Thyroid Cancer Overdiagnosis

An article in the August 18 issue of the *New England Journal of Medicine* (2016;375:614–676) by authors representing the International Agency for Research on Cancer (IARC), a part of the World Health Organization, garnered worldwide media coverage with its contention that growing rates of thyroid cancer reported in recent decades in high-income countries are largely the result of overdiagnosis of tumors unlikely to cause symptoms or lead to death. The authors used cancer registry data from IARC's reference publication *Cancer Incidence in Five Continents* to estimate the number of overdiagnosed cases of thyroid cancer in 12 countries. In a related IARC press release, lead author Salvatore Vaccarella, PhD, an IARC staff scientist, commented on the finding that the largest increase has been observed in South Korea, where the incidence among individuals 15–79 y old (standardized to the world population) increased from 12.2 cases per 100,000 persons in 1993–1997 to 59.9 cases per 100,000 persons in 2003–2007. "Countries such as the USA, Italy, and France have been most severely affected by overdiagnosis of thyroid cancer since the 1980s, after the introduction of ultrasonography, but the most recent and striking example is the Republic of Korea," said Vaccarella. "A few years after ultrasonography of the thyroid gland started being widely offered in the framework of a population-based multicancer screening, thyroid cancer has become the most commonly diagnosed cancer in women in the Republic of Korea, with $\sim$90% of cases in 2003–2007 estimated to be due to overdiagnosis." The estimated fraction of overdiagnosed cases in women during the same period ranged between 70% and 80% in Australia, France, Italy, and the United States, and was $\sim$50% in Japan, the Nordic countries, and England and Scotland. In men, patterns of changing overdiagnosis were similar but less pronounced, with far fewer cases reported ($\sim$70% in France, Italy, and the Republic of Korea; 45% in Australia and the U.S.; and $<$25% in other countries studied). The authors estimated that $>$470,000 women and 90,000 men may have been overdiagnosed with thyroid cancer in the 12 countries during the 2 decades studied. These increases were attributed entirely to greater access to ultrasound, CT, and MR imaging and to increased access to medical surveillance, resulting in identification of small papillary lesions unlikely to be symptomatic or lead to progressive disease. The study identified no environmental or other likely causes of increased disease. The report cautioned against systematic population screening of the thyroid and routine workup of small nodules and suggested that "watchful waiting approaches should be considered a research priority and a preferable option for patients with low-risk papillary thyroid cancers." "The drastic increase in overdiagnosis and overtreatment of thyroid cancer is already a serious public health concern in many high-income countries, with worrying signs of the same trend in low- and middle-income countries," said IARC Director Christopher Wild, PhD. "It is therefore critical to have more research evidence in order to evaluate the best approach to address the epidemic of thyroid cancer and to avoid unnecessary harm to patients."

New England Journal of Medicine
International Agency for Research on Cancer

Cancer Survival and Insurance Coverage

Two studies e-published on August 8 ahead of print in *Cancer* provided data suggesting that oncology patients in the United States who are uninsured or on Medicaid tend to be diagnosed later, have less optimal treatment, and experience poorer overall survival than individuals with private health insurance.

Rong et al. from the Johns Hopkins University School of Medicine and Bloomberg School of Public Health (Baltimore, MD) and Sun Yat-sen University (Guangzhou, China) reported on a population-based study of the association between insurance status and survival in adults with glioblastoma multiforme (GBM). The study used data from 2077–2012 from the Surveillance, Epidemiology, and End Results (SEER) database on 13,665 adult patients with GBM as primary diagnoses. Survival was analyzed, with additional analyses to account for confounding demographic and clinical variables. In the patients studied 558 (4.1%) were uninsured, 1,516 (11.1%) had Medicaid coverage, and 11,591 (84.8%) had private insurance. Insured patients were more likely to be older, women, white, married, and have smaller tumor sizes at diagnosis. Older age, male sex, large tumor size at diagnosis, and being uninsured or insured by Medicaid were predictors of worse outcomes. Survival numbers for those newly diagnosed with GBM improved for each discrete year of the study, whereas no such improvement was noted in uninsured or Medicaid-insured patients. "We have found that non-Medicaid insured patients have a significant survival benefit over uninsured and even Medicaid-insured patients," said Wuyang Yang, MD, a research fellow at Johns Hopkins Hospital and coauthor of the study, in an interview with Reuters Health. "Within the context of the current study, we cannot confirm the underlying reason for these associations."

In a second study, Markt et al. from Harvard University, the Dana–Farber Cancer Institute, and Brigham and Women's Hospital (all in Boston) reported on insurance status and disparities in disease presentation, treatment, and outcomes for men with germ cell tumors. The SEER database was accessed to identify $>$10,000 men diagnosed with germ cell gonadal neoplasms from 2007 to 2011. Uninsured patients and patients on Medicaid were found to have a greater risk of metastatic disease at diagnosis than insured patients. Among those with metastatic disease, uninsured and Medicaid patients were more likely to be diagnosed with intermediate/poor-risk disease and were less likely to undergo lymph node dissection. Those without insurance or on Medicaid were more likely to die of the disease than were individuals with insurance.

In a related editorial in the same issue of *Cancer*, Halpern and Brawley, from Temple University College of Public Health (Philadelphia, PA) and Emory University (Atlanta, GA), respectively, noted that "Although these 2 studies involved 2 very different types of cancer affecting 2 very different patient groups, the similarity of the results is striking.... These 2 studies join a long litany of studies demonstrating that a substantial number of Americans diagnosed with cancer die prematurely. The underserved deserve service. Adequate health care should be considered an inalienable human right, and greater emphasis is needed on realizing strategies that will make this happen throughout the continuum of cancer care."

Cancer

VA Proposal on Nurses and Imaging

On May 25, the Department of Veterans Affairs (VA) released a proposed rule to grant advanced practice registered nurses (APRNs) the authority to perform a range of patient procedures, including advanced imaging services. In a move to "increase veterans' access to qualified health care professionals and services," Section 17.415 (d)(1)(i) of the proposed rule would allow certified nurse practitioners (CNPs) to "order, perform, supervise, and interpret laboratory and imaging studies." On July 18 SNMMI joined multiple other professional organizations in urging members to respond with comments to the VA. Four days later, SNMMI submitted its own comments criticizing the proposed rule in a lengthy letter signed by Sally Schwarz, MS, RPh, SNMMI President, and Sara G. Johnson, MBA, CNMT, NCT, SNMMI–Technologist Society President. The writers noted that although "SNMMI applauds the VA's attempt to provide better health services for our nation's veterans, SNMMI believes that this proposed rule would undermine the quality of care the VA hopes to deliver." The letter went on to detail the complex requirements for delivery of high-quality nuclear medicine procedures, as well as the rigorous training and certification required for physicians. The requirements for Nuclear Regulatory Commission regulation and Authorized User status were reviewed, as well as radiation safety training. The specific training required for Nuclear Medicine Technologists and Nuclear Medicine Advanced Associates (NMAAs) was also reviewed. "By employing NMAAs, rather than CNPs, the VA could accomplish its goals of providing a quality care as efficiently as possible," SNMMI suggested. The letter writers summarized their opposition: "Allowing CNPs to 'perform,' 'supervise,' and 'interpret' laboratory and imaging studies will compromise, not enhance, the level of care received by veterans. Additionally, while combining all imaging services under a CNP may seem more efficient, CNPs' lack of qualifications could result in dangerous misdiagnoses, improper utilization of imaging procedures, and a general deterioration in the level of care the VA is able to provide to veterans." Although the window for public comment closed on July 25, revisions to and finalization of the proposed rule may take a number of months. The full proposed rule is available at: https://www.federalregister.gov/articles/2016/05/25/2016-12338/advanced-practice-registered-nurses.

Federal Register
SNMMI

NIH: Precision Medicine and Health Disparities

The National Institute on Minority Health and Health Disparities, part of the National Institutes of Health, announced on July 28 the commitment of ~$31 million over 5 y to a new program for Transdisciplinary Collaborative Centers (TCCs) for health disparities research. The centers will explore the potential for precision medicine to promote health equity and advance the science of minority health and health disparities.

Priority research areas include: development of new tools and analytic methods for integrating patient data with information about contextual factors acting at the community or population level to influence health outcomes; development of pharmacogenomic and other precision medicine tools to identify critical biomarkers for disease progression and drug responses in diverse populations; translation of pharmacogenomic discoveries into clinical practice, including effective treatments; investigation of facilitators and barriers to implementing precision medicine approaches in disparity populations; and understanding mechanisms that lead to differential health outcomes in common diseases in minorities and disparity populations.

The TCCs will function as regional coalitions of research institutions and partners working to develop and disseminate effective health interventions that can be implemented in real-world settings. TCCs supported through this initiative are expected to focus on at least 1 priority research area, each combining expertise in precision medicine, population health disparities, and the science of translation, implementation, and dissemination to address 1 or more documented health disparities. The proposed work must focus on 1 or more health disparities populations, which include Blacks/African Americans, Hispanics/Latinos, American Indians/Alaska Natives, Asian Americans, Native Hawaiians and other Pacific Islanders, socioeconomically disadvantaged populations, and rural populations. Each center will support 2–3 multidisciplinary research projects examining complementary aspects of precision medicine, focusing on interactions between biologic, behavioral, and contextual predictors of disease vulnerability, resilience, and response to therapies in patients from disadvantaged communities.

The first precision medicine TCC cooperative agreement awards, each providing up to $1.5 million in direct costs annually over 5 years, were made to Vanderbilt University Medical Center (Nashville, TN), Stanford University (Palo Alto, CA), and the Medical University of South Carolina (Charleston).

National Institutes of Health