# ACCELERATING IMPLEMENTATION OF EVIDENCE-BASED CANCER PREVENTION AND SCREENING STRATEGIES

## What is the recommendation?

Conduct implementation research to accelerate the adoption and deployment of sustainable, evidence-based cancer prevention and screening interventions at multiple levels and in different clinical and community settings. Advances in implementation science directed at the full integration of current evidence-based cancer prevention and screening interventions in 3 specific target areas across the country would dramatically accelerate progress in diminishing the cancer burden in the United States by averting an estimated 389,900 new cancer cases and 318,500 cancer deaths annually. Three high priority, high impact areas through which we can build the science of implementation are: HPV vaccination, colorectal cancer (CRC) screening, and tobacco control. This recommendation would significantly impact cancer outcomes in the general population as well as among populations that experience persistent cancer disparities (e.g. low income, minority, rural, and other underserved populations).

This recommendation will serve as a robust platform for accelerating the implementation of additional forthcoming population-level, cancer prevention and control recommendations resulting from other Cancer Moonshot initiatives, which could avert additional cases of cancer and deaths.

## Where are we now?

In the US, we do not routinely implement proven cancer prevention and screening interventions on a large scale. Instead, we allow millions of people to develop and die from highly preventable forms of cancer. Furthermore, by not implementing these interventions in ways that reach populations with greatest need, we permit disparities to persist.

## Summary of the current state of the science/practice

There now are proven cancer prevention strategies that, if widely used, would reduce cervical cancer mortality by 90%, CRC cancer mortality by 33-70%, and lung cancer by 60-95%, with relatively rapid returns. Yet, these strategies are not scaled sufficiently, leaving millions of Americans at high risk for preventable disease and death. If we can succeed in identifying effective implementation strategies for the three exemplar areas, we can not only make tremendous strides in improving health in these specific areas, but can also apply this knowledge toward implementing the full complement of evidence-based cancer interventions. Below is a current state of the science for each of the three exemplar areas:

- Persistent infection with oncogenic HPV types has a causal role in nearly all cervical cancers and in many vulvar, vaginal, penile, anal, and oropharyngeal cancers, with HPV 16 and 18 contributing the majority of these cancers [1,2]. Over 30,000 HPV-related cancers are diagnosed each year [3] in the US with great costs not only for treating these cancers but for treating pre-invasive disease, genital warts, and other conditions caused by HPV infection [4]. HPV vaccines (2-valent, 4-valent, and now 9-valent) are efficacious in reducing infection with

cancer-causing strains of HPV and reducing pre-invasive cervical lesions [5-8]. Unlike countries with national vaccination programs that report vaccination rates as high as 95% (e.g., Australia, Rwanda, UK), rates of the vaccine series completion are woefully low in the US – 40% among girls and 22% among boys (age 13-17, 2014).

- About 1 in 3 adults between 50 and 75 years old – about 23 million people -- are not up-to-date for CRC screening [9]. Populations with documented low screening rates include Hispanics, American Indians/Alaska Natives, Asians, rural populations, foreign-born, and those with lower education and income [10]. Equally important is the timely follow up for abnormal screening tests, which is lower in safety-net systems serving low-income and under-insured patients than in other settings [11].
    - 40 million US adults currently smoke [12]. Between 50-65% of all smokers will die from a tobacco-related disease, on average 14 years younger than non-smokers [13-14]. Lung cancer is the leading cancer killer in both men and women in the US; in 2015, about 30% of all cancer deaths were from lung cancer—a largely preventable disease [15]. There is very strong evidence on the benefits of comprehensive tobacco control (e.g. the effectiveness of clinical interventions for cessation [16], the impact of coverage for cessation medications on their uptake [17], taxes and public policies limiting tobacco use). Yet, this evidence has not been implemented consistently or adequately across the US. Among cancer patients/survivors, persistent tobacco use is estimated as at least 10% and causes adverse clinical outcomes resulting in a compelling need to improve implementation of evidence-based treatment of tobacco dependence in cancer care settings (US Department of Health and Human Services, 2014).

## Barriers to progress and/or emerging opportunities

The major barrier relates to the lack of empirical support for large-scale implementation strategies to optimize use of proven cancer prevention and screening interventions. We selected HPV vaccination, CRC screening, and tobacco control, because these are examples where substantial progress has been made in identifying interventions that work, providing remarkable opportunity for acceleration of the uptake of these modalities in the population. Below are barriers specific to each area. Please note that in some of these, there are barriers related to regulatory and policy issues, which have been listed in a different document.

- Major reasons for low HPV vaccination rates include failure of physicians to recommend the vaccine during routine well-child visits, parental fears about the vaccine and possible side effects, lack of knowledge about the vaccine and its cancer prevention efficacy, cultural and spiritual practices in some populations, and mis-information about the relationship of the vaccine to sexual promiscuity [18,19]. The HPV vaccine should be regarded as cancer prevention – to avoid mis-association with sexual promiscuity. New HEDIS (2017) [19] and current Affordable Care Act provisions would support this strategy.
- Barriers for CRC screening include failure of physicians to recommend it to patients, lack of identification of those needing screening by electronic health records (EHR), and the belief that colonoscopy is the only screening tool. Moreover, discussion about the test itself and the function of the colon reduce discussion of the test by people who need it.

- Using the evidence available right now, there are extraordinary opportunities to dramatically reduce tobacco-related cancer morbidity and mortality. However, a major barrier relates to our limited knowledge about how to best implement and sustain comprehensive tobacco control in a range of situations, including where there is limited state-level policy support, through existing health-related infrastructure (e.g. cancer centers, health insurance products), and where tobacco-related disparities are high.

### Key research priorities

Over the next 5 years, we encourage research that advances implementation science to develop and test effective, scalable multi-level (e.g. individual, family/caregiver, provider, system, community) and sustainable interventions in community settings to: 1) increase HPV vaccination initiation and completion rates; 2) increase CRC screening and follow-up of abnormal findings; and 3) reduce tobacco use. This research would directly impact cancer outcomes in the population and among populations that experience persistent cancer disparities (e.g. low income, minority, rural, and other underserved populations), as well as provide an evidence base to apply to the implementation of other cancer interventions. Below are specific research recommendations for each area; each should especially focus on safety-net settings such as health department clinics and federally qualified health centers (FQHCs).

To increase HPV vaccination rates in girls and boys, develop research to: 1) identify, understand, and develop strategies for bundling the recommendation for HPV vaccine with the Tdap and MCV4 vaccines at well-child visits at age 11-12; and 2) test multi-level implementation science approaches to improving rates of catch-up vaccination among girls age 13-26 and boys age 13-21 in all health care and other appropriate venues.

To increase CRC screening and follow-up rates, develop research to: 1) identify, understand, and develop multi-level strategies for increasing CRC screening and follow up of positive test results; and, 2) disseminate effective multilevel interventions in primary care settings.

For tobacco control research, develop a program of research to determine: 1) what factors lead to successful implementation of evidence-based comprehensive tobacco control strategies (CTCS) at the state level and through other systems (e.g. cancer centers), and to reduce the variability in implementation across states; and, 2) what factors can be modified to increase the percentage of low income and other under-served smokers that have access to and use CTCS.

### Rationale for investing

Advances in implementation science are needed to accelerate the development and testing of effective, scalable strategies to optimize reach and overcome multi-level/multi-focal barriers to the adoption, implementation and sustainability of evidence-based prevention and screening interventions. The three exemplar areas were specifically selected because they are ripe for acceleration using implementation science, and at the same time can have a profound impact on cancer mortality. Together, they have the potential to save upwards of 318,000 lives annually and to prevent cancer in 389,900 people. Specific justifications for each area are:

- New 9-valent HPV vaccine will cover over 90% of cancer-causing HPV infections. In addition if 2 doses of the vaccine are approved in the US, opportunities to provide full coverage for many children will increase.
- We have CRC screening modalities that work, the capacity to implement these, and effective models for implementation. We also have evidence-based recommendations for follow-up of abnormal CRC screening tests.
- We have tobacco control strategies that work and effective models for implementation.

### New or expanded research resources

- Develop new resources (registries, standardized outcomes tools), improve current resources and leverage existing NIH-funded network infrastructures (e.g., Cancer Centers, NCORP, CTSA) to rapidly develop and test implementation strategies for evidence-based interventions and evaluate and improve measures for implementation research and practice.
- Designated resources for development and maintenance of EHR capacity for implementation of evidence-based cancer prevention strategies in health care delivery settings.
- Examine current repositories of evidence-based practices and implementation strategies; and strengthen their potential usability for dissemination and efficient implementation of evidence-based interventions.
- Develop common measurement tools and centralized data capture platforms for key implementation constructs.
- Electronic technologies to establish: 1) state vaccine registries with reporting and surveillance capabilities; and 2) local and national reporting of CRC screening surveillance (as opposed to relying on self-reported data such as BRFSS).
- Training programs for clinicians and scientists in effective implementation research methods, especially those working in underserved communities.

### New scientific approaches

- Implementation research should be conducted on how to tailor and deploy evidence-based interventions at multiple levels (e.g. individuals, providers, systems, communities) and in different clinical and community settings.
- Empirical research to understand how to increase: 1) acceptance of the HPV vaccine as a cancer prevention strategy; 2) acceptance of CRC screening modalities (i.e., stool tests, endoscopy) in the public, especially among underserved communities and moving away from primarily or solely marketing colonoscopy for screening; and 3) acceptance of tobacco as the primary preventable cause of cancer that can be overcome through comprehensive efforts across multiple settings, including health care systems, cancer care delivery, schools, workplaces, communities, and in public policies.

### Concrete actions to take in the next 1-5 years

We believe that developing a research resource that includes evidence-based implementation strategies and a repository of implementation data focused on implementation in the three focal areas as well as others would be transformative through the accumulation of evidence-based strategies under a single entity. This would also provide a setting for archiving what strategies do not work and/or need to be de-implemented.

We also believe that development of a cohort of rapid implementation studies would significantly accelerate the field. Specific research within this group of studies could be conducted on scale-up, spread, combination of practices, and the context in which key prevention and treatment strategies become widely adopted, or not.

## What does success look like?

Success would result in greatly reduced incidence of and mortality from preventable cancers, within 5-10 years. Success would also include research to identify effective implementation strategies that can be used across a wide range of cancer targets and discoveries. Specific metrics of success for each of the three exemplars include:

For HPV vaccination:

- Vaccination rates for girls and boys aged 13 of 80% for 3 shots (or 2 shots if US moves to that schedule). Based on Australia's experience, reduction in high grade cervical lesions will be seen within 5 years [20].
- Reduction of vaccine-type HPV prevalence in girls and boys by 50% within 5 years (from 11%-5%) [21].
- Reduction in 6 types of HPV-related cancers (cervical, vulvar, vaginal, penile, anal, oropharyngeal) until the majority are eliminated. Currently, 6 cancers are known to be caused by HPV – approximately 26,900 annually. It is estimated that with high levels (>80%) of HPV vaccine coverage in girls and boys, up to 26,900 of these cancers could be prevented annually as well as up to 6,100 deaths [22].

For CRC screening:

- Increasing CRC screening rates to 80% by 2018 would prevent an estimated 43,000 new cases and 21,000 deaths annually [23], and eliminating disparities in screening, and stage of disease in 5 years and incidence and mortality by 10 years.

For tobacco control:

- Increased percentage of smokers, and particularly low income smokers and other under-served smokers, with *access* to CTCS; 90% of state Medicaid programs and 90% of health insurers offering access to medications and counseling on all insurance products.
- Increased *use* of CTCS by low income and other under-served smokers; at least 50% of these smokers accessing CTCS annually.
- These recommendations would avert up to 320,000 new cancer cases and 291,400 cancer deaths. The overall impact for all-cause morbidity and mortality would be significantly greater [24].

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# Implementation of Integrated and Evidenced-based Symptom Management Throughout the Cancer Trajectory

## What is the Recommendation?

Poorly controlled symptoms cause unacceptable suffering for cancer patients and cancer survivors. This promotes the discontinuation of effective treatments and decreases survival. Poorly controlled symptoms also add to health care costs and are the most common reason for cancer patients' use of emergency departments and unplanned hospitalizations. Symptoms profoundly impact the quality of life of patients, survivors and their families and disrupt important societal and family roles. We are at a tipping point, that with new investment and a clear charge, symptoms can be dramatically reduced through the testing and implementation of technology-assisted comprehensive models of supportive care. Improved symptom care would significantly contribute to the efficacy of new and existing treatments by increasing patients' adherence and persistence with treatment through the completion of therapy. The Moonshot Initiative provides the opportunity to boldly address this issue.

*Therefore, we recommend a strategic investment through implementation science approaches to accelerate the clinical adoption of technology-aided comprehensive and integrated systems that systematically-gather and monitor patient-reported symptom outcome data (PRO) and provide actionable decision support approaches utilizing evidence-based cancer symptom management guidelines to treat symptoms as they emerge throughout the cancer continuum.*

Cancer treatments have successfully extended the survival and even cured an increasing number of people. Currently 5 percent of the population in the United States (approximately 15.5 million people) are cancer survivors, a figure that is anticipated to increase to 20.5 million by January 2024 (*American Cancer Society. Cancer Facts & Figures 2016. Atlanta: American Cancer Society; 2016)*. Annually 650,000 cancer patients are treated with chemotherapy and 470,000 receive radiation alone or in combination with chemotherapy (www.cdc.gov/cancer/providers.htm) (1). However both disease and treatment cause deleterious symptoms and side effects which occur during the course of treatment or can continue or appear long after treatment is completed (2). All patients experience unpleasant side effects, but nearly a third of those receiving chemotherapy or radiation therapy, (> 350,000 patients annually) report three or more co-occurring moderate to severe symptoms during treatment (3), which contributes to lower functional status and quality of life (4), leads to multiple costly visits to the emergency departments (with over half resulting in hospitalization) (5, 6), and can cause treatment delays and discontinuation of therapy (7-10). Treatment delays and lack of persistence with treatment due to symptoms are particularly concerning because they decrease treatment effectiveness and increase the risk for recurrence and death. Even after an initial successful treatment, patients requiring maintenance therapy (hormonal therapy or chemotherapy) experience unpleasant symptoms and often decide to stop taking the medication. Adherence and persistence with treatment is particularly important given the growing number of oral therapies both for initial treatment and maintenance therapy (11-13). Studies show, for example that up to 50% of breast cancer patients receiving hormonal therapy discontinue it before completing the recommended

5-year treatment, even though it is proven to significantly prolong disease free survival. The most common reason given for discontinuance is poorly controlled symptoms related to the treatment (14, 15). When symptoms are poorly controlled, cancer treatment adherence is particularly challenging for the medically underserved and those with low health literacy (16). Poorly controlled symptoms have also been shown to increase the likelihood of patients leaving the workforce and not returning to work, even those who were disease free (17-19). Given all of the evidence of the harmful effects of poorly controlled symptoms, there is a compelling need to improve symptom care so that patients and survivors have optimal quality of life, ensure their adherence to treatment, and improve the therapeutic response and extend survivals possible with current and emerging cancer treatments.

*Barriers to Progress:*

*Lack of a systematic and effective way of* ***assessing and addressing*** *disease and treatment related symptoms.* Symptoms and many side-effects are patient-reported experiences that present in varying patterns and intensities mostly when patients are at home after receiving treatment and during the survivorship period. This presents both assessment and management barriers for the cancer care team to remotely monitor symptoms and implement appropriate care. Patients and their family caregivers also find it difficult to know when and how to effectively communicate concerns. There is increasing recognition of the essential need for the implementation of tools to remotely collect patient-reported symptom data, bring poorly controlled symptoms to the attention of the cancer care team, and use the patient-reported outcome (PRO) data to guide symptom control efforts (20). PRO data has yet to be automatically integrated within the electronic health record or included in big data resources thus limiting our ability to utilize patient symptom reports to directly improve patient care or to track and benchmark symptom outcomes (21). We are now at a critical juncture to exploit these advances to reduce symptom burden through the convergence of electronic health records with systems that can collect PRO data electronically.

*Poor implementation of evidence-based guidelines for symptom management:* National evidence-based guidelines for symptom management and supportive care throughout the care trajectory (from diagnosis throughout cancer survivorship/end-of-life) are widely available and promulgated by a number of cancer organizations including the National Comprehensive Cancer Network (NCCN), the Oncology Nursing Society (ONS), Multinational Association of Supportive Care in Cancer (MASCC) and the American Society of Clinical Oncology (ASCO). Despite the availability of these systematic assessment tools and evidence-based supportive care guidelines, they are not systematically used in practice nor are they provided to clinicians in a readily actionable format and, as a result, cancer patients and survivors do not benefit from evidence-based approaches to reduce their symptom burden. Thus, utilizing what is already known and implementation science approaches, there is an immediate and enormous opportunity, if adequately resourced, to dramatically decrease the burden of poorly controlled symptoms and, as a result, reduce suffering, improve the quality of life of cancer survivors, increase treatment adherence, improve the willingness of patients to participate and persist with clinical trials, and decrease symptom-related avoidable emergency department and unplanned hospitalizations and their associated costs.

*Opportunity and Priorities for Accelerated Implementation:*

The field of symptom management in cancer is at a tipping point where the gap between current and more effective supportive and palliative care provision could be rapidly closed if we capitalize on recent scientific advances including the valid measurement and reporting of patient-reported outcomes (PROs), current evidence-based symptom treatment guidelines, and the integration and clinical adoption of comprehensive supportive care delivery models that improve cancer symptom care and outcomes. Technology-aided solutions now allow the development of efficient, comprehensive systems to monitor patient-reported symptom experience, coupled with a systematic approach to guideline-based symptom care, provided when and where the patient needs it (22-25). Like precision medicine that treats the signature components of the individual tumor, precision care tailors symptom care to the individual patient's signature symptom pattern as it emerges over time. It also helps overcome current access barriers and patient factors that interfere with effective symptom care such as geographic distance of the patient's residence from the cancer treatment facility. Thus, we recommend that funding from the "Moonshot Initiative" be invested in accelerating the implementation of systematically gathered patient-reported outcomes (PRO) and the adoption of evidence-based cancer symptom management guidelines to decrease the deleterious effects of cancer and its treatment.

*Systematic Implementation of Patient-Reported Outcomes*: Systematic symptom assessment, not confined to clinic/office visits, is a key component of improving symptom care throughout the cancer trajectory. There are recent advances in the systematic collection of patient-reported symptoms and functional status data through validated patient-reported outcome (PRO) tools such as those available through the NIH-supported PROMIS and PRO-CTCAE initiatives. The accelerated funding of implementation science research on how to deploy these PRO measurement technologies, would rapidly remove the current communication barrier between cancer care providers and their patients/survivors and family caregivers, providing the mechanism to report poorly controlled symptoms whenever and wherever they are present. There is also a need for research on how to integrate these systems into care delivery (including the electronic health record), the most effective ways for the cancer care team (and primary care providers involved in the care of survivors) to act upon the PRO data and intensify symptom care, how to optimize use in diverse patient populations, how to expand their use with patient self-management strategies and e-Health applications, and how to use these systems to effectively address supportive and palliative care access barriers including outreach to underserved, rural, and frontier communities.

*Implementation of Symptom Management Guidelines*: Despite the availability of assessment tools and national evidence-based supportive care treatment guidelines, they are not systematically used in practice and, in particular, there is often a failure to intensify symptom care when initial symptom treatment is unsuccessful. Thus, there is an immediate and enormous opportunity to dramatically improve the quality of life of cancer patients and survivors if the gap could be closed between what is currently known about assessment and treatment of symptoms and what is currently done in practice. There is a need to accelerate innovative approaches and

systems that make existing evidenced-based supportive and palliative care guidelines actionable. Approaches must be efficient, use technology and assist health care providers to rapidly evaluate symptom data and utilize decision support systems for evidence-based approaches to treat poorly controlled symptoms whenever and wherever patients and survivors need help. Implementation research in this area could provide evidence on ways to more rapidly disseminate care guidelines in general.

*Implementing Patient Self-Care and Family Caregiver Support*: Although symptom management requires assessment and care by the cancer team, patients and their family caregivers must be knowledgeable and adopt both cognitive and behavioral approaches for self-management. Since cancer treatment is almost exclusively given on an outpatient basis, patients and their caregivers are dealing with symptoms and toxicities at home, on their own. Further research is urgently needed to test innovative ways to remotely engage and support patients and families in self-management behaviors, integrate and test new technologies and develop strategies that engage and support self-management in underserved populations such as low health literacy, non-English speakers, racially and ethnically diverse populations and those living in remote rural and frontier communities.

*Identifying optimal cancer care models.* There is a need to test and disseminate optimum models for the delivery of coordinated symptom care throughout the cancer trajectory. These models include evolving approaches toward delivery of primary and specialized forms of supportive and palliative care. Effective models would promote the coordination of care within the cancer team and with others involved in the care of the survivor, particularly the primary care provider, leading to improved support for adherence with oral therapies, reinforcement of optimal self-management strategies and timely provision of intensified symptom care for poorly controlled symptoms including assistance for cancer family caregivers. Implementation science approaches are required to determine optimal care models that include technology and bridge gaps in communication, coordination and provision of care and self-management support for patients and their family caregivers. In addition, current reimbursement mechanisms also hamper adoption of innovative symptom care models and systems, particularly care delivery that extends to the home or involves support to family caregivers and updated health policy and value-based reimbursement remedies are needed to ensure widespread uptake.

Technology-aided solutions now allow the development of efficient, comprehensive systems to monitor patient-reported symptom experience, coupled with a systematic approach to guideline-based symptom care, provided when and where the patient needs it. Like precision medicine that treats the signature components of the individual tumor, precision care tailors symptom care to the individual patient's signature symptom pattern as it emerges over time. It also helps overcome current access barriers and patient factors that interfere with effective symptom care such as geographic distance of the patient's residence from the cancer treatment facility.

Strategy: We therefore propose the following key priorities for accelerating research that, with additional investment and strategic focus, would transform symptom care and improve cancer outcomes in a short period of time. These strategies focus on accelerating two concurrent

opportunities: 1) To improve the systematic collection, integration, monitoring and benchmarking of PRO data and 2) To develop and deploy into cancer care settings, technology-aided comprehensive, integrated symptom monitoring and management systems.

- Conduct research that identifies the best approaches by which patient-reported symptom (PRO) data can be systematically and rapidly collected and used to trigger a coordinated actionable response within the cancer care team (and with others involved in the care of the survivor), that results in effective symptom control, improved quality of life, persistence with therapeutic cancer treatments and reduction in avoidable health care utilization.

- Promote the automatic integration of PRO data into the Electronic Health Record (EHR) and into all large cancer-related databases so outcomes can be closely tracked and more comprehensively capture the entire cancer experience so that gaps that require further research can be easily identified and benchmarking can accelerate systematic improvements in symptom outcomes. This would include the development of compatible software to provide seamless transitions between stand-alone PRO data collection packages and dissemination within EHRs and migration into large data sets.

- Through implementation science research, determine the optimal mechanisms (effective and scalable in different cancer care models) and support systems to accelerate the adoption and use of evidence-based guidelines to prevent, control, and manage symptoms related to cancer and its treatment within the cancer team and with others involved in the care of the survivor and provided to the patient and/or family caregiver wherever they reside.

<u>What is needed to achieve this:</u> The first step is to conduct a demonstration project to show the capability of comprehensive prototype systems that combine the various elements of symptom monitoring using PRO data, automated self-management coaching, and guideline-based decision support, to reduce symptoms and alter providers' management strategies for poorly controlled symptoms. Various prototypes models are already under development including several that have been funded by NCI. Once these system capabilities and outcomes are demonstrated, then multilevel interventions will be needed to address the integration and clinical adoption of these systems. This will require a combination of implementation efforts, research, overcoming technical barriers, and policy changes, which will be best accomplished in collaborative efforts across a variety of agencies and organizations. The combination of providing the appropriate technology to practices plus an incentive through a mandate (e.g. Committee on Cancer - CoC) will help with the final level of implementation and dissemination.

*Patient Reported Outcome Specific Needs:*

- To overcome technical barriers there needs to be a seamless interface for telehealth (phone, web, and handheld or wearable devices) that allow the reporting of patient symptoms with the major EHR systems, with easy to utilize and tailored assessment tools that address the range of symptoms associated with the prescribed treatment and type

of cancer, and populate the EHR systems including providing visualization of data and symptom patterns and indicate meaningful symptom scores requiring clinical attention and measuring effectiveness of interventions, triggering further actionable responses if not achieved. This will require industry-academic partnerships to engage vendors like Epic and Cerner and others.

- Research is needed in how to best visualize PRO information so the cancer care team can make rapid recommendations and management decisions in conjunction with easy-to-use decision support aids that seamlessly display current evidence-based approaches to symptom care.
- For systematic tracking of patient-reported outcomes, a standard set of measures should be adopted so that outcomes can be compared, allowing identification of best practices and symptoms in need of further research. The Centers for Medicare and Medicaid Services, which are involved in an effort to collect PRO data from a large number of health facilities, have identified PRO data elements that are relevant to symptom management.
- Meaningful score thresholds need to be defined for alerts and clinical action. There should be PRO value metrics for oncology endorsed by the National Quality Forum (NQF) and efforts to promote best practices and systematic improvement in patient-reported outcomes as a standard of care in oncology.
- Feasibility studies across diseases and care settings should be established to find best ways to engage patients and clinicians to work PRO reporting and management systems into practice and workflow. This would require participation of community stakeholders to develop and test implementation models in practice. Capability to tailor to specific treatment or disease symptom patterns and differing patient populations such as low literacy, ethnic, cultural or geographic differences will increase meaningful assessment and patient and survivor engagement in their use.
- There should be demonstration projects with the FDA in the use of these data for drug assessment.
- Ultimately the reporting and rapid collection of PROs and use of PRO symptom data to promptly intensify symptom care would be a requirement/standard of care expectation of all major cancer professional, public and advocacy groups (e.g., by the CoC, ASCO QOPI, ONS, ONC, etc.) and would also be integrated into all large cancer databases including SEER. Clinical trials also could collect PRO data and use PRO data to track side effects and determine why certain patients experience toxicities whereas other patients do not.

*Evidence-Based Symptom Guideline Specific Needs:*

- Discrepancies in supportive care guidelines across groups that promulgate these guidelines should be identified and consensus developed for best practices and efficiencies in rapidly updating as new science is produced.
- A systematic process should be utilized to identify symptoms that currently require evidence-based guidelines development and enact an inter-professional process to rapidly develop new guidelines.
- Evaluation studies are needed that test symptom decision support systems that interface

with the EHR and PRO data and link appropriate guideline recommendations for poorly controlled symptoms so that clinicians can rapidly and efficiently provide further evidenced-based care.

- There is a need to test technology-aided tools and e-Health approaches that provide symptom self-management coaching for patients and family caregiving as symptoms emerge and that assist patients to maintain the highest level of physical functioning and emotional wellbeing throughout the continuum of cancer (22-25). These patient-facing tools should be integrated with the patient reported symptom assessment system and the clinician decision support system so there is a comprehensive and coordinated approach to symptom care.
- Studies are needed to tailor symptom coaching so it is acceptable and engages patients/survivors and family caregivers. This includes tailoring for underserved populations such as low health literacy, non-English speakers, racially and ethnically diverse populations and those living in rural and frontier communities.
- There is a need for research projects that evaluate these comprehensive symptom care systems and identify their impact on symptom burden, quality of life, adherence and persistence with treatment, ability to maintain family and societal roles,, earlier identification of adverse events and late effects and decrease avoidable health care utilization (emergency department and unplanned hospitalizations).
- Implementation science studies are required to find best practices to engage clinicians to adopt and integrate guideline-based decision support symptom management systems into practice and workflow.
- Mechanisms for reimbursement of remote symptom monitoring and symptom care are required and incentives for adoption and maintenance of technology-aided systems will be needed for widespread clinical adoption.

Demonstration Project: A demonstration project to test prototype comprehensive symptom monitoring and management systems is being proposed (see Appendix). The demonstration project is designed to test existing automated, telehealth or e-health systems that track PRO's and symptoms, coaches patients/family caregivers and alerts providers when symptoms are poorly controlled and through decision support, prompts clinicians in the use evidence-based guidelines to respond.

What does success look like?

1) Systems for the routine monitoring and management of patient-reported symptoms are the standard of care for cancer patients in all care settings throughout the cancer continuum (from diagnosis throughout survivorship and at end-of-life) and tailored to differing patient and survivor needs. These systems rapidly link the cancer patient/survivor/family caregiver with knowledgeable and prepared health care providers for poorly controlled symptoms and provide timely self-management resources that effectively and efficiently control adverse symptoms and enable optimal quality of life. These systems are tailored to the needs of diverse communities and populations including those that live at a distance from their cancer treatment facility. There is adequate reimbursement for the deployment and use of these systems.

2) Routinely collected self-reported symptom data is an integral element of all national cancer databases and is actively utilized to a) revise and update evidence-based guidelines, b) track patient-reported outcomes, c) make comparisons, share best practices and encourage the attainment of a high standard for symptom control and supportive care nationally, and d) are systematically mined to identify gaps and new scientific questions that should be addressed through symptom science to improve outcomes.
3) Patients no longer dread the deleterious symptoms of cancer and its treatment, they are able to persist with and benefit from recommended therapy and participate in clinical trials, they are able to maintain optimal well-being and stay engaged in meaningful family and societal roles and there is a marked decrease in cancer care costs related to emergency department visits, urgent care, and unplanned hospital admissions.
4) Symptom Prevention and Management Research will fuel future discoveries including
    a. Research that solves symptom monitoring and management implementation barriers and integration into the mainstream of cancer care including the electronic health records. Scalability and widespread adoption will require collaboration with the commercial sector.
    *b.* Testing of innovative ways to remotely engage and support patients and families in self-management behaviors that can be integrated within comprehensive symptom management systems.
    c. New science that discovers innovative and improved approaches to accelerate precision care and addresses unanswered symptom science questions including:
        i. Identifying effective approaches and interventions to <u>prevent</u> symptoms.
        ii. Understanding who is at highest risk for particular symptoms and adverse outcomes (i.e. genetic, genomic and biomarkers of symptoms), how to tailor symptom care for these high risk groups, and determine who benefits most/least from specific symptom treatments.
        iii. Understanding mechanisms of effective symptom interventions (genetics, genomics and pathways) and utilize this information to develop additional treatments.
        iv. Understanding how to a<u>ccelerate recovery</u> from symptoms, and determine how to <u>optimize health and maintain wellbeing</u> of patients/survivors and their family caregivers throughout the cancer continuum.
        v. Determine best practices to tailor symptom care for underserved populations such as those with low health literacy, non-English speakers, racially and ethnically diverse populations and those living in remote rural and frontier communities.

# Appendix:
## Symptom Management Demonstration Project Proposal

*Improving Quality of Life through Precision Care to Monitor and Alleviate Symptoms*

State of the Science: *A Major Unmet Medical Need and Societal Concern: Diminished quality of life due to poorly controlled symptoms*

- Poorly controlled symptoms cause unacceptable suffering for cancer patients, survivors and their families, lowers the quality of life, interferes with adherence and continuation of lifesaving or life-extending therapies and adds to avoidable health care costs.
- Deleterious symptoms and side effects caused by cancer and its treatments occur in most patients, with nearly a third of patients receiving chemotherapy and/or radiation therapy (> 350,000 new patients per year) reporting 3 or more co-occurring moderate to severe symptoms (2, 3). Many symptoms occur during the course of treatment and for many survivors, they continue or appear as late effects long after treatment is completed.
- Poorly controlled symptoms contribute to [4-19]
    - lower physical functioning, psychological distress and suffering, loss of employment or extended medical leaves, and lower quality of life
    - multiple costly emergency department visits with over half resulting in unplanned hospitalizations
    - treatment delays, lack of adherence and discontinuation of therapy which decreases treatment effectiveness and increases the risk of recurrence and can lead to decreased survival and death.
    - refusal to participate in clinical trials
    - caregiving burden and stress for family caregivers
- Adherence and persistence with treatment is particularly important given the growing number of oral therapies both for initial treatment and as maintenance therapy after successful initial treatment [11-13]. Poorly controlled symptoms are the primary reason for lack of adherence [14-15].
- Intensifying symptom care is particularly difficult because symptoms fluctuate and occur after patients are at home in between scheduled clinic visits or after treatment ends making it difficult to monitor and communicate concerns between the cancer care team and patient/family caregivers.
- There are inadequate reimbursement models for symptom monitoring and symptom management nor are there incentives to adopt technology-assisted symptom monitoring and management systems.
- There is a compelling need to improve symptom care so that patients and survivors have optimal quality of life, ensure their adherence and persistence with treatment, and improve the therapeutic response and extended survivals possible with current and emerging cancer treatments.

New Science Creating an Exceptional Opportunity to Accelerate Research

- Symptom burden could be swiftly and significantly reduced through implementation science approaches to the application of current, evidenced-based advances to monitor and treat symptoms.
- Technology-aided solutions now allow the development of efficient, comprehensive systems to monitor patient-reported symptom experience, coupled with a systematic approach to guideline-based symptom care, provided when and where the patient needs it. Like precision medicine that treats the signature components of the individual tumor, precision care tailors symptom care to the individual patient's signature symptom pattern as it emerges over time. It also helps overcome current access barriers and patient factors that interfere with effective symptom care such as geographic distance of the patient's residence from the cancer treatment facility.
- Recent advances in technology-aided measurement and reporting of patient-reported symptom outcomes (PROs), such as PRO-CTCAE (26), now permits the deployment of automated measurement technologies which would provide the mechanism for patients to report poorly controlled symptoms whenever and wherever they are present.
- National cancer symptom and palliative care evidenced-based guidelines are readily available and regularly updated by a number of professional organizations. However, these guidelines are underutilized and not provided in a decision-support format that can be easily utilized in clinical settings (27, 28). This gap in actionable guidelines that facilitate adoption of current best symptom care practices could be quickly closed and achieve immediate patient benefit by utilizing implementation science approaches to promote adoption and development of decision-support systems for symptom management.
- While symptom management requires assessment and care by the cancer team, patients and their family caregivers must be knowledgeable and adopt both cognitive and behavioral approaches to symptom self-management. There is now an opportunity to capitalize on technology and e-Health approaches and integrate innovative self-management coaching and support for patients and family caregivers into emerging integrated comprehensive symptom care systems.
- Thus, there is an immediate and enormous opportunity to dramatically improve the quality of life and decrease the suffering of cancer patients and survivors by the development and deployment of comprehensive integrated models of coordinated symptom care aided by technology.

Demonstration Project Proposal to Address this Grand Challenge to Eradicate Symptoms

- A demonstration project would test prototypes of automated telehealth or e-health comprehensive and integrated PRO symptom management systems (22-25) that implement remote PRO symptom monitoring, tracking all common and expected symptoms (both physical and psychosocial), coach patients/family caregivers on self-management and alert cancer care providers of poorly controlled symptoms. The cancer care providers would be prompted through decision support aids to use evidence-based

symptom and palliative care guidelines to promptly intensify symptom care and would monitor effectiveness of interventions and alert clinicians when inadequate.

- Implementation of the demonstration project could take a variety of forms.
    - It could be conducted between an NCI designated cancer center and a Minority Underserved NCORP which would allow testing of the system in two different care settings.
    - Systems could be tested broadly across cancers commonly found in community oncology practices or could be narrowed to specific cancers such as non-Hodgkin lymphoma, breast or colorectal cancer in cancer centers where disease-specific specialty care is provided.
    - Systems could be tested that match patient/survivor needs during each phase of the cancer continuum- from diagnosis and treatment, transitioning to post treatment, recurrence free survivorship as well as advanced stage cancer including palliative and hospice care.
    - It could demonstrate the ability to bridge inequities in care through tailored approaches that effectively address patient and family caregiver needs in rural and frontier communities, ethnic and racial minorities, non-English speakers, or those with low health literacy.
- To explore potential scale-up and implementation issues, process and outcomes variables should be collected. Process variables could include patient/survivor and clinician adherence, engagement and satisfaction with the system, workflow issues, variation in provider type and process for responding to symptom alerts, and system level implementation barriers. Outcomes should include symptom severity and symptom reduction overall and by individual symptoms, physical functioning, treatment adherence and persistence, work absenteeism and presentism and health care utilization (emergency department visits and unplanned hospitalizations).

<u>Fueling Future Discoveries:</u> *New Opportunities Stemming from the Knowledge to Achieve Effective Symptom Prevention and Treatment*

- In addition to this demonstration project of system prototypes, future research is needed to address implementation issues and best practices to continually update and integrate these systems into care delivery including the electronic health record and collaborations needed for integration and commercialization.
- Further research will be needed to test innovative, technology-aided ways to remotely engage and support patients and families in self-management behaviors and incorporate these approaches into comprehensive symptom management systems.
- New science that discovers innovative and improved approaches to accelerate precision care and addresses unanswered symptom science questions including:
    - Identifying effective approaches and interventions to <u>prevent</u> symptoms.
    - Understanding who is at highest risk for particular symptoms and adverse outcomes (i.e. genetic, genomic and biomarkers of symptoms), how to

tailor symptom care for these high risk groups, and determine who benefits most/least from specific symptom treatments.

- Understanding mechanisms of effective symptom interventions (genetics, genomics and pathways) and utilize this information to develop additional treatments.
- Understanding how to accelerate recovery from symptoms, and determine how to optimize health and maintain wellbeing of patients/survivors and their family caregivers throughout the cancer continuum.
- Determine best practices to tailor symptom care for underserved populations such as those with low health literacy, non-English speakers, racially and ethnically diverse populations and those living in remote rural and frontier communities.

## Summary

For decades, cancer patients and survivors have suffered from poorly controlled symptoms that have lowered their quality of life, interfered with adherence and persistence with lifesaving or life-extending therapies and added to avoidable health care costs. These symptoms do not cease with the completion of treatment and profoundly affect day-to-day functioning and the quality of people's lives. While there has been progress in treating cancer with growing survival and cures, to date there has been limited research dollars and science focused on addressing symptom burden, thus symptom burden has not diminished proportionally with other progress in the field. With an accelerated investment and focus on advancing symptom science, significant and meaningful progress can now be achieved in eliminating symptom burden as an expected companion to cancer and its treatment. An initial demonstration of the capability of scalable comprehensive integrated systems that facilitate ongoing monitoring and management of symptoms and encourage patient engagement and self-management will propel the field rapidly forward and provide gains that will otherwise take decades to achieve given the current pace of research.

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