OXFORD

JNCI J Natl Cancer Inst (2017) 109(9): djx070

doi: 10.1093/jnci/djx070
First published online July 26, 2017
Editorial

EDITORIAL

US Cancer Statistics of Survival: Achievements, Challenges, and Future Directions

Shahinaz M. Gadalla, Brigitte C. Widemann

Affiliations of authors: Clinical Genetics Branch, Division of Cancer Epidemiology and Genetics (SMG), and Pediatric Oncology Branch, Center for Cancer Research (BCW), National Cancer Institute, National Institutes of Health, Bethesda, MD

Correspondence to: Brigitte Widemann, MD, Center for Cancer Research, Pediatric Oncology Branch, National Cancer Institute, 10 Center Drive, Building 10, CRC, 1W3742, Bethesda, MD 20892 (e-mail: widemanb@mail.nih.gov).

Cancer remains the second leading cause of death in the United States, with an estimated 600 920 cancer deaths in 2017 (1). In this issue of the Journal, the American Cancer Society, the Centers for Disease Control and Prevention, the National Cancer Institute (NCI), and the North American Association of Central Cancer Registries deliver their annual update on US cancer incidence and mortality trends (2). The report shows that during 1999 to 2013, cancer rates continued to decrease in men and remained stable in women. In contrast, mortality rates statistically significantly decreased in men and women (1.8% and 1.4% per year, respectively). Cancer site–specific statistics showed few exceptions. While these results are encouraging overall, they raise critical questions: Why do we see rate increases in some cancers? How can we decrease cancer mortality more rapidly? Can we address mortality risk factors within the current standard of care more effectively? Will the surge in new targeted anticancer therapeutics translate to a peak drop in cancer mortality soon?

The reported increase in the incidence of certain cancers, such as cancers of the liver, pancreas, thyroid, female breast, and uterus, is alarming, but a fraction of them may be explained by known risk factors such as the expanding obesity epidemic (3). Approximately 38% of US adults and 17% of children and adolescents are obese (4,5). The dramatic decrease in the incidence of cancers linked to tobacco smoking provides proof of concept that changing lifestyle risk factors is important in cancer control.

The identified geographic survival differences in this report—with survival for several common cancers being lowest in select Southern and Midwestern states and highest in Northeastern states—cannot be interpreted without considering the possible interaction with the population demographics and/or access to specialty care. Racial differences in cancer incidence and mortality have not changed from previous years. Access to and affordability of state-of-the art cancer care are important factors. Receiving care at an NCI-designated cancer center was linked to lower mortality in patients with incident cancers between 1998 to 2002 (6). Geocoding analysis suggested that people living in the Northeast may have better access to an NCI-designated cancer center, followed by those living in the West, the Midwest, and then the South (7).

In addition, research aiming at a comprehensive understanding of the possible genetic or biological mechanisms that may explain racial differences in cancer outcomes may play an important role in closing such gaps. For example, recent studies interrogating genome-wide germline single nucleotide polymorphisms may provide some explanation of the higher risk of death from leukemia in Hispanics described in this report (8,9). The Cancer Moonshot Blue Ribbon Panel Report (https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/blue-ribbon-panel) identified the development of a network for direct patient involvement in cancer research and expansion of proven prevention and early detection strategies as priorities to accelerate progress against cancer. With increased investment in these areas, there is hope for greater patient enrollment in clinical trials overall, and in particular for minorities, which would allow comparing treatment effects and molecular tumor characteristics across racial groups.

The current development of cancer-targeted therapies focus on tumors with oncogenic mutations, such as anaplastic lymphoma kinase (*ALK*) or epidermal growth factor receptor (*EGFR*) in non–small cell lung cancer (10,11) or inherited breast cancer susceptibility genes (*BRCA1/2*) in breast and ovarian cancers (12), has resulted in smaller subgroups within common cancers. For example, during the past five years, the US Food and Drug Administration (FDA) approved five EGFR inhibitors and three ALK inhibitors for non–small cell lung cancers harboring these mutations. New FDA-approved drugs for these subgroups may

Received: March 16, 2017; **Accepted:** March 23, 2017

result in survival improvement that may be undetectable when the focus is on cancers based on pathologic and not molecular classification. Also, some of the new drug approvals are for rare cancers such as medullary thyroid carcinoma (13). The capture of tumor molecular characteristics through cancer registries would allow for a more precise evalulation of the effect of new therapies on mortality rates in targeted cancer subgroups.

Unlike adults, cancer mortality in children age 0 to 14 years during 2010 to 2014 decreased despite the statistically significant increase in cancer incidence across evaluated racial groups. A recent analysis covering the time frame from 1975 to 2010 showed a mortality decline between 1975 to 1998 and a plateau from 1998 to 2002, followed by a decline between 2002 and 2010, with similar trends in children age 15 to 19 years (14). The observed timeline change in childhood cancer mortality could be attributed to advances in the treatment of childhood acute lymphoblastic leukemia (15,16) and solid tumors (17) accomplished through the Children's Oncology Group trials. Widespread participation of children with cancers in clinical trials, ranging from 60% to 90% compared with adult cancers, where trial participation is around 3%, likely enhanced faster changes in childhood cancer mortality. Increasing the enrollment of adults in clinical trials by overcoming known barriers to participation may substantially accelerate improvement in outcomes (18). Of note, while tremendous progress has been made in childhood cancers, fewer drugs are approved for children compared with adults. Accelerating access to new agents for children is critical for patients who do not have curative options or for tumors in which there has been little progress (19). Allowing enrollment of adolescents in disease- or target-appropriate adult oncology clinical trials is supported by the FDA and would provide access to this group—known to have lower trial enrollment—and potentially reduce mortality (20).

This year's report is the first to use a single database covering 89% of the US population for the main cancer incidence and mortality analyses, which increases the representation of the population and ensures generalizability of the results. However, different registries were used for more detailed information based on availability and years of collection. The current statistics do not reflect recent advances in targeted cancer therapies because of the long lag time between cancer diagnosis and reporting. The shift in the medical treatment of cancers from predominantly cytotoxic drugs to the addition of agents targeting molecular pathways, and more recently immunotherapy approaches, may result in clinically significant improvements. These treatment advances combined with increasing patient enrollment in clinical trials provide a prospect for more rapid improvement in cancer outcomes.

Funding

This work was supported by the Intramural Research Program of the Center for Cancer Research and the Division of Cancer Epidemiology and Genetics, National Cancer Institute.

Notes

The funders had no role in the writing of the editorial or the decision to submit it for publication. The authors have no conflicts of interest to declare.

References

1. American Cancer Society. *Cancer Facts and Figures 2017*. Atlanta, GA: American Cancer Society; 2017.
2. Jemal A, Ward E, Johnson C, et al. Annual report to the nation on the status of cancer, 1975–2014, featuring survival. *J Natl Cancer Inst*. 2017; 109(9): djx030.
3. Lauby-Secretan B, Scoccianti C, Loomis D, et al. Body fatness and cancer—viewpoint of the IARC working group. *N Engl J Med*. 2016;375(8): 794–798.
4. Ogden CL, Carroll MD, Flegal KM. Prevalence of obesity in the United States. *JAMA*. 2014;312(2):189–190.
5. Ogden CL, Carroll MD, Lawman HG, et al. Trends in obesity prevalence among children and adolescents in the United States, 1988–1994 through 2013–2014. *JAMA*. 2016;315(21):2292–2299.
6. Onega T, Duell EJ, Shi X, et al. Influence of NCI cancer center attendance on mortality in lung, breast, colorectal, and prostate cancer patients. *Med Care Res Rev*. 2009;66(5):542–560.
7. Onega T, Duell EJ, Shi X, et al. Geographic access to cancer care in the U.S. *Cancer*. 2008;112(4):909–918.
8. Yang JJ, Cheng C, Devidas M, et al. Ancestry and pharmacogenomics of relapse in acute lymphoblastic leukemia. *Nat Genet*. 2011;43(3):237–241.
9. Karol SE, Larsen E, Cheng C, et al. Genetics of ancestry-specific risk for relapse in acute lymphoblastic leukemia. *Leukemia*. 2017; in press.
10. Solomon BJ, Mok T, Kim DW, et al. First-line crizotinib versus chemotherapy in ALK-positive lung cancer. *N Engl J Med*. 2014;371(23):2167–2177.
11. Shaw AT, Gandhi L, Gadgeel S, et al. Alectinib in ALK-positive, crizotinib-resistant, non-small-cell lung cancer: A single-group, multicentre, phase 2 trial. *Lancet Oncol*. 2016;17(2):234–242.
12. O'Sullivan Coyne G, Chen AP, Meehan R, et al. PARP inhibitors in reproductive system cancers: Current use and developments. *Drugs*. 2017;77(2): 113–130.
13. Bible KC, Ryder M. Evolving molecularly targeted therapies for advanced-stage thyroid cancers. *Nat Rev Clin Oncol*. 2016;13(7):403–416.
14. Smith MA, Altekruse SF, Adamson PC, et al. Declining childhood and adolescent cancer mortality. *Cancer*. 2014;120(16):2497–2506.
15. Schultz KR, Bowman WP, Aledo A, et al. Improved early event-free survival with imatinib in Philadelphia chromosome-positive acute lymphoblastic leukemia: A children's oncology group study. *J Clin Oncol*. 2009;27(31): 5175–5181.
16. Seibel NL, Steinherz PG, Sather HN, et al. Early postinduction intensification therapy improves survival for children and adolescents with high-risk acute lymphoblastic leukemia: A report from the Children's Oncology Group. *Blood*. 2008;111(5):2548–2555.
17. Womer RB, West DC, Krailo MD, et al. Randomized controlled trial of interval-compressed chemotherapy for the treatment of localized Ewing sarcoma: A report from the Children's Oncology Group. *J Clin Oncol*. 2012;30(33): 4148–4154.
18. Unger JM, Cook E, Tai E, et al. The role of clinical trial participation in cancer research: Barriers, evidence, and strategies. *Am Soc Clin Oncol Educ Book*. 2016; 35:185–198.
19. Adamson PC. Improving the outcome for children with cancer: Development of targeted new agents. *CA Cancer J Clin*. 2015;65(3):212–220.
20. Chuk MK, Mulugeta Y, Roth-Cline M, et al. Enrolling adolescents in disease/target-appropriate adult oncology clinical trials of investigational agents. *Clin Cancer Res*. 2017;23(1):9–12.