



Current state of funded National Institutes of Health grants focused on individuals living with advanced and metastatic cancers: a portfolio analysis

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Abstract

Purpose The National Cancer Institute has supported cancer survivorship science for many years, yet few funded studies have examined the needs of individuals living with cancer that is advanced or has metastasized. This report analyzes currently active National Institutes of Health (NIH) grants focused on survivorship for patients living with advanced or metastatic cancers to identify emerging research topics in this population and gaps in current science.

Methods A search of all NIH research grants that received funding in Fiscal Year 2020 focused on this population was conducted, excluding grants with a primary focus on end-of-life care, tumor progression or staging and grants for which the only outcome was survival.

Results A total of 25 active grants met the inclusion criteria. Most were funded using the R01 grant mechanism and included a range of cancer types and topics such as palliative/supportive care, psychosocial support, health services, and symptom sequelae.

Conclusions Although currently funded grants focus on several important topics, gaps in the portfolio remain. There is a need to enhance the grant portfolio of research studies focused on the longitudinal examination of unmet needs, models of care delivery, impact of innovative therapies, and the impact of financial hardship for individuals living with advanced or metastatic cancer.

Implications for Cancer Survivors This review of current NIH studies suggests a need for expanded research on individuals living with advanced or metastatic cancer. Moving forward, enhancing research focused on key gap areas will be critical to improve care and outcomes for this growing population.

Keywords Metastatic cancer · Survivorship · Advanced cancer · Cancer survivor

Introduction

There were an estimated 16.9 million cancer survivors in the USA in 2019 [1], and this number is expected to grow. Patients living with advanced or metastatic cancer represent a survivor population that is markedly different from those who were diagnosed at earlier stages and who are treated with curative intent. Those with advanced or metastatic disease are a diverse population that is living longer (likely due to advances in innovative therapies and supportive care) and has

significant unmet needs in areas such as symptom management, psychosocial support, and health services [2]. Though much research on advanced/metastatic cancer survivors has been focused on end-of-life needs, it is critically important to address the other needs of those living with cancer [3].

The National Cancer Institute (NCI) within the National Institutes of Health (NIH) has invested substantial funds in survivorship science for several decades. Much research has targeted the needs of cancer survivors, including describing, preventing, and managing short- and long-term physiological and psychosocial sequelae. The extent and breadth of funded research that has focused on advanced/metastatic cancer survivors, however, is unknown.

Thus, to describe research that is currently being conducted and identify gaps in the science, we examined active NIH grants focused on the needs of those living with advanced or metastatic cancer. Specifically, we aimed to answer the following questions: (1) what are the key characteristics of the

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populations studied (e.g., cancer type, age, sex, inclusion of caregiver, focus on underserved population); (2) what are the primary areas of focus and research designs (intervention versus observational) among the studies; and (3) what are the scientific gaps in the NIH grant portfolio?

Methods

This analysis examined all NIH research project, training, and cooperative agreement grant awards with human subjects that received funding for any year of their grant between October 1, 2019, and September 30, 2020. We utilized key words to identify grants that focused on populations with advanced or metastatic cancer and identified 1033 active awards (Fig. 1). After excluding 772 studies of non-human animals, we reviewed the remaining 261 active grants for possible inclusion.

Our primary focus was understanding current NIH research focusing on the survivorship needs of individuals diagnosed with advanced or metastatic disease. We excluded grants that focused on end-of-life care, tumor progression or staging, as well as grants for which overall survival was the only outcome, to avoid overlap with the well-described existing evidence on these topics. We identified 25 active grants for this analysis after reviewing titles and abstracts, project aims, and eligibility criteria (Fig. 1).

Coding procedures were consistent with prior NIH-wide portfolio analyses [4]. After extracting general grant characteristics (e.g., NIH Institute, funding mechanism, funding opportunity announcement (FOA)), two co-authors (MAM, LG)

extracted, separately coded, and then compared all 25 grants for selected characteristics (Table 1). To code primary area of focus, we utilized topics from a previous review of NIH survivorship grants [5]. Differences in coding were discussed to reach consensus about coding decisions.

Results

The 25 grants were funded by four NIH Institutes, with NCI funding 16 grants (64%) and the National Institute for Nursing Research funding 6 grants (24%) (see Table 1). Over half of the grants were funded through R01 grants (60%). Nine grants focused on patients with multiple specified cancer types; four grants did not specify a specific cancer type, four grants focused on breast cancer only, and two grants focused on lung cancer only. One grant was not specific to cancer type, but instead focused on individuals who received targeted therapies.

Nearly all grants included only middle-aged or older adult cancer survivors (96%), with one grant focused on adolescent and young adult (AYA) survivors. Most grants included both females and males (84%). Caregivers were included in eight grants, with the majority (28%) including both the caregiver and the survivor. Nine grants (36%) focused on one or more minority and/or medically underserved population (e.g., rural, older adult, African American, Hispanic/Latino, or low-income survivors).

The primary area of focus among the grants was most often early palliative/supportive care (28%) or psychosocial support (24%). Other areas of focus included physiological sequelae

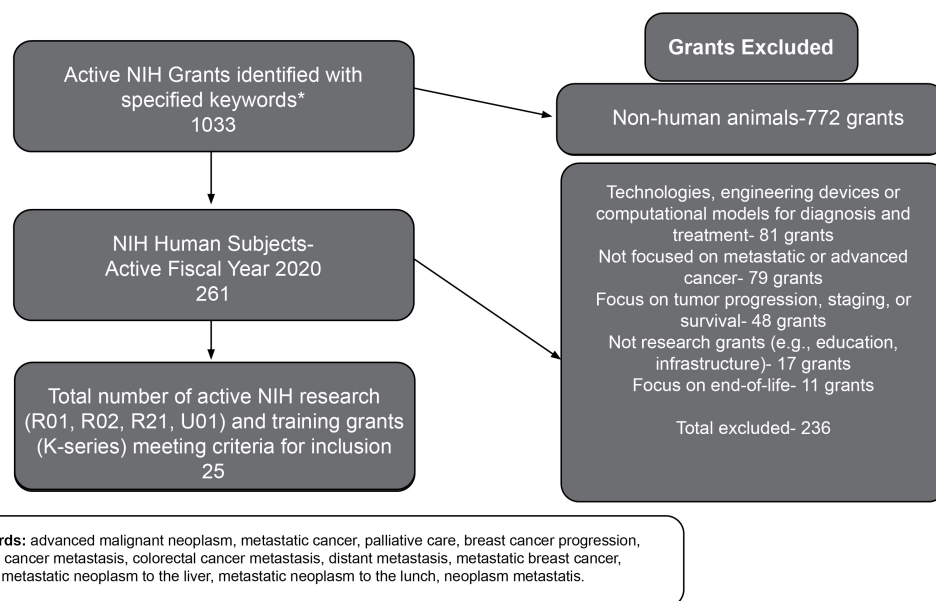


Fig. 1 Flow diagram for selection of NIH-funded metastatic/advanced cancer survivorship grants

Table 1 Characteristics of active NIH grants focused on individuals living with advanced and metastatic cancers ($n=25$)

Characteristic	<i>n</i> (%)
Funding institute	
National Cancer Institute	16 (64)
National Institute of Nursing Research	6 (24)
National Institute on Aging	1 (4)
National Institute of Arthritis and Musculoskeletal and Skin Diseases	2 (8)
Grant mechanism	
R01	15 (60)
R21	4 (16)
K07, K08, K23, K99 (Training grants)	4 (16)
R03	1 (4)
U01	1 (4)
Funding opportunity announcement (FOA) type	
Targeted FOAs	12 (48)
Investigator initiated FOA	8 (32)
Mentored Training FOA	5 (20)
Cancer type	
Multiple specified cancer types	9 (36)
Any cancer type	4 (16)
Breast cancer only	4 (16)
Any cancer based on metastases	2 (8)
Lung cancer only	2 (8)
Any cancer based on treatment	1 (4)
Gastrointestinal cancers only	1 (4)
Prostate cancer only	1 (4)
Gynecological cancers	1 (4)
Primary area of focus	
Palliative/ supportive care	7 (28)
Psychosocial support	6 (24)
Physiological sequelae only	5 (20)
Physiological and psychosocial sequelae	3 (12)
Health behaviors (physical activity)	3 (12)
Polypharmacy	1 (4)
Time since metastatic diagnosis	
Not specified	19 (76)
Less than 1 year	4 (16)
Not specified, but receiving first line treatment	2 (8)
Study population	
Adult	24 (96)
Adolescent and young adult (AYA)	1 (4)
Pediatric	0 (0)
Sex	
Both	21 (84)
Female	4 (16)
Male	0 (0)
Inclusion of caregiver	
No inclusion of caregiver	17 (68)
Caregiver and patient/survivor included	7 (28)
Caregiver only included	1 (4)
Focus on minority or medically underserved population*	

Table 1 (continued)

Characteristic	n (%)
No focus on minority or medically underserved populations	16 (64)
Rural	4 (16)
African American	3 (12)
Older adults	2 (8)
Hispanic/Latino	1 (4)
Low-income country	1 (4)
Socioeconomic disadvantaged	1 (4)
Study design	
Intervention study	18 (72)
Observational study	7 (28)
Length of follow-up	
1 to 6 months	17 (68)
7 to 12 months	4 (16)
Variable based on time enrolled in study	2 (8)
No follow-up (cross-sectional study)	2 (8)

*Some grants focused on more than one underserved population, so percentages do not add up to 100%

only, both physiological and psychosocial sequelae, and physical activity. Most of the grants were intervention studies (72%), and the focus of the intervention was most often psychosocial support (33.3% out of 18 intervention studies) or early palliative/supportive care (38.9%). Most grants had a length of follow-up between 1 month and 6 months (68%).

Discussion

The purpose of this report was to examine emerging research on individuals living with advanced or metastatic cancer through an analysis of current NIH grants, and identify gaps in this area. Our review included 25 funded grants across four NIH institutes. Below we highlight notable findings of this analysis and point to the need for future work.

First, it is promising that a quarter of the grants reviewed focused on the delivery of early palliative/supportive care. National guidelines have recommended early integration of supportive and palliative care delivered concurrently with treatment [6]. Questions remain, however, relative to the timing, delivery, types of providers, and key components of supportive care for metastatic survivors who are living longer; future work is needed in these areas.

One notable gap in this portfolio is the limited attention to the longer-term needs of advanced/metastatic survivors. Most grants reviewed followed study participants for up to 6 months and many were focused on first-line treatment or the first year following diagnosis of advanced disease. There is a pressing need to conduct longitudinal studies to examine symptom sequelae and supportive care needs for the growing population of individuals with advanced disease living for extended

periods of time. In order for longitudinal cohort or other observational studies to be conducted, methodological research is also needed to determine best approaches to capturing disease progression in medical records. Currently, it is difficult to identify metastasis in electronic health records (EHR) or registry data [7]. Novel approaches such as the use of natural language processing as a way to mine the EHR and clinic notes [8] offer potential opportunities, but require more investigation.

We also identified only one grant focused on survivors treated with newer targeted and emerging therapies. While advances in innovative treatments can extend overall survival, there may also be unintended consequences, including the possibility of short- and long-term toxicities and adverse health effects, increased uncertainty and fear of recurrence, caregiver distress and burden, and the need for enhanced communication [2], areas in which research is needed. The inclusion of caregiver/patient dyads in almost a third of grants was seen as a strength in this portfolio review, given the increasing burden placed upon caregivers to provide care and support for their loved ones with advanced/metastatic disease [9]. While the focus of these grants was most often psychosocial support, future research should identify ways to optimally support the caregiver/patient dyad through treatment decision-making, and with financial hardship and uncertainty that may result from long-term periods of disease.

In addition, none of the currently funded studies focused on models of care delivery for individuals with advanced or metastatic cancers. Though research is beginning to examine transitions in care after completion of treatment [10], there is a clear need for care models that better address those living with advanced disease. As treatments often lead to poor long-term

side effects and comorbidities, it is critical to determine optimal care pathways to improve survivor outcomes (e.g., provider type, care delivered).

Most grants in this analysis were funded through R01 grants, used to support large research projects with strong preliminary data. Largely absent from this current NIH portfolio of metastatic cancer survivorship research are grants funded under the R21 and R03 mechanisms. These mechanisms support smaller research projects that are innovative and exploratory in nature and may provide foundational work to support future larger studies on issues for this population.

Finally, the gaps identified in this portfolio analysis signal a need for the NIH and NCI to explore innovative models of funding, including those that allow for extended periods of longitudinal follow-up, as well as support for innovative yet foundational pilot studies of potential interventional strategies. In addition, it may be necessary to create opportunities to extend treatment trials of innovative therapies to include examination of persistent or late-onset physical and psychosocial sequelae. A key next step in this work is to identify priorities for funding that considers the current state of the science and these gaps in the portfolio.

This review should be viewed in light of certain limitations. First, studies funded by outside agencies and foundations are not represented in this report. In addition, this analysis was limited to currently funded grants to provide a snapshot of emerging research. Thus, it did not include an exploration of trends which may be useful for future efforts. We also did not include infrastructure grants and networks, including the NCI Community Oncology Research Program (NCORP). Finally, we did not examine unfunded grant applications. It is therefore unknown whether studies proposed but not funded are fundamentally different from those described in this review.

Summary

This grant portfolio review reflects the current state of NIH-funded grants focused on survivorship issues in patients living with advanced and metastatic cancer, a population with substantial needs. Although currently funded grants focus on several important topics for these survivors, including early palliative care, psychosocial support, and symptom sequelae, gaps in the portfolio remain. Moving forward, research that focuses on the longitudinal examination of unmet needs, models of care delivery, impact of innovative therapies, and the impact of financial hardship will be critical to improve care and outcomes for individuals living with advanced or metastatic cancer.

Author contribution All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by all authors. The first draft of the manuscript was written by MM, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Declarations

Disclaimers The article was prepared as part of the authors' (MAM, GT, ET, PJ, AWS, LG) official duties as employees of the US Federal Government. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the National Cancer Institute.

This study has not been previously presented.

Conflict of interest The authors declare no conflict of interest.

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