Cancer survivor late-effects, chronic health problems after cancer treatment: what's the evidence from population and registry data and where are the gaps?

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Purpose of review
Improvements in cancer treatment have led to more people living with and beyond a cancer diagnosis but survivors may have increased health problems as they age. The purpose of this review is to critically evaluate population data exploring incidence of late effects for cancer survivors.

Recent findings
18 studies were identified between 2013 and 2023 that explored the impact on survivors' physical and emotional health. Patients who had been treated at least 2 years previously for cancer had significant cardiovascular risk factors compared with age-matched controls. Women with breast cancer were more likely to have cardiovascular disease, including hypertension, arrythmias and congestive heart failure. This was associated with anthracyclines and/or trastuzumab as part of systemic anti-cancer therapy. Survivors of colorectal cancer were three times more likely to have acute kidney injury than age-matched controls. Stress and mood disorders were higher in survivors of testicular cancer and prostate cancer.

Summary
Population studies are important to identify the 'real world' consequences of cancer and its treatment beyond clinical trials. Knowledge is critical for managing an ageing cancer population. Data to personalise cancer survivorship care, not only helps determine potential health risks, but can improve secondary prevention, emotional health, recovery, and long-term outcomes.

Keywords
cancer survivors, chronic health, cohort studies, late effects, population

INTRODUCTION

The number of cancer survivors has grown rapidly over the last decade, because of the improvements in cancer screening, diagnosis, and treatment. It is predicted that by 2030 more than 4 million people in the United Kingdom [1] and by 2040, 40 million people in the United States [2], will be living with and beyond a cancer diagnosis. As the number of people with cancer live longer, they continue to experience a wide range of chronic health and emotional problems that can impact their quality of life (QOL) [3,4,5▪,6]. Health problems because of surgery, radiotherapy and systemic anti-cancer therapy (SACT) can persist as long-term symptoms which continue up to 12 months as well as late effects which can emerge years after cancer therapy. Long-term symptoms, such as fatigue, chronic pain, depression, lymphoedema, peripheral neuropathy, emotional and sexual concerns are commonly reported by patients after cancer treatment [7▪]. These can impact healthcare utilisation [5▪,8] and return to work [9–11]. Late effects that impact on an individual's longer-term health as they age are not as well documented. There is a paucity of multi-domain late effects data from clinical trials and population studies are valuable in providing information on a wider demographic and over a longer time interval. Healthcare

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KEY POINTS

- Late effects of cancer treatment continue to cause physical and psychological problems up to 10 years after therapy.
- Women treated for breast cancer had greater incidence of cardiovascular disease than women of a similar age without cancer.
- Comorbidities (2 or more), older age and obesity increased an individual's risk of cancer treatment-related cardiovascular late effects.
- People treated for non-Hodgkin lymphoma and recipients of bone marrow transplant were at greater risk of a second cancer after cancer treatment.
- Cancer survivors report lower cognitive function and have a higher incidence of depression than age-matched controls without cancer.

providers need to know who is at higher risk, trajectories of symptoms over time and who may need more supportive care to mitigate symptoms and promote health [12▪▪].

The purpose of this narrative review was therefore to critically review population and cohort studies to identify the prevalence of long-term and late effects in adult cancer survivors who have undergone modern cancer therapies compared with populations without cancer or its treatment.

We reviewed published studies from 2013 to 2023 on PubMed and Google scholar. Search terms included 'cancer survivors' AND adult AND 'late OR adverse effects' OR 'chronic health' Studies excluded were of childhood and 'young adult' survivors. Our focus was on cancer survivors who experience cancer as adults and therefore experience late effects as they age. The initial 135 papers identified were screened, and 18 studies were identified as population and cohort studies that explored physical health, chronic symptoms, and emotional health of cancer survivors. The studies were from 10 countries with data collected from cancer registrations, integrated health services, hospital episode statistics as well as subgroup samples of patient reported outcomes (PROs). Two countries routinely sampled random cohorts of the population and collected PRO data to complement cancer registry and clinical information. Included studies were in people treated for cancers of the breast, testicular, anal, colorectal, prostate, head and neck, blood, including lymphoma.

Determining if chronic health problems and late effects are linked to previous cancer treatment, this is best done by identifying excess morbidity. This is calculated by comparing those who have been treated for cancer, with age-matched comparative populations who have not received cancer treatment and identifying the predictive risk through a multivariate approach. Most studies identified non-cancer age and sex matched controls as a comparative sample from registry and healthcare data records. Three studies used a 'within group' comparator of patients being treated for the same cancer but treated differently for example different chemotherapy drugs or radiotherapy fields. Three studies had no comparative sample. Study results were grouped according to the physical late effects and cancers (Table 1), emotional and cognitive late effects (Table 2).

PHYSICAL LATE EFFECTS OF CANCER TREATMENT

Cardiovascular risk factors (CVRFs), such as hypertension, arrythmias, diabetes and obesity were significantly higher in cancer survivors than comparative populations (Table 1) [13,14▪▪]. Two or more CVRFs at cancer diagnosis led to greater cardiovascular disease (CVD) after cancer treatment and this then impacted on patients' overall survival (Table 1) [13,15]. Those populations at higher risk of CVRF were women treated for breast cancer, people treated for multiple myeloma, lung cancer or non-Hodgkin lymphoma (NHL) and those women who were older [13,14▪▪,16].

Trastuzumab, used as an adjuvant chemotherapy for breast cancer, increased women's risk of heart failure from 1.5 years after therapy; the 5-year cumulative risk of heart failure was 5.2% for women on this drug compared with 2.5% for those women who did not receive trastuzumab [17]. Radiotherapy to the left side of the chest was not associated with CVD [16]. However, cardiac arrythmias were the most reported CVD symptom affecting 12% of women and myocardial infarction in 1.7–2% [16]. These two studies used within group comparisons, comparing risk of differing therapies rather than age-matched controls that would identify if women with breast cancer were at higher risk of CVD.

Another important risk factor for the occurrence of CVD after cancer treatment is the use of anthracyclines as part of SACT with the number of cycles impacting on cumulative dose and CVRF. A study of the 5-year cumulative risk of congestive heart failure (CHF) in patients treated for diffuse large B-cell and follicular lymphoma was five times higher [HR = 5.00 (95% CI 1.4–18.5)] compared with those treated without anthracyclines 5.4% vs 0.7% experienced CHF. This was higher with higher intensity treatment (six cycles) [18]. CVD was also observed

Table 1. Population studies (2013–2023) of physical and emotional late effects for cancer survivors

Author and country	Population	Comparator	Timing and assessment	Late and chronic effects	Factors impacting occurrence of LE
Armenian *et al.* 2016 [13] USA	Retrospective cohort study of *long-term cancer survivors*, >40 years at diagnosis, between 2000 and 2007 sample of 36 232. Cancer registry data was linked with integrated managed care organisation. Study explored risk of CVD of long-term survivors compared with non-cancer comparisons	Age matched comparison of people without cancer (n = 73 545)	Data collected from routine care data. Treated at least 2 years previously	Survivors had significant (P < 0.01) CVRFs compared with non-cancer controls. People with multiple myeloma IRR 1.70, lung cancer IRR 1.58, non-Hodgkin lymphoma IRR 1.41 and breast cancer IRR 1.13 had higher risk scores than controls	Cancer survivors with 2 or more CVRF had the highest risk of CVD compared with controls (IRR 1.83–2.59, P < 0.01) Overall survival was worse among cancer survivors who developed CVD than those who did not (P < 0.01)
Falstie-Jensen *et al.* 2020 [20] Denmark	Retrospective matched cohort study of 44 574 women treated for non-metastatic *breast cancer* treated between 1996 and 2009. Study investigated the incidence of hypothyroidism after treatment	Age matched comparison of women without cancer	Danish registry study data, was matched to health records diagnostic codes, and levothyroxine prescriptions	Breast cancer survivors had a slightly higher incidence of hypothyroidism than controls 5-year cumulative incidence, 1.8% (95% CI = 1.7–1.9)	Women who received radiotherapy to the lymph nodes had an elevated risk of hypothyroidism (HR = 1.31; 95% CI 1.4–1.51)
Goldhar *et al.* 2016 [17] Canada	Retrospective population-based cohort study of 19 074 women with *breast cancer*, treated with adjuvant chemotherapy and 17% with trastuzumab, diagnosed between 2003 and 2009. Study explored new onset heart failure (HF) at a median of 5.9 years	Within group comparator of women not treated with trastuzumab as part of adjuvant therapy	Data collected from Ontario Canada, cancer registry and linked to administrative databases for cardiac risk factors, comorbidities, and use of trastuzumab and other chemotherapy	Women treated with trastuzumab were more likely to develop HF in the 1.5 years after treatment. Those on trastuzumab had a higher 5-year cumulative incidence than women on chemotherapy alone (5.2% vs 2.5%, P < 0.001)	Trastuzumab increased risk of HF
Koric *et al.* 2022 [14] USA	Population based retrospective cohort study of 6641 women with *breast cancer*, treated between 1997 and 2009. Study to evaluate CVD and possible risk factors	Age matched comparison of people without cancer	Women identified from the Utah cancer registry database who had survived 10 years	Breast cancer survivors had an increased risk of newly diagnosed diseases of the circulatory system (HR = 1.32; 99% CI 1–1.75) 10–15 years following cancer diagnosis compared with the matched population	Women with more comorbidities had a higher risk of CVD beyond 10 years (HR = 2.64; 95% CI 1.08–6.45). Older age, obesity, lower education and family history of CVD were risk factors for CVD

Table 1. (*continued*)

Author and country	Population	Comparator	Timing and assessment	Late and chronic effects	Factors impacting occurrence of LE
Merzenich *et al.* 2022 [16] Germany	Retrospective cohort of 11 982 women treated with radiotherapy for *breast cancer* between 1998 and 2008. Study to explore cardiac toxicity through mortality data and patient self-reported comorbidity data (*n* = 5388)	Within group comparator of women treated for left- or right-sided radiotherapy fields	Median follow-up of 11.1 years	There was no significant association of morbidity and mortality from cardiac events and laterality of radiation therapy. Arrhythmia was the most reported CVD symptom, 12%, MI 1.7–2%	Prior cardiac disease, higher age at diagnosis, were associated with increased cardiac mortality. Being treated more than 10 years ago chemotherapy was associated with higher overall mortality (HR = 1.51; 95% CI 1.39–1.65)
Andresen *et al.* 2023 [21] England	Retrospective matched cohort study of 20 340 health records of people receiving *colorectal cancer* treatment between 1997 and 2018. Study identified incident acute kidney injury (AKI) compared with individuals without cancer	Age matched comparator from 100 058 cancer free individuals	AKI identified by routine serum creatine levels	AKI was significantly higher than matched controls (HR = 2.16; 95% CI 2.05–2.27). Risk was highest in the first year after diagnosis (HR = 7.47, 95% CI 6.66–8.37) and reduced overtime. Still an increased risk at 5 years post treatment	Association between AKI and colorectal cancer treatment was greater for younger patients, men and those with pre-existing chronic kidney disease
Zhang *et al.* 2022 [19] Sweden	Retrospective registry study of 197 699 people diagnosed with *colorectal cancer* between 2007 and 2015. Study explored the mortality patterns and risks of cardiovascular disease events	No comparative normative data	Median follow-up of 37 months 79 455 deaths occurred of which 29.29% died through non-cancer events which CVD made up 41.69%	The 1, 3 and 5-year cumulative rate for CVD was 12.20%, 24.25% and 30.51%, respectively	Age, race, marital status, tumour size, stage, surgery, and chemotherapy were independent risk factors of CVD
Chen *et al.* 2019 [15] Taiwan	Retrospective cohort study of 3016 people diagnosed with *nasopharyngeal cancer* between 2005 and 2012. Study explored occurrence of ischaemic stroke in survivors following radiotherapy or concurrent chemotherapy	Age, matched non-cancer comparative population	Median follow-up 4.3 years	Significant cumulative risk of ischaemic stroke ($P < 0.001$). Prevalence 3× higher than that of controls. Those who had ischaemic stroke and concurrent chemotherapy had higher mortality	Those diagnosed younger had early occurrence of ischaemic stroke (10 years earlier than those of similar age without cancer). Comorbidities (diabetes, hypertension, prior CVD and AKI) increased risk

Table 1. (*continued*)

Author and country	Population	Comparator	Timing and assessment	Late and chronic effects	Factors impacting occurrence of LE
Baech *et al.* 2018 [18] Denmark	Retrospective registry cohort study of 2440 patients treated for *diffuse large B-cell and follicular lymphoma* from 2000 to 2012 Study to explore impact of poly-chemotherapy regimens on cardio toxicity	Comparison reference group 446 (18.3%) patients treated without anthracycline chemotherapy	Study population 1994 (81.7%) treated with anthracycline containing chemotherapy. Median follow-up 3.8 years	5-year cumulative risk of CHF compared with the reference group for 3–5 cycles of anthracyclines was Adjusted HR = 5.0 (95% CI 1.4–18.5) 5.4% of sample developed CHF compared with 0.7% for those who did not have anthracyclines	6 or more courses of anthracyclines increased risk of CHF 7.9% Age was a significant risk factor, radiotherapy and sex were not associated with CHF
Bilmon *et al.* 2014 [22] Australia	Population based study of *7765 BMT recipients* who had autologous HCT, from registry data recorded 1992–2007. Data linkage with cancer registrations and national death index Study to quantify second cancer risk	Comparison with non-cancer population	Median follow-up 2.5 years	Second cancer risk was moderately increased compared with a general population SIR 1.4, 95% CI 1.2–1.6 Significantly elevated risk for those treated for AML/myelodysplastic syndrome (SIR 20.6), melanoma (SIR 2.6) and non-Hodgkin's lymphoma (SIR 3.3)	At higher risk of second cancer were men, those transplanted at a younger age (more aggressive therapies) Melanoma risk elevated for men >45 years when treated with HCT Lung cancer risk elevated for Hodgkin lymphoma and older age

AKI, acute kidney injury; BMT, bone marrow transplant; CHD, congestive heart failure; CRVFs, cardiovascular risk factors; CVD, cardiovascular disease; HCT, haematopoietic stem cell transplant; HF, heart failure; HR, hazards ratio; IR, incidence ratio; IRR, incidence rate ratio; MI, myocardial Infarction; PSS, perceived stress scale; SIR, standardised incidence rate.

in those treated for colorectal cancer, with 1-, 3- and 5-year cumulative rates for CVD being 12.20%, 24.25% and 30.51%, respectively [19]. The prevalence of ischaemic stroke was three-times higher in those treated for nasopharyngeal cancer than those in a comparative non-cancer population [15]. Risk factors, such as being diagnosed younger and those with prior CVRFs, increased risk of ischaemic stroke [15].

Hypothyroidism was more prevalent in women previously treated for breast cancer than age-matched non-cancer controls. Falstie-Jensen *et al.* [20] used both medical and prescription records to determine the diagnosis as this is often under reported in medical records. Women who received both radiotherapy and chemotherapy with treatment not only to their breast and chest wall but additionally the supraclavicular lymph nodes were at higher risk of hypothyroidism.

Acute kidney injury (AKI) was significantly higher in those treated for colorectal cancer than age-matched controls without cancer (HR = 2.16; 95% CI 2.05–2.27) [21]. Risk of AKI was determined by serum creatine levels and was highest in the first year after diagnosis (HR = 7.47; 95% CI 6.66–8.37) and decreased over time although people still had a 26% increased risk of AKI at 5 years compared with the matched population.

The standardised incidence rate of a second cancer in those previously treated with an autologous haematopoietic stem cell transplantation for AML and myelodysplastic syndrome was 20.6 [22]. Recipients were at elevated risk if they were younger when transplanted and received more aggressive chemotherapy. Melanoma risk was higher for men older than 45 years when they were treated for Hodgkin lymphoma [22].

EMOTIONAL HEALTH, COGNITION, AND LATE EFFECTS IMPACT ON QUALITY OF LIFE

Long-term and late effects of cancer and its treatment impact on survivors' quality of life (Table 2). Women treated for breast cancer more recently reported poorer physical and mental health than in earlier cohorts. Women with higher comorbidities had greater functional limitations which was negatively associated with health-related quality of life (HRQOL) [23▪]. Foster *et al.* [24] found that 30%

Table 2. Population studies (2013–2023) of emotional, chronic symptoms and cognitive late effects for cancer survivors

Author and country	Population	Comparator	Timing and assessment	Late and chronic effects	Factors impacting occurrence of LE
Oerlemans *et al.* 2013 [25] Netherlands	Longitudinal population registry study of those treated from 1999 to 2009 for *non-Hodgkin's lymphoma*. Study to assess fatigue and quality of life of a sample of 824 survivors (80% response rate) plus a 1-year follow-up questionnaire	Age and sex matched non cancer normative population	PROs data from EORTC QLQ-C30 and fatigue assessment scale	Survivors of NHL reported more clinically relevant fatigue up to 10 years post diagnosis than age matched controls. 22% reported deterioration in fatigue, 19–23% reported improvement in fatigue, 44–45% reported persistent fatigue	Survivors who reported greater fatigue were more likely to have stage IV disease and had more comorbid disease
Oerlemans *et al.* 2022 [26▪] Netherlands	Population registry study of 6786 long-term *cancer survivors*, including cohorts of patients with colon, rectum, prostate, thyroid cancer, Hodgkin lymphoma (HL), non-Hodgkin lymphoma (NHL), chronic lymphocyte leukaemia (CLL), multiple myeloma (MM) and melanoma Study to investigate the level of perceived cognitive functioning of cancer survivors	Age and sex matched non cancer normative population	PROs sent to a sub sample (76% response rate). EORTC QLQ-C30	Survivors reported lower self-perceived cognitive function than controls. Largest difference was for those with thyroid cancer HL, NHL, CLL and MM	Cognitive function was perceived as worse for survivors <50 years
Burrell *et al.* 2023 [23▪] USA	Retrospective cohort study of older adults treated for *breast cancer* before 1995–2015. Data collected from SEER database. Random sample of 34 706 patients sent QOL questionnaires. Study to identify differences in QOL for survivors of breast cancer treated at 3 different time periods	No comparator	Average age of participants 76.17 years 35% received treatment before 1995. 48% received treatment 1996–2005 18% received treatment 2006–2015	Higher comorbidity count and functional limitations was negatively associated with QOL. Those more recently diagnosed had poorer physical and mental health	Increased comorbidity as patients aged Better general health perceptions were associated with better QOL
Foster *et al.* 2021 [24] UK	Retrospective study of 8438 *breast cancer* survivors treated between 2006 and 2010 aged 40–70 years. Study explored the link between comorbidities and depression	No comparator	Data from a UK biobank linked with data from cancer registries in the UK. Self-reported comorbidities and PHQ-2 health questionnaire for depression	32.9% of women reported comorbidities and 30.1% experiencing 2 or more chronic health conditions. Hypertension, chronic pain, and asthma were the commonest reported conditions. 5.3% of women had depression	Women who had multiple comorbidities had a higher incidence of depression

Table 2. (*continued*)

Author and country	Population	Comparator	Timing and assessment	Late and chronic effects	Factors impacting occurrence of LE
Bentzen *et al.* 2013 [27] Norway	Retrospective survey of population of 199 people with *anal cancer* treated with chemo-radiation from 2000 to 2007. Survey sent out and 64% (n = 128) returned questionnaires	Comparative non cancer population age matched	Late effects were identified via QLQ-C30 and QLQ-CR29 questionnaires. Median time since treatment was 66 months (5.5 years)	Cancer survivors had poorer QOL than comparator group with significant ($P < 0.001$) impairment in physical function. Increased scores of fatigue dyspnoea and insomnia. Symptoms of diarrhoea, faecal incontinence, anal pain, and sexual dysfunction were common	Factors leading to greater symptoms not explored
Ekels *et al.* 2022 [12▪▪] Netherlands	Population registry study of 669 patients diagnosed between 1999 and 2014 for *indolent non-Hodgkin lymphoma* Study of long-term HRQOL and persistence of symptoms after treatment	Comparative non cancer population age and sex matched	PROs collected for EORTC QLQ-C30 and CLL-16 (74% response rate)	Up to one third experienced long-term symptoms. 36% reported persistent fatigue 33% persistent neuropathy 25% role functioning impairment Symptoms 2–3 times higher than controls	Those with comorbidities, psychological distress, younger age, shorter time since diagnosis and no partner were associated with worse outcomes ($P < 0.05$)
Kreiberg *et al.* 2020 [28] Denmark	Cross-sectional population study of men treated for *testicular cancer* between 2014 and 2916, 2252 men were sent questionnaires (PSS) Study to identify prevalence of stress post treatment	Comparative population (n = 61 927) of men without cancer sampled at random	Median time since diagnosis 19 years Stress determined by PSS scores of ≥16	Men with testicular cancer had higher levels of stress than reference population. Ratio = 1.56 (95% CI 1.40–1.73)	Those men who had received chemotherapy and radiotherapy had greater levels of stress
Hu *et al.* 2023 [29] USA	Cohort study of 18 134 men with *prostate cancer* between 2014 and 2017 Study to assess incidence of mental health disorders among men with prostate cancer	Comparison with 73 470 age, matched men without cancer	Data from electronic health records	Mood disorders, including depression among men with prostate cancer was higher than the general population even 10–16 years after treatment	Higher risk of mental health disorders among men from lower socioeconomic status ($P > 0.0001$) and increased duration of androgen therapy ($P < 0.03$)

AKI, acute kidney injury; BMT, bone marrow transplant; CHD, congestive heart failure; CRVFs, cardiovascular risk factors; CVD, cardiovascular disease; HCT, haematopoietic stem cell transplant; HF, heart failure; HR, hazards ratio; HRQOL, health-related QOL; IR, incidence ratio; IRR, incidence rate ratio; MI, myocardial infarction; PSS, perceived stress scale; QOL, quality of life.

of women with breast cancer reported two or more comorbidities and these were associated with depression (OR = 6.06, 95% CI 3.63–10.14). Chronic long-term symptoms and HRQOL impacts are also described in those previously treated for indolent NHL up to 10 years post diagnosis. This includes 36% of people reporting fatigue and 33% reporting neuropathy. For 25% of NHL survivors, this impacted HRQOL role functioning as measured by EORTC QLQ-C30 [12▪▪]. Fatigue was also reported as being significantly higher in those treated for NHL compared with a matched non-cancer population; 19–23% reported an improvement in fatigue over time and 44–45% reported constant fatigue up to 10 years post diagnosis [25]. Lower than average emotional functioning, cognitive problems and higher fatigue levels are seen in many cancer survivors (Table 2). In a study from the Netherlands, the largest difference in cognitive function from the comparative non-cancer

population was seen in those treated for thyroid and haematological cancers [26▪].

Those treated with chemoradiotherapy for anal cancer also reported a poorer QOL and worse social and role functioning as measured by EORTC QLQ-C30 than a non-cancer comparative population [27]. The high symptom burden of fatigue, diarrhoea, faecal incontinence, anal pain, impotence and reduced sexual interest all impacted HRQOL. Men treated previously for testicular cancer had higher levels of stress than men without cancer [28]; this was also the case for men with prostate cancer who had more mood disorders [29] than men without cancer of a similar age. Mental health disorders were higher in those with lower socioeconomic status and in men who had increased use of androgen deprivation therapy [29].

DISCUSSION

The objective of this review was to provide a broad overview of the prevalence of physical and emotional long term and late effects in adult survivors through analysis of recent published population and cohort studies. The data from 12 of these studies was compared with age-matched non-cancer controls. The value of this comparison is that this allows the researchers to calculate the excess comorbidity for cancer survivors over those who have not received cancer treatment and determine the functional and HRQOL impairments beyond normal ageing. Three studies used a 'within group' comparator of patients being treated for the same cancer, but treated differently, which meant they were more likely to have biases. Studies without comparators lack clarity as to whether these symptoms or emotional problems are cancer treatment related or within population norms. Comparisons to an age, sex and non-cancer matched population is very important in the interpretation of longitudinal findings to understand the nature of cancer as a chronic illness.

These mainly registry, data linkage and PROs studies describe a range of physical and emotional late effects that were experienced by people living with and beyond their cancer diagnosis. These large studies highlight that not everyone experiences long term and late effects, but recognise that a significant proportion experience fatigue, mood disorders and increased comorbidities months to years after cancer treatment. Studies identified in the review were predominantly focused on adult survivors with one predominantly looking at adults over 65 years of age. There is a dearth of studies that explore rarer cancers and analysis of cancer in ethnic populations. Few of the studies identified ethnicity or were able to explore ethnic differences in late effect prevalence. The advantage of using national or regional registry data is the inclusion of a wide geographic reach but also the inclusion of survivors who would be less likely to participate in clinical trials. This is because there are disparities in recruitment to clinical trials which are often based on performance status or access to specialist centres. Many clinical trials fail to actively recruit patients from ethnic and lower socioeconomic groups. Population registry data should therefore provide a wealth of information on patients' ethnicity and sociodemographic characteristics unfortunately registry and clinical records poorly report ethnicity and socioeconomic status.

CVRF were identified as significantly higher in cancer patients than those without cancer and these are often associated with cardiovascular late effects and poorer overall survival [13]. Comorbidities are increasingly being seen in younger people with hypertension and obesity becoming more prevalent in non-cancer populations. Identification of those cancer survivors at higher risk of CVD is important as guidelines recommend that healthcare professionals mitigate late effects with changes to therapy and comorbidity management [30]. The recent publication of international cardio-oncology guidelines provides an important clinical pathway for those at moderate to higher risk of CVD with a critique of assessment, long-term monitoring, and management [31▪▪]. Secondary prevention and lifestyle interventions reduce risks of both recurrence and CVD, but the challenge is in identifying those at higher risk of late effects and implementing early prehabilitation and lifestyle interventions through multi-disciplinary care [32,33]. Surveys highlight that adherence to guidelines for cancer survivors is suboptimal in both secondary and primary care [34,35]. A recent survey of medical oncologists in the United States found that only 46% provided survivorship care plans for women with breast cancer, 34% assessed for emotional distress and only 34% screened for additional cancers. Reasons listed were a lack of disease-specific training, lack of understanding of survivorship issues and that women were not routinely informed about potential late effects after treatment [36]. This study explored the medical roles, but there is also a need to consider the referral and access to the broader multi-professional team to address the wide range of problems that occur in cancer survivors. Clearly significant challenges still exist in the provision of survivorship care and management of late effects.

Observational and population studies can provide complementary evidence to guide knowledge translation [37]. Analysis of primary care records and linkage to clinical data can identify late effects, interpreting the association of comorbidities and

cancer treatment which can complement clinical trial data and inform clinical practice [38]. Clinical trials are constrained by several factors; selected populations, i.e. excluding those who are older, those in lower socioeconomic groups and those from ethnic minorities who are less likely to enter a clinical trial as well as the short follow-up after treatment. A recent review of published breast cancer clinical trials found that only 20% included patients over the age of 65 years and that only 50% reported toxicities [39]. This impacts the external validity of results [40,41]. Population and cohort studies can be useful for insights into rare cancers and exploring cancer treatment efficacy beyond clinical trials [42,43▪], providing real-world outcomes beyond that of the short time frame of clinical trials and highlighting long term and late effects of cancer treatment. Studies that included PROs increase the quality of information and measure the personal impact of symptoms on survivors HRQOL rather than what is documented in routine clinical records [44]. Random sample study populations collecting PROs [23▪,45] gave greater granularity and understanding of late effects that complemented the data linkage to clinical records but encountered challenges with increasing missing PROs data over time.

Consensus and policy groups have recognised evidence and service gaps in survivorship care and late effects management, across many countries and have called for better strategies and further research to improve the health of cancer survivors [46–49]. There have been calls for cancer care providers to adapt to changing cancer survivor demographics within older cancer populations but clearly, as seen in this review, late effects occur in those who are also younger with excess morbidity prevalent in all age groups compared with age-matched non-cancer populations. Improving coordination with primary care teams to provide services over a longer time-period is essential for all cancer patients [49,50▪,51]. These would provide not only assessment for recurrence, screening for second cancers, but a focus on optimising health through physical and emotional recovery underpinned by behavioural change [51–53].

CONCLUSION

Cancer survivors have a greater risk of chronic health and emotional problems than age-matched comparative populations. This review of population studies highlights the increased risk for CVD, AKI, hypothyroidism, fatigue, poorer cognition, and depression which impacted survivors' quality of life and for some overall survival. Most of these studies are on women with breast cancer and their long-term health impacts, but in the context of a growing number of survivors, there is a need for more population data studies on other cancer groups, such as head and neck cancer. We know very little about late effects in people treated for cancer from different ethnic groups and there is a need for more research in this area. These types of studies provide important information on demographic and clinical associations and the predictive risk of late effects. More research is needed on how we can use this information at point of therapy and beyond to mitigate long term and late effects. The future points to using such information to personalise survivorship care, so we can improve the recovery of cancer survivors and optimise individuals' physical and emotional health.

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Conflicts of interest

There are no conflicts of interest.

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- ▪ of special interest
- ▪▪ of outstanding interest

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