

REVIEW

A Bibliometric Analysis of the Landscape of Cancer Rehabilitation Research (1992–2016)

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Abstract

Cancer rehabilitation research has accelerated as great attention has focused on improving survivorship care. Recent expert consensus has attempted to prioritize research needs and suggests greater focus on studying physical functioning of survivors. However, no analysis of the publication landscape has substantiated these proposed needs. This manuscript provides an analysis of PubMed indexed articles related to cancer rehabilitation published between 1992 and 2017. A total of 22 171 publications were analyzed using machine learning and text analysis to assess publication metrics, topic areas of emphasis, and their interrelationships through topic similarity networks. Publications have increased at a rate of 136 articles per year. Approximately 10% of publications were funded by the National Institutes of Health institutes and centers, with the National Cancer Institute being the most prominent funder. The greatest volume and rate of publication increase were in the topics of Cognitive and Behavioral Therapies and Psychological Interventions, followed by Depression and Exercise Therapy. Four research topic similarity networks were identified and provide insight on areas of robust publication and notable deficits. Findings suggest that publication emphasis has strongly supported cognitive, behavioral, and psychological therapies; however, studies of functional morbidity and physical rehabilitation research are lacking. Three areas of publication deficits are noted: research on populations outside of breast, prostate, and lung cancers; methods for integrating physical rehabilitation services with cancer care, specifically regarding functional screening and assessment; and physical rehabilitation interventions. These deficits align with the needs identified by expert consensus and support the supposition that future research should emphasize a focus on physical rehabilitation.

Cancer rehabilitation research has accelerated in the last two decades as greater attention has been drawn to the functional needs of cancer survivors and as disability prevention achieved prominent attention alongside antineoplastic treatment outcomes (1–3). Recent efforts from the National Institutes of Health's Rehabilitation Medicine Department (4) the Cancer and Aging Research Group (5), the Oncology Nursing Society (6), the Academy of Oncology Physical Therapy (7), and interdisciplinary published reports (8,9) have aimed to share expert opinion and coalesce consensus around existing research gaps and to prioritize areas of need to guide future research. In 2015, the National Institutes of Health's Rehabilitation Medicine

Department's Cancer Rehabilitation Initiative recommendations included stronger efforts to integrate cancer rehabilitation care models into oncology care, incorporating functional morbidity screening and assessment tools into oncology care planning and promoting comprehensive care planning to maximize interventions that improve physical function in cancer survivors (4). In 2016, Lyons et al. (8) conducted a Delphi study querying national subject matter experts to identify and rank priorities in cancer rehabilitation research based on areas of greatest need. Their findings identified consensus on high priority topics such as epidemiology of disability among cancer survivors, functional assessment and long-term functional

Received: January 5, 2018; Revised: April 19, 2018; Accepted: May 22, 2018

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outcomes in survivors, optimal clinical measures of physical function, cost and quality analyses of functional screening and therapeutic interventions, and effectiveness of therapeutic interventions to improve physical function in survivors. In 2015, the Cancer and Aging Research Group (CARG) issued a report (5) to guide future research trials in geriatric oncology and suggested that efforts should test interventions to optimize physical performance, nutrition status, and cognition during cancer treatment and to standardize cancer care plans based on geriatric assessment findings. The CARG report specifically called out the need for standardized functional assessment with an emphasis on physical domains, from the point of diagnosis through cancer care. These consensus reports concordantly agree that greater research emphasis is needed to better measure and manage physical function.

Outside of these individual consensus efforts, a detailed analysis of the existing research publication landscape has not been undertaken to elucidate the body of published evidence. A detailed analysis of the existing body of oncology-related functional rehabilitation research publications can provide insight on areas where the evidence is robust, highlight areas where publication deficits exist, and identify specific areas where opportunities exist to guide future physical rehabilitation research. This work can also serve as a baseline from which to benchmark future growth and development of the field.

This report presents a bibliometric analysis of the published literature on cancer rehabilitation as indexed in PubMed over the past 25 years. It seeks to identify trends in the publication rates among common research topics and explores how these topics have been studied in different cancer types. Beyond looking at the sheer volume of publications, this analysis leverages machine learning methodology to provide a more detailed and descriptive perspective on published topic areas beyond traditional search methods. The results will augment recent consensus efforts and enable researchers to better align their research inquiries to address areas where evidence is lacking to meet the identified needs of the field. Further, these results may be beneficial to inform funding agencies regarding the areas of greatest research opportunities.

Methods

A search for publications related to cancer and rehabilitation was conducted using the public version of PubMed in July 2017. The search included title, abstract, key word, and MeSH terms and was limited to articles published from 1992 through 2016. The full records of the search results were downloaded in XML format, and the relevant publication metadata from the original XML file were extracted using an R script.

The publication metadata were analyzed to identify the number of articles per year, MeSH terms, and reported funding agency. PubMed includes funding information in its article metadata if the authors cite a specific grant number from selected US, UK, or other international funding agencies. As a result, PubMed funding data are only reliable for these select agencies.

To quantify the degree to which articles investigated the use of rehabilitation therapies in specific cancer populations, the cooccurrence of MeSH terms for rehabilitation with terms for specific cancer types was analyzed. For example, the number of articles in which the terms “breast neoplasms” and “adaptation, physical,” or “prostatic neoplasms” and “exercise therapy” both occurred was calculated as a way of gauging the amount of

research performed on various rehabilitative therapies in specific types of cancers. To focus on the most frequently occurring therapies and cancer types, cooccurrence values were calculated for cancer and therapy terms that each appeared in at least 150 articles in the data set.

A Latent Dirichlet Allocation (LDA), a topic modeling technique, was then used to identify more specific research topics within the articles. LDA is frequently used in computer science, bibliometrics, and digital humanities to identify discrete topics in large amounts of unstructured text (10,11). The LDA program creates its own set of term vocabularies based on the frequency with which terms cooccur in the document set. Once the vocabulary has been created by the program, the algorithm assigns a probability that a document belongs to a specific topic based on the frequency with which terms appear in each document.

For this analysis, the vocabulary was set to identify 50 common topics, and the algorithm ran on the text from the articles' abstracts. A primary topic was assigned to each article in the analysis based on the topic to which it had the highest probability of belonging. Names were assigned to each topic based on the abstract and MeSH terms that most frequently occurred and through manual inspection of the articles within a topic. The topic assignments were used to calculate the number of articles per topic per year and per funding agency.

Finally, a topic similarity network was created to identify relationships and overlaps among these topics. For each article, the two topics to which it had the highest probability of belonging were identified, and that article topic list was used as an edge list, or a list of connections among topics. A network was then extracted from that edge list in which two topics are connected if the algorithm identifies them as being the highest two probabilities for one or more articles in the data set. The network was clustered to identify communities of related topics using the Louvain method, as above.

The publication count, LDA, and some network analyses were performed with the R programming language in RStudio (<https://rstudio.org>). The code is publicly available on GitHub (<https://github.com/christopherBelter/pubmedXML>). Other network analyses were performed using the Science of Science Tool (<https://sci2.cns.iu.edu/user/index.php>), and all network visualizations were created using Gephi (<https://gephi.org/>) (12,13).

Results

The search string (given in the [Supplementary Materials](#), available online) identified 22 171 publications (79.0% original research, 15.0% reviews, 5.0% Comment, Letter, and Editorial, 1.0% Other) were identified. From 1992 to 2016, publications increased at an average rate of 136 articles per year (Figure 1). A notable escalation in the overall publication rate is evident in the 2002–2005 time frame and continues thereafter. Funding analysis revealed that 2300 (10.0%) publications were funded by the National Institutes of Health (NIH) institutes and centers, more than any other reported funding source (Figure 2). The National Cancer Institute (NCI) is the clear leader in funding cancer rehabilitation research, with strong co-funding relationships with the National Institute for Nursing Research (NINR) and the National Institute on Aging (NIA). The strongest linkages for interinstitute research support occurred between the NCI and NINR (14).

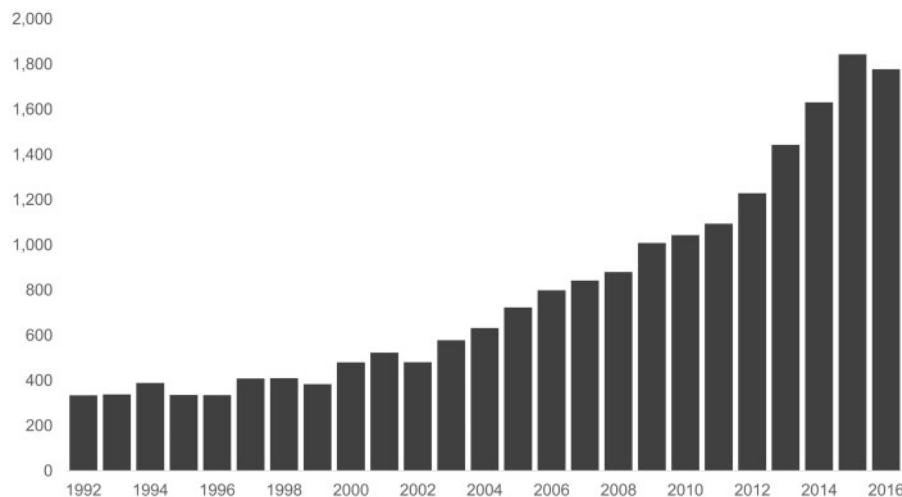


Figure 1. PubMed search results: articles per year. The decline in 2016 may reflect an indexing delay rather than a decline in publications.

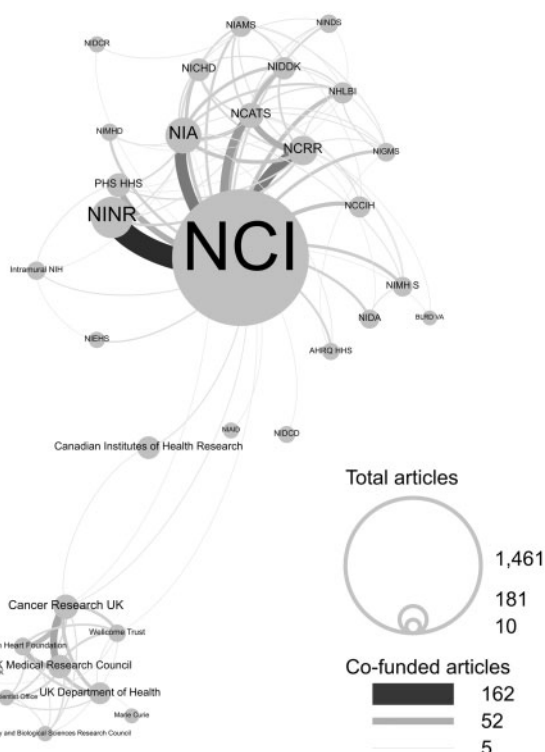


Figure 2. Total number of reported articles published per funder and co-funding relationships. NCATS = National Center for Advancing Translational Sciences; NCCIH = National Center for Complementary and Integrative Health; NCI = National Cancer Institute; NCRN = National Center for Research Resources; NHLBI = National Heart, Lung and Blood Institute; NIA = National Institute on Aging; NIAMS = National Institute of Arthritis and Musculoskeletal and Skin Diseases; NICHD = National Institute of Child Health and Human Development; NIDA = National Institute on Drug Abuse; NIDDK = National Institute of Diabetes and Digestive and Kidney Diseases; NIGMS = National Institute of General Medical Sciences; NIH = National Institutes of Health; NIMH = National Institute of Mental Health; NINDS = National Institute of Neurological Disorders and Stroke; NINR = National Institute for Nursing Research; PHS HHS = Public Health Service, Health and Human Services.

MeSH Analysis

Seven MeSH terms (Figure 3) demonstrate a notable (>2000.0%) escalation over the 25-year timeline. Articles using the MeSH

terms Exercise Therapy, Exercise, Depression, and Fatigue demonstrated the greatest volume change and rate of increase over time.

Articles per MeSH term are compared with MeSH cancer disease terms in Figure 4. Breast Neoplasms represent the greatest volume of publications, with the MeSH terms Psychological Adaptation and Exercise Therapy being most represented. Figure 4 highlights evident deficits in rehabilitation research across cancer types outside of breast, prostate, and lung.

Latent Dirichlet Allocation

LDA topics derived from the publications' abstracts provide a more detailed perspective on the specific topics most frequently occurring in the literature. The greatest increase in volume and rate of publication was in the topics of Cognitive and Behavioral Therapies and Psychological Interventions, followed by Depression and Exercise Therapy. The increase in the topic area Gene Expression and Cell Function seen from 2013 to 2014 is attributed to an indexing change in PubMed and is considered an artifact of this change. In the fall of 2013, MeSH integrated the Genetic Home Reference disease vocabulary, which covers human diseases and conditions with genetic components (15,16). Although detailed review of this specific topic is beyond the scope of this paper, the topic area of Gene Expression and Cell Function includes some disease biomarker and exercise research. However, the topic primarily includes a large number of vocabulary terms related to drug trials and gene therapy, which skews the topic relevance to cancer survivor rehabilitation.

Research Topic Network Analysis (Figure 5) highlights areas where clusters of inter-related topics cooccur and provides insight on relationships between prominent topics of interest. Four topic network clusters were identified by the Louvain method and represent areas of strong intrarelation among publications; 1) Surgical Intervention, 2) Assessment and Therapeutic Intervention, 3) Patient Experience and Clinical Case Management, and 4) Epidemiology and Special Populations. The greatest volume of publications, as depicted by the representative topic bubble size, center on Surgical Interventions including Reconstructive Surgeries, Surgical Precautions, and Postoperative Complications. The magnitude of the relationships among topics can be observed both within and between topic clusters, as

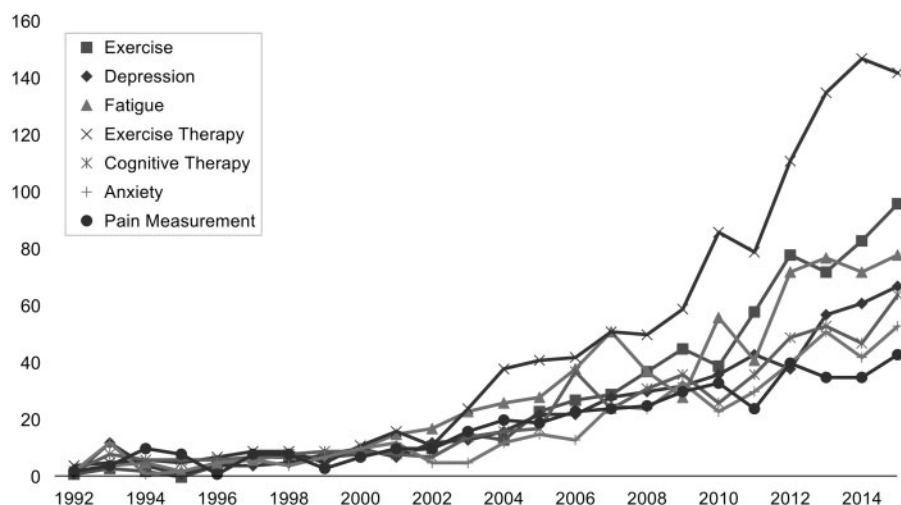


Figure 3. Articles per MeSH term per year.

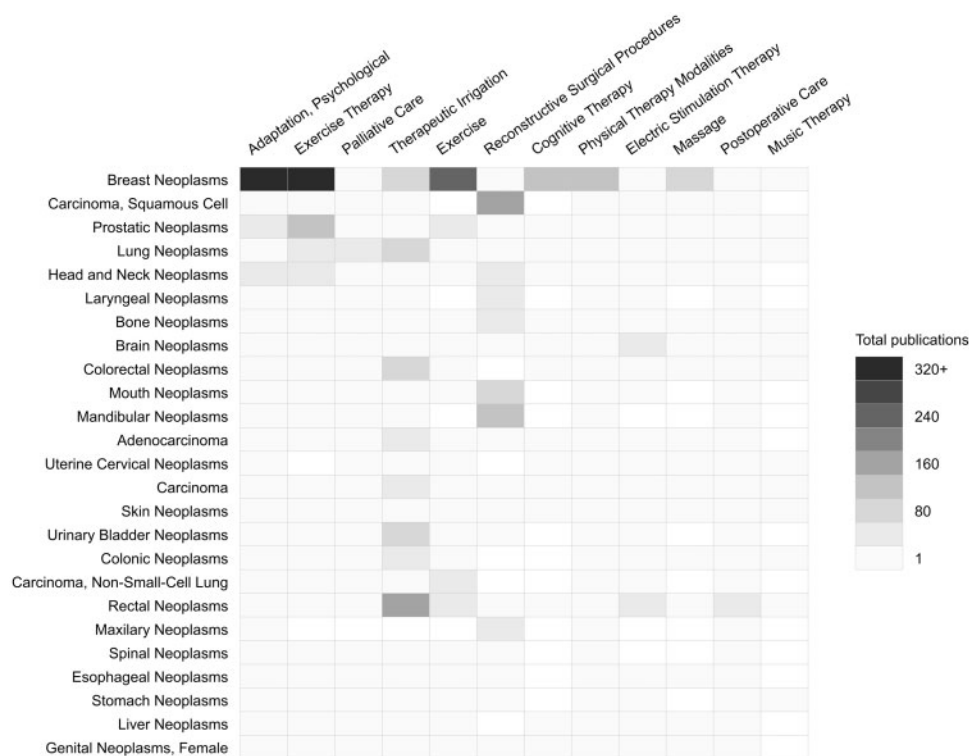


Figure 4. Articles per MeSH rehabilitation term within each MeSH cancer term.

depicted by the network line connections, with thicker lines representing greater numbers of articles using common terms. Figure 6 depicts LDA-derived topics with the greatest (>1500%) increase in publications over time.

The Surgical Intervention cluster emphasizes the topics of Reconstructive Surgery and Postoperative Procedures and Complications (Figure 5). The cluster shows strong associations among topics related to the Brain and Spinal Cord, reflecting a prominent relationship with rehabilitation for individuals with neoplasms in these systems. Additionally, a close relationship is noted with the topic of Speech and Swallowing Therapies.

The linkages between the Surgical Intervention cluster and the Assessment and Therapeutic Intervention cluster are less robust (Figure 5). Strong relationships are seen crossing these two clusters in the topic areas of Lymphedema and Cardiovascular Conditions. There is a lack of robust relationship between the Surgical Interventions and many of the specific physical rehabilitative therapies in the Therapeutic Interventions cluster.

The Assessment and Therapeutic Intervention cluster focuses heavily on topic areas including Psychological Intervention, Cognitive and Behavioral Therapies, and Exercise Therapy (Figure 5). Symptom-specific, impairment-based

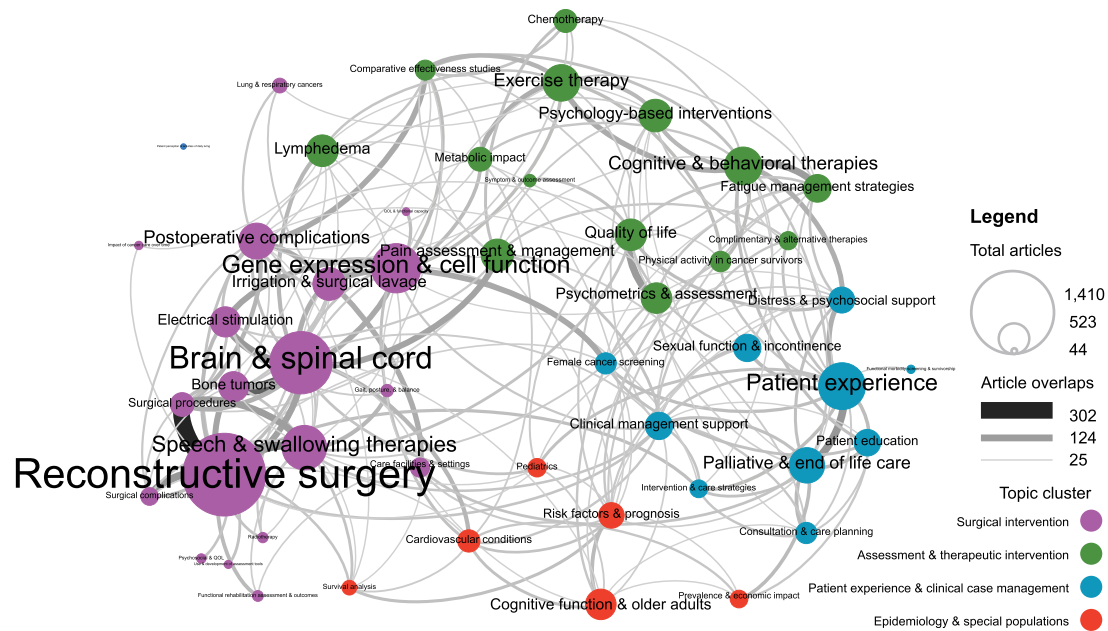


Figure 5. LDA research topic cluster network: inter- and intrarelations.

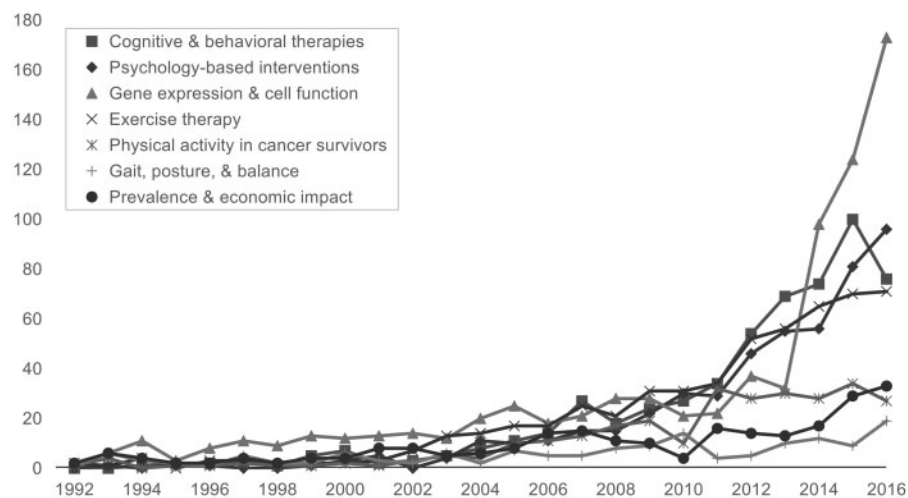


Figure 6. Latent Dirichlet Allocation analysis: increase in topic area articles per year.

research on topics such as Pain, Fatigue, and Lymphedema also feature prominently. Exercise publications cluster closely with pain, fatigue, and quality of life; however, the distant relationships between Exercise and topics such as Cardiovascular Disease, Cognition, or Sexual Functioning indicate that exercise studies are not prominently related to research in these areas. The topic of Chemotherapy features prominently in this cluster and is closely related to Exercise Therapy, Fatigue Management, and Cognitive and Behavioral Therapies.

The Patient Experience and Clinical Case Management cluster prominently features the topics of Patient Experience, Distress, and Psychosocial Support (Figure 5). This finding is supported in the MeSH analysis as these were among the most prominent terms identified in publications. Distress and Psychosocial Support are large topics of emphasis with strong linkages to Patient Experience and to various areas within the

Assessment and Therapeutic Intervention cluster. Specifically, there is a robust relationship between the topics of Distress, Psychosocial Support, and Cognitive and Behavioral Therapies, suggesting strong mechanisms for identification and management of these conditions. The topic areas of Sexual Function and Incontinence occur in this cluster and have close association with Distress; however, they are not linked to the cluster of Therapeutic Interventions, suggesting a strong emphasis on screening and assessing the distress associated with Sexual Function but a lack of research on triage and intervention to manage these issues. Comparatively, the number of studies on Functional Morbidity Screening is extremely small in this cluster, indicating a dearth of published research in this area. Further, the topic of Functional Morbidity Screening only has a relationship with one other topic (Patient Experience) and no relationship with the Therapeutic Interventions cluster.

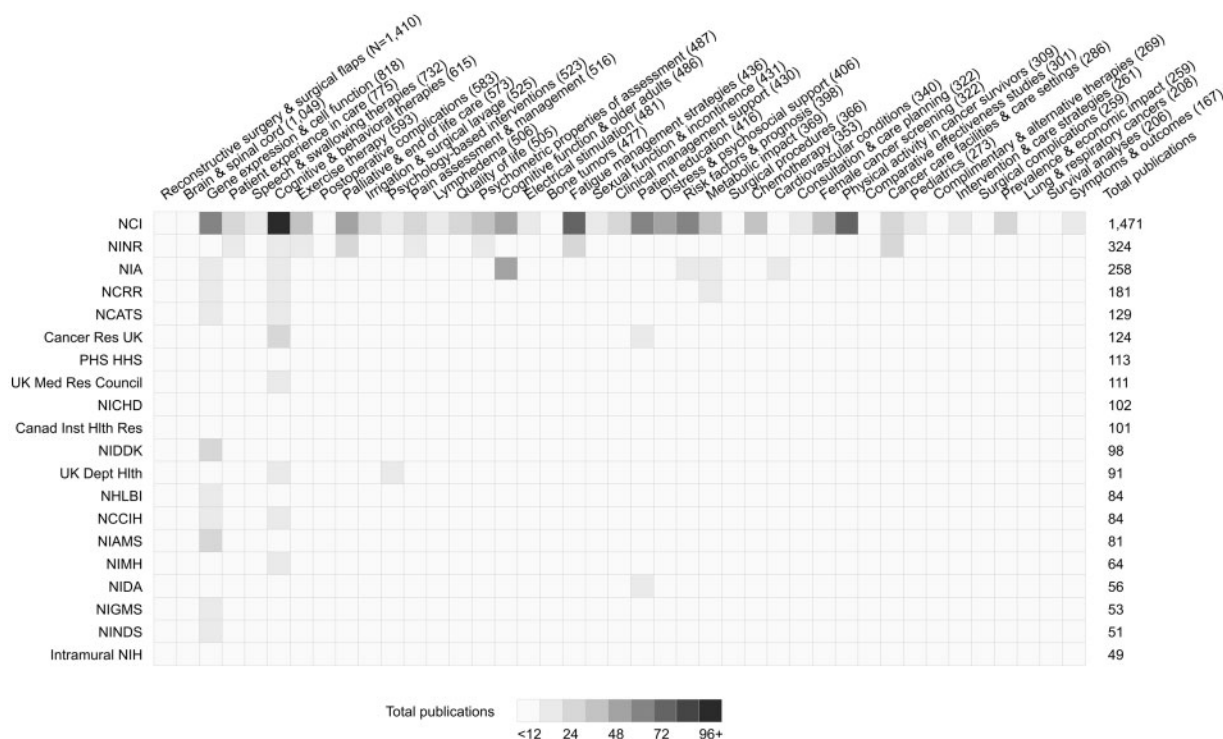


Figure 7. Latent Dirichlet Allocation analysis: rehabilitation topic areas identified by funder. NCATS = National Center for Advancing Translational Sciences; NCCIH = National Center for Complementary and Integrative Health; NCI = National Cancer Institute; NCRR = National Center for Research Resources; NHLBI = National Heart, Lung and Blood Institute; NIA = National Institute on Aging; NIAMS = National Institute of Arthritis and Musculoskeletal and Skin Diseases; NICHHD = National Institute of Child Health and Human Development; NIDA = National Institute on Drug Abuse; NIDDK = National Institute of Diabetes and Digestive and Kidney Diseases; NIGMS = National Institute of General Medical Sciences; NIH = National Institutes of Health; NIMH = National Institute of Mental Health; NINDS = National Institute of Neurological Disorders and Stroke; NINR = National Institute for Nursing Research; PHS HHS = Public Health Service, Health and Human Services.

The final cluster of Epidemiology and Special Populations is a smaller grouping and represents associations among publications related to Risk Factors, Disease Prognosis and Survival, Economic Impact of Survivorship, Cognition, and Cardiovascular Conditions (Figure 5). It also includes research publications on the topics of Pediatric and Older Adult populations. Lacking is a relationship between this cluster and the Assessment and Therapeutic Intervention cluster, indicating little published research on how rehabilitative or symptom management interventions might influence cancer treatment adherence, mortality, disease prognosis, recurrence risk, or impact health care economics.

Analyzing the LDA topic areas by the reported funding agencies provides insight on the level of funding directed to support these topics (Figure 7). The LDA reveals that the NCI's topic areas of greatest concentration have historically been Cognitive and Behavioral Therapies, Fatigue Management Therapies, and Physical Activity in Cancer Survivors. Looking across all reported funding agencies, Cognitive and Behavioral Therapies and Gene Expression and Cell Function are the most published research topics in cancer rehabilitation. The two most prominent topic areas of publication overall, Reconstructive Surgery and Brain and Spinal Cord, are not largely funded by any of the agencies in this analysis.

Discussion

Overall, cancer rehabilitation publications increased by 810% over this period, growing slower than the rate of general cancer research (1056%) but at a faster pace than general rehabilitation

research (386%). Although the year-over-year rate of publication grew steadily, averaging 136 articles per year, a pronounced increase in the yearly rate of publication is noted between 2002 and 2004, as seen in Figure 3. This increase may be attributable to historical changes in legislation that heightened national focus on cancer rehabilitation. The Health Omnibus Program Extension Act of 1988 amended the NCI's mandate to include "rehabilitation from cancer treatments." This only translated into extramural research funding when the NCI's Office of Cancer Survivorship (OCS) was established in 1996. The uptick in publications in the early 2000s may reflect the latency time between the establishment of the OCS's extramural portfolio and the time for that research to come to fruition. Furthermore, in 2005, the Institute of Medicine (now the National Academy of Medicine) issued a seminal report, "Cancer Patient to Cancer Survivor: Lost in Transition" (17), that recognized cancer rehabilitation as a part of cancer survivorship care, potentially driving the continued escalation in the rate of publications from 2006 onward. Although the overall trend in cancer rehabilitation publications is positive, our more detailed topic analysis suggests that research efforts are lagging for various aspects of physical rehabilitative interventions.

The predominant topics of research publication over this 25-year period included Psychological-Based Interventions, Cognitive and Behavioral Therapies, and Exercise Therapy (Figures 6 and 7). Results demonstrate a large volume of publications on Distress Screening and robust relationships between Distress, Patient Experience, and Psychological-Based and Cognitive and Behavioral Therapies, suggesting that there is a large body of research that has focused on identification and

management of these issues through therapeutic interventions. Although addressing psychosocial and psychological components of care is important to functional recovery after cancer treatment, there is a clear lack of research on physical rehabilitative interventions, as suggested by this analysis. Patients often report that anxiety, depression, and distress are the result of physical functional impairments and disability related to cancer treatments (18,19). Future research on physical function may help to improve the understanding and management of the root cause of functional morbidity and its related distress. Moreover, the lack of research emphasis on physical function should also be considered as a factor in the relative under-recognition of the benefits of rehabilitation and underutilization of physical rehabilitation interventions in oncology populations (20,21). Rehabilitation strategies for the management of physical dysfunction are well established, but our results demonstrate that the translation of this research to the field of oncology has languished (22).

This analysis identifies that there is limited research in the topic area of Functional Morbidity Screening. The lack of screening for physical morbidity inhibits the identification of limitations that may trigger referrals to appropriate types of rehabilitation interventions to restore physical function and reduce disability levels among cancer survivors (9). In rehabilitation research, screening and assessment tools for identification of functional impairments are plentiful, but as this analysis reflects, effort has not been undertaken to study which tools are most sensitive for identifying cancer treatment-related functional impairment. An important perspective to consider is that many of the prominently studied oncology-specific distress screening tools capture information regarding symptom presentation rather than functional impairment (21). This has led to an emphasis on clinical interventions for symptom management rather than a focus on alleviating physical morbidity. The paucity of research publication in the Functional Morbidity Screening topic area suggests missed opportunities to identify and alleviate functional impairments proactively. The need for more research on functional screening and assessment was also identified as an area warranting attention in a recent report from the NIH initiative in cancer rehabilitation (4), and is further supported by the Cancer and Aging Research Group (CARG) (5), which specifically cited the need for future trials to measure physical function before the initiation of treatment and to monitor function throughout the duration of medical treatment. Targeted efforts to fund trials that address the broader spectrum of physical functional morbidity screening and assessment and symptom-based screening could be a way to expand this body of evidence.

This analysis reveals notable escalation of Exercise Therapy and Exercise research publications. It is difficult, however, to discern the type of exercise as articles tagged with the MeSH term "Exercise Therapy" do not delineate the specific type of exercise studied, which could range from physical activity to cognitive exercises. An important observation, however, is that Exercise Therapy publications are prominent across the most common cancers: breast, prostate, and lung, as well as head and neck. Outside of breast and prostate cancers, Exercise Therapy publications fail to eclipse more than 100 articles across all remaining cancers over the period of this timeline (Figure 4). This is consistent with an NCI portfolio analysis of funded grants FY2004–2014 showing that most physical activity studies focused on breast, prostate, colorectal, or lung cancer survivors (23) and is supported by the CARG recommendations and Oncology Nursing Society (ONS) research agenda (6), which

suggest that there is a need for survivorship research beyond the most commonly diagnosed cancers. This deficit is of great importance as we look to the future and see a growing population of cancer survivors across all disease types (24). Medically directed cancer treatments are widely variable, and findings from breast cancer exercise research, for example, may not be easily or validly extrapolated to individuals with acute myelogenous leukemia. As survival increases across all cancers, it is important to identify new research approaches that may better serve the needs of these varied populations. A recent shift in pharmaceutical clinical trials toward tumor agnostic drug trials may provide an exemplar for future research trials to study physical function across disease types. Additional consideration is warranted regarding epigenetics so that tailored interventions may be provided to those most likely to respond based on individual factors rather than disease state.

This analysis provides little evidence regarding systems of rehabilitation care and their interface with and impact on oncology outcomes. For example, publications in the Surgical Intervention cluster are prominent; however, this research is poorly linked to the Therapeutic Intervention cluster. This may be driven by barriers to research and care and the complexities of payment models that are often prohibitive to aligning therapeutic interventions with postacute rehabilitation services (25), which may deter such research. Newer models such as prehabilitation and Early Recovery After Surgery (ERAS), studied in the colorectal and lung cancer populations, could help to improve the linkages between surgical interventions and therapeutic interventions for preventive, restorative, and supportive care (26–28). Future clinical trials could seek to study rehabilitation interventions delivered at various time points during cancer medical therapies and in varied settings to understand their impact on both short-term and long-term functional recovery for cancer survivors, as well as the potential impact on adherence and tolerance to medically directed cancer treatments. Further, few relationships exist between the Therapeutic Intervention cluster and topics such as Risk Identification and Disease Prognosis, suggesting that there has been little research focusing on important health services questions regarding rehabilitation services. Early work in lung cancer exercise trials suggests that exercises reduces postoperative complications and reduces hospital readmissions, suggesting a cost benefit to exercise. Additionally, although a number of observational trials suggest that physical activity contributes to improved overall survival, reduced recurrence rates, and improved disease-free survival time, there is no evidence of those relationships in this analysis, suggesting a great opportunity to study the impact of rehabilitation interventions on these end points. Although some work has been done examining the feasibility of various models of cancer rehabilitation service delivery at varying time points along the continuum of care (29–31), the need for future research to optimize care delivery was identified in the NIH initiative recommendations and has been expanded upon in various expert opinion publications (4,9,32,33).

Our analysis reveals a lack of notable publication on many commonly occurring functional impairments amenable to rehabilitation such as neuropathy, bone fragility, and joint and soft tissue restrictions. These issues are prevalent and functionally debilitating (34). Moreover, rehabilitative interventions are highly effective in mitigating the functional disability associated with these conditions. This analysis also identifies no substantial publication evidence regarding radiation therapy and its impact on function. Radiation therapy is prevalent in cancer care and incites a high degree of associated functional

Table 1. Rehabilitation research gaps

Area of research opportunity	Research questions
Populations of cancer survivors	Efficacy and effectiveness of exercise and rehabilitation interventions on oncologic populations other than breast, prostate, lung, and colorectal Longitudinal studies to identify late effects of cancer treatments and their functional impact on the survivor population
Enhanced rehabilitation care delivery	Optimal timing and dosing of perioperative rehabilitative therapies including prehabilitation and postacute care Optimal strategies for comprehensive screening of both psychosocial and functional morbidity including timing and frequency over the duration of cancer medical care and through survivorship Meaningful functional changes that trigger referrals for appropriate types of rehabilitation interventions Clinical objective measurement tools and patient self-reported measures that can track changes over time both during and after cancer treatments
Rehabilitative interventions that may alleviate cancer treatment-related physical impairment and functional disability	Physical, functional rehabilitation intervention, beyond psychological interventions Therapeutic interventions to prevent or treat common symptoms and side effects such as neuropathy, bone fragility, and joint and soft tissue restrictions The impact of therapeutic interventions on late effects of cancer treatment such as falls, return to work, accelerated aging, cognition, and overall functional performance Radiation therapy-related functional morbidity and therapeutic interventions that support physical function after radiation therapy both in the short and long term Strategies to coordinate distress screening with the therapeutic interventions that alleviate underlying physical limitations The effects of physical rehabilitation and exercise intervention on cancer treatment adherence, medical treatment tolerance, overall survival, post-treatment employment, and post-treatment health care utilization; this includes pragmatic trials to document the utility of rehabilitation services integrated into cancer care and their impact on health care utilization end points

morbidity, including cardiotoxicities, skin and soft tissue contractures, fatigue, nerve conduction disruption, and cognitive and memory impairment (35). One reason for the dearth of research in these areas is perhaps the prolonged latency until these impairments surface and negatively impact function. Studying late effects in prospective clinical trial cohorts is complicated by study designs that traditionally fail to follow individuals for a prolonged period during and after cancer treatment despite wide recognition that the late effects of cancer treatment have been known to cause substantial disability (36,37). Longitudinal studies (eg, NCT00760656, NCT00027118, <https://clinicaltrials.org>) have been successfully deployed in cancer rehabilitation, and investigators should consider opportunities to expand the use of this methodology. Additionally, large-scale, cross-sectional population-based descriptive research focusing on late functional impairments could also potentially alleviate this gap.

This analysis provides some perspective on funding sources, as reported in PubMed. The NIH funded 2300 of the 22 171 articles, with the NCI being the most prominent funder. The NIH therefore cumulatively supported approximately 10% of the articles in this analysis, representing less than 0.01% of the NIH's overall publication output. Therefore, although researchers have historically looked to the NIH as a primary funding body, the effort dedicated to cancer rehabilitation research is minimal. Considering the growing population of cancer survivors and the sheer magnitude of cancer treatment-related functional morbidity, expansion of funding portfolios in favor of the physical needs of cancer survivors could serve to address the greatest areas of need.

Many HHS publications have shared funding sources, and strong relationships are noted between the NCI and the NINR and NIA (Figure 2). There is little relationship, however, between the NCI and the Eunice Kennedy Shriver National Institute of

Child Health and Human Development's National Center for Medical Rehabilitation Research (NCMRR), whose portfolio and focus are specifically on reduction of physical disabilities through scientific research, a scope of work well aligned with the needs of cancer survivors.

Research Agenda for Future Work

This analysis underscores the critical need to enhance the science regarding physical functioning of cancer survivors. The deficits identified in this analysis not only support recent expert opinion recommendations but go a step further in suggesting areas of specific opportunity to better align future research to suit the needs of the field. We suggest three major areas of emphasis for future research work, in alignment with the aforementioned expert opinions: 1) rehabilitation research across populations of cancer survivors, 2) research on enhancing physical rehabilitation care delivery, and 3) research on specific rehabilitative interventions that may alleviate cancer treatment-related physical impairment and functional disability. Table 1 outlines this proposed future agenda.

The alignment between these efforts not only speaks to the apparent need but also creates an opportunity to develop a collaborative research agenda that could influence funding agencies and organizations. Although independent investigators may seek to meet these needs through research trials, this analysis suggests that they may have difficulty identifying funding sources aligned with the areas of greatest need. To achieve better equity in funding distribution, research agencies could seek to extend efforts to address the shortcomings identified by this analysis and supported by these consensus-based research prioritization efforts. Filling gaps according to a prioritized research agenda could ultimately serve to develop the body of

evidence around comprehensive functional rehabilitation for cancer survivors.

It cannot be overstated that many factors that have accelerated the rate of publication over time were related to federal legislative and regulatory initiatives targeting improved survivorship care. Recent changes and developments in cancer care standards, specifically the Commission on Cancer's (CoC's) accreditation standards (38) regarding distress screening and survivorship care planning, have likely led to the prominence of specific topic areas and relationships around Patient Experience and Distress. Although these standards are aimed at improving survivorship care, the emphasis on distress screening alone is skewed and should incorporate functional morbidity screening to enable identification of physical impairments and enable referral for optimal functional rehabilitative interventions. Emerging evidence suggests that distress screening tools may be inadequate to appropriately promote triage of many common physical functional problems associated with cancer treatment (18). Future research to study the impact of these standards on care delivery pathways, triage, and rehabilitative interventions that improve morbidity is needed. One notable set of standards that may facilitate greater attention to cancer rehabilitation is the Commission for the Accreditation of Rehabilitation Facilities (CARF) Cancer Rehabilitation Specialty Program Standards (<http://www.carf.org/Programs/Medical/>). These standards provide a framework for comprehensive cancer rehabilitation care service delivery and could catalyze research investigating the impact of rehabilitation services on cancer care outcomes.

The recent Cancer Moonshot coalition is an emerging initiative where this analysis could be impactful to increase awareness and instigate a change in the funding trends toward greater support of the physical and functional aspects of survivorship care. Cancer and rehabilitation professional societies could seek collaborative mechanisms to improve upon targeted legislation, regulatory standards, and other policy drivers that emphasize the rehabilitation needs of cancer survivors.

The National Cancer Institute is well positioned to bring attention to these gaps and to work in collaboration with other institutes to identify funding mechanisms to alleviate them. Additionally, other federal agencies and private funding organizations could look to examine this body of evidence more closely to contextualize the gaps and needs for funding and shared research priorities. In 2016, NCMRR released a National Institutes of Health Research Plan on Rehabilitation that specifically outlined opportunities, needs, and priorities in rehabilitation research (39). The plan specified a need to broaden rehabilitation research across the institutes at the NIH and identified priorities that align with the gaps identified in this analysis. Although the NCI is the largest funder of cancer rehabilitation research, collaborative efforts with the NCMRR, the Trans-NIH Medical Rehabilitation Coordinating Committee, and the National Advisory Board for Medical Rehabilitation could catalyze greater collaborative efforts.

Limitations

The funding source reports in this analysis may not be comprehensive beyond the US Department of Health and Human Services. Not only is there uncertainty about the level of reporting compliance among publications, work that was funded but is incomplete and work that was never completed will not be evident in this analysis. This analysis also does not include

funding reports from the Department of Defense or the Department of Veterans Affairs, both of which provide federal funding for rehabilitation research and likely have some cancer-related work in their portfolios.

This analysis queried only the PubMed database. Although there are many additional databases that catalog biomedical research publications, PubMed is noted to include the highest quality peer-reviewed research while eliminating extraneous and more obscure quasi-experimental, non-peer-reviewed publications (40). Exploring publications indexed in other medical scientific databases could provide opportunities for future efforts that may seek to go into greater detail within the topic areas outlined here.

These LDA topic areas and their identified associations were completely created by artificial intelligence; therefore, while the topics present a generalized understanding of common groupings identified by machine-driven analysis, a deeper, detailed scoping activity within each topic area could provide greater insight into the specific types of rehabilitation interventions used, the exposure of various populations to rehabilitative services, and the overall effectiveness of rehabilitation interventions in improving cancer survivorship outcomes.

Summary

This analysis explores historical trends in the topic areas most prominently published in cancer rehabilitation. Rehabilitation medicine is a broad topic encompassing diverse areas of practice focusing on preventive, restorative, supportive, and palliative care interventions that aim to maximize the overall function of an individual cancer survivor. This analysis should serve to support prioritization of topics for cancer rehabilitation research as it provides insight on many of the existing deficits in the scientific body of evidence. In general, there are notable gaps in studying physical and functional recovery from cancer treatment. Investigators should consider these shortcomings as a rationale to support future research. Institutions and funding organizations should seek to direct funding and productivity efforts to improve our understanding of how to optimize recovery of physical function during and after cancer treatment. Additionally, regulatory and standard-setting bodies should view these findings with interest and seek to facilitate greater access to rehabilitation care to improve outcomes for survivors.

Notes

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The views and opinions expressed are the authors' own and do not reflect the view of the National Institutes of Health, the Department of Health and Human Services, the Department of Veterans Affairs, or the US Government.

References

- Alfano CM, Kent EE, Padgett LS, Grimes M, de Moor JS. Making cancer rehabilitation services work for cancer patients: Recommendations for research and practice to improve employment outcomes. *PM&R*. 2017;9(9):S398–S406.
- Klepin HD, Geiger AM, Tooze JA, et al. Physical performance and subsequent disability and survival in older adults with malignancy: Results from the health, aging and body composition study. *J Am Geriatr Soc*. 2010;58(1):76–82.
- Bauer UE, Briss PA, Goodman RA, Bowman BA. Prevention of chronic disease in the 21st century: Elimination of the leading preventable causes of premature death and disability in the USA. *Lancet*. 2014;384(9937):45–52.
- Stout NL, Silver JK, Raj VS, et al. Toward a National initiative in cancer rehabilitation: Recommendations from a subject matter expert group. *Arch Phys Med Rehabil*. 2016;97(11):2006–2015.
- Mohile SG, Hurria A, Cohen HJ, et al. Improving the quality of survivorship for older adults with cancer. *Cancer*. 2016;122(16):2459–2568.
- Knobf M, Cooley ME, Duffy S, et al. The 2014–2018 Oncology Nursing Society Research Agenda. *Oncology nursing forum*; 2015;42(5).
- Pfalzer LC, Stout NL, Harrington S, Fisher MI. Toward a research agenda for oncology physical therapy. *Rehabil Oncol*. 2017;35(2):99–101.
- Lyons KD, Radomski MV, Alfano CM, et al. Delphi study to determine rehabilitation research priorities for older adults with cancer. *Arch Phys Med Rehabil*. 2017;98(5):904–914.
- Cheville AL, Mustian K, Winters-Stone K, Zucker DS, Gamble GL, Alfano CM. Cancer rehabilitation: An overview of current need, delivery models, and levels of care. *Phys Med Rehabil Clin N Am*. 2017;28(1):1–17.
- Blei DM. Probabilistic topic models. *Commun ACM*. 2012;55(4):77–84.
- Blei DM, Ng AY, Jordan MI. Latent Dirichlet Allocation. *J Mach Learn Res*. 2003;3(jan):993–1022.
- Bastian M, Heymann S, Jacomy M. Gephi: An open source software for exploring and manipulating networks. *ICWSM*. 2009;8:361–362.
- Jacomy M, Heymann S, Venturini T, Bastian M. Forceatlas2, a continuous graph layout algorithm for handy network visualization designed for the Gephi software. *PLoS One*. 2014;9(6):e98679.
- Reigle BS, Campbell GB, Murphy KB. *Cancer Rehabilitation and the Role of the Rehabilitation Nurse*. Chicago, IL: Association of Rehabilitation Nurses; 2017.
- Schulman J-L. What's new for 2014 MeSH. *NLM Technical Bulletin*. 2013 December 18. https://www.nlm.nih.gov/pubs/techbull/nd13/nd13_mesh.html. Accessed December 7, 2017.
- Tybaert S. MEDLINE data changes - 2014. *NLM Technical Bulletin*. 2013 December 04. https://www.nlm.nih.gov/pubs/techbull/nd13/nd13_medline_data_changes_2014.html. Accessed December 10, 2017.
- Hewitt M, Greenfield S, Stovall E. *Cancer Patient to Cancer Survivor: Lost in Transition*. Washington DC: National Academies Press; 2006.
- VanHoose L, Black LL, Doty K, et al. An analysis of the distress thermometer problem list and distress in patients with cancer. *Support Care Cancer*. 2015;23(5):1225–1232.
- Gao W, Bennett MI, Stark D, Murray S, Higginson IJ. Psychological distress in cancer from survivorship to end of life care: Prevalence, associated factors and clinical implications. *Eur J Cancer*. 2010;46(11):2036–2044.
- Pergolotti M, Deal AM, Lavery J, Reeve BB, Muss HB. The prevalence of potentially modifiable functional deficits and the subsequent use of occupational and physical therapy by older adults with cancer. *J Geriatr Oncol*. 2015;6(3):194–201.
- Cheville AL, Beck LA, Petersen TL, Marks RS, Gamble GL. The detection and treatment of cancer-related functional problems in an outpatient setting. *Support Care Cancer*. 2009;17(1):61–67.
- Gilchrist LS, Galantino ML, Wampler M, Marchese VG, Morris GS, Ness KK. A framework for assessment in oncology rehabilitation. *Phys Ther*. 2009;89(3):286–306.
- Alfano CM, Bluethmann SM, Tesauro G, et al. NCI funding trends and priorities in physical activity and energy balance research among cancer survivors. *J Natl Cancer Inst*. 2015;108(1):djv285.
- American Cancer Society. *Cancer Treatment and Survivorship Facts & Figures 2016–2017*. Atlanta, GA: American Cancer Society; 2016.
- Fu JB, Bianty JR, Wu J, Ngo-Huang A, Shin KY, Bruera E. An analysis of inpatient rehabilitation approval among private insurance carriers at a cancer center. *PM&R*. 2016;8(7):635–639.
- Carli F, Silver JK, Feldman LS, et al. Surgical prehabilitation in patients with cancer: State-of-the-science and recommendations for future research from a panel of subject matter experts. *Phys Med Rehabil Clin N Am*. 2017;28(1):49–64.
- Singh F, Newton RU, Galvão DA, Spry N, Baker MK. A systematic review of pre-surgical exercise intervention studies with cancer patients. *Surg Oncol*. 2013;22(2):92–104.
- Sebio Garcia R, Yáñez Brage MI, Giménez Moolhuyzen E, Granger CL, Denehy L. Functional and postoperative outcomes after preoperative exercise training in patients with lung cancer: A systematic review and meta-analysis. *Interact Cardiovasc Thorac Surg*. 2016;23(3):486–497.
- Blaney J, McCollum G, Lorimer J, Bradley J, Kennedy R, Rankin J. Prospective surveillance of breast cancer-related lymphoedema in the first-year post-surgery: feasibility and comparison of screening measures. *Support Care Cancer*. 2015;23(6):1549–1559.
- Sandmæl JA, Bye A, Solheim TS, et al. Feasibility and preliminary effects of resistance training and nutritional supplements during versus after radiotherapy in patients with head and neck cancer: A pilot randomized trial. *Cancer*. 2017;123(22):4440–4448.
- Sommer MS, Trier K, Vibe-Petersen J, et al. Perioperative Rehabilitation in Operable Lung Cancer Patients (PROLUCIA): A feasibility study. *Integrat Cancer Ther*. 2016;15(4):455–466.
- Alfano CM, Zucker DS, Pergolotti M, et al. A precision medicine approach to improve cancer rehabilitation's impact and integration with cancer care and optimize patient wellness. *Curr Phys Med Rehabil Rep*. 2017;5(1):64–73.
- Stout NL, Binkley JM, Schmitz KH, et al. A prospective surveillance model for rehabilitation for women with breast cancer. *Cancer*. 2012;118(S8):2191–2200.
- Silver JK, Baima J, Mayer RS. Impairment-driven cancer rehabilitation: An essential component of quality care and survivorship. *CA Cancer J Clin*. 2013;63(5):295–317.
- Stubblefield MD. Neuromuscular complications of radiation therapy. *Muscle Nerve*. In press.
- Ness KK, Mertens AC, Hudson MM, et al. Limitations on physical performance and daily activities among long-term survivors of childhood cancer. *Ann Intern Med*. 2005;143(9):639–647.
- Stein KD, Syrjala KL, Andrykowski MA. Physical and psychological long-term and late effects of cancer. *Cancer*. 2008;112(11 Suppl):2577–2592.
- American College of Surgeons. *Cancer Program Standards 2012: Ensuring Patient-Centered Care*. Chicago, IL: American College of Surgeons; 2012.
- Eunice Kennedy Shriver National Institute of Child Health and Human Development and the NIH Medical Rehabilitation Coordinating Committee. Committee NMRC. *National Institutes of Health Research Plan on Rehabilitation*. Rockville, Maryland: Department of Health and Human Services; 2017.
- Falagas ME, Pitsouni EI, Malietzis GA, Pappas G. Comparison of PubMed, Scopus, Web of Science, and Google Scholar: Strengths and weaknesses. *FASEB J*. 2008;22(2):338–342.