BMJ Open

Psychological aspects in patients with advanced cancer receiving lifelong systemic treatment: protocol for a scoping review

Evie E M Kolsteren ,[1] Esther Deuning-Smit,[1] Judith B Prins,[1] Winette T A van der Graaf,[2,3] Carla M L van Herpen,[4] Sophie Lebel,[5] Belinda Thewes,[6] Linda Kwakkenbos,[7] José A E Custers[1]

To cite: Kolsteren EEM, Deuning-Smit E, Prins JB, *et al*. Psychological aspects in patients with advanced cancer receiving lifelong systemic treatment: protocol for a scoping review. *BMJ Open* 2021;**11**:e042404. doi:10.1136/bmjopen-2020-042404

► Prepublication history and additional material for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2020-042404).

EEMK and ED-S contributed equally.

Received 06 July 2020
Revised 29 December 2020
Accepted 10 January 2021

For numbered affiliations see end of article.

Correspondence to
Evie E M Kolsteren;
evie.kolsteren@radboudumc.nl

ABSTRACT

Introduction A better understanding of the molecular, genetic and immunological characteristics of cancer and the introduction of new systemic treatment regimens in the last decades, has led to better treatment outcomes and increased survival rates for patients with previously short lived cancers. However, there is no uniform description to refer to this growing group of patients with advanced cancer who now respond to new systemic treatments for longer periods. Furthermore, little is known about the unique psychological challenges these patients face, living with ongoing uncertainty about the course of their disease and life expectancy. The objective of this scoping review is to identify the psychological aspects experienced by, and the definitions used to refer to patients with advanced cancer receiving lifelong systemic treatment.

Methods and analysis This review will be among the first to summarise literature on the psychological issues in the growing group of advanced cancer patients undergoing long-term systemic treatment. Articles will be retrieved from six databases (MEDLINE, Embase, Web of Science, PsycINFO, CINAHL and the Cochrane Database of Systematic Reviews) and reviewed for eligibility by two investigators independently. Definitions and psychological challenges will be extracted and narratively summarised following a descriptive approach. Furthermore, results will contribute in providing a uniform definition for this patient group, and help to identify knowledge gaps to give direction to further research in this field.

Ethics and dissemination No ethical approval is required. The results of the scoping review will be submitted for publication to a scientific journal and presented at relevant conferences.

Strengths and limitations of this study

- This scoping review is a first step to summarising knowledge in the unexplored field of psychological aspects of living with advanced cancer and receiving lifelong systemic treatment.
- An extensive literature search will be performed using six databases with a peer-reviewed search strategy according to the scoping review guidelines.
- The absence of an existing consensus on the definition of our target group could have consequences for the specificity of the search strategy.

INTRODUCTION

Recently, there have been major improvements in survival rates for some cancers with a previously poor prognosis, as a result of the increased understanding of the molecular, genetic and immunological basis of cancer and the introduction of new systemic treatment regimens. An example is the development of immunotherapies, which has transformed the treatment paradigm for many patients with cancer. In particular, monoclonal antibodies targeting the programmed cell death 1 receptor (PD-1) and its ligand, PD-L1, have exhibited impressive activity and have become standard therapy for several types of cancer such as melanoma, non-small-cell lung cancer and lymphoma.[1] Furthermore, identification of several types of cancer as mutation driven has facilitated the development of therapies such as targeted kinase inhibitors, which has revolutionised treatment options and outcomes. For example, imatinib mesylate was found to improve the recurrence-free survival for advanced unresectable or metastatic gastrointestinal stromal tumours (GIST), the most common sarcoma of the intestinal tract, as first-choice treatment option.[2–4] Sunitinib has been approved as the second-line treatment and regorafenib as third-line treatment of metastatic GIST, providing unresectable or metastatic patients a prolonged survival from less than 1 year prior to the development of these therapies to more than 5 years at the present time.[5 6] However, while studies have mainly focused on evaluating new treatments in terms of progression-free and overall survival rates,

little is known about the psychological, emotional and social challenges patients face when living longer with advanced cancer and receiving ongoing treatment.[7]

Existing literature and treatment guidelines document the physical and psychological impact of cancer diagnosis, treatment and side effects, both in the curative and palliative setting. By contrast, patients with advanced cancer on lifelong therapy have not yet been well studied, though diagnoses of incurable cancer and lifelong treatment with possible side effects can have substantial consequences for patients, their families, workplaces and healthcare resources in the coming years. These patients have very limited or no options for cure and must cope long term with a life-limiting illness. Literature suggests that uncertainty about the future accounts for a considerable emotional burden for patients with cancer and their relatives,[8–10] but little is known about the psychological burden of living with long-term continuing uncertainty. While the new medical treatments show promising results, it is often unknown whether an individual patient will respond to the treatment and if so, how long until progression of disease occurs. This may lead to feelings of fear, anxiety, hopelessness and helplessness.[8 9] Furthermore, most treatment regimens are accompanied with frequent medical procedures including scans, which might induce scan-associated distress, anxiety, fear of progression and uncertainty, which makes decisions on how to arrange extended lifetime even more challenging.[11]

An important barrier to summarising the literature on psychological challenges in patients with advanced cancer receiving lifelong treatments is the absence of a unified definition of this group. Authors have referred to this group as 'patients with metastatic cancer',[10] 'patients with incurable cancer',[9 12] 'patients with advanced cancer',[7 13 14] 'patients with chronic cancer'[15] and 'metastatic cancer survivors'.[9] Defining this specific patient group might be challenging but is an essential step in order to develop optimal care models and guidelines and to synthesise the available evidence relating to this group of patients.[16] To date, no studies systematically mapped the findings on psychological aspects in the group of patients with advanced cancer receiving lifelong treatments. Therefore, in order to fully explore this area, a broad literature overviewwould be an adequate first step to gain insight, and it might give direction to future research and aid healthcare providers to address psychological well-being in clinical practice.

Objectives

The overall objective of this scoping review is to identify, summarise and synthesise knowledge about psychological aspects in patients with advanced cancer receiving lifelong treatment. More specifically, this review aims to answer the following questions:

- What is known about psychological aspects and concepts that are relevant for this patient group?
- What descriptions or definitions are used to refer to this patient group?
- What are the knowledge gaps regarding psychological aspects in patients with advanced cancer?

METHODS AND ANALYSIS

A scoping review is rigorous like a systematic review, however, in contrast to a systematic review it serves the purpose of exploring a broader topic by summarising key concepts, types of evidence and research gaps, regardless of study design and quality.[17] The scoping review will be conducted following the five stages of the framework of Arksey and O'Malley[17] and later adaptations of Levac *et al*.[18] and The Joanna Briggs Institute[19]: (1) identifying the research questions; (2) identifying eligible studies (search terms and inclusion/exclusion criteria); (3) study selection; (4) charting the data and (5) collating, summarising and reporting the results. The results will be reported according to the guideline Preferred Reporting Items for Systematic Reviews and Meta-Analysis: extension for Scoping Reviews (PRISMA-ScR).[20]

Stage 1: identifying the research questions

The research question was developed and refined through an iterative process, leading to the following: 'What has been reported about the psychological aspects in patients with advanced cancer receiving life-long systemic treatment?'. An exploratory search in PROSPERO, the international prospective register of systematic reviews of the National Institute for Health Research,[21] and the Cochrane library, revealed no comprehensive reviews addressing a similar research question.

Stage 2: identifying relevant studies

Searches are aimed to include studies that involve adult patients (≥18 years of age) with a current diagnosis of advanced cancer receiving lifelong systemic treatment including targeted therapy, immunotherapy, hormone therapy or chemotherapy. Studies on patients receiving treatment with curative intent or end-of-life care will be excluded. Studies must describe at least one psychological outcome in this patient population as a primary outcome, for instance psychological symptoms, psychiatric disorders, emotions, distress, quality of life, coping, concepts like uncertainty, hope or optimism, or patients' needs and concerns. Both non-empirical articles (eg, expert opinion papers) and empirical quantitative or qualitative articles (eg, trials or interview studies) will be assessed. Eligible conference abstracts and abstracts of non-published papers will only be included on account of finding the full text paper.

Project team members identified key free text and index terms based on a preliminary search in MEDLINE. The MEDLINE strategy was further refined in collaboration with an academic librarian with expertise in systematic and scoping review searching, and peer reviewed similar to the methods described in the Peer Review of Electronic Search Strategies (PRESS) guideline.[22] Decisions regarding use of free-text fields, focus of subject headings and filters were guided by a balance between

completeness and feasibility, as recommended in scoping review guidelines.[18 23] The MEDLINE strategy (online supplemental material 1) was then adjusted to the electronic databases Embase, CINAHL, PsycINFO, Web of Science and the Cochrane Database of Systematic Reviews, tailoring vocabulary and syntax for optimal electronic searching. The search strategy will be limited to studies published after 2000, since new systematic treatment options for advanced cancer emerged in the last two decades, and will not be limited by language. Additional eligible articles will be identified through hand searching the reference lists of the final selected articles.

Stage 3: study selection

Results retrieved from all databases will be imported into the reference management software EndNote[24] and duplicate references will be removed using the comprehensive stepped procedure described by Bramer *et al*.[25] The references will then be transferred into Rayyan, a web application for systematically reviewing literature, to log the screening process and to visualise disagreements in screening between researchers.[26] Study selection will be performed in three steps. First, a manual based on the above mentioned inclusion and exclusion criteria will be developed. The manual will be pilot tested in a sample of 100 references and adapted if necessary. Second, title and abstract of all references will be assessed on eligibility by two researchers independently. Disagreements will be discussed until consensus is reached, and if necessary by consulting a third independent researcher. Third, full-text articles will be independently reviewed on eligibility by two researchers. Disagreements will again be discussed to reach consensus on final inclusion. A PRISMA-ScR flow chart will be developed to report the whole process of selection of articles.[20]

Stage 4: charting the data

A standardised data extraction form will be developed. First, two researchers will independently apply this form to a subsample of the included articles (ie, 10%) and compare the results in order to ensure consistency in data extraction. If necessary, the data extraction form will be revised by an iterative process in consultation with the research team until consensus is reached. Second, complete data extraction will be performed by one researcher and verified by a second researcher. Extraction results will be discussed at several moments during the review process until consensus is reached, if necessary by involving a third researcher.

We anticipate to extract the following data: (1) author(s); (2) publication year; (3) country; (4) publication type and/or study design; (5) sample size and patient characteristics; (6) reported psychological aspects; (7) methods for data collection and analysis; (8) psychological measurement instruments; (9) results of reported psychological aspects; (10) terminology used to refer to 'advanced cancer patients'; and if applicable (11) definition of 'advanced cancer'. The Standard Quality Assessment Criteria for Evaluating Primary Research Papers, containing one checklist for qualitative studies and one checklist for quantitative studies will be used to assess the quality of articles.[27]

Stage 5: collating, summarising and reporting the results

First, the individual study characteristics will be presented in tables, providing an overview of study designs, patient populations, reported psychological outcomes, psychological measurement instrumentsand analysis methods that have been used to study the psychological aspects in advanced cancer patients. Second, reported psychological aspects will be summarised. Findings from the quantitative studies will be narratively summarised. Findings from the qualitative studies as reported in the results sections will be extracted and synthesised into overarching psychological themes. We will choose an appropriate qualitative synthesis method in accordance with the nature of the original papers. Third, an overview of the terminology and definitions used to refer to advanced cancer patients on lifelong systemic treatment will be given. Elaboration on this overview will guide in providing a uniform definition. The overall synthesis of the available literature contributes to the identification of knowledge gaps to guide further research in this area.

Patient and public involvement

No patient involved.

ETHICS AND DISSEMINATION

A scoping review does not require ethical approval since it synthesises publicly available literature. The results of the scoping review will be submitted for publication to a scientific journal and presented at relevant conferences.

Author affiliations
[1]Medical Psychology, Radboud Institute for Health Sciences, Radboud university medical center, Nijmegen, The Netherlands
[2]Medical Oncology, Netherlands Cancer Institute, Amsterdam, The Netherlands
[3]Medical Oncology, ErasmusMC Cancer Insititute, Erasmus University Medical Center, Rotterdam, The Netherlands
[4]Medical Oncology, Radboud Institute for Health Sciences, Radboud university medical center, Nijmegen, The Netherlands
[5]School of Psychology, University of Ottawa, Ottawa, Ontario, Canada
[6]School of Psychology, Sydney University Medical Society, Camperdown, New South Wales, Australia
[7]Clinical Psychology, Radboud University Behavioural Science Institute, Nijmegen, The Netherlands

Acknowledgements The authors gratefully acknowledge the helpful comments of the research group and consulted stakeholders.

Contributors EEMK, ED-S and JAEC conceived the study, outlined the protocol and are guarantor of the review. EEMK and ED-S contributed equally to this work. JBP, WTAvdG, CMLvH, SL, BT and LK further revised the paper and approved the final text.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

ORCID iD

Evie E M Kolsteren http://orcid.org/0000-0003-2590-9352

REFERENCES

1 Nipp RD, Gainor JF. A coming of age for immune checkpoint inhibitors in cancer. *Immunotherapy* 2019;11:647–50.
2 Blanke CD, Demetri GD, von Mehren M, *et al*. Long-Term results from a randomized phase II trial of standard- versus higher-dose imatinib mesylate for patients with unresectable or metastatic gastrointestinal stromal tumors expressing kit. *J Clin Oncol* 2008;26:620–5.
3 DeMatteo RP, Ballman KV, Antonescu CR. American College of surgeons Oncology Group (ACOSOG) intergroup adjuvant GIST study Team. adjuvant imatinib mesylate after resection of localised, primary gastrointestinal stromal tumour: a randomised, double-blind, placebo-controlled trial. *Lancet* 2009;373:1097–104.
4 Demetri GD, von Mehren M, Blanke CD, *et al*. Efficacy and safety of imatinib mesylate in advanced gastrointestinal stromal tumors. *N Engl J Med* 2002;347:472–80.
5 Demetri GD, van Oosterom AT, Garrett CR, *et al*. Efficacy and safety of sunitinib in patients with advanced gastrointestinal stromal tumour after failure of imatinib: a randomised controlled trial. *Lancet* 2006;368:1329–38.
6 Demetri GD, Reichardt P, Kang Y-K, *et al*. Efficacy and safety of regorafenib for advanced gastrointestinal stromal tumours after failure of imatinib and sunitinib (grid): an international, multicentre, randomised, placebo-controlled, phase 3 trial. *Lancet* 2013;381:295–302.
7 Rogiers A, Boekhout A, Schwarze JK, *et al*. Long-Term survival, quality of life, and psychosocial outcomes in advanced melanoma patients treated with immune checkpoint inhibitors. *J Oncol* 2019;2019:1–17.
8 Dunn J, Watson M, Aitken JF, *et al*. Systematic review of psychosocial outcomes for patients with advanced melanoma. *Psychooncology* 2017;26:1722–31.
9 Langbaum T, Smith TJ. Time to study Metastatic-Cancer survivorship. *N Engl J Med* 2019;380:1300–2.
10 Levy D, Dhillon HM, Lomax A, *et al*. Certainty within uncertainty: a qualitative study of the experience of metastatic melanoma patients undergoing pembrolizumab immunotherapy. *Support Care Cancer* 2019;27:1845–52.
11 Bauml JM, Troxel A, Epperson CN, *et al*. Scan-associated distress in lung cancer: Quantifying the impact of "scanxiety". *Lung Cancer* 2016;100:110–3.
12 Okuyama T, Akechi T, Mackenzie L, *et al*. Psychotherapy for depression among advanced, incurable cancer patients: a systematic review and meta-analysis. *Cancer Treat Rev* 2017;56:16–27.
13 Coens C, van der Graaf WTA, Blay J-Y, *et al*. Health-Related quality-of-life results from PALETTE: a randomized, double-blind, phase 3 trial of pazopanib versus placebo in patients with soft tissue sarcoma whose disease has progressed during or after prior chemotherapy-a European organization for research and treatment of cancer soft tissue and bone sarcoma group global network study (EORTC 62072). *Cancer* 2015;121:2933–41.
14 Thewes B, Husson O, Poort H, *et al*. Fear of cancer recurrence in an era of personalized medicine. *J Clin Oncol* 2017;35:3275–8.
15 Efficace F, Breccia M, Cottone F, *et al*. Psychological well-being and social support in chronic myeloid leukemia patients receiving lifelong targeted therapies. *Support Care Cancer* 2016;24:4887–94.
16 Surbone A, Tralongo P. Categorization of cancer survivors: why we need it. *J Clin Oncol* 2016;34:3372–4.
17 Arksey H, O'Malley L. Scoping studies: towards a methodological framework. *Int J Soc Res Methodol* 2005;8:19–32.
18 Levac D, Colquhoun H, O'Brien KK. Scoping studies: advancing the methodology. *Implement Sci* 2010;5:69.
19 The Joanna Briggs Institute. Methodology for JBI Scoping Reviews Joanna Briggs Institute Reviewers' Manual Edition, 2015. Available: http://joannabriggs.org/assets/docs/sumari/Reviewers-Manual_Methodology-for-JBIScoping-Reviews_2015_v2.pdf [Accessed 9 Sep 2019].
20 Tricco AC, Lillie E, Zarin W, *et al*. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med* 2018;169:467.
21 National Institute for health research. *Prospero*, 2019.
22 McGowan J, Sampson M, Salzwedel DM, *et al*. PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. *J Clin Epidemiol* 2016;75:40–6.
23 Colquhoun HL, Levac D, O'Brien KK, *et al*. Scoping reviews: time for clarity in definition, methods, and reporting. *J Clin Epidemiol* 2014;67:1291–4.
24 Endnote. Endnote, 2019. Available: www.endnote.com [Accessed Mar 2020].
25 Bramer WM, Giustini D, de Jonge GB, *et al*. De-duplication of database search results for systematic reviews in endnote. *J Med Libr Assoc* 2016;104:240–3.
26 Ouzzani M, Hammady H, Fedorowicz Z, *et al*. Rayyan-a web and mobile APP for systematic reviews. *Syst Rev* 2016;5:210.
27 Kmet LML, Cook, LS RC. *Standard quality assessment criteria for evaluating primary research papers from a variety of fields. Alberta heritage foundation for medical research (AHFMR*. Edmonton: AHFMR - HTA Initiative #13, 2004.