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Implementation Framework for NCCN Guidelines

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Rapid advances in the oncology field over the past 2 decades has provided a better understanding of cancer biology, which has led to the development of many new and more effective therapeutic options. Better disease characterization fostered the evolution of precision oncology. Nevertheless, unless biomedical advances are accompanied by a parallel improvement in healthcare delivery, many patients will not fully benefit from them. Translational research bridges the gap between bench and bedside by creating an evidence base. However, translational research does not address the range of real-world patients, disease states, and resource availability, nor does it leverage knowledge gained from other sources. Furthermore, translational research does not monitor real-world activities. Therefore, a chasm can exist between how patients do in clinical trials and the real-world experience of patients outside of trials.

Implementation science can bridge the gap between available best evidence and actual patient care.¹ Implementation science ensures that providers can apply evidence consistently and efficiently and can monitor adherence to recommended interventions. It is the last and most critical step in adopting evidence-based practice. Implementation science begins with developing or adapting guidelines that synthesize the evidence and use it to make recommendations for patient management.² Best practices incorporate evidence generated from classic studies with pragmatic research and the clinical experience of expert clinicians (Figure 1).

For more than 2 decades, NCCN has created a variety of resources to assist healthcare professionals provide better care to patients with cancer. NCCN has developed evidence-based, consensus-driven guidelines (available at NCCN.org) used both in the United States and around the world to outline step-by-step clinical decision-making, from risk assessment and screening through palliation and end-of-life care.³

To create the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines), multidisciplinary panels of experts selected from the 27 NCCN Member Institutions evaluate the data at each point in disease management and reach evidence-based consensus on appropriate interventions. To keep pace with rapidly evolving data, the NCCN Guidelines are updated continuously. Strong emerging experience suggests that

Figure 1. Process of guideline development and update.

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patients treated in accordance with the NCCN Guidelines have better outcomes in several cancer types.⁴⁻¹⁰ Further, NCCN has a variety of tools to help clinicians implement the guidelines in clinical practice, including compendia enumerating recommended uses of imaging, biomarker testing, and drugs and biologics; chemotherapy order templates; and patient versions of the NCCN Guidelines.

NCCN Guidelines have also been adapted to various regions to meet the regulatory environments, medical expertise, and patient characteristics in those regions.^{11,12} Finally, to facilitate use of the NCCN Guidelines by practitioners in middle and lower resource settings and provide treatment recommendations applicable to different levels of healthcare resources, NCCN developed Frameworks for Resource Stratification.¹³

The frameworks preserve the context of the full NCCN Guidelines, yet provide a strategy for providing the highest quality healthcare in resource-limited environments to efficiently improve patient outcomes (Figure 2). The frameworks, which use a modification of the model developed by the Breast Health Global Initiative, stratify recommendations for care into 4 resource levels: Basic Resources, Core Resources, Enhanced Resources, and NCCN Guidelines. Resource stratification can help build an incremental, step-by-step roadmap from a basic level of care to more comprehensive care, through a set of rational improvements in applying resources.

These levels were originally designed to be used for regional allocation of resources; however, as different regions have considered adoption, a variety of additional models are being considered. In many lower resource countries, advanced medical facilities equipped with complex medical equipment and expert clinicians are centralized to a small number of tertiary care centers. Geographically dispersed, smaller regional centers provide less-specialized care, and a local clinical system provides basic care. The frameworks might be used to identify the types of interventions that should be available at each of these care sites.

In other cases, an individual setting or region might have access to interventions that are stratified at different levels, and may wish to develop a mosaic to match the resources available. For example, an otherwise low-resource setting might have radiation therapy capability but limited access to pharmaceuticals. In that case, a care model might be envisioned that includes elements of both basic and core resources.

Additionally, NCCN Evidence Blocks help users of the NCCN Guidelines prioritize recommendations. Given increasing interest in the escalating cost of cancer treat-

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NCCN Framework Definitions	
The NCCN Framework™ outlines a rational approach for building cancer management systems to provide the highest achievable cancer care by applying available and affordable services in a logical sequence. Each NCCN Framework™ builds on the one before it, with incremental changes to the allocation of resources, providing a structure for improving cancer care. Treatment recommendations applicable to each NCCN Framework can be viewed within the context of the NCCN Guidelines®.	
Basic Resources	Basic Resources include essential services needed to provide basic minimal standard of care.
Core Resources	Core Resources include those provided in the Basic Resources Framework plus additional services that provide major improvements in disease outcomes (e.g. survival) and that are not cost prohibitive.
Enhanced Resources	Enhanced Resources include those provided in the Core Resources Framework and additional services that provide lesser improvements in disease outcomes and/or services that provide major improvements in disease outcome but are cost prohibitive in lower resource settings.
NCCN Guidelines	The NCCN Guidelines are evidence-based, consensus-driven recommendations made by the NCCN Guidelines panels. They include services from the Enhanced Resources Framework and additional services that provide minor improvements in disease outcomes, interventions that are cost prohibitive in lower resource settings, and/or services that do not provide improvement in disease outcomes but are desirable services.
NCCN believes that the best available resources should be provided. If Basic Resources for cancer treatment are unavailable, palliative and best supportive care should be provided.	
From NCCN Framework for Resource Stratification of NCCN Guidelines (NCCN Framework™). NCCN Web site. Available at: https://www.nccn.org/framework/ . Accessed September 19, 2017.	

Figure 2. NCCN Stratification Framework definitions.

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Robert W. Carlson, MD

Robert W. Carlson, MD, is the Chief Executive Officer of NCCN. He joined NCCN as CEO in January 2013 following an esteemed history of leadership positions within the organization including, most notably, representative to the NCCN Board of Directors, Chair of the Breast Cancer Guidelines Panel, member and founding Chair of the Breast Cancer Risk Reduction Guidelines Panel, and Chair of the Survivorship Guidelines Panel.

Prior to his appointment as CEO at NCCN, Dr. Carlson served as Professor of Medicine in the Division of Oncology and Stanford Medical Informatics at Stanford University Medical Center, as well as Medical Director of inpatient oncology and hematology at Stanford Cancer Institute.

Dr. Carlson is a graduate of Stanford University Medical School, and he completed his internship and junior residency in internal medicine at Barnes Hospital Group in St. Louis before returning to Stanford University to complete his senior residency. He earned a Bachelor of Science with distinction from Stanford University, specializing in biological sciences. Dr. Carlson is board certified in Medical Oncology and Internal Medicine.

ment, NCCN decided to add an affordability measure that takes into account the total medical costs of providing a regimen, including cost of the drug, administration, supportive care, management of expected toxicities, and likelihood of hospitalization. The information provided by the NCCN Evidence Blocks allows comparison of regimens across these 5 domains based on the values of the individual clinician and patient. They can also be used in concert with the frameworks by users of the NCCN Guidelines to help prioritize which agents and combinations to select. The goal is to provide clinicians and patients the opportunity to make decisions based on the patient's values through shared decision-making models (Figure 3).¹⁴

All of these resources provide guidance in deciding what should be available in a particular setting, but recommendations must be tailored to individual circumstances to be maximally helpful in implementing high-quality care. Developing an implementation model will help translate this abundant knowledge into action and improve delivery of evidence-based medicine in a variety of resource settings.

Guiding Principles to Develop the Implementation Model

A practical model that can be used widely in different settings should:

- Be explicit and easy to understand and use;
- Be flexible and adaptable to different settings;
- Build on the previous experience of NCCN in different regions in the world;
- Enable users to optimize use of available NCCN resources, such as Frameworks for Resource Stratification of NCCN Guidelines and NCCN Evidence Blocks; and
- Be an educational resource to train healthcare professionals in implementation sciences.

Steps of the Implementation Model

The implementation model was developed considering these guiding principles. It consists of 5 steps (Figure 4).

Step 1: Select the Most Appropriate Guidelines Stratification

Although NCCN introduced 4 distinct strata of guidelines for practical reasons, many healthcare settings include a mixture of elements of several resource levels. Therefore,

Figure 3. NCCN Evidence Blocks.

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Figure 4. NCCN Guideline Implementation Model.
Abbreviation: EHR, electronic health record.

centers may probably have resources that span ≥ 2 strata. Healthcare units should use the available interventions that lead to optimal outcomes; generally, this equates to the highest level of resources available. We recognize that scarce resources may need to be allocated to patients whose disease and clinical circumstances are most likely to benefit. Therefore, a high-cost intervention such as radiation therapy might be reserved for circumstances when substantially improved outcomes are expected.

When adapting a guideline for use by a healthcare unit, a multidisciplinary healthcare team familiar with the resources of that healthcare unit should review the strata, comparing them with available resources, and select the level that is most suitable to their setting. Once they select a baseline resource level, they review other levels to determine whether any recommendations should be shifted up or down for the healthcare unit's implementation.

Step 2: Guidelines Modification

Step 2.1: Setting the Boundaries of Compromise

The adaptation team should decide which resources are required to provide care in its setting and when to select a higher or lower resource option. This task is challenging and can be performed only by local teams with the support of the regional and national infrastructure. Many variables influence specific decisions, including:

- Available resources in the healthcare system;
- Available resources in the region and the ability to refer patients;
- National policies and infrastructure; and
- Acceptance of resource-based restriction on patient autonomy; patients may prefer some treatment options over others based on their own perceptions, circumstances, and values. However, scarce resources need to be allocated fairly.

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Practical challenges related to end points and outcomes must be considered. Which end points drive decision-making? When should patients be triaged to another center or treatment facility? Available resources will be a critical element in this selection. Will the team members require better overall survival, longer progression-free survival, better quality of life, or preservation of organ function? Will better cosmetic effect be sufficient? If a particular end point is identified, then what increment in outcome justifies referral? If the higher resource choice offers a better survival rate, what is the threshold considered acceptable to compromise? Is it 1%, 5%, or more or less? The team should adopt general rules and consider them with each modification.

For patients with adequate personal resources, the health system's strata may become less relevant. Those patients may refuse to compromise on the quality of their care and elect to travel to more advanced centers for treatment at their own expense. Or they may not elect treatment with limited benefits in order to reduce the financial burden on the family.

Step 2.2: Modify Recommendations

Once a core set of criteria and recommendations based on the NCCN Frameworks is identified, the guidelines can be adapted to account for biological differences in the population and the availability of interventions in the country. Every modification should be justified and supported by a rationale and references, if available. Figure 5 was developed and used to modify guidelines by MENA (Middle East and North Africa)/NCCN and proved very simple and easy to use.¹²

Step 2.3: Prioritize Regimens or Medications

NCCN Guidelines usually list multiple regimens and agents that have evidence for a particular indication. Therefore, one may find dozens of treatment options for a particular clinical scenario (eg, first-line chemotherapy for metastatic lung cancer). The choices of systemic therapy may be limited, especially at the core and basic levels, but using the Evidence Blocks may help local experts prioritize medication choices based on their settings. Because the Evidence Blocks were developed using US pricing structures, users in other areas of the world may find it most efficient to concentrate on the first 4 criteria—efficacy, safety, quantity/quality of evidence, and consistency of evidence—and then generate their own, locally based estimates of affordability. This affordability may also change over time based on negotiations and pricing.

Step 3. Operationalize the NCCN Guidelines

After finalizing the local version of the guidelines, the team should create the process and tools to integrate these guidelines in the healthcare workflow based on available systems and processes. This may include using clinical pathways in the electronic or paper records, or creating order sets or checklists and alert systems, for example. In some cases, it will involve reallocation of resources to ensure that at least basic care or

NCCN Guidelines Version: _____

Page No.	Setting	Suggested Modifications	Reason/Justification	Reference

Reference: (list detailed reference information)

Figure 5. NCCN Guidelines modification form.

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palliation is provided. The developers may also consider which criteria should be used to refer a patient to another center. Pursuing further treatment outside the current centers may not be possible. If a tertiary government cancer center does not have access to effective treatment (eg, trastuzumab), should the physician inform the patient about a private center that offers the treatment, likely at the patient's own expense, and have the patient decide?

Step 4: Monitoring and Feedback

Monitoring 2 types of measures for guideline implementation is critical. The first is adherence to guidelines (process measures) and the second is impact of implementation on patient outcome (outcome measures). These data then can be used to modify the NCCN Guidelines in an iterative process to add real-life data and experience related to the particular setting.

Step 5: Incorporate Findings Into Guidelines

As a result of the implementation and evaluation process, findings will determine what does and does not work in that setting. Local teams should be aware of regional data as emerging pragmatic evidence for or against a particular approach. These data should be considered in the next implementation cycle, along with the new version of NCCN Guidelines and emerging evidence relevant to that setting.

Conclusions

The proposed NCCN Guidelines Implementation Model will enable healthcare professionals worldwide to benefit from the vast resources and knowledge base created by NCCN, and incorporate relevant local data and resources into practical steps to bring patients the best possible care that can be delivered in that setting.

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