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The 2014 Surgeon General's Report: "The Health Consequences of Smoking-50 Years of Progress":

A Paradigm Shift in Cancer Care

Graham W. Warren, MD, PhD^{1,2,3}, Anthony J. Alberg, PhD, MPH^{3,4}, Andrew S. Kraft, MD^{3,5}, and K. Michael Cummings, PhD, MPH^{3,6}

¹Department of Radiation Oncology, Medical University of South Carolina, Charleston, South Carolina

²Department of Cell and Molecular Pharmacology and Experimental Therapeutics, Medical University of South Carolina, Charleston, South Carolina

³Hollings Cancer Center, Medical University of South Carolina, Charleston, South Carolina

⁴Department of Public Health Sciences, Medical University of South Carolina, Charleston, South Carolina

⁵Department of Medicine, Medical University of South Carolina, Charleston, South Carolina

⁶Department of Psychiatry and Health Behavior, Medical University of South Carolina, Charleston, South Carolina

On rare occasions, clinicians are presented with evidence supporting a paradigm shift in clinical care. On January 17, 2014, the Surgeon General's report (SGR), "The Health Consequences of Smoking–50 Years of Progress," was published updating the evidence of the adverse effects of tobacco on health. Of course, the evidence linking smoking to a wide range of health consequences has been well established for decades. However, what was new in this report, and that is specifically relevant to clinicians involved in caring for patients with cancer, is the finding that tobacco smoking is causally associated with adverse health outcomes in patients with cancer. As noted in the executive summary and described in detail in the section on cancer, the report concludes the following:

- In patients with cancer and survivors, the evidence is sufficient to conclude a
 causal relationship between cigarette smoking and adverse health outcomes.

 Quitting smoking improves the prognosis of patients with cancer.
- 2. In patients with cancer and survivors, the evidence is sufficient to conclude a causal relationship between cigarette smoking and increased all-cause mortality and cancer-specific mortality.

Corresponding author: Graham Warren MD, PhD, Department of Radiation Oncology, Medical University of South Carolina, 169 Ashley Ave, MSC 318, Charleston, SC 29425; Fax: (843) 876-2297; warrengw@musc.edu.

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3. In patients with cancer and survivors, the evidence is sufficient to conclude a causal relationship between cigarette smoking and an increased risk of second primary cancers known to be caused by cigarette smoking, such as lung cancer.

4. In patients with cancer and survivors, the evidence is suggestive but not sufficient to conclude a causal relationship between cigarette smoking and the risk of disease recurrence, poorer response to treatment, and increased treatment-related toxicity.

The SGR concluded that continued smoking after a cancer diagnosis causes adverse health effects and increases both cancer-specific and all-cause mortality. The evidence further points toward smoking increasing cancer treatment toxicity, cancer recurrence, and the risk of developing a second primary cancer, though the current evidence fell short of establishing a causal relationship. Moreover, these findings are systemic, affecting both tobacco-related and non-tobacco-related cancer disease sites across all treatment modalities including surgery, chemotherapy, and radiotherapy. These conclusions are based on rigorous review of the scientific evidence including a stringent multilevel peer-review process. Conclusions of causation are considered the highest-level evidence and are based on the consistency, strength, specificity, and coherence of the association between tobacco and health outcomes.

In the past, causal relationships reported in SGRs have led to substantial legislative, societal, and medical changes, including the requirement of health warnings on cigarettes, limits on cigarette marketing, restrictions on smoking in public spaces, mass media counter marketing campaigns, and higher taxes on cigarettes.² For example, evidence presented in the 2006 SGR concluding that "second hand smoke exposure causes disease and premature death in children and adults who do not smoke" and that there was no risk-free level of secondhand smoke exposure³ led to substantial changes in smoke-free public policies. In 2005, there were 7 states with active comprehensive smoke-free air laws, 1 state in which a comprehensive law had passed but was not active, and 2 states with strong laws in effect.⁴ By 2013, there were 26 states with active comprehensive laws and 9 states with strong laws in effect. The 1990 SGR⁵ concluded that smoking cessation decreased the risk of lung cancer, other cancers, heart attack, stroke, and chronic lung disease. This causal evidence and benefit of smoking cessation provided support for the creation or expansion of national smoking cessation resources such as the National Quitline (1-800-QUIT-NOW), the Public Health Service smoking cessation guidelines (last updated in 2008),⁶ and nationwide tobacco control efforts. In summary, causal relationships presented in the SGR are tied to substantial historical changes in public policy with subsequent improvements in public health.

To our knowledge, before the 2014 SGR, there was no assessment of the evidence evaluating the effect of smoking on outcomes among patients with cancer. Based on the results of the 2014 SGR, as oncologists, we are now charged with purpose based on the conclusion that "the evidence is sufficient to conclude a causal relationship between cigarette smoking and adverse health outcomes." Given the new conclusions, patients should be advised that smoking has immediate and profound adverse implications for their prognosis by causing adverse outcomes, increasing all-cause mortality, and increasing cancer-specific mortality. No longer can oncologists rely solely on the risk of developing cancer due to smoking.

Oncologists are now charged with addressing the causal relationship between smoking and adverse health outcomes in their patients.

The 2014 SGR provides highly pertinent and useful information that oncologists can use to discuss and treat tobacco use in patients with cancer. Cigarette smoking is now causally associated with cancers of the oropharynx, larynx, esophagus, lung (including trachea and bronchus), stomach, liver, pancreas, kidney and ureter, bladder, cervix, and colorectum, as well as acute myeloid leukemia. Causal relationships are established for noncancer adverse effects on virtually every organ system including impaired immune function and type II diabetes. Secondhand smoke adversely affects adults and children with causal relationships on the respiratory, cardiovascular, aerodigestive, and reproductive systems. Smoking exerts adverse effects among both men and women regardless of race, ethnicity, education, or socioeconomic status. It is important to note that changes in cigarette design have caused an increased risk of some health conditions such as adenocarcinoma of the lung, thus negating any possible suggestion that newer cigarettes are safer. Smoking also diminishes overall health status leading to increased absenteeism from work and increased use of health care resources and increased cost. The biologic and clinical effects of tobacco continue after a cancer diagnosis, making this body of information highly useful in discussions with patients with cancer.

Given the additional finding that nicotine addiction results in approximately 20% to 30% of patients with cancer persisting in smoking even after a cancer diagnosis, more needs to be done to help patients with cancer refrain from smoking. Unfortunately, smoking is not well addressed in clinical practice or clinical trial design. Based on the causal findings in the 2014 SGR, it would be reasonable and justified that all cigarette packs be required to carry an instruction advising those with cancer to avoid smoking completely (ie, "If you have cancer, DO NOT use this product"). The current warning, which discusses the risks of smoking, is too vague and nonspecific to convey the actual harms associated with smoking for a patient undergoing therapy for cancer.

With an appropriately increased emphasis being placed on high-quality cancer care centered on evidence-based medicine using trained staff and advanced medical technology to actively inform patients of treatment options and to deliver effective cancer treatment, ^{10,11} a new emphasis must also now be placed on addressing nicotine addiction in patients with cancer. Fortunately, recent recommendations for addressing tobacco use in patients with cancer have been provided by both the American Society of Clinical Oncology¹² and the American Association for Cancer Research. ¹³ All patients should be assessed for tobacco use on a repeated basis, patients must be offered tobacco cessation support, clinical trials should include tobacco assessments, and tobacco should be considered as a confounder or effect modifier in clinical trials design. Conclusions from the 2014 SGR now advance these recommendations; cancer patients and survivors should now be advised that smoking causes adverse outcomes, increases all-cause mortality, and increases cancer-specific mortality.

The conclusions of the 2014 SGR regarding patients with cancer should be viewed as a beginning, not an ending. Research is still needed to understand how and why smoking causes adverse outcomes in these patients. We can infer the physiologic effects of smoking

on organ systems (such as heart disease, pulmonary disease, etc) from the wealth of evidence already presented; however, we lack inference regarding the interaction between smoking and the physiologic risks associated with cancer therapy, such as heart disease from cardiotoxic chemotherapy or the risk of a second primary tumor from radiotherapy. We can infer the biologic effects of smoking on normal noncancer cell physiology, but we have very limited information regarding the biologic effects of smoking on cancer cells with a spectrum of active mutations that drive changes in proliferation, migration, invasion, angiogenesis, immunomodulation, and cell death. We can also conclude that smoking cessation will manifest in health benefits for patients with cancer, as evidenced by improved prognosis in former smokers compared with current smokers, as summarized in the 2014 SGR. However, we have yet to fully understand the evidence behind the clinical benefits of smoking cessation during the time surrounding a cancer diagnosis.

Findings from the 2014 SGR warrant a paradigm shift in cancer care. The days when tobacco smoking among patients with cancer could be shrugged off as a pleasure for these individuals to enjoy during a difficult time are long gone. In fact, in some patients with cancer, the potential gains in survival from smoking cessation may arguably outweigh the benefits from current standard-of-care cancer treatments. In combination with ongoing advances in targeted and individualized medicine, clinicians and oncologists are now tasked with the responsibility of addressing tobacco use in their patients as a matter of providing evidence-based quality cancer care.

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