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Title

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Journal

Nature reviews. Clinical oncology, 16(8)

ISSN

1759-4774

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Publication Date

2019-08-01

DOI

10.1038/s41571-019-0226-0

Peer reviewed

RISK FACTORS

Health burden in cancer survivors: below the tip of the iceberg

Eden R. Brauer and Patricia A. Ganz 

In recent decades, cancer survival has improved dramatically, resulting in a growing population of cancer survivors with chronic health needs and disease risks. While large epidemiological studies are useful in tracking broad trends in health outcomes of cancer survivors, they lack the level of detail needed to inform the delivery of appropriate clinical care and optimal allocation of resources.

Refers to Kjaer, T. K. et al. Long-term somatic disease risk in adult Danish cancer survivors. *JAMA Oncol.* 5, 537–545 (2019).

Owing to major advances in cancer screening, early detection and treatment over the past few decades, many individuals are living well beyond their initial cancer diagnosis and treatment. In the USA, the number of cancer survivors is currently estimated to be ~16.9 million, which is ~5% of the population¹. The 5-year survival across all adults diagnosed with cancer is now nearly 67%², with many survivors living ≥ 15 years after their original diagnosis³. Furthermore, older survivors are the fastest growing group (FIG. 1). These trends, while representative of major successes in cancer care, have necessitated a paradigm shift in how we think about long-term health outcomes and the quality of life of cancer survivors.

Cancer survivorship research has predominantly focused on tracking and describing the experiences and health outcomes of this previously overlooked, rapidly growing, yet poorly understood population of long-term survivors. Landmark studies, especially among childhood cancer survivors, have revealed that both having cancer and receiving treatment are associated with increased risks of physical and psychosocial morbidities many years later^{4,5}. Survivors of cancers occurring during adulthood are now also surviving for a long time after treatment; therefore, a growing interest exists in the long-term health burdens that might accrue decades after initial diagnosis. However, the extent to which the needs of cancer survivors differ from those

of the general population of ageing adults is poorly defined. The majority of studies in this area are often derived from self-reported national survey data⁶. Merged cancer registry and health insurance claims data have been used in a number of jurisdictions to look at post-cancer treatment outcomes in selected populations (such as the [SEER Medicare database](#) in the US and the [Evaluative Clinical Sciences Research Platform](#) in Ontario, Canada), but these often lack data on important sociodemographic variables and other details relating to long-term outcomes.

In an effort to differentiate the consequences of cancer and its treatment from the pathological aspects of normal ageing, Kjaer and colleagues⁷ recently utilized nationwide, population-based cancer registry data to examine the incidence and temporal patterns of long-term diseases in adult cancer survivors in Denmark. Using a cohort-cohort design, the researchers identified survivors ≥ 40 years of age when diagnosed with 1 of the 12 most common cancers in the Danish Cancer Registry between 1997 and 2014 ($n = 458,646$) and assigned five individuals without cancer (a 1:5 ratio) who were otherwise matched in terms of age, sex and income ($n = 2,121,567$). These data were linked with another national registry in order to investigate the occurrence of diseases that resulted in hospital-based care across 11 broad (level 1) ICD-10 disease categories (such as diseases of the circulatory system) and to include any comorbid conditions occurring in the 3 years before a diagnosis of cancer. Cancer survivors had a significantly higher risk of hospitalization for somatic disease than that of matched individuals without cancer across most disease categories and subgroups. Hazard ratios for the majority of disease outcomes were highest in the first few years after diagnosis and then levelled out to some degree, but most remained significantly higher than those of individuals without cancer.

While data from this study contribute to the ongoing epidemiological evaluation of long-term disease risk in adult cancer

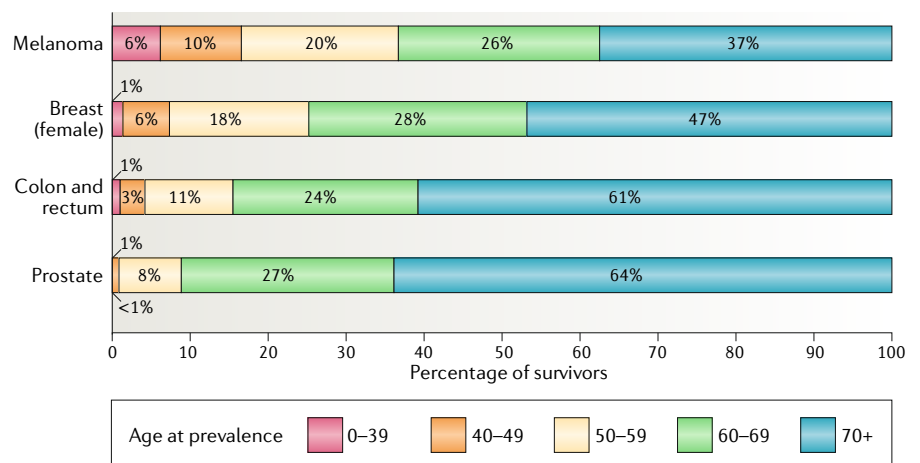


Fig. 1 | Age distribution for four common cancers in the USA, noting large number of older survivors. Reproduced with permission from REF.¹¹, Wiley-VCH.

survivors, it provides only a general overview and, aside from indicating an increased need for health-care services, does not provide sufficient detail to guide programme planning or changes in health policy. Furthermore, the generalizability of the findings to other populations that are less demographically homogeneous and/or do not have universal access to health-care might be limited. For example, the burden of chronic disease before the development of cancer in a population with less access to health-care might influence the subsequent trajectory of survivorship health problems. Similarly, the stage of cancer might be more advanced in other settings and/or populations, thus requiring more intensive cancer treatments, which can have more severe late-onset adverse effects. The lack of information on specific cancer treatments received by patients in the registry is a limitation, especially given that specific treatment exposures are known to contribute to long-term disease risks (for example, complications associated with off-target effects of thoracic radiation on the heart), and the general nature of the major disease categories provide a 'tip of the iceberg' view of the implications of a cancer diagnosis, from which opportunities for intervention are not visible.

To develop meaningful programmes for research into the outcomes of cancer survivors, more specific data on patient and treatment characteristics, as well as on the type and severity of long-term health outcomes, are needed. Efforts are currently underway to try to capture more detailed information on the post-treatment experiences of cancer survivors that could inform future approaches to clinical care. In a series of studies^{8,9}, Hashibe and colleagues used data linkages between a statewide cancer registry, electronic health records from major health systems, and birth, death and residential records to identify high-risk groups among survivors of thyroid cancer. By incorporating details related to treatment regimens, sociodemographic

characteristics and more-specific ICD-9 categories (such as atrial fibrillation versus diseases of the circulatory system) with cancer registry-level data, a more complete understanding of patient outcomes can be achieved. Progress has been made in documenting the long-term health risks and disease burdens of cancer survivors, although optimal models of survivorship care have not been fully developed or evaluated. Current opinion favours a risk-stratified approach based on treatment intensity, wherein low-risk survivors (such as those who had breast ductal carcinoma in situ) are transitioned to primary care for follow-up care, while high-risk survivors (such as those who required allogeneic stem cell transplantation) continue to receive specialized oncology care, and the intermediate-risk group are generally managed according to a shared care model. A more detailed approach to examining cancer survivorship outcomes similar to that adopted by Hashibe et al.^{8,9} could provide a basis for delineating risk strata and informing appropriate care models.

Clearly, long-term health risks associated with cancer and its treatments take on more tangible meaning as survivors become more likely to live long enough to have them. Growing old is becoming common among cancer survivors; therefore, the oncology community faces a new challenge of understanding the long-term and late-onset effects of cancer and its treatment in the context of ageing. The emerging theory of accelerated ageing, in which these effects (disease and treatment effects versus ageing effects) are not distinct outcomes but rather deeply intertwined processes, further complicates this issue¹⁰. According to this theory, intrinsic and extrinsic stressors during cancer treatment can drain the physiological reserves of an individual, resulting in an accelerated ageing process and an altered trajectory of decline in general health. Preparing health-care systems to deliver high-quality, risk-stratified care to the growing number

of long-term cancer survivors will require a sophisticated understanding of the interplay between cancer-related risks of morbidity as individuals age over time.

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<https://doi.org/10.1038/s41571-019-0226-0>

1. Bluethmann, S. M., Mariotto, A. B. & Rowland, J. H. Anticipating the "Silver Tsunami": prevalence trajectories and comorbidity burden among older cancer survivors in the United States. *Cancer Epidemiol. Biomarkers Prev.* **25**, 1029–1036 (2016).
2. National Cancer Institute. Cancer stat facts: cancer of any site. *SEER* <https://seer.cancer.gov/statfacts/html/all.html> (2019).
3. De Moor, J. S. et al. Cancer survivors in the United States: prevalence across the survivorship trajectory and implications for care. *Cancer Epidemiol. Biomarkers Prev.* **22**, 541561–541570 (2013).
4. Oeffinger, K. C. et al. Chronic health conditions in adult survivors of childhood cancer. *N. Engl. J. Med.* **355**, 1572–1582 (2006).
5. Armstrong, G. T. et al. Aging and risk of severe, disabling, life-threatening, and fatal events in the childhood cancer survivor study. *J. Clin. Oncol.* **32**, 1218–1227 (2014).
6. Yabroff, K. R. et al. Burden of illness in cancer survivors: findings from a population-based national sample. *J. Natl Cancer Inst.* **96**, 1322–1330 (2004).
7. Kjaer, T. K. et al. Long-term somatic disease risk in adult Danish cancer survivors. *JAMA Oncol.* **5**, 537–545 (2019).
8. Blackburn, B. E. et al. Aging-related disease risks among young thyroid cancer survivors. *Cancer Epidemiol. Biomarkers Prev.* **26**, 1695–1704 (2017).
9. Park, J. et al. Risk factors for cardiovascular disease among thyroid cancer survivors: findings from the Utah Cancer Survivors Study. *J. Clin. Endocrinol. Metab.* **103**, 2468–2477 (2018).
10. Henderson, T. O., Ness, K. K. & Cohen, H. J. Accelerated aging among cancer survivors: from pediatrics to geriatrics. *Am. Soc. Clin. Oncol. Educ. Book* **34**, e423–e430 (2014).
11. Miller, K. D. et al. Cancer treatment and survivorship statistics, 2016. *CA Cancer J. Clin.* **66**, 271–289 (2016).

Competing interests

The authors declare no competing interests.

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