

# Social inequalities and cancer: the imperative to act

Christopher P. Wild

“We are not concerned with the very poor. They are unthinkable, and only to be approached by the statistician or the poet. This story deals with gentleness, or with those who are obliged to pretend that they are gentleness.”

*Reproduced with permission from The Provost and Scholars of King's College, Cambridge and The Society of Authors as the Literary Representative of the Estate of E.M. Forster*

## Cancer, a disease of difference

Cancer is a disease of difference. It can occur in almost any part of the body, and within any particular organ may originate from more than one type of cell. Differences abound at the molecular level, where a unique, complex array of genetic and epigenetic alterations is acquired in each tumour, albeit generally affecting a common set of key molecular pathways. These alterations collectively shape the malignant phenotype. The natural history of each cancer is also unique: cancers progress through different stages, which may or may not include recognizable precancerous lesions, in processes that can span decades. These combined molecular, cellular, and morphological differences determine the inherent

nature of each individual tumour. In turn, these resultant characteristics influence the requirement for particular treatments from the available spectrum of therapeutic modalities. These characteristics also provide the theoretical foundation of the new era of precision cancer medicine; an example is immunotherapy, which specifically seeks to target the underlying cancer pathways in a given patient.

Cancer is a disease of difference not only at the micro or molecular level but also at the macro or societal level. The overall cancer incidence (excluding non-melanoma skin cancers) differs markedly worldwide; annual age-standardized rates in men and women combined are about 300 per 100 000 in Australasia, North America, and

western Europe, and one third of that in India and in many countries in the Persian Gulf and sub-Saharan Africa (Bray et al., 2018). The global increase in cancer burden is projected to fall most heavily on the low- and middle-income countries; this is predominantly a reflection of demographic changes (Stewart and Wild, 2014).

Country-specific incidence rates for cancers of specific organ sites vary more dramatically than the overall cancer incidence rates do (Bray et al., 2018). For example, oesophageal cancer is one of the most common cancers in men in parts of eastern and southern Africa but is generally uncommon in western and central Africa. The estimated age-standardized rate of liver cancer in Mongolian women is 40–50 times

that in Norwegian women. Dramatic geographical variations in incidence largely reflect the prevalence of and level of exposure to different risk factors. As a consequence, cancer patterns can change over time within a country. While cervical cancer rates in the Nordic countries have fallen markedly over the past few decades, there have been striking increases in parts of central and eastern Europe; these increases reflect changing sexual practices, an associated increased prevalence of human papillomavirus (HPV) infection, and a continued absence of effective screening programmes. For example, incidence rates in Bulgaria and Romania are now similar to those in several sub-Saharan African countries (Bray et al., 2018).

Similarly to the observations on incidence, cancer mortality and survival vary worldwide. In high-income countries such as Australia, the Republic of Korea, and the USA, an average of 9 out of 10 women diagnosed with breast cancer survive the disease; in parts of Africa and India, the proportion is closer to 1 in 2 (Allemani et al., 2018). Underlying these statistics are distinct cancer journeys experienced by women in these different parts of the world, from the awareness of symptoms onwards. Although data are sparse, in low- and middle-income countries the evidence of less favourable cancer outcomes is clear. A particularly poignant example is childhood leukaemia. Progress to high survival estimates in wealthier countries contrasts starkly with the desperately low survival rates that continue to be seen in economically poorer settings, despite the availability of inexpensive and effective treatments that

can offer decades of additional life to those children with access (Petridou et al., 2015; Allemani et al., 2018).

### **Cancer differences reflect social inequalities**

How far do these differences that characterize cancer reflect social inequalities? One does not have to look too hard or too long for evidence of an impact. For example, the hepatitis B virus (HBV) vaccine was available much earlier in the wealthier countries, which had a lower prevalence of chronic HBV infection and a lower incidence of liver cancer, than in the economically poorer countries where it will eventually make its greatest impact. An unfolding and related example is that of the new and effective, but expensive, drugs to treat hepatitis C virus (HCV) infection. There is also a risk that availability of the HPV vaccine will repeat the history of the HBV vaccine, unless forceful strategic measures are taken to enable access where infection is most common. Tobacco control measures have started to drive down cigarette smoking and lung cancer rates in several high-income countries, but the prevalence of smoking continues to climb in some low- and middle-income countries. The national differences in exposures and in the availability of preventive interventions are most often mirrored by shortfalls in terms of access to early detection, treatment, and palliative care.

The above-mentioned inequality in cancer rates between countries is paralleled within countries. Among countries with very high or high Human Development Index (HDI), survival rates are higher among inhabitants with high socioeconomic status (SES) than among those with low SES. In the USA, for 14 of 21

cancer sites diagnosis at a more advanced stage was strongly associated with measures of poverty; for the other 7 sites there was no significant difference, but these were cancers that were difficult to diagnose early (Boscoe et al., 2016). In low- and middle-income countries, childhood cancer survival rates were uniformly worse in groups with lower SES (Gupta et al., 2014); a gradient in survival by SES is also striking in the USA (Petridou et al., 2015). Even in countries with widely accessible high-quality health care and health insurance, differences in childhood cancer survival by SES persist (Adam et al., 2016).

The effects of inequalities on cancer incidence and mortality within countries also manifest themselves in the case of vulnerable or neglected groups. For example, in Australia, Canada, New Zealand, and the USA, the incidence rates of several preventable cancers, such as those of the cervix, liver, and lung, are generally higher in the Indigenous populations than in the non-Indigenous populations. Some cancers associated with behaviours typical of those countries (so-called industrialized lifestyles) are less common among Indigenous populations, for example, breast and colorectal cancers (Moore et al., 2015). Other vulnerable groups may also have cancer rates that differ from those of the general population. For example, HIV-positive women have far higher rates of cervical cancer than HIV-negative women do, because of their greater susceptibility to HPV infection (Clifford et al., 2005).

When cancer statistics are compared with different parameters of wealth, education, and life expectancy (as for the HDI) or other SES indicators, it is important to remain

conscious of the distinction between analyses made between countries and those made within countries. Several cancers have lower incidence rates in low- and middle-income countries because the risk factors that accompany wealth or industrialization have not yet become prevalent, illustrating the benefits of remaining free from these carcinogenic risks. Avoiding repeating the mistakes of the wealthy countries is a cancer control opportunity in itself. Despite lower incidence rates for some cancers, mortality rates in low- and middle-income countries may be similar to those in high-income countries because of a lack of access to timely diagnosis and treatment; a global comparison of breast cancer incidence and mortality rates is a prime example (Bray et al., 2018).

Between-country comparisons primarily reflect inequalities in the overall pattern of exposure to risk factors, as well as in the availability of and access to the relevant health services. Comparisons within a country reveal how inequalities between groups of fellow citizens affect their cancer outcomes, at least partially reflecting differences in access to the available health services. International comparisons can guide national cancer control priorities, whereas the subtleties of cancer patterns within countries may reveal important indicators for targeted cancer control measures.

### Detailing the nature of social inequalities and cancer

Although the inequalities narrative of “poor is worse” may hold as a general truth where cancer is concerned, the details merit scrutiny, particularly within countries. For some can-

cers, including those of the thyroid, prostate, breast, and colon, the incidence is higher among groups with higher SES. For cancers of the thyroid, prostate, and breast, this at least partially reflects detection of an excess of early-stage cancers as a result of differential participation in cancer screening, either organized or opportunistic. Although there are net benefits of screening for breast cancer in terms of reduced mortality (Lauby-Secretan et al., 2015), this is not the case for thyroid or prostate cancer, where benefits are lacking and overdiagnosis and overtreatment are common (Vaccarella et al., 2016; Martin et al., 2018). In the USA, thyroid cancer incidence was reported as being higher among the more affluent, whereas the diagnosis rates of late-stage thyroid cancer did not differ by level of affluence (Boscoe et al., 2016). In contrast, although the incidence of prostate cancer was also higher among the more affluent, late-stage prostate cancer was diagnosed more frequently in those in the poorer groups. These types of comparisons merit further study, taking account of health services accessed by different societal groups.

The incidence of colon cancer rises as countries transition to higher levels of human development (Arnold et al., 2017). This partly reflects increased exposure to known risk factors, including obesity, physical inactivity, and a high intake of red and processed meat. However, when increasing exposure to such risk factors accompanies a country’s transition to a higher HDI, it is often the groups with the lowest SES that sooner or later experience the highest exposures and associated cancer incidence rates. There may be an initial, generalized increase in

exposure, but this is usually followed by a divergence between the groups with higher and lower SES as the problem is identified and addressed by cancer control measures; such measures are differentially adopted across strata of SES. The tobacco epidemic has certainly followed this pattern in some countries. Another striking example is childhood obesity; national rates are starting to level off or fall in some high-income countries but continue to rise in countries still undergoing transition (Abarca-Gómez et al., 2017). The effects are more subtle within a country, however. It is the SES groups with access to energy-dense diets that are at increased risk of obesity; in high-income countries, this tends to be those with lower SES, and in low- and middle-income countries, this tends to be those with higher SES (Wang and Lim, 2012). For example, in the United Kingdom, 13% of children living in the most deprived areas are obese compared with 6% in the least deprived areas, and the gap is widening (Statistics Team, NHS Digital, 2018).

Precise measurement of inequalities is required to test hypotheses in well-designed studies. The measures of inequality used may encompass many components, but analysis at such a level of agglomeration can mask important individual elements within a composite measure. Scope is also crucial. There are well-described variations in exposures to risk factors that vary with SES, such as tobacco use, alcohol consumption, obesity, and poor-quality diet. However, the relevant measures of inequality extend further into broader social determinants of disease, including housing, education, and transport (McDaniel et al., 2019). The disaggregation of both exposures to risk factors and cancer

outcome data at the national level serves to reveal differences in incidence, mortality, survival, and other parameters such as disability-adjusted life years by sex, age, race, ethnicity, education, occupation, residence, wealth, social capital, social standing, and social support structures (e.g. access to health systems). The deeper one delves, the greater are the differences revealed in cancer rates as a result of social inequalities.

Cancer inequalities are not restricted to measures of the physical nature of cancer. Cancer is *lived* differently. There are national and subnational differences in understanding of and beliefs about cancer, what causes it, and how to prevent it. There are also differences in symptom presentation, access to early detection and diagnosis, participation in cancer screening programmes, and access to preventive interventions. In all of these areas, knowledge and beliefs, which may vary with SES, have a bearing on cancer outcomes (McCutchan et al., 2015). Variations in knowledge about the disease accompany and often influence the lived experience of a cancer diagnosis, treatment, and care. Access to and the user-friendliness of some of the new information technologies, including social media, are less influenced by SES; such technologies can therefore be tailored to inform specific groups within populations that are difficult to reach by traditional means, in turn reducing inequalities (Viswanath et al., 2012).

In summary, social inequalities form an intimate component of the observed differences in cancer rates between and within countries. Social inequalities are even written into the text of the altered genomes of cancer cells, referred

to at the beginning of this chapter, as the links between exposures and tumour-specific mutations are elucidated (Hollstein et al., 2017). To develop fully adequate cancer control programmes that benefit the whole population, an understanding of the role of social inequalities in all aspects of the cancer continuum not only is required but also must be translated into action.

### **The role and commitment of IARC as the cancer agency of the World Health Organization**

In this context, what is the rationale for a new IARC Scientific Publication on social inequalities and cancer, given that in 1997 IARC published a Scientific Publication titled *Social Inequalities and Cancer* (Kogevinas et al., 1997)?

First, the state of the science merits, or even calls out for, a full consideration of the available evidence. A wealth of data has been accumulated over the past two decades, data that are far more extensive, encompassing more disciplinary divides, than in the original publication. IARC is perfectly situated to take on the task of assimilating and critically evaluating this wealth of information, and can maintain an international perspective while highlighting the outstanding gaps in knowledge and the relatively low levels of investment in this area compared with others in cancer research and control.

Second, the possibility of translating the scientific evidence on social inequalities and cancer – these precious building blocks – into practice and delivering change has perhaps never been better. There is a timeliness of opportunity, and this could mark one of those all-too-

rare occasions where the science might just coalesce with the political priority being given to noncommunicable diseases, including cancer. The United Nations Sustainable Development Goals not only recognize noncommunicable diseases as a barrier to sustainable development but also provide the more fundamental starting point of reducing inequalities as a social goal, a matter of justice and human rights. In turn, universal health coverage, a cornerstone of the World Health Organization, is another key part of the solution, enabling everyone to have access to “preventive and curative healthcare services, without falling into poverty” (Vázquez and Ghebreyesus, 2017). Universal health coverage can enable access to some of the fundamental components of comprehensive cancer control measures for all.

Third, anyone who has experience of the cancer burden internationally can testify to the fact that the disease places a universally heavy social and economic burden on individuals, families, communities, and populations. More than that, as outlined in this book, cancer is a universal illustration of inequality between human beings in terms of risk of developing the disease, timely diagnosis, access to treatment and care, knowledge, the chance to experience life beyond a cancer diagnosis, and even hope. Social responsibility also drives IARC, as an international research agency with a public health focus, to use science to effectively decrease inequalities in cancer.

There are many areas of social inequalities and cancer to cover in this volume, but three stand out as fundamental to the goals of IARC.

*Data collection.* There is a need to capture data on the many dimensions of social inequalities that have an impact on the cancer burden. The former Director-General of the World Health Organization, Dr Margaret Chan, used to say, “What gets measured gets done.” In much of the population-based research on cancer, information on a sufficiently broad range of social and economic parameters is simply not collected. Without the data, there is no reliable basis for analysis and evidence-based change. Therefore, unsurprisingly for a cancer research agency, the collection of higher-quality and more systematic data on social inequalities and cancer must be prioritized.

*Prioritizing prevention.* Emphasizing prevention as a core component of reducing social inequalities in cancer is also critical. Primary prevention offers an effective mech-

anism to reach the greatest proportion of a given population and hence would tend to reduce inequalities. However, a disproportionately lower level of investment is allocated to preventing cancer compared with investments made in other areas, such as development of some of the high-tech medical devices and precision cancer medicines whose introduction may even exacerbate the existing inequalities. At the very least, every new cancer control initiative should be evaluated for whether it will reduce or increase the social inequalities faced in cancer. In terms of research funding, prevention is the poor relative within the full spectrum of cancer control, particularly given the limited scope for private sector investment. This situation poses a strategic question for public and civil society investment in terms of what priorities are set for cancer research funding.

*Evidence-based.* Finally, in seizing this window of opportunity and seeking to bring the science to bear on policies to reduce social inequalities in cancer, there is a need to be rigorous in the description of the extent and limits of the available data. One must tread carefully to avoid crossing the line between science and advocacy. In his remarkable chapter titled “Poverty and cancer” in the 1997 IARC publication, the former IARC Director Lorenzo Tomatis wrote, “In discussing poverty and health, one enters a territory in which the borders between public health, the social sciences and politics are indistinct” (Tomatis, 1997). In producing the current volume this statement was kept in mind as the authors analysed what is known and what is not, and spelled out clearly the implications of both.

## Key points

- Cancer occurrence, causes, outcomes, and required control measures differ markedly both between and within countries. However, these differences are not neutral in nature but instead frequently reflect social inequalities in the distribution of cancer risk factors and access to prevention measures, early detection, treatment, and care, with a consequent impact on survival and quality of life after a cancer diagnosis.
- A number of important steps are needed to reduce social inequalities in cancer: (i) inequalities need to be fully documented through well-designed research studies; (ii) greater emphasis should be given to prevention in general, with primary prevention offering an effective mechanism to reach the greatest proportion of a given population; and (iii) all cancer control measures should be evaluated as to whether inequalities are reduced or exacerbated by their implementation.
- The agenda to reduce social inequalities in cancer aligns perfectly with the United Nations Sustainable Development Goals, which not only recognize noncommunicable diseases as a barrier to sustainable development but also provide the founding principle that reducing inequalities is a social goal. Above all else, therefore, our motivation for addressing social inequalities in cancer should be one of justice and human rights.

# References

- Abarca-Gómez L, Abdeen ZA, Hamid ZA, Abu-Rmeileh NM, Acosta-Cazares B, Acuin C, et al.; NCD Risk Factor Collaboration (NCD-RisC) (2017). Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet*. 390(10113):2627–42. [https://doi.org/10.1016/S0140-6736\(17\)32129-3](https://doi.org/10.1016/S0140-6736(17)32129-3) PMID:29029897
- Adam M, Rueegg CS, Schmidlin K, Spoerri A, Niggli F, Grotzer M, et al.; Swiss Paediatric Oncology Group; Swiss National Cohort Study (2016). Socioeconomic disparities in childhood cancer survival in Switzerland. *Int J Cancer*. 138(12):2856–66. <https://doi.org/10.1002/ijc.30029> PMID:26840758
- Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Nikšić M, et al.; CONCORD Working Group (2018). Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. *Lancet*. 391(10125):1023–75. [https://doi.org/10.1016/S0140-6736\(17\)33326-3](https://doi.org/10.1016/S0140-6736(17)33326-3) PMID:29395269
- Arnold M, Sierra MS, Laversanne M, Soerjomataram I, Jemal A, Bray F (2017). Global patterns and trends in colorectal cancer incidence and mortality. *Gut*. 66(4):683–91. <https://doi.org/10.1136/gutjnl-2015-310912> PMID:26818619
- Boscoe FP, Henry KA, Sherman RL, Johnson CJ (2016). The relationship between cancer incidence, stage and poverty in the United States. *Int J Cancer*. 139(3):607–12. <https://doi.org/10.1002/ijc.30087> PMID:26991033
- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 68(6):394–424 <https://doi.org/10.3322/caac.21492> PMID:30207593
- Clifford GM, Polesel J, Rickenbach M, Dal Maso L, Keiser O, Kofler A, et al.; Swiss HIV Cohort Study (2005). Cancer risk in the Swiss HIV Cohort Study: associations with immunodeficiency, smoking, and highly active antiretroviral therapy. *J Natl Cancer Inst*. 97(6):425–32. <https://doi.org/10.1093/jnci/dji072> PMID:15770006
- Gupta S, Wilejto M, Pole JD, Guttmann A, Sung L (2014). Low socioeconomic status is associated with worse survival in children with cancer: a systematic review. *PLoS One*. 9(2):e89482. <https://doi.org/10.1371/journal.pone.0089482> PMID:24586813
- Hollstein M, Alexandrov LB, Wild CP, Ardin M, Zavadil J (2017). Base changes in tumour DNA have the power to reveal the causes and evolution of cancer. *Oncogene*. 36(2):158–67. <https://doi.org/10.1038/ncr.2016.192> PMID:27270430
- Kogevinas M, Pearce N, Susser M, Boffetta P, editors (1997). *Social inequalities and cancer*. Lyon, France: International Agency for Research on Cancer (IARC Scientific Publications, No. 138). Available from: <http://publications.iarc.fr/293>.
- Lauby-Secretan B, Scoccianti C, Loomis D, Benbrahim-Tallaa L, Bouvard V, Bianchini F, et al.; International Agency for Research on Cancer Handbook Working Group (2015). Breast-cancer screening – viewpoint of the IARC Working Group. *N Engl J Med*. 372(24):2353–8. <https://doi.org/10.1056/NEJMs1504363> PMID:26039523
- Martin RM, Donovan JL, Turner EL, Metcalfe C, Young GJ, Walsh EI, et al.; CAP Trial Group (2018). Effect of a low-intensity PSA-based screening intervention on prostate cancer mortality: the CAP randomized clinical trial. *JAMA*. 319(9):883–95. <https://doi.org/10.1001/jama.2018.0154> PMID:29509864
- McCutchan GM, Wood F, Edwards A, Richards R, Brain KE (2015). Influences of cancer symptom knowledge, beliefs and barriers on cancer symptom presentation in relation to socioeconomic deprivation: a systematic review. *BMC Cancer*. 15(1):1000. <https://doi.org/10.1186/s12885-015-1972-8> PMID:26698112
- McDaniel JT, Nuhu K, Ruiz J, Alorbi G (2019). Social determinants of cancer incidence and mortality around the world: an ecological study. *Glob Health Promot*. 26(1):41–9. <https://doi.org/10.1177/1757975916686913> PMID:29187122
- Moore SP, Antoni S, Colquhoun A, Healy B, Ellison-Loschmann L, Potter JD, et al. (2015). Cancer incidence in indigenous people in Australia, New Zealand, Canada, and the USA: a comparative population-based study. *Lancet Oncol*. 16(15):1483–92. [https://doi.org/10.1016/S1470-2045\(15\)00232-6](https://doi.org/10.1016/S1470-2045(15)00232-6) PMID:26476758
- Petridou ET, Sergentanis TN, Perlepe C, Papatoma P, Tsilimidos G, Kontogeorgi E, et al. (2015). Socioeconomic disparities in survival from childhood leukemia in the United States and globally: a meta-analysis. *Ann Oncol*. 26(3):589–97. <https://doi.org/10.1093/annonc/mdl572> PMID:25527416
- Statistics Team, NHS Digital (2018). *Statistics on obesity, physical activity and diet*. NHS Digital. Available from: <https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-obesity-physical-activity-and-diet>.
- Stewart BW, Wild CP, editors (2014). *World cancer report 2014*. Lyon, France: International Agency for Research on Cancer. Available from: <http://publications.iarc.fr/396>.
- Tomatis L (1997). Poverty and cancer. In: Kogevinas M, Pearce N, Susser M, Boffetta P, editors. *Social inequalities and cancer*. Lyon, France: International Agency for Research on Cancer (IARC Scientific Publications, No. 138); pp. 25–39. Available from: <http://publications.iarc.fr/293>.
- Vaccarella S, Franceschi S, Bray F, Wild CP, Plummer M, Dal Maso L (2016). Worldwide thyroid-cancer epidemic? The increasing impact of overdiagnosis. *N Engl J Med*. 375(7):614–7. <https://doi.org/10.1056/NEJMp1604412> PMID:27532827
- Vázquez TR, Ghebreyesus TA (2017). Beating NCDs can help deliver universal health coverage. *Lancet*. 390(10101):1473–4. [https://doi.org/10.1016/S0140-6736\(17\)32470-4](https://doi.org/10.1016/S0140-6736(17)32470-4) PMID:28952441
- Viswanath K, Nagler RH, Bigman-Galimore CA, McCauley MP, Jung M, Ramanadhan S (2012). The communications revolution and health inequalities in the 21st century: implications for cancer control. *Cancer Epidemiol Biomarkers Prev*. 21(10):1701–8. <https://doi.org/10.1158/1055-9965.EPI-12-0852> PMID:23045545
- Wang Y, Lim H (2012). The global childhood obesity epidemic and the association between socio-economic status and childhood obesity. *Int Rev Psychiatry*. 24(3):176–88. <https://doi.org/10.3109/09540261.2012.688195> PMID:22724639