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Multimorbidity in patients living with and beyond cancer: protocol for a scoping review

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ABSTRACT

Introduction The number of people living with and beyond cancer is increasing rapidly. Many of them will experience ongoing physical or psychological sequelae as a result of their original cancer diagnosis or comorbidities arising from risk factors common to cancers and other long-term conditions. This poses the complex problem of managing cancer as a 'chronic' illness along with other existing comorbidities. This scoping review aims to map the literature available on multimorbidity in patients living with and beyond cancer, to explore, quantify and understand the impact of comorbid illnesses to inform work around cancer care in UK primary care settings.

Methods and analysis This review will be guided by Joanna Briggs Institute Reviewer's manual for scoping reviews. A systematic literature search using Medical Subject Heading and text words related to cancer survivors and multimorbidity will be performed in MEDLINE, CINAHL, Embase and Web of Science, from 1990. Results will be described in a narrative style, reported in extraction tables and diagrams, and where appropriate in themes and text.

Ethics and dissemination The scoping review will undertake secondary analysis of published literature; therefore, ethics committee approval is not required. Results will be disseminated through a peer-reviewed scientific journal and presented in relevant conferences. The scoping review will inform understanding of the burden of multimorbidity for cancer survivors, thus allow families, practitioners, clinicians and researchers to take the steps necessary to improve patient-centred care.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ A novel and original exploration of how multimorbidity impacts those living with and beyond cancer.
⇒ This review will extend the current reviews as it focuses on cancer survivors from the 10 most common cancers with highest survival rates.
⇒ It uses robust methodology following latest guidelines for scoping reviews.
⇒ Following the guidelines of scoping reviews, quality appraisal of included studies was not undertaken.

INTRODUCTION

The estimated number of patients living with and beyond cancer (sometimes called 'cancer survivors') is increasing rapidly in the UK; 50% of people diagnosed with cancer in England and Wales survive their disease for 10 years or more.[1] Currently, 1.8 million people are living with and beyond cancer in the UK.[2] This trend is also evident worldwide. In 2040, an estimated 28.4 million new cancer cases are expected to be diagnosed worldwide, up 47% from the 19.3 million cases diagnosed in 2020, assuming national rates remain constant.[3] Due to better screening, diagnosis and treatment, long-term survival for patients with cancer is improving and doubled in the last 40 years in the UK.[1] Worldwide, the population of patients living with and beyond cancer is expanding at a pace of around 2% each year.[3] This poses the complex problem of managing cancer as a 'chronic' illness along with other existing comorbidities.

Multimorbidity is defined as 'co-occurrence of multiple chronic or acute diseases and medical conditions within one person'.[4] Multimorbidity, as defined, encompasses comorbidity which is a medical condition that exists along with index condition, and is becoming an issue of growing importance. Nearly two-thirds of cancer survivors in the UK are over 65 years old,[5] many of whom already suffer from one or more comorbid illness.[6] Multimorbidity impacts every stage of cancer, from prevention to detection through to end-of-life care. It potentially affects the development, stage at diagnosis, treatment and outcomes of people with cancer.[7] Prevalence of one comorbid condition in patients with cancer ranges from 40% to 55% and prevalence of multimorbidity ranges from 15% to 27%.[8–10] Although the incidence of cancer among children and young adults is low, their high overall survival rates means that this group of patients living with and beyond cancer will be increasing in the next few decades. The current prevalence of cancer globally in the age group below 50 is 1%.[3] Patients with history of cancer are significantly more likely to report a comorbid condition compared with patients with non-cancer even after

adjustment for age.[11] The lack of systematic measurement of comorbidities in cancer clinical trials limits the evidence base for making informed decisions for this group of patients. In order to provide personalised care and support for these patients, types of multimorbidity and their impact need to be explored.[12]

Cancer treatment is associated with several long-term sequelae such as chronic fatigue, sexual dysfunction, anxiety, depression and lymphoedema among many others.[13–15] The detection of cancer may be influenced by multimorbidity, with some patients having their cancer diagnosed sooner due to frequent interactions with healthcare providers, while others being diagnosed later if they share the same symptoms as a comorbid disease, as in the case of chronic obstructive pulmonary disease (COPD) and lung cancer.[16] Patients with cancer and comorbidity are less likely to receive cancer treatment with curative intent.[8] The presence of comorbidity leads to the increased complexity of health needs for patients living with and beyond cancer, which cannot be catered for by current single-disease model. A call has been made[17] 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.

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 Better Cancer Care in Scotland.[2] In addition, the National Cancer Research Institute and James Lind Alliance[18] made significant effort to publish the 'the top 10 research priorities for people living with and beyond cancer'. The findings of this scoping review will particularly address research priority three—which is better coordination of care for people with complex health needs (ie, multimorbidity). Currently, the guidelines for improving life for patients with cancer have a single disease focus, limiting their application in patients with multiple comorbid illnesses. This is because little is known about the impact and burden of additional comorbidities in this group of patients, especially in the UK. Recognising and managing comorbid illnesses will allow new insights in developing a patient centred, personalised model of care—which is one of the main goals of the National Health Service in the UK.

STUDY OBJECTIVE

Multimorbidity impacts cancer survivors in many ways. Although some research has been conducted in multimorbidity and improving care for cancer survivors, there is little research to date linking cancer to multimorbidity and its impact on cancer survivors.[19] This scoping review aims to summarise published evidence exploring the association between cancer survivorship and other long-term conditions.

METHODS AND ANALYSIS

There are many potential approaches available when reviewing and synthesising the literature. Scoping reviews are recommended for mapping the existing literature and summarising the findings especially when a topic 'has not yet being extensively reviewed'.[20] Given the variability of the available literature on multimorbidity in cancer survivors and the breadth of the research aims of this study, a scoping review was deemed the most suitable type of review method for this study. Methods for this scoping review were developed based on the Joanna Briggs Institute Guidelines[21] and further enhanced by methodological guidelines developed by Levac *et al*, which describe six framework stages used below.[22] Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for scoping reviews (PRISMA-ScR)[23] will be followed to report the results of this scoping review.

Identifying the research question

Research questions were derived using the Population–Concept–Context acronym recommended by the Joanna Briggs Institute.[24] The *population* is adult cancer survivors, with cancer survivorship as defined or implied in the included articles. Cancer survivors from the 10 most common cancers with the highest survival rates in the UK will be included in this review to focus on the areas with greater need of interventions. The 10 cancers are: prostrate, breast, non-Hodgkin's lymphoma, bowel/colorectal, kidney, head and neck, bladder, leukaemia, uterine and myeloma.[1] The *concept* is the multimorbidity. Multimorbidity has been defined as the presence of two or more long-term conditions thus for the purpose of this review, multimorbidity is defined as the presence of any long-term condition in addition to the index cancer.[25] The *context* is any geographical setting and any care setting excluding paediatrics or childhood cancer centres. The types of evidence that will be included are peer-reviewed research articles using quantitative methodology published in English language. The inclusion and exclusion criteria are stated in table 1 below.

The overall research question for this scoping review is: what evidence is available around multimorbidity in adult cancer survivors? The following subquestions will be explored in relation to people living with and beyond cancer:

1. What is the reported prevalence of multimorbidity in patients living with and beyond cancer?
2. Is there any association between multimorbidity and ethnicity or social deprivation in cancer survivors?
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? (see explanation of health status below)
4. What are the reported risks of survivors experiencing adverse health consequences and multimorbidity arising from their cancer or cancer treatment?
5. Does being a cancer survivor affect the care received for multimorbidity, and in what way?

Table 1 Inclusion and exclusion criteria based on population–concept–context mnemonic

	Inclusion criteria	Exclusion criteria
Population	► Cancer survivors. ► Adult population (age ≥18). ► Participants assessed for the presence of multimorbidity. ► Patients with any of the 10 types of cancer specified in this review.	► Childhood cancer survivors.
Concept	Studies assessing: ► Multimorbidity burden. ► Quality of life in relation to multimorbidity. ► Multimorbidity as a result of cancer treatment. ► Healthcare use in relation to multimorbidity.	► Cancer related drugs/drug trials. ► Cancer was not the main focus of the study. ► Studies focusing on health behaviour.
Context	► Any geographical setting. ► Any care setting.	► Paediatric setting or childhood cancer centres.
Type of evidence	► Publications after 1990 and before 2021. ► English articles. ► Peer-reviewed articles. ► Primary research only. ► Quantitative and mixed-methods study design.	► Reviews, commentaries and editorials. ► Qualitative study design. ► Grey literature.

Health status may include, but is not limited to: quality of life (QoL), health-related quality of life measurements, instruments that are used to assess QoL such as the Patient Health Questionnaire (PHQ)−9 to evaluate depression; the Generalised Anxiety Disorder Scale−7 for anxiety; PHQ-15 for somatisation; and the WHO Quality of Life Instrument-Short Form (Bref); activities of daily living (disability-adjusted life year).

Identifying relevant studies

The following databases will be searched for articles published between 1990 and 2021 (inclusive): MEDLINE, CINAHL, Embase and Web of Science. The year 1990 was chosen as the cut-off date because 'comorbidity' was introduced as a Medical Subject Headings (MeSH) term in 1990. Also, cancer mortality started declining in the 1990s.[26] The search will be carried out using Ovid platform for MEDLINE and Embase and other databases will be searched through their own searching platforms. To ensure inclusion of all relevant studies, reference lists of included studies (forward and backward citation) will be screened for new articles. To ensure transparency and replicability, the MeSH search strategy that will be adopted is presented here (box 1). The search strategy was developed in consultation with an experienced medical librarian. As scoping reviews are iterative, it is expected that the proposed search terms may need to be refined as the extent of literature is explored.[27]

Study selection

Studies will be considered for inclusion if they relate to multimorbidity in cancer survivors. To facilitate the study selection process, literature search results will be uploaded to the EndNote reference management software. From these references, the exclusion process will be documented. A two-stage process will be followed using the inclusion and exclusion criteria by two authors independently. At first, authors will screen titles and then abstracts of the searched studies and record their decisions on an eligibility form. Any disagreements between the two authors will be discussed among themselves first; if not resolved, then it will be reviewed by a third author. To resolve question on eligibility, additional information from the authors will be sought when required. After screening titles and abstracts, the two authors will also read and consider the full papers for the review independently; those articles omitted will have reported evidence as to why this was appropriate. Reasons for exclusion will be recorded. Number of studies identified and selected will be presented in the results section using the standard PRISMA flowchart following the PRISMA guidelines.[28] Details of the review decision process with regards to identification, screening, eligibility and included studies will be shown in this flowchart.

Extracting and charting the results

Two authors will read the articles independently and record data extraction in a charting form. Data extracted will include general study information, methodology, definition of multimorbidity, definition of survivorship, intervention details and all reported outcomes relevant to the review. The purpose of the data charting process is to produce a detailed description of the findings corresponding to this scoping review's objective and research questions. To help collect and sort key pieces of information from the selected articles, a concept charting form has been created (see box 2). The charting process in a scoping review is iterative, hence the charting form will be continuously updated.[24] A formal quality assessment will not be conducted as it is not part of the scoping review methodology.[27]

Collating, summarising and reporting the results

Due to the heterogeneity of the available evidence, meta-analysis and statistical methods of synthesis will not be performed. The aim of the scoping review is to summarise the reported results that have been conducted in this area and provide a narrative summary. An overall summary of all papers will be presented in a table format using the extraction chart as a guide. Then, findings will

Box 1 MeSH (Medical Subject Headings) terms/Text words

Cancer

1. (neoplasm$ or cancer$ or tumor$ or tumour$ or carcinoma$ or leukem$ or leukaem$ or malignan$ or oncolog$).ti,ab.
2. (breast cancer or mammary cancer or breast carcinoma or breast metastasis).ti,ab.
3. (prostat$ or prostatic adenocarcinoma or prostatic carcinoma or cancerous prostate or metastatic prostate cancer).ti,ab.
4. (non-hodgkin$ lymphoma or NHL or chronic lymphocytic leukemia or small lymphocytic lymphoma or Burkitt lymphoma or CLL or SLL or $lymphoma$).ti,ab.
5. (bowel or colorectal or colon or rectum or anal or small bowel or large bowel).ti,ab.
6. (kidney or renal cell adenocarcinoma or renal cell).ti,ab.
7. (head and neck or larynx or throat or lips or mouth or nose or salivary gland$ or $nasal or laryngeal or oesophageal or tonsil or pharyngeal or tongue).ti,ab.
8. (bladder or urolethial or urinary bladder or squamous cell bladder or adenocarcinoma bladder).ti,ab.
9. (Leukaemia or Leukemia or Acute myeloid leuk$ or AML or acute lymphoblastic leuk$ or ALL or chronic myeloid leuk$ or CML or chronic lymphocytic leuk$ or CLL or Hairy cell leuk$).ti,ab.
10. (uterine or uterus or womb or uterine sarcoma or endometrial).ti,ab.
11. (myeloma or multiple myeloma or light chain myeloma or non-secretory myeloma or plasma cell).ti,ab.
12. exp humans/ not animals.sh. not Drug Design/
13. 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
14. 1 and 12 and 13

Comorbidity

15. Comorbidity/
16. (Multimorbid$ or multi-morbid$ or Co-morbid$).ti,ab.
17. Chronic Disease/ or (Chronic adj5 (illness$ or condition$ or disease)).ti,ab.
18. (Long term adj5 (condition$ or illness$ or disease$)).ti,ab.
19. 15 or 16 or 17 or 18

Impact of comorbidity

20. Prevalence/ or Incidence/
21. Quantitative Research/ or Quantitative.mp
22. Primary care.mp. or Primary Health Care/ or Secondary care.mp. or Secondary Care/ or Community Care.mp or Community Health Services/ or Ambulatory Care.mp. or Ambulatory Care/ or Delivery of Health Care/ or Integrated/ or Preventive Health Services/ or Family Practice/ or Shared care.mp or Collaborat$ care.mp
23. Health/ or Health status/ or Health Status Indicator/ or Mental Health/
24. Survival Analysis/ or Progression-free survival/ or disease-free survival/ or Overall Survival/
25. (Well-being or Well being).mp. or Holistic.mp or Continuity of Care.mp or Continuity of Patient Care/ or (Fragmented adj5 care).mp or (joined-up or Joined Up).mp or Integrated care.mp or Diversity of Care.mp.
26. Psychosocial.mp. or Stress, Psychological/ or Social Support/ or Psycho-social.mp or Quality of Life/ or Experience of Illness.mp or Experience adj5 Illness or Attitude to Health/ or Quality of Life.mp or Happ$.mp or Emotion$.mp. or Emotions/
27. Patient satisfaction.mp. or Patient Satisfaction/ or Quality of Health Care/ or Delivery of Health Care/ or Patient Experience.mp or Satisfaction.mp or Information Preferences.mp
28. Access to Health Care.mp. or Health Services Accessibility/ or Life Change Events/
29. (Patient-centred care or Patient centred care or Patient-centred or Person-centred or Patient centred or Person centred).mp or Patient-Centered Care/
30. Survivor$.mp. or Survivors/ or Living with and beyond cancer.mp.
31. Epidemiology
32. 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31
33. 14 and 19 and 31

be grouped according to the subquestions in this review. For example, question one focuses on prevalence of multimorbidity in cancer survivors. For this section, a summary of reported prevalence of multimorbidity from all included studies will be presented in tabulated form and the key findings will be provided as textual summary. The process will then be iterated for each question in this review. A section summarising how 'cancer survivorship' or 'multimorbidity' was defined in the studies will also be included.

The quantitative outcomes will be assessed using the following measurements (if they are available in the paper):

- Reported prevalence or multimorbidity in cancer survivors in the different types of cancer.
- Reported incidence and prevalence of comorbidity/multimorbidity arising from cancer treatments.
- Any other numerical outcomes related to multimorbidity will be summarised.

Ethics and dissemination

This protocol describes the scoping review that will conduct secondary analysis of data already published in the literature. Therefore, it does not require ethical approval. Results will be disseminated through a peer-reviewed publication. In addition, results will be disseminated through networks of scientists, healthcare professionals and cancer survivorship researchers, as well as at relevant conferences.

Patient and public involvement

No patient involved.

Box 2 : Draft data charting form

- ⇒ Author.
- ⇒ Year of publication.
- ⇒ Country and setting where the study was published/conducted.
- ⇒ Study population.
- ⇒ Study design (eg, observational, randomised controlled trial) and study size.
- ⇒ Cancer site/s included.
- ⇒ Definition of cancer survivorship (if available).
- ⇒ Outcomes of relevance to the review.

DISCUSSION

The scoping review's objective is to explore and map how multimorbidity has been reported to impact patients living with and beyond cancer. It is anticipated that this review will build on the knowledge base to support evidence based and conceptually informed personalised model of care.

The purpose of this a priori protocol is to guide the authors in the review process, enhance methodological rigour and increase transparency around how results are obtained. The results of this scoping review will inform a broad audience. This includes cancer survivors, their families, healthcare practitioners and researchers with an interest to gain a better understanding of the impact of multimorbidity in cancer survivors. Assessment of the prevalence of multimorbidity in this patient group underpins healthcare planning. Policymakers need assessments of burden of disease if they are to plan and resource services that can effectively reduce the burden of cancer. The insights obtained from this review will make a significant contribution to care pathways of patients with cancer with other long-term conditions. This is becoming increasingly important given the growing rate of cancer, particularly in an ageing population and the shifting emphasis on patient care.

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Competing interests None declared.

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