Hypothesis/Commentary

Cancer Epidemiology, Biomarkers & Prevention

The Evolving Scale and Profile of Cancer Worldwide: Much Ado About Everything

Freddie Bray

Abstract

Today, cancer is responsible for one in three premature deaths from noncommunicable diseases worldwide, and the number of annual cancer diagnoses will rise to well over 20 million by the year 2030. That cancer is of profound importance to future global health reflects both recent gains in human development as well as mortality transitions that are centuries old. Still, cancer is complex, and the extensive geographical and temporal heterogeneity alerts us to the need for targeted, local approaches to cancer control. The study of trends in specific cancer types remains essential in monitoring and evaluating such strategies and as a descriptive tool for hypothesizing possible contributory factors. Of greatest necessity is an expansion of the availability of high-quality data. To improve the limited cancer incidence data available in low- and middle-income countries (LMIC), the Global Initiative for Cancer Registry Development (http://gicr.iarc.fr) is an international partnership supporting countries to redraw the surveillance map. *Cancer Epidemiol Biomarkers Prev; 25(1); 3–5. ©2015 AACR.*

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Using national estimates from GLOBOCAN (1) and the high-quality incidence from population-based cancer registries (PBCR) compiled in the *Cancer Incidence in Five Continents* series (2), Torre and colleagues (3) elucidate the key patterns and trends in common cancers worldwide, and the future prospects for cancer control action. As a report card on the global burden, the study documents the rising number of cancer cases and the significant impact the disease now imposes on every world region. Although there remains considerable diversity in the cancer profiles regionally, cancer has become a significant public health problem irrespective of level of income.

Globally, almost 22 million new cancer diagnoses are predicted in 2030 based solely on population ageing and population growth, a 53% increase on the 14.1 million new cases in 2012. Such projected increases are likely underestimated when observable recent trends in common cancers are factored in (4). The greatest proportional increases will be in countries currently indexed with the lowest levels of human development. Given the burden will overwhelm many lower-income countries and the costs of cancer diagnosis and therapy are set to continue to escalate, an acceleration of primary prevention measures and their local integration into existing health structures has been called for; prompt action will ultimately lead to net savings (5).

The cancer transition can be linked to gains in human development in individual countries: incidence rates of certain cancers (lung, breast, colorectum) are increasing in many low- and middle-income countries (LMIC), whereas several major cancers, associated with infection or poverty (cervix, stomach, liver), appear on the decline. A broad explanation for the rising incidence is the shifting distribution of risk determinants in transitioning countries toward those seen mainly in high-income settings (4). As the authors note (3), among the key factors are smoking, excess body weight, and physical inactivity, alongside altered childbearing patterns.

It is instructive to examine cancer as one of several major noncommunicable diseases (NCD) contributing to the global disease burden, and the underlying reasons for their remarkable prominence today: deaths from NCDs comprise more than two thirds of all deaths globally, whereas cancer is responsible for close to one in three premature NCD deaths (defined as ages below 70 years), and the leading premature cause of death in 48 countries (http://www.who.int/gho/en/). That NCDs and specifically cancer will have profound importance on future global health reflects both recent gains in human development and mortality transitions that are centuries old. The evolution can be viewed as part of an continuing epidemiologic transition, whereby improvements in nutrition, sanitation, hygiene and medical interventions, and the near eradication of malnutrition and pandemics of infection has led to an age of "degenerative and man-made diseases" (6). Quantification of the resulting demographic transition characterized by fertility declines, increasing longevity, and a large and rising number of persons diagnosed with NCDs, is fundamental to public health planning (7). The growing elderly population and marked declines in cardiovascular disease now observed in many highly-developed countries increases the relative share of cancer mortality, heightens the influence of cancer on future mortality patterns, and places the disease as the main obstacle to continued improvements in life expectancy.

Still, there is much geographical and temporal heterogeneity in regions and countries, and deviations from this simple epidemiologic model alert us to the need for targeted, local approaches to cancer control. Examples include the double burden of cancer (high residual burden of infection-related plus increasing westernization-related cancers) reported in Eastern Africa (8), the increasing risk of death from cervical cancer among young women in many middle- and high-income countries in Eastern Europe

Cancer Surveillance Section, International Agency for Research on Cancer, Lyon, France.

Corresponding Author: Freddie Bray, International Agency for Research on Cancer, 150 cours Albert Thomas, F-69372 Lyon Cedex 08, France. Phone: +33 4 72 73 84 53; E-mail: brayf@iarc.fr

doi: 10.1158/1055-9965.EPI-15-1109

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and the Former Soviet Union (9), and the high rates of lung and cervical cancer in many indigenous populations relative to their nonindigenous counterparts in four of the highest income countries (10).

Turning to the rationale for such temporal studies as a cornerstone of descriptive epidemiology, the paper by Torre and colleagues (3) is one study among hundreds of expositions of cancer trends over time published each year in peer-reviewed journals. That their number has exponentially grown over the last half century emphasizes their continued relevance, coupled with an expansion of the availability of routine data worldwide, particularly in high-income counties. In measuring how risk of cancer evolves at the population level, the study of cancer trends provides clues to the underlying determinants but also a means to monitor and evaluate cancer control strategies. Changes in cancer incidence rates over time allow, in the absence of artifacts, consideration of plausible mechanisms of, and changes in, environmental exposures, time-lagged by an approximation of the latency period. The marked variations in rates across populations and over time, as reported by Torre and colleagues (3), are considered by Doll and Peto as fundamental evidence of the avoidability of cancer (11): genetic factors only have a minor impact on time trends of cancer, unless there are sufficiently large migrational influxes and exoduses in the population under investigation (12). These should be readily identified, and in addition, would impact on the trend rather slowly relative to environmental determinants (13). That said, an inherent weakness in temporal studies is that rapid detection of changing trends is not easily achieved for most cancers in most populations (14). Hypotheses are more readily generated when changes in trends impact over a relatively short timeframe rather than over a number of decades (14). Vivid examples in recent times involve the increasing use of diagnostic techniques and a subsequent increased detection of asymptomatic disease. A rapid rise in prostate cancer incidence in the Nordic countries (15) following the commercial availability of the PSA test, and the equivalent trend in thyroid cancer incidence in South Korea, in an era of fine-needle biopsy testing and new imaging technologies (16).

As Estève has noted, each of the stages of data collection, analysis, and presentation bring their own set of problems (17). Even at the major cancer site level, there are issues concerning data quality and other detectable artifacts in interpreting time trends meticulously addressed by Muir and colleagues (18). In most instances, specific problems with a given site are recognised and the effects on the time trend, at least in terms of its likely consequence on the true underlying trend, reasonably well understood. As for methods, age-period-cohort (APC) analyses remain a vital tool in descriptive epidemiology, despite the overhead of understanding required in appropriately dealing with the non-identifiability of the linear components of age, period, and cohort effects in APC models, as definitively reviewed and clarified by Clayton and Schifflers (19, 20) and the approaches of Holford (21, 22). Such analyses have an illustrious history in cancer epidemiology. Early seminal work included studies from Korteweg (23) and Case (24) examining lung cancer mortality, MacMahon investigating breast cancer incidence (25) and Barrett applying cohort-based methods to bladder cancer mortality (26). Innovative generational studies sought to explain whether adult disease rates are a product of earlier life: Beral hypothesized a link between birth cohort trends in cervical cancer incidence and corresponding rates of sexually-transmitted diseases (27), and Moller postulated that the reduced incidence of testicular cancer among males born during World War II in Denmark resulted from an altered supply of provisions during the German military occupation (28). Today, APC modeling is easily undertaken in statistical packages (e.g., http://www.stata-journal.com/article.html?article=st0211). The commands implemented provide unique solutions assumptions on the net drift (20), ideally founded on biologic or epidemiologic evidence defined *a priori* (21). In spite of this, many temporal studies continue to focus on displays of trends in age-standardized rates at the exclusion of graphical and model-based APC approaches.

If we agree the investigation of cancer trends over time are still highly relevant, if complex and with some limitations, are there areas requiring further exploration or better measurement? Combined exploration of trends of incidence, mortality, and survival are still seldom undertaken even where the underlying data are available and of reasonable quality. Their routine study serves to confirm and clarify the often complex underlying biologic, epidemiologic, and clinical processes, surely missed by the common focus on a single measure. Equally, the study of cancer-specific incidence stratified by defined histologic groups or anatomical subsite can provide insight where there is evidence of subgroup heterogeneity in cancer biology and etiology, or amenability to prevention, early diagnosis and screening. Despite their research potential, interpretation remains confined to a limited number of datasets where the proportion of cases with unspecified histology is relatively low.

Without doubt, the biggest advance would be an expansion of availability and better measurement of data in every country of the world, an immense but not insurmountable problem in an era of e-health and m-health. Only one-third and one-fifth of (mostly high-income) countries are presently able to report high quality incidence and mortality data, respectively. For incidence, reliable local information at the population level is feasible even in the lowest income settings, through the planning and development of PBCR (29). These institutions represent a critical means to support national prioritization and evaluation of targeted and resource-dependant cancer control measures. As a means to improve the limited data in LMIC, the Global Initiative for Cancer Registry Development (GICR, http://gicr.iarc.fr) is an international partnership that shares resources, exchanges information and develops joint strategies to aid countries in producing local cancer data of high quality for cancer control action. The approach has been endorsed by WHO in supporting countries to plan and develop PBCR as a means to collect cancer incidence by type, one of 25 indicators used to monitor the Global Action Plan on NCDs 2013-20 via the Global Surveillance Framework. More recently, the UN Sustainable Development Goals (https://sustainabledevelopment.un.org/) includes a specific target and a priority for all countries worldwide of a one-third reduction in premature mortality from NCDs by 2030. In a complementary vein, Bloomberg Philanthropies have formed partnerships and alliances in their Data for Health initiative (http://www.bloomberg.org/program/public-health/data-health/), an ambitious global programme that includes efforts to improve the collection of deaths information in 20 LMIC over the next years. An

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equivalent investment in cancer registries in countries in transition would ensure future updates of the global review in this issue (3) are enriched and enlivened by more comprehensive, comparable and accurate data, serving both global and national cancer planning purposes.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Received October 16, 2015; accepted October 29, 2015; published OnlineFirst December 14, 2015.

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