12+ years since diagnosis	Cancer	Quality of life
Kang Y.M. (2017)	Taiwan	Cross-sectional	32,689	≥18	Colorectal	Patients undergoing curative surgery	Radiotherapy	Pelvic fracture risk
Kent (2014)	USA	Cross-sectional	16,095 cancer survivors and 1,224,529 individuals without a history of cancer	≥65	Kidney, bladder, pancreas, upper gastrointestinal, oral cavity & pharynx, uterine, cervical, thyroid, melanoma, chronic leukemia, non-Hodgkin lymphoma, and multiple myeloma	3+ years post diagnosis	Cancer	HRQOL
Kenzik K. (2016)	USA	Retrospective Cohort	5,991	≥65	Prostate, breast, colorectal, lung, bladder, kidney, head and neck, and gynecologic cancer and non-Hodgkin lymphoma	Not defined	Pre vs post cancer diagnosis, functional impairment	Comorbidity cluster

Khan N.F. (2011)	UK	Retrospective Cohort	26,213 survivors, 104,486 matched control	≥18	Breast, colorectal or prostate cancer	5+ years since diagnosis	Cancer	Comorbidities arising from treatment - Hypothyroidism, heart failure, coronary artery disease, lymphoedema, erectile dysfunction, incontinence, osteoporosis, coronary artery disease
Khan N.F. (2010)	UK	Cross-sectional	21,366 survivors; 21,366 controls	≥18	Breast, colorectal or prostate cancer	5+ years since diagnosis	Cancer	Chronic disease care
Kim S.H. (2017)	Korea	Cross sectional	5274 cancer survivors and 20,703 and 21,096 gender- and age-matched controls without and with chronic disease	≥18	Colorectal, breast, cervical, lung, thyroid, prostate, and bladder	Average 6.4 years since diagnosis	Cancer	Prevalence of metabolic syndrome
Kim S.H. (2008)	Korea	Cross sectional	1,933	≥18	Breast	In remission	Fatigue and depression	Quality of life
Kuijer A. (2018)	USA	Retrospective Cohort Study	888	18-40	Breast	1+ year after diagnosis	Treatment modality	Patient-reported postoperative arm swelling and decreased range of motion
Kurnit K.C. (2015)	USA	Retrospective cohort	23,227 survivors, 142,601 controls	≥18	Uterine	Not defined	Cancer	Prevalence of comorbidities
Lakomy D.S. (2021)	USA	Cross-sectional	302	≥18	Uterine	Median 6.7 years post surgery	Treatment modality	Pelvic floor dysfunction (PFD)
Landis S. (2011)	Netherlands	Retrospective cohort	1,499	≥18	Squamous cell head and neck cancer (SCCHN)	6 months post diagnosis	Cancer	Incidence of comorbidity after cancer treatment
Leach C. (2015)	USA	Prospective cohort	1,527	≥21	Breast, prostate, colorectal, and gynecological cancer	4+ years since diagnosis	Cancer, ethnicity and other demographics	Prevalence of cancer before and after diagnosis
Lim M. (2018)	Korea	Retrospective cohort study	14,797 endometrial cancer survivors	≥18	Endometrial	2 months after diagnosis	Cancer	Incidence of colorectal cancer as 2nd cancer
Louwman (2010)	Netherlands	Cross-sectional	72,153 patients	≥18	Oesophagus, stomach, colon/rectum, pancreas, lung, melanoma, breast, cervix uteri, corpus uteri, ovary, prostate, bladder, kidney, and non-Hodgkin's lymphoma (NHL)	Not defined	Socio-economic status	Comorbidity
Maharjan M. (2017)	Nepal	Cross-sectional	107	≥18	Breast	6+ months after surgery	Mastectomy	Quality of life
Mao J.J. (2007)	USA	Cross-sectional	1,904 cancer survivors and 29,092 controls	≥18	All	Diagnosis to 11 years	Age & comorbidity	Symptom burden
Mason S. (2018)	England	Cross-sectional	1231	≥18	Bladder	1-5 years post diagnosis	Treatment modality	Cancer specific Health related Quality of life
Miaskowski C. (2017)	USA	Cross-sectional	1450	≥18	Head & Neck	Completed chemotherapy 3+ months ago	Treatment modality	Quality of life

Möhl A. (2020)	Germany	Prospective cohort	3813 survivors, 7341 population-based controls	50-74	Breast	10+ years post diagnosis	Cancer	A modified Charlson Comorbidity Index (mCCI)
Mols F. (2008)	Netherlands	Prospective cohort	525 with prostate cancer and 65 with both prostate cancer and Diabetes Mellitus	18-75	Prostate	5+ years post diagnosis	Cancer, Diabetes	Comorbidity, Health-related quality of life (HRQOL)
Mols F. (2009)	Netherlands	Cross-sectional	780	18-75	Prostate	5+ years post diagnosis	Treatment modality	Bowel, urinary and sexual problems
Mustafa Ali (2016)	USA	Retrospective cohort	1126	≥18	Breast	0 months-5+ years since therapy ended	Cancer	34 conditions related to treatment
Nakash O. (2013)	Israel	Cross-sectional	66,387 total; 357 active cancer, 1373 cancer survivors, 64,657 cancer-free respondents	≥18	All	Patients in remission or cured	Active cancer, cancer survivor, cancer free, country level income	Common mental disorders, service use
Ng H.S. (2018)	Australia	Retrospective, rolling cohort study	23,376 survivors and 233,760 control group	All age	Breast	Diagnosis - 10 years post diagnosis	Cancer, time since diagnosis	Comorbidity incidence
Ng H.S. (2018)	Australia	Retrospective Cohort	A total of 13,824, 13,581 and 12,809 respondents aged 25 years and over from NHS 2007-08, 2011-12 and 2014-15 respectively	≥25	All	Anyone who ever had cancer	Time, cancer	Prevalence of comorbidity - 12 disease groupings
Ng H.S. (2018)	Australia	Retrospective, rolling cohort study	3,689 survivors; 36,890 control	All ages, although most are >65	Prostate	Followed from diagnosis until 10 years	Cancer	Prevalence of comorbidity
Ogle K.S. (2000)	USA	Cross-sectional	15,626	≥40	Lung, colon, urinary bladder, rectum, Oesophagus, stomach, skin, liver, salivary gland, mesothelioma, eye	2-8 weeks after diagnosis	Cancer	Prevalence of comorbidity
Okura Y. (2019)	Japan	Prospective cohort	26,235 de novo cancer patients; 16,130 survivors	≥18	All	5 years post diagnosis	Time since diagnosis	Prevalence of cardiovascular disease
Osthus A. (2012)	Norway	Prospective cohort study	106 recently diagnosed, 72 survivors	≥18	Head and Neck	18 months post diagnosis	Comorbidity, Time since diagnosis	Health related quality of life (HRQOL)
Paskett E. (2009)	USA	Cross-sectional	245	≥18	Breast	9-16 years post diagnosis	Chemotherapy dose	Quality of life
Pate A. (2020)	USA	Cross-sectional	403 survivors; 401 controls	≥18	Colorectal	≥5 years from diagnosis	Comorbidity	Quality of life
Penedo F (2005)	USA	Prospective cohort	204 men (85 non-Hispanic white, 37 African-American, and 82 Hispanic men)	≥50	Prostate		Ethnic group membership	QOL
Pergolotti M. (2017)	USA	Cross-sectional	768	≥65	All	1+ year since diagnosis	Comorbidity burden	Health related quality of life (HRQOL)
Petrova D. (2021)	Spain	Cross-sectional	853 recent survivors, 1220 long-term survivors	18-80	Breast, Gynaecological, Genitourinary, Gastrointestinal, Melanoma, Skin non-melanoma, Skin other types	Diagnosis to 20+ years	Physical comorbidities, time since diagnosis	Depression

Piccirillo J.F. (2000)	USA	Retrospective cohort study	3,378	18-95	Head & Neck compared to colorectum, lung, breast, gynaecological sites and prostate	1+ year since diagnosis	Severity of cancer	Comorbidity, two-year survival
Pinheiro L. (2016)	USA	Retrospective cohort	3,000	20-74	Breast	9+ months since diagnosis	Race	Health related Quality of Life
Poll-Franse L.V.V. (2007)	Netherlands	Prospective Cohort study	475	≥18	Prostate	Diagnosis to 4 years follow up	Comorbidity & treatment modality	Health related quality of life
Rebegea L. (2015)	Romania	Retrospective cohort	305	28-82	Breast	Diagnosis to 18 months follow up	Treatment modality	Risk of arm lymphedema
Reeve B. (2014)	USA	Prospective cohort study	697	46-82	Prostate	3+ months since diagnosis	Comorbidity	Health related Quality of Life
Rohan E.A. (2015)	USA	Cross-sectional	52,788 cancer survivors; 4001 colorectal cancer survivors	≥18	Colorectal	Ever had a cancer diagnosis	Colorectal cancer vs other cancers vs no cancer	Comorbidity, health behaviours and health related quality of life
Schmidt M.E. (2012)	Germany	Prospective Cohort study	1,928 disease-free cancer survivors and comparisons with fatigue and QoL scores from the general population	50-75	Breast	3.6+ years since diagnosis	Fatigue, treatment modality	Quality of life
Sanford N.N. (2019)	USA	Retrospective cohort	115,091	≥18	Multiple	2+ years since diagnosis	Cancer	Chronic pain prevalence, mental health and functional limitations of survivors with chronic pain
Sarfati D. (2016)	New Zealand	Cross-sectional	14,096	≥25	Colon, rectal, breast, ovarian, uterine, stomach, liver, renal or bladder	Within 5 year of diagnosis	Cancer	Prevalence of chronic conditions; Survival
Schoormans D. (2015)	Sweden	Cross-sectional	2,552 survivors; 5,140 non-cancer patients	≥18	Breast	0-10+ years since diagnosis	Cancer	Impact of time since diagnosis and comorbidity Health related quality of life
Soisson S. (2018)	USA	Retrospective cohort	2648 endometrial cancer survivors; 10,503 general population	≥18	Endometrial	1+ years since diagnosis	Cancer	Long-term genitourinary outcomes
Siembida E.J. (2021)	USA	Cross-sectional	2,019	≥65	Prostate, colorectal, non-small cell lung, Non-Hodgkin lymphoma, female breast, uterine, or cervical	6+ months since diagnosis	Individual comorbid conditions, as opposed to total comorbidity burden	Health-related quality of life (HRQOL)
Snyder C.F. (2013)	USA	Cross-sectional	8,661 cancer survivors; 17,322 controls	≥65	Colorectal, Prostate and Breast	3+ years since diagnosis	Cancer	Quality of comorbid condition care
Song L. (2014)	USA	Cross-sectional	193 pairs were matched based on 7 sociodemographic and health-related factors	≥50	Prostate	5+ years since diagnosis	Cancer	Quality of life (QOL), health status, and the relationships between them
Strongman H. (2019)	UK	Retrospective cohort	108,215 cancer survivors; 523,541 controls	≥18	20 most frequent adult cancers	12 months after diagnosis	Cancer	Risk of cardiovascular diseases
Thong M.S. (2011)	Netherlands	Prospective cohort	1,811 men	≥39	Prostate	0-5 years since diagnosis	Diabetes	Health related quality of life (HRQOL)

Thong M.S. (2011)	Netherlands	Prospective cohort	848 survivors		Colon	Up to 10 years post diagnosis	Chemotherapy	General and disease specific health status
Thyo A. (2019)	Denmark	Cross-sectional	2, 402	≥18	Colorectal	2.9+ years since diagnosis	Cancer	Long-term female sexual dysfunction
Trentham-Dietz A. (2003)	USA	Cross-sectional	726 women (502 women with diagnoses of colon cancer and 224 women with diagnoses of rectal cancer)	43-85	Colon cancer, colorectal cancer	7-11 years post diagnosis	Cancer	Health-related quality of life (physical component summary score, mental component summary score)
Vissers P.A.	Netherlands	Cross-sectional	3,792	≥18	Thyroid cancer, colorectal cancer, and non-Hodgkin's and Hodgkin's lymphoma	6+ months since diagnosis	Comorbidity	Health related quality of life (HRQOL)
Wallander M. (2019)	Sweden	Retrospective cohort	179,744 men	≥18	Prostate	7-11 years since diagnosis	Androgen deprivation therapy (ADT)	Risk of incident fractures and non-skeletal fall injuries
Wang F. (2014)	China	Cross-sectional	111 survivors, 111 controls	25-70	Breast	A diagnosis of breast cancer in the 2 years before the survey	Cancer	Depression and anxiety status
Wang J.W. (2016)	China	Cross-sectional	1,398	≥18	Colorectal	Not mentioned	Comorbidities	Quality of life
Wang L. (2018)	Canada	Cross-sectional	26	≥18	Colorectal	Completed curative treatment	Pre-operative radiotherapy (PRT)	Quality of Life
Weaver K. (2013)	USA	Cross-sectional	1,582	≥21	Breast, prostate, colorectal, and gynaecologic cancer	4-14 years after diagnosis	Cancer	Prevalence of cardiovascular risk factors
Wennstig A. (2020)	Sweden	Cross-sectional	60,217 cancer survivors; 300,791 non cancer patients	≥18	Breast	Not mentioned	Adjuvant radiotherapy (RT); women with right side breast cancer (BC); left side BC; without BC	Ischemic heart disease (IHD)
Yan R. (2019)	China	Cross-sectional	1,546		All	0-5 years since diagnosis	Chronic comorbid diseases	Anxiety and depression
Yancik R. (1996)	USA	Cross-sectional	7,600	≥18	Breast, cervix, ovary, prostate, colon, stomach, and urinary bladder cancer	15 years from diagnosis	Cancer	Prevalence of comorbid conditions
Zeynalova N. (2019)	Germany	Cross-sectional	9315 participants, 954 (10.2%) cancer patients	≥18	All	Ever had a diagnosis of cancer	Cancer	General anxiety level measured by Generalized Anxiety Disorder Scale (GAD-7)