How can global incidence estimates support childhood cancer control?

Sputnik/Science Photo Library

Published Online
February 26, 2019
http://dx.doi.org/10.1016/S1470-2045(19)30039-7

See Articles page 483

Information about the incidence of cancer is collected, analysed, and disseminated by population-based cancer registries. It is the basis for a planned response to demands on health services, the evaluation of the effect of interventions, and the study of associations between putative risk factors and variations in cancer incidence. Efficient cancer registration has become a landmark of a well-functioning advanced public health system, although it tends to be an exception, rather than the rule, in low-income countries.[1]

In *The Lancet Oncology*, Zachary Ward and colleagues[2] propose a microsimulation model of estimation of childhood cancer incidence in 200 countries and territories worldwide, by age group and tumour type. Using this novel approach, they determine not only the numbers of diagnosed but also undiagnosed paediatric cancers. These estimates are supported by a theoretical cancer diagnosis cascade, supplemented by demographic data, recorded data from population-based cancer registries, and proxy parameters of access to primary care and referral to a non-oncology specialised care reported in the WHO Global Health Observatory. The model is calibrated to agree with the published registries' data.[1] The authors calculate that 397 000 new cancers occurred in the world's childhood population (age 0–14 years) in 2015. This number includes 224 000 diagnosed cases and 172 000 presumed undiagnosed cases.[2] Although the global estimate of diagnosed cancers is relatively close to the 200 000 cases predicted in GLOBOCAN for 2018,[3] or 215 000 annual cases during the 2000s, the number of undiagnosed cases expands the global estimate by almost 80% (172 000 of 224 000). The proportion of undiagnosed cases varies from more than a half of the total numbers in Africa, south-central Asia, and Oceania to only a few percent in North America.[2] The methodology of the study is innovative and appealing, given that it quantifies for the first time the number of undiagnosed cases, and the potential needs for paediatric oncology care.

For the **International Agency for Research on Cancer annual cases during the 2000s** see https://www.iarc.fr/wp-content/uploads/2018/07/pr241_E.pdf

Population-based cancer registries use international standards to ensure high quality and comparability of their data. However, even the best quality registries are unable to capture data for undiagnosed cancers, since they are not revealed by medical services. Treatment cannot be provided and the patients will almost certainly die, although cancer will not be listed on a death certificate, unless a careful autopsy is done. The cause of death would be either ill-defined or likely to fall into a category of infectious diseases.

For the **WHO mortality database** see https://www.who.int/healthinfo/mortality_data/en/

What are the underlying reasons for a failure to diagnose cancer in a child in low-income and middle-income countries? Reaching the frontiers of medical knowledge would only be relevant in a tiny proportion of patients with rare or new entities, while uninformed family attitude towards the symptoms, together with the prohibitive cost of care, might explain a large degree of underdiagnosis.[4] In all age groups, the majority of preventable cancer deaths have been ascribed to a failure to seek care, although the limited capacity of health-care systems was also implicated.[5] In children, cancer will rarely be considered a diagnostic option by primary care providers. Their vigilance will influence referral to a specialised institution, which might also depend on the adequacy of facilities, trained personnel, and diagnostic procedures.[6]

To what extent should individual countries rely on the national estimates developed by Ward and colleagues?[2] Where national data are available and used in the presented model, the proposed estimates should be robust. Yet the only way to validate these new estimates is for countries to ensure efficient provision of representative data.[7] Only local surveillance systems can provide the data necessary for planning and evaluation of childhood cancer burden and services.

What needs to be done? First, increasing registration coverage and improving the data quality of existing registries would help to reduce the estimation error, which is equivalent to 21 000 cases globally, based on the 95% uncertainty interval.[2] This process includes improving staffing and equipping pathology laboratories to enable accurate diagnosis. Second, developing efficient vital statistics systems would help to ensure registration completeness and unveil the magnitude of underdiagnosis of cancer. Currently, some mortality statistics are available in only four of

34 low-income countries and in 21 of 47 lower-middle-income countries. Finally, research programmes investigating potential cancer determinants, especially in the areas with the least described cancer burden and highest prevalence of infections, would enable validation of the estimates developed by Ward and colleagues,[2] and possibly suggest solutions to childhood cancer management in these populations.[8]

Eva Steliarova-Foucher
Section of Cancer Surveillance, International Agency for Research on Cancer, WHO, Lyon CEDEX 08, France
steliarova@iarc.fr

I declare no competing interests. The author is a staff member of WHO. The author alone is responsible for the views expressed in this Comment and they do not necessarily represent the decisions, policy, or views of WHO.

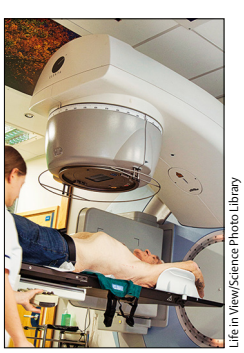
1 Steliarova-Foucher E, Colombet M, Ries LAG, et al. International incidence of childhood cancer, volume 3. 2017. Lyon, France: International Agency for Research on Cancer. http://iicc.iarc.fr/results/ (accessed Dec 20, 2018).
2 Ward ZJ, Yeh JM, Bhakta N, Frazier AL, Atun R. Estimating the total incidence of global childhood cancer: a simulation-based analysis. *Lancet Oncol* 2019; published online Feb 26. http://dx.doi.org/10.1016/S1470-2045(18)30909-4.
3 Global Cancer Observatory: Cancer Today. International Agency for Research on Cancer. 2018. https://gco.iarc.fr/today (accessed Dec 20, 2018).
4 Magrath I, Steliarova-Foucher E, Epelman S, et al. Paediatric cancer in low-income and middle-income countries. *Lancet Oncol* 2013; **14:** e104–16.
5 Kruk ME, Gage AD, Joseph NT, Danaei G, Garcia-Saiso S, Salomon JA. Mortality due to low-quality health systems in the universal health coverage era: a systematic analysis of amenable deaths in 137 countries. *Lancet* 2018; **392:** 2203–12.
6 Kruger M, Hendricks M, Davidson A, et al. Childhood cancer in Africa. *Pediatr Blood Cancer* 2014; **61:** 587–92.
7 Boerma T, Victora C, Abouzahr C. Monitoring country progress and achievements by making global predictions: is the tail wagging the dog? *Lancet* 2018; **392:** 607–09.
8 Barr AL, Young EH, Smeeth L, et al. The need for an integrated approach for chronic disease research and care in Africa. *Glob Health Epidemiol Genom* 2016; **1:** e19.

CHISELing a path forward in the treatment of early-stage non-small-cell lung cancer

Rapid technological changes inherently conflict with the slow pace of evidence-based medicine. In technology-driven specialties such as radiation oncology, it is difficult for randomised data to keep up as treatment tools evolve. Often, new approaches are introduced into clinical practice without supporting level 1 evidence. Adoption of a useful technology into clinical practice without level 1 evidence from randomised controlled trials allows immediate access for patients, and if the technology proves beneficial, outcomes are improved. But premature adoption of a technology that is later proven to be unhelpful leads to unnecessary cost and possibly harm. Differentiating between these two scenarios in advance, before randomised controlled trials, is often impossible. Moreover, even when randomised controlled trials are launched, a large proportion of them fail, leaving us without a high level of evidence despite enormous efforts.[1] Even successful trials can be irrelevant if a technology has drastically improved since the trial was launched.

One example of this conflict is the widespread adoption of proton therapy (an expensive technology that might better spare healthy tissues than conventional photon treatment) without level 1 evidence of benefit. Only now, decades after its introduction, are large randomised controlled trials underway. With one study already reporting negative results,[2] albeit using an older technology, the results of the forthcoming randomised trials are far from certain. Nonetheless, in some centres, proton therapy is aggressively marketed, their websites promoting incorrect claims that are not supported by data.[3] We should be mindful that medical reversal—the abandonment of a treatment previously presumed to be beneficial—is common in medicine.[4] Until randomised controlled trials are done, establishing whether a new technology represents a true step forward, or a step in the wrong direction, is difficult.

In the context of these difficulties, the completed phase 3 CHISEL trial by David Ball and colleagues reported in *The Lancet Oncology*[5] is a major step forward. CHISEL tested the effect of stereotactic ablative radiotherapy (SABR) in early-stage non-small-cell lung cancer (NSCLC) and compared the therapy with older radiotherapy techniques. CHISEL enrolled patients with peripherally located stage 1 NSCLC who were either unfit for surgery or refused surgery, and randomly assigned them to either conventional radiotherapy (66 Gy in 33 fractions of 2 Gy or 50 Gy in 20 fractions of 2·5 Gy) or SABR (54 Gy in three 18 Gy fractions or 48 Gy in four 12 Gy fractions). SABR achieved improvements


Life in View/Science Photo Library

Published Online
February 12, 2019
http://dx.doi.org/10.1016/S1470-2045(18)30953-7

See Articles page 494