2015 Strategic Priorities

Symptom Management & Quality of Life Steering Committee (SxQoL SC)

In 1983, the National Cancer Institute created the Community Clinical Oncology Program Network (CCOP) to: **1)** efficiently conduct cancer clinical trials, **2)** engage community oncologists in the conduct of clinical trials, **3)** extend access to clinical trials to cancer patients treated in the community, and **4)** expedite the dissemination of empirical findings into community-based oncology practices. In 2014, the CCOP was transformed into the National Cancer Institute Clinical Oncology Research Program (NCORP). NCORP provides the opportunity for world-renown oncology professionals and scientists to design and conduct cancer screening, prevention, treatment, control and care delivery research in a community setting.

A priority in NCORP is to increase the knowledge base for effective symptom management through the conduct of *research as part of cancer control clinical trials* focusing on: 1) identifying effective treatments to ameliorate and/or prevent toxicities, side effects and symptoms arising from cancer and its treatments, 2) elucidating biopsychosocial pathways through which symptoms, toxicities and side effects arise, 3) discovering mechanisms of action whereby interventions are effectively treating or preventing symptoms, toxicities and side-effects, and 4) developing novel biomarkers to predict risk for symptoms, toxicities and side effects, as well as individual patient response to available interventions. This is especially true in cancer control studies that test novel approaches to treating symptoms, toxicities and side effects stemming from cancer and its treatments rather than preventing or treating the actual disease. This area of cancer control research is also often referred to in oncology as symptom science. In support of this mission, the SXQOL Steering Committee is leading strategic planning efforts to maximally utilize NCORP resources to conduct rigorous cancer control research in a cost-effective and efficient manner that will have the greatest chance of rapidly, significantly and positively affecting cancer care in the United States and globally. This prioritization document addresses the “symptom” half of the Symptom Management and

Quality of Life Steering Committee charge, which is to promote the best symptom science possible with available resources.

The process for research strategic planning followed the procedures outlined in the SXQOL Steering Committee Plan for Research Priority Setting (Version October 30, 2014). In turn, this research strategic plan document was prepared with input from stakeholders including: 1) members of the NCORP SXQOL Steering Committee, 2) NCI staff in the Divisions of Cancer Prevention and Cancer Control and Population Sciences, 3) Cancer Patient and Lay Caregiver Advocates, 4) Principal Investigators of NCORP Research Bases, 5) Principal Investigators and Administrators of NCORP Community Partners and 6) Participants in NCI Clinical Trials Planning Meetings. The SXQOL Steering Committee and its stakeholders also considered information from several sources, including several national and international groups comprised of eminent scientists, clinicians and patient advocates that identified critical knowledge gaps in cancer control research and symptom science. The committee reviewed findings and suggestions from the:

1) *2009 NCI CIPN Clinical Trials Planning Meeting Working Group,*
2) *2010 NCI CCOP Strategic Planning Committee*
3) *2010 NCI CRF Clinical Trials Planning Meeting Working Group,*
4) *2011-2013 NCI SxQOL SC Cancer-Related Fatigue Working Group,*
5) *2012-2014 NCI NCTN Working Group,*
6) *2014 NCI SxQOL SC,*
7) *2014 NCI SxQOL SC Translational Research Working Group*
8) *2012-2014 MASCC International Fatigue Study Group, and*
9) *2012-2014 MASCC International Fatigue and Biomarkers Working Group.*

Toxicities, side effects and symptoms are expected but unwanted sequelae of a cancer diagnosis and its treatments. Some toxicities, side effects and symptoms occur in the acute setting immediately before or after diagnosis and during treatment. While some of these acute sequelae may subside and return to pre-diagnosis or pre-treatment levels, many will never return to baseline levels and become chronic persisting long after definitive treatments end. Some of these chronic toxicities, side effects and symptoms will also continue to escalate and worsen for months or years after

treatments are complete. Moreover, cancer and its treatments also portend late effects that arise for the first time months or years after treatments are finished. These toxicities, side effects and symptoms encompass a wide variety of physiological, psychological and sociological problems and can involve intricate interactions among numerous biopsychosocial and cultural systems.

Despite advances in the treatment of cancer and improvements in the length of survival, these toxicities, side effects and symptoms interfere with the completion of cancer treatments, negatively affect prognosis, increase the chances of recurrence, increase the occurrence of second cancers, result in multiple co-morbidities, increase healthcare costs and increase mortality. In turn, patients experience impairments in a wide variety of quality of life domains. Therefore, it is critical to identify the most clinically noxious toxicities, side effects and symptoms and to develop effective treatments to prevent and manage them in order to also improve the quality of life experienced by survivors. This is a critically important public health imperative across a broad landscape. Although *all* toxicities, side effects and symptoms experienced by patients are important, identification and prioritization of a specific set of high priority areas where focused research efforts in NCORP can rapidly, significantly and positively affect cancer care in the United States and globally is essential.

NCORP SXQOL Overarching High Priority Strategic Research Foci

The SXQOL and its stakeholders identified overarching guidelines for high priority research foci including:

1) Studies that are particularly suited for the NCORP mechanism and support through public funding agencies rather than studies that would be supported by private industry
2) Studies that address toxicities, side effects and symptoms with a high level of clinical relevance
3) Studies that address toxicities, side effects and symptoms with high levels of prevalence, incidence, severity, morbidity and/or mortality
4) Studies that are feasible and practical to conduct using the NCORP mechanism and in the community oncology environment

5) Studies that do not create excessive patient or provider burden

6) Studies across all types of cancer

7) Studies across all types of cancer treatments for the disease

8) Studies investigating all types of treatments for toxicities, side effects and symptoms, such as behavioral, integrative, nutraceutical, pharmaceutical and others.

9) Studies that test supportive care treatments that will be well-suited for broad dissemination in the community oncology environment

10) Studies that address needs across all adolescent, young adult and adult populations affected by cancer and its treatments (e.g., patients, survivors, providers and caregivers)

11) Studies that address the needs of underserved and underrepresented populations (e.g., geriatric patients, caregivers, lesbian, gay, bisexual and transgender patients, ethnic, racial, rural, low socio-economic status)

12) Studies across the entire cancer trajectory from pre-treatment through long-term survivorship and palliative care

13) Studies that utilize a clearly articulated and plausible theoretical framework

14) Studies that include clearly articulated and testable biopsychosocial mechanistic hypotheses

15) Studies that utilize rigorous research designs including single and multi-arm, as well as, randomized and non-randomized clinical trials

16) Studies that utilize valid and reliable objective (e.g. clinical, biomarker), and subjective (e.g. patient-reported, proxy and provider), biopsychosocial endpoints

17) Studies that include a strong cadre of multidisciplinary research teams

18) Studies that are supported by rigorous and compelling preliminary pre-clinical and clinical research

19) Studies that address translational science across the entire spectrum from T1 through T4 (e.g., bench to bedside to community dissemination/implementation)

NCORP SXQOL High Priority Areas for research

Importantly, one of the *major strengths* of research in the SXQOL portfolio is that it addresses a wide variety of toxicities, side effects and symptoms across all cancers, all populations affected by cancer, all types of cancer treatments, and all phases of the cancer trajectory from pre-treatment through long-term survival and palliative care. Unlike other NCTN disease site steering committees, the mission and purpose of the research supported through the SXQOL is broad and all-encompassing stemming from the necessity to address a myriad of challenges experienced by patients and clinicians. In an effort to preserve this strength of the SXQOL portfolio as cited in the NCTN working group review report of July, 2014, we will continuing to focus on a wide variety of toxicities, side effects and symptoms. As such, the committee will accept concepts and approve studies related to any toxicities, side effects or symptoms for which there is high clinical need, defined mechanistic hypotheses, sufficient preliminary data and high probability of practical success in completing the study within the NCORP network.

With this in mind, the SXQOL steering committee and its stakeholders have identified the following areas as toxicities, side effects and symptoms where there is a particularly high clinical need, emerging knowledge regarding potential biopsychosocial mechanistic pathways, and strong preliminary data to warrant larger longitudinal, prospective, cohort studies and large phase II and phase III randomized clinical trials. The SXQOL steering committee, its stakeholders and participants in NCI Clinical Trials Planning Meetings believe that focused research in these areas has the greatest potential to rapidly, significantly and positively affect cancer care in the United States and globally in the next few years. These areas include:

NCORP SxQOL First Tier High Priority Areas for Research

1) Cognitive Impairment
2) Neurotoxicity
3) Cardiovascular Toxicity
4) Fatigue
5) Cancer Specific Pain

NCORP SxQOL Second Tier High Priority Areas For Research

6) Sleep Disorders
7) Bone Health Toxicity
8) Metabolic Toxicity
9) Psychological Distress

In summary, the SxQOL SC along with its stakeholders have identified a clear and present need for more research in the field of symptom science where some, but not necessarily all, of the greatest opportunities for significant growth in the field of symptom science is through increasing the scientific foci on these high priority areas as part of cancer control clinical trials conducted via NCORP. Leveraging the NCORP network as a premier venue to test important hypotheses related to symptom science in these high-priority areas is not just a good option, it is absolutely the optimal option, because no other NIH or NCI network or program has the equivalent expertise, experience or infrastructure to do this type of cancer control science as rigorously, quickly, cost-effectively or efficiently in the United States or internationally.