Robert Henry: In mid-January, UnitedHealthcare announced that it was adopting the National Comprehensive Cancer Network (NCCN) Compendium for coverage purposes. Do you think it is going to influence physicians in the trenches? Also, many guidelines are issued, but they are often ignored. How has the NCCN reached what appears to be a consensus?

Bill McGivney: Indeed, there have been about 3500 guidelines written over the years. The majority of them have found their way to wastepaper baskets or reside in nice leather-bound editions on shelves. There are a variety of reasons why the NCCN guidelines have been widely recognized and applied by clinicians. The guidelines represent the evaluation of evidence and the integration of expert judgment in a consensus fashion by experts from leading NCCN institutions in the world. One of the keys clearly is that they are up to date, which is obviously crucial in oncology in particular and in medicine in general, because it is all moving extremely rapidly. In the pharmaceutical industry, the research product lines (the pipeline) are quite full with agents. At the NCCN, we strive to provide recommendations for diagnosis, imaging, drug therapies, radiation, surgery, and so on, along a continuum-of-care basis, and this is done with a sense of urgency to keep them up to date.

This is likely one reason that has made the guidelines particularly worthwhile. They are widely recognized as the standard for clinical policy and oncology in the United States. They are available free of charge, which helps, and finally, relevant to the rapid advancements in science and oncology, they came at the right time and the right place. The NCCN guidelines have met the needs of clinicians, especially in the community setting. Community oncologists tend to treat multiple tumor types and, as a result, are in greater need of

The NCCN Compendium for Cancer Management

Interview with Bill McGivney, PhD

Early in 2008, American Health & Drug Benefits asked Dr Bill McGivney to discuss the National Comprehensive Cancer Network Drugs and Biologics Compendium and guidelines, which represent the evaluation of current evidence on cancer management and the integration of expert judgment in a consensus fashion by oncologists from National Comprehensive Cancer Network institutions. Several advantages that may explain the increasing popularity and acceptance of the Compendium and the guidelines are the authoritative nature of the National Comprehensive Cancer Network experts, the rapid updates, and the free online access. The Centers for Medicare & Medicaid Services reference the guidelines specifically on coverage questions related to oncology and is currently evaluating whether to recognize the Compendium as a basis for Medicare coverage decisions for cancer patients. A decision is expected in June 2008. In January 2008, UnitedHealthcare announced that it would be using the Compendium as a basis for their coverage decisions for patients with cancer, a fact that may influence other private health insurance companies to follow suit. In this interview, Dr McGivney discusses some of the unique features of the guidelines and the Compendium and what differentiates them from available guidelines and compendia of other cancer organizations, including the American Society of Clinical Oncology. [AHDB.2008;1(5):40-44.]
an up-to-date set of guidelines that keep pace with the scientific and clinical advances.

Our surveys show that 96% of oncologists think that the NCCN guidelines are important to use when making decisions about patient care, and of these, 64% say they strongly agree that the guidelines are important. Increasingly, we see that physicians believe that the guidelines are also helpful for interacting with managed care companies. We have seen, particularly in the past 4 or 5 years, that managed care companies increasingly use the guidelines as one of the bases, if not the basis, for coverage policy. Some companies contact us to ask for our position on specific clinical issues and about the appropriateness of the use of a particular technology in the specific indication. In these situations, the NCCN responds rapidly to such information requests about our guideline recommendations.

With regards to national coverage determinations, the Centers for Medicare & Medicaid Services (CMS) references the NCCN guidelines specifically on questions related to oncology. We also see that with private payors. As a result, the NCCN has looked to put our information in formats that can be used by payors.

About 3 years ago, we looked at all the drugs and biologics recommendations in our guidelines to see what format would be best for payors. Since the late 1980s, when states started to adopt the legislation that became law requiring that private payors at least referred to the 2 compendia—the American Hospital Formulary Service Compendium and the US Pharmacopeia Drug Information Compendium (also known as AHFS and USP-DI)—and if there were indications for drugs in those compendia then they had to cover such indications in that state, we decided that there was certainly an important role for us to play, particularly in cancer, because of our guideline recommendations, and we had the most up-to-date compendium. Indeed the other 2 compendia tended to be outdated, especially for cancer.

So about 3 years ago we decided to develop the format for the Compendium, that is, to translate and transpose the recommendations about drugs and biologics into a compendium format, which is what we have today. On our website, which has free access, we have more than 13,000 registered users for the Compendium, which is the only product that we require registration for, but it is still free. About 5397 are self-identified physicians. Among the 13,000, about 2500 are nurses. Approximately 1000 individuals have identified themselves as managed care professionals, and 500 are involved in the employee world.

### Key Points

- The NCCN Compendium is becoming a standard for clinical policy in oncology in the United States.
- CMS is currently evaluating whether to adopt the Compendium as a basis for Medicare coverage for cancer patients. Earlier this year, UnitedHealthcare announced it would base its coverage policies for drugs and biologics in cancer care on the NCCN Compendium.
- More than 1 million people worldwide have accessed the guidelines and the Compendium online at www.nccn.org this year.
- The guidelines are being updated on an ongoing basis, consistent with the rapid advancements in science and in cancer therapy specifically.

**Henry:** These are the medical directors at the Fortune 500 company types?

**McGivney:** I am not sure. We have not checked for their degrees, but because they identify themselves as being associated with employers, it is likely they are medical directors or they work with the medical directors at companies that are interested in the expensive drugs and biologics that they may be purchasing.

**Henry:** That brings to mind the issue of cost. If we define value as being a balance of cost, quality, and access, unlimited quality would come at an unlimited price tag and, therefore, will deprive healthcare resources, which are being allocated anywhere else. Does the Compendium relate to cost at all?

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**McGivney:** Our guidelines do not explicitly address cost. We do not directly attempt to resolve the major health policy concern of increasing expenditures, particularly in drugs and biologics, and in cancer care. Rather we focus on the safety and effectiveness of treat-
ments and make recommendations that are based on data and evidence to enhance the efficiency and the utilization of the drugs. Also, my personal opinion is that the decisions about the pricing of drugs need to occur outside of the clinical decision-making setting. It is a public policy issue that relates to employers as purchasers, payors, and manufacturers.

**Henry:** Can the guidelines help in cost-efficiency by targeting the right patients toward the diagnostics? To what degree do the guidelines help in finding the right patient and eliminating waste use through improved diagnostics, genomic testing?

**McGivney:** It is certainly very important to be informed about the potential risks and benefits of any therapy. Patients should have authoritative information in user-friendly formats. In my personal opinion, the negative side tends to be when the patient is asked to share a significant burden of the costs of therapy and thus is asked basically to perform a cost-effectiveness analysis on their therapeutic options.

I think the guidelines tend to pinpoint with respect to the data regarding certain patient subpopulations, which patients are appropriate for the use of which drugs. The indications of our drug compendium compared with other compendia are more specific, because they are drawn from the guidelines that basically communicate what is appropriate in terms of the context of care. So, for example, if you look at a particular drug in the metastatic setting in our guidelines and in the Compendium, you may see in this specific recommendation that it is only for patients who have a performance status of 0 to 2, which may eliminate 30% to 40% of that patient population, because they have a performance status of 3 and 4. Other compendia are not that specific.

The specificity in our guidelines lends itself to enhancing efficiency. If UnitedHealthcare is using the NCCN Compendium as the basis for coverage determination about drugs and biologics, the Compendium will be used more and more by payors and by physicians. We are currently developing a set of standard chemotherapy order templates for individual practices for the ordering and use of chemotherapy or biologics. So if you are a community practice and you are using the NCCN standard or templates, and you have UnitedHealthcare patients, you know that for those patients, their therapy will be covered if based on the NCCN order templates.

**Henry:** How does UnitedHealthcare or any of the payors roll this out? How do they implement the Compendium?

**McGivney:** My understanding of the UnitedHealthcare rollout is that they have sent notices to employers, to practices, and to providers in their network, indicating that they are going to do this. They are going to cover all the category 1, 2A, and 2B recommendations in the NCCN Compendium. Category 3 recommendations, which are quite infrequent, will be referred for medical review. Category 3 issues will go down to the next set of compendia that may be required by the plans in a particular state and to the medical literature specifically.

In terms of frequency, for example, we looked at the way UnitedHealthcare is going to be managed, at least for an initial period of time, and for the 1564 indications in our compendium, only 6 indications would be category 3 indications that may be referred for medical review based on the way UnitedHealthcare is managing the system initially.

**Henry:** Are the guidelines and the Compendium evaluating health-related quality-of-life issues?

**McGivney:** Yes, that comes into play specifically. Certainly in terms of adverse events there are discussions and different branches in the guidelines, and therefore in the Compendium, about patients who may not be able to tolerate more aggressive treatments. Some of that is dependent on age and some on previous reactions to administration of drugs. We address the issues of pain, fever, neutropenia, and fatigue.

The guidelines have all 3 major components: the algorithms are major branches, with specific recommendations, and they are accompanied by long discussion manuscripts that review the evidence that supports the recommendations but also addresses controversial issues. The component is a large reference section.

**Henry:** What are the differences between what you are seeking to do with NCCN guidelines versus what the
The NCCN guideline development was initiated in 1995, 2 years before I joined. They are comprehensive, proceeding from identification of a suspicious lesion or symptoms all the way through work-up, diagnosis, treatment, follow-up, general surveillance, long-term surveillance, and if recurrence occurs, obviously, management of that recurrence. The expert panels are also multidisciplinary in nature, because cancer care can involve surgery, radiation, or drugs. ASCO’s guidelines are important as well, but are more focused, like technology assessments that look at a specific technology class.

The NCCN success may be explained by the context it provides, such as where the diagnostics should be provided, where the follow-up imaging test should be provided, where the drug therapy should be provided, and if such options fail, what to do next. We have developed quality measures of NCCN guideline recommendations. Some believe we need to measure many points along the continuum of care.

Again, NCCN guideline recommendation is a process measure. We first put our guidelines online in 2002, and we had about 100,000 visitors, but this year for the first time we passed the 1 million mark. We are at 1.18 million unique visitors—tremendous utilization of the guidelines by clinicians, consumers, patients, and international visitors.

And we are expanding. Right now we have just 5 doctoral level people that take all the different diagnoses and divide them up and track those areas. In addition, we know when the US Food and Drug Administration (FDA) is going to be required to act on something that is in the pipeline, so we track that and we update the guidelines continually.

We also have agreement collaboration with the American Cancer Society to develop patient guidelines; about 600,000 booklets of patient guidelines given out every year. These are also available on our website.

And we have just signed an agreement with Cerner—one of the largest hospital information system companies in the country—to imbed our information in decision support tools. We are in negotiations with a major company to develop software programs to evaluate the quality of care, and it is based on the 2006 CMS quality demonstration program in oncology for Medicare. We developed a tool with Medicare that could be used to evaluate the quality of care of clinicians, and we are working to develop that as a software program that would be made available to all constituencies and the healthcare community based on the NCCN guidelines and the Compendium.

Henry: What is the status of the Compendium with CMS?

McGivney: I am confident that we will be recognized by CMS. [A decision is expected in June 2008, just around the time this article will appear in print.] We have had a very collaborative relationship with them. They have asked for things that have been beneficial to the users. We have certainly paid particular heed to their “Federal Register” notices. Our Compendium online has an alphabetical listing and index by generic name of all the drugs and biologics in the Compendium. We have made available the total information in all pharmacologic characteristics and actions by directly linking from each drug to the most recent FDA label. It can be searched by disease, histology, brand names, and so on. CMS is interested in compendia that are available to their beneficiaries free of charge. Ours is the only compendium that is available free to all just by visiting our website.
Stakeholder Perspective

Economic/Societal Costs of Adding a Compendium to the Federal Registry

PHARMACY DIRECTORS: No one questions the benefits of the National Comprehensive Center Network (NCCN) Drugs and Biologics Compendium as a resource for listing of medically interesting literature, studies, and results. Nevertheless, the NCCN Compendium has not passed the test of need to replace or be added to the Centers for Medicare & Medicaid Services compendia listings.

The NCCN website lists 21 sponsoring pharmaceutical companies as financial supporters. Although these are fully disclosed, the aspect of potential bias remains for information being ported to clinicians as to appropriate drug therapy and drug use in manners that may promote greater drug utilization than necessary. The NCCN is suggestive on its website of being a vehicle for funding of clinical studies; this too adds a degree of concern because of unknown elements of the clinical trial agreement and the resulting free flow of all reported data from the clinical study, both good and not so good.

Many point to increased survivorship from cancer, and certainly many aspects of modern medicine contribute to this fact; the reality is that these advancements have not been driven by “guidelines” but by experimental outcomes based on evidence and superiority of one therapy compared with another, using active agents and not placebo. Medicine is not lacking for trial outcomes that are rapidly reported by investigators, followed by the oversight committees, and ended quickly when observed advantage or disadvantage is seen in the intermediary results. Clinical trials are tracked by the National Institutes of Health as well as by the US Food and Drug Administration (FDA).

As Dr McGivney notes in the interview, many guidelines are indeed published, and most are not used or are ignored, because of perceptions of bias or known bias; the many views of the NCCN online only indicates that a search tool listed a website as a “hit,” and curiosity may have led to further investigations. These investigations, as Dr McGivney notes, are not well documented as to content reviewed and do not necessarily indicate that the site is the destination for guideline development or prescribing purposes. Many hits on a website do not signify a preponderance of support by oncologists.

Healthcare in the United States consumes approximately 16% of the nation’s gross domestic product, with an upward trend. So while we can point to having the most costly and advanced technology worldwide, the metrics for measurement of healthcare success are often receiving a failing grade when compared with metrics being reported by lesser advanced and financially able countries.

Embellishing the NCCN as a compendium would be far-reaching both for therapy and as societal costs. As a society, we must remain steadfast in the approach to disease management and therapy to use proved therapies. Evidence-based medicine in relation to determining the best therapy, based on data from well-designed studies with an adequately powered number of subjects, supports a qualified confidence level in the results.

The FDA has similar responsibilities to that of the National Institute for Health and Clinical Excellence in matters of drug regulatory management and approvals, but the US-based clinical studies very often have too few subjects to elicit a high-confidence rating, and the studies often use a placebo for comparison. In contrast, European studies involve therapeutically active comparators with high scrutiny for statistical significance for outcome measures.

The official compendium in the federal registrar is currently used to host appropriate off-label use of drug therapy, the issues of Medicare’s national coverage determinations, as well as Part D medications and Medicaid reimbursement. Based on the expected expansion because of dueling listings, the overall expense to society will increase with the addition of any compendium to the federal registry. Adding more references as “official” can only add to the complexity of determination of medical necessity for off-label medications, resulting in the continuation of a broken system.

References

Thomas Kaye, RPh, MBA
Sr. Pharmacy Director
Passport Health Plan, AmeriHealth Mercy