

# Research Agenda of the Oncology Nursing Society: 2019–2022

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**PROBLEM STATEMENT:** To define the Oncology Nursing Society Research Agenda for 2019–2022.

**DESIGN:** Multimethod, consensus-building approach by members of the Research Agenda Project Team.

**DATA SOURCES:** Expert opinion, literature review, surveys, interviews, focus groups, town hall, and review of research priorities from other cancer care organizations and funding agencies.

**ANALYSIS:** Content analysis and descriptive statistics were used to synthesize research priority themes that emerged.

**FINDINGS:** Three priority areas for scientific development were identified: symptom science, health disparities, and palliative and psychosocial care in oncology. In addition, cross-cutting themes that provide context and elaboration for these priorities emerged.

**IMPLICATIONS FOR NURSING:** The Research Agenda can be used to focus oncology nurses' research, scholarship, leadership, and health policy efforts to advance quality cancer care, inform research funding priorities, and align initiatives and resources across the ONS enterprise.

**KEYWORDS** research; symptom science; health disparities; palliative care; psychosocial care

**ONF, 46(6), 654–669.**

**DOI** 10.1188/19.ONF.654-669

The Oncology Nursing Society (ONS) promotes excellence in oncology nursing and quality cancer care. In keeping with this mission, since 2001, ONS has developed and disseminated a Research Agenda identifying priority areas where new knowledge is urgently needed. The purpose of the Research Agenda is two-fold: it includes both the development and dissemination of contemporary research priorities needed to advance cancer care and delineates critical areas to be considered by research funders.

A multimethod approach was used to develop the Research Agenda. ONS identified content experts to serve on the project team. This team was broken into smaller work groups to address various tasks that needed to be accomplished to update the Research Agenda. The first work group was convened to review the previous process used to formulate the prior ONS Research Agenda and discuss the best way to update the process in a scientifically rigorous yet time- and resource-efficient manner (Knobf et al., 2015). The previous process spanned multiple years and involved surveying ONS members, publishing survey results, and then convening an expert panel to update the Research Agenda based on survey responses. Given the low response rates (11%) and the lack of a clear set of focused research priorities that emerged from analysis of the survey results, an alternative approach was discussed to actively engage ONS members with expertise in research together with other key stakeholders to yield a focused set of research priorities (LoBiondo-Wood et al., 2014).

A condensed process was recommended by the work group to identify a focused set of contemporary

research priorities. As Figure 1 illustrates, the first step in the process consisted of conducting a targeted survey and interviews with ONS members with research expertise as well as key stakeholders from funding agencies to identify research priorities needed to transform cancer care. Once this information was gathered and collated, the entire project team convened to discuss the results, review relevant literature, and examine research priorities from other professional organizations and funding agencies.

Once content areas where new knowledge is needed had been identified, work groups were convened to draft research priorities within each topical area. A consensus-building process consisting of iterative cycles of peer review and refinement of the research priorities was used to generate and approve the initial draft of the Research Agenda. Once the draft was approved, the Research Agenda was shared with a broader group of ONS members at the annual ONS Congress. The feedback from these sessions was presented to the Research Agenda team for consideration and inclusion in the agenda. The final Research Agenda was approved by the ONS Board of Directors. An evaluation process will be used to refine the process.

The purpose of this article is to disseminate the Research Agenda to the ONS membership and the larger interprofessional oncology community. The 2019–2022 Research Agenda provides a scientific road map that may be used to inform research, scholarship, leadership, and health policy efforts to advance quality cancer care, inform research funding priorities, and align initiatives and resources across the ONS enterprise.

The 2019–2022 Research Agenda project team identified three overarching priority areas where new scientific knowledge is needed: symptom science, health disparities, and palliative and psychosocial care in oncology. In addition, four cross-cutting themes emerged that add context and elaboration to these priorities: aging, survivorship, healthcare delivery models, and advanced research methods (see Figure 2). The following summary presents each research priority separated into three sections, including the context of the problem, research gaps, and the research priorities.

### Symptom Science: Immunotherapy and Emerging Therapies

Immunotherapy (IO) is one of the fastest-emerging areas of cancer treatment, and the availability of this new class of agents has created a paradigm shift in the treatment of many malignancies. The initial research

priority related to IO focuses on immune checkpoint inhibitor (ICPI) therapies because so many new agents targeting this mechanism have received recent U.S. Food and Drug Administration (FDA) approval (Hargadon, Johnson, & Williams, 2018). Other emerging IOs, including chimeric antigen receptor (CAR) T cells and combinatorial therapies (Holzinger & Abken, 2020) are also relevant within the context of this priority as the science evolves (Iafolla et al., 2018; Tang, Shalabi, & Hubbard-Lucey, 2018). The immune checkpoint pathway, part of the adaptive immune system, serves to balance the body's responses to foreign antigens and prevents autoimmune dysfunction. Tumors have the capacity to exploit these pathways, thereby evading immune surveillance. Inhibitory

## FIGURE 1. Oncology Nursing Society (ONS) Research Agenda Process

### Data Collection

- Targeted surveys and interviews
- Experienced researchers
- Novice researchers
- Key stakeholders

### Draft Research Priorities

- Research Agenda expert panel
- Review of survey results
- Review of literature
- Review of research priorities from other organizations

### Gather Input

- ONS membership input
- Focus groups
- Town hall meetings at ONS Congress

### Refine Research Priorities

- Research Agenda expert panel
- Review of feedback from ONS membership

### ONS Board of Directors

- Review and approval

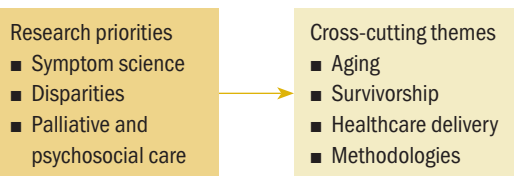
### Dissemination

- Research Agenda expert panel
- Review of feedback from ONS Board of Directors
- Finalize Research Agenda.
- Disseminate findings through publication and meetings at ONS Congress.

### Evaluation of Impact

- Research Agenda expert panel
- Reconvene to evaluate process.
- Develop criteria to evaluate dissemination and impact of Research Agenda process.

**FIGURE 2. 2019–2022 Research Agenda Priorities and Cross-Cutting Themes**



ICPIs targeting cytotoxic T-lymphocyte antigen 4 and programmed cell death protein 1 (PD-1) and its ligand (PD-L1) are the inhibitory ICPIs that have received the most study to date. ICPIs that target each of these checkpoints have been approved for use as first- and second-line therapy for metastatic disease in several malignancies, as well as in the adjuvant setting (Hargadon et al., 2018).

Although generally well tolerated, ICPI is associated with a unique profile of adverse effects referred to as immune-related adverse events (irAEs) (Friedman, Proverbs-Singh, & Postow, 2016; Postow, Sidlow, & Hellmann, 2018). irAEs reflect a generalized inflammatory reaction and can lead to significant morbidity. Although any organ system can be affected, the most common irAEs involve the gastrointestinal tract, endocrine glands, skin, and liver. Less often, the central nervous system and cardiovascular, pulmonary, musculoskeletal, and hematologic systems are involved.

There is interest in understanding factors that influence patients' responses to ICPI and irAE development. Clinical trials have observed variability in the therapeutic response to ICPI based on the tumor microenvironment, tumor burden, PD-L1 expression, age, and gender (Yan et al., 2018). Diversity of the gut microbiome is associated with improved response to ICPI, and antibiotic use may abrogate this response (Chaput et al., 2017; Havel, Chowell, & Chan, 2019; Matson et al., 2018).

### Research Gaps

ICPI therapies have been associated with numerous adverse events. Adverse events of cancer therapies are typically graded and reported by clinicians using the National Cancer Institute's Common Terminology Criteria for Adverse Events (U.S. Department of Health and Human Services, 2017). Systematic reviews of clinical trials describe significant gaps in the grading, reporting, and attribution of irAEs of patients treated with ICPI (Chen, Razak, Bedard, Siu, & Hansen, 2015). Although patients may derive clinical benefit from

ICPI, few studies have examined changes in symptoms, quality of life, physical function, and/or cognition using tools that are specific to the unique symptom and irAE profile associated with these therapies (Hall et al., 2019; Mendoza, 2018). To date, the patient experience has been captured using generic instruments developed for clinical trials on cytotoxic agents (Hall et al., 2019). Therefore, current instruments used may not accurately reflect the patient experience, underscoring the need to develop patient-reported outcomes (PROs) that are specific to ICPI.

Because patients are living longer after ICPI, it is unclear what will be the profile of late- and long-term adverse events (Johnson et al., 2015). A gap exists in identifying the impact of factors such as age, gender, diet, weight, exercise, stress, sleep patterns, and the environment, individually and collectively, on the development of irAEs across patient populations and over time (Andrews, Reuben, Gopalakrishnan, & Wargo, 2018; Elias, Hartshorn, Rahma, Lin, & Snyder-Cappione, 2018; Idorn & Thor Straten, 2017; King-Kallimanis, Kanapuru, Blumenthal, Theoret, & Kluetz, 2018; Rassy, Ghosn, Rassy, Assi, & Robert, 2018; Sattar, Kartolo, Hopman, Lakoff, & Baetz, 2019; Soldati et al., 2018; Wallis et al., 2019; Yan et al., 2018).

New knowledge is also required to provide the evidence base for optimal supportive care during and following treatment with IO. Although clinical practice guidelines have been developed to guide clinicians in the management of irAEs, those recommendations are based largely on a consensus of clinical expert opinion, rather than empirical evidence (Brahmer, Lacchetti, & Thompson, 2018; Haanen et al., 2017; Thompson et al., 2019). Oncology nurse scientists have significant expertise in the testing of symptom-focused interventions and, therefore, are well-poised to address this knowledge gap (Miaskowski, Barsevick, et al., 2017).

### Research Priorities

Areas for future research were developed based on the current state of the science and gaps identified by the expert panel, and included the following recommendations:

- Develop, test, and refine reliable, valid, and sensitive PRO tools to capture treatment experiences in patients receiving IO, and link those measures to clinical decision support and treatment pathways to improve clinical outcomes.
- Characterize variability in presentation, trajectory, and management of the irAEs across various patient populations.

- Examine factors (age, gender, diet, weight, exercise, stress, and sleep patterns) that may influence patient responses to ICPI therapy and irAE development.
- Conduct randomized trials to test the efficacy of supportive care interventions to alleviate irAEs.

### Symptom Science: Precision Health and Biosignatures

In alignment with a number of precision health initiatives (Ashley, 2015; Fiore & Goodman, 2016; Ginsburg & Phillips, 2018; McCarthy, 2016; National Research Council, 2011), oncology nursing research is focused on the identification of phenotypic and molecular characteristics that will identify individuals at highest risk for greater symptom burden, as well as target novel and effective supportive care interventions, thereby improving patient outcomes.

At the current time, oncology nurse scientists have made significant contributions to precision health in the areas of symptom management, quality of life, and functional status during and following cancer treatment (Hickey et al., 2019). Patients undergoing treatment for cancer experience multiple co-occurring symptoms. The pattern of symptoms has been classified based on the severity of specific symptoms or symptom clusters among patients with a variety of cancer diagnoses (Mazor et al., 2018; Russell et al., 2019; Sullivan et al., 2018) and by treatments (Abid et al., 2017; Miaskowski, Conley, et al., 2017; Wright et al., 2019). In addition, research is uncovering underlying genomic variations that increase the risk for adverse symptom experiences (Dhruva et al., 2015; Kober et al., 2016; Miaskowski, Conley, et al., 2017; Page et al., 2018).

Determining optimal approaches to reveal the underlying mechanisms of individual variability in symptom experiences requires a comprehensive understanding of the potential factors that contribute to higher symptom burden. Defining individual biosignatures may aid in this process. Biosignatures reflect both genomic and phenotypic components and may include biomarkers and integrative “omics,” as well as lifestyle, environmental, and psychosocial factors (Institute of Medicine, 2008). A number of approaches are available to obtain this information. The use of valid and reliable self-report measures along with the measurement of various biomarkers has provided some of the most salient information about the mechanisms underlying symptom experiences (Dhruva et al., 2015; Kober et al., 2016; Page et al., 2018).

Identifying biosignatures for common individual symptoms and symptom clusters will require the collection and analysis of multiple factors that accurately capture phenotypic and molecular characteristics. In addition to determining phenotypic characteristics, measuring different types of biomarkers (e.g., genomic, metabolomics, proteomic, epigenomic) is an essential component of this research. By definition, a biomarker is a defined characteristic that is measured as an indicator of normal biological processes, pathogenic processes, or responses to an exposure or intervention (Califf, 2018; FDA-NIH Biomarker Working Group, 2016). Biomarkers provide an indication of molecular functioning and can be applied to risk assessment, diagnosing or monitoring a state or condition, and/or evaluation of an intervention (Califf, 2018). Nurse scientists have incorporated many types of biomarkers into studies that target symptom experiences as well as functional status and responses to biobehavioral interventions (Ferranti, Grossmann, Starkweather, & Heitkemper, 2017).

### Research Gaps

A significant gap in the development of a precision health approach to symptom science is that most of the research on individual and/or multiple symptoms relies on statistical approaches that model means and standard deviations. However, a large amount of the individual variability and the latent patterns in patients' symptom experiences will not be reflected through such statistical modeling. In contrast, there is increasing interest in using finite mixture modeling approaches that are more flexible about the distributional shape of the data, and can be used both to draw inferences and to explore the data to derive clusters or trajectory groups. In addition, the use of heterogeneous measures across studies makes it difficult to aggregate data to support integrative analysis across studies (Hesse, Moser, & Riley, 2015; Yu & Zeng, 2018). Strengthening the use of common data elements in symptom science, including patient demographics, self-reported symptoms, behavioral factors, and biological measures, sets the stage for integrative data analysis, which has been a key priority of the National Institute of Nursing Research (Page et al., 2018; Redeker et al., 2015).

More information is needed about the phenotypes of individuals with stable symptoms as well as individuals whose symptoms are changing over time. A better understanding of those characteristics of patients with fluctuating symptoms will predict patients who, at baseline, are at greatest risk for adverse symptoms,

allowing clinicians to target intensive symptom screening and management approaches. Such predictive analytics will also support the delivery of anticipatory patient and family education and other preemptive interventions to improve symptom outcomes. There is also a knowledge gap with respect to the phenotype(s) of symptom burden in the survivor population. Although the number of survivors is increasing, there has been little exploration of symptom clusters in survivors, and most of the work that has been conducted has limited the focus to symptom clusters in breast cancer survivors. A majority of the reports of the symptom experience in cancer survivors emphasize the occurrence, severity, and management of single symptoms (Kim, Kim, Lim, & Kim, 2018; Nho, Kim, Park, & Kweon, 2018). Cross-sectional and longitudinal studies are needed to characterize the symptom experiences of patients with cancer in different age groups, with different types of cancers and treatments, and across the cancer control continuum. Also urgently needed are studies to identify effective interventions to mitigate and manage symptom clusters, both during and following cancer treatment and at the end of life (Miaskowski, Barsevick, et al., 2017). Conducting and analyzing such intervention studies, particularly those testing complex, multicomponent interventions, will require knowledge of advanced methods, including adaptive research designs and personalized dynamic treatment regimens, and the statistical methods needed to conduct finite mixture modeling and to examine mediation and moderation of treatment effects.

Determining optimal methodologic approaches to identify patients at risk for a higher symptom burden is an area that warrants additional research. The use of large data sets that include biological determinants may expedite filling this gap in knowledge. For example, a study by Papachristou et al. (2018) used predictive modeling and a robust dataset to predict which patients would be most likely to have severe symptoms during a cycle of chemotherapy.

Although many biosignature studies do capture data over time, the number of time points may be limited. Newer approaches, such as ecological momentary assessment, that capture the dynamic nature of patients'/survivors' symptom experiences and their associated biomarker profiles, are warranted. Approaches that incorporate web-based patient and survivor interfaces, such as the Electronic Patient Self-Reporting of Adverse Events: Patient Information and aDvice (eRAPiD) system (Absolom, Gibson, & Velikova, 2019; Cowan et al., 2016) or the Symptom Care at Home System, may be helpful for real-time

symptom reporting (Mooney, Whisenant, & Beck, 2019). However, characterizing individual variability in symptom experiences will require a multifaceted approach that also includes wearable devices and genomic/epigenomic evaluations, as well as the collection of patients, treatment, biobehavioral, and psychosocial factors to optimize the identification of symptom biosignatures (Lucas et al., 2018).

### Research Priorities

Areas for future research that were developed based on the current state of the science and gaps identified by the expert panel included the following recommendations:

- Harmonize assessment measures and strengthen the use of common data elements.
- Identify the optimal approaches to characterize patients' and survivors' symptom profiles and their associated genotypes and phenotypes.
- Comparatively evaluate approaches to examine the mechanisms underlying variation in patients' and survivors' symptom experiences.
- Determine optimal methodologic approaches to predict patients and survivors at greatest risk for symptom burden.
- Establish the biosignature (i.e., phenotypic and molecular characteristics) of common individual symptoms and symptom clusters in patients and survivors.
- Develop and test interventions to manage single symptoms and symptom clusters.

### Health Disparities

The National Institutes of Health (NIH) has designated several groups, including Blacks/African Americans, Hispanics/Latinos, American Indians/Alaska Natives, Asian Americans, Native Hawaiians and other Pacific Islanders, socioeconomically disadvantaged populations, sexual and gender minorities, and rural communities, as groups who are underserved and who may experience disparities in health outcomes and access to care (NIH, 2019). An analysis of U.S. socioeconomic and racial/ethnic disparities in incidence and mortality from all cancers, combined from 1950 to 2014, demonstrates that those who live in more areas with fewer resources, and those with lower levels of education and income, have higher cancer incidence and mortality rates compared with those with more resources (Singh & Jemal, 2017). In addition, those who identified as lesbian, gay, bisexual, transgender, or queer (LGBTQ) are at higher risk for specific cancers compared to heterosexuals (Hudson



et al., 2017). Disparities with respect to incidence and mortality are most prominent among those with lung, colorectal, cervical, stomach, and liver cancers, and these trends in disparities are increasing.

Similarly, there is a higher incidence of cancer-related deaths in rural populations compared to those living in urban communities. Risk factors for adverse outcomes in rural populations include tobacco use, sedentary behavior, and higher rates of obesity (Henley et al., 2017). Many barriers to accessing cancer care and participating in cancer clinical trials that exist for minorities and other vulnerable populations are also experienced by those living in rural communities. These barriers include lower rates of insurance coverage, poverty, transportation problems, and difficulties in accessing cancer screening, diagnosis, and staging services (Charlton, Schlichting, Chioreso, Ward, & Vikas, 2015).

### Research Gaps

In 1993, the U.S. government mandated that NIH-funded clinical trials must include women and minorities and must assess outcomes by gender and race or ethnicity. However, roughly 25 years after this mandate, the proportion of racial/ethnic minorities enrolled in cancer clinical trials does not reflect the U.S. general population (Chen, Lara, Dang, Paterniti, & Kelly, 2014). An analysis of 782 published clinical trials showed overall enrollment of women at 46%. However, 15% of trials enrolled less than 30% women, only 26% reported at least one outcome by gender, and 13% reported outcomes by race or ethnicity. Progress has been meager, with no changes or improvements made in inclusion, analysis, or reporting by sex, race, or ethnicity compared to studies conducted prior to this mandate (Geller et al., 2018). Research also continues to identify factors related to health disparities in cancer incidence; for example, approximately 40% of all cancers diagnosed are associated with obesity and women and non-Hispanic Blacks/African Americans are among those at highest risk (Steele et al., 2017).

Very limited research has focused on the care of LGBTQ patients with cancer. Cancer outcomes in this population have been understudied, and the information that is known is less likely to reach oncology care professionals (Margolies & Brown, 2018). An analysis of NIH-funded sexual and gender minority research indicated that 75% of projects focused on HIV/AIDS, whereas only 10% focused on cancer (the second leading cause of death in this population) (NIH, 2015). There is an urgency to better understand the

specific needs and experiences of sexual and gender minorities and to improve access to care and care quality for this population, as well as to improve their participation in clinical trials (Quinn et al., 2015).

Similarly, limited research has focused on rural populations, a group that has a higher incidence of cancer-related deaths and prominent risk factors that include tobacco use, sedentary behavior, obesity, and barriers to accessing needed care (Henley et al., 2017). Of note, the availability of cancer care providers in rural areas is lacking; less than 3% of physicians practice in rural areas. To reduce travel time to large metropolitan hospitals, reduce family burden and stress, and reduce healthcare and out-of-pocket costs for the system and patients, alternative models of healthcare delivery need to be evaluated to identify those who provide quality, cost-effective care (Blake, Moss, Gaysynsky, Srinivasan, & Croyle, 2017; Hazin & Qaddoumi, 2010; Sabesan, Simcox, & Marr, 2012).

As a result of the rising cost of cancer treatment, Altice, Banegas, Tucker-Seeley, and Yabroff (2016) observed that 47%–49% of cancer survivors reported experiencing financial distress, and 12%–62% reported being in debt because of their treatment. A population-based study identified several factors associated with cancer-related financial difficulties, including younger age, being a member of a minority group, and recent receipt of chemotherapy and/or radiation therapy. Survivors who had financial problems were more likely to delay or forego medical care, prescription medications, dental care, glasses, and mental health care. To minimize additional health disparities among disadvantaged groups, it is critical to conduct research identifying effective approaches to address the financial burden of cancer care.

### Research Priorities

Priorities for continued research include the following:

- Develop and test interventions to increase minority and vulnerable population participation in cancer clinical trials.
- Examine the effects on cancer outcomes of social determinants of health (i.e., physical, social, and economic factors).
- Develop and test interventions to address health disparities related to behavioral factors such as obesity, physical inactivity, diet, tobacco use, and immunizations that can prevent malignancies associated with human papillomavirus and hepatitis B.
- Evaluate interventions to address financial toxicity associated with cancer treatment.

- Examine the role of technology, including telehealth strategies, to improve access to care, particularly among rural populations.

### **Palliative Care and Psychosocial Oncology**

The National Consensus Project (NCP) of Quality Palliative Care developed guidelines for quality care, which were endorsed by 80 organizations, including ONS. Palliative care attends to the physical, functional, psychological, practical, and spiritual consequences of a serious illness through early integration of these needs and concerns into the plan of care. As such, palliative care improves quality of life for the patient and his or her family (Ahluwalia et al., 2018).

Palliative care has been integral to oncology care; cancer is recognized as an illness with a significant quality-of-life burden for patients and their family caregivers. The NCP guidelines recognize eight dimensions of palliative care, including structure and processes of care; physical aspects of care; psychological and psychiatric aspects of care; social aspects of care; spiritual, religious, and existential aspects of care; cultural aspects of care; care of the patient nearing the end of life; and ethical and legal aspects of care. Palliative care is now available in most oncology care settings and has demonstrated significant benefits to patients, families, and health systems. The availability of quality palliative care services is of particular importance given the shift to outpatient care and the aging of the population. There is also a strong recommendation for specialty palliative care to be accompanied by generalist-level palliative care, meaning palliative care provided by oncology nurses, physicians, and other cancer clinicians. Models of palliative care continue to evolve in oncology settings, with increasing attention being given to each of the eight domains across the trajectory of cancer diagnosis, treatment, survivorship, recurrence, and end of life.

### **Research Gaps**

Ahluwalia et al. (2018) examined 139 systematic reviews to synthesize the evidence about the components and effectiveness of palliative care and to identify research gaps. Despite the volume of evidence supporting the benefits of palliative care, much of the evidence is of low quality because of inconsistent findings, the lack of precise effect estimates to support the clinical significance of intervention effects, and a reliance on study designs with a high risk of bias. High-quality evidence does exist that supports the delivery of home-based palliative care; the expansion

of these services will be essential as the population ages. Challenges that need to be addressed include the assessment and treatment of symptom burden, particularly given the multimorbidity (defined as two or more chronic conditions) that is experienced by 70% of adults aged 75 years or older (Ritchie & Zulman, 2013). Expansion and testing of new care delivery models, particularly among those in rural areas who may have difficulty accessing palliative care services, are needed (Hui & Bruera, 2015).

A significant gap in knowledge was noted with respect to the provision of culturally sensitive palliative care. Given the importance of acknowledging and incorporating sociocultural norms into care, additional research in this area is needed. Similarly, Ferrell and Wittenberg (2017) found that the majority of research conducted with family caregivers of adults with cancer had been conducted in predominantly White populations.

It is important to focus on both patient and family caregiver needs because family caregivers often experience increasing distress as the patient's function declines (Northouse, Williams, Given, & McCorkle, 2012; Williams & McCorkle, 2011). Although the testing of caregiver interventions has received greater emphasis recently, the next step in the research is to determine which type or types of interventions work best to improve outcomes, and then to manualize these research-tested interventions for implementation in real-world settings (Ferrell & Wittenberg, 2017; Kent et al., 2016).

### **Research Priorities**

Priorities for continued study include the following:

- Develop and test interventions for culturally sensitive palliative and psychosocial oncology care.
- Examine the effects of telehealth on improving patient and caregiver symptoms and health outcomes.
- Determine the most effective interventions to improve patient and caregiver health-related quality of life (HRQOL), satisfaction with care, and use of healthcare resources.
- Determine the effects of early/integrated palliative care intervention on patient and family caregiver outcomes (e.g., symptoms, HRQOL, psychological health, rehospitalizations).
- Understand the impact of single or multiple symptoms on function, disease outcomes, HRQOL, and treatment decision making in seriously ill older adults with cancer, particularly those with multiple comorbidities.

## Cross-Cutting Themes

Four cross-cutting themes emerged as important and timely considerations as clinicians, scientists, and policy makers use this Research Agenda to prioritize their activities. These cross-cutting themes include aging, survivorship, healthcare delivery implications, and advanced research methods. A brief description of each of these themes, highlighting their relevance to contemporary oncology nursing research, is presented. Advanced research methods that have the potential to improve the rigor, depth, and efficiency of research and accelerate the translation of new knowledge into clinical practice are highlighted.

### Aging

Cancer incidence is expected to rise 67% in those aged 65 years or older from 2010 to 2030, compared to a rise in incidence of only 11% for those younger than age 65 years. It is also estimated that, by 2040, 73% of cancer survivors in the United States will be 65 years or older (National Cancer Institute, 2019). Older adults typically have other medical conditions that need to be considered when choosing cancer treatment. Research is needed to identify the most effective care delivery models for delivering services to older adults with cancer, and to test, tailor, and target supportive care and rehabilitative interventions that can preserve and enhance HRQOL and function.

### Survivorship

The number of cancer survivors is projected to increase from 16.9 million in 2019 to 21.7 million by 2029, and many survivors are living longer (National Cancer Institute, 2019). In addition, many survivors, even among those who are cancer-free, must cope with the long-term effects of treatment, as well as psychosocial concerns such as fear of recurrence and being at high risk for developing other malignancies.

### Healthcare Delivery System Implications

Innovative models of care delivery and reimbursement are needed to deliver high-quality, cost-effective care, and to position nurses as leaders in transforming cancer care.

### Advanced Research Methods

Biobehavioral, population, and data science are advancing at a rapid rate, and developments in these offer oncology nurse scientists new tools, technologies, and methods related to research design, measurement, and data analysis. At the same time, the receipt of research funding from federal and other

sources is highly competitive. For oncology nurse scientists to be successful, innovative advanced research methods that have the potential to offer robust new insights and speed the translation of science into real-world settings need to be incorporated into research training programs and grant applications.

## Overview of Advanced Research Methods

To address the challenges of cancer care delivery research, a thorough understanding of contemporary research designs, methods, and data analytics is essential. New methods are continuously emerging, and scientists are required to leverage developments and techniques from a wide range of disciplines, both basic and translational. As such, continuous lifelong learning to extend and develop new skills is essential for all scientists. In addition, interprofessional collaboration is needed to bring expertise to bear on solving problems of interest to oncology nursing. The authors present a brief overview of some salient trends in advanced research methods, which include contemporary research designs, data science, team science, and implementation science. These topics were chosen because they are relevant to the current research environment and have the potential to speed translation of research findings into real-world practice settings.

### Contemporary Research Designs

Although randomized controlled trials (RCTs) are often the gold standard for determining intervention effects, alternative approaches to testing interventions are receiving increased attention and may be particularly useful in situations where individual randomization is not possible, contamination threatens internal validity, and investigators wish to test adaptive complex interventions. In these circumstances, several new research designs have emerged, including Multiphase Optimization Strategy (MOST), Sequential Multiple Assignment Randomized Trials (SMART), and stepped wedge or cluster randomized trial designs. MOST and SMART are related approaches and are used to adaptively test an intervention, thereby achieving a more effective, efficient, acceptable, and scalable intervention. They are ideal for optimizing multicomponent complex interventions, including mobile health efforts. For circumstances in which individual-level randomization is not possible, or desirable, a pragmatic trial using a stepped wedge or cluster randomized design allows an investigator to examine an intervention's real-world effectiveness across diverse patient groups while, at the same time, preserving the experimental control needed to draw conclusions about a cause and effect



relationship between the intervention and the outcome patient groups (Song, DeVito Dabbs, & Ward, 2016; Wilbur, Kolanowski, & Collins, 2016).

Optimal management of health conditions often require a sequential, individualized approach where treatment is adjusted over time in response to the specific needs of the individual. Adaptive interventions, also known as stepped care or dynamic treatment algorithms, are one way to provide individualized sequences of treatment. With an adaptive intervention, the dose and even the components of the intervention may be varied based on individual characteristics or tailoring variables (Almirall, Nahum-Shani, Sherwood, & Murphy, 2014). MOST and SMART approaches can be used to develop and test these types of individualized interventions. MOST systematically and efficiently optimizes behavioral interventions and consists of three phases: preparation, optimization, and evaluation (Collins, Nahum-Shani, & Almirall, 2014; Wyrick, Rulison, Fearnow-Kenney, Milroy, & Collins, 2014). In the preparation phase, efficacious components of the intervention are identified and optimization criteria are pre-selected, such as selecting specific outcomes and/or effect size. In the optimization or refinement phase, a series of experiments are conducted to obtain information about the performance of each component. Finally, a confirmatory RCT of the adaptive or optimized intervention versus a comparator is conducted during the evaluation phase.

The SMART trial design is a tool to identify the best time-varying adaptive intervention strategy and can be used within the refinement phase of MOST (Lei, Nahum-Shani, Lynch, Oslin, & Murphy, 2012; Sikorskii et al., 2017). SMART is a special type of factorial design and differs significantly from a standard RCT. The main goal for a SMART design is to construct an adaptive intervention based on data, whereas the main goal of an RCT is to evaluate an already developed intervention versus a comparator condition (Almirall et al., 2014). Another difference between a SMART and RCT design is that randomization takes place more than once in the SMART design. Each randomization corresponds to a decision point and aims to address a scientific question concerning two or more treatment options at that decision point.

The stepped wedge design involves the collection of observations during a baseline period in which no clusters are exposed to the intervention. Following this, at regular intervals or steps, a cluster (or group of clusters) is randomized to receive the intervention and all participants are once again measured. This

continues until all eligible participants or clusters have entered the intervention condition (Barker, McElduff, D'Este, & Campbell, 2016; Murray et al., 2018). A cluster randomized trial (CRT) is a trial in which individuals are randomized in groups—the group as a whole is randomized and not the individual. Stepped wedge and cluster randomized designs offer several advantages, although they are complex to design, perform, and interpret (Hemming, Carroll, Thompson, Forbes, & Taljaard, 2019). They may mitigate the concerns that arise when studying an intervention that is expected to produce positive effects, where it would be ethically or logistically problematic to withhold that treatment. In addition, because each cluster in the stepped wedge design receives both the control and the treatment condition by the end of the trial and each cluster switches randomly from control to treatment condition at different times, analyses comparing between- and within-cluster effects and the effects of time can be performed. Therefore, CRT and stepped wedge trial designs may have increased statistical power, compared to a traditional RCT, and may also help to surmount issues of feasibility, referral bias, and intervention contamination.

Traditional clinical trials are costly, may be slow to produce results, and have limited external validity (Ford & Norrie, 2016; Volpp, Terwiesch, Troxel, Mehta, & Asch, 2013). As a result, efforts are being made to strengthen the capacity to implement cost-effective, large-scale, pragmatic trials (Weinfurt et al., 2017). Technological advances have created the opportunity to use real-world data to improve current methods of generating clinical evidence to enhance healthcare interventions. Multiple sources of real-world data are available for use in pragmatic trials, which include electronic health records, insurance claims, patient registries, and digital health solutions (Khozin, Blumenthal, & Pazdur, 2017).

Pragmatic trials measure the effectiveness of interventions in real-world settings. As a result, eligibility criteria are typically broad and protocols are brief and designed so that data can be collected as part of routine care. In contrast, traditional explanatory RCTs measure the efficacy of an intervention and are conducted under ideal conditions using tightly controlled study protocol procedures, comparatively smaller sample sizes, and carefully selected participants for inclusion. The PRagmatic Explanatory Continuum Indicator Summary-2 (PRECIS-2) tool provides guidance to enable researchers to design a trial that matches the intention of the proposed study (Loudon et al., 2015).

## Data Science

Data science uses an interprofessional approach to solve complex problems and extract knowledge through methods, tools, and analytics that support the organization, integration, and analysis (including visual analysis) of digital data (Alyass, Turcotte, & Meyre, 2015; Broome, 2016; Founds, 2018). Typically, the data are of a scope and magnitude that can only be analyzed using computers for data storage and processing. Big data may include well-defined and/or structured data elements (e.g., patient-reported measures) as well as loosely defined and/or unstructured elements (e.g., data obtained from wearable devices and social media) (Westra et al., 2017). Big data resources that are useful for oncology nurse scientists include self-report and survey data sources, including those linked to cancer or practice registries. Other sources of big data include instrumented measurements (e.g., actigraphy), social media, electronic devices (e.g., robot/avatar), sensors (e.g., pulse oximeters, glucose monitors), electronic health records, mobile and geospatial applications, and wearable tracking devices (Brennan & Bakken, 2015). Big data management and analysis cannot generally be performed using software such as R or SAS because big data require computing infrastructures that are usually cloud-based and use algorithms to achieve data linkages and synthesis. For example, Apache Spark™ is a leading platform for large-scale structured query language, batch processing, stream processing, and machine learning. Apache Hadoop®, on the other hand, is currently the most widely used open-source distributed processing framework that manages data processing and storage for big data applications running in clustered systems. Hadoop handles various forms of structured and unstructured data, and supports advanced analytics initiatives, including predictive analytics, data mining, and machine learning applications.

Machine learning is often incorporated in data science. Machine learning is an artificial intelligence tool that uses advanced algorithms to structure, analyze, and aggregate large volumes of data. Machine learning (either supervised or unsupervised) is particularly useful in identifying patterns in big data (Bose, Maganti, Bowles, Brueshoff, & Monsen, 2019). Supervised machine learning usually aims to learn a function that best approximates the relationship between a set of predictors and one or more outcomes observed in a dataset (Papachristou et al., 2018). Unsupervised machine learning, in contrast, does not define predictors and outcomes a priori, but rather allows the analytic modeling to define the structure of

relationships among variables within a dataset (Bose & Radhakrishnan, 2018). After collecting and processing the structured data from machine learning tools, data scientists interpret, convert, and summarize the data so that they are useful for clinical decision making (Kwon, Karim, Topaz, & Currie, 2019).

A key priority is to strengthen the educational curriculum so that nurse scientists have the needed data science skills and quantitative competencies to lead and contribute to these research teams (Shea et al., 2019). Other challenges associated with the use of big data, including the identification and analysis of vast amounts of unstructured data, can prove too complex, expensive, and time-consuming to analyze (Westra et al., 2015). In addition, given that machine learning is algorithm-based rather than theory-based, it may be challenging to determine the importance of each variable in contributing to the statistical overall model. Therefore, machine learning is often used for predictive purposes rather than to draw inferences (Brennan & Bakken, 2015). Machine learning can be combined with classic inferential statistics to identify the variables that account for most of the variance in the overall model. Challenges exist in integrating disparate data (particularly real-time information) at the right time to make clinical decisions, and with interpretation and generalization of findings from studies that leverage big data to better understand health outcomes (Founds, 2018; Hesse et al., 2015).

## Team Science

Team science is a collaborative effort to address a scientific challenge that leverages the strengths and expertise of professionals trained in different fields (Little et al., 2017). Cross-disciplinary team science brings together investigators with diverse knowledge and skills, and may be particularly helpful for studies of complex problems with multiple causes. Team members with different training work together to integrate their perspectives in a single research endeavor and are able to address a broad array of complex and interacting variables and apply complementary research methods. Team science is seen as a promising approach to accelerate scientific innovation and the translation of scientific findings into effective policies and practices.

The increased complexity of cancer care requires that researchers move beyond the boundaries of their respective disciplines and gain knowledge about the principles of team science so that these insights can be leveraged in conducting observational research, testing new interventions, and evaluating care

delivery models (Hall et al., 2018; Osarogiagbon et al., 2016). Research training has typically been discipline-specific, with some overlap in research methods, but with very little emphasis on understanding the science of team science or gaining experience operating in interprofessional research teams. Models of research training for nurse scientists must also evolve and incorporate meaningful interprofessional cross-educational opportunities.

### Implementation Science

The translation of evidence-based interventions into healthcare settings has been a slow and arduous process. It takes, on average, 17 years for scientific evidence to be taken up in the practice setting (Balas & Boren, 2000). Implementation science has evolved to facilitate more rapid uptake of evidence-based practice. It is defined as the study of methods to promote the adoption and integration of evidence-based interventions and policies into routine health care.

An essential component of implementation science is evaluating the process of implementation and its impact on the adoption of the evidence-based practice of interest. Implementation science research employs a multilevel (system, provider, and patient), cross-setting, and transdisciplinary approach, and plays an important role in identifying barriers to, and enablers of, effective health care (Mitchell & Chambers, 2017). Through both theory and specific research methods, implementation science leverages that knowledge to anticipate barriers and facilitators, tests the efficacy of implementation strategies, and helps to understand contextual factors that enhance the uptake of evidence-based practice.

### Conclusion

The ONS Research Agenda synthesizes the state of the science in key areas of cancer care, identifies gaps, and proposes directions for continued research to address contemporary challenges in oncology nursing and to drive improvements in health outcomes, care quality, and access for patients across the cancer control continuum. The ONS Research Agenda identifies three priority areas where new knowledge is urgently needed: symptom science, health disparities, and palliative and psychosocial care in oncology. Considerations to enhance the significance, rigor, and relevance of oncology nursing science include a focus on priority populations (older adults and cancer survivors), innovative care delivery models, and advanced research methods and data analytics. This focused set of priorities serves to both concentrate

the professional efforts of scientists and clinicians and to direct resources for scientific training, career development, and research funding opportunities.

The ONS Research Agenda can be used to align initiatives and resources across the ONS enterprise, and provides direction for knowledge generation, evidence-based practice, and healthcare policy to support the delivery of quality cancer care.

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No relevant financial relationships to disclose.

Von Ah, S.J. Brown, Leak Bryant, Davies, Dodd, Ferrell, Hammer, Knobf, Knoop, Mayer, Miaskowski, Mitchell, Song, Watkins Bruner, Wesmiller, and Cooley contributed to the conceptualization and design. Von Ah, Davies, Dodd, Ferrell, LoBiondo-Wood, Mitchell, Song, Watkins Bruner, and Cooley completed the data collection. Ferrell provided statistical support. S.J. Brown, Leak Bryant, Davies, Ferrell, Knobf, Mayer, Miaskowski, Mitchell, Song, Watkins Bruner, Wesmiller, and Cooley provided analysis. Von Ah, C.G. Brown, S.J. Brown, Leak Bryant, Davies, Dodd, Ferrell, Hammer, Knobf, Knoop, Mayer, Miaskowski, Mitchell, Song, Watkins Bruner, and Wesmiller contributed to the manuscript preparation.

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