ONCOLOGY ISSUES

This publication is a benefit of membership Association of Community Cancer Centers

November | December 2018

Introducing supportive care and enhanced navigation into the curative treatment of cancer

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FROM THE EDITOR

ACCC and the Biden Cancer Initiative

BY JENNIE R. CREWS, MD, MMM, FACP

On Sept. 21, the Biden Cancer Initiative Summit convened in Washington, D.C., and was joined by 450 community summits across the country to bring together those who work to improve the cancer experience for patients and caregivers. The Summit reinforced "the urgency of now," a phrase coined by former Vice President Joe Biden, and builds on the Cancer Moonshot's original aim: to make a decade of progress in five years toward ending cancer. The day featured inspirational talks from cancer survivors, updates from prominent researchers, and presentation of the FIERCE Awards, which celebrate those making an impact in the areas of prevention, navigation, survivorship, and disparities.

The Summit also held working sessions to identify new focus areas for the Biden Cancer Initiative within clinical trials, navigation, survivorship, disparities, prevention, and more. Session outcomes included strategies to:

- Lower out-of-pocket costs for cancer treatment
- Increase HPV vaccination rates
- Demonstrate the return on investment for navigation services
- Improve patient access to their clinical and genomic data
- Meet the psychosocial, physical, and financial needs of survivors
- Promote education for early signs of hard-to-treat cancers
- Enhance patient awareness of clinical trial design and eligibility.

More than 55 new commitments were made by individuals and organizations to achieve these goals.

It's not a surprise that these strategies and goals align seamlessly with many ACCC initiatives. For example, ACCC has long recognized the financial burden that cancer brings to patients, families, and cancer programs, and continues to develop resources to help mitigate these economic pressures, including an annual Reimbursement & Patient Assistance Guide (accc-cancer.org/PatientAssistanceGuide) and the Financial Advocacy Boot Camp (accc-cancer.org/FANBootCamp). On the topic of HPV vaccination and its importance in reducing the incidence of certain types of cancer, ACCC awarded a 2016 ACCC Innovator Award to The Outer Banks Hospital for its partnership with North Carolina county health departments and school district leaders to develop a multifaceted educational campaign disseminated to primary care providers and parents of adolescents. Read more about this innovative outreach effort at accc-cancer.org/HPVHearne. Programs seeking to grow their navigation services or improve the psychosocial and physical care delivered to patients need look no further than the pages of this journal for articles like "Building a Comprehensive Rehabilitation Program" (accc-cancer.org/RehabBauer) and "Building a Navigation and Psychosocial Support Program from the Ground Up" (accc-cancer.org/NavMcNulty).

It's also not surprising that throughout the day, Summit speakers recognized the importance of community oncology in achieving Biden Cancer Initiative goals. ACCC's work in clinical trials and navigation was acknowledged during the event, and Dr. Jill Biden specifically recognized ACCC Secretary Krista Nelson, MSW, LCSW, OSW-C, BCD, during her opening remarks. Krista Nelson and her colleagues at Providence Cancer Center received a 2015 ACCC Innovator Award for the Providence Family Program, which offers effective communication techniques, coping strategies, and support for families adjusting to their "new normal" after a cancer diagnosis (accc-cancer.org/FamilyProgramNelson).

ACCC partners with many organizations focused on the needs of cancer patients and the cancer care team. I am honored to represent ACCC on the Biden Cancer Initiative Advisory Committee, and many of our members are involved with Initiative-related projects. We have the opportunity to continue working with the Biden Cancer Initiative on several of the highlighted projects, and I will continue to promote the value that community oncology and ACCC bring to these efforts. Who better understands and is motivated by the "urgency of now" than those who care for cancer patients and families every day? OI

Step out of the Now

BY TOM GALLO

In this issue's "From the Editor" column, Dr. Crews notes some of the ways ACCC's education and advocacy efforts have anticipated the priorities identified during the recent Biden Cancer Institute Summit, "The Urgency of Now." This makes perfect sense. As community cancer care providers ACCC members are on the front lines delivering care. ACCC members are the touchstone for real-world cancer care delivery—we live in the "now," as we meet the needs of our patients and our communities. The creativity and dedication that ACCC membership brings to identifying and overcoming the challenges of now while simultaneously looking to those of tomorrow is reflected in the articles contributed to each issue of this journal, in the sharing of effective practices through ACCC education projects, in the annual ACCC Innovator Awards, and in peer-to-peer discussions on ACCCExchange. As wave after wave of change reshapes oncology and healthcare, this community's voice contributes to the national conversation on cancer care through multiple collaborations, joining in coalitions and stakeholder groups for advocacy efforts; connecting to patient organizations to support common education goals, such as ACCC's Metastatic Breast Cancer project; and through advocacy for change needed now.

With this column, I'd like to encourage you to step out of the now and invite you to share your organizational and/or personal wisdom and experience by joining in my President's Theme: Reflect, Renew, Reignite: Creating a Resilient Oncology Team in Your Community. If you need inspiration for reflection, an exceptional resource is the National Academy of Medicine (NAM) Clinician Well-Being Knowledge Hub (nam.edu/clinicianwellbeing) where you'll find a wealth of articles, research studies, and other materials. The NAM Action Collaborative on Clinician Well-Being is a multiyear exploration of both individual and systemic steps for combatting the current pervasive burnout among healthcare professionals. The ACCC 2018 Institute for the Future of Oncology forum mirrored this approach, discussing both personal and institutional strategies to support a culture of wellness for cancer care providers and their patients. (You can read the Executive Summary of this meeting online at accc-cancer.org/TeamWellBeing.)

In October, two new discussion papers from the NAM Action Collaborative, "A Vision for a Person-Centered Health Information System" and "A Pragmatic Approach for Organizations to Measure Health Care Professional Well-Being," examine challenges familiar to ACCC members: healthcare IT and metrics to measure well-being. Both papers are available online at nam.edu.

Another starting point for reflection on renewal and steps to recharge your team could be the "IHI Framework for Improving Joy in Work." Developed by the Institute for Healthcare Improvement, this white paper outlines four steps for leaders to consider when reflecting on ways to reignite their teams:

1. Use improvement science to test approaches to improving joy in work in your organization.
2. Commit to a systems approach to making joy in work a shared responsibility at all levels of the organization.
3. Identify unique impediments to joy in the work in the local context.
4. Ask staff, "What matters to you?"

Before you head back into the now, share your experiences and wisdom as together we build oncology team resources for resiliency. Send your stories to mmarino@accc-cancer.org. OI

Coming in Your 2019 *ONCOLOGY ISSUES*

- Improving Cancer Screening and Treatment Through a Focused Prostate Evaluation Program
- Removing Barriers in Cancer Detection: Getting LDCT Lung Cancer Screening to Work Within a Network
- Enhancing Radiation Therapy Patient's QOL Through Fatigue-Centered Psychoeducation
- A Model Colon Cancer Awareness Screening Event
- Implementing Medical Scribes in a Community Cancer Center
- Evaluation of High-Risk Pulmonary Nodules and Pathologic Correlation in Patients Enrolled in an LDCT Program
- *One Best Practice*: Streamlining Workflow, Unifying Staff, and Reducing Redundancy
- Utilizing Bedside Yoga as a Nonpharmacological Intervention for Cancer Patients
- The Experience Engine: Personalizing the Patient Experience Through Technology
- Venous Thromboembolism Prevention in the Ambulatory Cancer Clinic
- ArtsCare: Professional Artists and Musicians as Members of the Multidisciplinary Cancer Care Team
- Providing Psychoeducation to Radiation Oncology Patients to Combat Fatigue: A Quality Initiative Pilot Study

PUBLICATION

Metastatic Breast Cancer

The ACCC Metastatic Breast Cancer project identified effective principles and practices in supporting this patient population. Read how three ACCC Cancer Program members demonstrate these principles as they prioritize meeting the unique needs of patients with advanced breast cancer. Plus, check out the project's new interactive resource center. Both at accc-cancer.org/metastaticbreastcancer.

RESOURCE

Integration of Pathology & Cancer Team

Greater understanding of cancer biology continues to reshape how we diagnose and treat cancer. Advances in targeted therapies and the demand for biomarker testing mandates closer integration between pathology and the cancer care team. At ACCC's Integration of Pathology in Oncology Care Leadership Summit, participants outlined action items to help bring processes and policies into closer alignment with scientific progress. Learn more at accc-cancer.org/pathology.

WEBINAR

Multidisciplinary Multiple Myeloma Care

Managing patients with multiple myeloma has become more complex. Through the ACCC Multidisciplinary Multiple Myeloma Care education project, access an on-demand webinar that reviews data and key findings from ASCO 2018, and then read a new publication that recaps multiple myeloma management updates and describes how three community cancer programs deliver care for this less commonly seen cancer at accc-cancer.org/multiple-myeloma.

RESOURCE

IO (Immuno-Oncology) Insights

The ACCC Immuno-Oncology Institute brought together leading experts in four Working Groups focused on current and future imperatives to advance access to and delivery of immunotherapy for cancer. Read IO Insights from these thought leaders in the areas of Big Data, Telemedicine, Multispecialty Coordination & Communication, and Training & Education at accc-cancer.org/immunotherapy; then join the discussion on ACCCExchange.

BLOG

2 CMS Memos Signal Significant Changes for MA & Part D Plans

ACCC remains concerned about the impact of the Prior Authorization and Step Therapy for Part B Drugs in Medicare Advantage memo and the Indication-Based Formulary Design Beginning in Contract Year (CY) 2020 memo and how they will impact ACCC cancer programs and their patients. Read more about these proposed changes at accc-cancer.org/acccbuzz.

Despite the high prevalence of obesity among U.S. adults, treatments for obesity remain low. Providers cite lack of time and lack of knowledge as major barriers to treating patients with obesity.

Source. Turner M, et al. Current knowledge of obesity treatment guidelines by health care professionals. *Obesity*. 23 March 2018. doi.org/10.1002/oby.22142.

5 Key Considerations to Make Your Wellness Programs Work Better

1. **Recognize that your employees are living and working longer.** Maintaining health is important for ensuring productivity and reducing healthcare costs.
2. **Understand that your employees are not living or working healthier.** This is the principal cause of rising healthcare costs and contributes to absenteeism and "presenteeism" (coming to work sick).
3. **Wellness programs can help fill the skill gap.** 8 in 10 employees surveyed say that the presence or absence of a wellness program would be key in their job-hunting decisions.
4. **Wellness embraces body and mind.** Physical health should be considered inseparable from mental and emotional health.
5. **Technology can hurt; technology can help.** Wellness programs can help employees be intentional and self-disciplined about how they use technology tools.

Source. 3BLMedia. 3blmedia.com/News/How-Make-Wellness-Programs-Work-Better-Workplace.

facts

Most States are Failing to Address Opioid Crisis

- Just **13** states and Washington, D.C., have implemented comprehensive, proven actions to eliminate opioid overdoses and help protect their residents.
- **14** states that received the highest mark of "Improving": Arizona, Connecticut, Delaware, Washington, D.C., Georgia, Michigan, Nevada, New Hampshire, New Mexico, North Carolina, Ohio, Rhode Island, Virginia, and West Virginia.
- These **8** states received a "Failing" mark: Arkansas, Iowa, Kansas, Missouri, Montana, North Dakota, Oregon, and Wyoming

Source. National Safety Council. safety.nsc.org/prescription-nation-facing-americas-opioid-epidemic.

Meal Delivery Programs May Reduce the Use of Costly Healthcare

- A medically tailored meal delivery service provided to homebound and critically or chronically ill individuals was associated with a **16%** net reduction in healthcare costs.
- Participants in two meal programs experienced fewer emergency department visits and emergency transportation services; patients receiving medically tailored meals also had fewer inpatient admissions.

Source. Berkowitz SA, et al. Meal delivery programs reduce the use of costly health care in dually eligible Medicare and Medicaid beneficiaries. *Health Affairs*. doi.org/10.1377/hlthaff.2017.0999.

New study finds that 24% of women seen in the obstetrics-gynecology setting met NCCN Guidelines for hereditary cancer genetic testing.

Source. DeFrancesco MS and Waldman RN. Hereditary Cancer Genetic Testing in Community-Based Obstetrics and Gynecology Settings. 2018 American College of Obstetricians and Gynecologists (ACOG) Annual Meeting.

Socioeconomic Status May Help Explain U.S. Childhood Cancer Survival Rates

- For **9** cancers, black children were significantly more likely to die than white children, with an increased risk ranging from **38%** with neuroblastoma, a form of brain cancer, to **95%** with astocytoma, a different type of brain cancer.
- For **6** cancers, Hispanic children were more likely to die than white children, with an increased risk ranging from **31%** with neuroblastoma to **65%** with non-Hodgkin lymphoma.
- These findings add to the large body of evidence linking factors like limited education, low income, and issues with the access and affordability of care to worse survival rates for cancer.

Source. Kehm RD, et al. Does socioeconomic status account for racial and ethnic disparities in childhood cancer survival? *Cancer*. 20 August 2018. doi.org/10.1002/cncr.31560.

To the Rules and Beyond: CMS, CMMI, and Administrative Power

BY BLAIR BURNETT

In September 2018, the Association of Community Cancer Centers (ACCC) submitted comments to the Centers for Medicare & Medicaid Services (CMS) in response to both the 2019 Physician Fee Schedule (PFS) and Hospital Outpatient Prospective Payment System (OPPS) proposed rules. The arrival of autumn signals seasonal changes, but one constant is the policy implications of the proposed Medicare payment rules for the upcoming calendar year.

Key Concerns in the Calendar Year 2019 PFS and OPPS Proposed Rules

Site-neutral payment structure and healthcare delivery remained a huge focus for CMS in the calendar year 2019 OPPS proposed rule as the agency sought to lessen the gap in payment differentials between nonexcepted and excepted hospital off-campus provider-based departments (PBDs). CMS is expected to finalize a proposal to reduce reimbursement to 40 percent of the OPPS rate for clinic visits, including hematology and oncology, as well as any excepted off-campus PBD that has engaged in service line expansion since November 2015. ACCC commented against both proposals in alignment with CMS's own Advisory Panel on Hospital Outpatient Payment, which finalized its recommendations in August. CMS continues to cite an "unnecessary increase" in the volume of outpatient clinic visits, but the 2019 OPPS Proposed Rule provides no data or analysis to support this claim, and the agency's proposals would drastically impact cancer delivery for patients across the country. Should the agency finalize these proposals, it is likely that providers will be forced to scale back services or close off-campus PBDs, requiring patients receiving treatment to seek care farther from their homes. For the intent of these proposals to be realized, hospitals must be given the flexibility to adapt use of PBDs to better meeting their patients' needs.

The 2019 OPPS proposed rule also included an additional Request for Information on the potential revitalization of Medicare's failed 2006-2008 Competitive Acquisition Program. ACCC commented strongly that CMS should ensure that any model based on Competitive Acquisition Program authority is voluntary for all participants, preserves patient access to treatment and provider flexibility, and promotes cost efficiency through more effective distribution and delivery of drugs and biologicals rather than utilization management tools.

The CMS Physician Fee Schedule 2019 proposed rule also signals significant changes on the horizon for cancer care delivery. Most notable, CMS proposed a consolidated reimbursement structure for levels 2-5 Evaluation and Management-coded visits. In comments to the agency, ACCC voiced strong concern over the impact of this policy proposal and stated that there is a continued need to work with other oncology patient and provider advocacy stakeholders before finalizing this consolidation. Due to the complexity of cancer treatment, oncology providers often use level 4 and 5 visits, and there is strong concern that condensing these evaluation and management codes will devalue the work of these providers. Accordingly, ACCC opposes this reimbursement structure.

Beyond PFS and OPPS: How Healthcare Leadership is Exercising Their Authority

Outside of the PFS and OPPS 2019 proposed rules, CMS and various members of the administration's healthcare leadership team have taken large actions to reform cancer care on regulatory authority alone. Most notable, CMS issued a policy memo stating that on Jan. 1, 2019, Medicare Advantage plans will be able to infuse step therapy as a utilization management tool for their beneficiaries accessing Medicare Part B drugs. ACCC has commented in opposition of this policy shift due to the access implication this regulation has for patients with cancer across the country; however, with regulatory authority and no comment period in sight, this change could potentially signal more movement to come. News of this memo was released on Aug. 7, 2018, and was followed by an Aug. 29 agency memo announcing changes to Medicare Part D plans and news of "indication-based pricing" in 2020. Even more important to remember: healthcare leadership under this administration has untapped regulatory authority for potential mandatory demonstrations to test other value-based arrangements through the CMS Center for Medicare and Medicaid Innovation. ACCC continues to work with CMS, the Center for Medicare and Medicaid Innovation, and other patient and provider stakeholder organizations to proactively address and understand how best to navigate the future cancer delivery landscape in 2019 and beyond. OI

Blair Burnett is senior policy analyst at ACCC.

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Still More ICD-10-CM Updates!

BY CINDY PARMAN, CPC, CPC-H, RCC

Effective Oct. 1, 2018, the Centers for Medicare & Medicaid Services (CMS) and the Centers for Disease Control and Prevention will add 279 new codes, revise 143 existing codes, and deactivate 51 codes in the *International Classification of Diseases*, Tenth Revision, Clinical Modification (ICD-10-CM) classification. There are also updates to the *2019 ICD-10-CM Official Guidelines for Coding and Reporting* that affect medical record documentation, code selection, and sequencing. Adherence to the guidelines when assigning ICD-10-CM diagnosis codes is required under the Health Insurance Portability and Accountability Act in all healthcare settings.

Guideline Updates

Though there are many changes to the official guidelines, below are key updates that will impact oncology physicians, practices, and hospitals (changes listed in **bold** text). In addition to these specific guidelines, there are updates on the application and sequencing of external cause of morbidity codes, particularly as they relate to hurricanes and other cataclysmic events. Additional instructions were added for reporting sepsis due to a postprocedural infection, hypertension with heart disease, myocardial infarctions, drug use during pregnancy, use of the Glasgow Coma Scale, body mass index (BMI) codes, and coding for burns, sexual exploitation, and factitious disorders.

- Section 1.A.15: The word "with" or "in" should be interpreted to mean "associated with" or "due to" when it appears in a code title, the Alphabetic Index (either under a main term or subterm), or an instructional note in the Tabular List.
- Section 1.B.14: **Code assignment is based on the documentation by patient's provider (i.e., physician or other qualified healthcare practitioner legally accountable for establishing the patient's diagnosis). There are a few exceptions, such as for** BMI, depth of nonpressure chronic ulcers, pressure ulcer stage, coma scale, and National Institutes of Health Stroke Scale codes, code assignment may be based on medical record documentation from clinicians who are not the patient's provider (i.e., physician or other qualified healthcare practitioner legally accountable for establishing the patient's diagnosis), because this information is typically documented by other clinicians involved in the care of the patient (e.g., a dietitian often documents BMI, a nurse often documents the pressure ulcer stages, and an emergency medical technician often documents the coma scale). However, the associated diagnosis (such as overweight, obesity, acute stroke, or pressure ulcer) must be documented by the patient's provider. If there is conflicting medical record documentation, from either the same clinician or different clinicians, the patient's attending provider should be queried for clarification.

For social determinants of health, such as information found in categories Z55-Z65, persons with potential health hazards related to socioeconomic and psychosocial circumstances, code assignment may be based on medical record documentation from clinicians involved in the care of the patient who are not the patient's provider because this information represents social information, rather than medical diagnoses.

BMI, coma scale, National Institutes of Health Stroke Scale codes, and categories Z55-Z65 should only be reported as secondary diagnoses.

- Section 1.C.19.d: **Z codes (other reasons for healthcare encounters) may be assigned as appropriate to further explain the reasons for presenting for healthcare services, including transfers between healthcare facilities. The *ICD-10-CM Official Guidelines for Coding and Reporting* identify which codes maybe assigned as principal or first-listed diagnosis only, secondary diagnosis only, or principal/first-listed or secondary (depending on the circumstances). Possible applicable Z codes include:**
  - **Z59.0: Homelessness**
  - **Z59.1: Inadequate housing**
  - **Z59.5: Extreme poverty**
  - **Z75.1: Person awaiting admission to adequate facility elsewhere**
  - **Z75.3: Unavailability and inaccessibility of healthcare facilities**
  - **Z75.4: Unavailability and inaccessibility of other helping agencies**
  - **Z76.2: Encounter for health supervision and care of other healthy infant and child**
  - **Z99.12: Encounter for respirator (ventilator) dependence during power failure.**

The external cause of morbidity codes and the Z codes listed above are not an all-inclusive list. Other codes may be

applicable to the encounter based upon the documentation. Assign as many codes as necessary to fully explain each healthcare encounter. Because patient history information may be very limited, use any available documentation to assign the appropriate external cause of morbidity and Z codes.

- Section 1.C.2.m: When a primary malignancy has been previously excised or eradicated from its site, there is no further treatment (of the malignancy) directed to that site, and there is no evidence of any existing primary malignancy **at that site**, a code from category Z85, personal history of malignant neoplasm, should be used to indicate the former site of the malignancy.

Subcategories Z85.0-Z85.7 should only be assigned for the former site of a primary malignancy, not the site of a secondary malignancy. Codes from subcategory Z85.8 may be assigned for the former site(s) of either a primary or secondary malignancy included in this subcategory.

Neoplasm Code Updates

There are several changes to the Neoplasm Table specific to neoplasms of the eye, providing the ability to report additional location specificity. Note that there are now detailed ICD-10-CM diagnosis codes to report lesions of the upper or lower eyelid. Table 1, page 10, outlines the 2018 and 2019 differences in the significant series of codes.

A new subcategory for C44.13 (sebaceous cell carcinoma of skin of eyelid, including canthus) has been introduced for 2019. The series of codes is inserted between the unspecified, basal, and squamous cell carcinoma of the canthus and the other unspecified carcinoma of the canthus. These codes are:

- C44.13 Sebaceous cell carcinoma of skin of eyelid, including canthus
  - C44.131 Sebaceous cell carcinoma of skin of unspecified eyelid, including canthus
  - C44.132 Sebaceous cell carcinoma of skin of right eyelid, including canthus
    - C44.1321 Sebaceous cell carcinoma of skin of right upper eyelid, including canthus
    - C44.1322 Sebaceous cell carcinoma of skin of right lower eyelid, including canthus
- C44.139 Sebaceous cell carcinoma of skin of left eyelid, including canthus
  - C44.1391 Sebaceous cell carcinoma of skin of left upper eyelid, including canthus
  - C44.1392 Sebaceous cell carcinoma of skin of left lower eyelid, including canthus

Endocrine Code Updates

Within the Endocrine chapter there are also grammatical revisions, as well as deletions and additions to the different subcategories. Subcategory code E72.53 has a revised definition for 2019 from hyperoxaluria to **primary** hyperoxaluria. Two of the disorders defined as part of code E72.8 (other specified disorders of amino-acid metabolism) were deleted and new codes were assigned to this category:

- **E72.81 Disorders of gamma aminobutyric acid (GABA) metabolism**
  - 4-Hydroxybutyric aciduria
  - Disorders of GABA metabolism
  - GABA metabolic defect
  - GABA transaminase deficiency
  - GABA-T deficiency
  - Gamma-hydroxybutyric aciduria
  - SSADHD
  - Succinic semialdehyde dehydrogenase deficiency
- **E72.89 Other specified disorders of amino acid metabolism**
  - Disorders of beta-amino acid metabolism
  - Disorders of gamma-glutamyl cycle

There was no change to code E75.2 (other sphingolipidosis), but one new subcategory was added and another included a revised definition:

- Code **E75.26 (sulfatase deficiency), multiple sulfatase deficiency** was added.
- Code E75.29 (other sphingolipidosis) was not changed but "sulfatase deficiency" was deleted from the definition.

Familial combined hyperlipidemia was deleted from the definition of code E78.4 (other hyperlipidemia) and the following subcategories were created:

- E78.41 Elevated Lipoprotein(a)
  - Elevated Lp(a)
- E78.49 Other hyperlipidemia
  - Familial combined hyperlipidemia

The following new code was created for plasminogen deficiency, and instructions for reporting this condition were updated throughout the Tabular List and Alphabetic Index:

- E88.02 Plasminogen deficiency
  - Dysplasminogenemia
  - Hypoplasminogenemia
  - Type 1 plasminogen deficiency
  - Type 2 plasminogen deficiency
  - Code also, if applicable, ligneous conjunctivitis (H10.51).

Use additional code for associated findings, such as:

- Hydrocephalus (G91.4)
- Ligneous conjunctivitis (H10.51)
- Otitis media (H67)
- Respiratory disorder related to plasminogen deficiency (J99).

Mental and Behavioral Code Updates

The following codes were added to the Mental and Behavioral chapter effective Oct. 1, 2018:

- Code F12.23 (cannabis dependence with withdrawal) was added as a subcategory under F12.2 (cannabis dependence). Cannabis withdrawal was deleted from inclusion under F12.288 (cannabis dependence with other cannabis-induced disorder).
- Code F12.93 (cannabis use, unspecified with withdrawal) was added as a subcategory to code F12.9 (cannabis use, unspecified).

The term "disorder" was added to inclusion term under F19.21 (other psychoactive substance dependence, in remission). The full inclusion statement now reads, "Other (or unknown) substance use disorder, severe, in sustained remission."

Signs and Symptoms Code Updates

New inclusion terms have been added to the subcategory codes related to R40.2 (coma), identifying eye opening, verbal, and motor score in relation to the specific ICD-10-CM code. Additional changes related to the coma category of codes are related to changing the age ranges covered, beginning at two years

(continued on page 12)

Table 1. Neoplasm Code Updates

2018 Code Descriptor	Expanded 2019 Code Descriptor
C43.1 Malignant melanoma of eyelid, including canthus	
C43.11 Malignant melanoma of right eyelid, including canthus	C43.111 Malignant melanoma of right **upper** eyelid, including canthus
	C43.112 Malignant melanoma of right **lower** eyelid, including canthus
C43.12 Malignant melanoma of left eyelid, including canthus	C43.121 Malignant melanoma of left **upper** eyelid, including canthus
	C43.122 Malignant melanoma of left **lower** eyelid, including canthus
C4A.1 Merkel cell carcinoma of eyelid, including canthus	
C4A.11 Merkel cell Acarcinoma of right eyelid, including canthus	C4A.111 Merkel cell carcinoma of right **upper** eyelid, including canthus
	C4A.112 Merkel cell carcinoma of right **lower** eyelid, including canthus
C4.A12 Merkel cell carcinoma of left eyelid, including canthus	C4A121 Merkel cell carcinoma of left **upper** eyelid, including canthus
	C4A122 Merkel cell carcinoma of left **lower** eyelid, including canthus
C44.1 Other and unspecified malignant neoplasm of skin of eyelid, including canthus	
C44.102 Unspecified malignant neoplasm of skin of right eyelid, including canthus	C44.1021 Unspecified malignant neoplasm of skin of right **upper** eyelid, including canthus
	C44.1022 Unspecified malignant neoplasm of skin of right **lower** eyelid, including canthus
C44.109 Unspecified malignant neoplasm of skin of left eyelid, including canthus	C44.1091 Unspecified malignant neoplasm of skin of left **upper** eyelid, including canthus
	C44.1092 Unspecified malignant neoplasm of skin of left **lower** eyelid, including canthus
C44.11 Basal cell carcinoma of skin of eyelid, including canthus	
C44.112 Basal cell carcinoma of skin of right eyelid, including canthus	C44.1121 Basal cell carcinoma of skin of right **upper** eyelid, including canthus
	C44.1122 Basal cell carcinoma of skin of right **lower** eyelid, including canthus
C44.119 Basal cell carcinoma of skin of left eyelid, including canthus	C44.1191 Basal cell carcinoma of skin of left **upper** eyelid, including canthus
	C44.1192 Basal cell carcinoma of skin of left **lower** eyelid, including canthus
C44.12 Squamous cell carcinoma of skin of eyelid, including canthus	
C44.122 Squamous cell carcinoma of skin of right eyelid, including canthus	C44.1221 Squamous cell carcinoma of skin of right **upper** eyelid, including canthus
	C44.1222 Squamous cell carcinoma of skin of right **lower** eyelid, including canthus
C44.129 Squamous cell carcinoma of skin of left eyelid, including canthus	C44.1291 Squamous cell carcinoma of skin of left **upper** eyelid, including canthus
	C44.1292 Squamous cell carcinoma of skin of left **lower** eyelid, including canthus

Table 1 (continued). Neoplasm Code Updates

C44.19 Other specified malignant neoplasm of skin of eyelid, including canthus	
C44.192 Other specified malignant neoplasm of skin of right eyelid, including canthus	C44.1921 Other specified malignant neoplasm of skin of right **upper** eyelid, including canthus
	C44.1922 Other specified malignant neoplasm of skin of right **lower** eyelid, including canthus
C44.199 Other specified malignant neoplasm of skin of left eyelid, including canthus	C44.1991 Other specified malignant neoplasm of skin of left **upper** eyelid, including canthus
	C44.1992 Other specified malignant neoplasm of skin of left **lower** eyelid, including canthus
D03.1 Melanoma in situ of eyelid, including canthus	
D03.11 Melanoma in situ of right eyelid, including canthus	D03.111 Melanoma in situ of right **upper** eyelid, including canthus
	D03.112 Melanoma in situ of right **lower** eyelid, including canthus
D03.12 Melanoma in situ of left eyelid, including canthus	D03.121 Melanoma in situ of left **upper** eyelid, including canthus
	D03.122 Melanoma in situ of left **lower** eyelid, including canthus
D04.1 Carcinoma in situ of skin of eyelid, including canthus	
D04.11 Carcinoma in situ of skin of right eyelid, including canthus	D04.111 Carcinoma in situ of skin of right **upper** eyelid, including canthus
	D04.112 Carcinoma in situ of skin of right **lower** eyelid, including canthus
D04.12 Carcinoma in situ of skin of left eyelid, including canthus	D04.121 Carcinoma in situ of skin of left **upper** eyelid, including canthus
	D04.122 Carcinoma in situ of skin of left **lower** eyelid, including canthus
D22.1 Melanocytic nevi of eyelid, including canthus	
D22.11 Melanocytic nevi of right eyelid, including canthus	D22.111 Melanocytic nevi of right **upper** eyelid, including canthus
	D22.112 Melanocytic nevi of right **lower** eyelid, including canthus
D22.12 Melanocytic nevi of left eyelid, including canthus	D22.121 Melanocytic nevi of left **upper** eyelid, including canthus
	D22.122 Melanocytic nevi of left **lower** eyelid, including canthus
D23.1 Other benign neoplasm of skin of eyelid, including canthus	
D23.11 Other benign neoplasm of skin of right eyelid, including canthus	D23.111 Other benign neoplasm of skin of right **upper** eyelid, including canthus
	D23.112 Other benign neoplasm of skin of right **lower** eyelid, including canthus
D23.12 Other benign neoplasm of skin of left eyelid, including canthus	D23.121 Other benign neoplasm of skin of left **upper** eyelid, including canthus
	D23.122 Other benign neoplasm of skin of left **lower** eyelid, including canthus

(continued from page 9)
of age as opposed to starting at zero years.

The subcategory of codes related to R82.99 (other abnormal findings in urine) had several inclusion terms deleted (cells and casts in urine, crystalluria, and melanuria) and was expanded to a new subcategory code allowing for more specification:

- R82.991 Hypocitraturia
- R82.992 Hyperoxaluria
  - Excludes 1: Primary hyperoxaluria (E72.53)
- R82.993 Hyperuricoscuria
- R82.994 Hypercalciuria
  - Idiopathic hypercalciuria
- R82.998 Other abnormal findings in urine
  - Cells and casts in urine
  - Crystalluria
  - Melanuria.

Subcategories R93.81 (abnormal radiologic findings on diagnostic imaging of testis) and R93.89 (abnormal findings on diagnostic imaging of other specified body structures) were expanded and redefined as follows:

- R93.81 Abnormal radiologic findings on diagnostic imaging of testis
  - R93.811 Abnormal radiologic findings on diagnostic imaging of right testicle
  - R93.812 Abnormal radiologic findings on diagnostic imaging of left testicle
  - R93.813 Abnormal radiologic findings on diagnostic imaging of testicles, bilateral
  - R93.819 Abnormal radiologic findings on diagnostic imaging of unspecified testicle
- R93.89 Abnormal findings on diagnostic imaging of other specified body structures
  - Abnormal finding by radioisotope localization of placenta
  - Abnormal radiological finding in skin and subcutaneous tissue
  - Mediastinal shift.

Z Code Updates

The subcategory Z83.4 (family history of other endocrine, nutritional, and metabolic diseases) was updated to reflect new codes for more specified detail related to family history:

- Z83.430 Family history of elevated lipoprotein(a)
  - Family history of elevated Lp(a)
- Z83.438 Family history of other disorder of lipoprotein metabolism and other lipidemia
  - Family history of familial combined hyperlipidemia.

In addition to these updates, ICD-10-CM includes changes to codes for Zika virus, malaria, somatoform disorders, puerperal psychosis, factitious disorders, hemifacial spasms, muscular dystrophy, blepharitis, lagophthalmos, ectropions, meibomian gland dysfunction, rosacea conjunctivitis, brow ptosis, plasminogen deficiency, cerebrovascular diseases, appendicitis, colorectal abscesses, gallbladder conditions, myalgia, urethral strictures, poisoning by ecstasy, and numerous codes for forced labor and forced sexual exploitation.

The Official Guidelines for Coding and Reporting, Addenda, code lists, and other files are available online at: cdc.gov/nchs/icd/icd10cm.htm. OI

Cindy Parman, CPC, CPC-H, RCC, is a principal at Coding Strategies, Inc., in Powder Springs, Ga.

ASSOCIATION OF COMMUNITY CANCER CENTERS

IMMUNO-ONCOLOGY INSTITUTE

As immunotherapy for cancer continues to evolve, ACCC adapts to meet the changing needs of the oncology community.

The ACCC Immuno-Oncology Institute is the only initiative dedicated to educating multidisciplinary teams to go beyond a clinical understanding of IO and tackle real-world implementation issues.

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The **Association of Community Cancer Centers (ACCC)** is the leading education and advocacy organization for the multidisciplinary cancer team. ACCC is a powerful network of 24,000 cancer care professionals from 2,100 hospitals and practices nationwide. ACCC is recognized as the premier provider of resources for the entire oncology care team. For more information, visit accc-cancer.org or call 301.984.9496. Follow us on Facebook, Twitter, and LinkedIn, and read our blog, ACCCBuzz.

The **ACCC Immuno-Oncology Institute** is the leader in optimizing the delivery of cancer immunotherapies for patients by providing clinical education, advocacy, research, and practice management solutions for cancer care teams across all healthcare settings.

Association of Community Cancer Centers

The ACCC Immuno-Oncology Institute is supported by Bristol-Myers Squibb (charitable donation); EMD Serono; Kite, a Gilead Company; and Merck & Co, Inc. (educational grant).

spotlight

Olathe Health Cancer Center
Olathe, Kansas

Serving Johnson, Franklin, Linn, and Miami counties, Olathe Health Cancer Center occupies a brand-new 25,000-square-foot building at Olathe Medical Park in Olathe, Kan. The cancer center formed through the purchasing and consolidation of two private programs: a medical oncology practice in 2014 and a radiation oncology practice in 2015. At that time, cancer care services were located on different floors of different buildings on the Olathe Medical Park campus. The physicians within those practices came together and decided that they needed to consolidate their services and create a one-stop shop in one building.

Together with the Olathe Health leadership team, physicians, nurses, administrative staff, and patients worked on their vision for the cancer center. One of the driving factors in the creation of the building was patient convenience, and an important part of this vision was to have all services on one floor, allowing for easier patient access and workflow. The center opened its doors to radiation patients on February 5, 2018, and to medical oncology patients 23 days later.

A One-Stop Shop

True to its vision, the new Olathe Health Cancer Center is a comprehensive destination for cancer patients. The center is staffed by two medical oncologists and a medical oncology physician assistant; two radiation oncologists; a physicist; three patient navigators; eight nurses; a part-time dedicated oncology social worker; and two dedicated financial counselors, one each for medical oncology and radiation oncology. Within the center sits a 19-chair infusion center, an on-site laboratory, and a dedicated oncology pharmacy staffed by an oncology pharmacist and two pharmacy technicians. The pharmacy is up to the specifications of USP-800 compliance and will be officially compliant soon. The center is accredited by both the Commission on Cancer and the National Accreditation Program for Breast Cancers.

The main conference room serves as the home for the cancer center's three tumor boards—breast, thoracic, and general oncology. When those aren't running, the conference room also serves as the home for Look Good, Feel Better courses and community outreach events. Also on site are a number of supportive services, including an appearance center for patients with comfort and cosmetic needs and a cancer rehab program with a specialization in lymphedema and cancer fatigue management. The center's radiation suite has a TrueBeam linear accelerator and a Big Bore computed tomography scanner. Patients who require inpatient care are referred a short distance to Olathe Medical Center's inpatient units. Cancer center physicians also participate in inpatient rounds at the hospital, bridging the gap between inpatient and outpatient care.

Community Cancer Care

Olathe Health is a two-hospital system that encompasses Olathe Medical Center and the more rural Miami County Medical Center. The bulk of the cancer center's referrals come from those two organizations, including higher complexity patients from Miami County. Olathe Health Cancer Center also participates in significant community

outreach efforts through health fairs, marketing campaigns, and social media.

Olathe Health Cancer Center has a network of community providers to supplement its on-site cancer care. The center has a strong alliance with local surgical specialists, as well as a pulmonary specialist and a thoracic surgeon. Patients who require transportation to and from appointments can receive aid through the cancer center's partnership with the American Cancer Society. For complementary and alternative medicines, the cancer center provides referrals to community providers; they are looking to implement on-site complementary and alternative medicine programs in the near future.

For clinical trials, Olathe Health works with Midwest Cancer Alliance, the outreach network of the National Cancer Institute-designated University of Kansas Cancer Center. Twenty-three trials are currently available for open enrollment in both medical and radiation oncology, and the enrollment rate for patients is around 5 percent. Olathe Medical Center's imaging pavilion can provide additional imaging for high-complexity patients, and the cancer center also conducts low-dose lung screening.

The CEO of Olathe Health, Frank Devocelle, who is retiring this year after 47 years with Olathe Health, envisioned the hospital's campus to be a comprehensive place for health and well-being. The establishment of a YMCA on campus grounds provides a unique partnership—a LIVESTRONG program hosted there offers a strong survivorship program for cancer patients from Olathe Health Cancer Center. A hospice house also resides on the campus grounds, and a community college down the block offers the majority of certified nursing assistant and nursing classes. OI

Select Support Services

- Appearance Center
- Look Good, Feel Better
- Fatigue management
- Social work

Number of new analytic cases seen in 2018: 599

tools

Approved Drugs

- On September 24, the Food and Drug Administration (FDA) approved **Copiktra™ (duvelisib)** (Verastem, Inc., verastem.com) for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukemia/small lymphocytic lymphoma after at least two prior therapies. It also received accelerated approval for the treatment of adult patients with relapsed or refractory follicular lymphoma after at least two prior systemic therapies.
- On August 27, AbbVie Inc. (abbvie.com) announced that the FDA approved **Imbruvica® (ibrutinib)** plus rituximab for the treatment of adult patients with Waldenström's macroglobulinemia.
- On August 17, the FDA approved **Keytruda® (pembrolizumab)** (Merck & Co., Inc., merck.com) in combination with pemetrexed and platinum as first-line treatment of patients with metastatic, nonsquamous non-small cell lung cancer (NSCLC) with no epidermal growth factor receptor (EGFR) or ALK genomic tumor aberrations.
- On August 16, the FDA approved **Lenvima® (lenvantinib)** (Eisai Inc., eisai.com) for first-line treatment of patients with unresectable hepatocellular carcinoma. Approval was based on an international, multicenter, randomized, open-label, noninferiority trial conducted in 954 patients with previously untreated, metastatic, or unresectable hepatocellular carcinoma.
- On September 28, the FDA approved **Libtayo® (cemiplimab-rwlc)** (Sanofi, sanofi.com, and Regeneron, regeneron.com) for the treatment of patients with metastatic cutaneous squamous cell carcinoma or locally advanced cutaneous squamous cell carcinoma who are not candidates for curative surgery or curative radiation.
- On September 13, the FDA approved **Lumoxiti™ (moxetumomab pasudotox-tdfk)** (AstraZeneca, astrazeneca.com) for the treatment of adult patients with relapsed or refractory hairy cell leukemia who have received at least two prior systemic therapies, including treatment with a purine nucleoside analog.
- On August 17, Bristol-Myers Squibb Company (bms.com) announced that the FDA has approved **Opdivo® (nivolumab)** for patients with metastatic small cell lung cancer whose cancer has progressed after platinum-based chemotherapy and at least one other line of therapy.
- On September 27, the FDA approved **Vizimpro® (dacomitinib)** (Pfizer Inc., pfizer.com) for the first-line treatment of patients with metastatic NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution mutations as detected by an FDA-approved test.

Approved Devices

- Roche (roche.com) announced that it has received approval from the FDA for the **cobas® EGFR Mutation Test v2** as a companion diagnostic test for Iressa.®
- On August 16, the FDA approved the **Dako PD-L1 IHC 22C3 PharmDx Assay** (Dako North America, Inc., agilent.com) as a companion diagnostic to select patients with locally advanced or metastatic urothelial carcinoma who are cisplatin-ineligible for treatment with Keytruda.®

Drugs in the News

- Medsenic SAS (medsenic.com) announced that the FDA has granted orphan drug designation to **Arscimed® (arsenic trioxide)** for the treatment of graft-versus-host disease.
- Aslan Pharmaceuticals (aslanpharma.com) announced that the FDA has granted orphan drug designation to **ASLAN003** for the treatment of acute myeloid leukemia.
- Aravive Biologics, Inc. (aravive.com) announced that the FDA has granted fast track designation to **AVB-S6-500** as a potential treatment for platinum-resistant recurrent ovarian cancer.
- Cellectar Biosciences, Inc. (cellectar.com) announced that the FDA has granted rare pediatric disease designation to **CLR 131** for the treatment of osteosarcoma, a rare pediatric cancer.
- Rafael Pharmaceuticals, Inc. (rafaelpharma.com) announced that the FDA has granted orphan drug designation to **CPI-613** for the treatment of peripheral T-cell lymphoma.
- Janssen Pharmaceuticals (janssen.com) announced that a new drug application (NDA) has been submitted to the FDA,

seeking approval of **erdafitinib** for the treatment of patients with locally advanced or metastatic urothelial cancer and certain fibroblast growth factor receptor genetic alterations whose tumors have progressed after prior chemotherapy.

- Bristol-Myers Squibb Company (bms.com) announced that the FDA accepted the company's biologics license application (BLA) for **Empliciti™ (elotuzumab)** in combination with pomalidomide and low-dose dexamethasone for the treatment of patients with relapsed/refractory multiple myeloma who have received at least two prior therapies, including lenalidomide and a proteasome inhibitor.
- Merck & Co., Inc. (merck.com) announced that the FDA has accepted and granted priority review for a new supplemental BLA seeking accelerated approval for **Keytruda® (pembrolizumab)** for the treatment of adult and pediatric patients with recurrent locally advanced or metastatic Merkel cell carcinoma.
- Merck & Co., Inc. (merck.com) also announced that the FDA has accepted and granted priority review for a new supplemental BLA seeking approval for **Keytruda® (pembrolizumab)** for first-line treatment of locally advanced or metastatic nonsquamous or squamous NSCLC in patients whose tumors express PD-L1 (tumor proportion score ≥1%) without EGFR or ALK genomic tumor aberrations.
- Amgen (amgen.com) announced that the FDA has approved a supplemental NDA to expand the prescribing information for **Kyprolis® (carfilzomib)** to include a once-weekly dosing option in combination with dexamethasone for patients with relapsed or refractory multiple myeloma.
- Loxo Oncology, Inc. (loxooncology.com) announced that the FDA has granted breakthrough therapy designation to **LOXO-292**, a selective RET inhibitor, for the treatment of patients with metastatic, RET-fusion-positive NSCLC who require systemic therapy and have progressed following platinum-based chemotherapy and an anti-PD-1 or anti-PD-L1 therapy and for the treatment of patients with RET-mutant medullary thyroid cancer who require systemic therapy, have progressed following prior treatment, and have no acceptable alternative treatment options.
- Y-mAbs Therapeutics, Inc. (ymabs.com) announced that the FDA has granted breakthrough therapy designation to **naxitamab**, in combination with GM-CSF, for the treatment of high-risk neuroblastoma refractory to initial therapy or with incomplete response to salvage therapy in patients older than 12 months of age with persistent refractory disease limited to bone marrow with or without evidence of concurrent bone involvement.
- OBI Pharma, Inc. (obipharma.com) announced that the FDA has granted orphan drug designation for **OBI-3424** for the treatment of acute lymphoblastic leukemia (ALL).
- Clovis Oncology, Inc. (clovisoncology.com) announced that the FDA has granted breakthrough therapy designation to **Rubraca® (rucaparib)** as a monotherapy treatment of adult patients with BRCA1/2-mutated metastatic castration-resistant prostate cancer who have received at least one prior androgen receptor-directed therapy and taxane-based chemotherapy.
- Karyopharm Therapeutics Inc. (karyopharm.com) announced that the FDA has accepted its NDA with priority review seeking accelerated approval for **selinexor** as a new treatment for patients with penta-refractory multiple myeloma.
- Bristol-Myers Squibb Company (bms.com) announced that the FDA accepted has its supplemental BLA for **Sprycel® (dasatinib)** in combination with chemotherapy for the treatment of pediatric patients with newly diagnosed Philadelphia chromosome-positive ALL.

Genetic Tests and Assays in the News

- On September 28, the FDA permitted marketing of the **clonoSEQ® assay** (Adaptive Biotechnologies, adaptivebiotech.com), a next-generation sequencing-based test for minimal residual disease in patients with ALL or multiple myeloma.
- On August 8, PapGene, Inc. (papgeneinc.com) announced that it had received breakthrough device designation from the FDA for the **PapGene test**, a multi-analyte liquid biopsy test that uses a combination of circulating tumor DNA and protein biomarkers to detect the presence of cancer in average-risk, asymptomatic individuals over the age of 65.

Devices in the News

- Qiagen N.V. (qiagen.com) announced that the FDA has approved a PMA Supplement, expanding the labeling claim of the ***therascreen*® EGFR RGQ PCR Kit** to allow its use as a companion diagnostic with Pfizer's Vizimpro® for first-line treatment of patients with NSCLC with EGFR exon 19 deletions or an exon 21 L858R mutation. OI

FDA Expands Use of Gardasil®9

On October 5, the FDA approved a supplemental application for **Gardasil9 (Human Papillomavirus 9-valent Vaccine, Recombinant)** (Merck & Co., Inc., merck.com), expanding the approved use of the vaccine to include individuals aged 27-45 years.

FDA Updates Prescribing Information for Keytruda® and Tecentriq®

Prescribing **Keytruda (pembrolizumab)** (Merck & Co., Inc., merck.com) and **Tecentriq (atezolizumab)** (Genentech, Inc., gene.com) now requires the use of an FDA-approved companion diagnostic test to determine PD-L1 levels in tumor tissue from patients with locally advanced or metastatic urothelial cancer who are cisplatin-ineligible.

The SCOOP Program

BY CHRISTOPHER KOPROWSKI, MD, MBA; EDITH J. JOHNSON, PHD, MBA;
KAREN SITES, BSN, RN, OCN; AND NICHOLAS PETRELLI, MD

Introducing supportive care and enhanced navigation into the curative treatment of cancer

Numerous studies have demonstrated the impact of the early introduction of palliative care for patients with advanced cancers.[1-4] One landmark study of patients with metastatic non-small cell lung cancer revealed not only an improvement in quality of life but also a two-month improvement in survival among patients receiving supportive care in addition to standard care.[5] Also noted in the study, care for these patients may have been less costly due to earlier introduction of hospice services and less chemotherapy prescribed and used. In a similar manner, the addition of nurse navigation has been shown in a randomized study to impact favorably on the patient.[6]

We hypothesized that introducing supportive care management and enhanced electronic aids to nurse navigation in selective curative cases could result in cost savings and enhanced patient experience for patients with advanced disease.

Improving Our Multidisciplinary Care Model

Christiana Care's Helen F. Graham Cancer Center and Research Institute, located in northern Delaware, is one of the busiest cancer centers in the region, with 3,300 new analytic cases a year. A high priority is placed on the multidisciplinary practice of oncology, with multidisciplinary clinics established for 14 different tumor sites. In our traditional multidisciplinary care model, patients were initially seen by a nurse navigator and physicians representing the three major oncologic specialties—medical, radiation, and surgical—with other support staff consulted as needed. Prior to 2016 our supportive and palliative care service had been generally uninvolved with curative cases as part of the multidisciplinary team.

In addition, under our traditional multidisciplinary care model, nurse navigators did not have access to electronic aids to promote effective care coordination. Unfortunately, because our nurse navigators were challenged with managing patient needs in a fragmented system, barriers to care coordination sometimes occurred, resulting in missed appointments, unaddressed nutritional and psychosocial needs, and unmanaged symptoms.

We hypothesized that introducing supportive care management and enhanced electronic aids to nurse navigation in selective curative cases could result in cost savings and enhanced patient experience for patients with advanced disease. To test this hypothesis, we developed and implemented the Supportive Care of Oncology Patients (SCOOP) Program, introducing a clinical pathway as the key program component in November 2016. Our pathway committee—comprised of leaders from Organizational Excellence, Medical Oncology, Radiation Oncology, Inpatient Oncology Nursing, Supportive and Palliative Care, and Psycho-

social Oncology—believed that all patients receiving concurrent chemotherapy and radiation with curative intent would most likely benefit from this type of program due to their substantial risk for medical complications like inanition, uncontrolled pain, and respiratory distress. However, due to resource limitations and for the purposes of data collection, we limited the SCOOP Program to patients receiving radiation and chemotherapy at the Helen F. Graham Cancer Center who were diagnosed with potentially curable thoracic, colorectal, or head and neck malignancies in our multidisciplinary clinics. Because a number of patients with these diagnoses with combined modalities were not seen initially in the multidisciplinary clinics and therefore received standard care, these patients were able to function as contemporary controls for the purposes of analysis. Patients seen in the multidisciplinary clinics prior to the initiation of the SCOOP Program functioned as historical controls.

Developing Our Clinical Pathway

In 2016 Christiana Care Health System established a formal structure based on a service line model. Senior administration felt that the traditional department organization would be inadequate to prepare the institution for a risk-based reimbursement environment, and nine different service lines were established. The departments retained their educational and credentialing responsibilities, but clinical strategy and tactics were passed to the service lines. Each service line was tasked with developing a clinical pathway. These pathways were not intended to be National Comprehensive Cancer Network guidelines but instead were viewed as an interdisciplinary effort to meet the triple aim of improving the patient experience, delivering better care, and reducing healthcare costs.[7] Accordingly, Christian Care Health System established a clinical value council that included the service line leaders as well as the chief clinical officer. The council's purpose is to maintain accountability for the clinical pathways and to disseminate and share information about these pathways for mutual benefit.

Within the cancer service line, the service line leadership team approved the SCOOP clinical pathway, and an integrated practice team was put together to develop and implement the pathway. Figure 1, right, illustrates the pathway governance structure. A pathway integration team was established at the institutional level to provide all of the necessary support to integrate the clinical pathway.

The solar system diagrams in Figure 2, page 22, illustrates the relationships within the integrated practice team and the pathway integration team services that are available to this team. Section heads within the Helen F. Graham Cancer Center made up the core members of the integrated practice team. Four team leaders were selected, including the associate service line leader, a project manager from organizational excellence, and chiefs of nurse navigation and care management. The pathway integration team provided critical expertise in areas such as data on admission, readmissions, and emergency department (ED) visits; educational tools; information from patient advisors; and data from patient charges.

The integrated practice team met on a regular basis, initially biweekly and then monthly. Core team members developed a current state process map of the opportunities for improving patient experience and quality of care from the time the patients were seen in the multidisciplinary clinic until one month following completion of their radiation therapy. Examples of the inadequacies noted included:

- Lack of standardized medical history forms
- Redundant visits
- Incomplete task performance by nurse navigators
- Insufficient involvement of supportive and ancillary services
- Poor ED communications
- Poor communication on discharge from the hospital and admission to non-cancer floors.

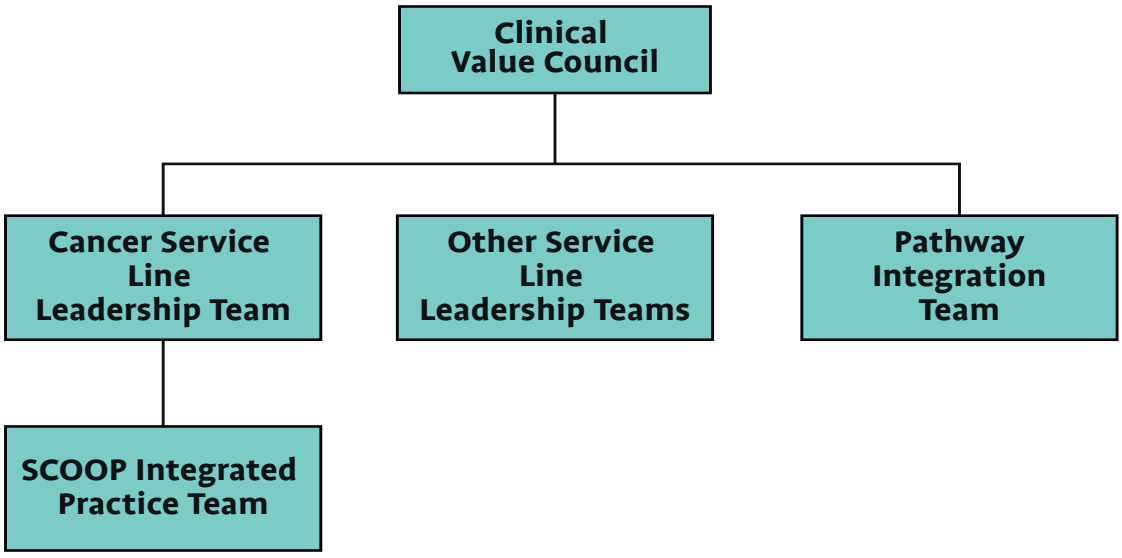
In discussion of the opportunities for enhancing the patient experience, it became obvious that our integrated practice team would have—in some instances—little short-term effect. For example, without restructuring the entire bed board assignments system, it was unlikely that the integrated practice team could influence patient admission to the cancer nursing unit. To counter this effect, the team developed an impact control matrix (Figure 3, page 23), identifying interventions in the top left as activities that the team felt would have the biggest impact on the patient and over which the team would have the most control. Our top priorities identified opportunities 1, 2, 3, 7, and 9 for our initial interventions. These included:

- Ensuring that all patients who will be receiving concurrent chemotherapy and radiation for either thoracic, head and neck, or colorectal malignancies with curative intent are screened by a member of the supportive and palliative care team at the time of the initial multidisciplinary visit.
- Developing a checklist for nurse navigation.
- Developing an enhanced electronic aid for navigation.
- Implementing a process by which palliative and supportive services such as nutrition, health psychology, and dentistry are automatically contacted to evaluate a patient unless nurse navigators opt out of such services at the time of the multidisciplinary visit.
- Developing an educational journal for patients that would help them self-navigate and reduce their anxiety.

Implementing the Clinical Pathway

Once these priorities were identified, the integrated practice team delegated implementation responsibilities to providers with feedback and education from appropriate integrated practice team members. Initially, ensuring that all eligible patients were placed on the clinical pathway proved challenging. Discussion with clinicians provided key insights. First, navigators were not aware that eligible patients were not being placed on the clinical pathway. Additionally, many eligible patients were not being referred to

Figure 1. Clinical Pathway Governance



the multidisciplinary clinics and instead were beginning treatments directly after consultation with the radiation and/or medical oncologist. Our initial analysis of compliance six months after clinical pathway implementation revealed a disappointing compliance rate of only 50 percent, mostly due to bypassing the multidisciplinary clinics. Nurse navigator consciousness was raised by repetitive reminders.

We countered the omission of multidisciplinary clinic referral by creation of a "re-entry" clinical pathway managed by the radiation oncology nurses, as well as substantial feedback to the physician providers. Radiation oncology nurses received a list of all SCOOP patients and were asked to compare it to their list of potentially eligible patients beginning treatment to identify discrepancies. If an eligible patient was determined to be off the pathway, he or she would be referred promptly to the newly created SCOOP multidisciplinary clinic, where patients would be seen by nurse navigators and relevant supportive care services early on in treatment but without the physician oncologic specialists whom they had already seen in consultation. As a result of these various interventions, the current overall participation of eligible patients is now 92 percent.

Next, we developed a checklist for nurse navigators that prescribed communication dates with the patient, captured scheduled visits, and assessed unmet needs among other mandatory tasks, such as opting out of individual supportive care interventions. We implemented the checklist and improved coordination of care using a platform called Aerial (Medecision, medecision.com). Intended primarily as an electronic platform for population health case management, the Christina Care Health System IT team—under the direction of the SCOOP integrated practice team—adapted the platform to assure task completion in a timely fashion by the nurse navigators. The electronic checklist helped nurse navigators improve care coordination and decrease gaps in care. These tasks include coordination of consults with oncologic physicians and other ancillary providers such as social work, behavioral health, nutrition, speech pathology, occupational and physical therapy, supportive care providers, and dental providers (when applicable). Collaborative communication occurs from the start of the electronic checklist. Tasks are automatically generated at various points based on the date of clinical pathway creation, treatment start, and treatment completion to correlate with disease and treatment needs.

The electronic checklist provides an automatic workflow versus manual entry, which decreases omission and error. The first step in the process is to enter patient characteristics in drop-down menus on the home page, thus initiating the electronic checklist.

(continued on page 24)

Figure 2. The SCOOP Integrated Pathway Team and Pathway Integration Team Partnership

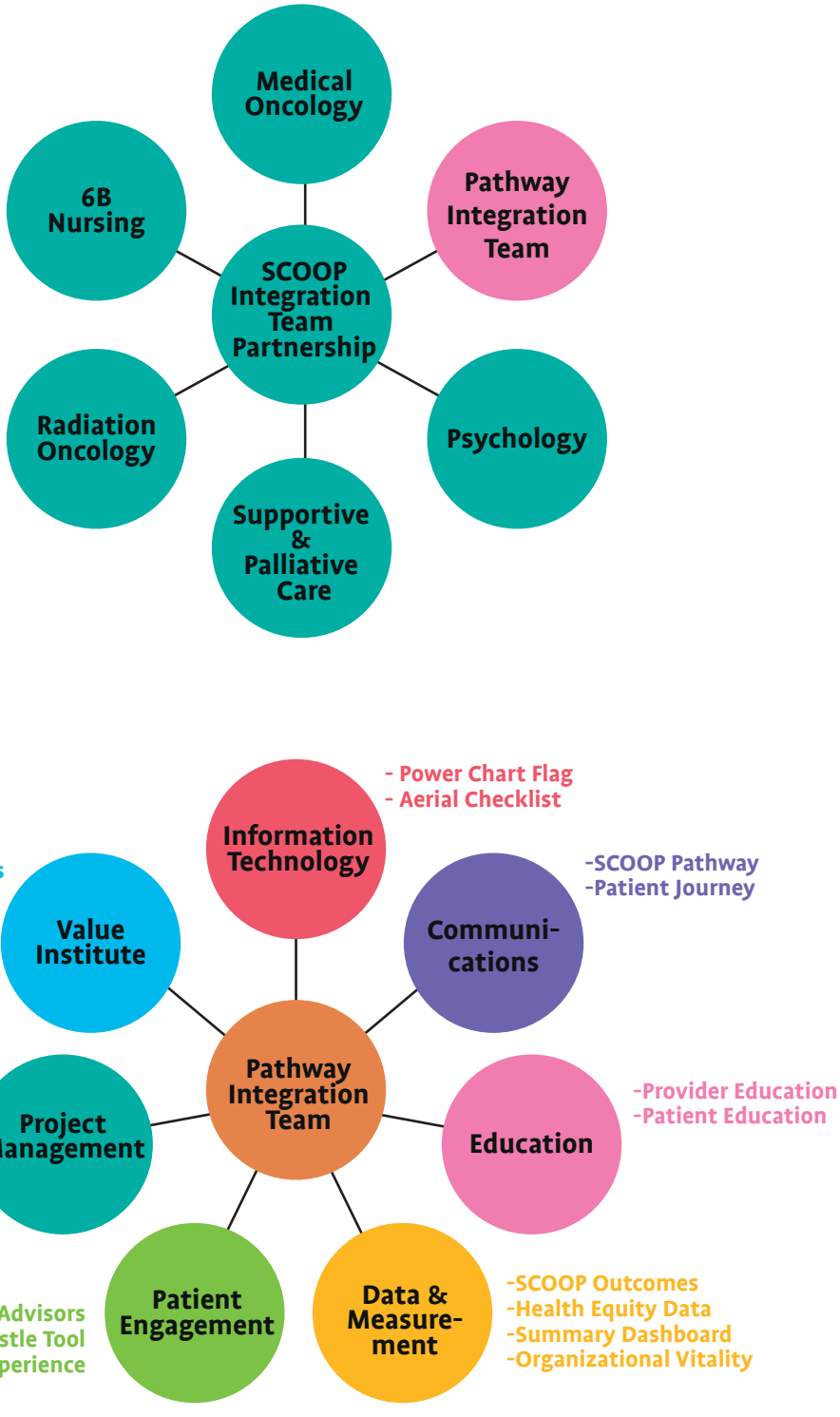
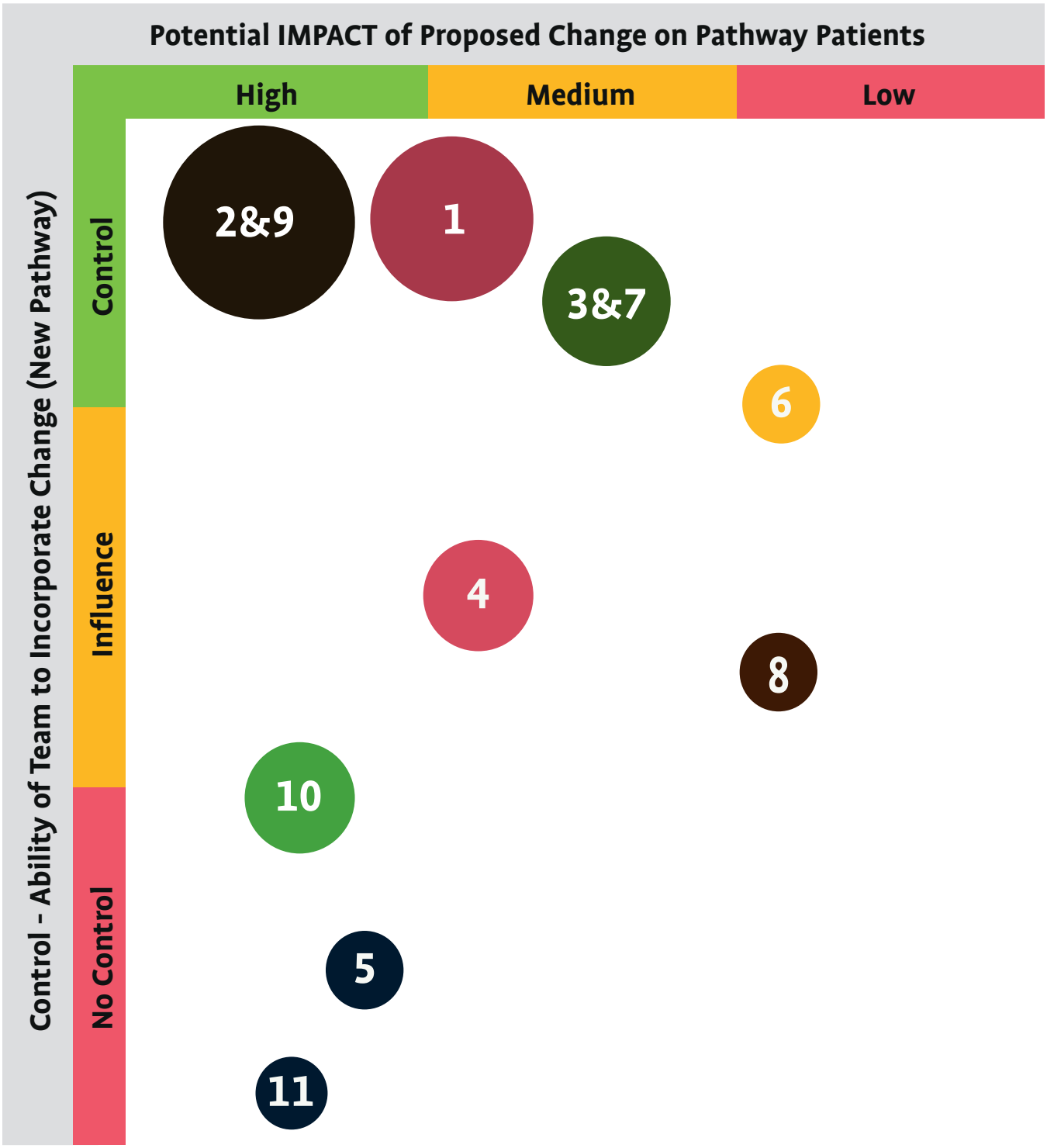


Figure 3. Impact Control Matrix for Proposed Change



(continued from page 21)

Once the required fields are completed, the software automatically generates a checklist that is patient specific and time driven. The checklist includes a series of tasks for nurse navigators to manage and complete. Though tasks may be delegated to and completed by certain consulted providers, navigators receive electronic notification of its completion and the task is not removed from their list prior to this notification. The electronic checklist and software provide navigators with a daily list of patient tasks. By clicking on individual patients, navigators become aware of necessary patient interventions.

In addition, the Aerial platform communicates with the hospital information system about clinical pathway patients and the navigator (as well as the oncologists) receives notification of ED visits, admission, and discharges when they are flagged by the information system. Once a discharge occurs, nurse navigators are tasked with reviewing patient discharge data, calling the patient, and assuring a smooth transition of care back to the outpatient oncology team. Figures 4 and 5, right, illustrate Aerial output of both task summaries and task details.

Finally, we collaborated with patient advisors to redesign our education journal to address unmet patient needs, such as what symptoms to expect from treatment, the goals of treatment, coping with unwanted emotions, and resources available in the cancer center to help patients through their treatment journey. Table 1, below, outlines the sections included in the revised patient education journal.

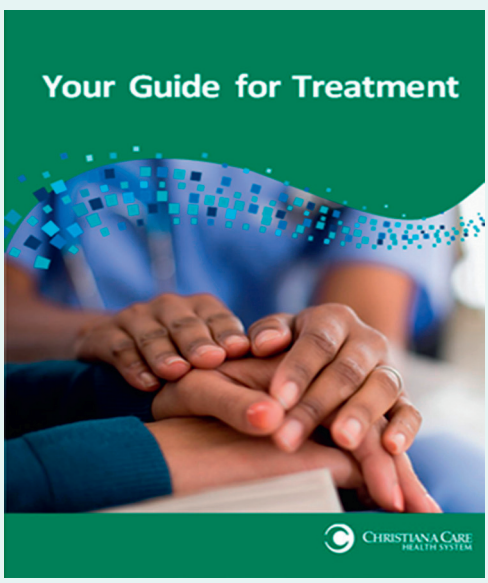
Our Results

When we examined our primary outcomes of ED visits, hospital admissions, and 30-day readmissions, it was clear from the outset that our SCOOP patients benefited from this multifactorial intervention. Table 2, page 26, shows data from the first year of the SCOOP Program, revealing striking differences between SCOOP patients and the contemporary controls (defined as SCOOP-eligible patients who were not on the clinical pathway). Moreover, current monthly data suggest that these results continue to be sustainable.

Nurse navigator task compliance was aided by the electronic platform. Already excellent (94 percent) at the onset of the SCOOP Program, over the course of the first 16 months, compliance increased to close to 100 percent (Figure 6, page 27).

Cost data were obtained from the pathway integration team, who were able to provide actual expenses incurred by the institution based on procedural charge codes. These cost data did not include reimbursement from the patient or third parties. Thus, these can be viewed as societal cost savings and would represent institutional savings in a capitated or bundled reimbursement environment but do not necessarily represent institutional savings in a fee-for-service environment. Table 3, page 26, shows the average cost savings for a SCOOP patient compared to a control patient (defined as SCOOP-eligible but not on the clinical pathway). Table 4, page 26, shows the average cost savings for a SCOOP patient since the start of the clinical pathway (Nov. 1, 2016. to May 31, 2018).

Table 1. SCOOP Patient Education Journal



- Welcome
- Map and How to Get Around the Campus
- Understanding Your Multidisciplinary Care Clinic Visit
- Your Treatment
  - Radiation
  - Chemotherapy and Medications
  - Surgery
  - Supportive and Palliative Care
  - Primary Care
- Coping and Emotions
- Nutrition and Well-being
- Symptoms and Side Effects
- Appointments
- My Medications
- After Treatment is Over

Figure 4. Aerial Daily Nurse Navigator Tasks

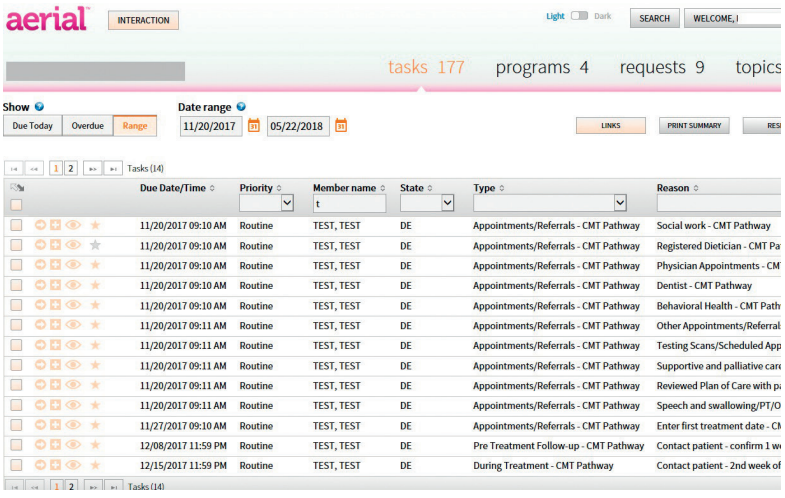
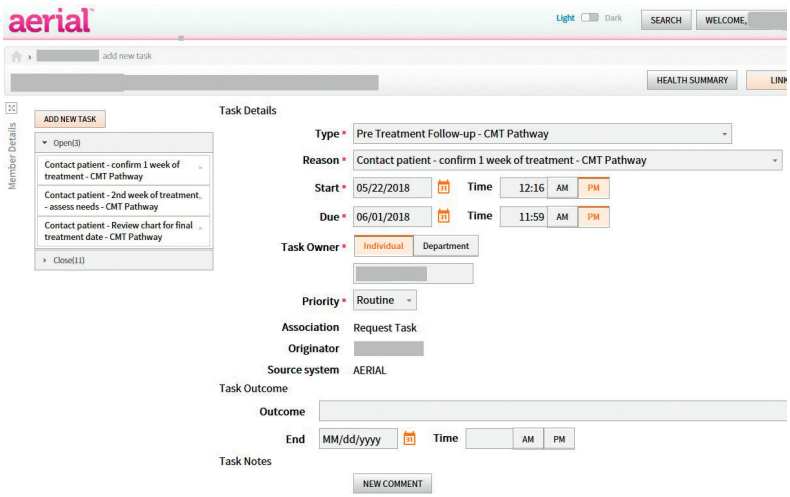


Figure 5. Aerial SCOOP Checklist Task Selection



Wrap-Up and Future Directions

Eighteen months ago, the Helen F. Graham Cancer Center and Research Institute instituted a program designed to provide the kind of supportive care services generally reserved for patients with advanced solid tumors into a population of patients being treated with curative intent but with sufficient acuity to suggest that they could also benefit from more intensive interventions. These interventions were combined with enhanced nurse navigation aided by an electronic platform. Our results with regard to prevention of ED visits, admission, and readmission strongly suggest a substantial benefit in the quality of life from a more intensive psychosocial approach for these cases. Not surprising, the decrease in admission and ED visits resulted in less procedural expense incurred and represented a substantial societal cost savings for these patients, likely improving relevant outcomes in a value- and risk-based environment.

We would like to expand the program to all patients with high acuity seen in our multidisciplinary clinics rather than limit the intervention to a select group of combined modality patients

(continued on page 27)

Table 2. SCOOP vs. Control Visit Data One Year After Program Implementation

ED Visits		
	SCOOP	**Control**
All patients	59	56
Number of ED patients	19	30
Total number of ED visits	37	63
Percentage of patients in ED	32.2	53.6
Hospital Admissions		
	SCOOP	**Control**
All patients	59	56
Number of patients admitted	15	19
Total number of admissions	25	34
Admission percentage by patients	25.4	33.9
Readmissions		
	SCOOP	**Control**
Number of 30-day readmissions	5	11
Number of admissions	25	34
Percentage of readmissions	20	32.4

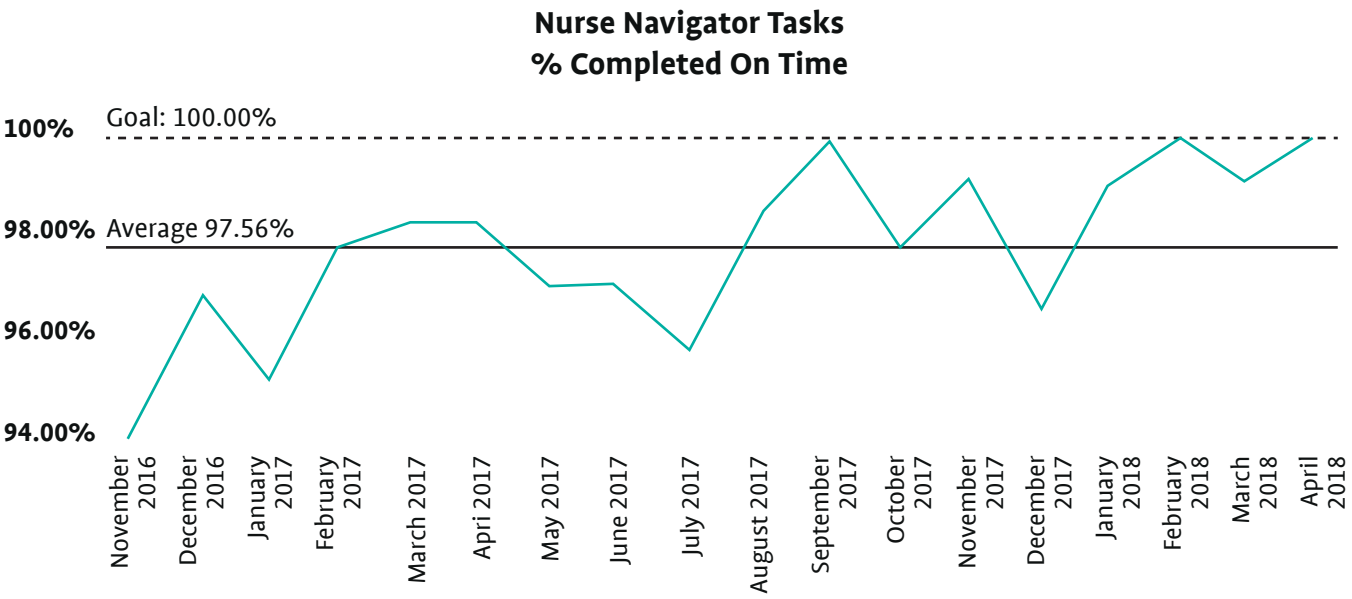
Table 3. SCOOP vs. Control One-Year Cost Analysis

	Control	SCOOP	Delta
Number of patients	54	57	—
Total cost	$371,640.00	$302,256.00	—
Cost per patient	$6,888.21	$5,337.83	$1,544.41

Table 4. SCOOP Program Annual Cost Savings

Year	Total Cost Savings	Number of SCOOP Patients	Average Number of Patients per Month
2016	$16,988.51	11	5.5
2017	$140,541.31	91	7.6
2018	$63,320.81	41	8.2
Total	$220,850.63	143	7.9

Figure 6. SCOOP Nurse Navigation Task Compliance



(continued from page 25)
being treated curatively. To do so would require greater staffing in our supportive care services and the institution of an objective measurement of individual patient acuity. We have also recently introduced a medical support unit manned daily by a nurse practitioner and allowing for urgent referrals, which we hope will further reduce ED visits and hospital admissions.

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References

1. Zimmermann C, Swami N, Krzyzanowska M, et al. Early palliative care for patients with advanced cancer: a cluster-randomised trial. *Lancet.* 2014;383:1721-1730.

2. Rummans TA, Clark MM, Sloan JA, et al. Impacting quality of life for patients with advanced cancer with a structured multidisciplinary intervention: a randomized controlled trial. *J Clin Oncol.* 2006;24:635-642.

3. Rabow MW, Dibble SL, Pantilat SZ, McPhee SJ. The comprehensive care team: a controlled trial of outpatient palliative medicine consultation. *Arch Intern Med.* 2004;164:83-91.

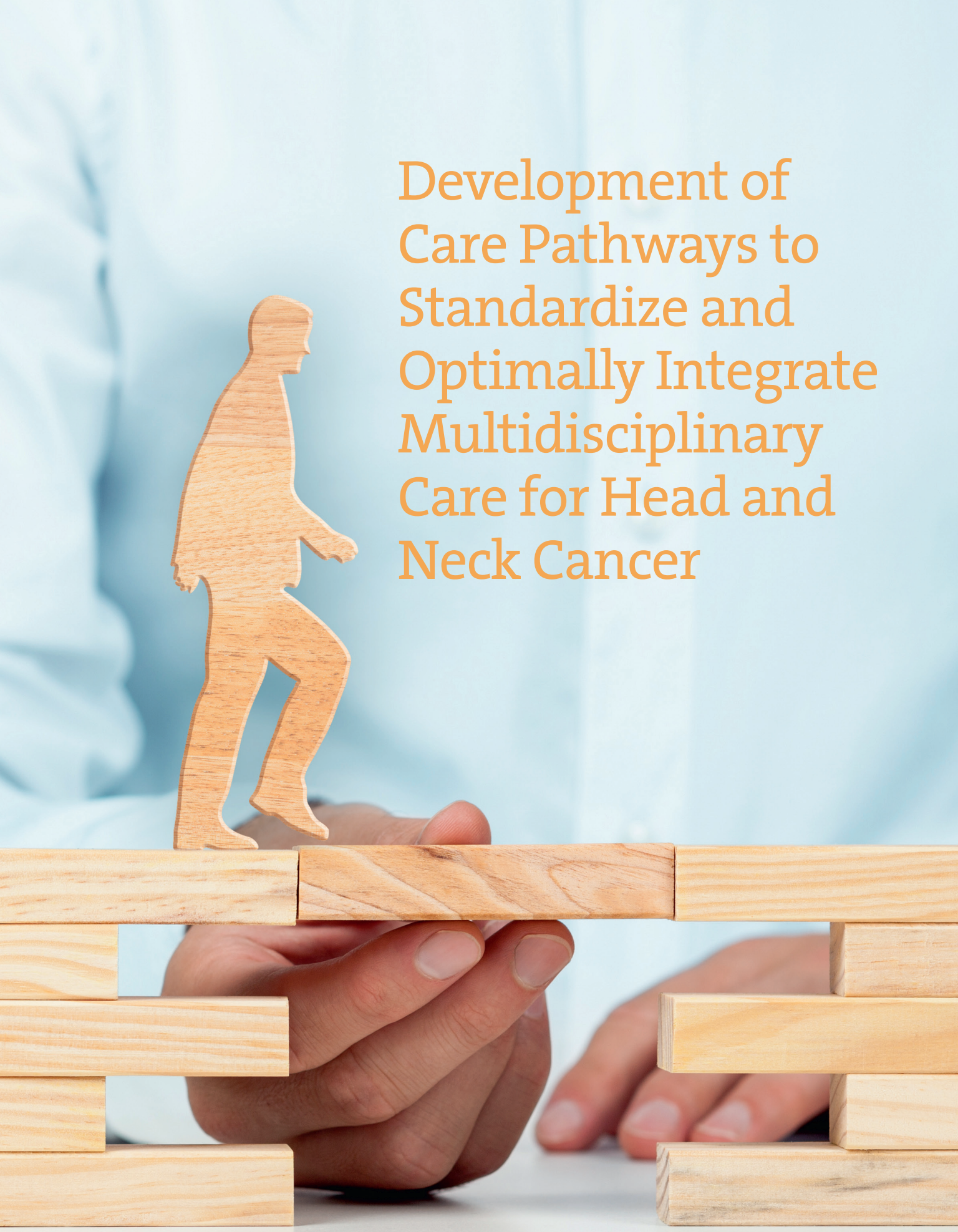
4. Bakitas M, Lyons KD, Hegel MT, et al. Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer: the Project ENABLE II randomized controlled trial. *JAMA.* 2009;302:741-749.

5. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med.* 2010;363:733-742.

6. Wagner EH, Ludman EJ, Aiello Bowles EJ, et al. Nurse navigators in early cancer care: a randomized, controlled trial. *J Clin Oncol.* 2014;32:12-18.

7. Berwick DM, Nolan TW, Whittington J. The triple aim: care, health, and cost. *Health Aff (Millwood).* 2008;27:759-769.

Development of Care Pathways to Standardize and Optimally Integrate Multidisciplinary Care for Head and Neck Cancer



BY ASSUNTINA G. SACCO, MD; CHARLES S. COFFEY, MD; PARAG SANGHVI, MD; GLORIA P. RUBIO, MS, RD, CNSC; JOSEPH CALIFANO, MD; JAYNA ATHAS, MS; GELINE J. TAMAYO, MSN, RN, ACNS-BC; KRISTEN LINNEMEYER, MA, CCC-SLP; LINDA C. BARNACHEA, PHARMD, BCOP; RYAN K. OROSCO, MD; KEVIN T. BRUMUND, MD; EZRA E.W. COHEN, MD; KATHRYN GOLD, MD; LOREN K. MELL, MD; ANDREW SHARABI, MD, PHD; GREGORY A. DANIELS, MD, PHD; YUKO ABBOTT, DSW, LCSW; RESENIA COLLINS, OTR/L, CLT-LANA; KATRINA CLYNCH†, NP-C; MONTSERRAT NOBOA, MPH; AND LIZA BLUMENFELD, MA, CCC-SLP, BCS-S

Head and neck cancer is the sixth most common cancer worldwide, with an estimated 600,000 new cases and 300,000 patient deaths reported annually.[1-3] In recent years, curative interventions have dramatically improved the five-year overall survival rate from 54.7 percent in 1992-1996 to 65.9 percent in 2002-2006.[4] This improvement is due in part to the increasing incidence of head and neck cancer caused by human papillomavirus (HPV).[5] In contrast to HPV-negative head and neck cancer, which is typically associated with tobacco and alcohol use, HPV-associated head and neck cancer is a distinct biological and clinical entity with improved treatment response and survival rates.[6-11] Because the majority of head and neck cancer patients present with locally advanced disease, curative treatment is often multimodal, including surgery, radiation, and/or chemotherapy.[12] The combined toxicity of these various interventions results in devastating disruption of quality of life (QOL), increased healthcare utilization, and poorer health outcomes.[13] Side effects carrying the greatest burden include dysphagia, dysarthria (difficulty swallowing), xerostomia (dry mouth), dental caries (tooth decay), pain, feeding tube dependence, lymphedema, and altered cosmesis (disfigurement).[14-17]

The high symptom burden across multiple functional domains has driven the need to incorporate supportive services during curative head and neck cancer treatment. The multidisciplinary team approach harnesses the combined contributions of physicians and ancillary providers to drive greater patient-centered care, addressing factors that heavily influence morbidity, mortality, and QOL. Numerous studies have investigated clinical and functional outcomes in institutions that offer multidisciplinary care.[18] David et al. reviewed 46,567 patients treated for squamous cell carcinoma of the oropharynx, larynx, and hypopharynx from the National Cancer Database, comparing survival rates between high- and low-volume facilities.[19] Patients treated in high-volume facilities with presumptive access to experienced multidisciplinary teams had improved survival compared to institutions with lower volumes and likely less multidisciplinary access.[19] Retrospective review of a single institution's adherence to treatment planning before and after implementation of multidisciplinary care practices revealed that implementation of this type of care led to:[20]

- Improved adherence to clinical quality indicators
- Higher rates of dental and nutritional assessments

The high symptom burden across multiple functional domains has driven the need to incorporate supportive services during curative head and neck cancer treatment. The multidisciplinary team approach harnesses the combined contributions of physicians and ancillary providers to drive greater patient-centered care, addressing factors that heavily influence morbidity, mortality, and QOL.

- Completed positron emission tomography (PET) scans
- Referrals to radiation and medical oncology
- Shorter length of inpatient stays postoperatively
- Reduced time from surgery to onset of adjuvant treatment.

The compelling body of evidence highlighting the benefits of multidisciplinary care prompted the National Comprehensive Cancer Network (NCCN) guidelines to include the following statement: "The management of patients with head and neck cancers is complex. All patients need access to the full range of support services and specialists with expertise in the management of patients with head and neck cancer for optimal treatment and follow-up. Outcomes are improved when patients with head and neck cancers are treated in high-volume centers."[21]

Care pathways have been proposed as a way to translate evidence-based practice and published national guidelines into an organization's care delivery model. Care pathways also carry the opportunity to hard-wire consistency and efficacious methodology in the provision of head and neck cancer care.

Though integration of multidisciplinary care may seem germane to the provision of curative head and neck cancer care, numerous implementation barriers such as insufficient facilities, lack of standardization, time constraints, and poorly developed interprofessional relationships have raised questions about its efficacy and value.[22] To overcome these barriers, Vanhaecht et al. defined *care pathway* as "a complex intervention for the mutual decision-making and organization of care processes for a well-defined group of patients during a well-defined period."[23] Care pathways have been clinically integrated for numerous healthcare conditions within the United States and abroad. Published benefits of care pathways include reduced lengths of hospital stay, reduced hospital costs, and improved patient outcomes with reduced complications.[24,25] This integrated model eliminates fragmentation, providing a structured, reproducible method for administering multidisciplinary care to individuals with a specific medical condition. Care pathways have been proposed as a way to translate evidence-based practice and published national guidelines into an organization's care delivery model. Care pathways also carry the opportunity to hard-wire consistency and efficacious methodology in the provision of head and neck cancer care. Growth in the multidisciplinary head and neck cancer team at our Head and Neck Center of Excellence provided an opportune time to develop and implement care pathway methodology.

Our Materials and Methods

Representatives across multiple disciplines participated in our care pathway development, including:

- Physicians (medical, radiation, and surgical oncology)
- Nursing
- Speech-language pathology
- Nutrition
- Physical and occupational therapy
- Social work
- Program administrator.

We conducted multiple small-group breakout sessions to create the care pathways, with decisions surrounding timing and frequency of visits based on specialty clinical expertise, recommendations from peer-reviewed literature and NCCN guidelines, and program feasibility. Our goal was to create treatment modality-specific rather than disease site-specific care pathways. All small groups included at least one representative from each discipline to ensure that physician-based and supportive services were appropriately represented.

We created each care pathway in a Microsoft Excel worksheet with the understanding that pathways were fluid documents subject to future modification. Each document followed a standardized format whereby the left-hand column listed each medical service as a separate row and each subsequent column was a specific time point across the care continuum that was marked when provision of a medical service was indicated. Following dissemination and approval of the care pathways from our multidisciplinary team at large, the second stage involved troubleshooting methods to optimize implementation. A workgroup (composed of our physicians, head and neck program directors, information technology support team, health system business office, and Moores Cancer Center healthcare administration) completed the following:

- Leveraged our shared electronic health record (EHR) to create order sets for referral generation
- Interfaced with our business office to implement a preauthorization process for certain ancillary services
- Implemented newly developed programs (patient navigation, head and neck cancer survivorship clinic)
- Expanded our resources and services for patient education.

Our Results

We created and implemented four care pathways, including two pathways each for single- and multimodality therapy rendered with curative intent. These care pathways are for:

1. Concurrent radiation with chemotherapy (Table 1, page 32)
2. Surgery followed by postoperative radiation (Table 2, page 34)
3. Surgery alone (Table 3, page 36)
4. Radiation alone (Table 4, page 38).

Below we detail our prescription of the various supportive services and the solutions we devised to contend with implementation barriers.

Speech-Language Pathology

The speech-language pathologist plays a critical role within the multidisciplinary head and neck cancer team. These professionals are directly responsible for administering diagnostic and therapeutic services addressing speech, voice, and swallowing functions. Curative head and neck cancer treatment generates acute and chronic deficits in these areas, causing a deleterious impact on QOL. The severity of QOL effects is directly related to tumor characteristics and prescribed cancer therapies, including site, modality, anatomic extent of treatment, and treatment dose(s). Published literature recommends a pre-treatment speech-language pathologist evaluation incorporating clinical, behavioral, and instrumental methods for all patients.[26] Results drive subsequent interventions and recommendations that optimize patient safety, education, and functional capacity.[26,27] NCCN guidelines recommend a formal baseline evaluation for patients with speech and/or swallowing dysfunction or whose treatment is likely to impair speech and/or swallowing.[21] NCCN also recommends routine evaluations until the patient has achieved a stable baseline post-treatment or indefinitely in certain cases.[21] Our care pathway workgroup integrated speech-language pathologist services in a calibrated fashion across the care continuum. Specific time points are driven by each treatment modality-specific care pathway (see Tables 1-4, pages 32–39). Though structured time points are delineated, services may be escalated based on severity of symptoms.

Nutrition

Poor nutritional status across the head and neck cancer care continuum is highly prevalent, underscoring the pivotal role that nutrition therapy plays for patients undergoing curative treatment. Altered nutrition and weight loss at baseline are typically driven by the underlying disease. Nutrition and weight loss are further exacerbated during and after treatment by therapeutic intervention and associated toxicity. Nutrition rates in head and neck cancer patients are as high as 52 percent at time of diagnosis and present in 44 to 88 percent of patients receiving radiation with or without chemotherapy.[28-30] The clinical significance of malnutrition is its association with increased rates of morbidity, mortality, and QOL disruption.[31] Weight loss before and during radiation is an independent prognostic indicator of five-year disease-specific survival.[29] These findings cement the role of the registered dietitian as a key member of the head and neck cancer multidisciplinary team.

Historically, prescription of feeding tube placement has been prophylactic or reactive, based primarily on provider recommendation and preference. NCCN guidelines now advise against prophylactic placement in patients with good performance status who do not have significant airway obstruction, significant weight loss, or severe dysphagia at baseline.[21] For patients who require enteral feeding, it is paramount for the registered dietitian to regularly communicate with the speech-language pathologist regarding status of swallowing function; this collaboration enables continued encouragement of oral intake during treatment (if safe to do so) and facilitates expeditious enteral wean. Our care pathway workgroup integrated dietitian services at baseline, a minimum of every two weeks during treatment, and specified time points post-treatment to provide patient-specific strategies to optimize nutrition and minimize unintentional weight loss.

Care pathways include both services to address any changes in neck or shoulder range of motion post-treatment. Occupational therapy instructs on upper extremity exercises post-operatively and educates patients on ways to maximize independence with ADLs.

Physical and Occupational Therapy

The tradeoff of curative head and neck cancer treatment is often residual physical disability, such as general deconditioning, trismus (reduced opening of the jaw), lymphedema, altered shoulder/neck range of motion, and reduced physical independence. Though physical therapy and occupational therapy interventions could potentially mitigate impairment and enable restoration of function in many instances, integration of these services for head and neck cancer is not well defined. NCCN guidelines broadly highlight the importance of physical medicine and rehabilitation and provide general principles and guidelines for physical and/or aerobic activity.[21,32] The absence of appropriate physiotherapy intervention would be especially detrimental to long-term function and QOL. Therefore, it was essential that we included physical therapy and occupational therapy in our care pathways to improve QOL and basic function through activities of daily living (ADLs), strengthening, and endurance exercise. Care pathways include both services to address any changes in neck or shoulder range of motion post-treatment. Occupational therapy instructs on upper extremity exercises post-operatively and educates patients on ways to maximize independence with ADLs. It also addresses head and neck lymphedema by providing education, evaluation, and complex decongestive therapy, which has been shown to improve symptomatology.[33] Physical therapy addresses mobility issues involving trismus (reduced opening of the jaw) and stiffness of the head, neck, and shoulders. Physical therapy also plays an important role in addressing strength and cardiorespiratory fitness both before and after treatment.[34,35]

Survivorship

The concept of cancer survivorship stems from a seminal publication in 2005, which highlighted the numerous unmet needs of a rapidly growing number of cancer survivors.[36] Though cancer

(continued on page 37)

Table 1. Concurrent Chemotherapy and Radiation Care Pathway

Service Line	Initial Visit	Treatment Phase					
		Week 1	Week 2	Week 3	Week 4	Week 5	
Head and neck surgery	x[1]						
Head and neck surgery admin	Outside slides and images requested						
Head and neck surgery nursing	Add to tumor boards, generate after-visit summary to include pathway timeline; needs assessment[2]						
Medical oncology (MD or NP)	x			3 weeks (with more frequent visits as needed)			
Radiation oncology	x	x	x	x	x	x	
Survivorship clinic	x						
Speech-language pathology	Baseline fluoroscopy/ endoscopy clinic visit		Visit, week 2 or 3			x	
Dietary	x			x		x	
Occupational therapy							
Physical therapy					x		
Navigator	x[3]						
Patient education	x						
Dental	x						
Audiology	x (as needed)	x (as needed, if on platinum with hearing change)					
Imaging	x						

[1]Initiate pathway-based referrals at initial visit. [2]Alert MD for patients needing social work, pastoral services, palliative care, integrative health. [3]Navigator at initial visit and at care transitions. [4]Transition to survivorship per guidelines.[5]Post-treatment PET/computed tomography will be ordered by radiation oncology.
MD = medical doctor.

			Post-Treatment					
	Week 6	Week 7	Month 1				Month 2	Month 4
			Week 8	Week 9	Week 10	Week 11		
	x (optional)							x[4]
	x			x				x[4]
	x	x				4-6 weeks after treatment, sooner if symptomatic	x	x[4]
								x[4]
		x		Scope and visit, week 9 or 10			Fluoroscopy as needed week 13	Scope/clinic swallow[4]
		x					As needed	
						x	As needed	
						x	As needed	
			x					
			x (as needed, if had platinum with hearing change)					
								x[5]

Table 2. Surgery Followed by Postoperative Radiation Care Pathway

Service Line	Initial Visit	Preop	Tumor Board	
Head and neck surgery	Establish staging, pathway,[1] surgical plan		x	
Head and neck surgery admin	Outside slides and images requested	Surgery date selected, postop appointment scheduled	x	
Head and neck surgery nursing	Add to tumor board; generate after-visit summary to include pathway timeline; needs assessment[2]		x	
Microvascular surgery		As needed		
Medical oncology (MD or NP)			x	
Radiation oncology		See patient preop, establish preauthorization for radiation therapy; place dental referral	x	
Survivorship clinic	x			
SLP (for noncomplex surgery, SLP may not be required)		Baseline visit for complex/ mucosal surgery: endoscopy, FEES, ±MBSS	x	
Dietary		Assessment and education session	x	
Occupational therapy		Lymphedema baseline		
Physical therapy				
Navigator	x[4]			
Education		x		
Dental	x			
Imaging	x			

[1]Initiate pathway-based referrals at initial visit. [2]Alert MD for patients needing social work, pastoral services, palliative care, integrative health. [3]Discharge order set to specify SLP for endoscopic swallow. [4]Navigator at initial visit and at care transitions. [5]Transition to survivorship per guidelines. ADLs = activities of daily living; FEES = fiberoptic endoscopic evaluation of swallow; MBSS = modified barium swallow study; MD = medical doctor; POD = post-operative day; SLP = speech-language pathology; UE ROM = upper extremity range of motion.

	Inpatient	Post-Surgery	During Adjuvant Radiation Therapy	Post-Radiation
	Inpatient and discharge order sets to reflect pathway	2-3 weeks (earlier as needed drains, bolsters, etc.)		4-6 weeks (earlier as needed), then transition to NCCN guidelines[5]
		(per plastic reconstructive surgeon)		
		As needed, pending path; if adjuvant chemo required, follow chemoradiation pathway		
		2-3 weeks	Weekly	4-6 weeks (earlier as needed), then transition to NCCN guidelines[5]
				4 months[5]
	Every patient, POD 0 or 1	Discharge order set[3] to reflect pathway, 1-2 weeks, FEES ± MBSS	Every 2 weeks (increased frequency as needed)	Clinic + FEES 2-3 weeks, as needed MBSS 4-6 weeks; then transition to NCCN guidelines[5]
	As needed (tube feeds, malnourished or high risk, MD or speech-language pathologist recommended)	1-2 weeks	Every 2 weeks (increased frequency as needed)	1-3 weeks, then transition to NCCN guidelines[5]
	All neck dissections—for UE ROM and ADLs	As needed (per inpatient recs)		4 weeks
	As needed, if nursing identifies need for assistance with out of bed mobility (neck dissection; microvascular)	As needed (per inpatient recs)		As needed
		x		
		x (for patients who do not expect radiation)		
				x

Table 3. Surgery Alone Care Pathway

Service Line	Initial Visit	Preop	Tumor Board	Inpatient	Post-Surgery
Head and neck surgery	Establish staging, care pathway,[1] surgical plan		x	Inpatient and discharge order sets to reflect pathway	2-3 weeks (earlier as needed drains, bolsters, etc.)
Head and neck surgery admin	Outside slides and images requested	Surgery date selected, postop appointment scheduled	x		
Head and neck surgery nursing	Add to tumor board; generate after-visit summary to include pathway timeline; needs assessment[2]		x		
Microvascular surgery		As needed		Microvascular surgeon to dictate rehab needs	x[5]
Survivorship clinic	x				
Speech-language pathologist (for complex surgery)		Baseline visit: endoscopy, FEES, ±MBSS	x	Every patient, POD 0 or 1	Discharge order set[3] to reflect pathway; 1-2 weeks, FEES ± MBSS
Dietary		Assessment and education session	x	As needed (tube feeds, malnourished or high risk, MD or speech-language pathologist recommendations)	1-2 weeks
Occupational therapy				All neck dissection-for UE ROM and OOB ADLs	As needed (per inpatient recommendations)
Physical therapy				As needed (neck dissection) if nursing identifies need for assistance with OOB mobility	As needed (per inpatient recommendations)
Navigator	x[4]				x[5]
Patient education		x			
Imaging	x				As needed

[1]Initiate pathway-based referrals at initial visit. [2]Alert MD for patients needing social work, pastoral services, palliative care, integrative health. [3]Discharge order set to specify SLP for endoscopic swallow. [4]Navigator at initial visit and at care transitions. [5]Transition to survivorship per guidelines. ADLs = activities of daily living; FEES = fiberoptic endoscopic evaluation of swallow; MBSS = modified barium swallow study; MD = medical doctor; OOB = out of bed; POD = post-operative day; SLP = speech-language pathology; UE ROM = upper extremity range of motion.

(continued from page 31)

survivorship research has primarily focused on the most common cancers, the rapidly changing landscape and toxicities associated with head and neck cancer mark a watershed of opportunity in this population. The goals of our newly formed survivorship clinic include:

- Prevention
- Detection and surveillance for cancer recurrence or development of second primaries
- Interventions for physical and psychosocial late effects from head and neck cancer and its therapies
- Improved care coordination with specialists and primary care providers.

These goals were in line with the consensus-based management strategies published by the American Cancer Society for head and neck cancer survivorship.[37] NCCN guidelines state that "an individual is considered a cancer survivor from the time of diagnosis, through the balance of his or her life."[32] NCCN recommends integration of survivorship care and care plan within one year.[21] Based on these recommendations, our nurse practitioner-run survivorship clinic was integrated into all four care pathways at baseline, 4 and 12 months post-treatment, and then annually (refer to Tables 1-4 and Figure 1, page 40, and Figure 2, page 41). In addition to the aforementioned goals, the nurse practitioner provides patients with a document detailing the summary of treatment received, information for surveillance recommendations and post-treatment needs, and healthy behavior recommendations per NCCN.[32]

Patient Navigation

The role of care navigation in head and neck cancer is designed to provide patients with clear, proactive guidance in traversing the complex structure of multidisciplinary cancer care. The National Cancer Institute describes patient navigation as the support and guidance provided to persons with abnormal screenings or new cancer diagnoses, including overcoming challenges and barriers to accessing the healthcare system in a culturally competent manner.[38] Integrating navigation within a care coordination model has reduced redundancies and delays in treatment, promoted greater participation in clinical trials, improved patient education and satisfaction, and reduced costs.[39,40] Though published literature typically describes nursing models for patient navigators, the American Cancer Society launched a patient navigator program in 2005, which includes a broad representation of individuals; some, but not all, have a healthcare background.[41] Our program implemented a philanthropy-funded, facilitated care navigation model led by a public health provider. Timed interventions for care navigation were designed to reduce vulnerable periods, including at initial diagnosis through treatment planning and across care transitions (Tables 1-4).

Audiology

Patients with head and neck cancers are at risk for progressive sensorineural hearing loss after receipt of chemotherapy with platinum derivatives such as cisplatin.[42] Therefore, proactive audiologic evaluations should be implemented at baseline, during, and after platinum-based treatment to prevent further deterioration of hearing and to counsel on compensatory communication strategies or incorporate assistive listening devices when indicated.[37,43,44] Published literature regarding ototoxicity management recommends complete audiologic examinations, including case history, otoscopy, tympanometry, pure tone audiometry, distortion product otoacoustic emissions, and patient counseling. These assessments should occur at baseline (prior to or within 24 hours after platinum administration), routinely during treatment, and post-treatment (months 1, 3, 6, 9, and 12 and then annually as indicated).[44-47] NCCN guidelines recognize audiology professionals as an important component of the multidisciplinary team for head and neck cancer, with evaluations being recommended "as clinically indicated."[21]

Our program implemented a philanthropy-funded, facilitated care navigation model led by a public health provider. Timed interventions for care navigation were designed to reduce vulnerable periods, including at initial diagnosis through treatment planning and across care transitions.

Incorporating published recommendations as well as feasibility based on hospital resources, we recommended audiology evaluations for patients receiving platinum-based chemotherapy at baseline, during, and after treatment as clinically indicated (Table 1).

Nuts and Bolts of Implementation

Successful implementation of the care pathways was contingent on addressing systematic barriers and maintaining a patient-centric focus. For example, entering orders for multiple individual referrals into the EHR is time-consuming and prone to unintentional omission. Therefore, we created pre-populated order sets in the EHR for each care pathway, which enables ordering providers to more efficiently and consistently place all relevant referrals amidst a busy clinic. Insurance authorization for each individual service is also triggered earlier, increasing the probability that services are rendered in parallel rather than sequentially. This latter point is especially critical because time to treatment initiation represents an independent risk factor for head and neck cancer survival outcome.[48] For ancillary services such as speech-language pathology, we worked with our business office to obtain preauthorization for all relevant services (consultation, diagnostic

(continued on page 42)

Table 4. Radiation Alone Care Pathway

Service Line	Initial Visit	Treatment Phase					
		Week 1	Week 2	Week 3	Week 4	Week 5	
Head and neck surgery	x[1]						
Head and neck surgery admin	Outside slides and images requested						
Head and neck surgery nursing	Add to tumor board; generate after-visit summary to include pathway timeline; needs assessment[2]						
Radiation oncology	x	x	x	x	x	x	
Survivorship clinic	x						
Speech-language pathologist	Baseline fluoroscopy/endoscopy/ clinic visit				x	As needed	
Dietary	x				x	As needed	
Occupational therapy							
Physical therapy					x		
Navigator	x[3]						
Patient education	x						
Dental	x						
Imaging	x						

[1]Initiate pathway-based referrals at initial visit. [2]Alert MD for patients needing social work, pastoral services, palliative care, integrative health. [3]Navigator at initial visit and at care transitions. [4]Transition to survivorship per guidelines. [5]Post-treatment PET/computed tomography will be ordered by radiation oncology. MD = medical doctor.

			Post-Treatment					
	Week 6	Week 7	Month 1				Month 2	Month 4
			Week 8	Week 9	Week 10	Week 11		
	x (optional)							x[4]
	x	x				4-6 weeks after treatment, sooner if symptomatic[5]		x[4]
								x[4]
			x	Scope and visit, week 9 or 10		Fluoroscopy, week 13	Scope/clinic swallow[4]	x[4]
			x			x	As needed	
						x	As needed	
						As needed	As needed	
			x					
								x[5]

Figure 1. Surveillance Plan Patient Handout

UC San Diego Head and Neck Cancer Center

Name _____

Blue blocks are NCCN-recommended follow-up. You may be seen more often, as indicated.

	Survivorship Clinic	Head and Neck Surgeon	Radiation Oncologist	Medical Oncologist	Speech Pathologist, Nurse, Social Worker, Dietitian	Dentist
Pretreatment	**All patients**	Chemoradiation Radiation Surgery	Chemoradiation Radiation	Chemoradiation	Chemoradiation Radiation Session with team	Chemoradiation Radiation
Post-treatment						
1 month				Chemoradiation	Chemoradiation Radiation Session with team	Chemoradiation Radiation
2 months			Chemoradiation Radiation			
4 months	**All patients**	Chemoradiation Radiation Surgery		Chemoradiation	Chemoradiation Radiation	Chemoradiation Radiation
6 months		Surgery	Chemoradiation Radiation	Chemoradiation	Chemoradiation Radiation	Chemoradiation Radiation
9 months		Chemoradiation Radiation Surgery				
12 months/ 1 year	**All patients**	Surgery	Chemoradiation Radiation	Chemoradiation	Chemoradiation Radiation	Chemoradiation Radiation
18 months		Chemoradiation Radiation Surgery				Chemoradiation Radiation
24 months/ 2 years	**All patients**	Surgery	Chemoradiation Radiation	Chemoradiation	Chemoradiation Radiation	Chemoradiation Radiation
32 months	**All patients**	Chemoradiation Radiation Surgery				Chemoradiation Radiation
40 months	**All patients**	*	*			Chemoradiation Radiation
48 months	**All patients**	*		*		Chemoradiation Radiation
56 months	**All patients**	*	*			Chemoradiation Radiation
Annually at 5 years	**All patients**	*		*		Chemoradiation Radiation

For help with pain, nausea, and constipation: Chemotherapy patients: Contact your medical oncology nurse: [Name].
Radiation-only and radiation-after-surgery patients: Contact your radiation nurse: [Name].
Surgery-only patients: Contact your surgical team: [Number].

Post-treatment imaging: (Chemotherapy patients: medical oncology; radiation-only and radiation-after-surgery patients: radiation oncology; surgery-only patients: surgical team):
1) Single baseline imaging 12-16 weeks after therapy, option for additional.
2) Patients 50 years or older and 20 pack-years smoking should have an annual low-dose chest computed tomography for at least two years.
3) Carotid ultrasound five years after neck radiation and repeat every 5 years if negative, otherwise refer to primary care physician.

Thyroid monitoring: every 6-12 months for patients with radiation therapy.
* For some patients, extended follow-up may be advised.

Figure 2. Electronic Order Set for Concurrent Chemotherapy and Radiation Care Pathway

REFERRALS

Referrals to Physician Providers

- ☐ Consult/Referral to Head and Neck/Surgical Oncology
  STAT, Internal referral
- ☐ Consult/Referral to Radiation Oncology
  STAT, Internal referral
- ☐ Consult/Referral to Head and Neck/Medical Oncology
  STAT, Internal referral
- ☐ Consult/Referral to Encinitas/Vista Medical Oncology
  STAT, Internal referral

Referrals for Supportive Services

- ☐ Referral Oncology Survivorship Clinic Head and Neck
- ☐ Referral to Patient Navigator—Head and Neck
  STAT, Internal referral
- ☐ Consult/Referral to Speech Pathology/Therapy Within Head and Neck Surgery
  STAT, Internal referral, NOTE: Dysphagia, dysarthria, or dysphonia are the only billable diagnoses for speech-language pathology services
- ☐ Video Swallow (Aspiration Evaluation)
  STAT, Normal
- ☐ Consult/Referral to Nutrition/Oncology (Moores Use Only)
  STAT, Internal referral
- ☐ Consult/Refer to UCSD Physical Therapy
  STAT, Internal referral, NOTE: Physical therapy referral is appropriate for the following patients: Patients with trismus; patients with temporomandibular joint (TMJ) symptoms; patients with neck range of motion issues
- ☐ Consult to UC Occupational Therapy
  STAT, Internal referral, NOTE: Occupational therapy referral is appropriate for the following patients: Patients with lymphedema; patients with symptoms related to scar tissue; patients with shoulder range of motion issues; patients with radiation fibrosis
- ☐ Consult/Referral to Audiology Clinic
  STAT, Internal referral
- ☐ Central Venous Catheter Service Request
  STAT, Normal
- ☐ Consult to Angio Interventional Rad
  STAT, Internal referral, Consult to Angio Interventional Rad for G-Tube Placement
- ☐ Consult Psychiatry Moores
  STAT, Internal referral
- ☐ Referral Psychology Moores
  STAT, Internal referral

Referrals for Imaging

- ☐ CT Soft Tissue Neck with Contrast
  STAT, Normal
- ☐ CT Chest with Contrast
  STAT, Normal
- ☐ PET/CT (Non-diag CT for AC) Skull to Mid-thigh
  STAT, Normal

(Note: Each care pathway [not shown herein] has its own prepopulated order set in the EHR.)

(continued from page 37)
studies, and treatment). Physical and occupational therapy services already engaged in a similar practice.

It was important to be mindful of the number and frequency of medical visits that our patients would encounter, particularly in light of symptom burden and psychosocial and economic restraints. The addition of the patient navigator to assist with care transitions reduced the number of missed consultations. Schedulers were also required to communicate with each other for improved visit coordination. Speech-language pathology and dietitian appointments are now scheduled on the same date, in this order, so that the dietitian has information related to swallow safety prior to providing dietary recommendations. Additionally, schedulers were instructed to arrange all medical visits in close proximity to avoid a prolonged wait or requirement of multiple trips. We also give patients EHR-generated, comprehensive calendars to improve visit adherence across the care continuum.

The genesis and evolution of our care pathways have provided a wealth of insights, highlighting both the strengths and weaknesses of our performance improvement initiative. The team was composed of representatives from numerous service areas—both outpatient and inpatient settings—which ensured a collective, cohesive multidisciplinary voice in all decision making and allowed for better management across vulnerable care transitions.

We developed an education course for new head and neck cancer patients to facilitate early introduction of multidisciplinary care practices. During this monthly meeting, the patient meets several allied health professionals and receives an overview of all supportive services. We also created a comprehensive booklet for patient education. Additionally, we created survivorship surveillance plans (based on NCCN guidelines) that are provided to patients as handouts.

Finally, we arranged for a small group of allied health professionals to meet after our weekly multidisciplinary tumor board to identify individuals with incomplete care pathway referrals or high-risk individuals already on a care pathway who may require more intensive support. This weekly patient care conference is a safety net to ensure maximal care pathway execution.

Closing Thoughts

The complexity of head and neck cancer management and associated morbidity demands accelerated efforts to provide highly integrated care. Because the ideal model for prescribing multidisciplinary care services is not well defined, it provided the ideal impetus for our care pathway performance improvement initiative.

The framework afforded by a well-defined care pathway enables predictability and consistency in both care delivery and cost. This model is becoming increasingly popular among healthcare systems and accountable care organizations seeking gross reductions in costly errors and redundancies that plague the existing status quo. Though cost savings was an important consideration, our primary aim was to define and describe the ideal multidisciplinary model that was feasible for our program and to identify areas requiring improvement. Our team elected to construct treatment-specific rather than disease site-specific pathways largely due to the unique symptoms and toxicities incurred by each treatment modality.

Though care pathway models support hard-wired consistency and reproducibility, we designed the process to be a guide rather than a precise recipe. Commonly, ancillary providers may need to increase the frequency of visits due to acute changes in function. It is therefore critical that the model remain fluid, allowing for modification and customization as needed to maximize patient safety and avoid adverse events and unplanned hospitalizations.

The genesis and evolution of our care pathways have provided a wealth of insights, highlighting both the strengths and weaknesses of our performance improvement initiative. The team was composed of representatives from numerous service areas—both outpatient and inpatient settings—which ensured a collective, cohesive multidisciplinary voice in all decision making and allowed for better management across vulnerable care transitions. Additionally, care navigation and survivorship were integrated to help engage patients and reinforce the clinical benefits of multidisciplinary care. In retrospect, the care pathways should have delineated a clear framework for the delivery of psychosocial, dental, and prosthodontic services, because they are critical to patient outcomes. At the time of article submission, our institution is finalizing recruitment efforts to secure a dedicated dentist/prosthodontist; in the interim, our patient navigator provides new patients with a list of community partners.

Independent of the care pathways, we did institute administration of the Patient Health Questionnaire 9 for new patients with head and neck cancers. The Patient Health Questionnaire 9 is a validated questionnaire to detect and assess depression severity.[49] Inclusion of this instrument was driven by the understanding that depression is highly prevalent in patients with head and neck cancers and may be associated with poorer survival outcomes.[50] Based on the patient's resultant score, an algorithm triggers appropriate referrals to psychiatry or primary care based on acuity and patient preference.

Finally, our team recognizes that mechanisms to measure adherence to care pathway use should have been developed. Such data would have provided an objective appraisal of progress to

date and facilitated practice modification to optimize adherence. Thus, our future directions will include:

- A modified algorithm for earlier identification of high-risk patients requiring feeding tube placement
- Inclusion of psychosocial and dental services
- Incorporation of mechanisms to measure care pathway adherence
- Rigorous evaluation of how our care pathways impact functional, oncologic outcomes, patient experience, and value. OI

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References

1. National Cancer Institute Surveillance, Epidemiology, and End Results Program. SEER Stat Fact Sheets. 2008. Available online at: http://seer.cancer.gov/statfacts/html/all.html. Last accessed April 30, 2018.

2. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. *CA Cancer J Clin.* 2015;65(2):87-108.

3. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. *CA Cancer J Clin.* 2016;66:7-30.

4. Pulte D, Brenner H. Changes in survival in head and neck cancers in the late 20th and early 21st century: a period analysis. *Oncologist.* 2010;15:994-1001.

5. Marur S, D'Souza G, Westra WH, Forastiere AA. HPV-associated head and neck cancer: a virus-related cancer epidemic. *Lancet Oncol.* 2010;11:781-789.

6. Gillison ML, D'Souza G, Westra W, et al. Distinct risk factor profiles for human papillomavirus type 16-positive and human papillomavirus type 16-negative head and neck cancers. *J Natl Cancer Inst.* 2008;100:407-420.

7. Schwartz SM, Daling JR, Doody DR, et al. Oral cancer risk in relation to sexual history and evidence of human papillomavirus infection. *J Natl Cancer Inst.* 1998;90:1626-1636.

8. Applebaum KM, Furniss CS, Zeka A, et al. Lack of association of alcohol and tobacco with HPV16-associated head and neck cancer. *J Natl Cancer Inst.* 2007;99:1801-1810.

9. Argiris A, Li S, Ghebremichael M, et al. Prognostic significance of human papillomavirus in recurrent or metastatic head and neck cancer: an analysis of Eastern Cooperative Oncology Group trials. *Ann Oncol.* 2014;25:1410-1416.

10. Fakhry C, Westra WH, Li S, et al. Improved survival of patients with human papillomavirus-positive head and neck squamous cell carcinoma in a prospective clinical trial. *J Natl Cancer Inst.* 2008;100(4):261-269.

11. Ang KK, Harris J, Wheeler R, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. *N Engl J Med.* 2010;363:24-35.

12. Seiwert TY, Cohen EEW. State-of-the-art management of locally advanced head and neck cancer. *Br J Cancer.* 2005;92:1341-1348.

13. Logan RM. Advances in understanding of toxicities of treatment for head and neck cancer. *Oral Oncol.* 2009;45:844-848.

14. Rieger JM, Zalmanowitz JG, Wolfaardt JF. Functional outcomes after organ preservation treatment in head and neck cancer: a critical review of the literature. *Int J Oral Maxillofac Surg.* 2006;35:581-587.

15. Connor NP, Cohen SB, Kammer RE, et al. Impact of conventional radiotherapy on health-related quality of life and critical functions of the head and neck. *Int J Radiat Oncol Biol Phys.* 2006;65:1051-1062.

16. Nguyen NP, Frank C, Moltz CC, et al. Impact of dysphagia on quality of life after treatment of head-and-neck cancer. *Int J Radiat Oncol Biol Phys.* 2005;61:772-778.

17. Smith BG, Hutcheson KA, Little LG, et al. Lymphedema outcomes in patients with head and neck cancer. *Otolaryngol Head Neck Surg.* 2015;152(2):284-291.

18. Lo Nigro C, Denaro N, Merlotti A, Merlano M. Head and neck cancer: improving outcomes with a multidisciplinary approach. *Cancer Manag Res.* 2017;9:363-371.

19. David JM, Ho AS, Luu M, et al. Treatment at high-volume facilities and academic centers is independently associated with improved survival in patients with locally advanced head and neck cancer. *Cancer.* 2017;123:3933-3942.

20. Kelly SL, Jackson JE, Hickey BE, Szallasi FG, Bond CA. Multidisciplinary clinic care improves adherence to best practice in head and neck cancer. *Am J Otolaryngol.* 2013;34:57-60.

21. National Comprehensive Cancer Network. Head and neck cancers 2018;Ver 2. Available online at: nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Last accessed April 30, 2018.

22. Blazeby JM, Wilson L, Metcalfe C, Nicklin J, English R, Donovan JL. Analysis of clinical decision-making in multi-disciplinary cancer teams. *Ann Oncol.* 2006;17:457-460.

23. Vanhaecht K, Sermeus W, Peers J, et al. The impact of care pathways for exacerbation of chronic obstructive pulmonary disease: rationale and design of a cluster randomized controlled trial. *Trials.* 2010;11:111-117.

24. Wentworth DA, Atkinson RP. Implementation of an acute stroke program decreases hospitalization costs and length of stay. *Stroke.* 1996;27:1040-1043.

25. Mosher C, Cronk P, Kidd A, McCormick P, Stockton S, Sulla C. Upgrading practice with critical pathways. *Am J Nurs.* 1992;92:41-44.

26. Logemann JA, Pauloski BR, Rademaker AW, Colangelo LA. Speech and swallowing rehabilitation for head and neck cancer patients. *Oncology.* 1997;11:651-656, 659; discussion 659, 663-654.

27. Gaziano JE. Evaluation and management of oropharyngeal dysphagia in head and neck cancer. *Cancer Control.* 2002;9:400-409.

28. Gorenc M, Kozjek NR, Strojan P. Malnutrition and cachexia in patients with head and neck cancer treated with (chemo)radiotherapy. *Rep Pract Oncol Radiother.* 2015;20(4):249-258.

29. Langius JAE, Bakker S, Rietveld DHF, et al. Critical weight loss is a major prognostic indicator for disease-specific survival in patients with head and neck cancer receiving radiotherapy. *Br J Cancer.* 2013;109:1093-1099.

30. Unsal D, Mentes B, Akmansu M, Uner A, Oguz M, Pak Y. Evaluation of nutritional status in cancer patients receiving radiotherapy: a prospective study. *Am J Clin Oncol.* 2006;29(2):183-188.

31. van Bokhorst-de van der S, van Leeuwen PA, Kuik DJ, et al. The impact of nutritional status on the prognoses of patients with advanced head and neck cancer. *Cancer.* 1999;86:519-527.

32. National Comprehensive Cancer Network. Survivorship 2017; Ver 3. Available online at: nccn.org/professionals/physician_gls/pdf/survivorship.pdf. Last accessed April 30, 2018.

33. Spotanski K, Ridner SH. Head and neck lymphedema. *National Lymphedema Network Lymph Link*. 2016;29(2):3-5.

34. Su T-L, Chen A-N, Leong C-P, et al. The effect of home-based program and outpatient physical therapy in patients with head and neck cancer: a randomized, controlled trial. *Oral Oncol.* 2017;74:130-134.

35. Guru K, Manoor U, Supe S. A comprehensive review of head and neck cancer rehabilitation: physical therapy perspectives. *Indian J Palliat Care.* 2012;18(2):87-97.

36. Press NA. From cancer patient to cancer survivior lost in transition. 2018. Available online at: georgiacore.org/articleImages/articlePDF_396.pdf. Last accessed April 30, 2018.

37. Cohen EE, LaMonte SJ, Erb NL, et al. American Cancer Society head and neck cancer survivorship care guideline. *CA Cancer J Clin.* 2016;66(3):203-239.

38. Freund KM, Battaglia TA, Calhoun E, et al. National Cancer Institute Patient Navigation Research Program: methods, protocol, and measures. *Cancer.* 2008;113:3391-3399.

39. Oncology Nursing Society. Oncology Nurse Navigator Core Competencies. 2013. Available online at: bit.ly/1PifoCx. Last accessed January 20, 2016.

40. Bensink ME, Ramsey SD, Battaglia T, et al. Costs and outcomes evaluation of patient navigation after abnormal cancer screening: evidence from the Patient Navigation Research Program. *Cancer.* 2014;120:570-578.

41. Esparza A. Patient navigation and the American Cancer Society. *Semin Oncol Nurs.* 2013;29(2):91-96.

42. Hitchcock YJ, Tward JD, Szabo A, Bentz BG, Shrieve DC. Relative contributions of radiation and cisplatin-based chemotherapy to sensorineural hearing loss in head-and-neck cancer patients. *Int J Radiat Oncol Biol Phys.* 2009;73:779-788.

43. American Academy of Audiology. Position statement and clinical practice guidelines: ototoxicity monitoring. 2009. Available online at: http://audiology-web.s3.amazonaws.com/migrated/OtoMonGuidelines.pdf_539974c40999c1.58842217.pdf. Last accessed April 30, 2018.

44. Foxhall LE, Rodriguez MA. *Advances in Cancer Survivorship Management*. 1st ed. New York, NY: Springer-Verlag;2015.

45. American Speech-Language-Hearing Association. Audiologic management of individuals receiving cochleotoxic drug therapy [Guidelines]. 1994. Available online at: www.asha.org/policy. Last accessed September 10, 2018.

46. American Speech-Language-Hearing Association. Ototoxicity monitoring protocol. 2013. Available online at: http://asha.org/uploadedFiles/ASHA/Article/Ototoxicity-Monitoring-Protocol-Flowchart.pdf. Last accessed April 30, 2018.

47. Campbell KC, Durrant J. Audiologic monitoring for ototoxicity. *Otolaryngol Clin North Am.* 1993;26:903-914.

48. Murphy CT, Galloway TJ, Handorf EA, et al. Survival impact of increasing time to treatment initiation for patients with head and neck cancer in the United States. *J Clin Oncol.* 2016;34(2):169-178.

49. Rieke K, Schmid KK, Lydiatt W, Houfek J, Boilesen E, Watanabe-Galloway S. Depression and survival in head and neck cancer patients. *Oral Oncol.* 2017;65:76-82.

50. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med.* 2001;16:606-613.

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Wheels Up:

Bringing Lung Cancer Education and Screening to Rural Patients

BY DEREK RAGHAVAN, MD, PHD, FACP, FRACP, FASCO;
MELLISA WHEELER, BSW, MHA; DARCY DOEGE, RN, BSN; AND JEN TOTA MCGIVNEY, MA

Lung cancer has been the center of great challenge and great hope over the past decade. Innovations in lung cancer treatments, including targeted therapies, genetic markers, and immunotherapy, have captured national headlines. These advancements have allowed people to live longer and better with late-stage lung cancer than they ever have before. Less public attention, however, has been given to rapid advancements in lung cancer screenings, which offer the potential to diagnose lung cancer at a stage early enough to cure it. Among those paying close attention was Derek Raghavan, MD, PhD, the president of Levine Cancer Institute, Charlotte, N.C., who recognized new possibilities with each new study.

New Data, Sparks a New Idea

In 2011 lung cancer screenings became more effective. In a large trial with more than 50,000 patients at more than 30 sites, the National Lung Screening Trial compared two methods of detecting lung cancer: a low-dose helical computed tomography (CT) and a standard chest X-ray. The low-dose CT detected lung cancer at earlier stages than the standard X-ray, making lung cancer screening as effective in preventing lung cancer deaths as mammograms are at preventing breast cancer deaths. Patients who had the low-dose CT had a 15 to 20 percent lower risk of dying from lung cancer than those who had the standard chest X-ray.

In 2013 lung cancer screenings became more systematic when the U.S. Preventive Services Task Force issued new lung cancer screening recommendations: annual screenings with low-dose computed tomography (LDCT) for adults between 55 and 80 years old with a 30-pack-per-year smoking history, who have quit within the last 15 years, or who still smoke. By applying these criteria, physicians could systematically screen those who are at the highest risk of lung cancer, increasing opportunities to diagnose at earlier stages, thus creating the opportunity to cure more frequently.

With lung cancer screening now more effective, systematic, and affordable, Dr. Raghavan began to look at ways to improve patient access. Specifically, how could Levine Cancer Institute deliver these critical screenings to their patients, including those in underserved communities?

In 2015 lung cancer screenings became more affordable: Medicare began to cover these scans for eligible patients, aged 65 years and older, with a 30-pack-per-year smoking history, and who have smoked during the past 15 years or continue to smoke.

With lung cancer screening now more effective, systematic, and affordable, Dr. Raghavan began to look at ways to improve patient access. Specifically, how could Levine Cancer Institute deliver these critical screenings to their patients, including those in underserved communities? Access barriers existed. For example,

despite coverage and/or patients who could afford to pay out of pocket for this screening, some rural hospitals lacked the LDCT scanners that make these early diagnoses possible. In search of solutions, Dr. Raghavan contacted the Director of Disparities and Outreach at Levine Cancer Institute (and the author of this article), Mellisa Wheeler. Dr. Raghavan proposed that Levine Cancer Institute send a mobile LDCT lung scanning unit to rural locations, and he contacted me—Mellisa Wheeler, BSW, MHA—to help him make this vision a reality. As the Director of Disparities and Outreach at Levine Cancer Institute, I have long shared Dr. Raghavan's commitment to serving underserved populations. With a mobile unit, Levine Cancer Institute could deliver these critical screenings to underserved communities and patients who otherwise might not be able to access them.

> Because we went into this situation unencumbered by a long history of other mobile units, we could really design our mobile unit to fit what we needed. Knowing too much sometimes causes a paralysis of sorts by overthinking, but not in this case. We just forged ahead.

I shared enthusiasm for the idea. There was just one problem, we learned. A mobile LDCT lung screening unit did not actually exist. Faced with two options—the first being acceptance of the status quo—Dr. Raghavan and I chose option two: acceptance that a mobile lung cancer unit did not exist *yet* and development of an even more ambitious plan.

We needed to think differently about how we were going to reach people. In healthcare, we think, if we build it, patients will come. And that's not the way that it happens. You have to go out and find people where they already are.

A Great Need in the Carolinas

What drove Dr. Raghavan and I was a belief that with the right operational approach, lung cancer deaths could see significant declines. It's a lofty goal. Lung cancer is still the deadliest cancer. Each year, lung cancer kills more Americans than the next three common cancers combined: breast, colorectal, and prostate. Late diagnoses are partly to blame for the high death rate. Typically, when people begin to feel symptoms, the disease has already progressed to an advanced stage when no cure is possible.

A lack of insurance contributes to these late diagnoses. Nearly half of North Carolina residents who make less than 133 percent of the federal poverty level lack health insurance. People with Medicaid, as well as the "working poor" who fall below the Medicaid threshold but are still unable to afford healthcare insurance, are not likely to come into a hospital unless it's an emergency. Too many people associate hospitals with bills they're unable to pay, so they stay away as long as possible. Thus, diagnoses for lung cancer often occur in the emergency department, after the disease has become metastatic.

Smoking, of course, is another contributing factor. Smoking is more than habit in our state—it's tradition. Tobacco has grown on this land for centuries, creating the livelihood for many rural families. Twenty percent of people in the rural Carolinas still smoke. And it's not just older people smoking. Younger people—even young kids—are picking up the habit, although the situation has improved in the last 10 to 15 years. Awareness of the impact of lung cancer or the existence of a screening for lung cancer does not reach all communities equally. And until it does, lung cancer will continue to strike in the Carolinas with a disproportionate force.

A Need for Early Diagnosis and Prevention

Dr. Raghavan and I recognized that late-stage lung cancer diagnoses are both deadly and, in some cases, preventable. By stage 3, lung cancer has spread to the lymph nodes. By stage 4, the cancer has spread throughout the body and no cure is possible. Yet nearly 70 percent of Atrium Health patients are diagnosed at stage 3 or higher. Nearly half in Mecklenburg County receive a diagnosis at stage 4. Dr. Raghavan and I believed that we could change those percentages by improving early diagnosis and prevention. Recognizing a need for a free screening to increase the ability to diagnose lung cancer earlier, as well as a need for lung health education to decrease smoking rates our community, we believed that a combination of education, screening, navigation, and intervention would provide continual care for everyone by:

- Teaching the risks
- Giving accurate and early diagnoses
- Guiding people through the healthcare system
- Treating people with a high standard of care.

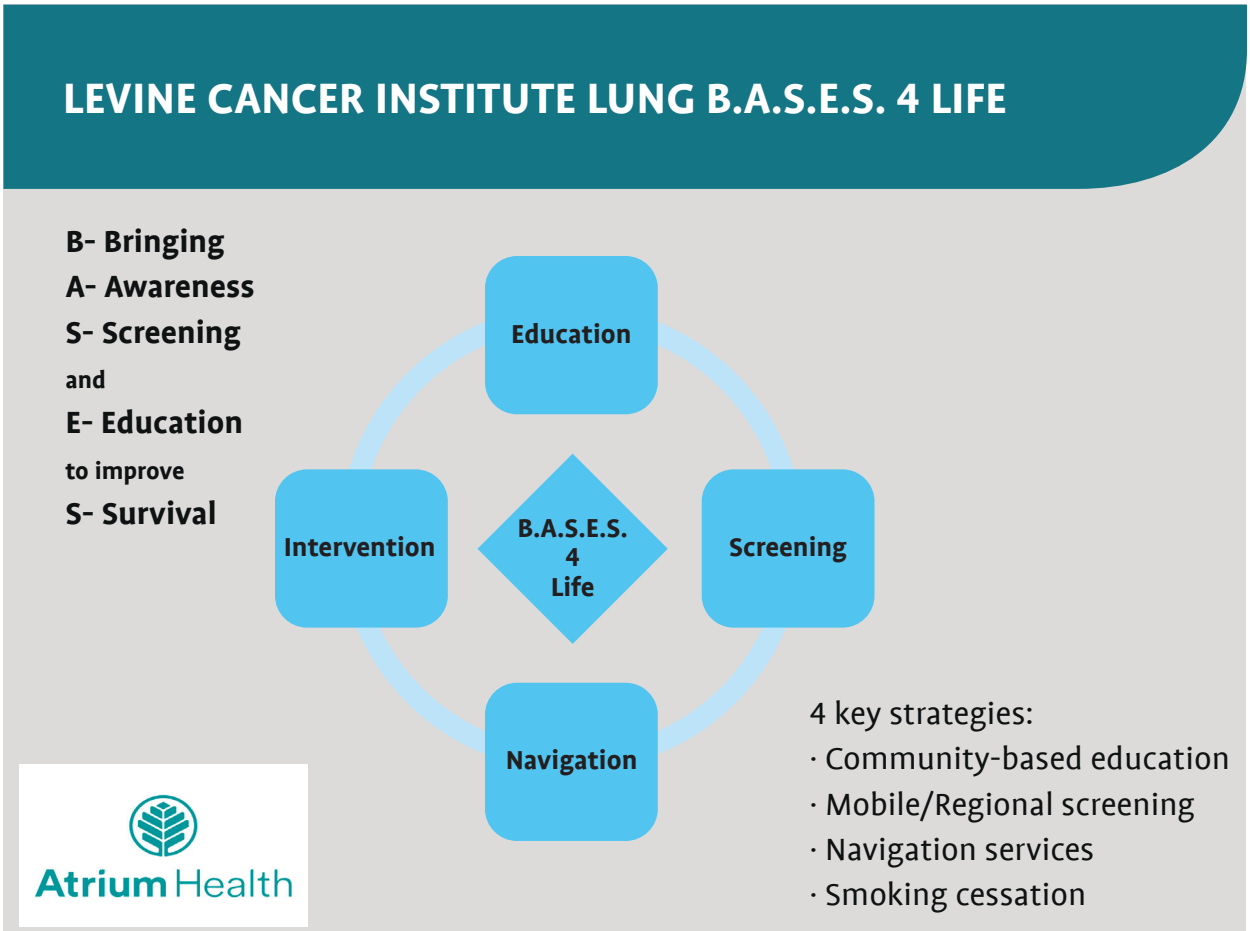
These four priorities—education, screening, navigation, and intervention—became the core components of our Lung B.A.S.E.S. (**Bringing Awareness, Screening & Education to improve Survivorship**) 4 Life program (see Figure 1, right).

Overcoming Initial Obstacles

The first two obstacles we faced were the largest. Literally. We needed a mobile LDCT machine and a bus large enough to hold the piece of equipment. Dr. Raghavan and I brought in a colleague at Levine Cancer Institute known for her innovation, collaboration, and tenacity—three skills this project needed. That colleague, Darcy Doege, BSN, RN, became the program's coordinator.

Our now three-person team faced some daunting practical challenges. For one, CT scanners are big and heavy. They can't be jostled much, presenting a problem about how to not only fit one inside a bus but also how to protect it from literal bumps in the road. And then there was an issue of the bus itself. Did one even exist that could fit a mobile CT scanner? Being first in this effort meant that there was no precedent and, hence, no ready answers.

Figure 1. Levine Cancer Institutes Lung B.A.S.E.S. 4 Life Program



The lack of precedent became one of the biggest assets to our project. Being first offered the opportunity to design a bus and a program specifically for this purpose and for this population. It spurred an innovative, flexible approach that resulted in the mobile unit not just serving our communities but becoming part of our communities. Relationships were formed, education shared, and lives saved.

I have been asked whether there were things I wish my team knew going into it if we had it all to do again, and my answer is "no." Because we went into this situation unencumbered by a long history of other mobile units, we could really design our mobile unit to fit what we needed. Knowing too much sometimes causes a paralysis of sorts by overthinking, but not in this case. We just forged ahead.

Finding Partners

To help brainstorm solutions for the mobile LDCT scanner and the bus, we looked to Samsung Neurologica, the creator of a mobile scanner for early diagnosis of strokes, and Frazer Ltd., a company that customized large vehicles. Bristol Myers Squibb Foundation supported our project with a grant, allowing Levine Cancer Institute to develop one of the first mobile lung cancer screening units in the country. This group of enthusiastic partners was committed to helping Lung B.A.S.E.S. 4 Life succeed.

Samsung Neurologica solved the challenge of creating a CT scanner that could fit on a bus by adapting the BodyTom CT, a portable LDCT scanner. The mobile unit has no restrictions for age or weight, offers wireless connectivity, and can perform axial, helical, and dynamic scanning (see photo on page 50).

Frazer designed a custom bus that was large enough not only to house the scanner but also to create a headquarters for the Lung B.A.S.E.S. 4 Life program (see photo on page 51). The company created a 35-ft. coach that is able to power the 32-slice LDCT scanner. The bus boasts low power consumption, as well as high-speed wireless Internet connection to allow for fast image transfer. The bus is comfortable for patients as well. It's completely handicapped accessible. Inside is a dressing area and features a Samsung tablet that is loaded with information, including a shared decision-making video that educates about risks and benefits of screening and smoking cessation.

A patient enters the BodyTom CT, a scanner developed by Samsung Neurologica specifically for the Lung B.A.S.E.S. 4 Life program.

Launching the Lung B.A.S.E.S. 4 Life Program

In April 2017, operations began. Levine Cancer Institute began to deliver mobile lung cancer screenings to rural communities through its Lung B.A.S.E.S. 4 Life program, focusing on those who fit the U.S. Preventive Services Task Force screening recommendations and who are either uninsured or on Medicaid.

"This type of patient would normally present to the emergency department with metastatic cancer," said Dr. Raghavan. "What we're trying to do is to find the disease when it's not metastatic. If you do the math, to provide palliative care to someone with metastatic lung cancer—particularly with some of these new expensive drugs—can cost a million dollars and eventually these patients die. If we can operate on these patients early, it costs about $40,000 to $50,000, or less, and there's a potential to cure them."

Lung cancer screening is only one part of the Lung B.A.S.E.S. 4 Life program, however. When patients come to the bus, our providers help them with whatever they need. For many patients, a screening on the bus becomes a first step to obtaining other types of care.

"People who haven't had the community wrap around them are suddenly experiencing a truly altruistic approach, which has really no secondary gain other than doing the right thing," says Dr. Raghavan.

Providers screening patients on the mobile unit have helped to diagnose heart disease in several patients and, in one instance, helped to detect a kidney cancer. For patients who discover a health issue while being screened on the mobile unit, Atrium Health will provide treatment for that issue—regardless of the patient's ability to pay. The mobile unit has become much more than a single lung cancer screening. It's become the start of relationships between people in underserved communities and the providers who can help them—and, it is hoped, the start of a journey to better health.

A lot of these interactions are about relationships, and that's one way we approach our screening programs differently. We are not just screening for disease and sending this person on their way. We're really looking at everything that patient is going through, from "Do you have a primary care physician? No? Let us find one for you" to "Do you need transportation resources? Let us get you plugged in." We even had a patient who was homeless and needed a place to shower, and we were able to help point him to a program where he could access the YMCA to take a shower every day. For more, read our patient case study on page 53.

Delivering High-Tech Operations, Human Touch

During the first year of Lung B.A.S.E.S. 4 Life, the mobile unit provided screenings in six counties in the Charlotte-Mecklenburg region: Anson, Lincoln, Mecklenburg, Stanly, Rutherford, and Burke. During the second year, the reach extended into Cabarrus, Cleveland, and Union counties. Soon, Polk and Columbus counties will be included as well. The hope is to expand the reach of the mobile unit into parts of the Carolinas that lack the technology to provide LDCT screening.

The program has created partnerships with community and indigent care clinics across the area, who invite the mobile unit into their towns and refer their patients for screenings.

The Lung B.A.S.E.S. 4 Life truck, custom designed by Frazer, Ltd.

Healthcare can be very siloed. We think, "We're this system and we do x, y, and z," and "You're that system and you do a, b, and c," and we don't communicate or network. Lung B.A.S.E.S. 4 Life has allowed us to reach out to community partners that never otherwise would have collaborated with our health system and bring them together to benefit patients. This outreach has become the vital component to the success of our mobile lung cancer screening unit. The success isn't due to the bus or the screening technology. It's due to empathy. Collaboration. The human elements. Every decision puts the patient at the center: Is this location convenient for the community? Do patients feel at ease on the bus? What other resources does this patient need to become healthy? Our mobile LDCT unit is more than technology; it's a philosophy of care. Our team operates under the mission that until every patient is seen, we can't stop doing what we do.

To do so, our team ensures that our mobile LDCT unit offers a comfortable, approachable experience. We don't make patients feel as though this is a screening that they must do. We teach the community that this is a screening that they deserve to have—that they're important, that their health is important, and that Levine Cancer Institute recognizes that importance and feels a responsibility to give them high-quality care.

"Patients come, and they love seeing the truck," Doege says. "Our team makes people feel welcome. We sit outside of the truck and make everything feel laid-back and approachable. People have been so appreciative." (See photos on pages 52 and 53.)

Our philosophy of care is represented in the repeated phone calls that Doege makes, encouraging patients to come to their upcoming appointments and providing her personal cell phone number to call if any problems arise. It's represented in the team members aboard the bus being able to talk to all types of people about all types of things, in learning to connect with community members as people before serving them as patients. It's represented in the story about Tiffany Williams Crank, a cancer program development specialist in the Lung B.A.S.E.S. 4 Life program, who noticed a long line of cars waiting for a food truck in one rural area. Crank went car window by car window, telling everyone in line about lung cancer screenings and performing interviews to check for their eligibility. That food truck line led two patients to be screened on the mobile LDCT unit.

> For patients who discover a health issue while being screened on the mobile unit, Atrium Health will provide treatment for that issue—regardless of the patient's ability to pay.

Our philosophy of care is based on the knowledge that vulnerable populations face barriers to care that often go overlooked by the medical community. In one case, a woman was going to miss her appointment for her lung screening. When the team called to check in on her, she told them that the bus ride she needed to get to her appointment would cost a dollar, and she

The Lung B.A.S.E.S. 4 Life truck provided screenings in six counties during its first year. Now, almost two years later, it will soon reach 11 counties across the Carolinas.

didn't have an extra dollar to spare. A member of Lung B.A.S.E.S. 4 Life team drove to her home to give the woman that dollar, and she made her appointment.

In another system, that patient would be labeled as non-compliant. There are so many barriers, and as healthcare providers, we must do everything in our power to break down these barriers for these underserved and at-risk patients. It's our moral obligation.

What's Next

Measuring the success of Lung B.A.S.E.S. 4 Life comes down to three main indicators:

1. How many people was our team able to cure?
2. Has our team improved the overall survival rate of our patients? In other words, has our team helped keep people alive longer and enjoying a better quality of life?
3. How many people has our team helped to stop smoking?

But our Lung B.A.S.E.S. 4 Life has its eyes set on an even loftier goal. This isn't a model that can change lung health only in the Carolinas. As our team grows and learns, we want to create a model that can be replicated across the country, connecting underserved communities with free lung cancer screenings that create a big impact—both on an individual and national level.

"My aim for this program is that it will be a game changer. That 10 years from now we're reducing the lung cancer death rate nationally," Dr. Raghavan says. "North Carolina has one of the higher death and incident rates for cancer, so if this program is successful, five years from now, the numbers of people dying from lung cancer will change disproportionately to the number of new cases."

As more people stop smoking, lung cancer rates are expected to decline. But even for current and previous smokers at risk, the team behind Lung B.A.S.E.S. 4 Life hopes that diagnoses will come earlier, cures will come more often, and the death rate for lung cancer will decrease. The goal of Lung B.A.S.E.S. 4 Life is, quite simply, for lung cancer to lose its position as the number one cancer killer. OI

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The Lung B.A.S.E.S. 4 Life truck, custom designed by Frazer, Ltd.

A Patient Case Study

The Lung B.A.S.E.S. 4 Life project began as a way to diagnose lung cancer earlier in underserved populations. But soon, it became its own philosophy of care.

Breathing problems brought Herbert Buff to the Good Samaritan Clinic in Morganton, N.C., a town about 90 miles west of Charlotte in the foothills of the Appalachian Mountains. It was spring of 2018, and Herbert thought that his asthma was flaring up. During his exam, the physician told Herbert that he was eligible for a free lung cancer screening. Even better, the physician told Herbert that he did not have to travel to a hospital for the screening—he could have it done aboard a bus outfitted as a mobile medical unit that would soon roll into to town. Herbert, who did not know that lung cancer had a screening, agreed. The screening would be free, and it wouldn't be a hassle, so he made an appointment.

The screening was no big deal, Herbert said. The people on the bus were friendly, and it was over and done quickly.

It soon became a big deal. Within 2 months of Herbert's free screening aboard the mobile medial unit, Herbert was in surgery for stage 1 lung cancer. The surgery was successful, the cancer is now gone, and Herbert reflects on how a seemingly minor decision changed his life.

"I learned that you can have lung cancer and not even know it," Herbert said. "The early screening might've saved my life. It might've given me quite a few years."

The end of Herbert's lung cancer did not mean the end of his relationship with the providers on the LDCT mobile unit. He's remained in contact with staff regarding his smoking habits. He hasn't quit smoking entirely, but he's cut down significantly, and he's working to do more, progress that he credits to the staff calling him after his surgery to check in on him.

"I'm working very, very hard on not smoking," Herbert says. "I went from a couple packs each day to just a couple cigarettes a day. One of the ladies from the bus called me the other day and said she was going to send me some more nicotine patches. Everyone from there is great. I couldn't be happier with the doctors and everything."

The Inherited Cancer Registry (ICARE) Initiative:

An Academic-Community Partnership for Patients and Providers

BY TUYA PAL, MD, FACMG; CRISTI RADFORD, MS, CGC; ANNE WEIDNER, MPH; ANN LOUISE TEZAK, MA, MPH; DEBORAH CRAGUN, PHD, MS, CGC; AND GEORGIA LOWREY WIESNER, MD, MS

Genetic testing for inherited cancer predisposition can reduce cancer associated morbidity and mortality.[1-3] Given that 5 to 15 percent of cancer may be due to inherited predisposition,[4-9] identification and management of those with inherited cancer predisposition offers the opportunity to refine cancer risks and personalize cancer prevention and treatment.[10-16] In fact, testing for inherited cancer to guide cancer treatment is becoming increasingly important to identify among cancer patients, with the recent U.S. Food and Drug Administration approvals for drug eligibility based on presence of inherited cancer predisposition due to germline DNA changes.[17-21] Moreover, the increasing use of tumor DNA testing to guide treatment has tremendous potential to identify individuals predisposed to inherited cancers if the changes are confirmed to be present in the germline.[22]

For individuals to benefit from cancer genetic risk assessment services (i.e., genetic counseling and testing), they must first be identified as at-risk, offered appropriate testing, receive accurate interpretation of their genetic test results, and access risk-appropriate cancer screening and prevention options. Yet data from us and others suggest limited knowledge about cancer genetics services among providers,[23-27] which is required to fully maximize the benefits of genetic testing for inherited cancer susceptibility. Furthermore, many physicians report a lack of confidence regarding their ability to interpret genetic test results, with a recent study suggesting that some patients receive non-guideline-adherent care recommendations, particularly among those with uncertain genetic test results.[28] This is particularly concerning given that the advances in sequencing technology and the availability of multigene panels have led to additional complexities with higher rates of uncertain

The increasing use of tumor DNA testing to guide treatment has tremendous potential to identify individuals predisposed to inherited cancers if the changes are confirmed to be present in the germline.

About Our Program

The Inherited Cancer Registry (ICARE) represents an academic-community partnership among healthcare providers, researchers, and individuals at an increased risk for inherited cancer. Through these partnerships, ICARE strives to fulfill its mission of ending the cycle of inherited cancer though research, education, and engagement. Established in the summer of 2010, ICARE has grown into one of the largest registries focused on individuals with inherited cancer predisposition, with more than 2,500 participants including 1,100 *BRCA*1/2 carriers and nearly 500 carriers of other inherited cancer genes. Provider and participant engagement has remained a key component that underlies the success of ICARE's ongoing efforts.

results and testing for genes with variable cancer risks, spectrum, penetrance, and evidence-based management guidelines.[27,29-31] Amidst the issues of quality and competency in the provision of genetic services, availability and access to cancer genetic risk assessment services through certified and credentialed genetics professionals is limited, particularly in rural areas,[32,33] certain states, and community oncology practices.[34-36] Consequently, healthcare providers with limited genetics proficiency and training order most genetic tests for inherited cancer susceptibility, which may result in guideline-discordant care.[23,24,26-28,37-39] Yet, restricting the provision of genetic services to only those with specialized training in clinical cancer genetics has raised concerns that this may reduce utilization of genetic services,[40] thus making it important to explore novel service delivery models through academic-community partnerships.

Ultimately, the expanding indications for BRCA testing, in conjunction with testing for genes with uncertain or moderate levels of cancer risk through multigene panel tests highlight the importance of data collected through registries such as ICARE.

In an effort to broadly share clinical cancer genetics expertise, the ICARE initiative was launched in 2010 along with the ICARE genetics case conference. Through engaging healthcare providers who offer genetic testing for inherited cancer predisposition, a community-academic partnership was formed. Healthcare professionals across the country were offered free educational resources, including access to the web-based genetics case conferences as well as regular newsletters outlining clinical and research updates pertaining to inherited cancers. The ICARE provider network has experienced ongoing expansion and encompasses genetic counselors, nurse practitioners, nurses, physician assistants, physicians, and other healthcare professionals (further referred to as provider partners). These provider partners refer their high-risk patients to participate in ICARE, which has resulted in its rapid growth. ICARE participants are also provided with regular clinical and research updates and opportunities, which has fostered their ongoing engagement in this initiative. From the outset, the ICARE initiative has simultaneously focused on research, education, and engagement, with details and accomplishments for each of these areas outlined in the ensuing sections.

Research

The ICARE initiative houses a research registry for individuals at high risk for inherited cancer predisposition. The registry has experienced continued growth as a result of provider partners referring their high-risk patients to the registry (Figure 1, right), thereby providing them with a research link as well as an opportunity to receive ongoing clinical and research updates. The registry consists of men and women interested in participating in studies about inherited cancer, including those with inherited cancer predisposition based on their genetic test result(s) or family history. Enrollment in the registry involves completing a consent form, through a traditional paper-based consenting method or online through the ICARE website (InheritedCancer.net). Participants are also asked to complete a baseline questionnaire and periodic follow-up questionnaires. To date, more than 2,500 high-risk patients have enrolled into ICARE, including more than 1,100 *BRCA* mutation carriers and nearly 500 participants with mutations in 40 other inherited cancer genes (Figure 2, right). Registry participants have been recruited throughout the United States and internationally (**Figure 3, page 58**), with participants representing 47 U.S. states, the District of Columbia, and 15 countries worldwide.

The data collected through the registry have enabled research efforts to broadly study the delivery of clinical cancer genetic services across diverse providers and settings. Such efforts include data suggesting that there is a higher uptake of cancer risk management options among *BRCA* carriers with longer genetic counseling sessions and when testing was performed by a genetics professional.[41] Furthermore, despite the existence of cancer genetic risk assessment standards put forth through multiple national organizations,[42-47] our data indicated higher adherence to nationally recommended genetic counseling practices and potential reduction in *BRCA* testing costs when services were delivered by genetics professionals.[39]

These registry participant-reported data (i.e., patient-level data) are consistent with provider-level data collected through surveying providers in Florida who order hereditary cancer genetic testing. Specifically, survey data was collected in 2010[24,48,49] and 2013[25] to better understand service delivery models, management practices, and educational needs across providers who order *BRCA* testing. Comparisons were made between those with certifications and/or credentials in genetics (called genetics professionals) to those without any formal training in genetics (called non-genetics professionals). Results of the 2010 provider survey showed that genetics professionals were significantly more likely to discuss the standard pre-test genetic counseling elements, accurately interpret test results, and recommend guideline-concordant management compared to providers without credentials or certifications in genetics.[24] Furthermore, survey respondents indicated both the need for and interest in ongoing educational opportunities and resources focused on clinical cancer genetics.[48] Data from the subsequent 2013

(continued on page 58)

Figure 1. ICARE Provider Partner Recruitment by Year

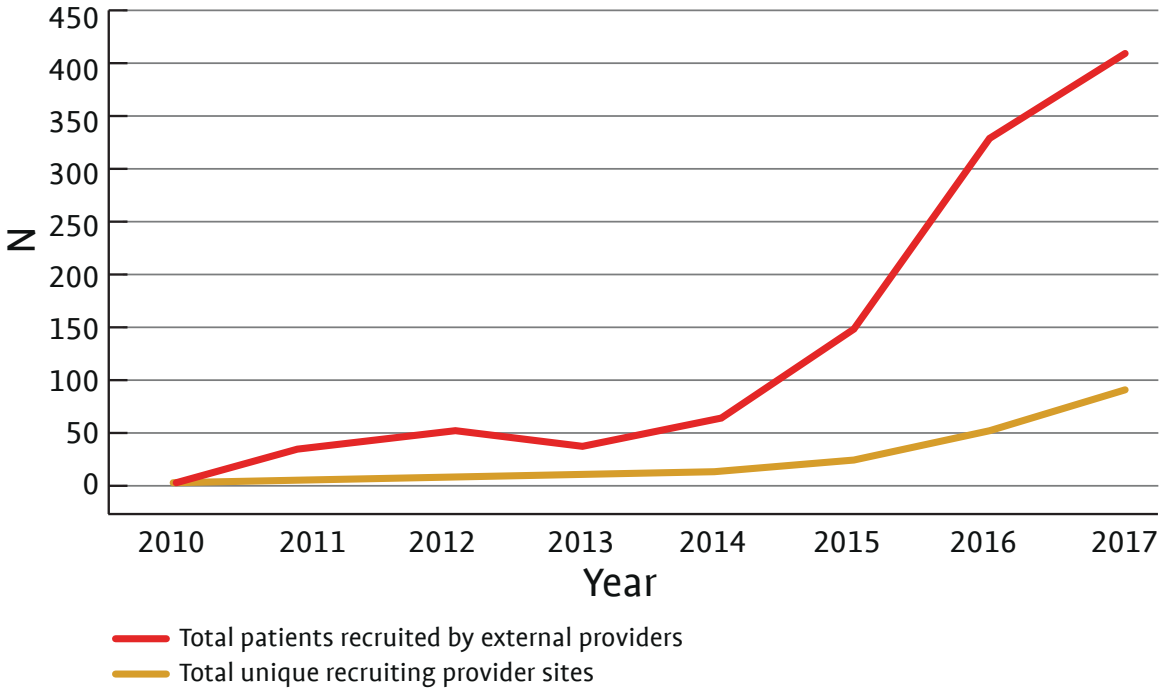
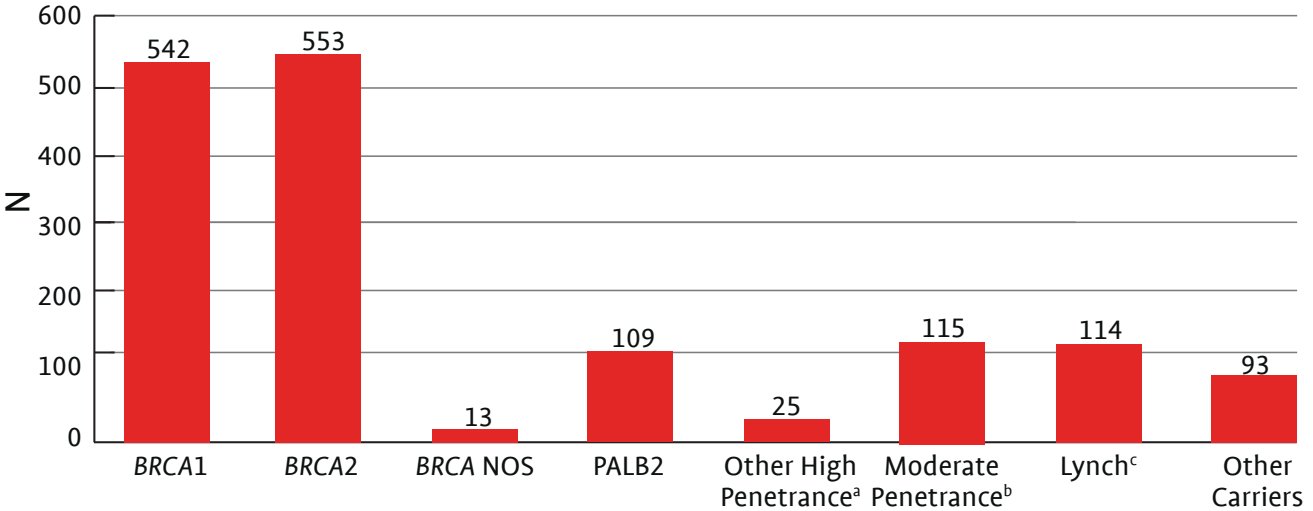
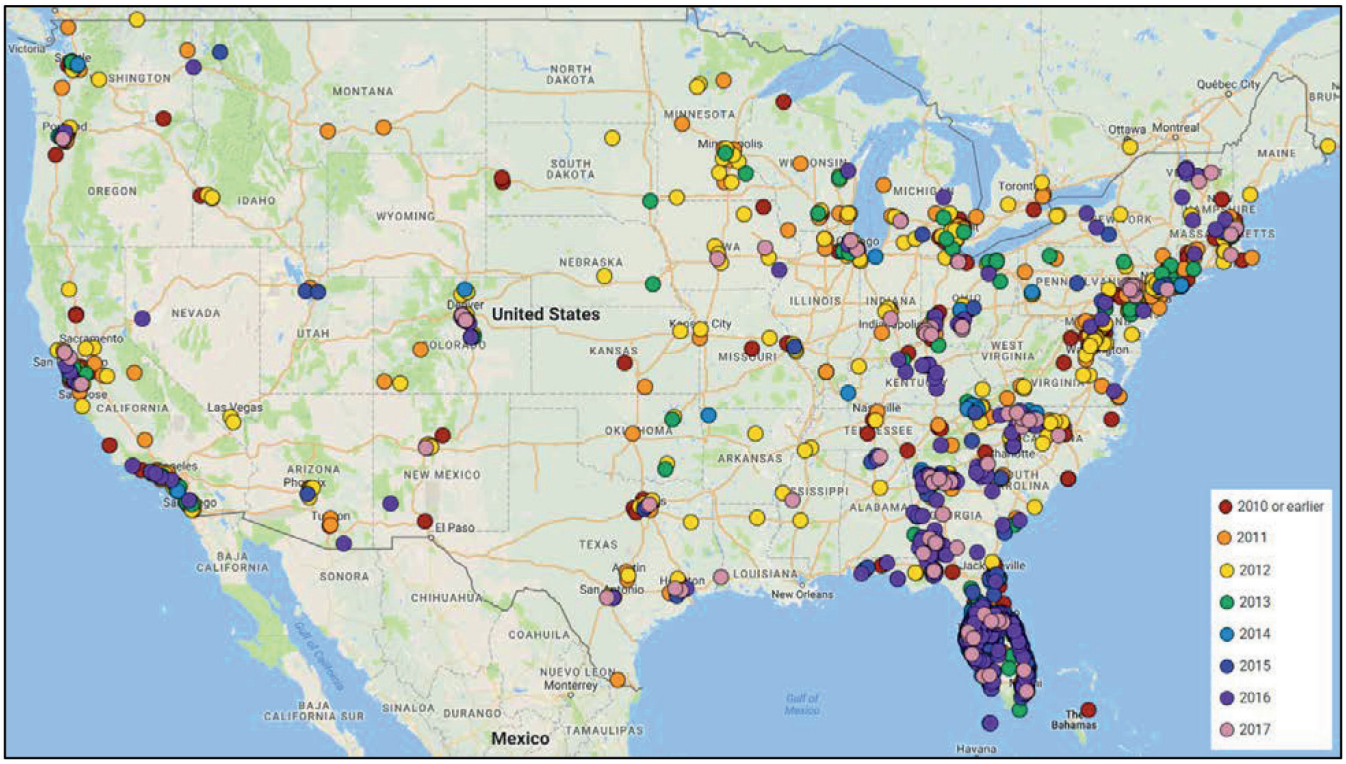


Figure 2. ICARE Carrier Count by Gene



[a] Includes *PTEN*, *TP53*, *STK11*, and *CDH1*
[b] Includes *ATM* and *CHEK2*
[c] Includes *MLH1*, *MSH2*, *MSH6*, *PMS2*, and *EPCAM*

Figure 3. Location of ICARE Registry Participants



(continued from page 56)

provider survey were consistent with the prior 2010 survey data, revealing significantly higher knowledge and guideline-adherent testing and cancer risk management recommendations among genetics professionals compared to non-genetics professionals.[25] Furthermore, genetics professionals had a greater awareness of recent changes in genetic testing and policies, particularly given that the 2013 survey was conducted after the fall of the *BRCA* patent and as multigene panel testing became more widely available. Overall, these efforts have confirmed both the benefits of and interest in the formation of academic-community partnerships where the expertise of genetics professionals may be maximally leveraged for patient benefit.

In addition to pursuing our own efforts focused on better understanding the delivery of cancer genetic risk assessment services, the research registry has enabled the contribution of data to international research efforts focused on optimizing management among *BRCA* carriers (as regularly updated on our website: inheritedcancer.net/publications). For example, findings from studies in which *BRCA* carriers from ICARE were included have shown that an oophorectomy may prevent premenopausal breast cancer in *BRCA2* but not *BRCA1* mutation carriers[50]; breastfeeding and oral contraceptive may be useful for the primary prevention of ovarian cancer among *BRCA* carriers[51]; and infertility treatment does not significantly increase the risk of ovarian cancer among *BRCA* carriers.[52]

In addition to efforts among *BRCA* carriers, it has become increasingly important to study patients who are carriers of other inherited cancer genes, including genes with moderate or uncertain levels of cancer risk and that lack evidence-based management options. These individuals have been increasingly identified with the expanded use of multigene cancer panels, which has also raised the complexity of testing and results interpretation.[53] There are currently almost 500 registry participants with mutations (i.e., pathogenic or likely pathogenic variants) in inherited cancer predisposing genes other than *BRCA1* or *BRCA2* (Figure 2), with ongoing efforts to study cancer risks and management practices among these individuals. These include focused efforts to study breast cancer outcomes among *PALB2* carriers in collaboration with colleagues from the University of Toronto (inheritedcancer.net/palb2-study), which has resulted in the recruitment of more than 100 *PALB2* carriers to ICARE. We have also

recently reported on *TP53* carriers in ICARE identified through multigene panel tests.[54] Our findings indicated that many of these individuals did not meet clinical diagnostic criteria for Li-Fraumeni syndrome, highlighting the substantial variations in clinical phenotypes among *TP53* carriers that may be taken into account when making cancer risk management recommendations.

Ultimately, the expanding indications for *BRCA* testing, in conjunction with testing for genes with uncertain or moderate levels of cancer risk through multigene panel tests highlight the importance of data collected through registries such as ICARE. Furthermore, data collected through registries such as ICARE have reinforced evidence-based care and the benefits of genetic testing and family history to help guide cancer care, primarily among high-risk individuals and families. These types of efforts are needed to generate observational and often longitudinal data to refine cancer risks and optimize management of patients at high risk for inherited cancer. They may also serve as the platform upon which interventional trials may be based.

Education

Educational efforts through the ICARE initiative have encompassed the dissemination of research findings and clinical updates to both provider partners and registry participants. Our published research results (as outlined previously) suggest limited proficiency in genetics among many testing providers[24,25] who are interested in educational opportunities,[48] reinforcing the need for our educational efforts. These ongoing efforts have been achieved through 1) regular web-based genetics case conferences for our provider partners and 2) biannual newsletters for both provider partners and registry participants through which clinical and research updates are provided and other research opportunities are highlighted.

ICARE Case Conference

The ICARE genetics case conference was initiated in June 2010 and initially hosted quarterly; however, the frequency increased to bimonthly in March 2011 and then to monthly since September 2015 to accommodate requests from provider partners. These virtually-hosted case conferences consist of clinicians who present interesting and challenging patient cases with inherited cancer predisposition, followed by a discussion and feedback about the case by a multidisciplinary group of attendees. These case conferences take place on a weekday during regular working hours and last for one hour.

Case conference attendance has continued to grow annually, as reflected in Figure 4 (page 60), with providers participating across the country and beyond. The diversity of attendees has fostered a unique forum for healthcare providers to network and communicate, as well as obtain feedback on complex cases. Many of the conferences focus on a particular inherited cancer predisposition topic, with past topics including uninformative negative test results, families with *PALB2* mutations, and the identification of germline findings through somatic testing. For some topics, a guest expert attends to provide deeper insight, such as presentation of unpublished clinical data and case commentary. A complete list of upcoming ICARE case conference dates and topics is made available and updated regularly on the ICARE website (inheritedcancer.net/case-conferences).

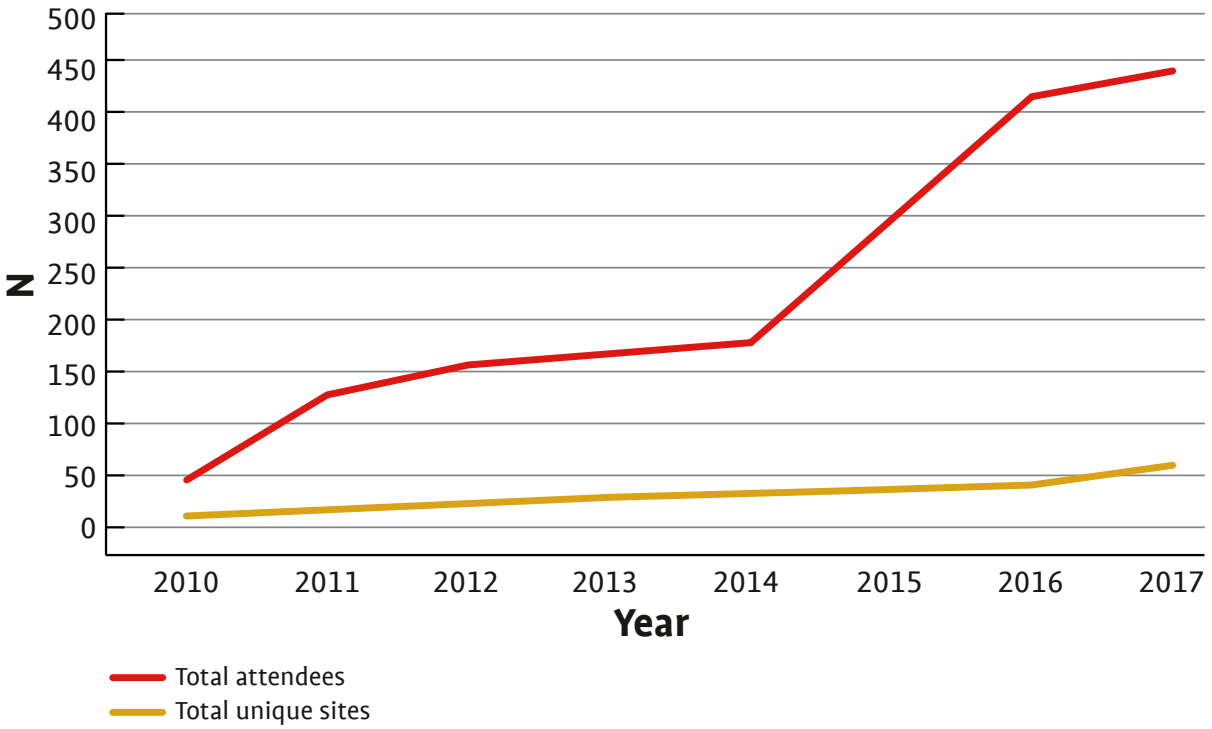
ICARE Newsletters

ICARE newsletters are developed and disseminated biannually to registry participants and provider partners and made freely available on the website (inheritedcancer.net/newsletters). The newsletters are a means by which new information is widely disseminated to these groups. Newsletters include clinical and research updates relevant to clinical cancer genetics and highlight other research and clinical trial opportunities for individuals with inherited cancer.

Many of the conferences focus on a particular inherited cancer predisposition topic, with past topics including uninformative negative test results, families with *PALB2* mutations, and the identification of germline findings through somatic testing.

These efforts have served to provide registry participants and provider partners with clinically relevant and practice-changing updates that may be pertinent to them. These include data on newer genes, clinical trials, U.S. Food and Drug Administration approvals for new drug treatments, updates to national practice guidelines, as well as new research to guide testing or management of individuals with inherited cancer predisposition. A community spotlight piece is featured in each newsletter, providing ICARE participants the opportunity to share their stories of navigating cancer prevention, screening, and treatment options for themselves and their families. Additionally, updates about the continued growth of the registry, published efforts in which our registry data were included, and information about new research and clinical updates are included in each newsletter. Overall, this effort has been met with much enthusiasm. Each ICARE newsletter dissemination effort is typically followed by an influx of questions and comments from registry participants and provider partners who email or call the study team. Moreover, with the rapid pace at which new information is generated, these newsletters have been welcomed by ICARE provider partners given that these function as a mechanism by which to deliver targeted information to this high-risk population. Over the past seven years, ICARE has developed 13 newsletters and disseminated more than 15,000 copies.

Figure 4. Genetics Case Conference Attendance by Year



Recognizing that it takes effort on the part of provider partners to refer patients, as well as the patients to enroll in the registry, we continuously strive to share information about publications and presentations made possible through their involvement.

Engagement

In conjunction with our educational efforts, we have actively promoted the engagement of provider partners and registry participants in our efforts, which we believe has been instrumental in expanding our provider network and registry growth. This engagement has been at the core of the ICARE initiative from the beginning and has served as a means to constantly reassess, reengage, and realign research and educational efforts to meet the evolving landscape of cancer genetic risk assessment services and the needs of provider partners and registry participants. For example, days and times for ICARE case conferences were guided through surveying provider partners to enhance broad attendance. Additionally, provider partners were surveyed to determine specific topics that may be of interest to them for a case conference, which guides upcoming case conference themes.

Registry participant and provider partner engagement works in synergy with both research and educational endeavors with the ICARE website serving as a centralized hub to keep registry participants and provider partners informed. Recognizing that it takes effort on the part of provider partners to refer patients, as well as the patients to enroll in the registry, we continuously strive to share information about publications and presentations made possible through their involvement. We include this type of information in our biannual newsletters in order for registry participants and provider partners to be aware that their efforts are contributing to research advances to guide care among those with inherited cancer or at risk for inherited cancer. Our website also includes up-to-date information on other educational and research-based initiatives that are in development or currently in practice within various professional and patient-based cancer communities or through ICARE. A public forum that may be viewed by provider partners and registry participants enables transparency in ICARE efforts and validates participation in ICARE is being used toward ICARE's mission.

Other avenues to enhance engagement in ICARE-focused efforts have included the implementation of a dedicated telephone line and e-mail address to provide centralized and ongoing access to the ICARE study team for both provider partners and registry participants. For provider partners, the ICARE team is available to provide guidance about general clinical, research, and recruitment questions and help connect providers to appropriate resources for their patients. Furthermore, registry participants recruited through provider partners are tracked, and this information is shared with the providers. Participants often contact the ICARE team with clinical questions (ranging from questions about other mutation-focused studies to questions about clarification on additional genetic testing or screening based on prior results), which are funneled back to the referring provider partner, underscoring the value of maintaining the link between participants and their referring healthcare providers within the ICARE database. For example, when gene panels became clinically available, the newsletter provided an update about new genetic tests being available. We received inquiries from participants about these tests and were able to refer them back to their provider for update testing. By constantly engaging with provider partners, the ICARE team has tailored its research and educational objectives to meet the needs of healthcare providers actively involved in the provision of cancer genetic risk assessment services. Similar to engagement with the providers, ICARE participants are kept informed about clinical and research updates via ICARE's website and biannual newsletter. Data from the research registry have facilitated patient participation in translational studies and multi-institutional consortia, and participants are able to track progress of these types of efforts through the website, newsletter updates, and individual inquiries to our study phone line or email.

Summary

The ICARE initiative is a novel program that provides research opportunities, education, and engagement about inherited cancers to patients and healthcare providers. It has experienced a tremendous growth trajectory for both registry participation and provider partnerships spanning across the United States and internationally since its foundation in 2010. The infrastructure and success of the ICARE initiative has resulted in the study team's ability to conduct its own hypothesis-driven research, participate in a number of grants, and contribute de-identified data to international efforts. Over the years, the development of a collaborative network of hundreds of unique healthcare providers has culminated in the recruitment of more than 2,500 participants to the research registry, who continue to be followed over time. These efforts will continue to enable ongoing information dissemination to healthcare providers, researchers, registry participants, and members of the general population, while providing an infrastructure to conduct clinical and translational research studies to achieve a mission—*to end the cycle of inherited cancer through research, education, and engagement.* OI

Get Involved

To learn more about how referring to ICARE may benefit you and your patients, please visit InheritedCancer.net or call 615-875-2444. There is no cost to participate.

Who Can Enroll in ICARE?

- Men and women
- Aged 18 or older
- Carries a gene mutation linked to an inherited cancer syndrome
- Gene status negative or unknown but personal and/or family history of cancer suggesting increased risk

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References

1. Watson M, Kash KM, Homewood J, et al. Does genetic counseling have any impact on management of breast cancer risk? *Genet Test*. 2005;9:167-174.

2. Roukos DH, Briasoulis E. Individualized preventive and therapeutic management of hereditary breast ovarian cancer syndrome. *Nat Clin Pract Oncol*. 2007;4:578-590.

3. Narod SA, Offit K. Prevention and management of hereditary breast cancer. *J Clin Oncol*. 2005;23:1656-1663.

4. Risch HA, McLaughlin JR, Cole DE, et al. Population BRCA1 and BRCA2 mutation frequencies and cancer penetrances: a kin-cohort study in Ontario, Canada. *J Natl Cancer Inst*. 2006;98:1694-1706.

5. Pal T, Permuth-Wey J, Betts JA, et al. BRCA1 and BRCA2 mutations account for a large proportion of ovarian carcinoma cases. *Cancer*. 2005;104:2807-2816.

6. John EM, Miron A, Gong G, et al. Prevalence of pathogenic BRCA1 mutation carriers in 5 U.S. racial/ethnic groups. *JAMA*. 2007;298:2869-2876.

7. Malone KE, Daling JR, Doody DR, et al. Prevalence and predictors of BRCA1 and BRCA2 mutations in a population-based study of breast cancer in white and black American women ages 35 to 64 years. *Cancer Res*. 2006;66:8297-8308.

8. Pearlman R, Frankel WL, Swanson B, et al. Prevalence and spectrum of germline cancer susceptibility gene mutations among patients with early-onset colorectal cancer. *JAMA Oncol.* 2017;3:464-471.

9. Dillon JL, Gonzalez JL, DeMars L, Bloch KJ, Tafe LJ. Universal screening for Lynch syndrome in endometrial cancers: frequency of germline mutations and identification of patients with Lynch-like syndrome. *Hum Pathol.* 2017;70:121-128.

10. Domchek SM, Friebel TM, Singer CF, et al. Association of risk-reducing surgery in BRCA1 or BRCA2 mutation carriers with cancer risk and mortality. *JAMA*. 2010; 304:967-975.

11. Finch AP, Lubinski J, Moller P, et al. Impact of oophorectomy on cancer incidence and mortality in women with a BRCA1 or BRCA2 mutation. *J Clin Oncol*. 2014;32:1547-1553.

12. Maxwell KN, Domchek SM. Cancer treatment according to BRCA1 and BRCA2 mutations. *Nat Rev Clin Oncol*. 2012;9:520-528.

13. Tinoco G, Warsch S, Gluck S, Avancha K, Montero AJ. Treating breast cancer in the 21st century: emerging biological therapies. *J Cancer.* 2013;4:117-132.

14. Robson M, Im SA, Senkus E, et al. Olaparib for metastatic breast cancer in patients with a germline BRCA mutation. *N Engl J Med*. 2017;377:523-533.

15. Le DT, Uram JN, Wang H, et al. PD-1 blockade in tumors with mismatch-repair deficiency. *N Engl J Med.* 2015;372:2509-2520.

16. Westdorp H, Kolders S, Hoogerbrugge N, de Vries IJM, Jongmans MCJ, Schreibelt G. Immunotherapy holds the key to cancer treatment and prevention in constitutional mismatch repair deficiency (CMMRD) syndrome. *Cancer Lett*. 2017;403:159-164.

17. Meehan RS, Chen AP. New treatment option for ovarian cancer: PARP inhibitors. *Gynecol Oncol Res Pract*. 2016; 3:1-8. Available online at: https://gynoncrp.biomedcentral.com/articles/10.1186/s40661-016-0024-7. Last accessed October 10, 2018.

18. Cragun D, Pal T. Identification, evaluation, and treatment of patients with hereditary cancer risk within the United States. *ISRN Oncol.* 2013;2013:260847.

19. Evans DG, Barwell J, Eccles DM, et al. The Angelina Jolie effect: how high celebrity profile can have a major impact on provision of cancer related services. *Breast Cancer Res.* 2014;16:1-6. Available online at: https://breast-cancer-research.biomedcentral.com/articles/10.1186/s13058-014-0442-6. Last accessed October 10, 2018.

20. Bradbury AR, Patrick-Miller L, Long J, et al. Development of a tiered and binned genetic counseling model for informed consent in the era of multiplex testing for cancer susceptibility. *Genet Med*. 2015;17:485-492.

21. Cragun D, Radford C, Dolinsky JS, Caldwell M, Chao E, Pal T. Panel-based testing for inherited colorectal cancer: a descriptive study of clinical testing performed by a U.S. laboratory. *Clin Genet.* 2014;86:510-520.

22. Mandelker D, Zhang L, Kemel Y, et al. Mutation detection in patients with advanced cancer by universal sequencing of cancer-related genes in tumor and normal DNA vs. guideline-based germline testing. *JAMA*. 2017;318:825-835.

23. Mai PL, Vadaparampil ST, Breen N, McNeel TS, Wideroff L, Graubard BI. Awareness of cancer susceptibility genetic testing: the 2000, 2005, and 2010 National Health Interview Surveys. *Am J Prev Med*. 2014;46:440-448.

24. Pal T, Cragun D, Lewis C, et al. A statewide survey of practitioners to assess knowledge and clinical practices regarding hereditary breast and ovarian cancer. *Genet Test Mol Biomarkers*. 2013;17:367-375.

25. Cragun D, Scherr C, Camperlengo L, Vadaparampil ST, Pal T. Evolution of hereditary breast cancer genetic services: are changes reflected in the knowledge and clinical practices of Florida providers? *Genet Test Mol Biomarkers*. 2016;20:569-578.

26. Wideroff L, Vadaparampil ST, Greene MH, Taplin S, Olson L, Freedman AN. Hereditary breast/ovarian and colorectal cancer genetics knowledge in a national sample of U.S. physicians. *J Med Genet.* 2005;42:749-755.

27. Blazer KR, Nehoray B, Solomon I, et al. Next-generation testing for cancer risk: perceptions, experiences, and needs among early adopters in community healthcare settings. *Genet Test Mol Biomarkers*. 2015;19:657-665.

28. Kurian AW, Li Y, Hamilton AS, et al. Gaps in incorporating germline genetic testing into treatment decision-making for early-stage breast cancer. *J Clin Oncol.* 2017;35:2232-2239.

29. Caswell-Jin JL, Gupta T, Hall E, et al. Racial/ethnic differences in multiple-gene sequencing results for hereditary cancer risk. *Genet Med*. 2017;20:234-239.

30. Tung N, Domchek SM, Stadler Z, et al. Counselling framework for moderate-penetrance cancer-susceptibility mutations. *Nat Rev Clin Oncol.* 2016;13:581-588.

31. Manolio TA, Murray MF. The growing role of professional societies in educating clinicians in genomics. *Genet Med*. 2014;16:571-572.

32. Bookman T. More people seek genetic testing, but there aren't enough counselors. 2016. Available online at: https://www.npr.org/sections/health-shots/2016/04/18/473066953/more-people-seek-genetic-testing-but-there-arent-enough-counselors. Last accessed October 10, 2018.

33. Occupational employment statistics: occupational employment and wages, May 2015: 29-9092 genetic counselors. Available online at: https://www.bls.gov/oes/2015/may/oes299092.htm. Last accessed March 30, 2016.

34. Acheson LS, Stange KC, Zyzanski S. Clinical genetics issues encountered by family physicians. *Genet Med.* 2005;7:501-508.

35. Vig HS, Armstrong J, Egleston BL, et al. Cancer genetic risk assessment and referral patterns in primary care. *Genet Test Mol Biomarkers*. 2009;13:735-741.

36. Radford C, Prince A, Lewis K, Pal T. Factors which impact the delivery of genetic risk assessment services focused on inherited cancer genomics: expanding the role and reach of certified genetics professionals. *Genet Couns*. 2014;23:522-530.

37. Cragun D, Bonner D, Kim J, et al. Factors associated with genetic counseling and BRCA testing in a population-based sample of young black women with breast cancer. *Breast Cancer Res Treat.* 2015;151:169-176.

38. Cragun, D, Sherr C, Camperlengo L, Vadaparampil S, Pal T. Evolution of hereditary breast cancer genetic services: are changes reflected in the knowledge and clinical practices of Fl providers. *Genet Test Mol*. 2016;20(10):569-578.

39. Cragun D, Camperlengo L, Robinson E, et al. Differences in BRCA counseling and testing practices based on ordering provider type. *Genet Med.* 2014;17:51-57.

40. Whitworth P, Beitsch P, Arnell C, et al. Impact of payer constraints on access to genetic testing. *J Oncol Pract*. 2017;13:e47-e56.

41. Pal T, Lee JH, Besharat A, et al. Modes of delivery of genetic testing services and the uptake of cancer risk management strategies in BRCA1 and BRCA2 carriers. *Clin Genet*. 2013;85:49-53.

42. ACOG committee opinion no. 527: Personalized genomic testing for disease risk. *Obstet Gynecol*. 2012;119:1318-1319.

43. Robson ME, Bradbury AR, Arun B, et al. American Society of Clinical Oncology policy statement update: genetic and genomic testing for cancer susceptibility. *J Clin Oncol*. 2015;33:3660-3667.

44. Moyer VA. Risk assessment, genetic counseling, and genetic testing for BRCA-related cancer in women: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med*. 2013;160:271-281.

45. Genetic/familial high-risk assessment: breast and ovarian. In: *NCCN Practice Guidelines*. 2017. Available online at: https://www.nccn.org/professionals/physician_gls/pdf/genetics_screening.pdf. Last accessed October 10, 2018.

46. NAPBC/CoC. *2014 Breast Center Standards Manual Through the National Accrreditation Program for Breast Centers* (NAPBC). 2015. Available online at: https://www.facs.org/~/media/files/quality%20programs/napbc/2014%20napbc%20standards%20manual.ashx. Last accessed October 10, 2018.

47. NAPBC/CoC. *Cancer Program Standards: Ensuring Patient-Centered Care*. Chicago, IL: 2016. Available online at: https://www.facs.org/quality-programs/cancer/coc/standards. Last accessed October 10, 2018.

48. Cragun D, Besharat AD, Lewis C, Vadaparampil ST, Pal T. Educational needs and preferred methods of learning among Florida practitioners who order genetic testing for hereditary breast and ovarian cancer. *J Cancer Educ*. 2013;28:690-697.

49. Vadaparampil ST, Scherr CL, Cragun D, Malo TL, Pal T. Pre-test genetic counseling services for hereditary breast and ovarian cancer delivered by non-genetics professionals in the state of Florida. *Clin Genet*. 2014;87:473-477.

50. Kotsopoulos J, Huzarski T, Gronwald J, et al. Bilateral oophorectomy and breast cancer risk in BRCA1 and BRCA2 mutation carriers. *J Natl Cancer Inst*. 2017;109:1-7.

51. Kotsopoulos J, Lubinski J, Gronwald J, et al. Factors influencing ovulation and the risk of ovarian cancer in BRCA1 and BRCA2 mutation carriers. *Int J Cancer*. 2015;137:1136-1146.

52. Gronwald J, Glass K, Rosen B, et al. Treatment of infertility does not increase the risk of ovarian cancer among women with a BRCA1 or BRCA2 mutation. *Fertil Steril*. 2016;105:781-785.

53. Cragun D, Kinney AY, Pal T. Care delivery considerations for widespread and equitable implementation of inherited cancer predisposition testing. 2017;17:57-70.

54. Pal T, Brzosowicz J, Valladares A, Wiesner GL, Laronga C. Identification and management of TP53 gene carriers detected through multigene panel testing. *South Med J*. 2017;110:643-648.

Supportive Oncodermatology

Addressing dermatologic adverse events associated with oncologic therapies

BY STEPHANIE KAO, BA, AND ADAM FRIEDMAN, MD

Supportive oncodermatology is an emerging collaborative subspecialty between oncology and dermatology that aims to address dermatologic events associated with cancer therapy. An estimated 1.685 million new cancer diagnoses were made in 2016—many of these patients will require chemotherapy and/or radiotherapy and become part of the estimated 15.5 million living cancer survivors in the United States.[1] With the rapid development and utilization of targeted therapies, a rise in both established and new cutaneous toxicities has been witnessed. For example, in 2008, 8.04 percent of 384,000 adverse events reported from Phase I and II cancer therapeutic trials were dermatologic.[2] Despite the frequency of dermatologic adverse events, efforts in supportive care in oncology have thus far been prioritized for gastrointestinal, hematopoietic, and constitutional toxicities based on data generated from epidemiological quality of life (QOL) studies.

The spectrum of dermatologic adverse events from cancer treatments has a profound impact on the physical, emotional, financial, and psychosocial well-being of patients. In a study by Gandhi et al.,[3] 379 cancer survivors were surveyed using a validated QOL tool to determine the impact of their dermatologic symptoms. Sixty-seven percent felt that their dermatologic toxicities were worse than what they had expected, 84 percent were not referred to a dermatologist, and 54 percent thought that they would have felt better had they been referred to a dermatologist.[3] With the success of targeted anti-cancer therapies leading to a growing number of cancer survivors, we are also beginning to see long-term dermatologic effects of targeted therapies, many of which are underreported and overlooked. Knowledge of dermatologic toxicities is not only important for physicians so that prophylactic and reactive interventions can be instituted but also to provide realistic expectations to patients and prepare them for the potential and expected sequelae. Therefore, there is a clear need to establish communication between oncologists and dermatologists in order to effectively assess and manage dermatologic adverse events associated with cancer therapy—the core mission of the field of supportive oncodermatology.

The spectrum of dermatologic adverse events from cancer treatments has a profound impact on the physical, emotional, financial, and psychosocial well-being of patients.

Dermatologic Adverse Event Management

Over 50 distinct dermatologic toxicities have been reported in association with more than 30 anti-cancer agents.[4] Here we will focus on the most common documented adverse events:

- Hand-foot skin reaction
- Nail changes
- Papulopustular eruptions (an acne-like rash)
- Pruritus (severe itching)
- Secondary malignancies
- New neoplasms
- Chemotherapy-induced alopecia (hair loss or spot baldness).

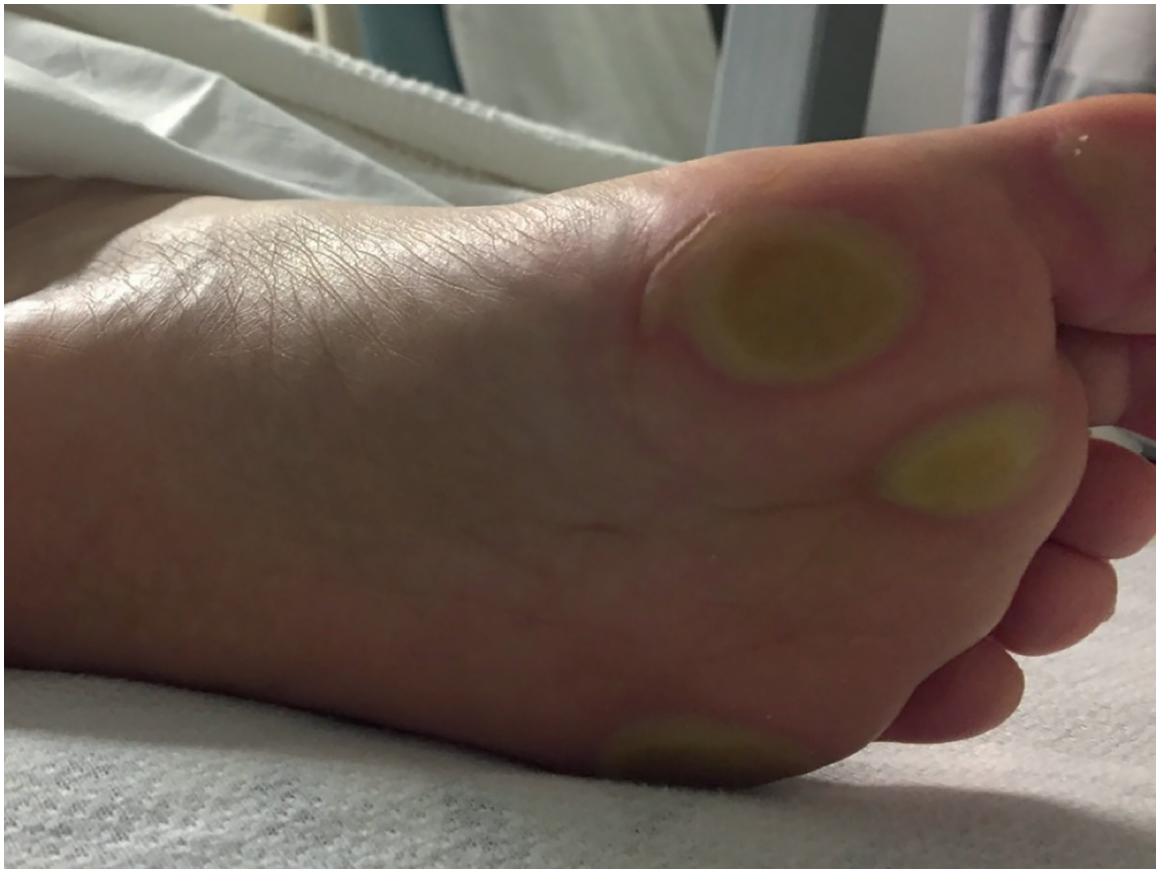
Hand-Foot Skin Reaction

Hand-foot skin reaction is one of the most common cutaneous side effects affecting 9 to 62 percent of patients on targeted cancer therapies.[5] It is associated with multikinase inhibitors such as sorafenib, sunitinib, pazopanib, and bevacizumab that specifically

target the vascular endothelial growth factor pathways implicated in angiogenesis, a process that provides the blood supply critical for development and invasive potential of many solid tumors, notably in advanced renal cell carcinoma and hepatocellular carcinoma.[6,7] Hand-foot skin reaction clinically appears within six weeks of treatment initiation and most commonly within the first two to four weeks.[8] It usually presents as tender, hyperkeratotic plaques surrounded by a peripheral halo of erythema and is sometimes accompanied by superficial blistering and callus formation (see photo, below). These lesions usually affect flexural surfaces subject to increased pressure and friction such as the digits, finger webs, palms, heels, soles, and periungual regions.[9] The thickened lesions limit weight-bearing and range of motion, two impairments that have shown to limit activities of daily living and debilitate patient QOL. Additional symptoms of hand-foot skin reaction include paresthesia (abnormal sensation such as tingling, tickling, pricking, numbness or burning of a person's skin with no apparent physical cause), burning, pain, and decreased tolerance to contact with hot objects.

Physicians must be able to distinguish between hand-foot skin reaction as described here and the hand-foot syndrome reported with conventional cytotoxic therapies such as cytarabine, doxorubicin, capecitabine, and 5-fluorouracil.[10] Hand-foot syndrome presents as diffuse symmetric paresthesias, erythema (superficial reddening of the skin), and edema that localizes to flexural surfaces with associated pain and tenderness.[8] Hand-foot skin reaction, in contrast, is characterized by the localized hyperkeratotic lesions with surrounding erythema and distinct histopathological features. The pathogenesis of hand-foot skin reaction is unknown, but a dual blockade of vascular endothelial growth factor and platelet-derived growth factor receptors may cause drug leakage from capillaries damaged by subclinical trauma and inhibit vascular repair pathways.[11] This hypothesis is supported by the increased severity of hand-foot skin reaction with increased activity and friction.

Due to its negative impact on patient QOL, hand-foot skin reaction can result in dose reduction or interruption of therapy. For example, in Phase II studies, patients treated with sorafenib



Hand-foot skin reaction, caused by a multikinase inhibitor chemotherapeutic, affecting the pressure baring areas of the plantar aspect of the foot.

for prostate cancer and lung cancer experienced dose reductions due to hand-foot skin reaction toxicity (10 percent and 31 percent, respectively).[12]

Prevention involves prophylactic removal of hyperkeratotic (thickened outer layer of skin) areas on the palms and soles. Additionally, patients should be advised to make lifestyle modifications such as wearing soft, orthotic shoes to cushion calluses and cotton socks and avoiding tight-fitting soles, running, or any exercise that creates unnecessary friction in the palms and soles.[13] Recently, researchers have attempted to identify prophylactic therapies to prevent hand-foot skin reaction. A randomized trial using a prophylactic urea-based cream in patients with hepatocellular carcinoma treated with sorafenib found that those treated had universally decreased grades of hand-foot skin reaction from 73.6 percent to 56 percent and delayed onset of hand-foot skin reaction from 34 days to 84 days.[14]

Treatment recommendations for each stage of hand-foot skin reaction are shown in **Table 1, page 68**.[8,15] These recommendations address the different stages of hand-foot skin reaction that the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events Version 4.0 (NCI-CTCAE Version 4.0)[16] uses to grade severity of this adverse event.

Nail Changes

Nail changes are a distressing and frequently underreported chemotherapy side effect that can cause considerable cosmetic concern, pain, infection, and impact to QOL. The clinical presentation of nail toxicities varies, and classification schemes from the NCI are used to grade severity (see Table 2, page 68).[15] Onycholysis (painless separation of the nail from the nail bed) occurs as acute damage to the nail bed epithelium and is common with taxanes such as docetaxel and paclitaxel, first- or second-line chemotherapy agents used against breast cancer. Taxane-induced onycholysis occurs in up to 44 percent of patients, with docetaxel as the more commonly offending agent (see photo on page 69). Additional taxane-related nail changes include[17]:

- Dark pigmentations
- Beau's lines (deep grooved lines that run from side to side on the fingernail or the toenail)
- Subungual hemorrhage
- Transverse loss of the nail plate
- Thinning and ridging of the nail plate
- Subungual hyperkeratosis (abnormal thickening of the outer layer of the skin)
- Acute painful, paronychia (an infection of the skin around a fingernail or toenail)
- Discoloration.

The integrity of peripheral nerves may be necessary for the development of nail abnormalities and two mechanisms have been proposed: taxanes may activate nociceptive C-fibers that release neuropeptides and trigger neurogenic inflammation or release prostaglandins from sympathetic postganglionic terminals.[18] Current management of taxane-induced nail changes includes hand protection with gloves and moisturizers. Although there are no approved treatments, research has explored the application of regional cooling via frozen glove and sock therapy. Scotte et al. reported that the incidence of nail changes decreased from 51 percent to 11 percent in the hands and 21 percent to 0 percent in the feet with the use of frozen gloves and socks.[19]

Other chemotherapeutic agents can also cause nail alterations. The anthracyclines, such as doxorubicin, daunorubicin, and idarubicin, cause diffuse and banded patterns of nail pigmentation that resolve with discontinuation of therapy and subsequent nail growth.[20] Multikinase inhibitors and epidermal growth factor receptor inhibitors (EGFRIs) can cause paronychia, fissures, slow nail growth, subungual splinter hemorrhages, and onycholysis.[21] The most commonly seen nail changes associated with targeted therapy include paronychia and periungual pyogenic granuloma-like lesions. These nail changes typically occur one to six months after therapy initiation and most commonly affect the big toe and thumbs. These alterations can persist for months despite treatment interruption and are often complicated by secondary infections.

Unfortunately, there are no approved treatments for targeted therapy-associated nail changes. As such, management strategies should be aimed at minimizing periungual trauma, decreasing periungual inflammation, preventing secondary infection, and eliminating excessive granulation tissue.

Unfortunately, there are no approved treatments for targeted therapy-associated nail changes. As such, management strategies should be aimed at minimizing periungual trauma, decreasing periungual inflammation, preventing secondary infection, and eliminating excessive granulation tissue.[22] Physicians can help minimize periungual trauma by instructing patients to wear comfortable shoes with wide toe boxes, wear gloves while cleaning, and trim their nails. Topical corticosteroids and anti-inflammatory dose tetracyclines are recommended to combat periungual inflammation and antimicrobial vinegar soaks are recommended to prevent secondary infection. Additionally, silver nitrate, electrocautery, and nail avulsion are recommended to eliminate excessive granulation tissue.[23,24] For fissures, many patients have found success with thick moisturizers, bleach soaks to prevent infection, liquid glues, propylene glycol, salicylic acid, and topical steroids for red itchy areas.[25]

(continued on page 69)

Table 1. Treatment Recommendations for NCI-CTCAE Version 4.0 Grades of Hand-Foot Skin Reaction

Grade	Description	Recommendation	Change in Dose
1	Minimal skin changes or dermatitis with no pain (erythema, edema, or hyperkeratosis)	• Avoid hot water • Moisturizing creams • Thick cotton gloves and/or socks • Lifestyle modifications	No change; maintain current dose of multikinase inhibitor
2	Skin changes (e.g., peeling, blisters, bleeding, edema, or hyperkeratosis) with pain, limiting instrumental activities of daily living	• Continue with grade 1 care • Urea 20%-40% cream • Tazarotene 0.1% cream • Fluorouracil 5% cream • Clobetasol propionate 0.05% ointment • 2% Lidocaine for pain • Nonsteroidal anti-inflammatory drugs, codeine, pregabalin for pain	50 percent dose reduction for 7 to 28 days
3	Severe skin changes (e.g., peeling, blisters, bleeding, edema, or hyperkeratosis) with pain, limiting self-care activities of daily living		50 percent dose reduction or interrupt treatment until symptoms improve to Grade 0 or 1

Table 2. NCI Criteria (Common Terminology Criteria for Adverse Events, Version 4.0) for Classification of Nail Changes

CTCAE Version 4 Toxicity	Grade 1	Grade 2	Grade 3
Nail discoloration	• Asymptomatic; clinical or diagnostic observations only • Intervention not indicated		
Nail loss	• Asymptomatic separation of nail bed from nail plate • Nail loss	• Symptomatic separation of nail bed from nail plate • Nail loss • Limits activities of daily living	
Nail ridging	• Asymptomatic; clinical or diagnostic observations only • Intervention not indicated		
Nail infection	• Localized • Local intervention indicated	• Oral intervention indicated (e.g., antibiotic, antifungal, antiviral)	• Intravenous antibiotic, antifungal, or antiviral intervention indicated • Radiologic or operative intervention indicated
Paronychia	• Nailfold edema or erythema • Disruption of cuticle	• Localized intervention indicated • Oral intervention indicated (e.g., antibiotic, antifungal, antiviral) • Nailfold edema or erythema with pain • Associated with discharge or nail plate separation • Limits activities of daily living	• Surgical intervention or intravenous antibiotics indicated • Limits self-care activities of daily living

Onycholysis, separation of the nail plate from the nail bed, caused by taxane-derived chemotherapeutics such as docetaxel and paclitaxel.

(continued from page 67)

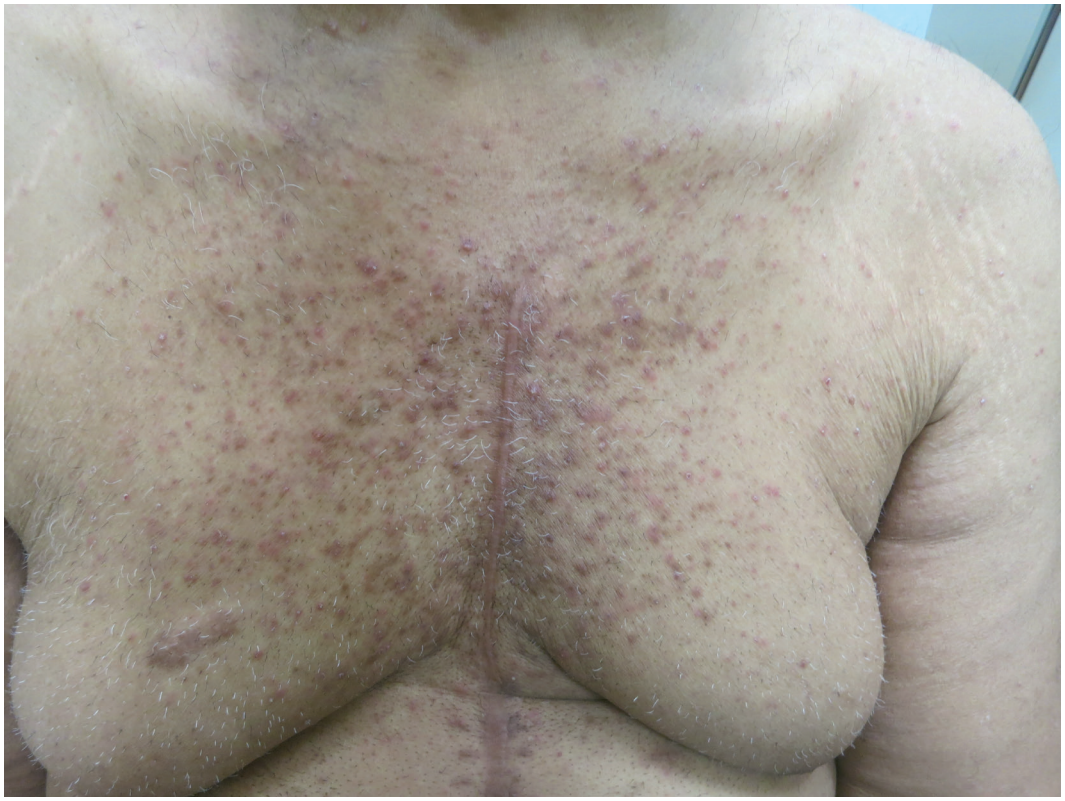
Papulopustular Eruptions

Papulopustular eruptions are the most clinically significant dermatologic toxicities that have been reported with use of virtually all targeted cancer therapies. Of note, this adverse event most commonly occurs with EGFRIs and HER2 inhibitors. EGFRIs are used in the treatment of several malignancies including colorectal, head and neck, non-small cell lung, and breast cancers.[25] Among patients treated with EGFRIs, up to 90 percent have experienced papulopustular eruptions.[26]

The rash usually develops during the first two to four weeks after initiation of therapy as pruritic and tender erythematous papules and pustules in skin with a high density of sebaceous glands such as the scalp, face, neck, chest, and back (see photo on page 70).[22] Mechanistically, the inhibition of EGFR-mediated signaling pathways affects keratinocytes by inducing growth rest and apoptosis, increasing cell attachment that inhibits cell migration and maturation, and stimulating inflammation.[27] Interestingly, there is a relationship between the development of the papulopustular rash and response to chemotherapy and consequent survival, making the eruption a potential marker of response and/or survival. Multiple studies with erlotinib and cetuximab have reported a positive correlation between therapy-induced rash and clinical outcome.[28,29] Though a herald of positive treatment outcomes, it is noteworthy for its impact on psychosocial well-being and can have negative effects on dose intensity.

Patients experiencing papulopustular rashes while on EGFRIs have higher median scores than patients on other targeted therapies in the symptom, emotion, and function subdomains (37.5, 50.0, and 16.7, respectively) of the Skindex-16 assessment, a patient-reported QOL measure used in dermatology. As such, these data suggest that the psychosocial burden associated with EGFRI sequelae is more severe than with other anticancer therapies.[30] Moreover, a survey of oncologists revealed that 32 percent of providers discontinued therapy and 76 percent modified the dose when the rash was severe.[31]

Because the eruption predictably occurs within the first month of therapy, preventive management is recommended: a prophylactic therapeutic cocktail of hydrocortisone 1 percent combined with moisturizer, sunscreen, and doxycycline 100 mg bid during the first six weeks of treatment has been found to delay the first occurrence of skin toxicity in a randomized controlled study.[32] Reactive recommendations include the use of medium- to high-potency topical corticosteroids. Several case reports and studies have demonstrated successful treatment of EGFRI-induced rash with low-dose isotretinoin without chemotherapy dose reduc-



Papulopustular eruption on the chest most frequently caused by EGFR inhibitors.

tion.[33-35] The promising use of isotretinoin is further supported by patient reports of improved quality of life.[36]

Papulopustular rashes occur less frequently and are milder with the multikinase inhibitors sorafenib and sunitinib, HER2 inhibitor pertuzumab, and dual EGFR and HER2 inhibitor lapatinib.[37,38] Recent case reports have paradoxically reported more severe papulopustular eruptions with the HER2 inhibitor trastuzumab.[38] There are no approved treatments for HER2 inhibitor- and multikinase inhibitor-induced rashes. Nevertheless, guidelines of prevention and treatment of EGFRI-induced papulopustular rash may be applicable.

Pruritus

Pruritus is a common adverse event associated with EGFRIs. Its incidence is 22.7 percent, with the highest occurrence associated with panitumumab (54.9 percent).[40] Though the pathophysiology of pruritus remains unclear, targeted agents such as EGFRIs may inhibit the EGFR of basal keratinocytes, perturbing normal epidermal physiology.[41] Additionally, EGFRI-induced pruritus may be associated with an increased number of dermal mast cells surrounding adnexal structures. These mast cells may recruit mediators that activate sensory nerves, which trigger itch.[42,43]

Current management options for pruritus require a tailored approach of stabilized hypochlorous acid 0.045 percent, pramoxine 1 to 2.5 percent, strontium 4 percent, capsaicin 0.1 to 8 percent, and menthol 1 to 2 percent for mild to moderate pruritus. Severe pruritus warrants the use of high dose anti-epileptics, antidepressants, and anti-psychotics. Additionally, a therapeutic cocktail of ketamine 5 to 10 percent, lidocaine 5 percent, and amitryptiline 5 percent in a lipoderm base that targets ion channels has found success in itch management.[44] Patients should be counseled on how to break the itch-scratch cycle by[45]:

- Keeping fingernails short
- Wearing loose clothing
- Using a humidifier
- Restricting bath and shower time and using lukewarm water
- Avoiding cleansers with a high pH or containing alcohol.

Secondary Skin Cancers

The overall five-year survival rate for children with cancer now exceeds 80 percent, resulting in more than 360,000 living survivors in the United States.[46] With this success comes a heightened recognition of the need to address treatment-related sequelae that may affect QOL. One such adverse event is anti-cancer therapy-associated secondary malignancies; these malignancies can be divided into two distinct groups: chemotherapy-related myelodysplasia and radiation-related solid second malignant neoplasm. Chemotherapy-related myelodysplasias are sequelae

that appear within three years from the primary cancer and are more commonly associated with alkylating agents or topoisomerase II inhibitors.[47] Radiation-related solid second cancers account for the largest burden of secondary malignancies (about 80 percent) and appear more than 10 years after the primary cancer. The most common radiation-associated solid tumor is non-melanoma skin cancer, particularly basal cell carcinoma, and the most well-established primary cancers that lead to radiation-related secondary malignancies include breast, lung, and thyroid cancers and brain tumors, sarcomas, and basal cell carcinomas.[48,49] These secondary cancers are leading causes of non-relapse late mortality and serious morbidity. As such, the Children's Oncology Group recommends that cancer survivors receive annual full-body skin checks after radiation treatment, especially of irradiated fields.[50] However, such frequent medical evaluation and potential biopsies can add to emotional and financial distress among cancer survivors, leading to a gap and possible omission of necessary care. One such example is seen in a study conducted by Nathan et al., where 26.6 percent of surveyed cancer survivors reported never having had a skin examination of irradiated areas.[51]

The problem, however, is not simply due to a patient lack of interest or adherence. In fact, cancer survivors are more likely to report an indicated skin examination if they receive follow-up care at a cancer center or are enrolled in a long-term follow-up program.[51] However, few survivors (12.4 percent in the Nathan et al. cohort) continue to receive regular care at a cancer center or have access to specialized survivorship clinics once they reach adulthood. Thus, assessment and management of secondary malignancies must be aimed at initiating early and maintaining regular surveillance screenings. Physicians across all specialties should pay careful attention to dermatologic changes in cancer survivors and equip patients with knowledge of their cancer therapy to encourage them to seek care focused on secondary malignancy detection.

Epidermal Neoplasms

Epidermal neoplasms are adverse skin reactions frequently associated with BRAF gene inhibitor therapy (vemurafenib, dabrafenib) used to treat metastatic melanoma. The characteristic keratinocyte proliferation found in all BRAF inhibitor-induced skin toxicities drives the formation of lesions such as squamous cell carcinoma, keratoacanthoma, and verrucous keratosis.[52] The mechanism behind BRAFI-induced squamous cell carcinoma is unknown, yet biochemical studies have shown that RAF blockade in wild-type BRAF cells, particularly in the presence of oncogenic RAS mutations caused by sun damage to keratinocytes, can lead to paradoxical mitogen-activated protein kinase (MAPK) pathway activation via dimerization of RAF isomers.[53-55] To support this theory, studies have shown a high prevalence of RAS gene mutations in cutaneous squamous cell carcinomas developing in patients treated with RAF inhibitors (see photo on page 72).[55] Therefore, the RAF inhibitor-driven activation of MAPK may unmask the oncogenic events in keratinocytes harboring preexisting RAS mutations caused by sun damage.[55]

Squamous cell carcinomas sometimes appear in an eruptive fashion within the first week after initiation of a BRAF inhibitor and generally regress after treatment is discontinued.[56] Management includes surgical excision if the squamous cell carcinoma is solitary or paucilesional and intralesional 5-fluorouracil, systemic retinoids, and electrodessication and curettage if the carcinomas are multiple or eruptive. Patients should be closely monitored with visits every four to six weeks.[52]

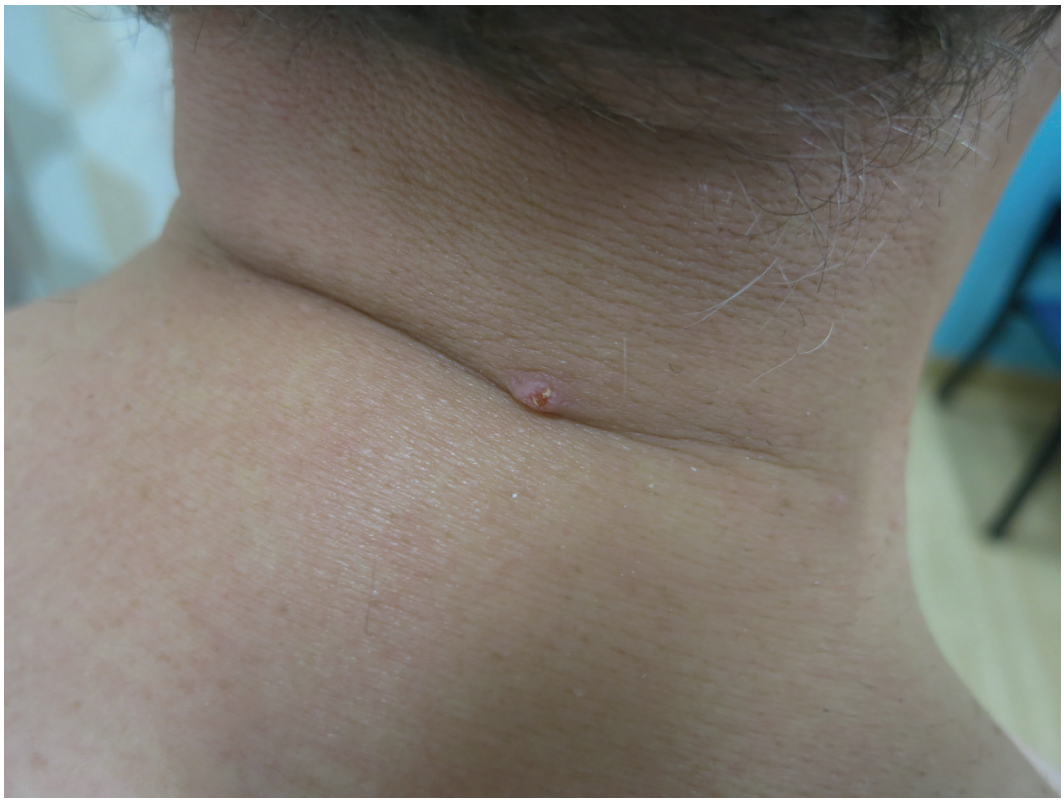
Verrucous keratoses are the most commonly encountered squamo-proliferative lesions induced by RAF inhibitors. The lesions tend to present in older patients between the first 6 to 12 weeks of RAF inhibitor therapy.[57] They appear as verruciform white keratotic papules that occur in a widespread distribution in photoexposed and non-photoexposed skin (see photo on page 73). Pathologically, the lesions exhibit minimal to mild atypia, papillomatosis, acanthosis, hypergranulosis, and hyperkeratosis of the epidermis.[56,58] Though verrucous keratoses are not malignant in nature, the variation of epidermal dysplasia and occasional presence of acantholysis suggest that these lesions may potentially be premalignancies. As such, patients with verrucous keratoses should be monitored closely for squamous cell carcinoma transformation; early cryotherapy can be very effective against these keratoses.

Chemotherapy-Induced Alopecia

Chemotherapy-induced alopecia is one of the most common and distressing adverse events in patients with cancer. Sixty-five percent of patients with cancer overall experience chemotherapy-induced alopecia, 47 percent consider it the worst side effect of chemotherapy, and 8 percent of women decline chemotherapy due to fear of hair loss.[59] Chemotherapy-induced alopecia has a large psychosocial impact on patients by serving as a visual reminder and public statement of their cancer. It additionally leads to impairments such as decreased self-esteem, decreased sensuality and sexuality, and negatively affected social interactions.[60]

There are two major types of chemotherapy-induced alopecia: telogen effluvium and anagen effluvium. Telogen effluvium rarely involves more than 50 percent of scalp hair and consequently produces a level of hair thinning.[61] This type of hair loss occurs when a larger than normal proportion of anagen hairs on the scalp moves into the telogen phase of the hair cycle.[62] This premature shift in the hair cycle terminates as hair shedding that is most profound three to four months after chemotherapy exposure. Anti-cancer agents that frequently lead to telogen effluvium include methotrexate, 5-fluorouracil, and retinoids.

In anagen effluvium, the second major type of chemotherapy-induced alopecia, chemotherapy targets the rapidly growing inner root sheath cells, which leads the hair to either fall out with mild pressure or break off when it reaches the scalp surface. The hair then remains in the resting telogen phase for the rest of the treatment duration.[62] The most notable chemotherapy-induced alopecia chemotherapeutics include cyclophosphamide, etoposide, topotecan, and paclitaxel. Though hair does regrow, the new hair often presents with a different color and/or texture.



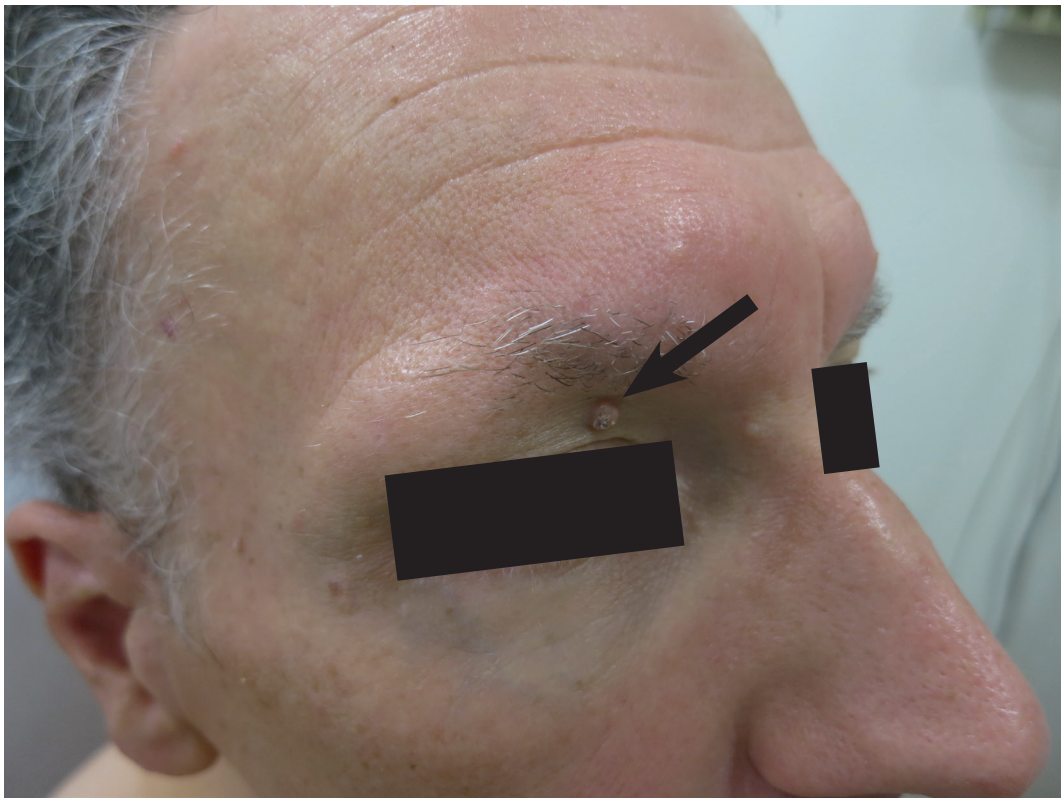
Cutaneous squamous cell carcinoma, an epidermal neoplasm, developing on the nape of the neck in a patient treated with the BRAF inhibitor, Vemurafenib.

Sadly, permanent alopecia can develop as a result of chemotherapy. In a study looking at alopecia in children following chemotherapy and hematopoietic stem cell transplantation, Choi et al. found that:[63]

- 12 percent of 159 pediatric patients surveyed developed permanent chemotherapy-induced alopecia
- 67.1 percent had reduced hair density
- 58.3 percent experienced a change in hair color (with 79.8 percent reporting lighter hair color)
- 78.8 percent had altered texture (80.8% reported thinner hair).

Risk factors for permanent chemotherapy-induced alopecia in pediatric patients following hematopoietic stem cell transplantation include younger age at time of transplant and treatment with thiotepa.[63] Among patients with breast cancer, the highest incidence of all-grade alopecia was observed in those treated with topical formulations of tamoxifen.[64]

Current management options include topical minoxidil and scalp cooling therapy for alopecia prevention. One milliliter of 2 percent minoxidil applied to the scalp twice daily during chemotherapy accelerated the time to first hair regrowth by 50 days.[65] Prophylactic application of 2 percent topical minoxidil, however, failed to prevent chemotherapy-induced alopecia during chemotherapy.[66,67] Scalp cooling is a supportive care intervention that is applied concurrently with chemotherapy. It is hypothesized to prevent chemotherapy-induced alopecia by either slowing down scalp cellular metabolism or by reducing blood perfusion and subsequently chemotherapy delivery to the scalp.[68] Overall, scalp cooling has a good safety profile with no reported cases of systemic reactions. Common adverse events include cold intolerance; heavy cap weight; mild, transient headache; anxiety; nausea; dizziness; and chest pain.[69] Patient tolerance to scalp cooling is unpredictable and highly variable. Discomfort and side effects can contribute to early discontinuation of scalp cooling, with studies finding that patient dropout occurs mostly in the first cycles and rarely later in treatment.[70,71] Concerns about and limited data on scalp metastases have hindered physicians from recommending scalp cooling to patients. In 2009 Lemieux et al. followed 640 patients with breast cancer for approximately 5.5 years; 553 received scalp cooling and 87 did not receive scalp cooling. The study did not yield a significant difference in scalp metastases between the two groups; 6 patients (1.1 percent) in the scalp cooling group of 553 and 1 patient (1.2 percent) in the control group of 87.[72,73] The publication of multiple articles that show no increased risk for scalp metastases in breast cancer patients who used scalp cooling has bolstered the recent reconsideration of scalp cooling in American oncology clinics. The U.S. Food and Drug Admin-



Verrucous keratosis appearing inferior to the medial right eyebrow, a squamo-proliferative lesion induced by a BRAF inhibitor. This type of lesion tends to present in older patients between the first 6 to 12 weeks of treatment.

istration (FDA) recently reversed its 1990 ban on the sale of scalp cooling caps in the United States originally based on a lack of safety and efficacy data. In December 2015, the FDA awarded marketing clearance of the DigniCap® Cooling System (Dignitana AB, Sweden).[74] As of June 2016, 26 cancer treatment centers in the United States are currently offering or will offer DigniCap Cooling Systems as part of their cancer services.[75] Paxman Coolers® Ltd., another scalp cooling device, which demonstrated promising data through the Scalp Cooling Alopecia Prevention Trial, recently received FDA clearance.[76]

Conclusion

As more specialized cancer treatments come down the pipeline, successful assessment and management of dermatologic side effects is critical to achieving good outcomes for patients. Dermatologic problems associated with cancer therapies have been shown to negatively affect patient QOL and even interrupt or dose-modify treatment. Promising studies in recent years have shown that dermatologic toxicities are amenable to treatment and can be mitigated with conscientious monitoring by physicians. However, more research into the management of dermatologic reactions is needed in order to support the millions of patients diagnosed with cancer every year and the growing number of cancer survivors living with dermatologic side effects. Thus, it is crucial that oncologists and dermatologists communicate clearly with each other to address these often overlooked side effects. Supportive oncodermatology can bridge this gap in care by raising awareness of dermatologic adverse events, improving QOL in cancer patients, and ultimately maximizing the efficacy of anticancer therapies.

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References

1. Miller KD, Siegel RL, Lin CC, et al. Cancer treatment and survivorship statistics, 2016. *CA Cancer J Clin.* 2016;66(4):271-289.

2. Warren JL, Yabroff KR, Meekins A, et al. Evaluation of trends in the cost of initial cancer treatment. *J Natl Cancer Inst.* 2008;100:888-897.

3. Gandhi M, Oishi K, Zubal B, Lacouture ME. Unanticipated toxicities from anticancer therapies: survivors' perspectives. *Support Care Cancer.* 2010;18:1461-1468.

4. Balagula Y, Rosen ST, Lacouture ME. The emergence of supportive oncodermatology: the study of dermatologic adverse events to cancer therapies. *J Am Acad Dermatol.* 2011;65:624-635.

5. Chu D, Lacouture ME, Fillos T, Wu S. Risk of hand-foot skin reaction with sorafenib: a systematic review and meta-analysis. *Acta Oncol.* 2008;47(2):176-186.

6. Sawhney R, Kabbinavar F. Angiogenesis and angiogenic inhibitors in renal cell carcinoma. *Curr Urol Rep*. 2008;9:26-33.

7 Fischer A, Wu S, Ho AL, Lacouture ME. The risk of hand-foot skin reaction to axitinib, a novel VEGF inhibitor: a systematic review of literature and meta-analysis. *Invest New Drugs.* 2013;31:787-797.

8. McLellan B, Kerr H. Cutaneous toxicities of the multikinase inhibitors sorafenib and sunitinib. *Dermatol Ther.* 2011;24:396-400.

9. Autier J, Escudier B, Wechsler J, Spatz A, Robert C. Prospective study of the cutaneous adverse effects of sorafenib, a novel multikinase inhibitor. *Arch Dermatol.* 2008;144:886-892.

10. Gomez P, Lacouture ME. Clinical presentation and management of hand-foot skin reaction associated with sorafenib in combination with cytotoxic chemotherapy: experience in breast cancer. *Oncologist.* 2011;16:1508-1519.

11. Jain L, Gardner ER, Figg WD, et al. Lack of association between excretion of sorafenib in sweat and hand-foot skin reaction. *Pharmacotherapy.* 2010;30:52-56.

12. Azad NS, Aragon-Ching JB, Dahut WL, et al. Hand-foot skin reaction increases with cumulative sorafenib dose and with combination anti-vascular endothelial growth factor therapy. *Clin Cancer Res.* 2009;15:1411-1416.

13. Anderson R, Jatoi A, Robert C, et al. Search for evidence-based approaches for the prevention and palliation of hand-foot skin reaction (HFSR) caused by the multikinase inhibitors (MKIs). *Oncologist.* 2009;14(3):291-302.

14. Ren Z, Zhu K, Kang H, et al. Randomized controlled trial of the prophylactic effect of urea-based cream on sorafenib-associated hand-foot skin reactions in patients with advanced hepatocellular carcinoma. *J Clin Oncol.* 2015;33:894-900.

15. Chen AP, Setser A, Anadkat MJ, et al. Grading dermatologic adverse events of cancer treatments: the Common Terminology Criteria for Adverse Events Version 4.0. *J Am Acad Dermatol.* 2012;67:1025-1039.

16. NCI-CTCAE. Version 4.0. Available online at: http://evs.nci.nih.gov/ftp1/CTCAE/About.html. Accessed August 13, 2018.

17. Winther D, Saunte DM, Knap M, et al. Nail changes due to docetaxel—a neglected side effect and nuisance for the patient. *Support Care Cancer.* 2007;15:1191-1197.

18. Wasner G, Hilpert F, Baron R, Pfisterer J. Clinical picture: nail changes secondary to docetaxel. *Lancet*. 2001;357:910.

19. Scotte F, Banu E, Medioni J, et al. Matched case-control phase 2 study to evaluate the use of a frozen sock to prevent docetaxel-induced onycholysis and cutaneous toxicity of the foot. *Cancer.* 2008;112:1625-1631.

20. Borecky DJ, Stephenson JJ, Keeling JH, Vukelja SJ. Idarubicin-induced pigmentary changes of the nails. *Cutis.* 1997;59(4):203-204.

21. Shu KY, Kindler HL, Medenica M, Lacouture M. Doxycycline for the treatment of paronychia induced by the epidermal growth factor receptor inhibitor cetuximab. *Br J Dermatol.* 2006;154:191-192.

22. Lacouture ME, Anadkat MJ, Bensadoun RJ, et al. Clinical practice guidelines for the prevention and treatment of EGFR inhibitor-associated dermatologic toxicities. *Support Care Cancer.* 2011;19:1079-1095.

23. Ghodsi SZ, Raziei M, Taheri A, et al. Comparison of cryotherapy and curettage for the treatment of pyogenic granuloma: a randomized trial. *Br J Dermatol.* 2006;154:671-675.

24. Quitkin HM, Rosenwasser MP, Strauch RJ. The efficacy of silver nitrate cauterization for pyogenic granuloma of the hand. *J Hand Surg Am.* 2003;28:435-438.

25. Johnston JB, Navaratnam S, Pitz MW, et al. Targeting the EGFR pathway for cancer therapy. *Curr Med Chem.* 2006;13:3483-3492.

26. Perez-Soler R, Delord JP, Halpern A, et al. HER1/EGFR inhibitor-associated rash: future directions for management and investigation outcomes from the HER1/EGFR inhibitor rash management forum. *Oncologist.* 2005;10(5):345-356.

27. Kari C, Chan TO, Rocha de Quadros M, Rodeck U. Targeting the epidermal growth factor receptor in cancer: apoptosis takes center stage. *Cancer Res.* 2003;63:1-5.

28. Saltz LB, Meropol NJ, Loehrer PJ, et al. Phase II trial of cetuximab in patients with refractory colorectal cancer that expresses the epidermal growth factor receptor. *J Clin Oncol.* 2004;22:1201-1208.

29. Wacker B, Nagrani T, Weinberg J, et al. Correlation between development of rash and efficacy in patients treated with the epidermal growth factor receptor tyrosine kinase inhibitor erlotinib in two large phase III studies. *Clin Cancer Res.* 2007;13:3913-3921.

30. Rosen AC, Case EC, Dusza SW, et al. Impact of dermatologic adverse events on quality of life in 283 cancer patients: a questionnaire study in a dermatology referral clinic. *Am J Clin Dermatol.* 2013;14:327-333.

31. Hassel JC, Kripp M, Al-Batran S, Hofheinz RD. Treatment of epidermal growth factor receptor antagonist-induced skin rash: results of a survey among German oncologists. *Onkologie.* 2010;33(3):94-98.

32. Lacouture ME, Mitchell EP, Piperdi B, et al. Skin toxicity evaluation protocol with panitumumab (STEPP), a phase II, open-label, randomized trial evaluating the impact of a pre-emptive skin treatment regimen on skin toxicities and quality of life in patients with metastatic colorectal cancer. *J Clin Oncol.* 2010;28:1351-1357.

33. Bidoli P, Cortinovis DL, Colombo I, et al. Isotretinoin plus clindamycin seem highly effective against severe erlotinib-induced skin rash in advanced non-small cell lung cancer. *J Thorac Oncol.* 2010;5:1662-1663.

34. Requena C, Llombart B, Sanmartin O. Acneiform eruptions induced by epidermal growth factor receptor inhibitors: treatment with oral isotretinoin. *Cutis.* 2012;90(2):77-80.

35. Vezzoli P, Marzano AV, Onida F, et al. Cetuximab-induced acneiform eruption and the response to isotretinoin. *Acta Derm Venereol.* 2008;88:84-86.

36. Gutzmer R, Werfel T, Mao R, et al. Successful treatment with oral isotretinoin of acneiform skin lesions associated with cetuximab therapy. *Br J Dermatol.* 2005;153:849-851.

37. Lacouture ME, Wu S, Robert C, et al. Evolving strategies for the management of hand-foot skin reaction associated with the multitargeted kinase inhibitors sorafenib and sunitinib. *Oncologist.* 2008;13:1001-1011.

38. Drucker AM, Wu S, Dang CT, Lacouture ME. Risk of rash with the anti-HER2 dimerization antibody pertuzumab: a meta-analysis. *Breast Cancer Res Treat.* 2012;135:347-354.

39. Sheu J, Hawryluk EB, Litsas G, et al. Papulopustular acneiform eruptions resulting from trastuzumab, a HER2 inhibitor. *Clin Breast Cancer.* 2015;15:e77-e81.

40. Ensslin CJ, Rosen AC, Wu S, Lacouture ME. Pruritus in patients treated with targeted cancer therapies: systematic review and meta-analysis. *J Am Acad Dermatol.* 2013;69:708-720.

41. Peuvrel L, Bachmeyer C, Reguiai Z, et al. Semiology of skin toxicity associated with epidermal growth factor receptor (EGFR) inhibitors. *Support Care Cancer.* 2012;20:909-921.

42. Inami Y, Andoh T, Sasaki A, Kuraishi Y. Topical surfactant-induced pruritus: involvement of histamine released from epidermal keratinocytes. *J Pharmacol Exp Ther.* 2013;344:459-466.

43. Gerber PA, Buhren BA, Cevikbas F, et al. Preliminary evidence for a role of mast cells in epidermal growth factor receptor inhibitor-induced pruritus. *J Am Acad Dermatol.* 2010;63:163-165.

44. Lee HG, Grossman SK, Valdes-Rodriguez R, et al. Topical ketamine-amitriptylinelidocaine for chronic pruritus: A retrospective study assessing efficacy and tolerability. *J Am Acad Dermatol.* 2017;76:760-761.

45. Yosipovitch G. Chronic pruritus: a paraneoplastic sign. *Dermatol Ther.* 2010;23:590-596.

46. Mariotto AB, Rowland JH, Yabroff KR, et al. Long-term survivors of childhood cancers in the United States. *Cancer Epidemiol Biomarkers Prev.* 2009;18:1033-1040.

47. Bhatia S, Sklar C. Second cancers in survivors of childhood cancer. *Nat Rev Cancer.* 2002;2(2):124-132.

48. Oeffinger KC, Bhatia S. Second primary cancers in survivors of childhood cancer. *Lancet.* 2009;374:1484-1485.

49. Oeffinger KC, Baxi SS, Novetsky Friedman D, Moskowitz CS. Solid tumor second primary neoplasms: who is at risk, what can we do? *Semin Oncol.* 2013;40:676-689.

50. Children's Oncology Group. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers, version 4.0. Available online at: http://survivorshipguidelines.org. Last accessed August 13, 2018.

51. Nathan PC, Ness KK, Mahoney MC, et al. Screening and surveillance for second malignant neoplasms in adult survivors of childhood cancer: a report from the childhood cancer survivor study. *Ann Intern Med.* 2010;153:442-451.

52. Macdonald JB, Macdonald B, Golitz LE, LoRusso P, Sekulic A. Cutaneous adverse effects of targeted therapies: part II: inhibitors of intracellular molecular signaling pathways. *J Am Acad Dermatol.* 2015;72:221-236; quiz 237-238.

53. Poulikakos PI, Persaud Y, Janakiraman M, et al. RAF inhibitor resistance is mediated by dimerization of aberrantly spliced BRAF(V600E). *Nature.* 2011;480:387-390.

54. Sanchez-Laorden B, Viros A, Girotti MR, et al. BRAF inhibitors induce metastasis in RAS mutant or inhibitor-resistant melanoma cells by reactivating MEK and ERK signaling. *Sci Signal.* 2014;7(318):ra30.

55. Su F, Viros A, Milagre C, et al. RAS mutations in cutaneous squamous-cell carcinomas in patients treated with BRAF inhibitors. *N Engl J Med.* 2012;366(3):207-215.

56. Chu EY, Wanat KA, Miller CJ, et al. Diverse cutaneous side effects associated with BRAF inhibitor therapy: a clinicopathologic study. *J Am Acad Dermatol.* 2012;67:1265-1272.

57. Anforth RM, Blumetti TC, Kefford RF, et al. Cutaneous manifestations of dabrafenib (GSK2118436): a selective inhibitor of mutant BRAF in patients with metastatic melanoma. *Br J Dermatol.* 2012;167:1153-1160.

58. Harvey NT, Millward M, Wood BA. Squamoproliferative lesions arising in the setting of BRAF inhibition. *Am J Dermatopathol.* 2012;34:822-826.

59. Kanti V, Nuwayhid R, Lindner J, et al. Analysis of quantitative changes in hair growth during treatment with chemotherapy or tamoxifen in patients with breast cancer: a cohort study. *Br J Dermatol.* 2014;170:643-650.

60. Cho J, Choi EK, Kim IR, et al. Development and validation of Chemotherapy-Induced Alopecia Distress Scale (CADS) for breast cancer patients. *Ann Oncol.* 2014;25:346-351.

61. Olsen EA. Chemotherapy-induced alopecia: overview and methodology for characterizing hair changes and regrowth. In: Olver I, ed. *The MASCC Textbook of Cancer Supportive Care and Survivorship*. Boston, MA: Springer; 2010:381-386.

62. Yeager CE, Olsen EA. Treatment of chemotherapy-induced alopecia. *Dermatol Ther.* 2011;24:432-442.

63. Choi M, Kim MS, Park SY, et al. Clinical characteristics of chemotherapy-induced alopecia in childhood. *J Am Acad Dermatol.* 2014;70:499-505.

64. Saggar V, Wu S, Dickler MN, Lacouture ME. Alopecia with endocrine therapies in patients with cancer. *Oncologist.* 2013;18:1126-1134.

65. Duvic M, Lemak NA, Valero V, et al. A randomized trial of minoxidil in chemotherapy-induced alopecia. *J Am Acad Dermatol.* 1996;35:74-78.

66. Granai CO, Frederickson H, Gajewski W, et al. The use of minoxidil to attempt to prevent alopecia during chemotherapy for gynecologic malignancies. *Eur J Gynaecol Oncol.* 1991;12(2):129-132.

67. Rodriguez R, Machiavelli M, Leone B, et al. Minoxidil (Mx) as a prophylaxis of doxorubicin-induced alopecia. *Ann Oncol.* 1994;5:769-770.

68. Trüeb RM. Chemotherapy-induced alopecia. *Semin Cutan Med Surg.* 2009;28:11-14.

69. Macduff C, Mackenzie T, Hutcheon A, et al. The effectiveness of scalp cooling in preventing alopecia for patients receiving epirubicin and docetaxel. *Eur J Cancer Care (Engl).* 2003;12(2):154-161.

70. Shaw J, Baylock B, O'Reilly A, et al. Scalp cooling: a qualitative study to assess the perceptions and experiences of Australian patients with breast cancer. *Support Care Cancer.* 2016;24:3813-3820.

71. Peck HJ, Mitchell H, Stewart AL. Evaluating the efficacy of scalp cooling using the Penguin Cold Cap system to reduce alopecia in patients undergoing chemotherapy for breast cancer. *Eur J Oncol Nurs.* 2000;4(4):246-248.

72. Lemieux J, Amireault C, Provencher L, Maunsell E. Incidence of scalp metastases in breast cancer: a retrospective cohort study in women who were offered scalp cooling. *Breast Cancer Res Treat.* 2009;118:547-552.

73. Lemieux J, Provencher L, Perron L, et al. No effect of scalp cooling on survival among women with breast cancer. *Breast Cancer Res Treat.* 2015;149:263-268.

74. Food and Drug Administration, HHS. Medical devices; general and plastic surgery devices; classification of the scalp cooling system to reduce the likelihood of chemotherapy-induced alopecia. Final order. *Fed Regist.* 2016;81:7452-7454.

75. Shah VV, Wikramanayake TC, DelCanto GM, et al. Scalp hypothermia as a preventative measure for chemotherapy-induced alopecia: a review of controlled clinical trials. *J Eur Acad Dermatol Venereol.* 2018;32:720-734.

76. Nangia J, Wang T, Osborne C, et al. Effect of a scalp cooling device on alopecia in women undergoing chemotherapy for breast cancer: the SCALP randomized clinical trial. *JAMA.* 2017;317:596-605.

Best Practices for Implementing Cancer Immunotherapy in the Community

The Association of Community Cancer Centers (ACCC) recently hosted live continuing medical education (CME)-certified learning workshops at two community cancer programs to review current barriers to immunotherapy implementation in the community setting. During the workshops, an expert faculty panel engaged participants in discussion on the challenges that they may face as they integrate immunotherapy into their clinical practice, as well as practical solutions and strategies they can apply to overcome these barriers. This article summarizes the guidance and information provided by the faculty on the various issues raised during the workshop discussions.

Decision-Making in Therapy Selection

It is not always clear which checkpoint inhibitor, or combination regimen, provides better efficacy than others. In order to establish clarity as a foundation for therapy selection, it is critical for clinicians to review the available clinical data and, where available, comparator data, for the indication of interest. Clinical practice guidelines from the National Comprehensive Cancer Network (NCCN) provide evidence-based, tumor-specific recommendations and guidance for decision-making, and biomarkers for response also provide a valuable tool to guide therapy across malignancies (see Figure 1, right).

Response and Toxicity Monitoring

Monitoring response to therapy and managing immune-related adverse events (irAEs) pose additional challenges in using checkpoint inhibitors. Although most patients show response to treatment at approximately 6 to 10 weeks after therapy initiation, responses can be nuanced. For instance, pseudoprogression can occur (e.g., in about 10 percent of patients with melanoma), in which there is a transient worsening of disease prior to disease stabilization or regression. Clinicians should be familiar with response evaluation criteria monitoring parameters to measure treatment response.[1]

Early recognition of irAEs is essential for effective management; therefore, clinicians need to have a high index of suspicion for irAEs. The type and broad distribution of irAEs differ considerably from toxicities associated with chemotherapy, and immune-related side effects can also occur or recur months after discontinuation of therapy. Routine baseline monitoring prior to initiating therapy is paramount, and should, at minimum, include tests for renal, liver, and thyroid function, repeated at 4- to 6-week intervals. Immune-related adverse event management is based on the grade of severity. The most commonly encountered grade 1-2 irAEs are skin- and gastrointestinal-related, with differences noted across checkpoint inhibitors (e.g., colitis and diarrhea are more commonly associated with CTLA-4 agents). Although relatively uncommon, endocrine toxicities such as hypophysitis, hyper- or hypothyroidism, can be challenging to identify; however, they contribute to greater morbidity. Combination therapies increase the likelihood of patients experiencing irAEs. Fortunately,

most irAEs are manageable when recognized early and addressed immediately, and evidence-based guidelines provide recommendations for monitoring and managing immune-related toxicities.[2]

Enhancing Patient Care Through Multidisciplinary Team Communication

Effective irAE management starts with timely and current education for patients and their caregivers at treatment initiation and throughout treatment into survivorship. Such education should include:

- Information about mechanisms of action
- How checkpoint inhibitors differ from chemotherapy and other cancer therapies
- How to recognize irAEs during therapy as well as when treatment has ended
- The importance of ongoing communication with members of the oncology multidisciplinary team.

In addition, all clinicians involved in the care of patients treated with checkpoint inhibitors, such as providers in radiology, radiation oncology, and emergency medicine need ongoing education on these agents including mechanisms of action, how to recognize irAEs, how immunotherapy differs from chemotherapy, how to contact the treating oncology team, and more. Because irAEs involve many organ systems, specialists outside of the field of oncology need to become members of the multidisciplinary team to provide assessment, share their expertise about which laboratory panels to order in the event of emergent irAEs, and to support system-based irAE management. Establishing a list of "go-to" specialists and organizing multidisciplinary case-based irAE discussions before treatment initiation (e.g., via tumor boards and grand rounds) offer channels for cross-specialty communication, education, and a foundation for multidisciplinary collaboration. Figure 2, page 78, summarizes several tools that support multidisciplinary communication and education.

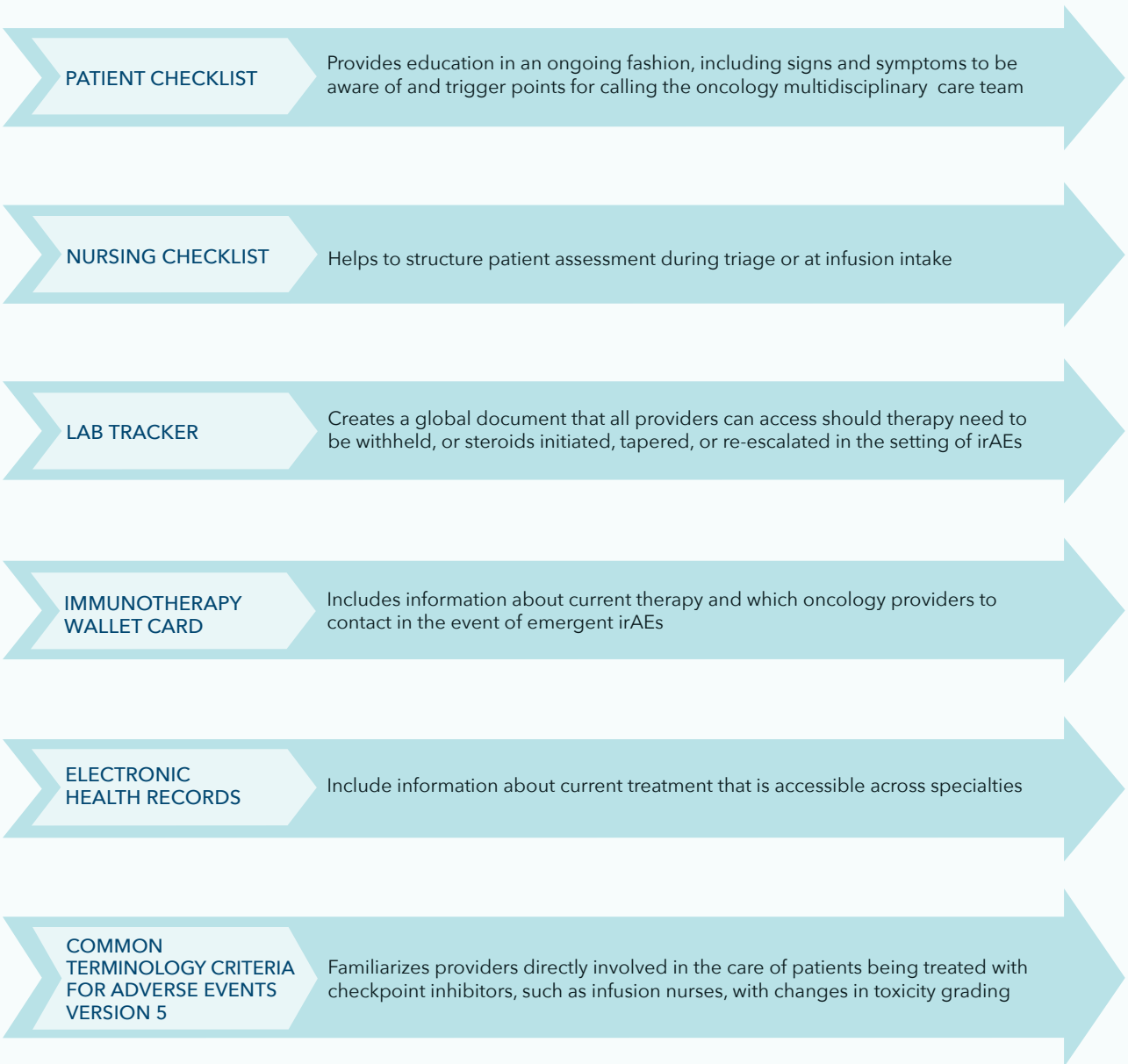
Optimizing Immunotherapy Reimbursement

Precertification for immunotherapy is resource and time intensive and many challenges persist. For instance, while payer policies lag behind new indications and medication approvals, payer

Figure 1. Biomarkers for Immunotherapy Response

PD-L1	MSI	TMB
Programmed death ligand-1 (PD-L1) expression correlates with response to checkpoint inhibitor therapy and is conducted via immunohistochemistry. Several studies are ongoing to answer questions about the role of biomarkers in therapy selection.	DNA mismatch repair system (MMR) failure causes microsatellite instability (MSI). MSI occurs most commonly in colorectal or endometrial cancer but can occur in every malignancy. MSI-high as measured by fragment analysis correlates to an increased neoantigen burden, which may respond more favorably to checkpoint inhibitor therapy.	Tumor mutational burden (TMB) measures the total number of somatic mutations identified per megabase of the genome coding area. Tumors with high TMB are likely to harbor neoantigens and might respond more favorably to immune checkpoint inhibitors.

Figure 2. Tools for Multidisciplinary Team Communication and Education



authorization requirements are continually expanding. Revenue work queues (e.g., JW modifiers) can streamline prior authorization practices, and trigger collation of the data necessary to support precertification as soon as immunotherapy is prescribed, including:

- Documentation of disease state
- Payer policies and practices
- Prior therapies received by patients
- Biomarker findings if required
- Concurrent indications that might preclude authorization.

Pharmacy staff should be armed with the most recent clinical data, published guidelines, insurance provider clinical policies, compendia, and national/local coverage determinations (NCD/LCD) in order to support precertification claims. It can also be useful to include guideline recommendations and FDA approvals as part

of a prior authorization claim, as well as any information on changes in therapy dosing and administration. Patients should be aware of their financial obligations before therapy initiation, and pharmacy staff can identify patients in need of assistance and access resources such as assistance programs for uninsured and/or underinsured patients. In order to optimize waste management, it is important to clarify if payers will allow for wastage billing.

Unfortunately, denials are common, and payers have strict guidelines and timelines about the appeals process. A denial management process that works with the revenue cycle can support routing claims in a timely fashion and ensure staff have access to the resources they will need to support an appeal (e.g., guidelines, NCD/LCD, clinical policies). Finally, it is important for oncology pharmacy staff to monitor trends with payers and hold them accountable if immunotherapy denials become an established pattern.

Conclusion

As part of the learning workshops process, the expert faculty collaborated with the participants at each cancer center to develop action plans for incorporating short-term and long-term changes in their practice aimed at improving the quality of patient care. The action plans drafted at these workshops covered creation of educational resources for the clinical staff and patients and information cards that can be used for patients going to the emergency room or for referring providers. Several changes are currently underway at the participating cancer centers including addition of immunotherapy information to an existing Oncologic Emergency Card that patients can present at the emergency room and the development of education materials for nurses and other healthcare providers on how to recognize and manage irAEs. Immediate changes like these demonstrate the effectiveness of onsite CME designed to identify solutions to local needs. ■

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References

1. Seymour L, Bogaerts J, Perrone A, et al. iRECIST: guidelines for response criteria for use in trials testing immunotherapeutics. *Lancet Oncol*. 2017;18(3):e143-e152.

2. Brahmer JR, Lacchetti C, Schneider BJ, et al. Management of Immune-Related Adverse Events in Patients Treated with Immune Checkpoint Inhibitor Therapy: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol.* 2018;36(17):1714-1768.

An article from the ACCC Immuno-Oncology Institute. Learn more at accc-cancer.org/immunotherapy.

This activity is supported by an educational grant from the Bristol-Myers Squibb Company.

ACCC Welcomes its Newest Members

Adventist Health Simi Valley
Simi Valley, Calif.
Delegate Rep: Teresa Lyon
Website: adventisthealth.org/Simi-Valley

University Health Care System
Augusta, Ga.
Delegate Rep: Sloan Maes, MSN, BSN
Website: universityhealth.org

Maroone Cancer Center
Cleveland Clinic Florida
Weston, Fla.
Delegate Rep: Angelia Palahunik, MHA
Website: my.clevelandclinic.org/florida/departments/cancer

Adventist Health Glendale
Glendale, Calif.
Delegate Rep: Jill Dickson, RN
Website: adventisthealth.org/glendale

Calvert Health Oncology Services
Calvert Health Medical Center
Prince Frederick, Md.
Delegate Rep: Kasia Sweeney
Website: calverhealthmedicine.org

A Reminder from ACCC's Bylaws Committee

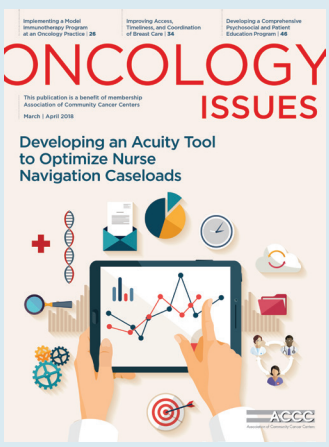
December 1, 2018, is the deadline for submission of any proposed amendments to the ACCC Bylaws. Proposed recommendations should be sent to Betsy Spruill at bspruill@accc-cancer.org. ACCC's Bylaws are available online at: accc-cancer.org/about/pdf/Bylaws-2016.pdf.

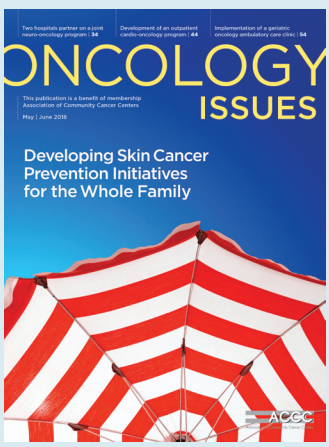
Open Positions on *Oncology Issues* Editorial Board

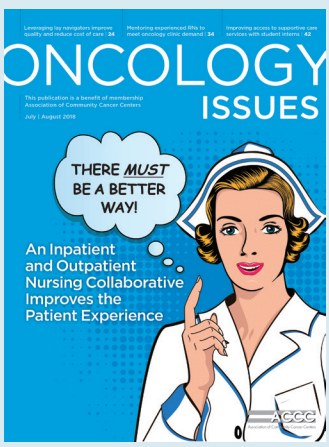
In 2019 ACCC will have openings for the following specialties on the Oncology Issues Editorial Board:

- Medical oncologist
- Surgical oncologist
- Cancer registrar/Data manager
- Pharmacist
- Radiation oncologist
- Cancer program administrator
- Radiation therapist

Interested candidates should email a one-page bio summarizing their oncology experience, areas of interest, and any relevant writing experience to: mmarino@accc-cancer.org.







ACCC 35th National Oncology Conference Takeaway—You've Got the Power!

More than 500 multidisciplinary cancer care providers convened in Phoenix last week, Oct. 17-19, to learn from featured speakers Vicki Hess, RN, MS, Employee Engagement Solutions, LLC; Julie Oehlert, DNP, Chief Experience Officer, Vidant Health; and Dale Dauten, The Innovators' Lab;® the 2018 ACCC Innovator Award winners; and speakers at "how-to" sessions spotlighting programs actively improving patient-centered care delivery about how interconnected the patient experience is with the cancer team's professional experience.

Reflect. Renew. Reignite

On Thursday morning, Oct. 18, ACCC Secretary Krista Nelson, MSW, LCSW, OSW-C, BCD, opened the conference in a guided mindfulness moment, setting the stage for messages of: engagement, empowerment, disrupting the status quo, daring to suggest new possibilities and share new perspectives, and expressing appreciation, throughout the conference.

Opening speaker Vicki Hess challenged attendees to imagine working in a "professional paradise." As an antidote to burnout, Hess reminded attendees, "Sometimes you need to fill your own cup and coming to this ACCC National Oncology Conference is one way to do it!"

Don't Burn Out, Power Up!

"Does your staff feel satisfied, energized, and productive at work?" Hess asked.

When cancer care teams are operating at peak performance, making a difference to patients, "most of the time it's not due to clinical skills alone," Hess said, "it's the bigger picture." What's needed to support optimal teamwork is a three-way partnership among individuals, leadership, and the healthcare organization. "The more empowered employees feel, the more they can create a professional paradise."

For individuals, empowerment starts with understanding that you have choices in how you respond to frustrating, overwhelming, stressful situations (or colleagues) in the workplace. A mindful approach and exercising your power to choose how you respond will boost your resilience, rather than drain your energy, according to Hess.

For example, when a staff member or colleague complains, engage them with empathy, "I hear we have a problem." Then ask, "What would the organization need to do to fix it? What would you like me to do? What's your role?"

Hess suggests the following steps may bolster your workplace resiliency:

- Lose the attitude. Don't hold on to frustrations.
- Encourage chronic complainers to step up and get involved.
- Don't take things personally.
- Spread appreciation. Shared appreciation brings bi-directional benefits. You feel good when you express appreciation and also when you're on the receiving end.
- Embody gratitude.
- Take a breath before responding.

For organizational change, Hess notes that the following are important prerequisites for moving toward a culture of empowerment:

- Gain consensus about what is acceptable at work and what is not
- Build trust
- Get feedback
- Hold staff accountable for being engaged
- And remember: How you define a problem is also how you define the solution.

More highlights from the ACCC 35th National Oncology Conference available at accc-cancer.org/oncologyconference.

Making the Most Out of Drug Representatives

How oncology practices can take advantage of free education opportunities without the hassle

BY CONNIE RENFROE

Medical science representatives possess critical information about new drug regimens, protocols, and indications. However, scheduling them often requires a part-time position that few practices can afford—it's a catch-22. In our oncology practice with two locations, a staff member spent about 20 hours per week managing pharmaceutical appointments.

It can take even longer when practices do not have consistent rules for when reps can visit. Often, reps show up unannounced, disrupting the patient check-in process and taking the focus off other administrative priorities such as insurance verification, pre-certification, and the accurate collection of demographic information.

Most practices value the education that reps provide but struggle to reduce the time spent coordinating the visits. The more reps there are to coordinate, the bigger the burden that is placed on administrative staff to control and manage the scheduling. Combine this with the added pressure of Medicare payment reform, shrinking margins, and increased post-payment audits, and an average practice can easily become overwhelmed. This is the situation my practice faced when I began looking for solutions to make the process of scheduling reps more efficient. I wanted to find a way to automate this process, with an immediate goal of improving staff satisfaction and a long-term goal of gaining more time for patient interaction.

Leveraging Technology

After a quick Google search, I found RxVantage, a free tool that digitizes the physician-rep relationship by allowing reps to self-schedule in custom online calendars. All I needed to do was identify our practice's availability for meeting with reps, grant staff access, and provide minimal internal training. Within an hour, we were up and running with the technology.

Now when reps come to the office seeking meetings, we simply direct them online, where they can log on and book an appointment. My practice can set up specific rules for booking, such as letting our most valued reps book more often than reps that our providers or staff don't find particularly valuable to our practice. Other advantages include the ability to:

- Search for current rep contact information by name, product, or company
- Request product information
- Confirm meetings
- Message reps directly without having to exchange email addresses.

Realizing ROI

Since going live with RxVantage, my practice has seen a significant return on investment, particularly in the realm of reducing the burden on our administrative staff. We are now able to manage reps using only an hour per month of administrative time. This streamlined process has allowed us to increase staffing at our front desk so that we can spend more time answering patient questions and collecting accurate insurance and demographic information, which ultimately improves our revenue cycle.

My practice has also been able to increase efficiency for our clinical staff. For example, our social workers and nurses use the rep scheduling tool to easily research grant and vendor-based patient assistance programs. By typing in the name of a drug, staff can quickly identify all updated patient assistance programs and forms that might be relevant rather than having to research programs individually.

If a practice is looking for ways to increase efficiencies without increasing administrative bandwidth, rep scheduling automation may be one solution. Consider these five steps:

1. ***Commit to rep education.*** Staying current with new oncology medications is no easy task, especially for independent practices that are not owned by or affiliated with a health system. That is why making time for reps is important. The free education that reps provide helps practices stay on top of new advancements, improve outcomes, and perhaps even reduce denials.
2. ***Identify practice availability.*** Reach a consensus on when the practice will see reps. Will it only be on a certain day of the week or certain time slots during each day? In our practice, we only see reps during lunchtime (i.e., 11:00 am-1:00 pm) daily.

(continued on page 84)

ASSOCIATION OF COMMUNITY CANCER CENTERS

FINANCIAL ADVOCACY NETWORK

800+ cancer programs and practices enrolled

1,500+ participants

Financial Advocacy Boot Camp

Powerful Training to Boost Your Financial Advocacy Skills!

Whether you're an experienced financial advocate or new to the field, now is the time to shape up your skills.

The ACCC Financial Advocacy Boot Camp offers a dynamic curriculum with the tools you need to help cancer patients navigate today's complex healthcare system. Topics include:

- Financial Advocacy Fundamentals
- Enhancing Communication
- Improving Insurance Coverage
- Maximizing External Assistance
- Developing and Improving Financial Advocacy Programs and Services

Enroll at
accc-cancer.org/FANBootCamp

"The Financial Advocacy Boot Camp explains all aspects of financial advocacy and is a great tool for new advocates and experienced professionals. Our team will be more prepared and confident with this tool."

– Angie Santiago, CRCS-I, Lead Financial Counselor – Oncology,
Thomas Jefferson University Health System,
Sidney Kimmel Cancer Center

Who Should Enroll?

Financial advocates, nurses, patient navigators, social workers, pharmacists and techs, medical coders, administrative staff, cancer program administrators, and other healthcare professionals.

Cost

FREE to ACCC and Oncology State Society Network members, and $149 for non-members. Join ACCC as an Individual Members ($149) to access this resource—and others—for free.

The ACCC Financial Advocacy Network is supported by:

Pfizer Oncology — *Cornerstone Partner*
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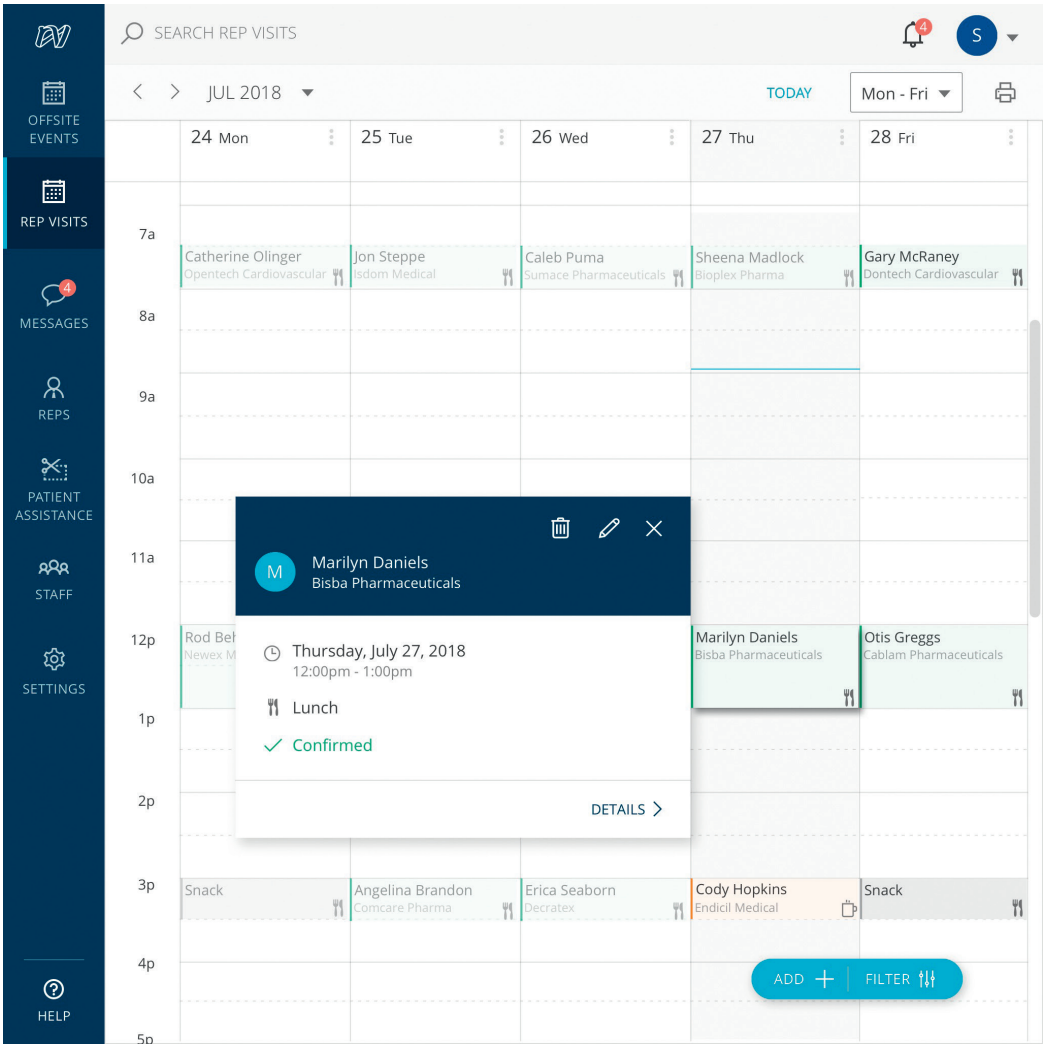
The **Association of Community Cancer Centers (ACCC)** is the leading advocacy and education organization for the multidisciplinary cancer care team. ACCC is a powerful network of 24,000 cancer care professionals from 2,100 hospitals and practices nationwide. ACCC is recognized as the premier provider of resources for the entire oncology care team. For more information, visit accc-cancer.org or call 301.984.9496. Follow us on Facebook, Twitter, and LinkedIn, and read our blog, ACCCBuzz.

The **ACCC Financial Advocacy Network** is the leader in providing professional development training, tools, and resources that will empower providers to proactively integrate financial health into the cancer care continuum and help patients gain access to high quality care for a better quality of life.

Association of Community Cancer Centers



Reps book appointments online so that all appointments are up to date for office staff to see.

(continued from page 82)

3. ***Automate the scheduling process.*** RxVantage intelligently connects physicians and medical staff members with reps who have the most relevant information, enabling practices to continue receiving in-person education with minimal time and effort.
4. ***Create policies and/or procedures.*** Our practice wrote an internal policy for our reps explaining check-in procedures, parking guidelines, and food and snack policies. Front office staff also have informational cards that are given to the reps and describe how they access the technology and self-schedule.
5. ***Dig into your data.*** How frequently do physicians meet with reps? RxVantage provides this information through distribution reports, helping practices understand how often reps visit individual practice locations and what products, services, and companies they represent. Does this frequency make sense given the cancers that are most prevalent in a specific geographic area, or should the practice bring in reps from additional manufactures to better align with cutting-edge treatments that enhance population health efforts?

Digitizing the process of scheduling reps has allowed my practice to do more with the same number of staff, helping us capitalize on the most limited commodity in today's practices: time. OI

Connie Renfroe is clinical practice manager at North Mississippi Medical Center-Hematology and Oncology, which serves 24 counties in north Mississippi and northwest Alabama from headquarters in Tupelo, Miss., and includes a regional network of more than 45 primary and specialty care clinics.

ASSOCIATION OF COMMUNITY
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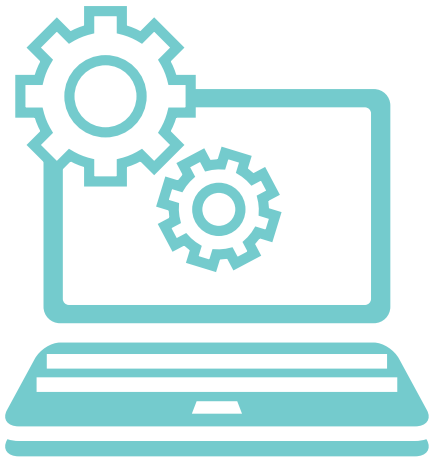
Advance your delivery of patient-centered care with the

HEALTH LITERACY GAP ASSESSMENT TOOL



Pinpoint where targeted health literacy efforts can lead to more effective communication in your cancer program.

ASSESS YOUR PROGRAM AT:

accc-cancer.org/health-literacy

A full report will be emailed upon completion. All results are confidential.

WHY TAKE THE ASSESSMENT?

1. Identify areas where simple quality improvement measures will enhance patient-centered care.
2. Understand if education efforts are effective for your patient population.
3. Create a case for leadership on the need to ensure alignment to standards created by the National Academy of Medicine (formerly, the Institute of Medicine).

ASSESSMENT DOMAINS INCLUDE:

- Health Literacy Program
- Staff Training
- Health Information
- Navigation
- Technology
- Quality Measurement and Improvement

Access robust resources for each domain online.

American Cancer Society®

American College of Surgeons
Inspiring Quality:
Highest Standards, Better Outcomes
100+years

AONN Academy of Oncology Nurse & Patient Navigator

Cancer Support Community
A Global Network of Education and Hope

Health Research for Action
UC Berkeley

NPAF
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Funding & support provided by Lilly | ONCOLOGY
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ACCC
Association of Community Cancer Centers

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IncyteCARES (**C**onnecting to **A**ccess, **R**eimbursement, **E**ducation and **S**upport) provides a single point of contact through a registered nurse, OCN®, to assist eligible patients and healthcare providers in obtaining access to Jakafi® (ruxolitinib) and to connect them with continuing support and resources. The program offers:

REIMBURSEMENT SUPPORT

- Insurance benefit verification
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ACCESS ASSISTANCE

- Copay/Coinsurance assistance
- Free medication program
- Temporary access for insurance coverage delays
- Referrals to independent nonprofit organizations and foundations

EDUCATION & SUPPORT

- Access to a registered nurse, OCN®
- Educational information for your patients about their condition and Jakafi
- Patient Welcome Kit

CONNECTION TO SUPPORT SERVICES

- Referrals for transportation assistance
- Access to patient advocacy organizations for counseling and emotional support resources

Connect with IncyteCARES

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visit IncyteCARES.com or call 1-855-4-Jakafi (1-855-452-5234).

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