Over the past 30 years, awareness and screening have led to an emphasis on early diagnosis of cancer. Although the goals of these efforts were to reduce the rate of late-stage disease and decrease cancer mortality, secular trends and clinical trials suggest that these goals have not been met; national data demonstrate significant increases in early-stage disease, without a proportional decline in later-stage disease. What has emerged has been an appreciation of the complexity of the pathologic condition called cancer. The word “cancer” often invokes the specter of an inexorably lethal process; however, cancers are heterogeneous and can follow multiple paths, not all of which progress to metastases and death, and include indolent disease that causes no harm during the patient’s lifetime. Better biology alone can explain better outcomes. Although this complexity complicates the goal of early diagnosis, its recognition provides an opportunity to adapt cancer screening with a focus on identifying and treating those conditions most likely associated with morbidity and mortality.

Changes in cancer incidence and mortality reveal 3 patterns that emerged after inception of screening (Table). Screening for breast cancer and prostate cancer appears to detect more cancers that are potentially clinically insignificant. Lung cancer may follow this pattern if high-risk screening is adopted. Barrett esophagus and ductal carcinoma of the breast are examples for which the detection and removal of lesions considered precancerous have not led to lower incidence of invasive cancer. In contrast, colon and cervical cancer are examples of effective screening programs in which early detection and removal of precancerous lesions have reduced incidence as well as late-stage disease. Thyroid cancers and melanoma are examples for which screening has expanded and, along with it, the detection of indolent disease.

Optimal screening frequency depends on the cancer’s growth rate. If a cancer is slow growing, screening is rarely effective. If a cancer is slow growing but progressive, with a long latency and a precancerous lesion (eg, colonic polyps or cervical intraepithelial neoplasia), screening is ideal and less frequent screening (eg, 10 years for colonoscopy) may be effective. In the case of an indolent tumor, detection is potentially harmful because it can result in overtreatment. These observations provide an opportunity to refocus screening on reducing disease morbidity and mortality and lower the burden of cancer screening and treatments.

In March 2012, the National Cancer Institute convened a meeting to evaluate the problem of “overdiagnosis,” which occurs when tumors are detected that, if left untreated, would not become clinically apparent or cause death. Overdiagnosis, if not recognized, generally leads to overtreatment. This Viewpoint summarizes the recommendations from a working group formed to develop a strategy to improve the current approach to cancer screening and prevention.

Periodic screening programs have the potential to identify a reservoir of indolent tumors. However, cancer is still perceived as a diagnosis with lethal consequences if left untreated.

An ideal screening intervention focuses on detection of disease that will ultimately cause harm, that is more likely to be cured if detected early, and for which curative treatments are more effective in early-stage disease. Going forward, the ability to design better screening programs will depend on the ability to better characterize the biology of the disease detected and to use disease dynamics (behavior over time) and molecular diagnostics that determine whether cancer will be aggressive or indolent to avoid overtreatment. Understanding the biology of individual cancers is necessary to optimize early detection programs and tailor treatments accordingly. The following recommendations were made to the National Cancer Institute for consideration and dissemination.

Physicians, patients, and the general public must recognize that overdiagnosis is common and occurs more frequently with cancer screening. Overdiagnosis, or identification of indolent cancer, is common in breast, lung, prostate, and thyroid cancer. Whenever screening is used, the fraction of tumors in this category increases. By acknowledging this consequence of screening, approaches that mitigate the problem can be tested.

Change cancer terminology based on companion diagnostics. Use of the term “cancer” should be reserved for describing lesions with a reasonable likelihood of lethal progression if left untreated. There are 2 opportunities for change. First, premalignant conditions (eg, ductal carcinoma in situ or high-grade prostatic intraepithelial neoplasia) should not be labeled as cancers or neoplasia, nor should the word “cancer” be in the name. Second, molecular diagnostic tools that identify indolent or low-risk lesions need to be adopted and validated. Another step is to reclassify such cancers as IDLE (indolent lesions of epithelial origin) conditions. An example is the reclassification of grade 1 papilloma to urothelial neoplasia of low malignant potential. Pre- sently, the rationale for reclassifying papilloma and grade 1 carcinoma as “papillary urothelial neoplasia of low malignant potential” was “to take the lowest grades of tumor, the most benign-appearing lesions, and remove the word carcinoma.” A multidisciplinary effort across the pathology, imaging, surgical, advocate, and medical communities could be convened by an independent group (eg, the Institute of Medicine) to revise the...
The National Lung Screening Trial conducted among individuals at risk for lung cancers such as active surveillance. Prognosis for precancerous lesions is crucial to informed decision making, including comfort with alternate treatment strategies to improve selection of patients for cancer screening. The ultimate goal is to preferentially detect consequential cancer while avoiding detection of inconsequential disease.

**Conclusion**

The original intent of screening was to detect cancer at the earliest stages to improve outcomes; however, detection of cancers with better biology contributes to better outcomes. Screening always results in identifying more indolent disease. Although no physician has the intention to overtreat or overdiagnose cancer, screening and patient awareness have increased the chance of identifying a spectrum of cancers, some of which are not life threatening. Policies that prevent or reduce the chance of overdiagnosis and avoid overtreatment are needed, while maintaining those gains by which early detection is a major contributor to decreasing mortality and locally advanced disease. The recommendations of the task force are intended as initial approaches. Physicians and patients should engage in open discussion about these complex issues. The media should better understand and communicate the message so that as a community the approach to screening can be improved.

**ARTICLE INFORMATION**


Conflict of Interest Disclosures: All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Thompson reported serving as a board member or consultant for, and receiving grants or grants pending, payment for lectures, patents, and honoraria from, a variety of sources. No other authors reported disclosures.

Additional Contributions: We thank Barnett Kramer, MD, MPH (Division of Cancer Prevention, National Cancer Institute [NCI]), for convening the brainstorming meeting held in March 2012. The authors chaired the NCI working group, which included Donald Berry, PhD, Mina Bissel, PhD, William Black, MD, Shelley Hwang, MD, Kenneth Kinzler, PhD, Peter Nelson, MD, David Ransahoff, PhD, Howard Parnes, PhD, Sudhir Srivastava, PhD, and Gilbert Welch, MD. Follow-up discussions and recommendations form the basis of this article.

Nadarajen A. Vydelingum, PhD, FSB, FRSPH (Division of Cancer Prevention, NCI), provided administrative support and coordination among the authors throughout the preparation of this article.

REFERENCES