

Cancer Surveillance Opportunities to Meet Prevention and Control Challenges

Paulo S. Pinheiro , MD, PhD^{1,2,*}

¹Sylvester Comprehensive Cancer Center, Miami, FL, USA and ²Department of Public Health Sciences, University of Miami School of Medicine, Miami, FL, USA

*Correspondence to: Paulo S. Pinheiro, MD, PhD, University of Miami School of Medicine, Clinical Research Building, 1120 N.W. 14th St, Miami, FL 33136, USA (e-mail: ppinheiro@med.miami.edu).

News from the latest Annual Report to the Nation of the Status of Cancer by Islami et al. (1) is largely positive. Cancer mortality overall continues to decrease; for most cancers, incidence is also decreasing. Substantial gains in survival for late-stage melanoma patients, attributable to state-of-the-art immunotherapies, herald major progress in our fight against cancer. Nonetheless, the report also contains some inauspicious news. Increasing incidence trends persist for childhood cancers, which, although not accompanied by increasing mortality, are worrisome nonetheless given the multiple health problems faced by childhood cancer survivors. Colorectal cancer mortality continues to increase among adolescents and young adults, mirroring obesity trends that show no signs of abating. Among adults, the increasing mortality trends for endometrial, oral, and brain cancers; a complex picture for liver cancer; and the heavy burden of lung cancer, despite decreasing trends, remain concerning.

Cancer surveillance programs, giving rise to the data in this annual report jointly issued by the Centers for Disease Control and Prevention, the North American Association of Central Cancer Registries, the American Cancer Society, and the National Cancer Institute, are unique in their truly universal, population-based coverage. The fact that all cancers are recorded in a given population de facto precludes selection issues that may bias even the most well-designed cohort studies. Ever evolving, existing cancer surveillance programs face numerous challenges, including the collection of consistent data to facilitate trend analyses while remaining flexible to adapt in response to identified needs. Yet they are uniquely positioned to lead in furthering our understanding of some of the more troublesome trends emerging on the cancer landscape.

The Surveillance, Epidemiology, and End Results program, which covers a fairly representative 37% of the US population, has spearheaded efforts to obtain additional informative data with direct clinical interest, including diagnostic and treatment variables garnered from linkages with claims data, electronic health records, pathology reports, and aggregators of pharmacy data (2-5). To achieve completeness for these data elements at a

level that would suffice for consideration as truly population based, 85% or higher, will naturally take some time.

Meanwhile, additional linkages with data from currently available national surveys, claims, registries, etc, should be explored; meaningfully integrating these with our cancer surveillance data could clarify and/or improve the accuracy of our trend depictions. To fill crucial knowledge gaps that would improve diagnosis and treatment for cancers with complex increasing trends, including liver and endometrial cancers, consideration of additional factors is imperative.

Liver cancer, a highly fatal malignancy, has been increasing since the 1980s (6). The current report highlights complex incidence trends: stabilization among males and a slowing of the increase among females. By race-ethnicity, liver cancer trends are quite distinct: a steadily decreasing trend among Asians, a more recent decrease among Black men, and ambiguous trends among Black women, Whites, and Hispanics. This complexity results from grouping together all cases of hepatocellular carcinoma (HCC) (responsible for approximately 80% of all liver cancers) regardless of etiology. Major causes of HCC include chronic infection with viral hepatitis B (HBV) and/or C (HCV), alcohol-related disorders, and nonalcoholic fatty liver disease (NAFLD) (6). Our recent study (7) linked registry data with individual-level discharge data to enable the calculation of incidence rates by distinct HCC cause for the first time, adding clarity to this muddled picture. Patterns differed considerably by sex, age, and race-ethnicity. Liver cancer affects men more than women; however, the nature of this pattern varies by cause: alcohol-related HCC is 5-6 times more common among men; HCV-HCC occurs nearly 4 times more; NAFLD-HCC and HBV-HCC occur twice as frequently among men (7). Age is also related to etiology: the median age for NAFLD-HCC is considerably older than for HCV-HCC, partially attributable to the known HCV high-risk birth cohort of 1945-1965 (8,9). Race-ethnicity also factors in: HBV-HCC incidence is highest among Asians, HCV-HCC among Blacks, alcohol-related HCC among Hispanic males, and NAFLD-HCC among Hispanics (7). As expected, because relative improvements in liver cancer incidence have been largely

Received: June 9, 2021; Accepted: June 28, 2021

© The Author(s) 2021. Published by Oxford University Press. All rights reserved. For permissions, please email: journals.permissions@oup.com

attributed to the treatment and control of HCV and HBV infections (6), the gains observed in the current report are most pronounced among Black males and Asians of both sexes. However, this decrease in hepatitis-related HCC is likely masking increasing trends in other causes, including NAFLD-HCC (6) and possibly alcohol-related HCC, considering the recent mortality increases from alcoholic cirrhosis (10). These etiology-specific HCC trends suggest Hispanics as a particularly vulnerable group, reinforcing the need for specific targeted cancer prevention strategies that address obesity and excessive alcohol use.

The publication of hysterectomy-corrected rates for uterine, cervical, and ovarian cancers on a national level, which is largely feasible (11-13), is long overdue. Continued publication of uncorrected rates, known to be affected by substantial differences in hysterectomy proportions by race-ethnicity, renders inaccurate indicators and underestimates the substantial Black-White mortality disparity for endometrial and cervical cancers. Additionally, attributing increases in endometrial cancer primarily to obesity trends requires further scrutiny because the nonendometrioid types (serous carcinomas and carcinosarcomas), which have worse prognoses (14,15), seem less related to obesity (16). Separate analyses for endometrioid and nonendometrioid types, as suggested by the report, would be informative.

Similarly, for oral cancer, which has intriguing trends (increases among Whites but decreases among Blacks), growth in the prevalence of HPV infection alone may not fully explain the observed patterns. Rather, the intricate interplay between HPV infection, alcohol use, and the unknown role of the more recent electronic nicotine delivery systems, combined with decreasing smoking prevalence, should be clarified.

Lastly, although continued decreases in lung cancer mortality earn deserved publicity, the burden remains considerable: lung cancer continues to account for the largest proportion of deaths from cancer. Although most cases are attributable to long-term smoking, lung cancer among never-smokers (LCNS) is also very prevalent. If considered by itself, LCNS would be the seventh-most common cancer (17). Moreover, it disproportionately affects racial-ethnic minority groups and women. Fortunately, LCNS tumors tend to have higher prevalence of the EGFR mutations and ALK rearrangements that respond favorably to targeted therapies, credited for the recent favorable trends in advanced non-small cell lung carcinomas (18). Examining LCNS separately on a population basis is warranted to avoid overlooking this subset of lung cancers, especially given the magnitude of the smoking-related burden, and to better understand its unique epidemiologic characteristics.

Cancer surveillance is a fundamental tool in our battle to reduce the burden of cancer. The annual reports allow us not only to track progress and measure successes but also to identify problem areas. Being responsive to these identified areas of interest would enable surveillance programs to further meet the needs of all those interested in cancer prevention and control, including clinicians, public health program developers, researchers, and policy makers.

Funding

Funding was provided by the Bankhead Coley Research Program of the State of Florida, Grant Number 20B16. Research reported in this publication was also supported by the National Cancer Institute of the National Institutes of Health under Award Number P30CA240139.

Notes

Role of the funder: The funder had no role in the writing of this editorial or the decision to submit it for publication.

Disclosures: The author declares no conflicts of interest.

Author contributions: Writing, original draft, review and editing—PSP.

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Data Availability

Not applicable .

References

1. Islami F, Ward EM, Sung H, et al. Annual Report to the Nation on the Status of Cancer, part 1: national cancer statistics [published online ahead of print]. *J Natl Cancer Inst.* 2021;113(12):1648–1669.
2. Surveillance, Epidemiology, and End Results Program. Overview of the SEER Program. <https://seer.cancer.gov/about/overview.html>. Accessed June 6, 2021.
3. National Cancer Institute. Enhancing observational data collection to inform precision cancer research and care. <https://cancercontrol.cancer.gov/sites/default/files/2020-08/Observational-Data-Midyear-Report.pdf>. Accessed June 6, 2021.
4. Rivera D, Rubinstein WS, Schussler NC, et al. NCI and ASCO CancerLinQ collaboration to advance quality of cancer care and surveillance. *J Clin Oncol.* 2019;37(15_suppl):e18317.
5. Duggan MA, Anderson WF, Altekruse S, et al. The Surveillance, Epidemiology, and End Results (SEER) program and pathology: toward strengthening the critical relationship. *Am J Surg Pathol.* 2016;40(12):e94–e102.
6. McGlynn KA, Petrick JL, El-Serag HB. Epidemiology of hepatocellular carcinoma. *Hepatology.* 2021;73(suppl 1):4–13.
7. Pinheiro PS, Medina HN, Callahan KE, et al. The association between etiology of hepatocellular carcinoma and race-ethnicity in Florida. *Liver Int.* 2020;40(5):1201–1210.
8. Ryerson AB, Ehemann CR, Altekruse SF, et al. Annual report to the nation on the status of cancer, 1975-2012, featuring the increasing incidence of liver cancer. *Cancer.* 2016;122(9):1312–1337.
9. Pinheiro PS, Callahan KE, Jones PD, et al. Liver cancer: a leading cause of cancer death in the United States and the role of the 1945-1965 birth cohort by ethnicity. *JHEP Rep.* 2019;1(3):162–169.
10. United States Department of Health and Human Services, Centers for Disease Control and Prevention. *United States Cancer Statistics - Mortality Data: 1999-2017, WONDER Online Database; 2020.* <https://wonder.cdc.gov/wonder/help/cancermort-v2017.html>. Accessed June 6, 2021.
11. Clarke MA, Devesa SS, Harvey SV, et al. Hysterectomy-corrected uterine corpus cancer incidence trends and differences in relative survival reveal racial disparities and rising rates of nonendometrioid cancers. *J Clin Oncol.* 2019;37(22):1895–1908.
12. Baldwin LA, Chen Q, Tucker TC, et al. Ovarian cancer incidence corrected for oophorectomy. *Diagnostics (Basel).* 2017;7(2):19.
13. Temkin SM, Minasian L, Noone AM. The end of the hysterectomy epidemic and endometrial cancer incidence: what are the unintended consequences of declining hysterectomy rates? *Front Oncol.* 2016;6:89.
14. Cote ML, Ruterbusch JJ, Olson SH, et al. The growing burden of endometrial cancer: a major racial disparity affecting Black women. *Cancer Epidemiol Biomarkers Prev.* 2015;24(9):1407–1415.
15. Johnson AL, Medina HN, Schlumbrecht MP, et al. The role of histology on endometrial cancer survival disparities in diverse Florida. *PLoS One.* 2020;15(7):e0236402.
16. Setiawan VW, Yang HP, Pike MC, et al.; The Australian National Endometrial Cancer Study Group. Type I and II endometrial cancers: have they different risk factors? *J Clin Oncol.* 2013;31(20):2607–2618.
17. Samet JM, Avila-Tang E, Boffetta P, et al. Lung cancer in never smokers: clinical epidemiology and environmental risk factors. *Clin Cancer Res.* 2009;15(18):5626–5645.
18. Howlader N, Forjaz G, Mooradian MJ, et al. The effect of advances in lung-cancer treatment on population mortality. *N Engl J Med.* 2020;383(7):640–649.