REDUCING SOCIAL INEQUALITIES IN CANCER: EVIDENCE AND PRIORITIES FOR RESEARCH

EDITED BY SALVATORE VACCARELLA, JOANNIE LORTET-TIEULENT, RODOLFO SARACCI, DAVID I. CONWAY, KURT STRAIF, AND CHRISTOPHER P. WILD

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Cover image: This photo by Johnny Miller from his photo series Unequal Scenes shows the physical divide that separates
Bloubosrand, a middle-class suburb northwest of Johannesburg, South Africa, from Kya Sands, an informal settlement
consisting of improvised housing made of plywood and corrugated metal.

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Foreword

Cancer is undoubtedly a disease of inequalities. At source, tackling these inequalities is a matter of social justice and human rights. In 1997, the International Agency for Research on Cancer (IARC) summarized the available evidence on the differences in cancer incidence, survival, and mortality between groups with different socioeconomic status in the volume *Social Inequalities in Cancer* in order to draw attention to this area of research.

The first studies showing socioeconomic differences in cancer outcomes date back to more than a century ago. There has been notable progress in understanding many major causes of cancer, such as tobacco use, alcohol consumption, obesity, poor diet, and other lifestyle factors, as well as exposure to certain infections, radiation, chemical agents in the workplace, and air pollution, and much of this knowledge has been translated into effective preventive interventions. Over the same period, there have been significant improvements in the early detection, diagnosis, and treatment of some cancer types, as well as in the provision of palliative care. However, in parallel with this progress there has been increasing recognition of the social inequalities which exist in accessing the benefits of that progress. Far from disappearing, social inequalities in cancer have persisted over time, albeit changing in nature and extent.

Social inequalities in cancer, therefore, remain as a crucial public health issue, affecting everyone but hitting particularly hard the most disadvantaged individuals. These inequalities entail major financial consequences for societies, in addition to the impact on health. Understanding how the phenomenon of inequalities evolves and is reshaped over time demands a broader perspective. Economic, social, political, legislative, and technological forces have an impact on the distribution of risk factors within a population, and also affect access to health services, which translate into the observed inequalities in cancer outcomes. There are also important psychosocial factors leading individuals with low socioeconomic status to adopt unhealthy behaviours and therefore be exposed to a greater variety, and higher intensity, of cancer risk factors compared with their fellow citizens. To monitor, investigate, and understand these issues, high-quality data on populations within populations are needed, and multisectoral action is required to find effective solutions to the prevailing social inequalities in cancer.

Research can provide the data needed to inform evidence-based interventions to reduce social inequalities in cancer. The research community has a duty to provide high-quality evidence and to ensure this knowledge is presented in a form which can be translated into effective cancer control policies that leave no one behind. In its role as an international cancer research agency and part of the World Health Organization, IARC is committed to this task. The present volume serves as a foundation not only to its own research but also to collaborative research efforts on social inequalities and cancer worldwide.

Dr Christopher P. Wild
Director, IARC

Preface

This IARC Scientific Publication aims to provide a comprehensive and timely overview of the most recent evidence on social inequalities in cancer, incorporating contributions from more than 70 authors, reviewers, and editors whose expertise spans a wide range of relevant disciplines. The publication was further informed by the discussions and conclusions of a workshop held by IARC in April 2018 in Lyon, France, to identify research priorities to reduce social inequalities in cancer, the results of which were summarized and published in *CA: A Cancer Journal for Clinicians* and are reproduced in the Conclusions at the end of this volume.

The first two chapters of this book describe the concept of cancer as a disease of difference, both biologically and socially (Chapter 1), and how social inequalities in cancer are addressed by the global public health agenda (Chapter 2). The subsequent 17 chapters are structured around three major themes and are complemented by exam-

ples and specific focuses: Part 1 gives an overview of the evidence of social inequalities in cancer that exist between and within countries, Part 2 describes the most important factors and mechanisms underlying these inequalities, and Part 3 identifies real-world examples of interventions that contribute to the reduction of social inequalities in cancer.

Part 1 includes descriptions of how social inequalities are important across the whole cancer continuum (Chapter 3), how they can be measured (Chapter 4, Focus 1, and Focus 2), and evidence of inequalities in cancer between countries (Chapter 5 and Focus 3) and within countries (Chapter 6, Focus 3, Focus 5, Focus 6, and Focus 7). It also describes the evidence of social inequalities in cancer risk factors and in access to health care (Chapter 7).

Part 2 starts with a description of the theoretical frameworks of cancer inequities (Chapter 8) and continues by highlighting important mechanisms such as income inequalities (Chapter 9), the role of health sys-

tems (Chapter 10), the economics of tobacco, alcohol, food products, and sugar-sweetened beverages (Chapter 11 and Example 1), and national and international legislation (Chapter 12). Part 2 concludes with a concrete example of a life-course approach to the study of socioeconomic determinants (Chapter 13).

Part 3 includes considerations of the impact of public health interventions to reduce social inequalities in cancer (Chapter 14), the research priorities for low- and middle-income countries (LMICs) (Chapter 15), the potential benefits of certain low-cost technologies and approaches in LMICs (Chapter 16 and Example 2), and the lessons learned from the response to the AIDS epidemic and their application to reduce social inequalities in cancer (Chapter 17). Part 3 closes by describing how the increasing use of technology could, if not regulated, lead to increasing rather than decreasing inequalities in cancer (Chapter 18), and how resources that could be used to control cancer in disadvantaged individuals

are instead allocated to fund the unnecessary and potentially harmful treatment of individuals with greater access to health care (Chapter 19).

Issues pertaining to cancer inequalities within specific regions of the world are also addressed and condensed in focus sections distributed through the book (Focus 4, Focus 8, and Focus 9).

This initiative was planned to stimulate the international community into acting on social inequalities and cancer, a topic that has been neglected in terms of both research and public health practice. The editors anticipate that this book, which includes detailed descriptions of specific examples of interventions that may reduce future inequalities in cancer, will also serve as a reference for policy-makers and public health officials.

Dr Salvatore Vaccarella

Contributors

Editors

The editors conceived and developed this initiative, participated in the meeting, wrote some of the material in the chapters, served as reviewers, and worked jointly to edit the overall text.

Dr Salvatore Vaccarella (Chair)
Infections and Cancer Epidemiology Group
Section of Infections
International Agency for Research on Cancer
Lyon, France

Dr Joannie Lortet-Tieulent
(Vice-Chair)
Infections and Cancer Epidemiology Group
Section of Infections
International Agency for Research on Cancer
Lyon, France

Professor Rodolfo Saracci
Senior Visiting Scientist
International Agency for Research on Cancer
Lyon, France

Professor David I. Conway
School of Medicine, Dentistry and Nursing
University of Glasgow
Glasgow, United Kingdom

Dr Kurt Straif
Section of Evidence Synthesis and Classification
International Agency for Research on Cancer
Lyon, France

Dr Christopher P. Wild
Director
International Agency for Research on Cancer
Lyon, France

Participants

Dr Ajay Aggarwal
Department of Cancer Epidemiology, Population and Global Health
King's College London
and
Guy's and St Thomas' NHS Foundation Trust
Department of Clinical Oncology
Guy's Hospital
London, United Kingdom

Professor Rifat Atun
Department of Global Health and Population
Harvard T.H. Chan School of Public Health
Boston, USA

Dr Partha Basu
Screening Group
Section of Early Detection and Prevention
International Agency for Research on Cancer
Lyon, France

Dr Melanie Bertram
Department of Health Systems
Governance and Financing (HGF)
World Health Organization
Geneva, Switzerland

Professor Tony Blakely
Department of Public Health
University of Otago
Wellington, New Zealand

Dr Evan Blecher
Health Policy Center
University of Illinois
Chicago, USA

Dr Freddie Bray
Section of Cancer Surveillance
International Agency for Research
on Cancer
Lyon, France

Dr Denise Brown
MRC/CSO Social and Public Health
Sciences Unit
University of Glasgow
Glasgow, United Kingdom

Professor Giuseppe Costa
Department of Clinical and
Biological Sciences
University of Turin
Turin, Italy

Dr Adam P. Coutts
Department of Sociology
University of Cambridge
Cambridge, United Kingdom

Professor Joan Cunningham
Menzies School of Health Research
Charles Darwin University
Melbourne, Australia

Dr Adel Daoud
Harvard School of Public Health
Harvard University
Boston, USA

Dr Louise Davies
Geisel School of Medicine at
Dartmouth
and
The Dartmouth Institute for Health
Policy and Clinical Practice
Dartmouth College
Lebanon, USA

Dr Catherine de Martel
Infections and Cancer Epidemiology
Group
Section of Infections
International Agency for Research
on Cancer
Lyon, France

Dr Esther de Vries
Department of Clinical Epidemiology
and Biostatistics
Pontificia Universidad Javeriana
Bogotá, Colombia

Dr Lynette Denny
Department of Obstetrics and
Gynaecology
University of Cape Town/Groote
Schuur Hospital
Cape Town, South Africa

Dr Miranda Fidler
Section of Cancer Surveillance
International Agency for Research
on Cancer
Lyon, France

Professor Gail Garvey
Wellbeing and Preventable Chronic
Diseases Division
Menzies School of Health Research
Brisbane, Australia

Dr Hellen Gelband
Centre for Global Health Research
University of Toronto
and
St. Michael's Hospital
Toronto, Canada

Dr Peter Godfrey-Faussett
Joint United Nations Programme on
HIV and AIDS
Geneva, Switzerland

Dr Joe Hasell
Oxford Martin Programme on Global
Development
Oxford Martin School
University of Oxford
Oxford, United Kingdom

Dr Rolando Herrero Acosta
Section of Early Detection and
Prevention
International Agency for Research
on Cancer
Lyon, France

Dr André Ilbawi
Department for Management of
Noncommunicable Diseases,
Disability, Violence and Injury
Prevention (NVI)
World Health Organization
Geneva, Switzerland

Dr Hyacinth Irving
Centre for Global Health Research
University of Toronto
and
St. Michael's Hospital
Toronto, Canada

Dr Farhad Islami
Surveillance and Health Services
Research
American Cancer Society
Atlanta, USA

Dr Ahmedin Jemal
Surveillance and Health Services
Research
American Cancer Society
Atlanta, USA

Professor Prabhat Jha
Centre for Global Health Research
St. Michael's Hospital
Toronto, Canada

Dr Michelle Kelly-Irving
Inserm Unit of Epidemiology and
Public Health
Université Paul Sabatier
Toulouse, France

Professor Nancy Krieger
Department of Social and
Behavioral Sciences
Harvard T.H. Chan School of Public
Health
Boston, USA

Dr Ivana Kulhánová
Section of Cancer Surveillance
International Agency for Research
on Cancer
Lyon, France

Professor Tezer Kutluk
Department of Pediatrics
Division of Pediatric Oncology
Hacettepe University Faculty of
Medicine and Cancer Institute
Ankara, Turkey

Dr Alastair H. Leyland
Social and Public Health Sciences
Unit
University of Glasgow
Glasgow, United Kingdom

Mr Jonathan Liberman
McCabe Centre for Law and Cancer
Melbourne, Australia

Dr Dana Loomis
IARC Monographs Group
Section of Evidence Synthesis and
Classification
International Agency for Research
on Cancer
Lyon, France

Professor Johan P. Mackenbach
Department of Public Health
Erasmus University Medical Center
Rotterdam, The Netherlands

Sir Michael Marmot
Institute of Health Equity
Department of Epidemiology and
Public Health
University College London
London, United Kingdom

Dr Valerie McCormack
Section of Environment and
Radiation
International Agency for Research
on Cancer
Lyon, France

Dr Alex D. McMahon
School of Medicine, Dentistry and
Nursing
University of Glasgow
Glasgow, United Kingdom

Dr Filip Meheus
Prevention and Implementation
Group
Section of Early Detection and
Prevention
International Agency for Research
on Cancer
Lyon, France

Dr Gwenn Menvielle
Equipe de Recherche en
Epidémiologie Sociale (ERES)
Institut Pierre Louis d'Epidémiologie
et de Santé Publique Inserm UMRS
1136/Sorbonne
Paris-Sorbonne and Pierre et Marie
Curie Universities
Paris, France

Ms Sujata Mishra
Centre for Global Health Research
Institute of Health Policy, Manage-
ment and Evaluation
University of Toronto
Toronto, Canada

Dr Salvatore Morelli
Stone Center on Socio-Economic
Inequality
City University of New York
New York, USA

Dr Raúl Murillo
Centro Javeriano de Oncología
University Hospital San Ignacio
Bogotá, Colombia

Professor Robert Newton
Health Sciences Department
University of York
York, United Kingdom

Dr Max Roser
Institute for New Economic Thinking
Oxford Martin School
University of Oxford
Oxford, United Kingdom

**Dr Rengaswamy
Sankaranarayanan**
Section of Early Detection and
Prevention
International Agency for Research
on Cancer
Lyon, France

Professor Diana Sarfati
Department of Public Health
University of Otago
Wellington, New Zealand

Dr Mary Schubauer-Berigan
IARC Monographs Group
Section of Evidence Synthesis and
Classification
International Agency for Research
on Cancer
Lyon, France

Dr Omar Shamieh
Department of Palliative Care
King Hussein Cancer Center
Amman, Jordan

Mr Michel Sidibé
Joint United Nations Programme on HIV and AIDS
Geneva, Switzerland

Ms Rebecca Siegel
Surveillance and Health Services Research
American Cancer Society
Atlanta, USA

Dr Mónica S. Sierra
Division of Cancer Epidemiology and Genetics
National Cancer Institute
Rockville, USA

Dr Isabelle Soerjomataram
Section of Cancer Surveillance
International Agency for Research on Cancer
Lyon, France

Professor Richard Sullivan
Conflict and Health Research Group
Centre for Global Health
King's College London
London, United Kingdom

Professor Rajaraman Swaminathan
Department of Epidemiology, Biostatistics, and Cancer Registry
Cancer Institute (WIA)
Chennai, India

Dr Andrea Teng
Department of Public Health
University of Otago
Wellington, New Zealand

Ms Nicole Valentine
Social Determinants of Health Unit
World Health Organization
Geneva, Switzerland

Dr Nadia Vilahur
IARC Handbooks Group
Section of Evidence Synthesis and Classification
International Agency for Research on Cancer
Lyon, France

Professor Paolo Vineis
Faculty of Medicine, School of Public Health
Imperial College London
London, United Kingdom

Other Contributors

The authors are grateful to the following experts who contributed by reviewing specific chapters of this book.

Dr Afsan Bhadelia
Global Health Systems Cluster
Department of Global Health and Population
Harvard T.H. Chan School of Public Health
Boston, USA

Professor Sofia Gruskin
Keck School of Medicine and Gould School of Law
Program on Global Health and Human Rights
and
Institute for Global Health
University of Southern California
Los Angeles, USA

Professor Martin McKee
London School of Hygiene and Tropical Medicine
London, United Kingdom

Dr Luc Morris
Department of Surgery
Memorial Sloan Kettering Cancer Center
New York, USA

Dr Catherine Sauvaget
Screening Group
Section of Early Detection and Prevention
International Agency for Research on Cancer
Lyon, France

The following participants also served as reviewers.

Dr Freddie Bray
Dr Partha Basu
Professor Giuseppe Costa
Dr Esther de Vries
Dr Lynette Denny
Dr Miranda Fidler
Dr Rolando Herrero Acosta
Dr Farhad Islami
Dr Ahmedin Jemal
Dr Ivana Kulhánová
Dr Alastair H. Leyland
Professor Johan P. Mackenbach
Dr Valerie McCormack
Dr Filip Meheus
Dr Raúl Murillo
Dr Rengaswamy Sankaranarayanan
Professor Diana Sarfati
Ms Nicole Valentine
Dr Nadia Vilahur
Professor Paolo Vineis

IARC Organizing Committee

Dr Salvatore Vaccarella
Dr Joannie Lortet-Tieulent
Professor Rodolfo Saracci
Professor David I. Conway
Dr Miranda Fidler
Dr Dana Loomis
Dr Nadia Vilahur
Dr Kurt Straif
Dr Christopher P. Wild

Administrative Assistance

Ms Philippine Gason
Infections and Cancer Epidemiology
Group
Section of Infections
International Agency for Research
on Cancer
Lyon, France

Production Team

Dr Elaine Rowan
Technical Editor

Dr Karen Müller
English Editor

Ms Sylvia Lesage
Publishing Assistant

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Abbreviations

ACE	adverse childhood experience
AIDS	acquired immune deficiency syndrome
ASR	age-standardized rate
ASRS	age-standardized relative survival
BMI	body mass index
CBE	clinical breast examination
CI	confidence interval
CIN	cervical intraepithelial neoplasia
DALYs	disability-adjusted life years
DEMETRIQ	Developing Methodologies to Reduce Inequalities in the Determinants of Health
DHS	Demographic and Health Surveys
ER	estrogen receptor
FNAC	fine-needle aspiration cytology
GDP	gross domestic product
HBCR	hospital-based cancer registry
HBV	hepatitis B virus
HCI	health concentration index
HCV	hepatitis C virus
HDI	Human Development Index
HEL	high education level
HICs	high-income countries
HIV	human immunodeficiency virus
HPV	human papillomavirus
IARC	International Agency for Research on Cancer
ICE	index of concentration at the extremes
IDP	internally displaced person
LEL	low education level
LMICs	low- and middle-income countries
m-Health	mobile health
NCD	noncommunicable disease

OS	overall survival
PBCR	population-based cancer registry
PED	price elasticity of demand
RII	relative index of inequality
RII$_L$	relative index of inequality, linear regression model
RII$_P$	relative index of inequality, Poisson regression
SEER	Surveillance, Epidemiology, and End Results Program
SEP	socioeconomic position
SES	socioeconomic status
SII	slope index of inequality
SSB	sugar-sweetened beverage
SVA	single-visit approach
UHC	universal health coverage
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV and AIDS
USS	ultrasound screening
VIA	visual inspection with acetic acid
WHO	World Health Organization
YLD	years lost because of disability
YLL	years of life lost

CHAPTER 1.

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 gentlefolk, or with those who are obliged to pretend that they are gentlefolk."

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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.

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CHAPTER 2.

Social inequalities, global public health, and cancer

Michael Marmot

Introduction

The World Health Organization and the Government of Uruguay held the Global Conference on Noncommunicable Diseases (NCDs) in Montevideo in October 2017, a most welcome initiative. The aim was to prepare for the third United Nations General Assembly high-level meeting on NCDs, another welcome development. At the Montevideo summit we discussed strategies to reduce the global burden of NCDs by both prevention and treatment. Inequalities in the burden of NCDs were not a strong feature of the meeting, however. They surfaced prominently to the extent that universal health coverage aims to deal with inequalities in access to health care; out-of-pocket payments for medical care can, and do, impoverish people globally. To avoid social in-

equalities in the occurrence of NCDs being the silent guest at the table, there but not openly acknowledged, I was invited to speak at the opening experts' plenary. I began along the following lines.

"NCDs are a global health problem. One purpose of our meeting here in Montevideo is to plan for an NCD summit to be held at the United Nations in New York in September 2018. If you attend that summit and, while there, go to Central Park for a little exercise in green space – good for mental as well as physical health – you may find your life at risk. Mown down by hordes of high-income joggers."

Much as I applaud people taking responsibility for their health, these high-income New Yorkers are atypical. Globally, the burden of NCDs is in middle-income and, increasingly,

low-income countries. Within countries, the so-called diseases of affluence are no longer; the lower people are in the social hierarchy, the higher their risk of NCDs. We cannot deal with NCDs without dealing with the social determinants of health inequalities.

There is a rumour going around that poor people are poor because they make poor choices, and that poor people are unhealthy because they make unhealthy choices. This rumour is, very largely, a myth. It has the causal connection backwards. More accurately, it is not mythical that the rumour exists – I read it in the press nearly daily – but the evidence points the other way. It is not poor choices that lead to poverty but poverty that leads to poor choices. An Indian villager is more likely to invest in longer-term strategies if the

harvest has been good. If it has been poor, he will focus on how to get calories for his family tomorrow, not on strategies for future prosperity. A single mother may respond to the admonition to read bedtime stories to her children – it's good for their long-term future – that she would if she could be sure that they would have a bed, let alone a book.

So it is with healthy choices. Under different circumstances, people with lower income would be more likely to adopt the choices that are good for health. Having time to think about exercise is a luxury that people at the economic margins may not have, quite apart from a lack of amenities; healthy food may be beyond a household budget. The stress of marginal employment would be happily forgone if better jobs were available.

Globally, to take effective action on NCDs, we need to address inequalities in NCDs, and this entails action on the social determinants of health. This chapter focuses on what we can do, but first we look at cancer in the context of inequalities in health.

Health inequalities: the gradient

All countries from which we have good data show inequalities in mortality. Such inequalities are not confined to poor health for the poor, but follow a social gradient (Marmot, 2015). In low-income countries, where the systematic collection of data on inequalities is uncommon, we have data on child mortality from Demographic and Health Surveys (Gwatkin, 2007). In country after country, the lower the wealth quintile, the higher the mortality rate of children under the age of 5 years.

Specific analyses from middle-income countries such as Brazil show

social gradients in adult mortality (Bassanesi et al., 2008). In high-income countries, the gradient is clear: higher socioeconomic position means lower mortality, whether socioeconomic position is measured by education level, income, occupational status, or degree of deprivation of area of residence. A recent publication from Lifepath, a European collaborative research programme, showed that in 48 cohorts low occupational status was associated with higher all-cause mortality (Stringhini et al., 2017).

If all societies have social and economic inequalities – in education level, income, occupational status, and living conditions – and the social gradient in health follows from

these social and economic inequalities, one might speculate that there will always be inequalities in health. Probably, there will be. However, the magnitude varies between countries and, over time, within countries. If the magnitude of inequalities, that is, the slope of the gradient, is not fixed, it suggests that action to reduce these inequalities should be possible.

First, consider the variation in health inequalities between countries: it is marked. In Europe, we calculated life expectancy at the age of 25 years by education level. In each country, men with a university education had a longer life expectancy than men with only a primary education (Fig. 2.1), but the gap varied (Marmot and UCL Institute of Health Equity,

Fig. 2.1. Life expectancy for men aged 25 years, by education level, in different European countries. ISCED, International Standard Classification of Education; levels 0–2, pre-primary, primary, and lower secondary education, or second stage of basic education; levels 5–8, first stage of tertiary and second stage of tertiary education. Source: Eurostat [demo_mlexpecedu] (2016).

Legend:
- Males, 25 years, Tertiary education (levels 5–8), Year 2016
- Males, 25 years, All ISCED 2011 levels, Year 2016
- Males, 25 years, Less than primary, primary and lower secondary education (levels 0–2), Year 2016
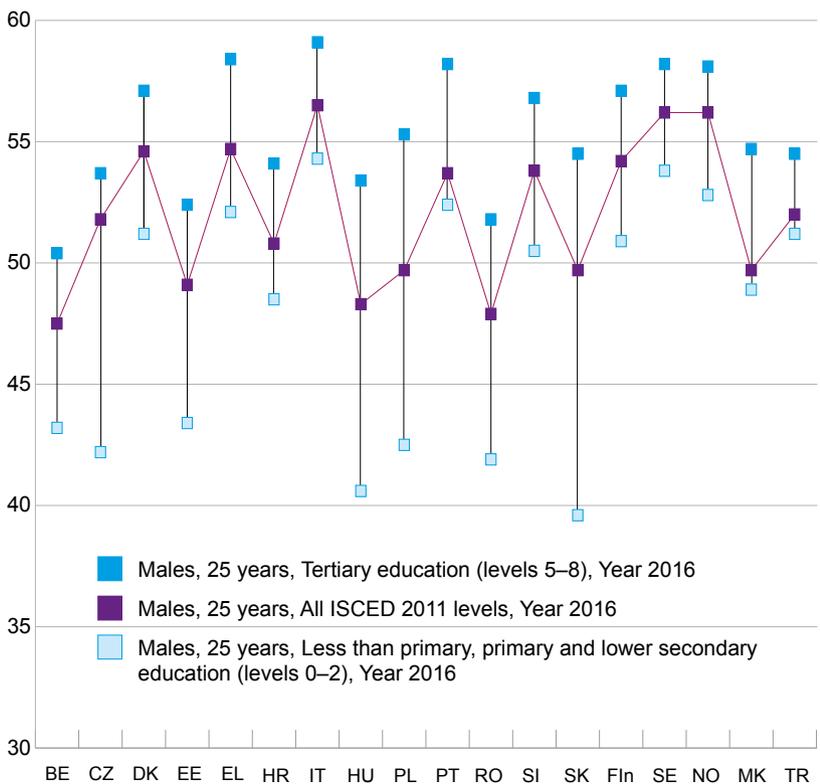
2013). Sweden has the second longest life expectancy at the age of 25 years, and a narrow gap between those with a primary education and those with a tertiary education. Men living in the countries located to the east of Sweden have a lower average life expectancy, and there is a wider gap in life expectancy between those with a primary education and those with a tertiary education. Looking at it a different way, the health disadvantage of living in these countries is greater for those with a primary education than for those with a tertiary education. They do know how to get good health in Bulgaria, Estonia, Hungary, and Romania … it happens for men with university education. It is those lower in the hierarchy who suffer most.

The magnitude of health inequalities also varies within countries over time. Part of that variation may result from conscious policy decisions. In England, Barr et al. (2017) looked at the gap in life expectancy between the poorest 20% of local authorities and the remainder; their results are summarized in Fig. 2.2. The New Labour government, elected in 1997, developed a national strategy to reduce health inequalities. In the period before the strategy was put in place, the health gap between the poorest 20% and the remainder was widening. During the period of the strategy, the gap narrowed. In the period after the strategy, when a Conservative-led coalition government changed policy direction, health inequalities increased again.

This simple correlation in time does not prove causation, nor does it tell us what feature, if any, of government policy might have made the most difference. What the data do show is that the magnitude of health inequalities can vary quite quickly.

Fig. 2.2. Trends in difference in life expectancy between areas of greatest deprivation and the average. Source: compiled from Barr et al. (2017).
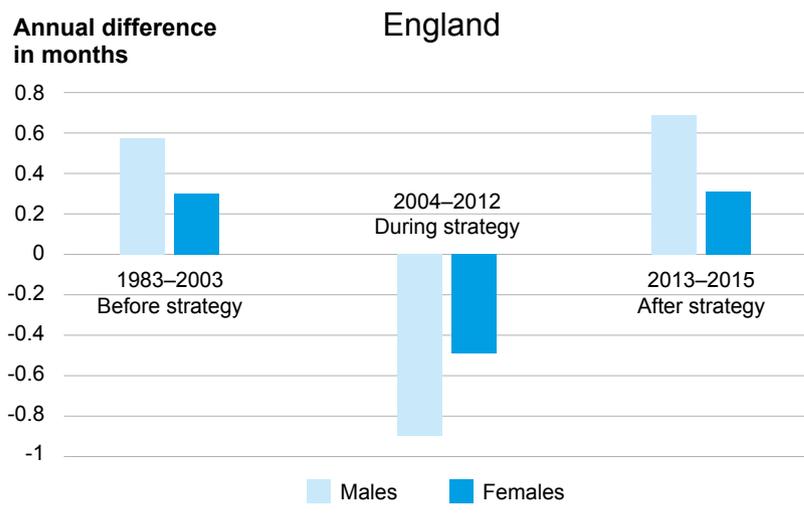
The data are, at the least, consistent with the notion that having an explicit policy to do something about the problem may help.

Cancer and health inequalities

Cancer has perhaps featured less than some other diseases in the consideration of health inequalities. This volume is a timely reminder that that should no longer be the case, as illustrated by Fig. 2.3. Although the contribution of cancer to absolute inequalities in all-cause mortality varies among countries, it is substantial in each case. Unexpectedly, cancer looms large in middle-income countries. It is, however, more difficult to obtain data on social inequalities. There are exceptions, such as the demonstration of inequalities by education level in Colombia, particularly for cancers of the stomach and cervix, both of which are linked to infection (de Vries et al., 2015).

Cancer inequalities: the causes

Cancer Research UK (Gordon-Dseagu, 2006) concluded that 40% of cancers in the United Kingdom are preventable, and that globally the estimate is similar (30–50%). According to Cancer Research UK, the routes to lower cancer risk are, in order of importance, to be a non-smoker, maintain a healthy weight, eat fruits and vegetables, consume less alcohol, be "SunSmart", eat less processed meat and red meat, eat a high-fibre diet, be physically active, and eat less meat.

Each of these is socially determined, and many show a social gradient; more unhealthy behaviours are observed in those lower in the hierarchy. It used to be thought that in low- and middle-income countries cigarette smoking was more common in groups with higher income or higher education level, unlike the gradient seen in high-income countries. This is no longer the case. In many lower- and upper-middle-income countries, smoking is more common lower in the hierarchy (Global Tobacco Economics Consortium, 2018). Similarly with obesity, the social gradient is clear in North America and Europe, as illustrated in Fig. 2.4

Fig. 2.3. Contribution of selected noncommunicable diseases to absolute inequality (all-cause) death rates between lowest and highest quintiles of community socioeconomic status for those aged 30–64 years. Source: reprinted from Di Cesare et al. (2013), copyright 2013, with permission from Elsevier.
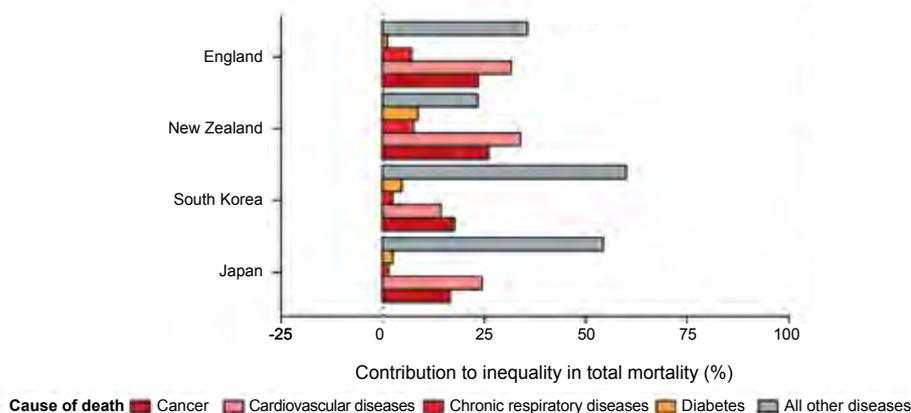
for 19 Member States of the European Union.

Worryingly, in Britain there is a social gradient in childhood obesity, which has been steepening over time (NHS Digital, 2017). Given that childhood obesity tracks into adulthood, we are facing increasing inequalities in obesity in the future.

I have placed emphasis on socioeconomic differences in health and disease. In the Commission on Equity and Health Inequalities in the Americas, established by the Pan American Health Organization, we are also concerned with ethnic and gender inequalities. We see that throughout the Americas, Indigenous groups are disadvantaged in terms of social determinants of health compared with non-Indigenous groups. In many countries of the Americas, including the USA, people of African descent are commonly subject to structural racism, which compounds socioeconomic disadvantage. These socioeconomic and ethnic disadvantages can combine with differences between sexes in social determinants of health.

Cancer inequalities: what can be done?

It can be argued that the mind is an important gateway by which social determinants affect health equity. The above-mentioned risks identified by Cancer Research UK are behavioural, that is, controlled by the mind. As I stated at the beginning of this chapter, however, it is inadequate to see these behaviours as simply being under the control of individuals without taking into account the social determinants that lead to inequalities in these behaviours.

A review of health inequalities in England, *Fair society, healthy lives: the Marmot review* (Marmot, 2010), identified six domains of recommendations to reduce avoidable health inequalities and promote health equity: (i) giving every child the best start in life; (ii) education and lifelong learning; (iii) employment and working conditions; (iv) a

Fig. 2.4. Obesity prevalence according to educational attainment, averaged over 19 European Union Member States. Source: reproduced from report by Robertson et al. (2007).
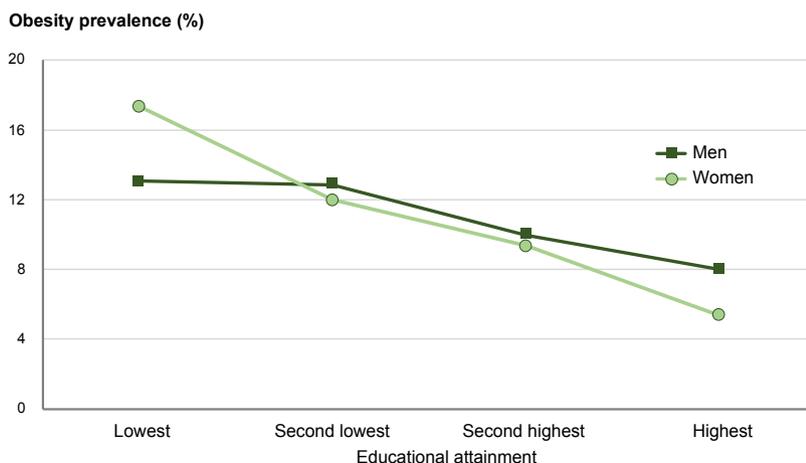
minimum income for healthy living (everyone should have at least the minimum income that would enable them to live a healthy life); (v) healthy and sustainable places and environments in which to live and work; and (vi) taking a social determinants approach to prevention, that is, not just looking at reducing smoking and unhealthy diet, for example, but also looking at the causes of the social distribution of these behaviours (the causes of the causes). To prevent inequalities in cancer, attention must be paid to these six domains through the entire life-course. In other words, promotion of health equity with respect to cancer should be part of a general approach to reducing health inequalities.

The argument I have just stated is not confined to cancer. In recent months, I have been invited to talk about social determinants and health equity to groups concerned with medical education, internal medicine, cardiology, surgery, paediatrics, thoracic medicine, mental illness, obstetrics and gynaecology, cancer control, primary care, pharmacy, early child development, violence, inclusion health, health psychology, psychosomatic medicine, vegetable summit, and concepts of honour, as well as public health and health promotion, urban renewal, local government, and community development.

The causes of cancer identified by Cancer Research UK are largely behavioural, but interventions to address these causes will also have an environmental component; examples are banning smoking in public places and encouraging active transport. Environmental, rather than simply behavioural, interventions will also be important in relation to other medical conditions: reducing air pollution, improving housing quality, and designing neighbourhoods to promote health and well-being.

We need to make common cause, not only to reduce inequalities in cancer and specific medical conditions but also to promote health equity more generally. A commitment to action on social determinants of health is urgently required.

Key points

- About 40% of cancers are judged to be preventable by simple lifestyle changes; these causes of cancer, smoking and obesity principal among them, are socially determined.

- These causes follow a social gradient, with lower socioeconomic position corresponding to higher risk. They contribute to inequalities in the occurrence of cancer.

- To make progress in reducing inequalities in cancer we must address the causes of the causes of cancer.

- Evidence shows that inequalities in mortality vary between and within countries. The implication is that inequalities are not fixed but can be improved.

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Introduction to Part 1

Freddie Bray and Ahmedin Jemal

If the cancer control continuum represents a framework to assess, plan, and prioritize information provision, etiology, prevention, early detection, diagnosis, treatment, survivorship, and end-of-life care of cancer, the measurement of social inequalities at each of these stages offers the opportunity to appraise progress in tackling the root causes of cancer inequalities, as part of cancer control policy.

Part 1 is centred on *evidence-based social inequalities in cancer*, a reformulation of Sackett's then-novel concept of evidence-based medicine (Sackett and Rosenberg, 1995), which describes the process in which caring for our citizens creates the need for evidence of disparities in the risk factors, diagnosis,

prognosis, and treatment of cancer; alongside related health-care determinants, these provide a means to formulate answerable questions that can be assessed and appraised in practice. This book summarizes evidence of social inequalities in cancer, and Part 1 comprises a series of chapters and focus sections that document valid and applicable evidence of social inequalities. The observations in Part 1 are then linked to the mechanisms that underpin social inequality in cancer in Part 2, and to specific examples of interventions that may reduce future inequality gaps in Part 3.

Part 1 starts with an essay on why cancer inequalities matter, given the amassed evidence that inequalities touch everyone (although the im-

pact is greatest on the poorest in the community), and describes how such inequalities are, by and large, avoidable. Thereafter, an appraisal is given of indicators essential to capture socioeconomic status and thus monitor and evaluate cancer inequalities; some guidance is also provided on how population-level indicators can be routinely collected. The remainder of the chapters represent a world view of the evidence of inequalities in more depth. Included are descriptive comparisons of the cancer burden, both between and within countries, and a review of some of the factors that may drive such inequalities: those related to risk (e.g. the prevalence of certain infectious agents, lifestyle factors, and occupational exposures) and

those connected to the underlying health systems and infrastructure (e.g. the availability of and access to early diagnosis and screening, treatment, and palliative care).

Importantly, this part of the book also takes a populations-within-populations approach to identify the marked cancer inequalities in marginalized and disadvantaged communities, including those of Indigenous populations, refugees, and ethnic minorities.

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CHAPTER 3.

Why social inequalities matter in the cancer continuum

Diana Sarfati

What do we mean by social inequality in the cancer continuum?

Social inequality in the cancer continuum refers to systematic differences between social groups that affect people's risk of developing cancer, the likelihood that they receive effective and timely (or any) treatment for the cancer, whether they survive, and whether they have access to palliative care. Such inequality can occur on many axes, including, but not limited to, a person's socioeconomic status (SES), race or ethnicity, sex, disability, sexuality, and geographical location. Marked, persistent social inequalities occur across the cancer continuum both between and within countries. They reflect the importance of social, economic, environmental, historical, and political contexts in determining who develops cancer, what kind of cancer they develop, and whether they survive or die from it. The relationships between these determinants and cancer outcomes are neither linear nor simple. They operate through multiple intersecting pathways, reflected in differential exposure to risk factors such as social factors (e.g. resources and support), living conditions (e.g. housing and overcrowding), behavioural factors (tobacco use, unhealthy diet), and different access to and through health services.

Terminology in this field is somewhat contentious. For clarity, the focus of this book is on differences that occur between social groups and that are amenable to reasonable action (Kawachi et al., 2002). The term inequity implies a judgement that differences are inherently unjust, for example the uneven distribution of access to cancer care services. This element of unfairness can sometimes be contentious and difficult to determine. The term inequalities, referring to differences between population groups, will therefore be used in this book (Kawachi et al., 2002). The term disparities is very closely aligned with inequalities, and is more commonly used in United States literature on this topic (see Box 3.1).

Why should we care about social inequalities in cancer?

Social inequalities occur at every step of the cancer continuum

Social inequalities are evident at every step of the cancer continuum, starting from the individual's exposure

Inequity in health:

"Health inequity refers to those inequalities in health that are deemed to be unfair or stemming from some form of injustice…. Because identifying health inequities involves normative judgment, science alone cannot determine which inequalities are also inequitable, nor what proportion of an observed inequality is unjust or unfair" (Kawachi et al., 2002).

Inequalities in health:

"Health inequality is the generic term used to designate differences, variations, and disparities in the health achievements of individuals and groups" (Kawachi et al., 2002).

Disparities:

Disparities in cancer are defined by the United States National Cancer Institute as "adverse differences in cancer incidence (new cases), cancer prevalence (all existing cases), cancer death (mortality), cancer survivorship, and burden of cancer or related health conditions that exist among specific population groups" (National Cancer Institute, 2018).

to risk factors and the likelihood of developing cancer, to whether information relating to the cancer is collected and counted, through access to screening and diagnostic facilities, and even to fundamental palliative care.

Social patterns of cancer incidence and mortality have been documented for decades, with many cancers occurring more frequently among groups with lower SES and other underserved populations. This is particularly true for cancers related to tobacco use (such as lung and oral cancers), chronic infections (including cervical, stomach, and liver cancers), and exposure to some dietary, reproductive, occupational, and environmental factors (see Chapter 7). There are also clear differences in the pattern of cancer incidence and mortality across countries according to their Human Development Index, which provides a measure of social and economic progress (Bray et al., 2012). Countries of lower Human Development Index have a substan-

tially higher proportion of cancers associated with chronic infection, but cancers associated with reproductive and dietary risk factors, which predominate in high-income countries (HICs), are also quickly increasing in importance.

The most fundamental requirement for identifying, monitoring, and addressing inequalities in cancer is the ability to generate relevant information from a functional cancer registry and mortality vital registration. Despite some progress, many low- and medium-income countries (LMICs) still do not have the capacity to produce even basic cancer intelligence. Of the 71 countries reporting such data in the CONCORD-3 study, only 27 were LMICs (Allemani et al., 2018). Within HICs, poor cancer outcomes among some underserved groups remain largely invisible because of a lack of adequate data, notably the plight of Indigenous populations (Sarfati et al., 2018).

People diagnosed with cancer in LMICs and among the most vulner-

able groups in HICs are more likely to be diagnosed with advanced disease, and have poorer survival (Dalton et al., 2008; Ellis et al., 2012; Cunningham et al., 2015; Singh and Jemal, 2017; Allemani et al., 2018). In LMICs there is also a lack of access to timely and effective cancer diagnosis and care, resulting in exceptionally poor outcomes for those diagnosed (Atun et al., 2015; Sullivan et al., 2015; Allemani et al., 2018; Wilson et al., 2018). Cancer screening programmes in LMICs are often either not available or poorly developed (Sankaranarayanan, 2014). In HICs, there is consistent and troubling evidence of ethnic or racial disparities in cancer care and outcomes, as well as evidence of less access to cancer screening, poorer cancer care, and less favourable outcomes among other disadvantaged groups (Smedley et al., 2002; Woods et al., 2006; Hill et al., 2013; Cunningham et al., 2015).

In many LMICs, the outcomes for cancer remain dismal. In countries without universal health coverage or other adequate safeguards, a diagnosis of cancer can be financially catastrophic for individuals and their families because of unaffordable out-of-pocket payments (Carrera et al., 2018; Jan et al., 2018).

Access to palliative care is a neglected aspect of global health (Fig. 3.1), and many people with cancer, including children in LMICs and underserved people in some HICs, die without access to adequate symptomatic relief, despite its relative affordability (Knaul et al., 2018). The lack of effective palliative care for many of the world's most vulnerable people has recently been described as a "medical, public health, and moral failing and a travesty of justice" (Knaul et al., 2018).

Fig. 3.1. Distributed opioid morphine-equivalent and estimated percentage of need that is met for serious health-related suffering. Source: reprinted from Knaul et al. (2018), copyright 2018, with permission from Elsevier. Data from International Narcotics Control Board and WHO Global Health Estimates, 2015 (http://www.who.int/healthinfo/global_burden_disease/en).
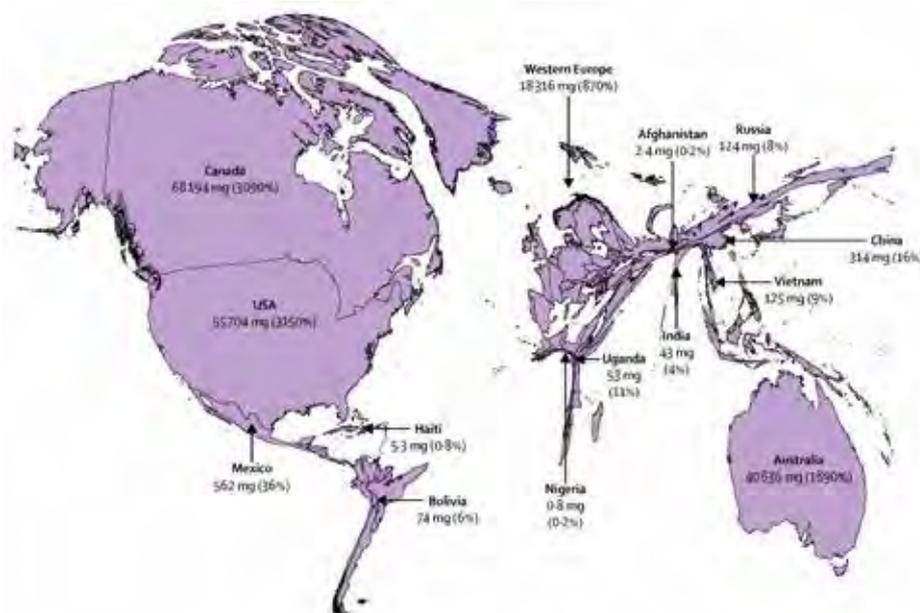
Despite these stark inequalities across the cancer continuum, cancer research remains focused on basic science and expensive treatments; there is very limited research on defining, identifying, and addressing social disparities in cancer (Krieger, 2005). Furthermore, most cancer research occurs in the context of HICs. For example, 73% of cervical cancer research is carried out in HICs compared with only 0.7% in low-income countries, despite the disproportionate burden of cervical cancer in LMICs (Ginsburg et al., 2017).

Each of these elements – social inequalities in cancer prevention, surveillance, treatment, and survival, as well as access to palliative care – is explored across several chapters of this book.

Social inequalities affect everyone

Although the poorest of the poor and the least privileged groups tend to have the worst health at both individual and country level, there is a demonstrable gradient highlighting how cancer mortality increases through all strata from those living in areas of least to greatest deprivation. For example, data from England show that cancer mortality is higher among those living in more deprived areas, with a clear gradient evident for both men and women (Fig. 3.2).

Fig. 3.2. Mortality rates (per 100 000) by deprivation quintile in England for all cancers combined (excluding non-melanoma skin cancers); 2007–2011 (European age-standardized).

a

All-cancer mortality rate per 100 000: Males

(1 = least deprived) NZDep2001 decile (10 = most deprived)

b

All-cancer mortality rate per 100 000: Females

(1 = least deprived) NZDep2001 decile (10 = most deprived)
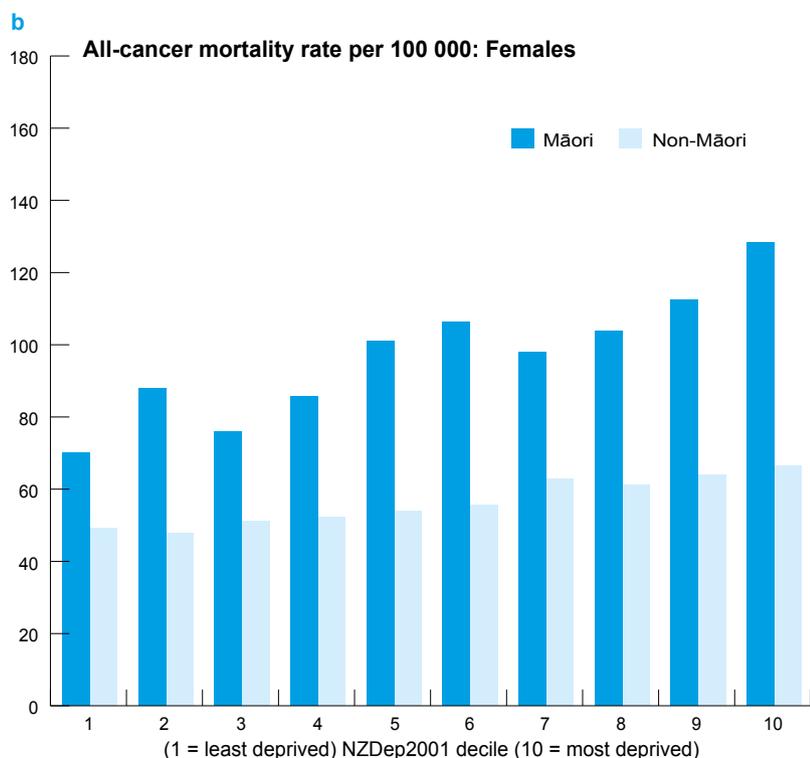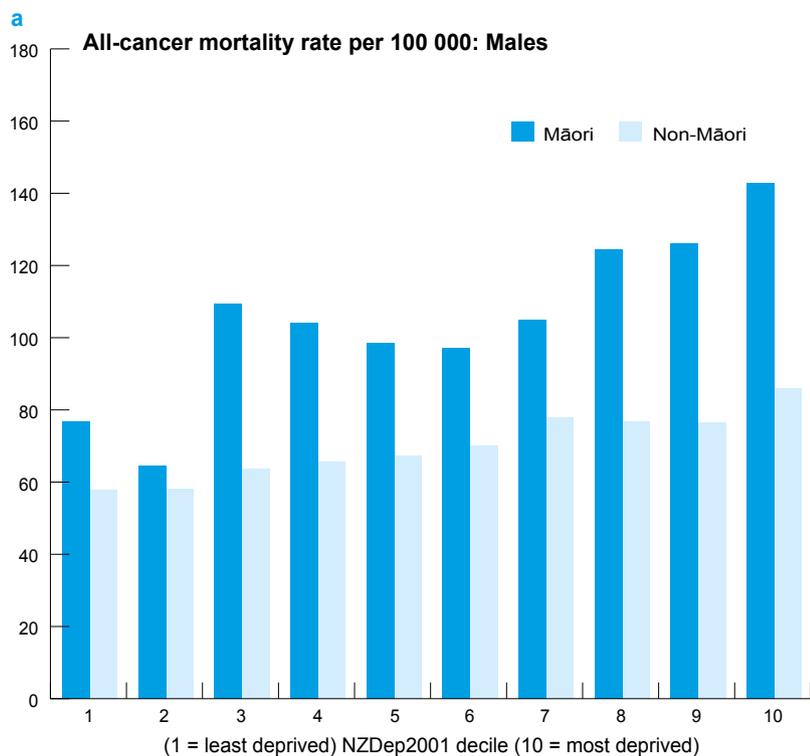
A similar pattern exists within New Zealand. A higher level of (area-based) deprivation is associated with higher mortality from cancer among males (Fig. 3.3a) and females (Fig. 3.3b). There are two additional points to note: (i) although a gradient is evident for both Māori and non-Māori populations, it is steeper for Māori, and (ii) at every level of deprivation, cancer mortality among Māori populations is substantially higher than that among non-Māori populations. These observations suggest that the disparities between ethnic groups cannot be explained by differences in SES only (Krieger, 2005; CSDH, 2008; de Souza et al., 2016).

The presence of such gradients means that interventions aiming to address inequalities have a potentially positive impact (theoretically, at least) on the health of entire populations. However, within and between countries some groups are disproportionately negatively affected by cancer, such as those living in poverty, Indigenous populations, ethnic minority groups, and those with mental illnesses (Valery et al., 2006; Dalton et al., 2008; Blakely et al., 2011; Bray et al., 2012; Ellis et al., 2012; Kisely et al., 2013; Cunningham et al., 2015; DeSantis et al., 2016; Singh and Jemal, 2017; Australian Institute of Health and Welfare, 2018; Bryere et al., 2018; Tweed et al., 2018). These groups have the potential to gain the most from such interventions.

The associations are strong and persistent

There are stark inequalities in cancer incidence and survival between those living in LMICs and those living in HICs. Although overall cancer incidence is higher in HICs, cancer rates are increasing more rapidly in

LMICs; the pattern of cancer sites is also different between HICs and LMICs (Farmer et al., 2010; Bray et al., 2012; de Souza et al., 2016). Indigenous populations, people living in poverty, and those who are part of ethnic minority groups or other disadvantaged groups tend to experience different patterns of cancer incidence; poorer cancer survival rates are observed among such groups compared with more privileged people, within both higher- and lower-income countries (Dalton et al., 2008; Blakely et al., 2011; Singh and Jemal, 2017; Allemani et al., 2018; Australian Institute of Health and Welfare, 2018; Bryere et al., 2018). Strong and persistent patterns exist, with systematic differences between social groups seen in nearly every context where they are investigated. The magnitude of the association with social factors is often greater than the association with so-called traditional risk factors for cancer. In New Zealand for example, the risk of cancer in the Māori population is higher than that in European New Zealanders by factors of 3–3.5 for lung cancer, 4–6 for stomach and liver cancers, and 2 for endometrial cancer (Teng et al., 2016; see Chapters 5 and 6 for more details).

Social inequalities are amenable to change

Social inequalities in cancer outcomes are not inevitable, but changing them is likely to require concerted action at many levels both within and outside of the health sector, and at both local regional and global levels. Strategies and policies focused on root causes, such as addressing unequal power and access to resources between groups, are likely to have an impact on the health status of populations generally and cancer

outcomes specifically. For example, global-level strategies that support sexual equality are likely to have a positive impact on women's cancers, particularly in LMICs (Ginsburg et al., 2017). International trade policies that encourage the production of and trade in foods high in saturated fats and sugars, or tobacco, are likely to increase the global burden of obesity- and tobacco-related cancers (Taylor et al., 2000; WHO, 2016). Similarly, policies within and between countries that counteract childhood poverty may have an impact on adult cancers through complex, but generally poorly understood, mechanisms. One example is policies to reduce overcrowding in children's living conditions; less overcrowding is associated with a lower risk of cancer-related chronic infections including *Helicobacter pylori* and hepatitis B virus (HBV) (Chapter 7; Teng et al., 2017).

Risk factors tend to be more prevalent in the lives of members of the most disadvantaged groups. The reasons for this are complex and multifaceted, including environmental factors (such as the availability of alcohol, tobacco, and healthy food), psychosocial factors (such as stress relating to material hardship, lack of control over one's life, and lack of social support), and cultural, historical, and economic factors (McKee and Shkolnikov, 2001; CSDH, 2008; Mackenbach et al., 2008). Many cancers in LMICs and excess cancers among disadvantaged groups within all countries are amenable to prevention through policies and strategies addressing risk factors of cancer such as: comprehensive tobacco control policies; strategies to address obesity, including supporting a healthy diet and increased physical activity; and policies for eq-

uitable access to high-quality vaccination and screening programmes (Farmer et al., 2010; de Souza et al., 2016; Plummer et al., 2016; Ginsburg et al., 2017; Sassi et al., 2018).

Access to affordable, appropriate, and effective health care with a focus on cancer prevention, diagnosis, and treatment is critical. There are vast disparities between the health care available in HICs and in LMICs, with populations in many LMICs experiencing very poor access to cancer treatment services (Farmer et al., 2010; Atun et al., 2015; Sullivan et al., 2015; de Souza et al., 2016; Ginsburg et al., 2017). A lack of universal health coverage in many LMICs is a barrier both to development and to addressing inequalities in cancer outcomes. Progress towards meeting the health-related United Nations Sustainable Development Goals of universal health coverage will have an effect on cancer inequalities both between and within countries (see Chapter 10).

There is also a growing body of evidence supporting the importance of early-life environment as an important determinant of future health (or ill health). Although evidence relating to the effect of early-life exposure to traditional risk factors for cancer (obesity, poor diet, and physical inactivity) on adult cancer risk is inconsistent, the increased risk of cancer in adults exposed to tobacco and to certain infections early in life is conclusive (Teng et al., 2016, 2017).

Evidence of the effectiveness of interventions to reduce inequalities within HICs is largely based on single aspects of complex systems (Masi et al., 2007; Glick et al., 2012; Gorin et al. 2012; McPheeters et al., 2012; National Cancer Institute, 2018). However, comprehensive systems-level approaches are most

likely to succeed (Smedley et al., 2002; Ministry of Health, 2003; Steinberg, 2008; Goss et al., 2009; Department of Health, 2011; National Cancer Institute, 2018), and there is some evidence that such broad, organized approaches may be effective in reducing inequalities within HICs. For example, socioeconomic inequalities in participation in screening for breast cancer and cervical cancer are less likely to be found in countries with organized screening programmes (Palència et al., 2010), socioeconomic disparities are more marked in the USA than in Canada, where universal health care is available (Gorey et al., 2009), and in New Zealand, ethnic disparities in cancer care and survival have decreased over time as a result of organized screening programmes that include an explicit focus on reducing inequalities (McLeod et al., 2010).

Addressing social inequality in health is a global priority

As outlined in Chapter 2, this book focuses on the evidence of the positive impact of aligning global cancer control activity with efforts to improve equality within global health agendas more generally, as well as the action being taken to achieve this goal. It builds on recent work, including the seminal report from the Commission on Social Determinants of Health (CSDH, 2008). A global conference held in Rio de Janeiro in 2011 resulted in the Rio Declaration on Social Determinants of Health (WHO, 2011), with a subsequent World Health Assembly resolution in 2012 endorsing this declaration and the importance of correcting inequities in health (WHA, 2012). These and other activities aim to progress and focus an agenda on supporting health equality within global, region-

al, and national health and development programmes, and to assist the achievement of the United Nations Sustainable Development Goals (Farmer et al., 2010; UICC, 2013; Stewart and Wild, 2014; UN, 2018). In 2017, the Seventieth World Health Assembly emphasized the importance of cancer prevention and control, with an explicit call to monitor and address inequality (WHA, 2017).

Social inequalities in cancer are often unfair

In the Rio Political Declaration on Social Determinants of Health (WHO, 2011), world leaders reaffirmed that "health inequities within and between countries are politically, socially and economically unacceptable, as well as unfair and largely avoidable". Systematic variations in who develops cancer, the type of cancer developed, and how and whether people survive cancer are seen both within and between countries (Krieger, 2005; Farmer et al., 2010; Blakely et al., 2011; Bray et al., 2012; de Souza et al., 2016; see also Chapters 5 and 6). Where these differences are preventable or amenable to reasonable action, they are not acceptable and require coordinated action. These inequalities reflect the environments in which people are born, live, and work, and, ultimately, the uneven distribution of resources and services within and between countries (CSDH, 2008). The obvious consequence of this is that addressing inequality in health requires action at all levels of society, not just within the health (or cancer) sector.

A clear example of this is the global distribution of infection-related cancers (Chapter 7). About 15% of the world's cancers are caused by infectious agents, particularly *H. pylori*, human papillomavirus (HPV),

HBV, and hepatitis C virus (HCV) (Plummer et al., 2016). The distribution of these cancers is strongly related to the socioeconomic development of countries; less than 5% of cancers in Australia, some European countries, New Zealand, and the USA are caused by infection, but this proportion rises to more than 50% of cancers in some countries in sub-Saharan Africa (Plummer et al., 2016). Within HICs, people who develop and die from infection-related cancers are disproportionately from low-income, ethnic minority, Indigenous, or other underserved groups (Dalton et al., 2008; Blakely et al., 2011; Singh and Jemal, 2017; Australian Institute of Health and Welfare, 2018; Bryere et al., 2018). These cancers are highly preventable with the availability of extremely cost-effective interventions (Farmer et al., 2010; Knaul et al., 2012; Gelband et al., 2015; de Souza et al., 2016; Plummer et al., 2016). The fact that inequalities in these cancers exist is a stark illustration of the inadequacy of current social, political, and economic policies, which, instead of promoting health for all, put the world's most vulnerable people at increased risk.

Global demographic trends are likely to affect inequality

Social inequalities are not static. Changes in population structures may exacerbate social inequalities in cancer outcomes, or create new inequalities. For example, population ageing results in an increasing burden of cancer, with the relative impact being greater for LMICs (Pilleron et al., 2018); without action, such trends are likely to exacerbate the differences between LMICs and HICs. Continuing global urbanization and the growth of urban slums

are leading to substantial challenges for health equity in general (CSDH, 2008). These trends tend to be associated with higher levels of overcrowding, reductions in physical activity, increased consumption of energy-dense and processed food leading to higher rates of obesity, and higher rates of hazardous alcohol consumption. All of these are risk factors for many cancers, and these trends tend to disproportionately affect the most disadvantaged groups (CSDH, 2008). Conflicts and other catastrophic events have also led to the forced emigration of entire populations, resulting in the dissolution of structures and processes to protect the health of those people (see Focus 6).

Social inequalities have major economic implications

There are good economic arguments for investing in health generally (WHO, 2001). If we assume that interventions that reduce inequalities in health have an upwards levelling effect, that is, the health of those in more disadvantaged groups is improved towards the level of those in less disadvantaged groups, then reductions in inequalities also result in better population health overall. In 2015, there were 17.5 million new cases of cancer and 8.7 million deaths from cancer worldwide;

numbers are expected to increase over the next decade, particularly in LMICs (Bray et al., 2012; Fitzmaurice et al., 2017). The global economic impact of cancer is substantial, conservatively estimated at US$ 1.16 trillion in 2010 (Stewart and Wild, 2014).

There are few studies based in HICs that have explicitly estimated the costs of inequality in either health generally or cancer specifically. However, Mackenbach et al. (2011) found that inequality-related losses accounted for approximately 20% of costs to the health-care system and 15% of costs to social security systems within the European Union. Mackenbach et al. (2011) also found that introducing an equity-focused tobacco policy that reduced smoking by one third among groups with low SES and one quarter among groups with high SES would result in improved health overall and a 7% reduction in costs relating to inequalities.

Although there is a scarcity of relevant research in LMICs, the evidence that exists suggests that there are several interventions that are likely to be cost-effective, even in the most constrained of settings (Horton and Gauvreau, 2015). These interventions relate to preventive strategies such as tobacco control, and the expansion of vaccination programmes and cervical screening

strategies (Horton and Gauvreau, 2015). One estimate is that investing US$ 100 million in core cancer prevention strategies in LMICs could result in savings of US$ 100 billion in treatment costs (Knaul et al., 2012). The expansion of cancer treatments, particularly surgery and radiotherapy, would also be expected to reduce the massive disparity in outcomes between those living in HICs and those living in LMICs (Atun et al., 2015; Horton and Gauvreau, 2015; Sullivan et al., 2015).

Conclusions

Inequalities in cancer care and outcomes both between and within countries are persistent and large, resulting in substantial human suffering and economic cost. They affect all populations, with the poorest of the poor most profoundly affected. They are, to a large extent, avoidable. Concerted and coordinated multisectoral action at regional, national, and global levels is urgently needed to prioritize cancer control, strengthen health systems, and monitor progress. The remainder of this book expands on these issues, providing detailed evidence of the extent of inequalities within and between countries, the drivers of those inequalities, and key approaches for tackling them.

Key points

- Marked, persistent social inequalities occur along the cancer continuum both between and within countries.
- Those living in low-income countries and underserved populations within high-income countries are particularly likely to have increased risks of cancers associated with tobacco use, chronic infections, and exposure to some dietary, reproductive, occupational, and environmental factors.
- Those living in low-income countries and underserved populations are less likely to have access to effective diagnostic, screening, treatment, and palliative care facilities.
- Reducing cancer inequalities is likely to require concerted action at many levels both within and outside of the health sector.

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FOCUS 1.

Changing social inequalities in cancer mortality: the value of linking census and health data

Andrea Teng, Tony Blakely, and Diana Sarfati

The monitoring of trends in social inequalities over time by the New Zealand Census Mortality Study and Cancer Trends project has informed policy, research, and prioritization agendas for more than a decade, including work that explicitly evaluates the cost–effectiveness of cancer-related interventions and their effect on inequalities (BODE3, 2018). Three decades of cancer trends by income and ethnicity have been analysed by linking mortality and registry data with census data for six national population cohorts from 1981 to 2011.

Cancer mortality has declined over time; however, improvements have been greater for European/Other populations (non-Māori, non-Pacific, and non-Asian ethnicities) and for the highest-income groups (Fig. F1.1) than for groups of other ethnicity and income. By 2006–2011,

Māori (Indigenous) populations were twice as likely to die from cancer than European/Other populations, and cancer had overtaken cardiovascular disease as the largest contributor to the excess mortality experienced by Māori women and low-income women (Teng et al., 2016).

Results suggest that the drivers of social inequalities in cancer are changing, with obesity-related cancers making an increasing contribution. This is a sentinel warning of the increasing relevance of obesity- and nutrition-related cancers in social inequalities. From 1981–1984 to 2006–2011, absolute inequalities more than tripled for breast cancer mortality in Māori women (rate difference, 6–20 per 100 000; *P* < 0.01) and for endometrial cancer incidence in Pacific women (rate difference, 11–37 per 100 000; *P* < 0.01) compared

with women of European/Other ethnicity (Teng et al., 2016). Over the same period, absolute inequalities in cancer for Māori populations were observed to significantly increase in terms of colorectal, male prostate, and female breast cancer mortality rates and colorectal, male liver, and female breast cancer incidence rates (Teng et al., 2016).

In the most recent cohorts, the difference in lung cancer mortality rates between the quintiles of lowest and highest income and between Māori and European/Other populations declined (Figs. F1.1 and F1.2). However, lung cancer was the largest contributor to the inequalities in cancer mortality experienced by Māori populations (which accounted for 47% of excess cancer deaths) and by low-income households (which accounted for 33% of excess

Fig. F1.1. Difference in cause-specific cancer mortality rates between Māori (Indigenous) populations and European/Other populations for both men and women aged 1–74 years during 1981–2011. Results are age-standardized to the WHO world population. Source: Teng et al. (2016). © Teng et al. 2016. Distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/).
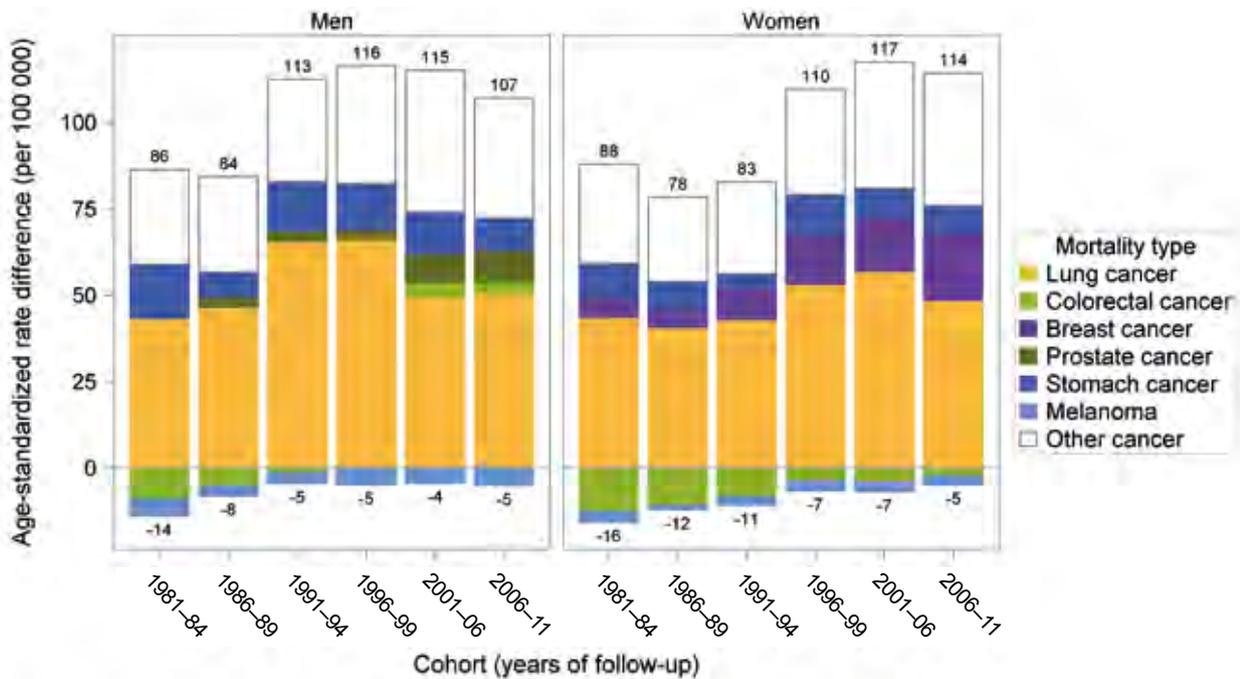
Fig. F1.2. Difference in cause-specific cancer mortality rates between the quintiles of lowest and highest income for men and women aged 25–74 years during 1981–2011. Results are age-standardized to the WHO world population. Source: Teng et al. (2017), with permission from John Wiley & Sons Inc.
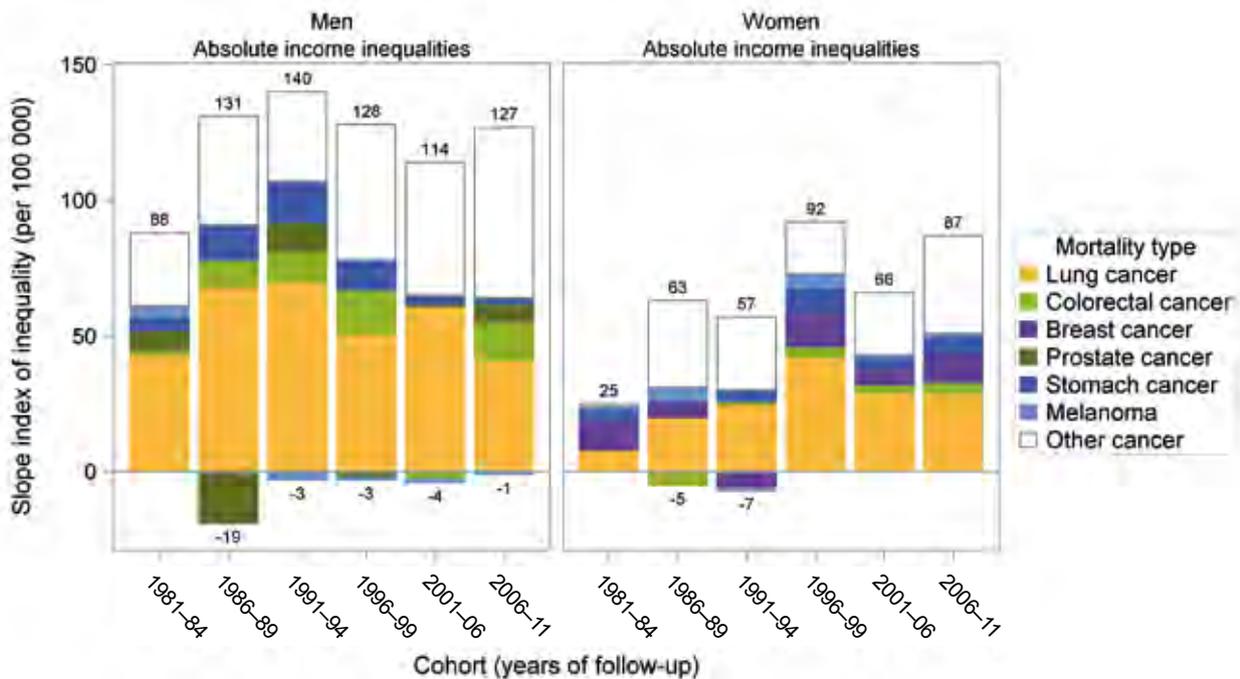
deaths) during 2006–2011 (Teng et al., 2017). Ongoing social disparities in smoking prevalence must continue to be addressed.

The New Zealand Census Mortality Study and Cancer Trends team has developed a tool for the simultaneous depiction of trends in cancer mortality and absolute and relative inequalities in cancer, for monitoring inequalities and setting goals (Blakely et al., 2017); data are freely available via the interactive Population Data Explorer (available from: nzcms-ct-data-explorer.shinyapps.io/version8/).

Monitoring social inequalities in cancer informs priorities for cancer prevention programmes and can enable progress towards equality to be evaluated. The trends observed during this study highlight the types of cancer that contribute to inequalities and the pathways over which inequalities take effect. Positive trends in equality in cancer are more likely to be achieved if effective tobacco control and obesity prevention measures benefit the social groups with the greatest prevalence of smoking and obesity.

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CHAPTER 4.

Measuring socioeconomic status and inequalities

David I. Conway, Alex D. McMahon, Denise Brown, and Alastair H. Leyland

"The true **measure** of any society can be found in how it treats its most vulnerable members."

Attributed to Mahatma Gandhi (our emphasis)

Introduction

In 2008, the World Health Organization's pioneering Commission on Social Determinants of Health measured the extent of health inequalities in the city of Glasgow, Scotland, as an example. The final report revealed that a boy in the deprived area of Calton had an average life expectancy of 54 years compared with a boy in the affluent suburb of Lenzie, only 12 km away, who could expect to live to an age of 82 years (CSDH, 2008): a gap of 28 years. Michael Marmot, chair of the World Health Organization Commission, later reflected in his book *The Health Gap* that this "was a tale of two cities ... and they are both in Glasgow" (Marmot, 2015). This is a most basic,

fundamental, and stark example of measuring health inequalities. The authors of this chapter all work in Glasgow, and are driven by the aim of tackling this inequality.

Measures of health inequality, which are determined by inequalities in income, wealth, and power (WHO, 2010), are a reflection of the levels of justice and fairness in society. The measurement of inequalities in health is essential to define, describe, and understand the nature of the public health problem; it is a crucial first step in the development of strategies and policies to tackle health inequalities, and in the monitoring and evaluation of the effectiveness of approaches.

Socioeconomic inequalities can exist both within and between coun-

tries (as detailed in Chapters 5 and 6), and they have an impact across the cancer continuum, from burden and risk, to early detection, diagnosis, and treatment (see Chapter 7), and to outcomes including quality of life, mortality, and survival. Inequalities also exist across other population groups and communities (defined by sex, age, race or ethnicity, geographical area, time periods, and health status, for example), although socioeconomic status (SES) is often a major factor in these differences (United Kingdom Government, 2010; Krieger, 2014). This chapter describes two key aspects of measurement and analysis of SES in relation to cancer: indicators of SES, and metrics of health inequality between socioeconomic strata.

Indicators of SES

SES or socioeconomic position is a theoretical construct of socioeconomic hierarchies with roots in the social theories of Weber and Marx (Lynch and Kaplan, 2000). SES is conceptualized through indicators or measures collected at the individual or area-based level. In social epidemiology, these indicators are used to capture and analyse the impacts of social determinants of health (Glymour et al., 2014). Several comprehensive reviews of SES indicators have discussed in detail the strengths and weaknesses of the different approaches to measurement (e.g. Liberatos et al., 1988; Berkman and Macintyre, 1997; Krieger, 2001; Galobardes et al., 2006a, b; Glymour et al., 2014). Drawing from and expanding on these reviews, we summarize individual indicators of SES, including examples of indicators and notes on their interpretation, in Table 4.1.

Table 4.1. Individual indicators of socioeconomic status: their measurement and interpretation

Indicator	Measurement and examples	Interpretation and comments
Income	Individual or household: monthly or annual; before taxes; equivalized (household income by household size) Government or state welfare benefit support; food stamps Absolute or relative poverty thresholds	Measures access to material resources (food, shelter, and culture) and access to services (health care, leisure or recreation activities, and education) Relates to social standing or prestige Reverse causality: health impacts on level of income Context-specific: country, sex, age
Education	Educational attainment: highest level attained; qualifications; years completed; ISCED	Reflects early-life SES, usually stable across the life-course Strong determinant of employment and income Influences position in society or social networks Affects access to health care or information Determines values, cognitive decision-making, risk taking, behaviours, and life skills Affects exposure to and ability to cope with stressors Reverse causality: childhood poor health impacts on school attendance and attainment Context-specific: country education system, age cohorts
Occupation	Employment or job history: longest, first, last; blue or white collar; manual or non-manual; "head of household"; RGSC; NS-SEC; European Socioeconomic Classification; American Census Classification; Wright's Social Classification (Wright, 1997); Lombardi et al. Social Classification (Lombardi et al., 1988); Erikson and Goldthorpe Classification (Erikson and Goldthorpe, 1992); country-specific classifications; ISEI; SIOPS Unemployment experience (ever or number of years) Type of contract: salaried or hourly wage; part-time, full-time, or zero-hours; short- or long-term contract; job insecurity	Reflects social standing or prestige, working relations and conditions Strong determinant of income Based on educational attainment Influences social networks, work-based stress, autonomy or control Reflects occupational hazards, exposures, or demands Excludes some groups (e.g. retired people, unpaid home workers or "housewives", students, some self-employed) Context-specific: country (level of industrialization or deindustrialization), age cohorts Unemployment has particular impacts on social exclusion and income, poverty, and access to health care Reverse causality: health impacts on (un)employment
Wealth	Assets (total or specific): land, property, livestock; housing tenure; ownership of car, refrigerator, television, etc.; DHS; FAS	Reflects material aspect of socioeconomic circumstances Relates to income Context-specific: country, rural or urban Reverse causality: health impacts ability to accumulate wealth
Housing	Housing quality or conditions: overcrowding (number of residents per number of rooms); dampness; housing type; water and sanitation	Direct impact: exposures for specific diseases Relates to material circumstances Context-specific: country development Reverse causality: health impacts on money available to spend on housing

Table 4.1. Individual indicators of socioeconomic status: their measurement and interpretation (continued)

Indicator	Measurement and examples	Interpretation and comments
Compositional	Combinations of SES metrics: education or income (study-specific); income and wealth (FAS); WAMI Historic indicators: Hollingshead index of social position; Duncan index; Nam–Powers socioeconomic status; Warner's index of status characteristics	Attempts to capture multiple dimensions of SES; however, composite indicators perhaps mask specific relationships and mechanisms which individual SES measurements provide
Childhood SES	Parental SES: parental (father's or mother's) occupation; household income or conditions; child-related benefits (e.g. entitlement to free school meals) Educational attainment (end of childhood or early years)	Used in life-course SES analyses to capture childhood socioeconomic circumstances
Subjective SES	Self-identification, comparison, or satisfaction: self-identification as upper, middle, or lower class; comparison of income with others; satisfaction with income; MacArthur Scales of subjective social status	Individual's perception of his or her socioeconomic standing Relates to objective indicators of SES Could be part of psychosocial pathway of health inequalities
Social capital	Social support, inclusion, or exclusion: more than 100 tools identified in recent systematic review (25 with validated psychometric elements; Cordier et al., 2017); CAMSIS	Commonly measures domains of connectedness, community participation, and citizenship; no single instrument measures all aspects within the three domains of social inclusion Hierarchical social interactions reflect social and material advantage; conversely, social exclusion from social and community life can result from economic deprivation and low SES

CAMSIS, Cambridge Social Interaction and Stratification Scale; DHS, Demographic and Health Surveys Wealth Index; FAS, Family Affluence Scale; ISCED, International Standard Classification of Education; ISEI, International Socioeconomic Index; NS-SEC, National Statistics Socioeconomic Classification (UK); RGSC, Registrar General's Social Classification (UK); SES, socioeconomic status; SIOPS, Treiman's Standard International Occupational Prestige Scale; WAMI, water and sanitation, the selected approach to measuring household wealth (assets), maternal education, and income index.

SES indicators have typically included individual measures of income, education, and occupational social class, and these measures have formed the mainstay of cancer socioeconomic analyses in relation to health and disease outcomes. Education level, followed by occupational social class and income, is widely used in analytical epidemiology investigating individual SES risk associations with cancer. Such associations are evident in the systematic reviews and meta-analyses of case–control and/or cohort studies across many cancer sites, including oral cavity (Conway et al.,

2008), lung (Sidorchuk et al., 2009), stomach (Uthman et al., 2013), colon and rectum (Manser and Bauerfeind, 2014), head and neck (Conway et al., 2015), and breast (Lundqvist et al., 2016). These analyses sought to both quantify the risk association of SES with cancer, and assess whether such associations are attenuated (explained) by behavioural risk factors. Measures of wealth have increasingly been a focus of health inequality studies, but have received limited attention in relation to cancer (Pollack et al., 2007).

Area-based socioeconomic indicators are summarized in Table 4.2.

These indicators are frequently used in descriptive epidemiological analyses of cancer registry data at the state or regional level (Harper and Lynch, 2005) or country level (Purkayastha et al., 2016), often to overcome the lack of individual-level SES data. At the global level, IARC is leading the field in the assessment of the burden of cancer using sophisticated measures that go beyond categorizations of developing versus developed countries, by using more sophisticated measures of development including the Human Development Index (Bray et al., 2012; Arnold et al., 2016). There are concerns that interpretations of

the association between area-based indicators and health outcomes are prone to the ecological fallacy, where all individuals living in an area are assigned an SES based on the characteristics of that particular area. However, people living in the same area will share many of the socioeconomic environmental circumstances that have an impact on health apart from (or over and above) individual SES factors (Berkman and Macintyre, 1997).

Within- and between-country inequalities in cancer mortality have also been regularly examined in Europe via educational attainment (Menvielle et al., 2008); see Chapter 6 for further details.

Recent studies have begun to investigate the contribution of multiple measures of SES to inequalities in cancer; this demonstrates the interconnectedness of different SES measures (Spadea et al., 2010; Sharpe et al., 2014). These studies highlight both the independent effects of different SES measures and the further elevated risk associations observed with combinations of SES indicators, for example, low educational attainment or living in a deprived community.

Table 4.2. Area-based socioeconomic indicators: their measurement and interpretation

Indicator	Measurement and examples	Interpretation and comments
Neighbourhood, community (small areas)	Deprivation indices (zip code or postal code) using composite of multiple census or administrative data: Townsend deprivation index (Townsend et al. 1988); Carstairs deprivation index (Carstairs and Morris, 1989); indices of multiple deprivation (e.g. SIMD); European Deprivation Index; single aggregate measure e.g. percentage of population living below the poverty line; urban or rural	Categorizes areas over a continuum from deprived to affluent Usually aggregates individual-level data rather than true area characteristics Infers individual's SES (but ecological fallacy of assigning all individuals in the area the same SES) Infers socioeconomic conditions of an area through the SES characteristics of the people living there, or other dimensions of the social and physical environment increasingly included in indices of multiple deprivation (e.g. access to services)
State, region, county level	Single aggregate measure: income-to-poverty ratio; median income; cost of living; poverty level; rural or urban; HDI (regional level)	Interpreted as per small areas; however, when inferring individual SES, the larger the areas the greater the likelihood of misclassification (underestimation of individual SES)
Country level	Country income or wealth: high-, middle-, or low-income countries; GDP; GDP per capita; GNI per capita Country development: MPI; HDI Country income inequality: Gini index; S80/S20 Country happiness: GNH; WHI	Provides between-country comparisons Country economic measures of national or county income or wealth estimated from economic output (productivity) by population MPI is a composite indicator of poverty (health, living standards) and HDI includes life expectancy, education, GDP; these indicate societal and economic conditions Context-specific: country, underlying demography Country income inequality describes, at the country level, the gap between the rich and poor (i.e. the share of income between higher and lower groups) Impacts on society as a whole, but particularly on those on lower incomes who suffer disproportionate health impacts and are prevented from realizing their human capital potential Happiness indicators are subjective ratings of life (based on small questionnaire sample), weighted by levels of GDP, life expectancy, generosity, social support, freedom, and corruption

GDP, gross domestic product; GNH, gross national happiness; GNI, gross national income; HDI, Human Development Index; MPI, Multidimensional Poverty Index; S20/S80, the ratio of the mean income received by the 20% of the population with the highest income to that received by the 20% of the population with the lowest income; SES, socioeconomic status; SIMD, Scottish Index of Multiple Deprivation; WHI, World Happiness Index.

Sociodemographic factors

In addition to the dominant effect of socioeconomic inequalities, there are also important inequalities related to other population demographic groups. These factors, summarized in Table 4.3, are also known as equality domains and have their origins in human rights (United Nations, 2018). The concept of the interrelationship between these various measures of social stratification and SES was named "intersectionality" by Crenshaw (1991), who proposed a theoretical framework for analysing the combined effects of multiple social categories.

The future of SES measurement

The cancer epidemiology scientific community has been challenged to characterize the exposome, which encompasses individual environmental exposures across the life-course from as early as the prenatal period, using similar conceptual approaches and level of rigour as those taken to map and study the genome (Wild, 2005). The concept has been refined and updated with a general external environment domain that includes SES factors: "social capital, education, financial status, psychological and mental stress, urban–rural environment, [and] climate" (Wild, 2012). More recently, a "socio-exposome" has been proposed to

Table 4.3. Sociodemographic factors: their measurement and interpretation

Indicator	Measurement and examples	Interpretation and comments
Race, ethnicity, caste, immigration	Ethnicity classifications: ESCEG; country-specific (e.g. UK Census, US NIH, or Indian Government Scheduled Castes and Scheduled Tribes) Immigration (legal or illegal): country of birth; time since arrival in new country; degree of acculturation	Difficult to assess (societies are increasingly diverse) Self-reported or self-declared race is superior to name search methods or analyses by country of birth Ethnicity differences reflect multiple factors, including educational, meaning there are different occupational opportunities for minority groups Relates to discrimination Paradox of migrants' health advantage, possibly due to higher SES of those able to migrate relative to health of destination countries; artefactual due to data limitations
Marital status and living arrangements	Living arrangements: with parent(s), child(ren), alone, as a couple, lone parent; residential care (numbers of household residents); prisoners	Marital status can infer social support, but also provides economic or material advantage and access to health care (USA) Adverse impacts on divorced and widowed Healthier selection effects of being married Context-specific: country, culture, age cohort effects Relates to household structure, social relationships, and to SES
Language isolation	For example, the US Census Bureau defines a "limited English speaking household" as one in which no member of age ≥ 14 years (i) speaks only English at home; or (ii) speaks a non-English language at home and speaks English "very well".	Relates to ethnicity, immigration status, and also SES Impacts on abilities to integrate into society and to navigate access to health, care, and public services Impacts on health literacy Context-specific: country, ethnic group
Disability	Self-identified; ICF (e.g. WHODAS, MDS); objective clinical measures (e.g. visual acuity, seizure history)	Includes physical and intellectual disabilities Impact directly on health outcomes, on SES circumstances Impacts on access to health care and participation in society Relates to discrimination Context-specific: country
Religion, faith, belief, religious practices	Assessed along with, but separately from, ethnicity: major, other, or no religion(s)	Impacts on belief system, behaviours (e.g. diet, reproductive health) Reflects SES Relates to ethnicity and identity Relates to discrimination Context-specific: country, age cohorts

Table 4.3. Sociodemographic factors: their measurement and interpretation (continued)

Indicator	Measurement and examples	Interpretation and comments
Sexual identity, sexuality	LGBTQ+ Sexual orientation, behaviour: KSOG; self-assessment; MSS	Can change over lifetime Impacts directly on health, e.g. sexually transmitted diseases Impacts on access to health care Relates to discrimination
Sex, gender	Trans-inclusive measures: two-step measures: (i) birth-assigned sex; and (ii) current gender identity	Women may be performing unpaid work at home in caring roles or be employed in lower-paid jobs, and have different educational and work opportunities Important to consider partner's SES also Relates to discrimination Context-specific: country, ethnic group
Age	Age (years), age groups, life stages (e.g. early years, middle age, older years), birth cohorts	Interactions between age and SES examined in life-course approaches SES fundamentally affects life expectancy Relates to discrimination

ESCEG, European Standard Classification of Cultural and Ethnic Groups; ICF, International Classification of Functioning, Disability and Health; KSOG, Klein Sexual Orientation Grid; LGBTQ+, lesbian, gay, bisexual, transgender, queer (or questioning); MDS, Model Disability Survey; MSS, Multidimensional Scale of Sexuality; NIH, National Institutes of Health; SES, socioeconomic status; UK, United Kingdom; US, United States; WHODAS, World Health Organization Disability Assessment Schedule.

capture the wide range of socioeconomic environments and influences (Senier et al., 2017). Socioeconomic measures and exposures need to be better and more comprehensively captured, so that cancer risks associated with socioeconomic factors and their interactions with physical environmental exposures and genetics can be investigated.

Analysis approaches

Risk association analyses between SES and health or disease (including cancer) are so well accepted that it is very unusual to investigate risk factors without adjusting for SES (Berkman and Macintyre, 1997). However, with the growing discipline of social epidemiology during the past decades, studies have increasingly reversed this logic and focused on socioeconomic factors as risk factors (Kawachi and Subramanian, 2018). Typically, analyses take the highest SES strata as the referent category and quantify the relative

risk associations in lower SES strata, quantifying inequalities between groups with different SES. These analyses can be influenced by the number and size of SES strata. Reducing the size (and increasing the number) of strata will increase the extent of inequalities observed between the extreme groups, with smaller strata implying more extreme social groupings. More sophisticated analyses of inequalities that make adjustments for such changes are therefore required (see the section on "Metrics of health inequalities" below).

Life-course analysis takes advantage of the ever-present and potentially changing socioeconomic circumstances at all stages of the life-course from birth (or in utero) to death (Ben Shlomo and Kuh, 2002; see also Chapter 12 for a detailed description); SES is therefore a time-varying exposure, and combinations of SES measures at different times across the life-course can be

used. Insights from life-course epidemiology have highlighted the limitation of capturing SES on the basis of data collected at a single time point in terms of investigating socioeconomic risk as well as adjusting for SES confounding in analyses. Although recognition of this limitation represents progress, investigating and disentangling all the processes occurring over a life-course (e.g. critical periods, social mobility, cumulative effects, or combinations of these) is challenging (Hallqvist et al. 2004). Much attention has been given to the effect of adverse SES in childhood and early life on the occurrence of disease in adulthood and later life, independent of adult SES; for example, children who experience conditions of overcrowding or poor hygiene are more likely to become infected with *Helicobacter pylori*, which increases the risk of stomach cancer in later life (Stemmermann and Fenoglio-Preiser, 2002). A few studies have investigated the association between cancer

risk and social mobility (Schmeisser et al., 2010; Behrens et al., 2016), and the cumulative effects of SES across the life-course are increasingly recognized as being associated with disease outcomes (Ben-Shlomo and Kuh, 2002).

Multilevel analysis is a form of regression analysis that takes into account the natural clustering of one unit of analysis (such as the individual) within another (such as the area of residence), and can be used to distinguish between contextual (macro) and compositional (micro) influences (Diez Roux, 2002). Even in the absence of any interest in contextual influences, multilevel analysis enables us to correct for the lack of independence between observations at the micro (e.g. individual) level. In assessing inequalities in health, multilevel analysis can be used to estimate a variance indicative of the size of inequality between areas or over time (Leyland, 2004), or to provide an appropriate estimate of a contextual effect, such as an indicator of area deprivation (Krieger et al., 2003).

Metrics of health inequalities

Numerous measures have been proposed as a means of measuring inequalities in health, whether in relation to cancer specifically (Harper and Lynch, 2005) or to health in general (Regidor, 2004a, b; Wagstaff and van Doorslaer, 2004; Blair et al., 2013). Aside from the longstanding debate about whether more emphasis should be placed on absolute or relative measures of inequality (Asada, 2010; King et al., 2012; Mackenbach, 2015), there is a realization that the actual metric chosen can influence the inequality observed and hence the monitoring of changes in inequality; as such, the choice of a measure or measures represents a value judgement (Harper et al., 2010; Kjellsson et al., 2015). For a detailed discussion of interpretation of measures of inequalities, see Chapter 14.

In Table 4.4 we present the definition of some of the most commonly used measures of inequality along with their strengths and limitations; see Munoz-Aroyo and Sutton (2007)

for further information on some of these measures. We also present the value and interpretation based on data for cancer mortality of men aged 50–59 years across quintiles of area deprivation in Scotland between 2012 and 2016 (the underlying data are shown in Table 4.5).

The complex methods shown in Table 4.4 have the advantage of taking into account all available information from the different groups and their SES. Although simpler measures do have their place, they do not represent the entire picture (Mackenbach and Kunst, 1997). The slope index of inequality (SII) and relative index of inequality (RII) compare the notionally most deprived individuals with the least deprived individuals in the population on an absolute and relative scale, respectively. Different methods have been proposed for calculation of SII, based on either a linear regression of the age-standardized rates weighted by the size of the socioeconomic groups (Pamuk, 1985) or on an additive Poisson regression of the number of deaths (Moreno-Betancur

Table 4.4. Measures of inequality applied to the example of cancer mortality of men aged 50–59 years in Scotland between 2012 and 2016 across quintiles of area deprivation

Measure	Definition	Advantages	Disadvantages	Interpretation[a]
Simple				
Rate difference (RD)	Absolute measure: difference in health between the most and least deprived group	Easy to calculate and interpret	Insensitive to group size; ignores information in the middle groups	The difference in the cancer mortality rate between the most and least deprived quintiles is 208 per 100 000 population
Rate ratio (RR)	Relative measure: ratio of the rates in the most deprived and least deprived groups	Easy to calculate and interpret	Insensitive to group size; ignores information in the middle groups	The cancer mortality rate in the most deprived quintile is 2.7 times that in the least deprived quintile
Population attributable risk (PAR)	Can be both absolute and relative; shows the improvement in health that would be possible if all groups had the same health as in the highest socioeconomic group	Uses information on all groups; sensitive to group size; can be used for ordered or non-ordered groups	Ignores association between SES and health; PAR is a theoretical figure (e.g. 1393 cancer deaths avoided if everyone reaches the lowest level of deprivation) which may not be achievable in reality	The proportion of cancer deaths attributable to deprivation is 39%; multiplying the PAR by the overall standardized deaths gives a total of 1393 cancer deaths that are attributable to deprivation

Table 4.4. Measures of inequality applied to the example of cancer mortality of men aged 50–59 years in Scotland between 2012 and 2016 across quintiles of area deprivation (continued)

Measure	Definition	Advantages	Disadvantages	Interpretation[a]
Complex				
Health concentration index (HCI)	Relative measure (from –1 to +1) of the extent to which a health outcome is concentrated among the most or least deprived groups; the larger the absolute value of HCI the greater the inequality; strong similarities to the Gini index; Koolman and van Doorslaer (2004) have shown that multiplying the absolute value of HCI by 75 gives the percentage linear redistribution required to arrive at a distribution with an HCI value of 0	Uses information on all groups; graphical representation of the concentration curve	Requires strict ordering of socioeconomic groups from lowest to highest	The HCI of –0.18 reflects higher cancer mortality among the most deprived groups; it is estimated that 13.5% redistribution is required to achieve an equal distribution of cancer mortality across the deprivation groups
Slope index of inequality (SII)	Absolute measure: the slope, obtained by linear or additive Poisson regression, describing the relationship between the mean health rate in a socioeconomic group and the cumulative percentage of the population, ranked by socioeconomic position	Uses information on all groups; sensitive to group size and to the mean health status of the population	Requires socioeconomic groups to be ordered	The cancer mortality rate difference across the population is 238 (linear model) or 203 (additive Poisson model) deaths per 100 000 population
Relative index of inequality – Poisson (RII_P)	Relative measure: the exponential of the slope, obtained by Poisson regression, describing the relationship between the mean health rate in a socioeconomic group and the cumulative percentage of the population, ranked by socioeconomic position	Uses information on all groups; sensitive to group size	Requires socioeconomic groups to be ordered	The RII_P of 3.3 is the relative risk of cancer mortality for the most deprived group compared with the least deprived group, while taking into account the deprivation distribution
Relative index of inequality – linear (RII_L)	Relative measure: SII, obtained by linear regression, divided by the population mean rate of health; an RII_L value of 0 suggests that there is no inequality; a value of 1 suggests that health rates in the most deprived areas are about 50% above average; the maximum value of RII_L is approximately 2	Uses information on all groups; sensitive to group size	Requires socioeconomic groups to be ordered	The RII_L of 1.15 means that the cancer mortality rate in the most deprived group is about 57% higher than the mean cancer mortality rate (and 57% lower than the mean in the least deprived group)

HCI, health concentration index; PAR, population attributable risk; RD, rate difference; RII_L, relative index of inequality – linear; RII_P, relative index of inequality – Poisson; RR, rate ratio; SES, socioeconomic status; SII, slope index of inequality.

[a] Interpretation of each measure is based on the example shown in Table 4.5.

Table 4.5. Number of deaths from all cancers of men aged 50–59 years in Scotland between 2012 and 2016, population estimates (2014), and age-standardized mortality rate by quintile of area deprivation

SIMD quintile[a]	Number of cancer deaths	Population	Age-standardized mortality rate (per 100 000 people)
Most deprived	1043	62 659	334
2	792	65 782	240
3	672	69 945	191
4	604	73 569	163
Least deprived	473	74 440	126
All Scotland	3584	346 395	207

SIMD, Scottish Index of Multiple Deprivation.

[a] Area deprivation assessed using the Scottish Index of Multiple Deprivation (Scottish Government, 2016).

Source: Mortality and population data from National Records of Scotland.

et al., 2015). These different methods produce results of similar magnitude and have the same interpretation; both estimate the absolute difference between the extremes of the distribution. RII can be estimated based on the linear regression model by dividing SII by the population rate (Pamuk, 1985), or through a (standard) multiplicative Poisson regression of the number of deaths (Moreno-Betancur et al., 2015). These methods (denoted RII_L and RII_P, respectively) provide different results with different interpretations as indicated in Table 4.4. The two indices are approximately related by the equation $RII_P \approx (2 + RII_L)/(2 - RII_L)$. When individual time-to-event data are available, SII and RII_P can be calculated using an additive hazards model and a Cox model, respectively (Moreno-Betancur et al., 2015). Despite having different interpretations, the health concentration index (HCI) and SII are approximately equivalent except for the presence of a multiplicative constant (Lumme et al., 2012). The estimate of the required redistribution of mortality across groups is obtained by multiplying the absolute value of HCI by 75 (Koolman and van Doorslaer, 2004).

SII and RII_L are decomposable; as such, they easily lend themselves to visualizations of inequalities and, in particular, to an investigation of the contribution of different causes to socioeconomic inequalities (Leyland et al., 2007). Examples of inequalities in cancer mortality by area-based SES in Scotland are presented in Fig. 4.1. The overall shapes of the graphs illustrate the inequality in all-cancer mortality. The widths of the different bands show the extent to which inequalities in cancer mortality are attributable to specific cancers. SII tends to be lowest for younger ages and increases for older ages, for which death rates are higher. Absolute inequalities are highest at the age of about 80–85 years for men (absolute rate difference of 1166 per 100 000 population between the most and least deprived) and about 75–80 years for women (absolute rate difference of 683 per 100 000 population). The RII_L peaks earlier, at the age of about 50–55 years for men (RII_L, 1.21) and 60–65 years for women (RII_L, 0.96). At younger ages, relative inequalities in cancer mortality tend to be due to causes such as colorectal cancer, brain cancer, my-

eloma and leukaemia, whereas at ages 40 years and older, the largest contribution to relative inequalities in cancer mortality is from lung cancer.

Conclusions

Measuring SES and social inequalities is essential to understanding the risk, burden, and impact of socioeconomic factors on cancer. Several indicators have been developed to capture SES, and sophisticated analytical methods have been developed to measure inequalities between socioeconomic strata. In line with the Commission on Social Determinants (CSDH, 2008), it is recommended that social inequalities in cancer be measured and monitored using both absolute and relative measures, ideally using both (or multiple) individual and area-based SES indicators. Improvements in data linkage will facilitate the assignment of SES indicators to cancer registry data. Finally, an improved understanding of the effect of socioeconomic factors on the burden of cancer will enable cancer control strategies to be better targeted at populations, communities, and individuals.

Fig. 4.1. Contribution of specific cancers to absolute and relative inequalities in all cancers. (a) SII and (b) RII$_L$ for men aged 15–90 years in Scotland between 2012 and 2016. (c) SII and (d) RII$_L$ for women aged 15–90 years in Scotland between 2012 and 2016. (b, d) Deaths are ordered from bottom to top in terms of contribution to RII$_L$ at peak (50–55 years). The order differs for males and females, but colours have been used consistently for each type of cancer. SII, slope index of inequality. RII$_L$, relative index of inequality. Area-based Scottish Index of Multiple Deprivation 2016 quintiles.
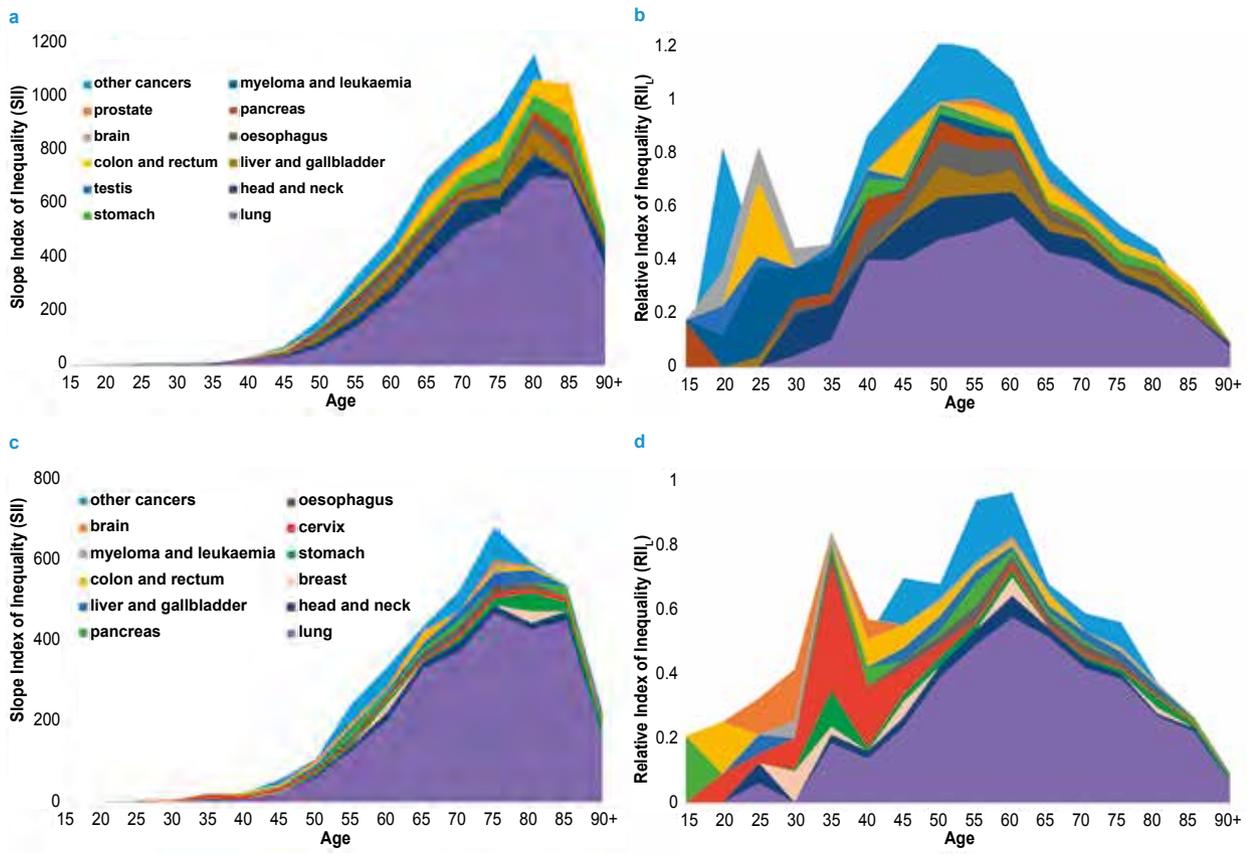
Key points

- Measuring socioeconomic status and inequalities is essential to understanding the risk, burden, and impact of socioeconomic factors on health, disease, and indeed cancer. It is an important step in developing strategies, policies, and interventions aimed at tackling these inequalities, and in monitoring and evaluating the impact of these interventions.

- Several indicators have been used in epidemiological research to capture socioeconomic status. These are typically education level, occupational social class, and income, but indicators of wealth and of area-based socioeconomic circumstances, as well as wider sociodemographic factors, are increasingly considered to be important.

- In both descriptive and analytical epidemiology studies, the link between socioeconomic status and health inequalities can be measured in absolute or relative terms; these capture different aspects of the inequality burden, and can differ in direction, magnitude, and resulting interpretations.

- It is recommended that social inequalities in cancer be measured and monitored using both absolute and relative measures.

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FOCUS 2.

Incorporating indicators of socioeconomic status or ethnicity in cancer registries

Esther de Vries and Freddie Bray

In order for a variable to be included in a population-based cancer registry, it is important to ensure from the outset that the indicator is feasible to collect in routine settings for virtually all cases within the health system. In practice, this means that the information should be available either routinely in the medical records or via cross-linkages with other databases (e.g. through matching unique identification). In addition, it is important that the variable is sufficiently robust to be stable during the periods before and after the occurrence of a cancer event. Lastly, in terms of the calculation of incidence or mortality rates, it is important that the variable can be stratified by year of diagnosis, age group, and sex. Ideally, this would be aligned with the equivalent strata available in the population censuses.

Example indicators of socioeconomic status include those based on the residential address of the patient (e.g. postal code area), whether it is a rural or urban area of residence, type of health insurance, tax or income data (cross-linked with identification number), and education level. Indicators such as profession, although potentially useful, are very difficult to capture in practice; type of occupation can change with time, and occupation is rarely mentioned in patient records.

If the interest is in outcomes other than incidence or mortality rates, the requirement for comparability of the indicator with census or population register data does not apply, and the list of potential indicators can be extended to any relevant variable that can be captured routinely for all patients. Such variables could be used to stratify analyses of, for example, survival time, stage distribution at diagnosis, and types of treatment received.

Indicators of education level tend to be invalid for younger age groups, because education has not yet been completed. In addition, in many regions with large informal economies, education level is not a very useful indicator. In such economies, informal employment income is often not related to education level, meaning that education level may not be linked to affluence; in particular, women may be dependent on the education level and financial status of their spouse. In general, education level is more often an indicator of the awareness of the need to consult a doctor and the likelihood of following and completing a treatment regime.

CHAPTER 5.

Social inequalities in cancer between countries

Miranda M. Fidler, Salvatore Vaccarella, and Freddie Bray

Introduction

Omran's theory of epidemiological transition focused on how changing health and disease patterns interact with societal, economic, and demographic factors (Omran, 1971). In particular, in the third stage of the transition, the model describes how chronic diseases increase as life expectancy rises beyond age 70 years and mortality from degenerative diseases is postponed to older ages. This late-stage transition is analogous to the rising prominence of noncommunicable diseases (NCDs), which in the past decades have surpassed communicable diseases as the leading cause of death worldwide (WHO, 2016).

Cancer has emerged as an important NCD. The growing elderly population and continuing declines in deaths from cardiovascular disease are steadily increasing the relative share of cancer mortality, heightening the influence of cancer on future mortality patterns and making the disease the main obstacle to continued improvements in life expectancy. With an estimated 14 million new cancer cases and 8 million cancer-related deaths occurring in 2012 worldwide (Ferlay et al., 2015), a growing recognition of cancer as a public health priority is exemplified by the adoption of a new cancer resolution by governments from around the world at the Seventieth World Health Assembly, in 2017 (WHA, 2017a, b).

Although once considered the preserve of the rich and of the inhabitants of the countries of highest income, cancer is a global problem that affects all nations; two thirds of cancer deaths occur in countries transitioning socially and economically to higher levels of the Human Development Index (HDI) (referred to here as "transitioning countries") (Bray et al., 2012; Ferlay et al., 2015).

The increasing magnitude of cancer is partly a consequence of declining fertility and increasing longevity (leading to population growth and ageing), but it is also the result of societal, economic, and lifestyle changes associated with globalization. In this chapter we present a global framework of the impact of cancer transitions on cancer occurrence worldwide. We

illustrate the profound effects on the patterns and trends in cancer that will lead to projected increases in the magnitude of the disease, and show how they can be linked to changing levels of human development.

We comment on inequalities between countries as a result of such transitions in terms of cancer incidence and mortality, using either the numbers of new cancer cases (or deaths) or incidence (or mortality) rates. An exploration of inequalities in cancer outcomes between countries, in terms of benchmarking cancer survival in transitioning countries, is provided in Focus 3.

Finally, it is important to note that the national measures examined in this chapter do not consider inequalities within countries; this topic is covered in Chapter 6.

The Human Development Index

As described in Chapter 4, HDI is a summary indicator of national average achievement in terms of three areas of human development: a long and healthy life (based on life expectancy at birth), knowledge (based on mean and expected years of schooling), and a decent standard of living (based on gross national income per capita) (UNDP, 2015, 2018). The composite measure ranges from 0 to 1, with lower values indicating the least developed nations in terms of human development and higher values representing the most developed nations. It is commonly presented according to the predefined cut-off points of the United Nations Development Programme, representing four tiers of HDI: low, medium, high, and very high.

As shown in Fig. 5.1a, low-HDI countries are largely concentrated in sub-Saharan Africa, although several

countries in this region have now transitioned to the group of medium-HDI countries, which are geographically diverse. High-HDI countries comprise the largest group, including many in Asia and South America. The group with very high HDI is closest to the traditional view of developed countries; it includes Australia, Europe, Japan, New Zealand, and North America as well as several countries in Asia, the Eastern Mediterranean, and South America.

Cancer burden and profile by HDI category in 2012

When HDI values are compared with the GLOBOCAN 2012 estimates of country-specific all-cancer incidence rates at the national level for 2012 (Ferlay et al., 2013), a strong link between HDI and incidence is observed; in particular, national incidence rates are increasing rapidly with increasing HDI levels (Figs. 5.1b and 5.2a). To illustrate, 41% of the total number of

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Fig. 5.1. Global maps of: (a) Human Development Index, 2012; (b) all-cancer age-standardized incidence rates per 100 000 people; and (c) all-cancer age-standardized mortality rates per 100 000 people. Source: reproduced from Ferlay et al. (2013).

a

Human Development Index Level 2012
Very High
High
Medium
Low

b

Age Standardized Incidence Rates
(per 100,000)
> 217.8
151 - 217.8
107.8 - 151
< 107.8

c

Age Standardized Mortality Rates
(per 100,000)
> 109.9
94.8 - 109.8
78.3 - 94.8
< 78.3

No data   Not applicable
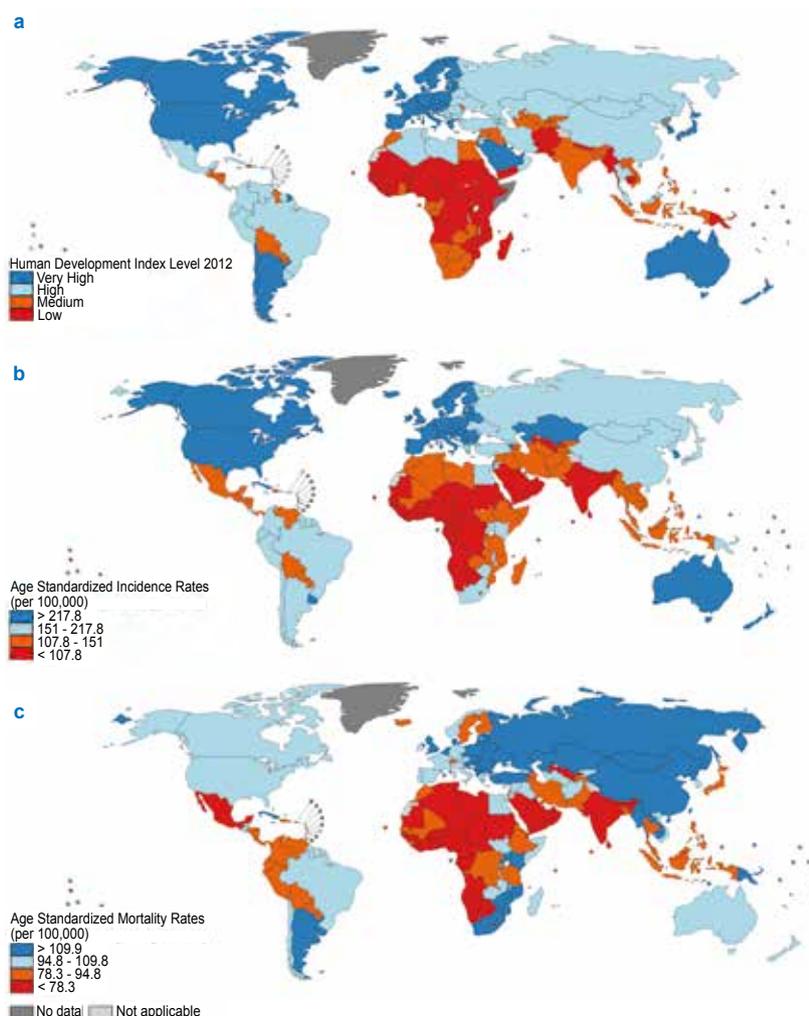
Fig. 5.2. Country-specific age-standardized all-cancer (a) incidence and (b) mortality rates by Human Development Index. Source: reproduced from Ferlay et al. (2013).
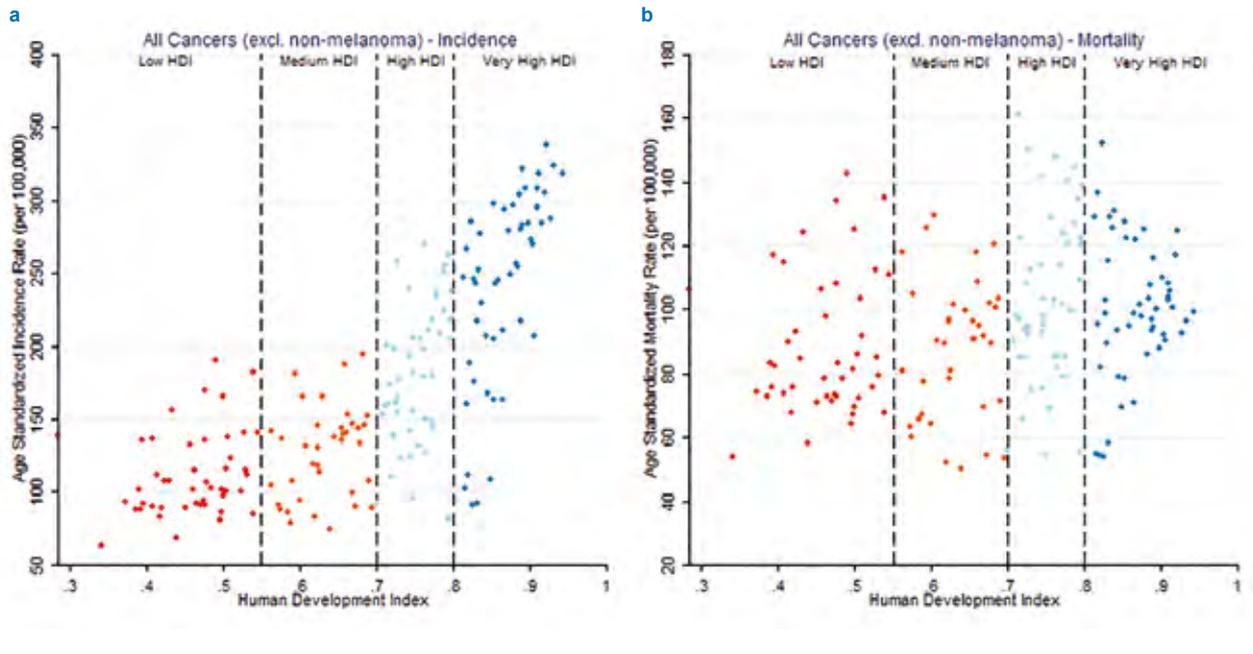
Fig. 5.3. The five most frequent cancer types in terms of incident cases and deaths, globally and by Human Development Index. Source: reproduced from Ferlay et al. (2013).
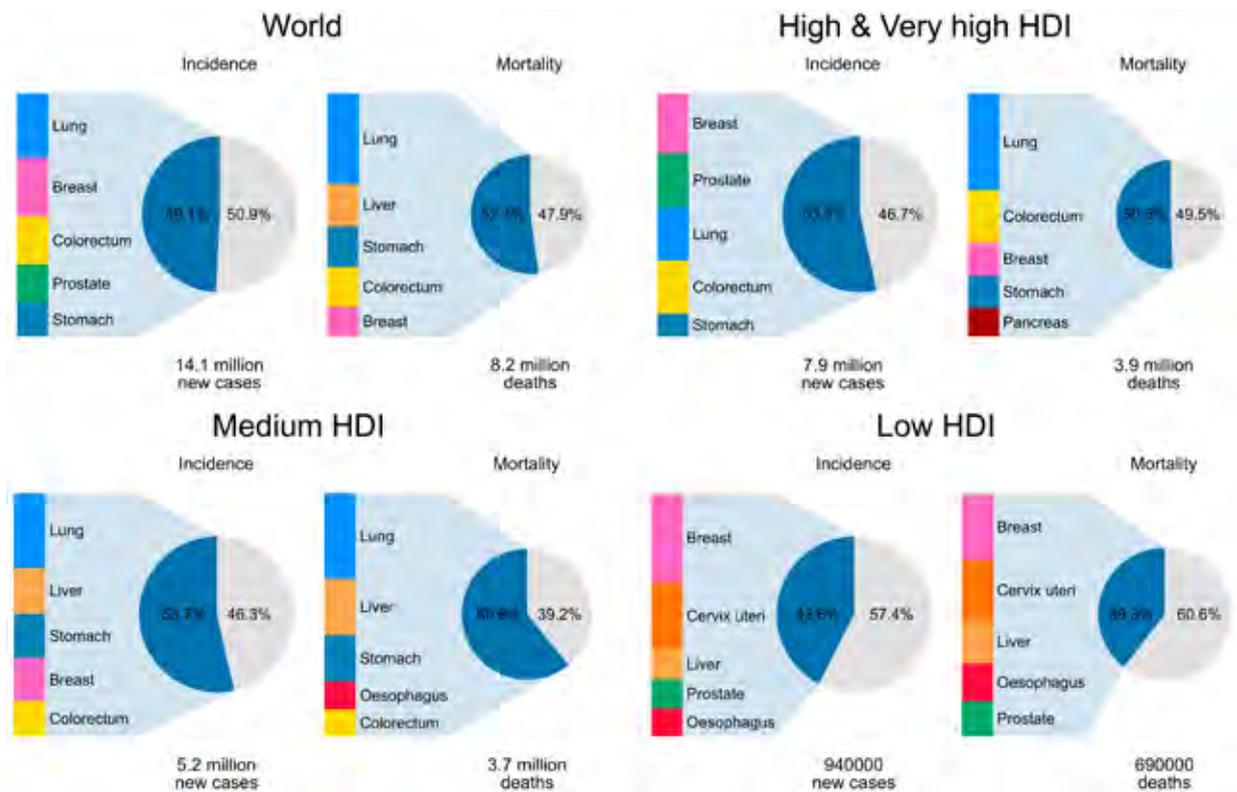
new cancer cases in 2012 occurred in countries with very high HDI, compared with 28%, 16%, and 6% in countries with high, medium, and low HDI, respectively (Ferlay et al., 2013). There is little correlation between the cancer mortality rates and the HDI level of any country, however, as illustrated in Figs. 5.1c and 5.2b.

The cancer profile of a country, that is, the five most common types of cancer in terms of both new cases and deaths, is dependent upon the HDI level (Fig. 5.3). The difference between countries with low HDI and high HDI is stark; a high residual burden of infection- and poverty-related cancers is observed in countries with low HDI, where cancers of the cervix, liver, and oesophagus are leading cancers, compared with countries with high or very high HDI, where the most frequent cancers are those of the prostate, breast, colorectum, and lung (Bray et al., 2004, 2010; Fidler et al., 2016). In countries with medium HDI, there is still a large burden of infection-related cancers, including cancers of the stomach, liver, and oesophagus. The increasing incidence burden of infection-related cancers with decreasing HDI level is highlighted when quantifying the population-attributable fractions by HDI level; in 2012, the proportion of new cancer cases attributable to infectious agents was 25.3%, 21.5%, 13.2%, and 7.6% in countries with low, medium, high, and very high HDI, respectively (Plummer et al., 2016).

Evidence of cancer transitions linked to HDI

Colorectal cancer rates can be considered a marker of human development; national incidence increases with some consistency with increasing HDI level; rates in countries with

Fig. 5.4. Temporal trends in age-standardized incidence rates (ASR) of colorectal cancer in men and in Human Development Index (HDI) for selected countries. *, countries without a national cancer registry, but combined regional registries. Source: reproduced from Forman et al. (2013).
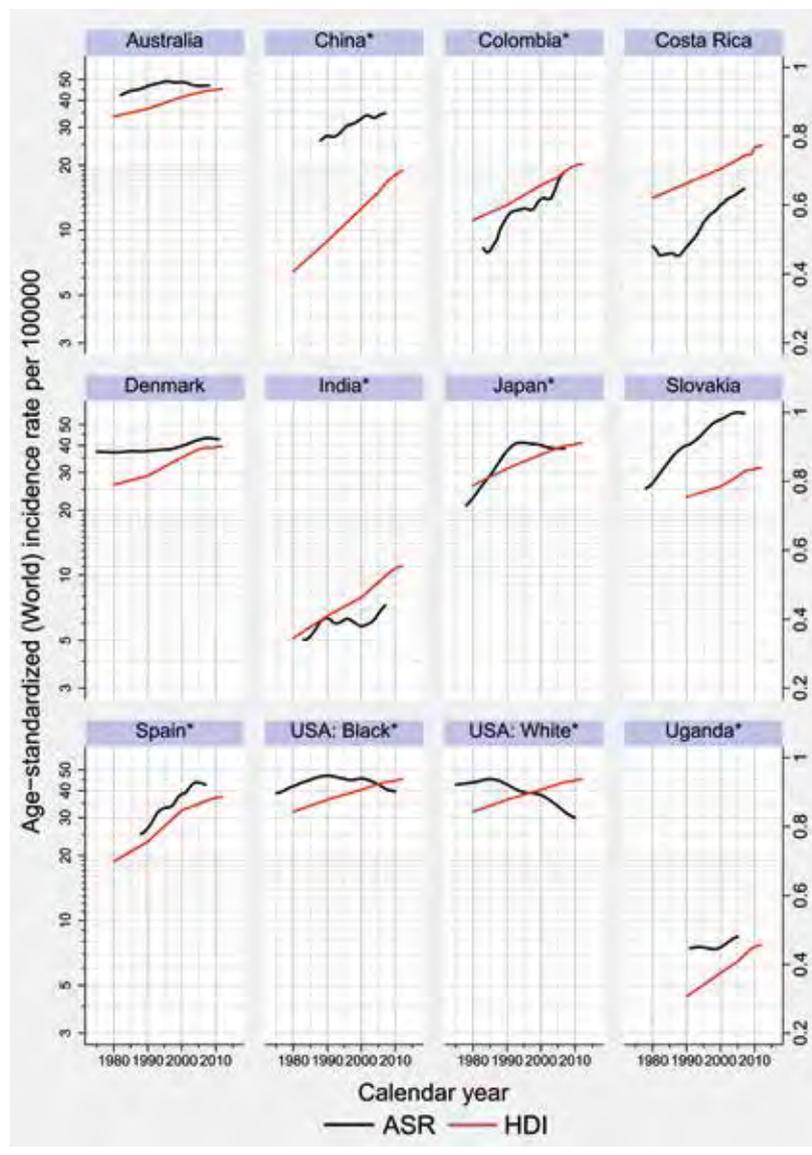
very high HDI are many times higher than those in countries with low HDI in both sexes (Bray, 2014). Trends in age-standardized incidence rates of colorectal cancer in men are plotted against trends in national HDI in selected countries (those with high-quality population-based cancer registries) in Fig. 5.4, in which is it evident that colorectal cancer incidence increases in parallel with

increasing HDI in most countries (Arnold et al., 2016; Fidler et al., 2017). It also appears that colorectal cancer incidence rates have stabilized or declined quite recently in several countries that have attained very high HDI levels, including Australia, Japan, and the USA; this may be due to multiple factors, including colorectal cancer screening and a changing prevalence of the

Fig. 5.5. Temporal trends in age-standardized incidence rates of breast cancer and cervical cancer for selected countries. *, countries without a national cancer registry, but combined regional registries. Source: reproduced from Forman et al. (2013).

with HDI level; the much higher incidence-to-mortality ratio in countries with high and very high HDI compared with countries with low HDI most likely reflects the inequalities in survival and prognosis between countries of different socioeconomic development.

Breast cancer is a highly frequent cancer across countries of all HDI levels (Fidler et al., 2016; Ginsburg et al., 2017), and a general observation has been one of rising incidence. This has been offset by declining incidence rates of cervical cancer in more developed and transitioning countries, the year in which the two cancers are equally common, with one trending up and other down, being a marker of the extent of transition in a given country (Stewart and Wild, 2014). Fig. 5.5 demonstrates that this convergence must have occurred in the distant past in countries with very high HDI (e.g. Australia, Denmark, and the USA), but occurred more recently for countries with medium or high HDI (e.g. Colombia, Costa Rica, and India).

On the basis of the trends from the high-quality cancer registry in Kampala in Uganda, a low-HDI country, this transition has yet to occur (Wabinga et al., 2014), with the incidence rate of cervical cancer remaining twice that of breast cancer. Trends are similar in the Barshi population in rural India (Badwe et al., 2014). The large differences in rates and the direction of trends are an indication of barriers to cervical cancer control in countries with lower HDI, where preventive and screening programmes have been largely absent. Conversely, the increasing burden of breast cancer is related to changes in reproductive and hormonal factors (some of which are considered protective for cervical cancer) and an increased prevalence of obesity

putative risk factors, protecting against the disease (Arnold et al., 2016). The corresponding decline in mortality rates is a direct result of falling incidence, but also a result of a number of improvements in treatment and cancer care.

The evolution of breast cancer and cervical cancer in women (Fig. 5.5) is another example of how HDI levels can be linked to changing

risks of specific cancers. Cervical cancer accounts for up to one third of all neoplasms diagnosed in both sexes in some countries with low HDI, particularly in sub-Saharan Africa, and breast cancer incidence rates in countries with very high HDI are approximately 3 times those in countries with low HDI. In contrast, mortality rates for breast cancer vary much less than incidence rates

at postmenopausal ages, as well as mammographic screening in countries with higher HDI (Bleyer and Welch, 2012).

Inequalities in cancer between countries with different HDI levels

Although countries with higher HDI have a greater share of the overall cancer incidence burden, mortality rates are disproportionately higher in countries with lower HDI, as are the inequalities related to premature mortality and life expectancy gains. Projections of cancer rates also indicate that the greatest proportional increases in the number of cancer diagnoses will occur in countries with lower HDI. Some examples of inequality are illustrated in the following.

Disability-adjusted life years

Disability-adjusted life years (DALYs) is a measure that combines the degree of illness and disability in patients and long-term survivors in terms of years lost because of disability (YLD) and the burden of cancer mortality in terms of years of life lost (YLL) to quantify the number of years of healthy life lost. When assessed at the global level for all cancers, measures of DALYs are actually rather similar across the four tiers of HDI (Fig. 5.6) (Soerjomataram et al., 2012a). However, inequalities in the contribution of YLL and YLD to total DALYs are evident between countries with different HDI levels. In general, individuals in countries with higher HDI were observed to live a greater number of years with disabil-

ity, whereas individuals in countries with lower HDI were observed to have a greater burden of premature mortality. When assessed by specific types of cancers, YLL was observed to be the main contributor to DALYs overall. YLD contributed to a greater proportion of DALYs in higher-HDI countries compared with lower-HDI countries, whereas YLL contributed to a greater proportion of DALYs in lower-HDI countries compared with higher-HDI countries, although the extent of these relationships varied with cancer site. The fact that the fraction of DALYs due to YLL was consistently greater in lower-HDI countries is an indication of the poor prognosis for cancer patients in developing countries, and highlights the need for prevention and treatment programmes in these countries

Fig. 5.6. Age-adjusted disability-adjusted life years per 100 000 people by cancer site and Human Development Index level. YLD, years lost because of disability; YLL, years of life lost. Source: reproduced from Soerjomataram et al. (2012b), copyright 2012, with permission from Elsevier.
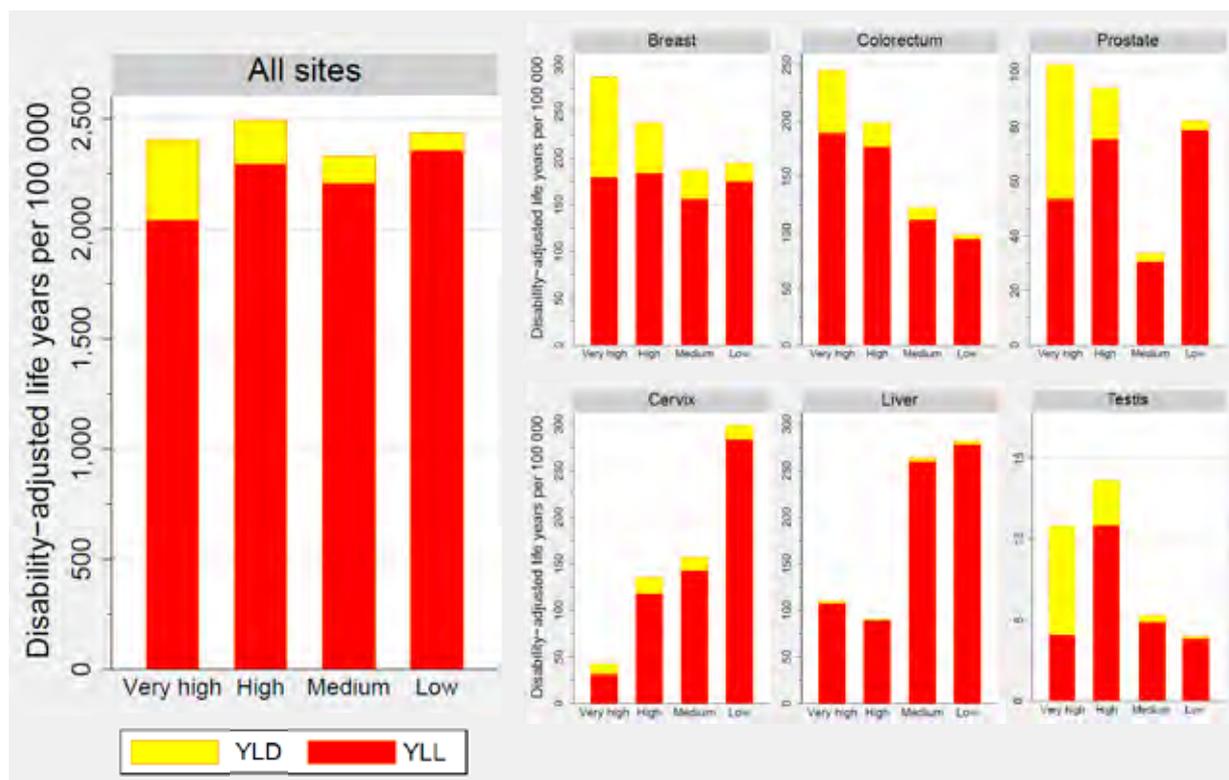
to reduce inequalities in non-fatal and fatal cancer-related outcomes worldwide.

Gains in life expectancy

In a study assessing the impact of all-cancer mortality trends on overall life expectancy over the period 1981–2010, countries with very high HDI were found to make larger gains in life expectancy relative to countries with medium and high HDI (Cao et al., 2017). More specifically, reductions in cancer mortality were responsible for improving life expectancy by 0.8 years for men and 0.5 years for women, respectively, for individuals aged 40–84 years in countries with very high HDI, whereas the corresponding gain was 0.2 years for both men and women in countries with medium and high HDI. Similar inequalities in life expectancy gains would have been observed in the hypothetical situation that all cancer deaths were eliminated: for the period 2006–2010, life expectancy gains were estimated to be 2.5 years for men and 1.9 years for women for individuals aged 40–84 years in countries with very high HDI, compared with 1.6 years for men and 1.5 years for women in countries with medium and high HDI. These results provide evidence of disproportional improvements in cancer rates according to HDI level, leading to widening gaps in life expectancy between more and less developed nations.

Future burden

The projections of future cancer burden depicted in Fig. 5.7 show how the increase in numbers of new cancer cases will be proportionally greatest in countries with lower HDI; it has been estimated that countries with low and medium HDI will experi-

Fig. 5.7. Projections of future cancer burden by Human Development Index (HDI) level. Source: reproduced from Ferlay et al. (2013).
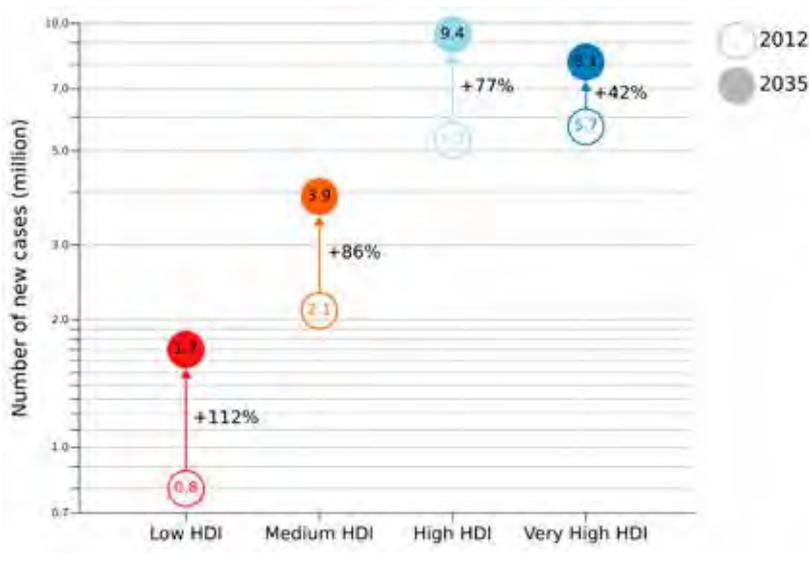
ence a 112% and 86% increase, respectively, in the incidence of cancer from 2012 to 2035. Because these countries are the least equipped to deal with such a pending increase in cancer patients, the projections highlight the necessity for investment in targeted, resource-dependent, effective, and cost-effective interventions that will reduce the burden of and suffering from the disease.

Evidence of regional diversity

Increasing average levels of societal and economic indicators are linked to a changing scale and profile of cancer at the individual and grouped HDI levels. However, this serves only to identify that a myriad of factors – some risk-related (reproductive, dietary, metabolic, and hormonal) and some systems-related (including the extent of cancer plans and the population-wide implementation of effective interventions) – can increase (or fail to reduce) the risk of developing or dying from certain (preventable or treatable) cancers. Fig. 5.3 also captures the complexity and diver-

sity of cancer patterns and trends. For example, breast cancer has the leading incidence rates worldwide irrespective of HDI level, yet stomach cancer remains a common cancer even within several countries with high and very HDI, and ranks as the fifth and fourth most common cancer in this tier in terms of incidence and mortality, respectively. The temporal development of cervical cancer is another example of a complex and diverse trend between countries. Although there have been systematic reductions in cervical cancer incidence in countries with medium and high HDI, the 40-year trends in incidence rates depicted in Fig. 5.8 highlight the recent increases in countries with high HDI (e.g. Belarus) and very high HDI (e.g. Japan). These increases can be linked to several factors, including changing sexual behaviours (increasing the risk of persistent infections by high-risk human papillomavirus subtypes), the continued absence of organized screening programmes (Vaccarella et al., 2013, 2016), and the low, or

Fig. 5.8. Age-standardized (World) cervical cancer incidence rates per 100 000 by calendar year for selected populations, 1975–2012. Source: reproduced from Forman et al. (2013).
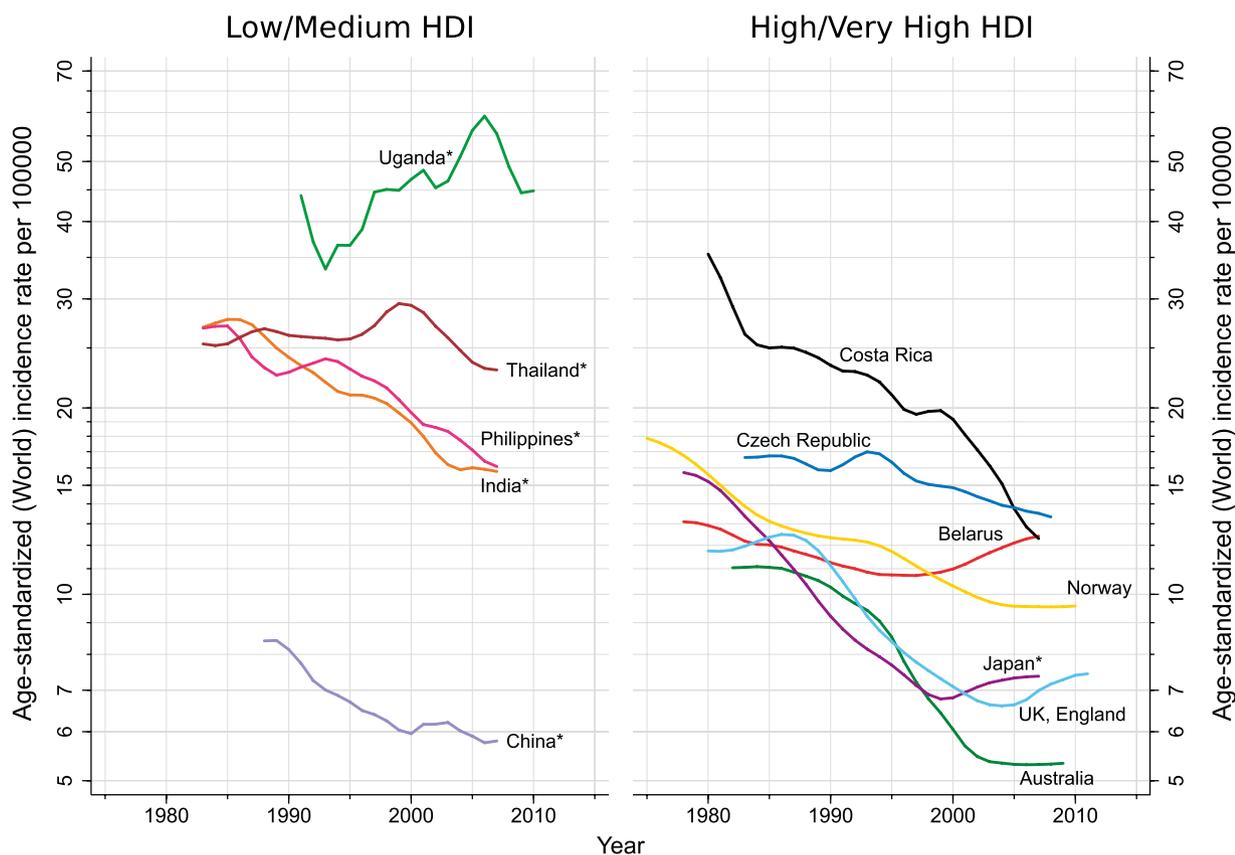
*: China (Hong Kong and Shanghai), India (Chennai and Mumbai), Japan (Miyagi, Nagasaki and Osaka), Philippines (Manila), Thailand (Chiang Mai), Uganda (Kampala).

diminishing, compliance in countries where screening programmes exist. As a consequence, the incidence of cervical cancer in these countries is increasing, particularly among recent generations of women.

Conclusions

That heterogeneity in the magnitude of cancer incidence within HDI levels remains is not surprising given the extent to which local risk factors, alongside the presence or absence of medical intervention, serve to modulate the national cancer burden. However, HDI level does provide a useful framework to map the continuing transitions in cancer and highlight the stark reality of the increasing burden in countries with lower HDI compared with countries with higher HDI. Although the cancer incidence rates are higher in countries with very high HDI, those living in countries with low HDI experience disproportionately higher mortality, and are projected to be most affected by the disease in the near future. These inequalities can only be expected to increase unless established effective and cost-effective interventions (WHA, 2017a, b; WHO, 2017) are urgently implemented.

Finally, with cancer projected to become the leading cause of mortality worldwide in the coming decades as deaths from cardiovascular diseases decline, it is increasingly evident that cancer control initiatives will also play an important role in decreasing inequalities in all-cause mortality. The development and implementation of effective, affordable, feasible, and sustainable cancer control measures in transitioning countries can therefore be seen as an effort to not only decrease inequalities in cancer but also decrease inequalities across the spectrum of causes.

Key points

• Major inequalities in cancer outcomes exist between countries. Assigned values of the Human Development Index (HDI), a proxy for the socioeconomic development of a country, can be linked to the corresponding cancer magnitude and profile to explain cancer transitions at the national level.

• The rapid rise in all-cancer incidence rates with increasing levels of HDI contrasts with the lack of a clear correlation between all-cancer mortality rates and HDI levels. A high residual burden of infection- and poverty-related cancers is observed in low-HDI countries. In several medium- and high-HDI countries, often those undergoing major social and economic transitions, marked declines in rates of these cancer types are offset by increasing rates of cancers more frequently observed in transitioned (very high HDI) countries.

• Premature cancer mortality in terms of years of life lost is highest in low-HDI countries and declines with increasing HDI. Conversely, for treatable cancers associated with major sequelae after diagnosis, the number of years of disability increases as HDI increases and is highest in countries with very high HDI.

• The global cancer burden is predicted to exceed 20 million new cancer cases annually by 2025, compared with an estimated 14.1 million new cancer cases in 2012; relative increases are greatest in lower-HDI countries.

• Although evident, the role of human development in global cancer transitions cannot be overgeneralized, given the complexity of the disease. There are clear examples of national and regional cancer diversity that depart from this model.

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FOCUS 3.

Cancer survival in countries in transition, with a focus on selected Asian countries

Rajaraman Swaminathan

Introduction

Cancer survival is one of the cornerstones of the cancer control triangle. Like for the other cornerstones of incidence and mortality, social inequalities in cancer survival have been observed (Schrijvers and Mackenbach, 1994; Kogevinas and Porta, 1997). However, although data on cancer survival are generally available from high-income countries (HICs) (Ries et al., 2006; Sant et al., 2009), data on cancer survival from low- and middle-income countries (LMICs) and from countries in transition are scarce, suffer from methodological or quality limitations, or do not include all cancer types. Furthermore, data collection is often separated by large periods, preventing the evaluation of trends in survival.

Apart from several isolated case series in LMICs or countries in transition, a few centrally planned international collaborative studies, such as Cancer Survival in Africa, Asia, the Caribbean and Central America (SurvCan) (Sankaranarayanan et al.,

1998; Sankaranarayanan and Swaminathan, 2011) and CONCORD (Coleman et al., 2008; Allemani et al., 2015), have been conducted. These collaborative studies have provided a template for the conduct of standard population-based cancer survival studies in LMICs, prompting a modest beginning, ensuring continuation, and also facilitating the systematic expansion to cover more regions.

Socioeconomic differences in cancer incidence and mortality are large, and it is generally acknowledged that such differences require suitable interventions in the area of primary prevention (Fox and Goldblatt, 1982; Volkonen et al., 1990; Swaminathan et al., 2009a; Bray et al., 2018). However, addressing the socioeconomic inequalities in cancer survival requires policy measures in the area of secondary prevention and treatment (Schrijvers and Mackenbach, 1994; Kogevinas and Porta, 1997). This focus addresses socioeconomic inequalities in cancer survival in several countries in Asia.

Between- and within-country relative survival rates from population-based cancer registries

Survival data from population-based cancer registry (PBCR) series provide an indication of average prognosis for all cancer types in a given region, generally with heterogeneous treatment status, and studies are heavily reliant on good-quality data and on the completeness of both the registration of cases and their follow-up. In addition to standard data quality control and centrally performed analysis, many registries in emerging economies in Asia and elsewhere, such as in Shanghai and Tianjin in China, in Costa Rica, in Cuba, and in Lampang in Thailand, have therefore adopted active methods to minimize the bias in survival rate estimation as a result of a lack of complete follow-up, thus allowing for more comparable survival statistics (Swaminathan et al., 2008a; Sankaranarayanan and Swaminathan, 2011; Allemani et al. 2015).

Age-standardized relative survival (ASRS) rates at 5 years after diagnosis in Asian countries are given in Fig. F3.1 both by country and by particular registries (rural or urban) within a country for cancer of the (a) breast, (b) mouth, and (c) colon, and (d) for lymphoid leukaemia. There is clear heterogeneity in ASRS rates 5 years after diagnosis both between and within several countries for different cancers (Fig. F3.1). The corresponding reference values of ASRS rates from the United States Surveillance, Epidemiology, and End Results Program (SEER) (Ries et al., 2006) and from the EUROCARE study on cancer survival in Europe (Sant et al., 2009) matched the highest values of ASRS rates observed in Asia. Within-country relative survival rates based on two or more PBCRs are reported for China, India, the Republic of Korea, and Thailand. The Republic of Korea reported the smallest inequalities in survival rates between the three urban registries (Busan, Incheon, and Seoul). Some differences were observed across China; these were most striking for lymphoid leukaemia, for which urban survival rates were much higher than those reported in the rural Qidong registry (Fig. F3.1d). Within-country differences in survival rates for all selected cancer types, with the possible exception of breast cancer, were observed in Thailand (a mixture of urban and rural populations) and in India (where the Bhopal, Chennai, and Mumbai registries cover urban populations and the Barshi and Karunagappally registries cover rural populations).

Overall, the 5-year ASRS rates within countries were higher in urban than in rural areas in the majority of

Fig. F3.1. Five-year age-standardized relative survival (ASRS) rates (%) by country (number of incident cases in parentheses) for 1990–2003 and by registries (period varies) for cancer of the (a) breast, (b) mouth, and (c) colon, and (d) for lymphoid leukaemia. SAR, Special Administrative Region. Source: compiled from Sankaranarayanan and Swaminathan (2011).

a

By Country

Country	Cases	ASRS rates (%)
China	(21810)	79.4
Korea	(9442)	78.6
Turkey	(1329)	77.2
Singapore	(3204)	76.4
Cuba	(2169)	70.4
Costa Rica	(2462)	69.6
Saudi Arabia	(298)	64.5
Thailand	(2354)	62.9
India	(10936)	51.6
Philippines	(1714)	47.4
Uganda	(162)	45.8
Gambia	(61)	12.5

By Registry

China
Registry	ASRS rates (%)
Hong Kong SAR	89.6
Tianjin	85.6
Shanghai	79.4
Qidong	58.3

Korea
Registry	ASRS rates (%)
Busan	80.6
Seoul	78.6
Incheon	78.5

India
Registry	ASRS rates (%)
Karunagappally	54.4
Barshi	52.7
Mumbai	51.6
Chennai	47.7
Bhopal	30.6

Thailand
Registry	ASRS rates (%)
Khon Kaen	65.6
Lampang	63.3
Songkhla	62.4
Chiang Mai	57.3

b

By Country

Country	Cases	ASRS rates (%)
China	(1134)	66.9
Korea	(523)	51.6
Singapore	(135)	49.2
Cuba	(260)	43.7
Pakistan	(413)	40.9
India	(4781)	36.7
Thailand	(560)	36.3

By Registry

China
Registry	ASRS rates (%)
Shanghai	70.9
Tianjin	69.2
Hong Kong SAR	64.5
Qidong	43.8

Korea
Registry	ASRS rates (%)
Incheon	54.4
Seoul	51.6
Busan	48.4

India
Registry	ASRS rates (%)
Karunagappally	45.3
Bhopal	37.5
Chennai	36.7
Mumbai	36.0
Barshi	26.1

Thailand
Registry	ASRS rates (%)
Khon Kaen	41.9
Lampang	37.2
Songkhla	35.3
Chiang Mai	22.0

c

By Country

Country	Cases	ASRS rates (%)
China	(18777)	58.0
Korea	(6699)	57.4
Singapore	(2501)	52.5
Turkey	(371)	52.2
Cuba	(1248)	46.4
Philippines	(145)	43.5
Thailand	(1151)	41.9
India	(1626)	17.8
Uganda	(51)	8.2

By Registry

China
Registry	ASRS rates (%)
Hong Kong SAR	63.2
Tianjin	61.9
Shanghai	54.0
Qidong	42.1

Korea
Registry	ASRS rates (%)
Seoul	65.7
Incheon	57.4
Busan	57.0

India
Registry	ASRS rates (%)
Mumbai	30.3
Bhopal	5.2

Thailand
Registry	ASRS rates (%)
Songkhla	52.8
Khon Kaen	44.3
Lampang	39.4
Chiang Mai	32.5

d

By Country

Country	Cases	ASRS rates (%)
Turkey, Izmir	(161)	50.1
China	(1289)	44.8
Singapore	(205)	42.9
Korea	(942)	38.5
Thailand	(278)	36.5
India	(1602)	16.0

By Registry

China
Registry	ASRS rates (%)
Tianjin	64.9
Hong Kong SAR	59.1
Shanghai	30.4
Qidong	5.4

Korea
Registry	ASRS rates (%)
Incheon	40.3
Seoul	38.5
Busan	32.7

India
Registry	ASRS rates (%)
Karunagappally	45.6
Chennai	16.4
Mumbai	15.5
Bhopal	12.6

Thailand
Registry	ASRS rates (%)
Lampang	44.1
Songkhla	36.5
Chiang Mai	15.4

instances. The large differences in survival observed within countries in some instances (e.g. lymphoid leukaemia in China and India, or colon cancer in India) probably reflect within-country inequalities between urban and rural populations in the availability of, development of, and accessibility of cancer-related health services, and possibly in other social and disease-related factors (Sankaranarayanan and Swaminathan, 2011).

Overall survival rates from hospital-based cancer registries in India

Survival data from hospital-based cancer registry (HBCR) series gen-erally provide the average prognosis among treated patients in a specific hospital, most probably representing the upper limit of average surviv-al in the region. HBCRs represent an information platform where the treatment factor is uniform and, if the hospital receives patients from all strata of society, any observed differences in overall survival (OS) rate will reflect the inequalities with respect to social and disease-relat-ed factors. Fig. F3.2 depicts 10-year and 5-year OS trends for several common cancers observed in a HBCR at the Cancer Institute (Wom-en's Indian Association), Chennai, India, during the two calendar pe-riods 1990–1999 and 2006–2011, by type of residence area (urban or rural) and education level. OS rates increased between the two time pe-riods for cervical cancer and breast cancer (at a faster rate in the 10-year vs 5-year data), but remained static for oral cancer. The increasing trend in OS rates for cervical cancer and breast cancer correlates well with reported achievements of clinical downstaging (the increase in the proportion of patients diagnosed at an earlier stage of the disease) and treatment milestones (the evolution of treatment protocols) over time in India (Shanta et al., 2013); however, for oral cancer, the unchanging high proportion of patients diagnosed at an advanced stage during both

Fig. F3.2. Five-year and 10-year overall survival (OS) trend for cancers of the (a) cervix, (b) breast, and (c) cheek observed in a hospital-based cancer registry including cases treated at the Cancer Institute, Chennai, India, during 1990–1999 and 2006–2011. Source: compiled from Swaminathan R, Rama R, Shanta V. Hospital Based Cancer Registry database, Cancer Institute (Women's Indian Association), Chennai, 2018.
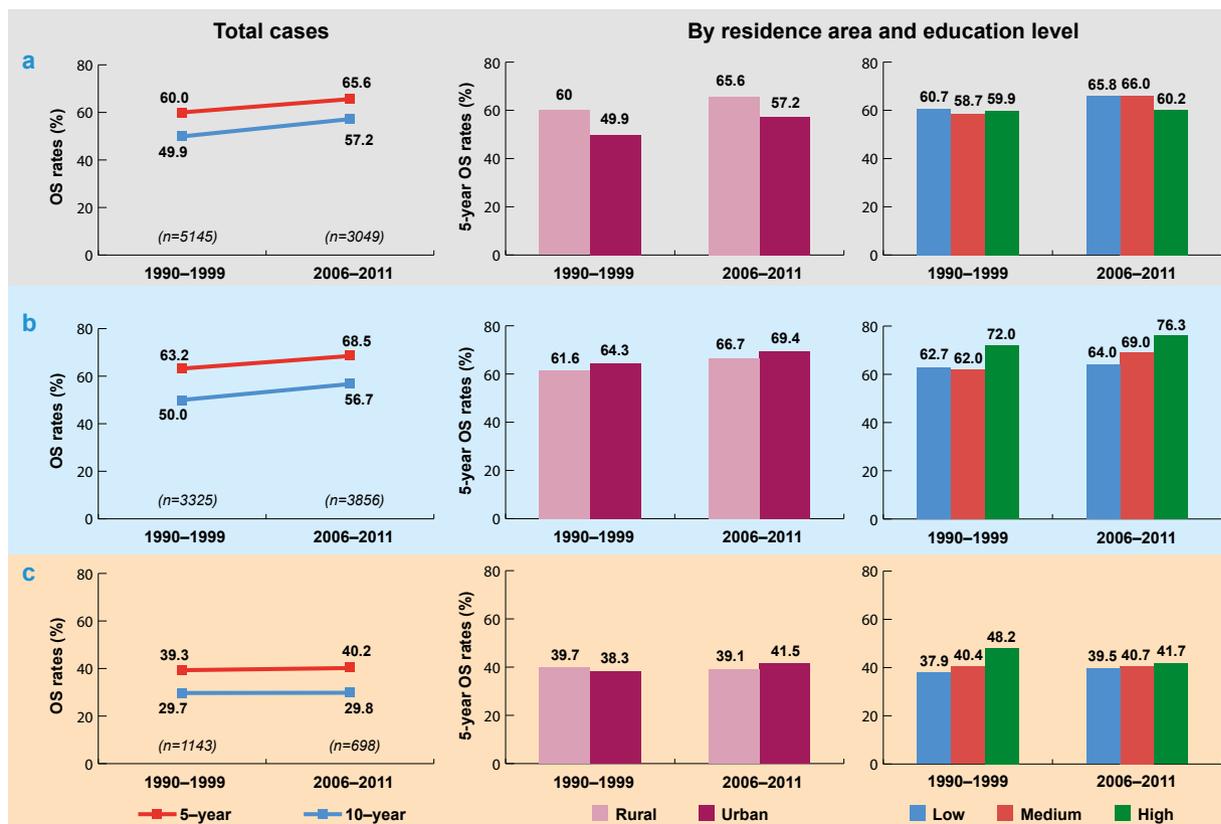
periods has rendered any advances in treatment irrelevant and negligible in terms of improving survival.

The contribution of social factors, namely type of residence area and education level, to OS rates was generally modest for these three cancer types in the Chennai region in India. The most marked differences were recorded in relation to breast cancer and education level during 2006–2011; the reported 5-year OS rate was an average of 12% higher for those with a high education level than for those with a low education level. In contrast, an inverse trend of OS rate with education level for cer-

vical cancer was seen during 2006–2011, correlating with the observed increased incidence (Swaminathan et al., 2009a); this result calls for policies to improve awareness of cervical cancer and its prevention and early detection, even in urban areas.

Within-state and residence area type comparisons of overall survival rates in India

Fig. F3.3 shows the 5-year OS rates in the Indian state of Tamil Nadu for selected cancer types, comparing data from a rural registry (PBCR of Dindigul), an urban registry (PBCR of Chennai), and a HBCR (Cancer Insti-

tute, Chennai, registry including only treated cases), with United States SEER data used as an external reference. Overall, clear heterogeneity is observed for cervical cancer OS rates, with the lowest survival rate observed in the rural area of Dindigul. Heterogeneity is also observed for breast cancer OS rates, although to a lesser extent.

In contrast, no differences in oral cancer OS rates are observed between the rural and urban registries or between the PBCRs and the HBCR; this is because in India more than 50% of patients present with stage IV oral cancer, even in a

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Fig. F3.3. Comparison of 5-year overall survival (OS) rates (%) between rural and urban population-based and hospital-based cancer registries in Tamil Nadu State, India, 1990–2003 (although the period varies for individual registries) and with United States SEER data for cancer of the (a) cervix, (b) mouth, and (c) breast, and (d) for leukaemia. HBCR, hospital-based cancer registry; PBCR, population-based cancer registry; SEER, Surveillance, Epidemiology, and End Results Program. Source: compiled from Swaminathan et al. (2009b).

Legend:
- Dindigul: Rural, PBCR, treated and untreated cases
- Chennai: Urban, PBCR, treated and untreated cases
- Cancer Institute (WIA): HBCR, treated cases only
- United States SEER data, White population
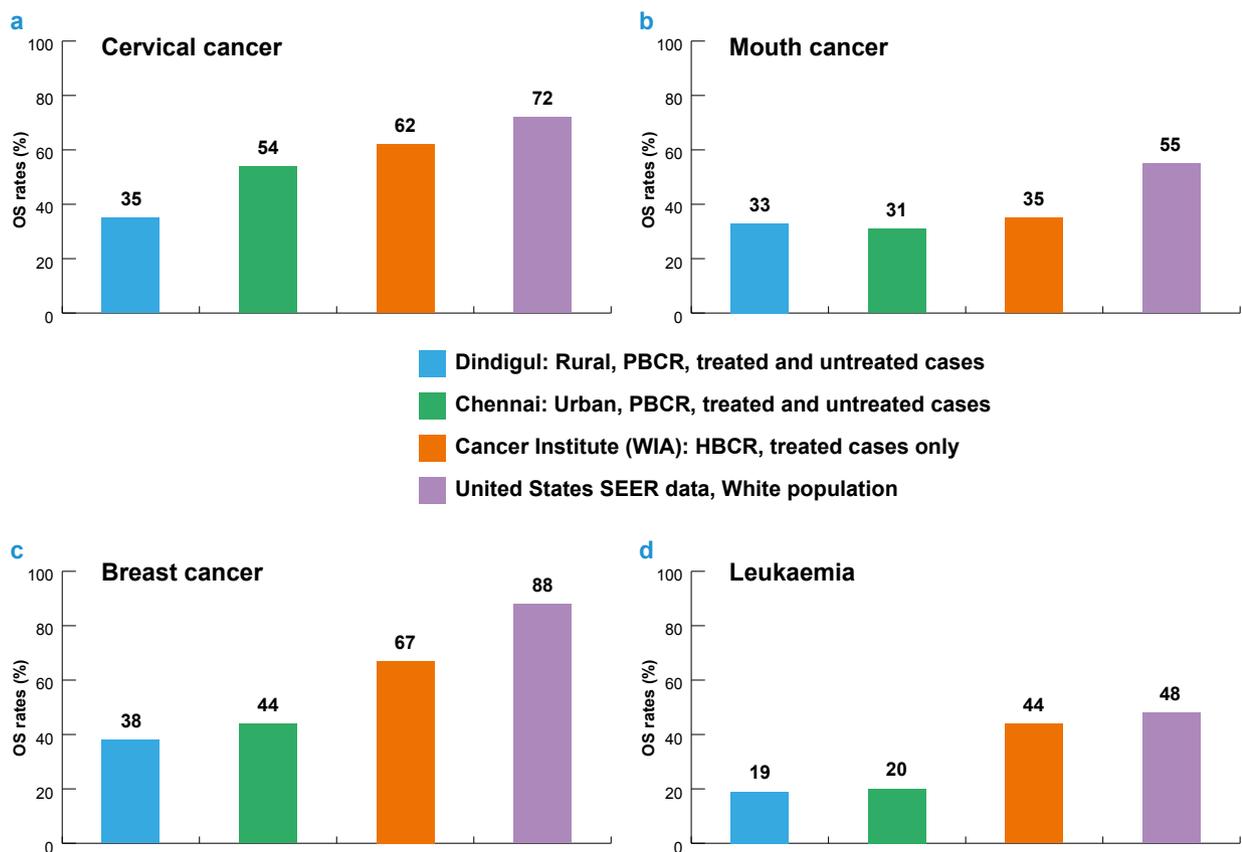
comprehensive cancer care facility (Swaminathan et al., 2009b).

Finally, the 5-year OS rates for leukaemia among the treated series in the Chennai HBCR are similar to those of the United States SEER White population, indicating that if an appropriate system is in place for correct referral of curable cancers to appropriate cancer centres and treatment is received, survival rates can be expected to be similar to those observed in HICs (Swaminathan et al., 2008b).

Comparison of cancer survival across different settings, with a focus on Asia and Africa

The inequalities in factors relating to the stage of disease at diagnosis and to access to health services

Fig. F3.4. Overall survival (OS) rates (%) among countries with health services with variable levels of development (high, intermediate, and low), 1990–2003 (period varies for individual registries), for cancer of the (a) large bowel and (b) breast by extent of disease (localized or regional), and for (c) Hodgkin and (d) non-Hodgkin lymphoma. Source: reproduced from Sankaranarayanan and Swaminathan (2011).
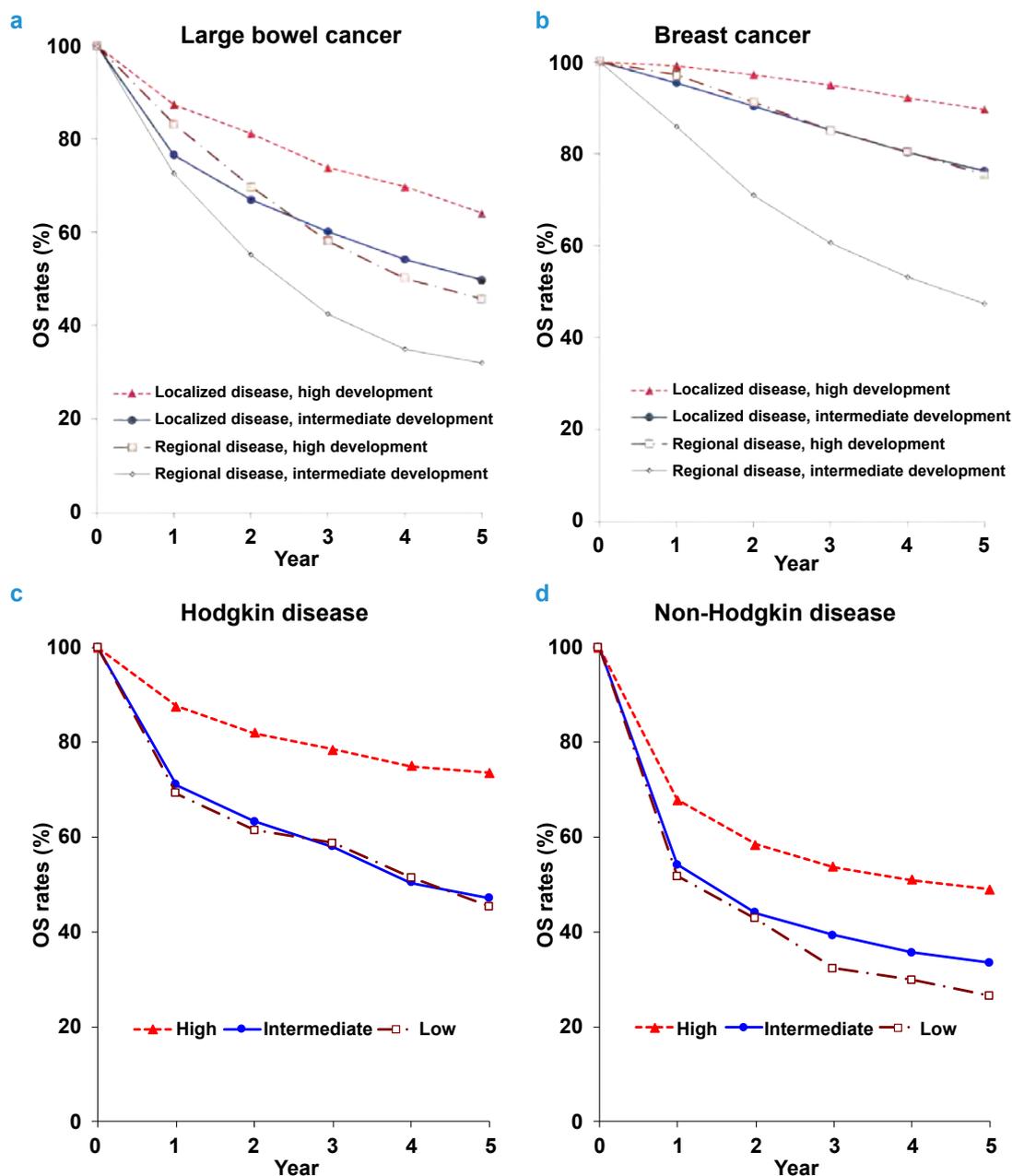
and treatment are among the major causes of the differential cancer survival patterns observed between most Asian countries; data quality issues, such as incomplete follow-up, differences in the proportion of death-certificate-only notifications, and inaccurate vital status, may also contribute. Fig. F3.4 shows the 5-year OS rates by clinical extent of disease for cancer of the (a) large bowel and (b) breast and by different levels of development of health services in selected countries (Sankaranarayanan et al., 2011) for (c) Hodgkin and (d) non-Hodgkin lymphoma.

In Fig. F3.4, health services with a high level of development are represented by Hong Kong Special Administrative Region, Singapore, and Turkey (specifically, the Izmir registry), health services with an intermediate level of development are represented by Costa Rica, Cuba, India, the Philippines, and Thailand, and health services with a low level of development are represented by The Gambia, Uganda, and Zimbabwe. Data from individual registries in the respective categories were pooled for this comparison of OS rates.

The OS rates of breast cancer patients with regional disease in countries with health services with a high level of development were similar to those of breast cancer patients with localized disease in countries with health services with an intermediate level of development; the two curves

of OS rates are superimposed (Fig. F3.4b). For patients with cancer of the large bowel, a very similar situation was observed (Fig. F3.4a). The differences in OS rates between localized and regional categories of cancer of the large bowel, regardless of level of development of health services, indicate the potential of early detection to increase survival (Fig. F3.4a). The difference in OS rates between localized and regional categories of breast cancer was larger among countries with health services with an intermediate level of development than among those with health services with a high level of development (Fig. F3.4b). Although some misclassification between localized and regional disease cannot be ruled out and the proportion of cases with missing stage information varies greatly by country, intercountry differences in the availability of and accessibility of early detection and appropriate treatment are predominantly responsible for these results.

In the case of Hodgkin lymphoma, given the generally good prognosis, the low OS rates and the minimal differences in 5-year OS rates between the intermediate and low categories of development of health services indicate that all levels of suboptimal treatment will lead to similar survival rates (Fig. F3.4c). Non-Hodgkin lymphoma is more heterogeneous, with variable clinical behaviour and

responses to treatment. The differences in OS rates for non-Hodgkin lymphoma between the countries with different levels of development of health services are therefore striking (Fig. F3.4d); these differences are possibly explained by the capacity of the health services to provide diagnosis, histological typing, accurate staging, and appropriate treatment (Sankaranarayanan et al., 2011).

Conclusions

It is evident from existing studies that inequalities exist and influence cancer survival patterns in countries in transition in Asia. Five-year OS rates show an increasing trend for most cancers, but relative survival differences persist between and within Asian countries, correlated with the level of development of health services, socioeconomic indicators such as area of residence (rural versus urban), or stage of disease at diagnosis. Care should be taken in future international studies to devise more suitable individual-level measurements of conceivable inequalities in social indicators (education level and occupation), disease (extent of disease or tumour stage), and treatment (access, modality, and compliance), as well as other population-level health-related factors (equality in availability and access), for a more objective appraisal over time of inequalities in cancer survival.

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FOCUS 4.

Social inequality in cancer: perspectives from Africa

Lynette Denny

Africa is a complex, heterogeneous continent characterized by premature death as a result of both communicable and noncommunicable diseases, high levels of poverty, poor-quality living and working conditions, poor governance, and high levels of conflict, civil disruption, and corruption. As a consequence, health tends to be neglected; the available funding and resources are insufficient to serve the needs of Africa's population of now more than 1 billion (Lingwood et al., 2008).

Cancer care has received little attention as a public health problem in Africa, largely because of the competing needs of the many countries, ranging from the predominance of malaria, tuberculosis, HIV, nutritional deficiencies, and maternal and neonatal mortality, to name a few health problems, to major issues surrounding access to clean water, sanitation, decent housing, and employment. The consequences of these competing needs are that although cancer is not the primary cause of morbidity and mortality in Africa, those who

do develop cancer have a very high case mortality rate, and more than 80% present with advanced-stage disease. Facilities for prevention (e.g. cervical cancer screening and human papillomavirus [HPV] vaccination) and early detection are limited, and they are barely available in the public sector. Access to diagnostic services (pathology, radiology, and laboratory testing) is limited, and such services are not accessible to most individuals, especially in rural areas. The training of health-care professionals in cancer care and management is minimal and is only available at very few of the 148 medical schools in Africa (Mullan et al., 2011). There is also a significant so-called brain drain of health-care professionals from Africa to other continents, where working conditions and salaries are much more favourable (Duvivier et al., 2017). Furthermore, access to treatment facilities (surgical oncology, radiotherapy, and chemotherapy) is very limited, and such treatment is prohibitively expensive for the majority of people with cancer.

Access to palliative care is also poor but has improved in the past 10 years; Hospice Uganda is leading the way and introducing home-based care and nurse-driven pain management with oral morphine. Of all the African countries, in only 11 countries do the residents have access to oral morphine.

The World Health Organization has strongly recommended that ministries of health adopt national cancer control programmes that encompass the entire continuum of cancer care, including: improving prevention and early detection and diagnosis, to reduce the proportion of patients who present with advanced-stage disease; developing support infrastructure for cancer care, to enable access to high-quality treatment; and providing palliation and rehabilitation services for cancer survivors. Efforts to create an aware and competent health-care workforce need to be prioritized, as well as the creation of a health system that is able to support the provision of cancer care.

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CHAPTER 6.

Social inequalities in cancer within countries

Salvatore Vaccarella, Esther De Vries, Mónica S. Sierra, David I. Conway, and Johan P. Mackenbach

Introduction

As well as the large variations in cancer incidence, survival, and mortality that are observed between countries (see Chapter 5), stark and consistent inequalities in cancer also exist between groups and individuals living within the same country. Socioeconomic inequalities in cancer incidence, survival, and mortality have been reported from all high-income countries (HICs) in which information on education level, occupational class, income, or other indicators of socioeconomic status (SES) is available and has been investigated in relation to cancer, as recorded in cancer or cause-of-death registries. These associations are subject to substantial variability, not only across the different cancer types but also between countries and over time.

In this chapter, these issues are illustrated by reviewing and analysing a unique collection of data on inequalities in cancer mortality rates by education level in 17 European countries over the period 1980–2015. In addition, a summary overview was undertaken of the literature currently available on socioeconomic inequalities in cancer in HICs and low- and middle-income countries (LMICs).

Cancer mortality data in European populations

Cancer mortality data by education level in 17 European countries were collected and harmonized within the framework of two European collaborative studies: Developing Methodologies to Reduce Inequalities in the Determinants of Health (DEMETRIQ; Gregoraci et al., 2017) and Lifepath (Stringhini et al., 2017; Vineis et al., 2017). A key feature of these data is that information on cancer mortality by education level is available for the entire population in most of the study countries. Social inequalities in cancer mortality and the corresponding 95% confidence intervals (CIs) were quantified by calculating the ratio of the age-standardized rates for individuals with a low education level (LEL) to those for individuals with a high education level (HEL) in each country. Country-specific and pooled estimates were

estimated for 18 cancer types (see Box 6.1).

Evidence of social inequalities for all cancers combined

Among men, mortality from all cancers combined was higher among LEL groups than among HEL groups in all study countries, with a pooled rate ratio of 1.75 (95% CI, 1.61–1.89). However, there was some variability between countries; relative inequalities in mortality were consistently larger in central and eastern Europe than in other European countries. Rate ratios ranged from a little below 1.4 in Spain and Sweden to almost 2.2 in Hungary and Estonia (Fig. 6.1). Relative inequalities were almost always smaller among women than among men (with the exception of Sweden, where inequalities were slightly higher among women); the pooled rate ratio for cancer mortality in LEL women versus HEL women was 1.34 (95% CI, 1.23–1.46). The pattern of variation between countries is also somewhat different for women than for men: among women, the relative inequalities in mortality were largest in northern Europe and central and eastern Europe, and smallest or almost absent in southern Europe. Rate ratios ranged from 1.0 in Italy, Slovenia, and Spain to about 1.6 in Norway and Denmark (Fig. 6.1).

Similar patterns, although with more pronounced contrasts between countries, were found for absolute inequalities in cancer mortality. Rate differences of cancer mortality varied by more than 4-fold among men (from ~80 per 100 000 in Sweden to ~360 per 100 000 in Hungary) and by even more among women (from ~0 in Italy, Slovenia, and Spain to ≥ 120 per 100 000 in Denmark and Norway; results not shown).

Evidence of social inequalities for specific cancer types

Cancer mortality rates were greater for LEL groups than for HEL groups for most cancer types, although substantial variability was found in the magnitude of the association for specific cancer types (Fig. 6.2). The largest inequalities were found for mortality rates of smoking- and alcohol-related cancers, including cancers of the larynx; buccal cavity and pharynx; oesophagus; and trachea, bronchus, and lung. These data suggest that the social patterning of smoking and excessive alcohol consumption plays an important role

Box 6.1. On the mortality data (DEMETRIQ/Lifepath).

Data were mostly derived from census-based mortality follow-up studies, but data from a few countries were derived from cross-sectional unlinked studies. Although data covered complete national populations for most of the studied countries, for England and Wales and France a 1% sample was used. For Italy and Spain, national data were available for the most recent time periods only; time trends for these countries were based on data from the regions of Turin and Barcelona, respectively. In addition to inequalities in mortality from all cancers combined, inequalities in mortality from 18 specific cancer types are shown (Fig. 6.2). Causes of death were coded according to the 10th revision of the International Statistical Classification of Diseases and Related Health Problems and previous editions for data from previous time periods. Mortality inequalities are shown by education level, with low education level (LEL) being defined as International Standard Classification of Education levels 1–2 (primary and lower secondary education) and high education level (HEL) being defined as levels 5–6 (tertiary education). Mortality rates per 100 000 person-years, age-standardized by the European Standard Population (Doll, 1976), were computed for each education level in each country. Inequalities were quantified by calculating the ratio of the age-standardized rates for LEL groups to that for HEL groups in each country. The corresponding rate ratios for middle versus high education level were computed but are not included or discussed in this chapter. To summarize inequalities in cancer mortality between countries, a random-effects meta-analysis was conducted and pooled estimates of the rate ratios were computed. In a graphical representation of the results for overall cancer (Fig. 6.1), rate ratios for each country are plotted as grey squares of size inversely proportional to the variance of the logarithm of the rate ratio. Diamonds represent summary rate ratios for the pooled data. Heterogeneity of the rate ratios between countries was also assessed. Time trends of overall cancer mortality by education level were computed and plotted for the available time points in each country. Finally, the estimated annual percentage change was computed for all-cancer mortality (Fig. 6.1) and for selected cancer types (Fig. 6.2) for each education level.

Fig. 6.1. Relative social inequalities in cancer mortality by education level in 17 European countries, by country, for the most recent data available for each country (from 2004 to 2013). The charts show rate ratios and corresponding 95% confidence intervals of mortality from all cancers combined for men (left) and women (right) with a low versus high education level, and a pooled rate ratio estimate obtained from a random-effects meta-analysis.
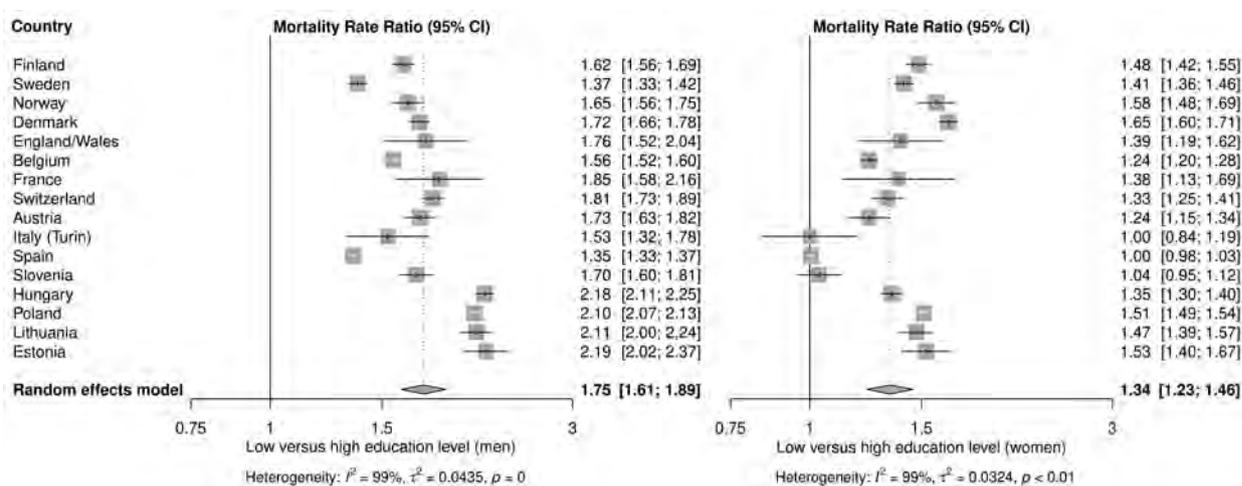
in generating inequalities in cancer mortality. Compared with HEL individuals, LEL individuals had mortality rates that were 2–3 times as high for cancers of the lung and oesophagus, 2–4 times as high for cancers of the buccal cavity and pharynx, and 3–5 times as high for cancer of the larynx.

Lung cancer was the main contributor to the differences between European countries in the magnitude of inequalities in cancer mortality shown in Fig. 6.1. This is unsurprising because lung cancer is a very common cancer and tobacco smoking, its main risk factor, is strongly associated with SES. In Europe, absolute inequalities in lung cancer mortality rates in men were largest in central and eastern Europe, followed by Belgium and Norway, whereas inequalities in women were largest in Denmark and Norway and very small in Italy and Spain (results not shown).

Large inequalities in cancer mortality rates were also observed for infection-related cancers, that is, cervical cancer (by a factor of 3 for LEL vs HEL), and stomach cancer and liver cancer (by a factor of 2 for LEL vs HEL) in both sexes. No differences in mortality rates were observed for breast cancer, and the only cancer for which mortality rates were higher among HEL men than among LEL men was cutaneous melanoma (Fig. 6.2).

Time trends

The remarkable inequalities described above are the result of major trends over time. Cancer mortality among HEL groups of men and women has almost universally declined, but trends in cancer mortality over the past decades have generally been more favourable among HEL groups than among LEL groups, for which cancer mortality rates have often remained stable or even increased (Fig. 6.3). For all cancers combined, annual percentage declines as well as absolute declines (not shown) were considerably larger among HEL individuals versus LEL individuals, particularly

among women (Fig. 6.4), meaning that both relative and absolute inequalities in cancer mortality have risen in many countries. However, inequalities in cancer mortality have reversed in some countries, for example Estonia and Hungary, from higher mortality among HEL groups in the early 1990s to higher mortality among LEL groups in the early 2010s (Fig. 6.3). Because cardiovascular disease mortality has declined at a greater rate and more uniformly than cancer mortality has (Bray et al., 2012; Torre et al., 2015; Townsend et al., 2016), among both HEL men and women and LEL men and women, inequalities in cardiovascular disease mortality have declined in many countries. Cancer has therefore become relatively more important as a cause of inequalities in total mortality in several populations, for example, among men in Austria, Belgium, England and Wales, Italy, Spain, and Switzerland, and among women in England and Wales, Italy, and Norway (results not shown).

Fig. 6.2. Relative inequalities in mortality from 18 specific cancer types in 17 European countries, according to the most recent data available for each country (from 2004 to 2013). The graphs show pooled rate ratio estimates and corresponding 95% confidence intervals of mortality for men (left) and women (right) with a low versus high education level, obtained from a random-effects meta-analysis.
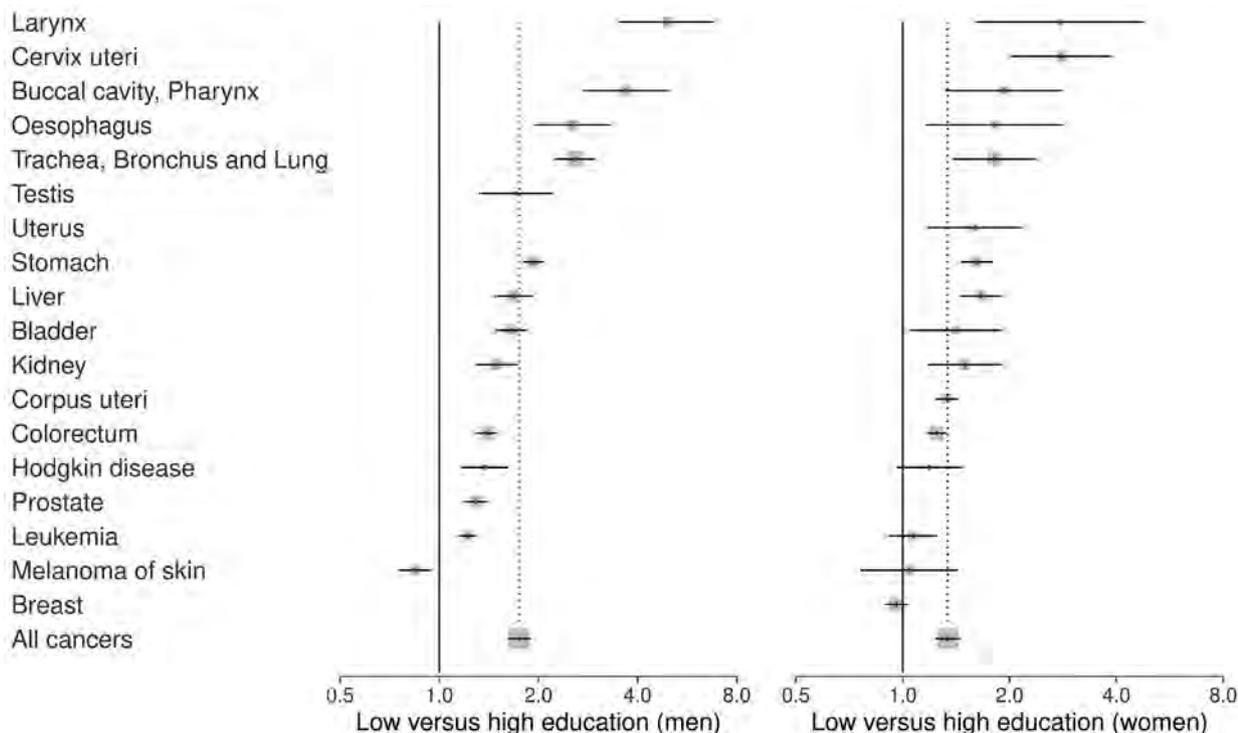
The magnitude and even the direction of temporal trends for groups with different education levels differ by cancer type, however. Declines were observed in most countries for several cancer types in both HEL and LEL groups, but were often greater in HEL groups, for example, cancer of the breast in women and cancers of the prostate, colorectum, and lung in men. Cervical cancer mortality rates decreased in both HEL and LEL groups in certain countries, but also increased in LEL groups in other countries. General declines were also observed for stomach cancer mortality rates, often more favourable to LEL groups versus HEL groups in some countries, but increases were also observed in HEL groups in other countries. Mixed trends in liver can-

cer mortality rates were observed, with increases for both HEL and LEL groups in several countries. Lung cancer mortality has generally increased among women, but more so among LEL groups versus HEL groups. The patterns described above are quite general, however; it is important to acknowledge that trends in specific cancer types may vary in magnitude and sometimes even in direction across different countries (Fig. 6.4).

Evidence of social inequalities in cancer within HICs

This section integrates the information provided above on social inequalities in cancer mortality in Europe with the most recent and highest-quality available evidence on social inequalities in cancer incidence in countries

classified as HICs by the World Bank (2018a). Several searches were undertaken in PubMed to identify key systematic reviews, meta-analyses, or significant cohort studies (published in the past 10 years) that focused on cancer incidence in relation to SES. Articles were reviewed, and data in relation to HICs or HIC groupings were abstracted.

Four cohort studies that investigated associations between SES and risk of cancer incidence (in all sites and across subsites) were identified: one in North America and three in European countries. Table 6.1 presents the data from these cohort studies on the risk associations by sex of LEL versus HEL groups (note that all cohort studies investigated multiple measures of SES; only education level is reported here). Despite

Fig. 6.3. Trends of age-standardized all-cancer mortality rates (European Standard Population) in deaths per 100 000 person-years in 17 European countries, using data from 1990–2012. The graphs show mortality rates for men (upper) and women (lower) with a low (left) and high (right) education level.
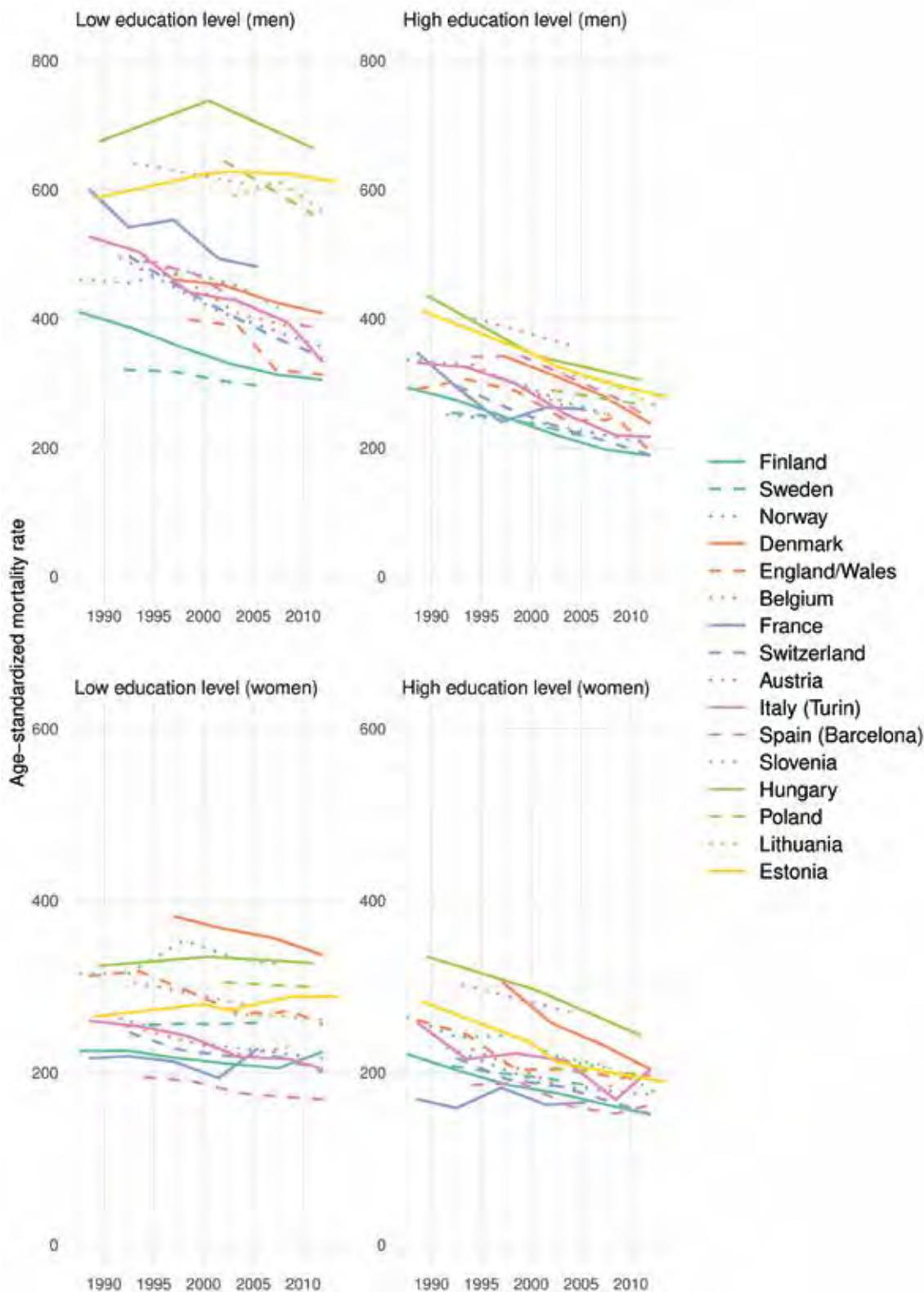
Fig. 6.4. Annual percentage change in age-standardized mortality rates from all cancers and specific cancer types in 17 European countries for men (blue) and women (red) with a low education level (vertical axis) plotted against those with a high education level (horizontal axis), using data from 1980–2015. A comparison of the magnitude of same-direction changes (decreases or increases) between the groups of different education level is provided by the dashed lines. For example, a blue dot in the lower left quadrant indicates that, in that specific country, cancer mortality rates decreased over time for men with both a low and a high education level; if the dot lies above the dashed line, then the decrease is greater for those with a high education level.
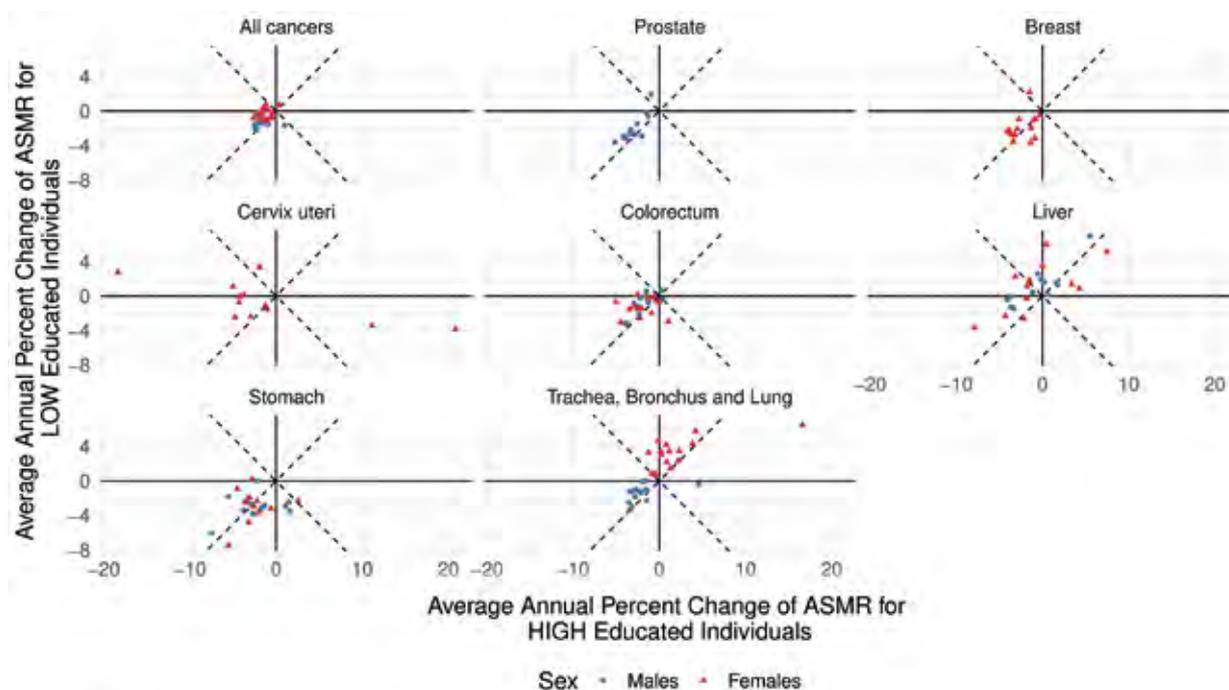
the different definitions of cancer used and differences in modelling approaches, the four cohort studies observed increased risks of cancer incidence for both sexes for LEL groups relative to HEL groups (Dalton et al., 2008; Mouw et al., 2008; Spadea et al., 2010; Sharpe et al., 2014). Across all cohort studies, those with the lowest levels of education had higher risks of cancers of the lung, upper aerodigestive tract, stomach, and cervix uteri relative to those with the highest levels of education. In contrast, LEL groups generally had a lower risk of cancers of the skin, prostate, and breast.

In addition to the four large cohort studies described above, there is a large body of evidence (usually in the form of case–control studies) from HICs investigating the relationship between SES and cancer incidence by cancer site. These studies are often collated within systematic reviews and are usually combined with meta-analyses, or in pooled data consortia. Data were abstracted from these studies by cancer type for HICs (Table 6.2). Unadjusted (or minimally adjusted) pooled estimates of the risk associations for LEL groups relative to HEL groups, or other SES measure where education level was not available, are shown (note again that some of these studies reported multiple measures of SES, although only data on education level are included here). In agreement with the results from the four cohort studies described above, the incidence of cancers of the lung, head and neck,

stomach, and cervix was increased for groups with lower SES relative to groups with higher SES. There was no clear relationship for cancers of the colon and rectum, and an inverse relationship was observed for breast cancer incidence (Table 6.2).

Evidence of social inequalities in cancer within LMICs

A literature review on social inequalities in cancer incidence and mortality in LMICs was conducted using PubMed, Scielo, and Bireme, and the reference lists from retrieved reports were reviewed to identify other sources. Keywords included inequalities, cancer, Latin America, Africa, Asia, and LMIC. Both ecological and individual-level indicators of inequality in cancer incidence and mortality

Table 6.1. Summary of results from selected cohort studies from high-income countries: relative risk of incidence of specific cancer types for those with a low education level compared with those with a high education level

Cancer site	Relative risk (low vs high education level)							
	Mouw et al. (2008), USA (1995–2004)[a]		Dalton et al. (2008), Denmark (1994–2003)[b]		Spadea et al. (2010), Turin, Italy (1985–1999)[b]		Sharpe et al. (2014), Scotland (1991–2006)[b]	
	Men	Women	Men	Women	Men	Women	Men	Women
Mouth and pharynx			1.43[c]	1.25				
Larynx			1.67[c]	3.23[c]				
Head and neck	1.29	1.21						
Upper aerodigestive tract					1.96[c]	1.10	1.82[c]	1.42[c]
Thyroid		1.01						
Oesophagus	2.00[c]		1.30[c]	0.87				
Stomach	1.67[c]	0.92	1.37[c]	1.23[c]	2.19[c]	1.48		
Pancreas		0.74	1.20[c]	1.22[c]				
Colorectal					0.89[c]	0.9		
Colon	1.10	1.37[c]	0.93	1.02				
Rectum	1.50	1.05	1.02	1.12				
Liver	1.28				1.05	1.09		
Lung	1.95[c]	1.43[c]	1.53[c]	1.85[c]	1.68[c]	0.59[c]	3.05[c]	1.94[c]
Pleura	4.56[c]							
Breast		0.83[c]		0.80[c]		0.66[c]		
Cervix		1.20		1.33[c]		2.13[c]		
Corpus/endometrium		0.65[c]		0.98				
Ovary		1.08		0.97				
Prostate			0.81[c]					
Prostate (localized)	0.85[c]							
Prostate (advanced)	0.89							
Testis			1.00					
Kidney	0.97	1.29	1.22[c]	1.54[c]				
Bladder	1.20[c]	0.67	1.15[c]	1.37[c]				
Malignant melanoma	0.53[c]	0.40[c]	0.65[c]	0.69[c]	0.34[c]	0.41[c]		
Brain and central nervous system	0.82		1.04	0.92				
Lymphoma	0.76[c]	0.99						
Non-Hodgkin lymphoma			1.10	1.14				
Hodgkin lymphoma			1.05	1.16				
Leukaemias	1.11	1.14	0.96	1.10				
All cancers	1.03	0.84[c]	1.10[c]	1.02	1.17[c]	0.78[c]	1.17[c]	0.99

[a] Estimates adjusted for age, sex, ethnicity, smoking, alcohol consumption, energy intake, body mass index (BMI), physical activity, marital history, and family history of cancer.
[b] Estimates adjusted for age, period, and multiple socioeconomic status variables.
[c] Estimates for which the 95% confidence interval excludes unity.

for countries classified as LMICs by the World Bank (2018b) were included. When several studies of inequalities were reported for certain cancer types within a particular country, the most recent and/or those report-ing the broadest age groups were used. Of note, most studies on social inequalities in cancer in LMICs report-ed only cancer mortality data; the very few publications that included individu-al-level data by education level almost exclusively reported mortality data (Attar et al., 2010; Dey et al., 2010a; Dikshit et al., 2012; de Vries et al., 2015, 2016, 2018; Tarupi et al., 2018). Published results are mostly limited to some countries in Latin America and

Table 6.2. Systematic reviews and meta-analyses of associations between socioeconomic status and risk of cancer incidence by site for high-income countries

Reference	Cancer site	Setting	No. of studies	Unadjusted pooled OR (95% CI) for groups with different levels of SES
Lundqvist et al. (2016)	Breast	Europe	8	All SES measures combined; high vs low SES: 1.25 (1.17–1.32)
Parikh et al. (2003)	Cervix	North America	10	Low vs high education level: 2.30 (2.01–2.65)
		Europe	8	Low vs high SES: 1.28 (1.10–1.49)
Uthman et al. (2013)	Stomach	HICs	19	Low vs high education level: 2.65 (1.64–4.30)
		North America	4	Low vs high education level: 2.37 (0.99–5.69)
		Europe	11	Low vs high education level: 2.92 (1.37–6.19)
Manser and Bauerfeind (2014)	Colon	North America	5	Low vs high education level: 1.03 (1.00–1.06)
	Rectum	Europe	9	Low vs high education level: 0.90 (0.76–1.07)
Conway et al. (2008)	Oral cavity	HICs	37	Low vs high education level: 1.85 (1.60–2.15)
Conway et al. (2015)	Head and neck	North America	15	Low vs high education level: 3.00 (2.05–4.39)
	Head and neck	Europe	11	Low vs high education level: 2.20 (1.55–3.11)
	Oral cavity			Low vs high education level: 2.06 (1.64–2.58)
	Oropharynx			Low vs high education level: 2.34 (1.66–3.31)
	Larynx			Low vs high education level: 2.99 (2.19–4.07)
Sidorchuk et al. (2009)	Lung	HICs	11	Low vs high education level (adjusted for smoking): 1.66 (1.10–2.51)
		North America	6	Low vs high education level: 2.13 (1.45–3.13)
		Europe	6	Low vs high education level: 1.61 (1.26–2.05)
Hovanec et al. (2018)	Lung	North America	2	Low vs high occupational SES (adjusted for smoking, exposures): 1.54 (1.61–2.09)
		Europe	10	Low vs high education level: 1.84 (1.61–2.09)

CI, confidence interval; HICs, high-income countries; OR, odds ratio; SES, socioeconomic status; vs, versus.

a few countries in Africa and Asia, and the majority are ecological studies, comparing regions or states with different SES indicators, such as percentage of illiteracy and mortality of children younger than 5 years.

Despite these limitations (see Box 6.2), studies in LMICs combining all-cancer incidence or mortality usually show inequalities, with generally higher rates among people with lower SES (Diez Roux et al., 2007; Cavalini and de Leon, 2008; Chiavegatto Filho et al., 2012; Dikshit et al., 2012; Oguntoke, 2014; de Vries et al., 2016; Wang and Jiao, 2016). These general patterns conceal large differences in the magnitude and even the direction of inequalities by cancer type, but

are consistent with those observed in HICs, described above. In general, studies based on individual SES data report the largest inequalities for smoking-related cancers and for infection-related cancers, such as those of the stomach, liver, and cervix. In contrast, breast cancer and colorectal cancer do not show a clear and consistent association with SES in LMICs (Dikshit et al., 2012; de Vries et al., 2015, 2018) (Table 6.3).

Discussion

In summary, major social inequalities in cancer exist within countries, with consistent evidence from HICs and LMICs. Disadvantaged individuals

and groups tend to have a different spectrum of cancers compared with people with higher socioeconomic status (SES), notably an excess of tobacco-related and infection-related cancers. Compared with groups with high SES, lower cancer incidence rates are observed in certain anatomical sites than in groups with lower SES. However, disadvantaged individuals systematically suffer from substantially higher mortality rates and lower survival rates than groups with higher SES for the large majority of cancer types. This is clearly evident in HICs where a substantial amount of data is available. Data from LMICs are more sparse, but the available evidence on social

Table 6.3. Evidence of associations between socioeconomic status and risk of cancer incidence or mortality by cancer site for low- and middle-income countries

Reference	Individual or ecological studies	Incidence or mortality	Setting	SES indicator	Measure	Results (95% CI or *P* value)
Cancer of the cervix						
de Vries et al. (2018)	Individual	Mortality	Colombia	Education level	RII	6.8 (6.2–7.5)
				Education level	MRR (low vs high)	4.7 (4.6–4.7)
Dikshit et al. (2012)	Individual	Mortality	India	Education level (illiterate vs senior secondary)	MRR	3.5
				Rural vs urban	MRR	1.13
Dey et al. (2010a)	Individual	Incidence	Egypt	Urban vs rural	IRR	3.1 (2.1–4.6)
Martínez and Guevel (2013)	Ecological	Mortality	Buenos Aires, Argentina	Worst vs best areas	Standardized MRR	1.75
Girianelli et al. (2014)	Ecological	Mortality	Brasilia, Brazil	HDI	Correlation	−0.38 (0.050)
				% individuals aged ≤ 25 yr with > 11 yr of schooling	Correlation	−0.57 (0.002)
				% young population illiterate	Correlation	0.18 (0.3588)
				% living below poverty line	Correlation	0.45 (0.020)
Oguntoke (2014)	Ecological	Incidence	Nigeria	% illiteracy	Correlation	0.16 (NS)
				% urbanization	Correlation	0.61 (< 0.05)
Palacio Mejía et al. (2003)	Ecological	Mortality	Mexico	Urban vs rural	MRR	3.07
Sánchez-Barriga (2012)	Ecological	Mortality	Mexico	Regional SES (low vs high, 2007)	MRR	1.38 (1.20–1.58)
Drumond and Barros (1999)	Ecological	Mortality	São Paolo, Brazil	Regional SES (low vs high)	MRR	1.92
Cancer of the stomach						
de Vries et al. (2015)	Individual	Mortality	Colombia	Education level (low vs high)	RII	M, 3.21 (2.48–4.17); F, 2.05 (1.48–2.83)
					MRR	M, 2.56 (2.29–2.86); F, 1.98 (1.75–2.24)
Dikshit et al. (2012)	Individual	Mortality	India	Education level (illiterate vs senior secondary)	MRR	M, 4.32; F, 4.97
				Urban vs rural	MRR	M, 1.60; F, 1.25
Drumond and Barros (1999)	Ecological	Mortality	São Paolo, Brazil	Regional SES (low vs high)	MRR	M, 1.30; F, 2.18
Sánchez-Barriga (2016)	Ecological	Mortality	Mexico	Regional SES (low vs high)	MRR	1.06 (NS)

Table 6.3. Evidence of associations between socioeconomic status and risk of cancer incidence or mortality by cancer site for low- and middle-income countries (continued)

Reference	Individual or ecological studies	Incidence or mortality	Setting	SES indicator	Measure	Results (95% CI or *P* value)
Cancer of the lung						
de Vries et al. (2015)	Individual	Mortality	Colombia	Education level (low vs high)	RII	M, 2.24 (1.65–3.04); F, 1.35 (0.90–2.03)
					MRR	M, 1.64 (1.47–1.82); F, 1.32 (1.16–1.50)
Dikshit et al. (2012)	Individual	Mortality	India	Education level (illiterate vs senior secondary)	MRR	M, 1.83
				Rural vs urban	MRR	M, 0.78; F, 0.95
Antunes et al. (2008)	Ecological	Mortality	São Paolo, Brazil	HDI of city areas	MRR (high vs medium)	M, 1.08 (1.00–1.16); F, 1.27 (1.11–1.45)
					MRR (low vs medium)	M, 0.74 (0.67–0.83); F, 1.01 (0.90–1.13)
Drumond and Barros (1999)	Ecological	Mortality	São Paolo, Brazil	SES condition region (low vs high)	MRR	M, 0.70; F, 0.88
Cancer of the breast						
de Vries et al. (2015)	Individual	Mortality	Colombia	Education level (low vs high)	RII	0.71 (0.58–0.89)
					MRR	0.93 (0.87–0.99)
Dikshit et al. (2012)	Individual	Mortality	India	Education level (illiterate vs senior secondary)	MRR	1.48
				Rural vs urban	MRR	0.94
Dey et al. (2010b)	Individual	Incidence	Egypt	Urban vs rural	IRR	3.73 (3.30–4.22)
Sánchez-Barriga (2015)	Individual	Mortality	Mexico	Education level (college vs no education)	MRR	1.28 (1.23–1.33)
Girianelli et al. (2014)	Ecological	Mortality	Brasilia, Brazil	% individuals ≤ 25 yr with > 11 yr schooling	Correlation	0.51 (0.006)
				% young population illiterate	Correlation	−0.22 (0.27)
				HDI	Correlation	0.32 (0.099)
				% living below poverty line	Correlation	−0.26 (0.188)
Oguntoke (2014)	Ecological	Incidence	Nigeria	% urbanization	Correlation	0.64 (< 0.05)
				% illiteracy	Correlation	0.22 (> 0.05)
Tumas et al. (2017)	Ecological	Incidence	Córdoba, Argentina	% households in neighbourhoods with unmet basic needs	IRR	1.128 (1.076–1.183)
Fei et al. (2015)	Individual	Incidence	China	Urban vs rural	IRR	1.86 (< 0.001)
	Ecological	Incidence	China	% illiteracy	Correlation	−0.288 (NS)
	Ecological	Incidence	China	Years of education	Correlation	0.640 (< 0.01)

Table 6.3. Evidence of associations between socioeconomic status and risk of cancer incidence or mortality by cancer site for low- and middle-income countries (continued)

Reference	Individual or ecological studies	Incidence or mortality	Setting	SES indicator	Measure	Results (95% CI or *P* value)
Girianelli et al. (2014)	Ecological	Mortality	Brasilia, Brazil	HDI	Correlation	0.32 (0.099)
				% aged < 25 yr with > 11 yr or schooling	Correlation	0.51 (0.0063)
				% aged < 25 yr illiterate	Correlation	−0.22 (0.2764)
				% below poverty line	Correlation	−0.26 (0.1878)
Drumond and Barros (1999)	Ecological	Mortality	São Paolo, Brazil	Regional SES (low vs high)	MRR	0.75
Cancer of the prostate						
de Vries et al. (2015)	Individual	Mortality	Colombia	Education level (low vs high)	RII	1.38 (0.83–2.32)
					MRR	1.04 (0.92–1.19)
Oguntoke (2014)	Ecological	Mortality	Nigeria	% urbanization	Correlation	0.51 (< 0.05)
				% illiteracy	Correlation	0.15 (NS)
Cancer of the colon and rectum						
de Vries et al. (2015)	Individual	Mortality	Colombia	Education level (low vs high)	RII	M, 0.99 (0.67–1.47); F, 0.94 (0.65–1.36)
					MRR	M, 0.91 (0.82–1.01); F, 1.01 (0.90–1.13)
Dikshit et al. (2012)	Individual	Mortality	India	Rural vs urban	MRR	M, 1.04; F, 1.12
Drumond and Barros (1999)	Ecological	Mortality	São Paolo, Brazil	Regional SES (low vs high)	MRR (colon)	M, 0.40; F, 0.62
Sánchez-Barriga (2017)	Individual	Mortality	Mexico	Regional SES (low vs high)	MRR	0.62 (< 0.05)
Cancer of the oral cavity and pharynx						
Dikshit et al. (2012)	Individual	Mortality	India	Education level (illiterate vs senior secondary)	MRR	M, 2.74; F, 5.60
				Rural vs urban	MRR	M, 0.96; F, 1.29
Attar et al. (2010)	Individual	Incidence	Egypt	Urban vs rural (head and neck)	IRR	M, 2.59 (2.26–2.97); F, 2.00 (1.64–2.43)
Oguntoke (2014)	Ecological	Incidence	Nigeria	% urbanization	Correlation	0.52 (< 0.05)
				% illiteracy	Correlation	0.10 (> 0.05)
Antunes et al. (2008)	Ecological	Mortality	São Paolo, Brazil	% low instruction	Correlation	0.308 (0.001)
				% academic degree	Correlation	−0.472 (< 0.001)
				HDI	Correlation	−0.348 (< 0.001)
Borges et al. (2009)	Ecological	Mortality	Brazil	Education	Correlation	0.569 (0.002)
				Unit increase per capita income	Correlation	0.734 (< 0.001)
Ferreira et al. (2012)	Ecological	Incidence	São Paolo, Brazil	HDI	MI	0.226 (0.01)
		Mortality		HDI	MI	0.337 (0.01)

CI, confidence interval; F, female; HDI, Human Development Index; IRR, incidence rate ratio; M, male; MI, Moran index; MRR, mortality rate ratio; NS, not significant; RR, relative risk; RII, relative index of inequality; SES, socioeconomic status; vs, versus; yr, year(s).

Note: RII is a regression-based index that summarizes the magnitude of SES as a source of inequalities in health (see Chapter 4).

Several limitations need to be acknowledged in studies of social inequalities in cancer within countries, and this is particularly true in LMICs. To produce individual-level comparisons of cancer burden according to SES, both the numerators (numbers of new cases or cancer deaths) and population data on the SES indicator (e.g. income, education level, place of residence, profession) of interest must be available. In some settings, it is difficult to obtain information on patient's SES or abstract this information from death certificates, and it is often even more difficult to obtain reliable information on the population distribution of SES indicators (the denominators) to be able to calculate rates and indices of inequality. It is probably because of this lack of data, as well as a lack of research based on cancer registry data in many LMICs, that published information on inequalities in cancer incidence and mortality with individual-level data is very scarce (see Focus 2). Comparing cancer incidence or mortality rates between regions within a country may also be challenging; SES indicators may differ substantially between different areas because of the presence of individual- and area-level effects and because of a possible ecological fallacy (in which all individuals in an area are assigned a SES on the basis of their area of residence). A caveat should also be added when interpreting education level for different birth cohorts, because the meaning of this variable and the consequent features of the SES associated with it may vary between generations.

inequalities in cancer within such populations points to similar conclusions as for HICs.

Despite the many tobacco control measures and prevention campaigns, lung cancer is still among the most frequently diagnosed cancer types in most countries (Ferlay et al., 2018). On a global scale, lung cancer is mostly caused by cigarette smoke and environmental contamination, factors that are strongly related to SES; the associations observed vary by country, however, probably as a result of the varying characteristics of the smoking epidemic. A lower education level is related to higher incidence and mortality rates of lung cancer and oral cancer (Conway et al., 2008; Dikshit et al., 2012; de Vries et al., 2015); exceptions have been observed in some rural areas in LMICs where low SES has been linked to a lower incidence of lung cancer, presumably because of a lower uptake of smoking among the most deprived groups of individuals in these areas (Dikshit et al., 2012). It is important to note that in some LMIC settings the types of housing and cooking methods, which are also associated with SES, are also important contributors to lung cancer risk (Hosgood et al., 2011; Jia et al., 2018).

About 85% of the global burden of cervical cancer occurs in LMICs, where it accounts for almost 12% of all cancers in women. In addition to LMICs having a higher burden of cancer incidence, survival, and mortality compared with HICs, large inequalities are also observed for cervical cancer within both HICs and LMICs; LEL women (Martínez and Guevel, 2013; Girianelli et al., 2014; Oguntoke, 2014; de Vries et al.,

2018) living in rural areas (Antunes et al., 2008; Cavalini and de Leon, 2008; Ferreira et al., 2012) and in areas of lower SES (Drumond and Barros, 1999; Sánchez-Barriga, 2012; Girianelli et al., 2014) have the highest cervical cancer incidence and mortality rates. These observations are probably explained by the lack or limited availability of and limited access to well-organized cervical cancer screening programmes (Murillo et al., 2012), and by the limited access to screening for disadvantaged individuals even in HICs (see Example 2). The large variation in the relative and absolute differences in mortality (by up to a factor of 7) represents an enormous potential for reduction of this disease, even among the groups with the lowest SES (Hall et al., 2019), particularly because of the availability of the highly effective human papillomavirus (HPV) vaccine and of HPV-based screening tests.

Incidence and mortality rates of stomach and liver cancer have been declining in many HICs but are still high in LMICs (Colquhoun et al., 2015; Petrick et al., 2016; Sierra et al., 2016), where the burden of the disease is highest (Ferlay et al., 2018). Stomach and liver cancer are also diseases of the groups of lower SES within both HICs and LMICs, with clearly increased rates among LEL groups and in rural populations (Drumond and Barros, 1999; Belon and Barros, 2011; Dikshit et al., 2012; Ferreira et al., 2012; de Vries et al., 2015; Sánchez-Barriga, 2016). The evidence of a social gradient for the infectious agents causally linked with stomach cancer (*Helicobacter pylori*) and liver cancer (hepatitis B and C viruses) is discussed in Chapter 7.

No clear social gradient is observed for breast cancer. Although incidence is much higher in HICs

than in LMICs (see Chapter 5) and breast cancer is often considered a disease of the affluent, data from both HICs and LMICs do not show clear associations between breast cancer mortality rates and SES (Dikshit et al., 2012; de Vries et al., 2015; Sánchez-Barriga, 2015). In HICs, breast cancer mortality rates used to be higher among HEL women, but they are now equally high among both LEL and HEL women. This could be explained by (i) strong declines in breast cancer mortality among HEL women, as a result of improvements in screening and treatment in this group, and (ii) slower declines (or even increases in some countries) in breast cancer mortality among LEL women, which may be due to an increased incidence as a consequence of a progressive transition towards delayed childbearing in this group of women, an established risk factor for breast cancer (Logan, 1953). In LMICs, living in rural areas seems to be consistently related to lower breast cancer risk (Dey et al., 2010b; Dikshit et al., 2012; Oguntoke, 2014; Fei et al., 2015); this is probably a result of childbearing-related factors, but also lower participation in screening (see Chapters 14 and 15). Although women with lower SES in LMICs may have a lower breast cancer risk, they also have a lower breast cancer survival rate, causing their mortality rates to be similar to those of women with higher SES.

In HICs, a social gradient was also observed with colorectal cancer, which is among the most frequently diagnosed cancer types in HICs and is also increasingly common in LMICs and emerging economies (Li et al., 1997; Ferlay et al., 2018). Screening and early detection combined with timely and effective treatment can greatly improve prognosis,

but 5-year survival has stagnated at about 65% in HICs and is only 30–45% in many LMICs (Allemani et al., 2015). Within LMICs, the association between colorectal cancer mortality and education level is unclear (Dikshit et al., 2012; de Vries et al., 2015; Sánchez-Barriga, 2017).

The only cancer for which mortality was higher among HEL men compared with LEL men in HICs was cutaneous melanoma, perhaps as a result of more intermittent sunlight exposure among HEL men (Fig. 6.2). For some specific cancer types, such as cancers of the thyroid, breast, and prostate, incidence was higher among people with high SES, even though mortality was not (or only to a lesser extent). The large discrepancy between incidence and mortality observed for certain cancers in HICs or emerging economies could be predominantly explained by the availability of and access to effective treatments and by the increased detection of clinically irrelevant cancers in individuals with better access to a health-care system (see Chapter 18). However, the discrepancy between incidence and mortality is smaller in LMICs than in HICs, predominantly because of lower survival rates in LMICs as a result of later diagnosis and poorer access to treatment.

Three potentially relevant arguments related to the observed patterns are proposed.

First, social inequalities in cancer mortality reflect social inequalities both in incidence and in survival. Socioeconomic inequalities in mortality from cancer types for which the effectiveness of life-prolonging treatment is still relatively low, such as lung cancer, are likely to be based on socioeconomic inequalities in incidence. However, for other cancers,

such as breast cancer, the balance may be different; socioeconomic inequalities in access to care and treatment may have a larger weight.

Second, social inequalities in incidence and survival must be based on inequalities in exposure to a large array of specific determinants of incidence and survival. On the basis of the literature, it is clear that health-related behaviours (such as smoking, excessive alcohol consumption, dietary factors, unprotected sex, and delayed childbearing), occupational and other environmental factors, and access to screening and treatment all play a role (see Chapter 7).

Tobacco use is certainly one of the most important factors underlying socioeconomic inequalities in cancer: the remarkably large inequalities in cancer mortality among both Danish and Norwegian women (Fig. 6.1) would not exist without the large inequalities in smoking-related cancers that have emerged within these countries, which are otherwise characterized by egalitarian social and health-care policies. It is therefore important to control the smoking epidemic (also focusing on targeting the underlying socioeconomic determinants of smoking), especially in some emerging economies and LMICs, such as in sub-Saharan Africa and Asia, where the epidemic is currently expanding (see Chapter 11 and Example 1).

Third, current inequalities in cancer mortality rates are the result of striking differences between socioeconomic groups in cancer mortality trends. For most cancer types, the trends of the past decades have been more favourable for groups with higher SES, who have apparently benefited more from advances in prevention and treatment of cancer.

This confirms the central idea of the so-called fundamental causes theory, which stipulates that, whenever opportunities for health improvement arise, groups with higher SES are in a better position to benefit, because they have greater access to an array of material and non-material resources, greater health literacy, and fewer financial barriers to health care. This suggests that redistributing specific risk factors for cancer is insufficient to eliminate inequalities in cancer, and that policies should also tackle the underlying inequality in social and economic resources.

Conclusions

The variability of inequalities in cancer incidence and mortality, both between countries and over time, is a major public health challenge. This variability clearly suggests that these inequalities are not based on immutable laws of nature but are potentially modifiable. The fact that cancer is gradually replacing cardiovascular disease as the main cause of inequalities in total mortality highlights the urgency for a stronger focus on equality in cancer prevention and treatment policies.

Key points

- Stark and consistent inequalities in cancer exist between groups and individuals living within the same country. Socioeconomic inequalities in cancer incidence, survival, and mortality have been reported from all high-income countries as well as low- and middle-income countries in which information on education level, occupational class, income, or other indicators of socioeconomic status (SES) is available and has been investigated in relation to cancer.

- Disadvantaged individuals and groups tend to have a different spectrum of cancers compared with people with higher SES, notably an excess of tobacco-related and infection-related cancers.

- Despite the substantial variability in the magnitude and direction of the association between SES and the outcomes of specific cancer types, for the large majority of cancer types groups with lower SES systematically have substantially higher mortality rates and lower survival rates than their more affluent fellow citizens.

- These remarkable inequalities are the result of major trends over time. Evidence from high-income countries has shown that cancer mortality rates among individuals with high SES have almost universally declined; over the past decades, however, trends have generally been more favourable among groups with high SES than among those with low SES, for which cancer mortality rates have often remained stable or even increased.

- The variability of inequalities in cancer incidence and mortality, both between countries and over time, is a major public health challenge. This variability clearly suggests that these inequalities are not based on immutable laws of nature but are potentially modifiable.

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FOCUS 5.

Social inequalities and cancer in Indigenous populations

Gail Garvey and Joan Cunningham

There are approximately 370 million Indigenous people spread across 70 countries worldwide (UN, 2009). They represent as many as 5000 different cultures and account for much of the world's cultural diversity (UN, 2009). Indigenous people live in a wide variety of environments and circumstances (UN, 2009). Despite this diversity, many Indigenous people around the world, in both high-income countries and low- and middle-income countries, continue to face substantial economic, health, and social disadvantages as a result of an enduring legacy of colonization, an ongoing marginalization and disempowerment, and the social, structural, and political arrangements of the countries in which they live (UN, 2009; Paradies, 2016).

Gaining an accurate statistical picture of the health and well-being of Indigenous populations is challenging. In some countries, the national information infrastructure is inadequate for the whole population; in others, high-quality data exist for the total population, but Indigenous people are not always identified as such in the relevant data collections. In addition, some Indigenous populations live on lands that cross modern-day national boundaries (e.g. the Sami in northern Europe), and many countries group together several distinct Indigenous populations using a single umbrella term (e.g. Aboriginal in Australia, First Nations in Canada, and Native American in the USA).

Despite the data limitations arising from such challenges, it is increasingly clear that cancer is an important health priority for Indigenous populations throughout the world both in absolute terms, as a leading cause of illness and death, and in relative terms, based on disparities in the cancer burden between Indigenous and non-Indigenous populations within countries. Furthermore, in an era of major advances in reducing the impact of cancer, there is evidence that disparities between Indigenous and non-Indigenous populations may be widening (Fig. F5.1).

Studies from around the world provide evidence that Indigenous populations experience significant disparities relative to the local non-Indigenous populations with respect to risk factor prevalence, cancer incidence, stage at diagnosis, care received, and disease outcomes (Moore et al., 2015; Ellison-Loschmann et al., 2017). Although variation exists between and within countries, Indigenous people are more likely to have cancers that are largely preventable, detectable by screening, and/or have a poor prognosis, such as lung, liver, and cervical cancers (Moore et al., 2015).

To date, published reports on cancer in Indigenous populations have come largely from Australia, Canada, New Zealand, and the USA; even in these countries, however, limitations in data quality and availability have generally precluded national-level reporting (with the exception of New Zealand) (Boyd et al., 2016). Data inadequacies have also limited the number of cross-country

Fig. F5.1. Trends in age-standardized mortality rates of all cancers combined, by Australian Indigenous status, 1998–2015. Source: compiled from Australian Institute of Health and Welfare (2018). Cancer in Aboriginal and Torres Strait Islander people of Australia. Cat. no.: CAN 109. Canberra, Australia: AIHW. https://www.aihw.gov.au/reports/cancer-screening/cancer-in-Indigenous-australians/contents/mortality.
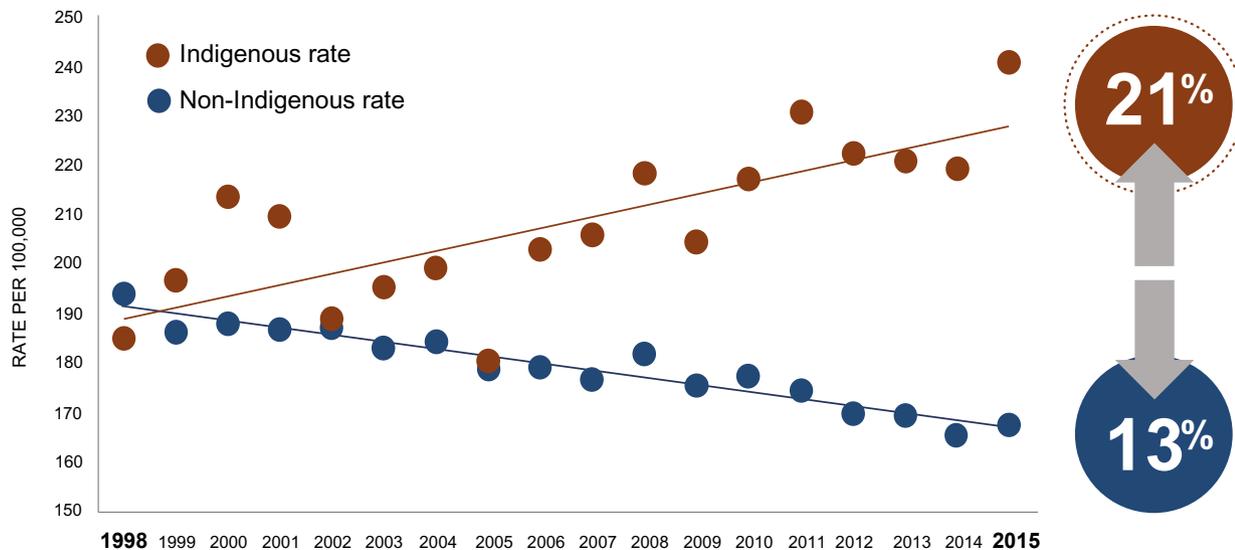
comparisons. Moore et al. (2015) reported higher incidence rates of preventable cancers for a range of Indigenous populations across Australia, Canada, New Zealand, and the USA, with some notable variations among groups (Moore et al., 2015). Systematic reviews of peer-reviewed literature have been used in some countries to overcome data inadequacies (Hassler et al., 2008; Moore et al., 2014). Moore et al. (2014) found higher incidence rates of cervical cancer in parts of Brazil, Ecuador, and Guyana for Indigenous women compared with non-Indigenous women; higher incidence rates of stomach cancer in regions of Chile and of gallbladder cancer in Bolivia and Chile were also reported for Indigenous populations compared with non-Indigenous populations (Moore et al., 2014). Within countries, data linkage has been used to overcome deficiencies in population-level cancer surveillance programmes to enable reporting for

Indigenous populations, for example in Australia (Whop et al., 2016), Canada (Sanchez-Ramirez et al., 2016), and the USA (Espey et al., 2008).

A broad range of factors may contribute to poorer cancer outcomes for Indigenous populations, including those relating to individual patients, health-care systems, and sociocultural and political contexts (Fig. F5.2). Although many of these interconnected and multifaceted factors are relevant for Indigenous populations globally, the relative importance of particular factors is likely to vary from place to place. In addition to the Indigenous-specific factors included in Fig. F5.2, patterns of cancer incidence and mortality in Indigenous populations are also strongly influenced by the prevalence of traditional risk factors such as tobacco use, excessive alcohol consumption, nutrition, and level of physical activity, as well as by social determinants such as education level, employment, in-

come, and housing (more information about the social determinants of cancer is provided in Chapters 3 and 7).

Key international bodies, including the Seventieth World Health Assembly and the Union for International Cancer Control, have recognized the need for specific, targeted cancer control strategies for population groups experiencing an inequitable cancer burden. Understandings of health and well-being are culturally bound (Petersen et al., 2004), and this needs to be considered in improving the performance of the cancer system with and for Indigenous people. For example, Cancer Care Ontario's Aboriginal Cancer Strategy aims to do this by honouring the Aboriginal Path of Well-being (Fig. F5.3) (Kewayosh et al., 2015). The development of shared principles and priorities to guide efforts to improve cancer outcomes for Indigenous populations is also critical. For example,

Fig. F5.2. Factors affecting cancer outcomes of Indigenous people. Design by Lea Bill and Alana Gall.
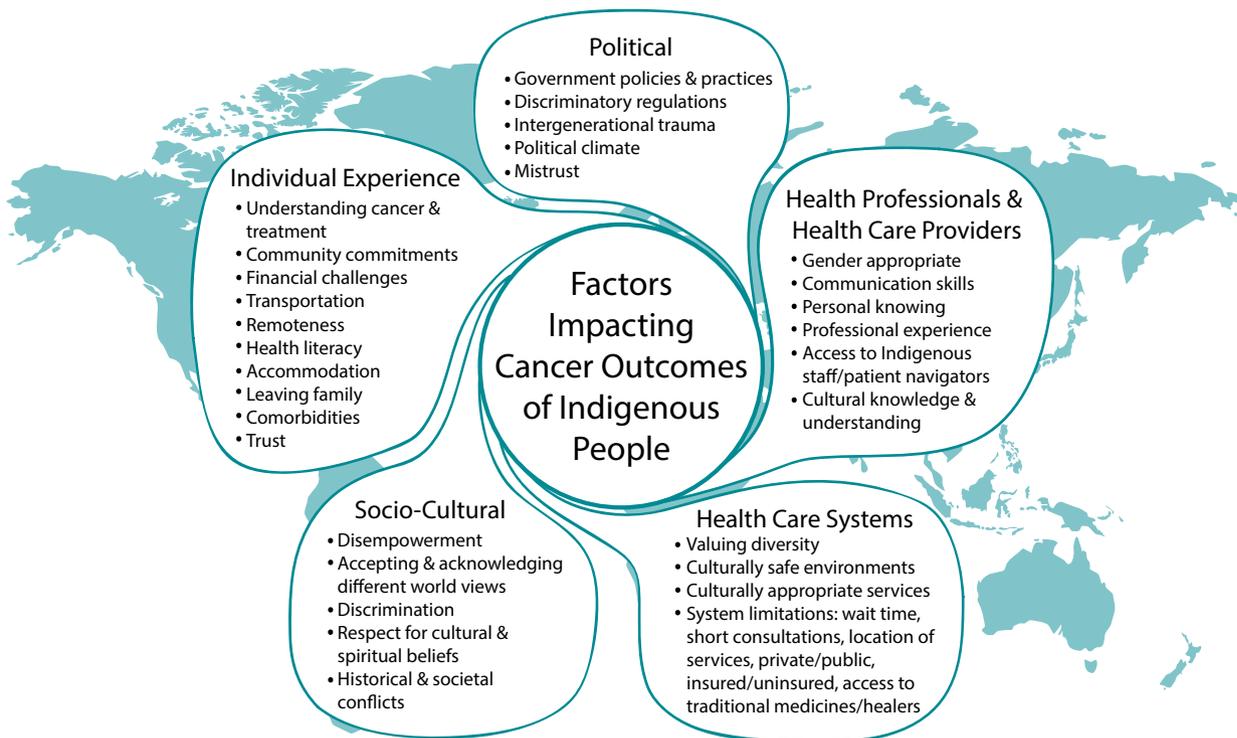
Cancer Australia, the Australian government's key cancer control agency, undertook extensive stakeholder consultation with a wide range of key Indigenous organizations and individuals, as well as with health service providers, governments, nongovernmental organizations, and researchers, to develop the National Aboriginal and Torres Strait Islander Cancer Framework (Cancer Australia, 2015). This framework is underpinned by four key principles: Indigenous engagement, Indigenous information and empowerment, working together, and evidence-informed practice. The key priorities address issues such as cancer-related health literacy, prevention and early detection, optimal treatment, supportive care, and service development, with a range of enablers highlighted (Cancer Australia, 2015).

Fig. F5.3. An example of incorporating Indigenous understandings of health and well-being into a jurisdictional cancer strategy: Cancer Ontario's Aboriginal Cancer Strategy II. Source: reproduced with permission from Kewayosh et al. (2015).
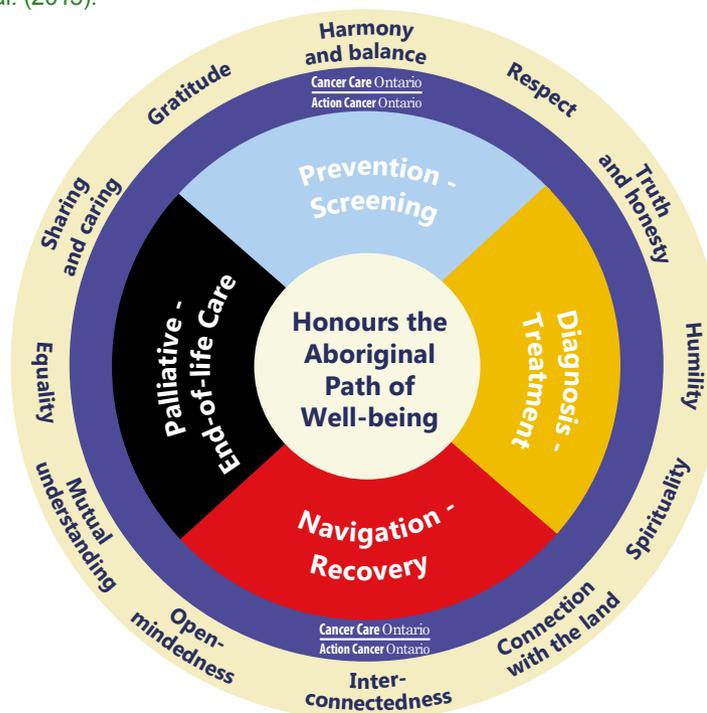
Addressing the excess cancer burden for Indigenous populations requires culturally appropriate public health interventions that are developed, implemented, and evaluated in partnership with Indigenous communities. Such community partnerships can have a positive impact in addressing cancer disparities providing they are built on trust, a shared commitment, agreement of the outcomes, and mutual benefit, and that Indigenous people are involved at all levels. An example of a successful collaborative partnership is the cancer prevention and screening practices project among Alberta First Nations communities (Voyageur et al., 2018). Providing patient navigators and conducting community education workshops can also play an important role in improving cancer screening rates and empowering Indigenous populations (Burhansstipanov et al., 2017).

Conclusions

Measuring the cancer burden of Indigenous populations is critically important, but gaps and challenges remain. In particular, reliable and accurate data are needed to develop appropriate cancer policy, priority setting, and service responses, and to monitor cancer outcomes over time. In addition to measuring traditional end-points such as morbidity and mortality, better information is also needed about quality of life, well-being, and the psychosocial impacts of cancer for Indigenous people. Sarfati et al. (2018) have described key issues relating to cancer surveillance among Indigenous populations and suggested a range of solutions to strengthen their visibility. In particular, it is critical to ensure that Indigenous people are centrally involved in determining appropriate data governance structures, including data ownership and access.

Improved measurement is necessary but by no means sufficient to reduce the cancer burden for Indigenous populations. Indigenous leadership, empowering Indigenous communities, and establishing authentic partnerships across the continuum of cancer care are vital to eliminating cancer inequalities. The development of a culturally competent health-care workforce and of culturally appropriate systems, services, and programmes is also needed. Research is required to identify and evaluate innovative approaches to cancer control across the cancer continuum.

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FOCUS 6.

Inequality and cancer: the conflict ecosystem and refugees

Richard Sullivan, Omar Shamieh, Tezer Kutluk, Adel Daoud, and Adam P. Coutts

The changing nature of global conflict and its impact on demographically transitioned societies

During the Hungarian Revolution in 1956, 200 000 people fled to neighbouring Austria. This uprising and its aftermath shaped the way humanitarian organizations would deal with refugee crises in the decades that followed. The decolonization of Africa produced the first of that continent's numerous refugee crises by the 1960s, a trend that has now reached a zenith with the largest global refugee crisis since the Second World War across Africa, Asia, and the Middle East. Traditional humanitarian action to support displaced populations in low-resource settings focused on emergency aid and the control of infectious diseases; this situation has changed to one where people are leaving lower-middle-income countries, such as the Syrian Arab Republic, to escape conflict, poverty, and/or oppression. As well as the inherent infectious diseases, cancer and other noncommunicable diseases (NCDs) are prevalent among refugees. New inequalities have emerged as a result of these new conflict-driven demographic dynamics. Migration patterns and sociocultural changes are radically altering exposure to cancer risk factors and access to cancer care. The geopolitical status and immediate surroundings of refugees and internally displaced persons (IDPs) – for example, a rural refugee camp, an urban detention centre, or an enclave – defines and exacerbates inequalities in cancer. Many countries and regions now experience oscillations between conflict and fragile states (so-called post-conflict states). This results in populations spending longer periods as refugees, further weakening state capacity to maintain health systems.

Contemporary conflicts and humanitarian crises have had significant impacts on demographically transitioned countries from Latin America (e.g. the Mexican Drug Wars) to the Middle East and North Africa (MENA) region (e.g. regional conflicts since the 2011 Arab uprisings), particularly across Iraq, Libya, and the Syrian Arab Republic. This has significant consequences for population health, including those

of refugees and IDPs, at a time when pre-existing and long-term vulnerabilities, including the endemic high levels of poverty, corruption, unemployment, and disease (both infectious and noncommunicable) burden, are becoming increasingly significant (ILO/UNDP, 2013; Coutts, 2015). The scale and scope of the ongoing refugee crisis has exposed both the fragile nature of the health and social protection systems for cancer care of refugee host countries, and inadequacies in international response mechanisms for supporting displaced populations with a high burden of NCDs. However, academic discourse and foreign policy agendas on the conflict-affected countries in the region frequently overlook health inequalities and the political economy of how health systems are designed, implemented, and governed.

It is apparent that existing health systems and medical approaches have not been able to properly address the rising burden of cancer and other NCDs experienced in conflict-affected countries (SPHN, 2016). Cancer has been neglected within the policy response to the humanitarian crisis and development (Coutts et al., 2015). Evidence from public health, sociology, and social epidemiology studies demonstrates that factors separate from the provision of health services, such as social, economic, and political factors, are increasing inequalities in cancer; any policy response must therefore reflect this (NCCDH, 2012). Indeed, a recent analysis of health inequalities including in NCDs in the Eastern Mediterranean Region highlights the absence of a political economy and multisectoral approach to understanding health and health-care issues (Mokdad et al., 2016). From

our research, it is clear that powerful vested interests, such as syndicates of hospitals and doctors, private sector health providers, and pharmaceutical and tobacco companies, have contributed to national inequalities in cancer through the inadequate health and social protection systems of conflict-affected countries (Coutts et al., 2013).

In addition to a high cancer burden, most countries in conflict have a long record of underinvestment in health research and its subsequent translation into adequately funded policies on a national level; this has given rise to critical skills shortages, insufficient capacity in health services, and poor health outcomes for the populations (Mateen et al., 2018). Viewed alongside the limitations of basic public health surveillance systems, these problems severely constrain governments and multilateral agencies in attempting to address the unprecedented inequalities in both short- and long-term cancer care for vulnerable domestic populations and refugees (Ismail et al., 2013).

The conflict ecosystem and inequalities

Today's refugee crisis brings the inequalities in cancer experienced by refugees and the impact of conflict on cancer care into sharp perspective. The cancer burden in transitioned middle-income countries is already high because of years of underinvestment in health services; conflict serves only to increase the inequalities experienced by both refugees and domestic populations of host countries.

The fragile and nascent cancer control programmes of countries in North Africa and sub-Saharan Africa mean that cancer care for domestic

populations is already limited. The influx to these countries of refugees, some of whom are seeking cancer care, has already had an impact on the availability of and accessibility of cancer care in Rwanda and the United Republic of Tanzania; of the more than 420 000 refugees who left Burundi during 2015–2017, 20% went to Rwanda and 54% went to the United Republic of Tanzania. The conflicts in Chad, Libya, and Mali and across the Sahel have also driven cancer patients into seeking care in Tunisia and across the Mediterranean Sea. Although many families in Libya have been able to pay out-of-pocket expenses for care, even basic treatment is unaffordable for most refugees from the Sahel region. The impact of Libyan refugees seeking cancer care has been 2-fold: contributing to the decline of Libyan cancer care by removing domestic remittances; and contributing to inequalities in outcomes for host-country populations by displacing domestic, publically insured patients in Tunisia.

The contribution to inequalities in cancer from the movement of refugees has also been seen in South-East Asia (Chongsuvivatwong et al., 2011). Inequality in outcomes and high levels of catastrophic expenditure on cancer treatment have been well documented. Countries such as Bangladesh and Myanmar have particularly unequal and fragile cancer care systems. However, during 2017 about 761 000 refugees were displaced from Myanmar to Bangladesh, essentially from one low-income setting to another, reversing the incremental improvements in cancer care (achieved from advances in treatment) and inadvertently increasing inequalities in outcomes as wealthier patients left Bangladesh to seek care in Northeast India. Ironically, this

secondary migration then places a strain on resources in an already constrained and deprived part of India, enhancing cumulative inequalities across the region.

Traditionally equitable health systems in Latin America, such as that of Columbia, are coming under huge strain from refugees escaping the civil unrest and collapsing economy in the Bolivarian Republic of Venezuela; about 68 000 refugees were absorbed in 2017 alone. Similarly, many refugees migrating across Europe find themselves passing through many of the more deprived central and eastern European countries that already have relatively poor cancer outcomes. In particular, the high number of children (~20% of the total refugee population; Carballo et al., 2017) has placed a significant burden on childhood cancer services in many countries (ExPO-r-Net, 2018). Refugees seeking cancer care contribute to complex patterns of displacement of domestic cancer patients, either through the volume effect or by the rising costs of treatment because of increased demand.

Inequalities in access to care, outcomes, and financial burden are also driven by conflict geography. The trapping of refugees in seam zones and enclaves, such as the Biddu enclave (a cluster of eight Palestinian villages in the West Bank surrounded by and cut off by Israeli settlements), or the isolation of communities (e.g. the Gaza Strip) as a result of conflict, drives inequalities in cancer. For example, breast cancer 5-year survival

is just more than 54% in these communities, compared with a regional average of nearly 74% (Khatib et al., 2017). Analysis by the United Nations High Commissioner for Refugees revealed that refugees in formal camp settings experience very poor cancer outcomes; even when the cancer has been diagnosed, they receive inadequate treatment, because the refugee camp care system is geared towards the treatment of communicable diseases (Spiegel et al., 2014). The clinical and surgical expertise within such a system is usually focused on trauma and benign disease (Trelles et al., 2015). Without referral or access to a country's dedicated cancer centre, access to curative or palliative treatment is beyond many refugees, especially those living in the informal "sans papiers" sector. Sexual inequality is also worsened by conflict in most settings; women experience significantly poorer cancer outcomes than men (Bigby and Holmes, 2005; Mokdad et al., 2016).

Addressing inequalities experienced by refugees or those affected by conflicts

Conflict changes therapeutic and social geographies through complex paths that drive inequalities in cancer by affecting not only refugees and IDPs but also the low-income domestic populations of host countries; furthermore, the reduction in the volume of the skilled workforce of the conflict-affected country contributes to inequalities in cancer for

those choosing to stay (Dewachi et al., 2014). Despite the recognition of ageing refugee populations and the rising number of transitioned countries affected by conflict, new frameworks for humanitarian medicine still do not address cancer (Spiegel et al., 2010). This is a fundamental gap and needs to be tackled if progress is to be made in addressing inequalities in cancer within these unique ecosystems. Even strategies aimed at providing care for patients with NCDs in emergencies are mostly silent on the best models of care and pathways, never mind the wider political economy of delivering cancer control (Slama et al., 2017). However, many host countries (e.g. Turkey) have developed interventions that deliver outcomes equal to those of the population of the host country (Kebudi et al., 2016). The Turkish government recently extended the coverage for cancer patients by abolishing the charges that had been applied to non-resident populations only. The common denominator among countries that have delivered such interventions is a prior history of and commitment to universal health coverage (Atun et al., 2013). The impact of absorbing refugees has exposed short- and long-term vulnerabilities in the health systems of host countries, but has also had the effect of forcing policy-makers to reform their health systems, particularly in light of the assessment of national resources (Coutts et al., 2013; Kaafarani et al., 2018).

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FOCUS 7.

Social inequalities in cancer burden between Black and White populations in the USA

Ahmedin Jemal and Rebecca Siegel

Inequalities in disease rates among racial or ethnic minority populations have been documented in many parts of the world, including England (non-Whites vs Whites) (Nazroo et al., 2007), Singapore (Malays or Indians vs Chinese) (Sabanayagam et al., 2010), the USA (Blacks, Hispanics, or Asians vs Whites), and Zimbabwe (Blacks vs Whites) (Chokunonga et al., 2016). These disparities may vary within and/or between countries and are largely based on differences in migration patterns, socioeconomic status (SES), and health systems. Blacks involuntarily immigrated to the USA during the period from the 16th century to the 18th century and are a particularly vulnerable population; disparities in cancer outcomes have been well documented since the 1970s (Burbank and Fraumeni, 1972). Because of the unique availability of long-term data on race in the USA, we can highlight these inequalities here.

Cancer death rates during 2011–2015 were higher in Black populations than in White populations for 9 of the top 15 cancers in men and women (Table F7.1), with the excess risk for some cancers persisting since the 1950s (Burbank and Fraumeni, 1972). The death rate for breast cancer in Black women was 40% higher than that in White women, despite a lower incidence rate (Siegel et al., 2018). The reasons for this disparity are complex, but it is predominantly due to inequalities in employment, wealth, education level, housing, and overall SES that contribute to excess exposure to cancer risk factors, and to barriers in both health literacy and access to good-quality health care, including primary prevention, early detection, and treatment (see Chapter 7). One study estimated that eliminating socioeconomic disparities in the USA could prevent twice as many cancer deaths as eliminating racial disparities (Siegel et al., 2011).

According to the United States Census Bureau, one quarter of Black people lived in poverty in 2015, compared with one tenth of White people. Poor health is not only strongly correlated with impoverishment but is also exacerbated by inequalities in medical advances in cancer control (because of slower dissemination to disadvantaged groups). For example, the racial disparity in tobacco-related cancer mortality began to narrow in the early 1990s because of faster declines in smoking among Black people (DeLancey et al., 2008), but the disparities in female breast cancer and colorectal cancer mortality continued to widen until recently (Fig. F7.1), coinciding with the increased uptake of screening and improved access to advances in treatment for these diseases for the Black population. Furthermore, recent studies reported that differences in insurance status (a proxy for health-care access) among non-elderly cancer patients accounted for more than one third of the Black versus White survival disparity for female breast cancer and one half of the Black versus White survival disparity for colorectal cancer; differences in tumour characteristics

Table F7.1. Cancer death rate ratios of Black versus White populations for the top 15 cancer types in Black men (left) and the top 15 cancer types in Black women (right), listed in descending order by rate ratio

Cancer type	Rate for Black men[a]	Rate for White men[a]	Rate ratio (95% confidence interval)[b]	Cancer type	Rate for Black women[a]	Rate for White women[a]	Rate ratio (95% confidence interval)[b]
Stomach	8.5	3.4	2.54 (2.46–2.62)	Stomach	4.0	1.7	2.37 (2.28–2.46)
Prostate	40.8	18.2	2.24 (2.20–2.27)	Myeloma	5.6	2.4	2.31 (2.24–2.39)
Larynx	3.4	1.7	1.95 (1.86–2.05)	Uterine corpus	8.5	4.3	1.99 (1.94–2.04)
Myeloma	7.6	4.0	1.90 (1.84–1.96)	Cervix uteri	3.8	2.1	1.83 (1.76–1.90)
Liver and intrahepatic bile duct	13.5	8.2	1.65 (1.62–1.69)	Breast	29.5	20.8	1.41 (1.40–1.43)
Colon and rectum	25.1	16.9	1.48 (1.46–1.51)	Liver and intrahepatic bile duct	4.7	3.4	1.39 (1.35–1.44)
Oral cavity and pharynx	4.9	3.9	1.26 (1.21–1.30)	Colon and rectum	16.5	12.1	1.36 (1.34–1.38)
Lung and bronchus	66.9	56.3	1.19 (1.18–1.20)	Pancreas	12.5	9.5	1.31 (1.29–1.34)
Pancreas	15.2	12.8	1.19 (1.16–1.21)	Urinary bladder	2.5	2.3	1.09 (1.04–1.14)
Kidney and renal pelvis	5.7	5.8	0.98 (0.95–1.01)	Kidney and renal pelvis	2.4	2.5	0.99 (0.95–1.03)
Leukaemia	7.6	9.5	0.80 (0.78–0.83)	Lung and bronchus	34.4	39.0	0.88 (0.87–0.89)
Oesophagus	6.0	8.0	0.75 (0.73–0.77)	Leukaemia	4.6	5.2	0.88 (0.85–0.91)
Non-Hodgkin lymphoma	5.5	7.8	0.71 (0.68–0.73)	Ovary	6.5	7.6	0.85 (0.83–0.87)
Urinary bladder	5.5	8.3	0.66 (0.63–0.68)	Non-Hodgkin lymphoma	3.4	4.7	0.74 (0.71–0.77)
Brain and ONS	3.3	6.1	0.54 (0.52–0.56)	Brain and ONS	2.2	4.0	0.55 (0.52–0.57)
All sites	246.1	200.6	1.23 (1.22–1.23)	All sites	163.2	143.6	1.14 (1.13–1.14)

ONS, other nervous system.

[a] Average annual rate per 100 000 people of non-Hispanic ethnicity during 2011–2015; age-adjusted to the 2000 United States standard population.

[b] Rate ratio is the 2011–2015 rate for Black populations divided by the rate for White populations before rounding; all results are statistically significant ($P < 0.05$), with the exception of kidney cancer for both sexes.

Source: compiled from Surveillance, Epidemiology, and End Results Program (SEER) (https://seer.cancer.gov/) SEER*Stat Database: Mortality – All COD, Aggregated With State, Total U.S. (1990–2016) <Early release with Vintage 2016 Katrina/Rita Population Adjustment>, National Cancer Institute, DCCPS, Surveillance Research Program, released May 2018. Underlying mortality data provided by NCHS (www.cdc.gov/nchs).

accounted for one quarter of the Black versus White survival disparity for both cancer types (Jemal et al., 2018; Sineshaw et al., 2018).

However, the disparity in cancer mortality with race in the USA varies substantially by state and age, partly reflecting differences in public policies that affect access to health care. For instance, the overall cancer death rate in 2015 in Blacks compared with Whites was 31% higher in

Fig. F7.1. Disparities in death rates for female breast cancer and colorectal cancer between Black and White populations in the USA.
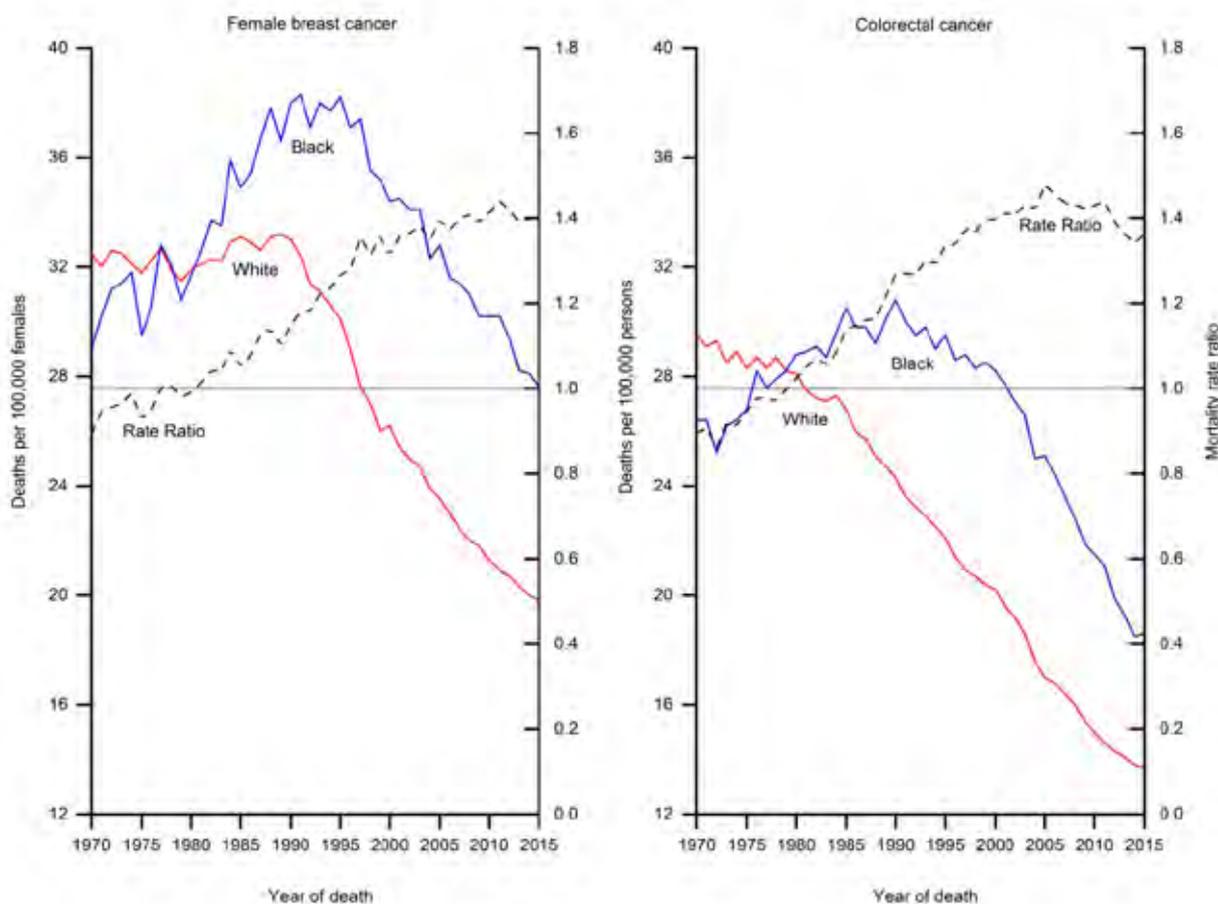
those younger than 65 years but only 7% higher in those aged 65 years and older (Siegel et al., 2018), partly because of access to universal health coverage through Medicare for older adults. Similarly, the excess risk of breast cancer mortality in Black women in 2015 ranged from a non-significant 8% in Massachusetts to more than 60% in Louisiana and Mississippi (DeSantis et al., 2017). Unique among all the other states, Massachusetts implemented sweeping health-care reform in 2006, resulting in the lowest uninsured rate in the country and significant reductions in all-cause and health-care-amenable mortality (Sommers

et al., 2014). Likewise, the state of Delaware almost eliminated a 50% excess in colorectal cancer mortality among Black people in less than a decade with the establishment of a comprehensive statewide colorectal cancer screening and treatment programme in 2002 (Grubbs et al., 2013). Delaware and Massachusetts serve as social laboratories, exhibiting the importance of removing barriers to primary prevention, early detection, and high-quality treatment in eliminating racial inequalities in cancer mortality.

Despite a concerted national public health effort to address racial disparities, both as a moral imperative

and to reduce the overall cancer burden, several challenges remain. For instance, research on the specific mechanisms that cause cancer disparities requires high-quality data not only on race and/or ethnicity but also on the mediators of health (e.g. SES, place of birth, and comorbidities), which are lacking at the individual level in the USA. In addition, racial gaps in cancer treatment have been perpetuated by the underrepresentation of Blacks in the oncology profession and in clinical trials because of shortfalls in recruitment and participation (Smedley et al., 2003). For example, although Black men in the USA have prostate cancer mortality

rates that are among the highest in the world (Siegel et al., 2018), the first prospective study of treatment for metastatic prostate cancer in Black men, specifically designed to reduce barriers to participation, was prematurely terminated because of insufficient patient accrual (Tsao et al., 2016).

Similarly to disadvantaged groups in many countries, Black people in the USA experience disparities in cancer incidence rates and outcomes largely because of deficits in a wide array of social resources that affect health. For most cancers that are amenable to early detection and treatment, such as colorectal cancer and breast cancer, the gap in Black versus White inequalities in cancer death rates in the USA dramatically widened as a result of progress in detection and treatment. Overcoming these disparities involves reducing socioeconomic inequalities and/or weakening the link between SES and health through multipronged approaches that increase access to care. Examples of such approaches in the USA are provided by Delaware and Massachusetts, whereby racial disparities and treatment-amenable mortality were reduced by removing barriers to prevention, early detection, and treatment services. In a longitudinal study of 75 countries, Maruthappu et al. (2016) found that the main factor that protected against increased cancer mortality associated with the global economic crisis during 2008–2010 was universal health coverage. With a gross domestic product (GDP) of US$ 15 trillion, the USA has the resources to be a global leader in eliminating disparities. The Patient Protection and Affordable Care Act (PPACA), which became law in 2010 and has expanded health insurance coverage to more than 20 million previously uninsured people, predominantly low-income and minority Americans, was a step in the right direction. However, the impact of the PPACA on reducing cancer inequalities has yet to be determined, especially given uncertainties about its future in the current political climate.

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CHAPTER 7.

Social inequalities in cancer risk factors and health-care access

Lynette Denny, Ahmedin Jemal, Mary Schubauer-Berigan, Farhad Islami, Nadia Vilahur, Miranda Fidler,
Diana Sarfati, Isabelle Soerjomataram, Catherine de Martel, and Salvatore Vaccarella

Introduction

Social gradients in cancer show complex patterns between and within countries (as documented in Chapters 5 and 6), which are driven by a multifaceted and concurrent interplay of different factors. Although all-cancer incidence rates are generally higher in more developed countries and generally increase with increasing levels of national socioeconomic development, the gradient is less clear for all-cancer mortality rates. Caution is certainly needed when interpreting cancer patterns between countries, because these are characterized by substantial heterogeneity and several exceptions. Within countries, however, mortality for the majority of cancer types is

disproportionately higher in groups with low socioeconomic status (SES) for almost all countries globally. The spectrum of certain types of cancer also varies with social condition. Infection-related cancers are generally more frequent in disadvantaged individuals and in inhabitants of low-income countries; other cancers, such as those of the breast, prostate, thyroid, and colon and rectum, have been, at least historically, associated with affluence. The social gradient in cancer may change over time, however, or even reverse. Countries that are undergoing a transition towards higher socioeconomic levels have, on average, higher standards of living, a wider range and larger supply of goods and services, higher life expectancy, and a lower rate of infec-

tion-related cancers. However, these improvements are often accompanied by changing environments, which support the uptake of certain cancer-causing behaviours and increased exposure to risk factors, affecting predominantly less affluent groups. High-quality health care, from prevention and early detection to treatment, is therefore of great importance in controlling and reducing cancer mortality. However, its availability is often prohibitive for people residing in less developed countries and limited for disadvantaged individuals in more developed countries, thus increasing social inequalities in cancer. Here, we provide a summary of the evidence on the social inequalities that exist in the distribution of major risk factors for cancer as well

as in the availability of and access to early detection and treatment of the disease, with a focus on how these inequalities have an impact across the whole cancer continuum. The mechanisms and the context underlying social inequalities in the risk factors for cancer and health-care access, and consequently cancer outcomes, are discussed in Part 2 of this publication.

Lifestyle factors

According to IARC, many cancer types are causally associated with tobacco use, alcohol consumption, and excess body weight (Table 7.1). Several cancers have also been associated with unhealthy diet (WCRF/AICR, 2018a). Tobacco use accounts for 21% of total cancer deaths worldwide, followed by unhealthy diet (8%), alcohol consumption (7%), and excess body weight (5%). The burden of these major risk factors varies within and across countries according to SES and other factors, such as: the level of economic development and transition to lifestyles typical of industrialized countries; the activities of the tobacco, fast food, sugar-sweetened beverage, and liquor industries; and public health policies (see Example 1 and Chapters 10 and 11).

Before the health hazards of smoking became public knowledge in the middle of the 20th century, in many high-income countries (HICs) the prevalence of smoking was highest in groups with higher SES. Over time, however, the burden of smoking shifted to groups with lower SES, because of inequalities in risk awareness and access to counselling and treatment services for tobacco dependence, combined with highly effective targeted marketing of tobacco to more disadvantaged

Table 7.1. Cancer types associated with tobacco smoking, alcohol consumption, and excess body weight according to IARC, and the magnitude of the associations

Exposure	Cancer type	Relative risk[a]
Tobacco smoking	Oral cavity and pharynx	5.7
	Oesophagus	4.3
	Stomach	1.8
	Colon and rectum	1.5
	Liver	2.1
	Pancreas	1.7
	Nasal cavity and paranasal sinuses	Not reported
	Larynx	17.4
	Lung	23.9
	Uterine cervix	1.9
	Ovary (mucinous)	Not reported
	Kidney (body and pelvis) and ureter	1.6
	Urinary bladder	3.9
	Bone marrow (myeloid leukaemia)	1.6
Alcohol consumption	Oral cavity and pharynx	3.1
	Oesophagus (squamous cell carcinoma)	3.6
	Liver	1.1
	Colon and rectum	1.4
	Larynx	1.1
	Female breast	1.5
Excess body weight	Oesophagus (adenocarcinoma)	1.5
	Stomach (cardia)	1.2
	Colon and rectum	1.1
	Liver	1.3
	Gallbladder	1.3
	Pancreas	1.1
	Female breast (postmenopausal)	1.1
	Corpus uteri	1.5
	Ovary	1.1
	Kidney	1.3
	Meningioma	1.2
	Thyroid	1.1
	Multiple myeloma	1.1

BMI, body mass index.

[a] Relative risks for tobacco smoking are for current versus never smokers (Carter et al., 2015); for alcohol use are for heavy drinking (> 50 g of alcohol or > 4 drinks per day) versus non-drinkers (Bagnardi et al., 2015); and for excess body weight are per 5 kg/m^2 increase in BMI, except for meningioma (overweight [BMI 25–29.9 kg/m^2] versus normal weight). Relative risks for excess body weight are from WCRF/AICR (2018b), except for those for meningioma (Niedermaier et al., 2015), thyroid cancer (Kitahara et al., 2016), and multiple myeloma (Teras et al., 2014).

Source: compiled from Carter et al. (2015), Bagnardi et al. (2015), WCRF/AICR (2018b), Niedermaier et al. (2015), Kitahara et al. (2016), and Teras et al. (2014).

Fig. 7.1. Current smoking prevalence among adults by sex and education level in selected countries. A lower education level was defined as elementary/primary school in Panama, the Philippines, and Turkey, primary school or less in Kazakhstan, less than primary school in Kenya, and 0–12 years of school with no diploma in the USA. A higher education level was defined as college/university or above in Kazakhstan, Panama, the Philippines, and Turkey, secondary school completed or above in Kenya, and a graduate degree in the USA. Source: compiled from the National Health Interview Survey for the USA and the Global Adult Tobacco Survey (WHO, 2018b) for other countries.
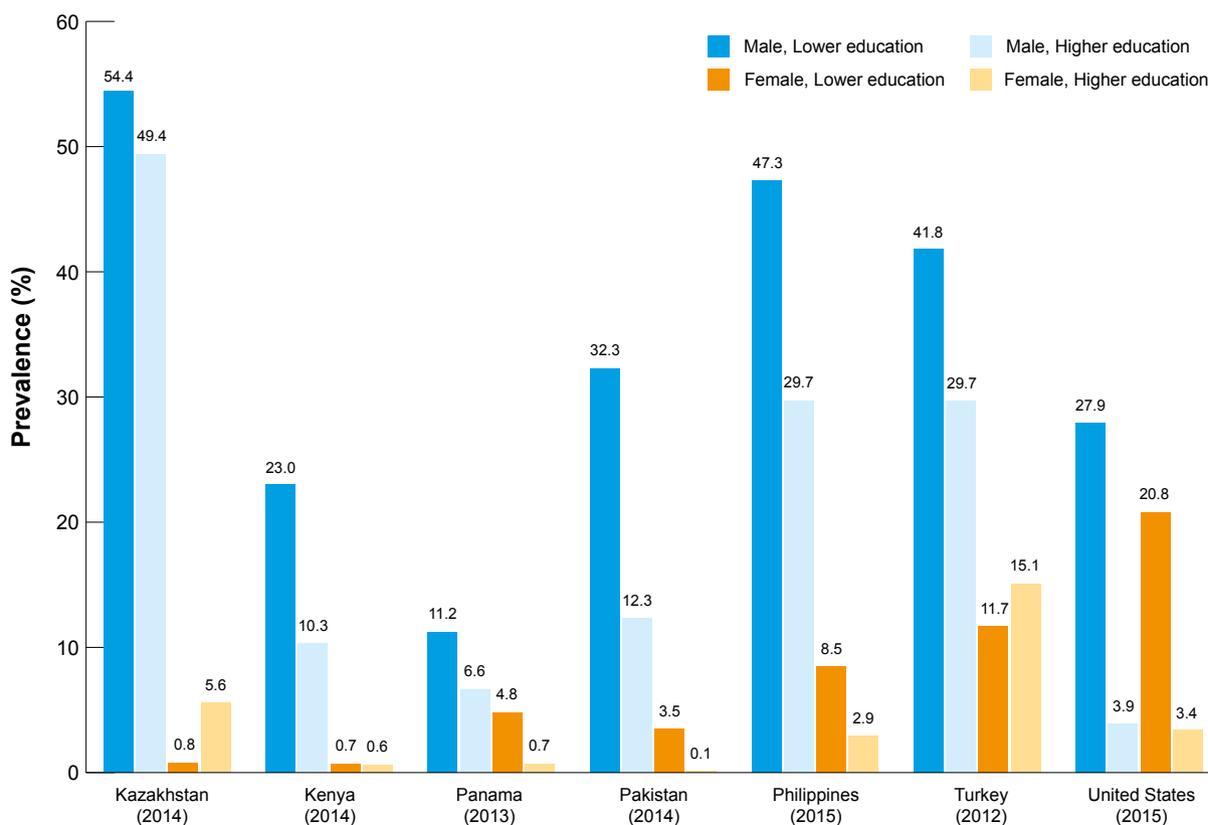
populations (Fig. 7.1) (Allen et al., 2017; Casetta et al., 2017; Sreeramareddy et al., 2018). A similar shift in the burden of smoking has occurred in many low- and middle-income countries (LMICs), particularly among men (Islami et al., 2015; Allen et al., 2017; Casetta et al., 2017; Sreeramareddy et al., 2018). In the few remaining low-income countries where the prevalence of smoking is still higher in groups with higher SES (Sreeramareddy et al., 2018), the burden is expected to shift to groups with low SES and other disadvantaged groups (e.g. ethnic minorities and Indigenous populations) in the

foreseeable future, unless concerted efforts are made to promote and apply tobacco control measures (Islami et al., 2015).

Although the prevalence of alcohol consumption is generally greater among people with higher versus lower SES, epidemiological studies suggest that people with lower SES and disadvantaged groups are at higher risk of some alcohol-related diseases, including head and neck cancers (Jones et al., 2015). This is largely thought to be due to higher rates of excessive drinking (e.g. binge drinking) among lower-SES individuals (Grittner et al., 2013).

Compared with people in affluent neighbourhoods, those in poorer neighbourhoods have a higher degree of stressors and fewer means to cope with them (Grittner et al., 2013) and the density of liquor stores is higher in poorer neighbourhoods (Berke et al., 2010). In LMICs, unrecorded (i.e. home-made) alcohol, which is more affordable than commercial alcohol, is consumed excessively, especially among the low-income population (WHO, 2018a). The World Health Organization estimates that unrecorded alcohol accounts for 9% of total alcohol consumption in HICs, 24% in upper-middle-income

countries, and 40% in other LMICs (WHO, 2018a) (see Chapter 11).

The prevalence of excess body weight has substantially increased globally in recent decades, because of the increased availability of low-cost, calorie-dense foods and the adoption of a more sedentary lifestyle (Abarca-Gómez et al., 2017; Bann et al., 2017). About 13% of the world's adult population is obese (body mass index $\geq$ 30 kg/m^2), and the prevalence is as high as 50% among women in parts of the Middle East and North Africa (Fig. 7.2) (Abarca-Gómez et al., 2017). In most HICs, people with lower SES are more likely to be obese or overweight than those with higher SES (Devaux

and Sassi, 2013; Bann et al., 2017). However, in some low-income countries (especially in parts of sub-Saharan Africa), the prevalence of overweight or obesity is often higher in people with higher SES and in urban areas (Madise and Letamo, 2017).

A major limitation in assessing SES inequalities in tobacco use, alcohol consumption, and unhealthy diet is a lack of representative data, particularly from LMICs. Evidence is therefore often based on small-scale epidemiological studies or surveys with heterogeneous inclusion criteria, some of which are conducted in clinics or urban areas only. There are also limited data on determinants of inequalities, and on the best ways to implement

effective preventive measures in each population. More research on the implementation of effective interventions at the community and individual levels is also needed in both LMICs and HICs. However, the prevalence of tobacco use, alcohol consumption, and unhealthy diet in middle- and high-income countries is generally higher among low-income populations, mainly because of inequalities in the application of effective interventions and in targeted marketing by the tobacco, fast food, sugar-sweetened beverage, and liquor industries. Elimination of this inequality requires public policies for equitable access to health care, policies against deceptive

Fig. 7.2. Prevalence of excess body weight (BMI $\geq$ 25 kg/m^2) and obesity (BMI $\geq$ 30 kg/m^2) among women aged 15–49 years by education level in selected low- and middle-income countries. Lower and higher education levels were defined as no education or primary education only and secondary or higher education, respectively. BMI, body mass index. Source: compiled from the Demographic and Health Surveys (https://dhsprogram.com/).
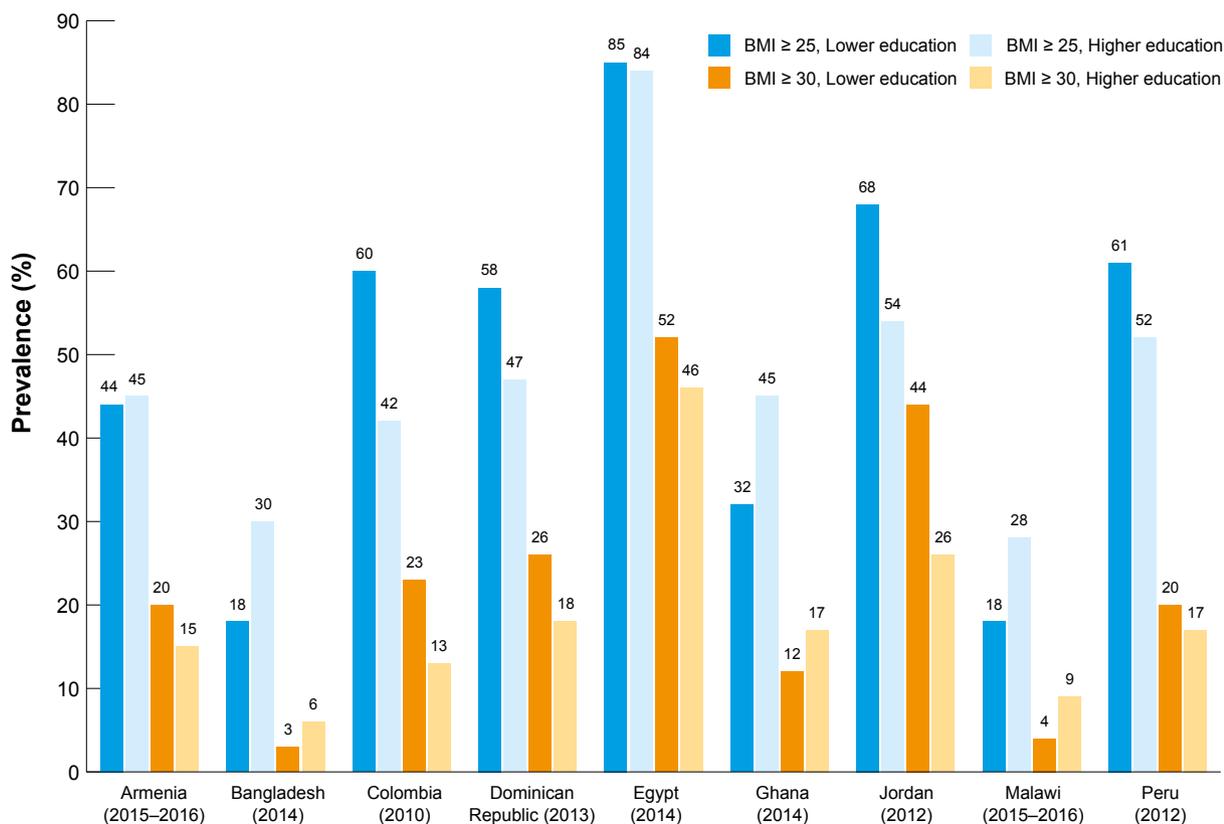
industry advertising, and programmes for the broad application of effective interventions.

Occupational exposures

The history of occupational epidemiology includes recognition that manual workers face unequal cancer risks as a result of varying levels of exposure to carcinogenic agents specific to their employment, and as a consequence of other risk factors associated with their typically lower SES. Formal investigation of the links between occupation and cancer was a development of the 20th century, via an exploration of the health effects of exposure to carcinogens in the mining and manufacturing industries (e.g. Pirchan and Sikl, 1932; Doll, 1952; Case et al., 1954). Subsequent research has facilitated the identification of at least 70 agents, mainly chemicals, metals, airborne particles, and radiation, as occupational carcinogens (Loomis et al., 2018).

Cancer risks are distributed unequally across occupational groups, with manual workers being the most severely affected (Hart et al., 2001; Vanthomme et al., 2017). Large surveys have shown that skilled and unskilled workers in occupations such as vehicle repair, metallurgy, and metal- or wood-working and in the chemical industry are often exposed to complex mixtures of carcinogenic substances (European Foundation for the Improvement of Living and Working Conditions, 2010, 2013, 2015). Reflecting both the uneven distribution of occupational cancer hazards and their often-complex nature, 12 different occupations (e.g. painters) and industries (e.g. rubber manufacturing) typically employing blue-collar workers are classified by the IARC Monographs as carcinogenic to humans (Loomis et al., 2018).

Even within occupations, important exposure and health disparities exist (Quinn et al., 2007). For example, mortality studies in United States steel workers revealed striking differences in cancer risk among groups defined by occupation, work location, and race; for respiratory cancer mortality, the highest rates were seen among African-American, compared with White, workers on the topside of coke ovens, who were believed to have the heaviest exposures to coke oven emissions (Lloyd, 1971; Birdsey et al., 2007). Disentangling the contribution of factors such as place of residence and access to health care from occupational exposure to carcinogens remains challenging. Occupational cohort studies typically lack data on workers' personal and social attributes, and are consequently unable to investigate influences beyond the workplace.

To address these challenges, researchers have used population-based studies to investigate the role of occupation in inducing cancer disparities. For example, in a study of mortality from potentially work-related cancers in 21 states of the USA, African-Americans experienced higher mortality from leukaemia and cancers of the lung, nasal cavity, and peritoneum relative to the average for all workers in the same age range (Loomis and Schulz, 2000). A study within the multicentre European Prospective Investigation into Cancer and Nutrition cohort showed that exposure to asbestos, heavy metals, and polycyclic aromatic hydrocarbons explained 14% of the socioeconomic inequalities observed in lung cancer incidence in men, independent of smoking and dietary factors (Menvielle et al., 2010). A recent study evaluated socioeconomic differences in adult cancer mortality in Belgium, using occupational group and employment status as measures of SES, to test the theory that inequalities in cancer arise largely from the differential distribution of economic resources (Vanthomme et al., 2017). Among the employed, inequalities in cancer mortality were observed by occupation, especially for cancers that are largely preventable.

Finally, ever-increasing economic globalization has amplified geographical aspects of occupational cancer disparities. For example, the adoption of bans or restrictions on the use of asbestos has probably helped to limit mesothelioma rates in certain HICs (Nishikawa et al., 2008). Without active intervention to reduce exposures in LMICs, the cancer burden from occupational exposures may continue to shift to these more vulnerable workers.

Environmental exposures

Inequalities in cancer from environmental exposures may arise from many causes. For example, poor indoor air quality can result from the use of coal-burning cooking stoves in unventilated homes; such practices, which are more frequent in LMICs, have been linked to lung cancer (Lan et al., 2002). Within a particular country, people experiencing poverty may live in areas with greater concentrations of carcinogens in air, soil, or water compared with areas where less deprived people live (Huang et al., 2017). Research on ambient air pollution provides an illustrative example of the scale of disparities between and within countries. Outdoor air pollution is classified by IARC as Group 1 (carcinogenic to humans)

(Loomis et al., 2013; IARC, 2016), causing lung cancer. WHO has estimated that outdoor air pollution accounted for about 400 000 lung cancer deaths worldwide in 2012 (WHO, 2016), representing 14% of the total mortality burden attributable to ambient air pollution. The same publication reported how unequally this burden was distributed within and across regions, with LMICs having the highest air-pollution-related lung cancer mortality and morbidity (Fig. 7.3). Social inequalities in the risk of lung cancer associated with exposure to outdoor air pollution can be demonstrated within a single country, region, or even city. Exposure to air pollution (Huang et al., 2017) and the incidence of related cancer (Apelberg et al., 2005) in the USA are highest for census tracts with high percentages of racial and ethnic minorities and of those living in poverty, although adjustment for smoking remains a challenging issue. A cohort study of mortality among more than 1 million adults

in Rome, Italy, showed gradients of increasing mortality risk ratios for exposure to fine particulate matter with area-based SES and education level (Cesaroni et al., 2013). Also, ethnically diverse neighbourhoods have the highest levels of air pollution in England and the Netherlands (Fecht et al., 2015). A better understanding of how environmental exposures and air pollution are distributed across the geographical space, particularly in disadvantaged areas, is therefore crucial to address environmental inequalities in cancer.

From a life-course perspective, in utero or early-life exposure to environmental carcinogens may substantially increase future disparities in cancer incidence and mortality. For example, unsafe management practices related to the disposal and recycling of end-of-life electrical and electronic equipment, so-called e-waste, have greatly increased in the past two decades in LMICs such as China, Ghana, India, Nigeria, the Philippines, Thailand, and Viet Nam.

E-waste handling can entail exposure via multiple routes to mixtures of many hazardous and often carcinogenic chemicals (e.g. arsenic, cadmium, chromium, and persistent organic pollutants, such as dioxins) (Baldé et al., 2015). Children or pregnant women are often involved in these unregulated activities or live in the surrounding contaminated areas. They may also be exposed through take-home contamination from a family member (Ceballos et al., 2017). Although the short-term health effects of e-waste exposure have been described, including pregnancy complications, adverse neonatal outcomes, and reduced lung function in children (Grant et al., 2013), the long-term effects on cancer risk remain largely unknown.

Infections

Infections with viruses, bacteria, and parasites have long been identified as strong risk factors for specific cancers (IARC, 2012) (Table 7.2). Worldwide, about 2.2 million (15.4%) of the total

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Fig. 7.3. Age-standardized disability-adjusted life years (DALYs) per 100 000 people attributable to ambient air pollution in 2012, by country. Source: reprinted from WHO (2016, p. 43).

DALYs per 100 000 population

0–299
300–679
680–999
1000–1499
≥1500
Data not available
Not applicable

Table 7.2. Cancer types and associated IARC Group 1 (i.e. carcinogenic to humans) infectious agents

Cancer type	Infectious agent (IARC Group 1)
Stomach	*Helicobacter pylori*
Liver (hepatocellular carcinoma and cholangiocarcinoma)	Hepatitis B virus, hepatitis C virus, *Opisthorchis viverrini*, *Clonorchis sinensis*
Cervix uteri	Human papillomavirus
Anogenital (penile, vulva, vagina, anus)	Human papillomavirus
Nasopharynx	Epstein–Barr virus
Head and neck (oropharynx, larynx, oral cavity)	Human papillomavirus
Non-Hodgkin lymphoma	*Helicobacter pylori*, Epstein–Barr virus, hepatitis C virus, human T-cell lymphotropic virus type 1 (HTLV-1)
Kaposi sarcoma	Human herpesvirus type 8/Kaposi sarcoma-associated herpesvirus (KSHV)
Hodgkin lymphoma	Epstein–Barr virus
Bladder	*Schistosoma haematobium*

Source: compiled from IARC (2012).

of 14 million new cancer cases that occurred in 2012 were attributable to infections. Of these, 770 000 were caused by *Helicobacter pylori*, 640 000 by human papillomavirus (HPV), 420 000 by hepatitis B virus (HBV), and 170 000 by hepatitis C virus (HCV) (Plummer et al., 2016).

The population-attributable fractions of infection-related cancers vary greatly by average level of socioeconomic development, as measured by the Human Development Index (HDI); the proportion of new cancer cases attributable to infections is highest (20–25%) in countries with medium and low HDI, intermediate (13.2%) in countries with high HDI, and lowest (7.6%) in countries with very high HDI (Plummer et al., 2016; see also Chapter 5). In absolute terms, half of the burden of infection-associated cancers (i.e. 1.1 million cases) occurs in countries with medium HDI. (At the time of the study this classification included China, a country with approximately half of the global burden of gastric cancer and liver cancer; more recently, China was reclassified as a high-HDI country.) The absolute burden of

infection-related cancers is expected to increase in countries with medium HDI, because of the large number of adults who were infected with carcinogenic microbes such as HBV or *H. pylori* in childhood.

Infection-related cancers are characterized by a strong socioeconomic gradient. The link between infections and cancer is reviewed here for some of the most important carcinogenic pathogens.

H. pylori *infection*

The bacterium *H. pylori* is estimated to cause 90% of non-cardia gastric cancer (Plummer et al., 2015). More than 70% of gastric cancer cases in 2012 occurred in countries in eastern Asia and Latin America, and 42% of all global cases of non-cardia gastric cancer in 2016 occurred in China alone (Ferlay et al., 2015). The incidence of gastric cancer was very high in HICs in Asia, such as Japan and the Republic of Korea. *H. pylori* is transmitted mainly in early childhood within the family, and often during bouts of gastroenteritis. Within any country or population, *H. pylori* infection and the resulting gas-

tric cancer disproportionately affect more disadvantaged groups (Power et al., 2005; Nagel et al., 2007).

Globally, the incidence and mortality rates of gastric cancer are declining by approximately 2.5% per year, partly because of the slow disappearance of *H. pylori* that accompanies the general progressive access to better living conditions (de Martel et al., 2013). However, because of the growth and ageing of the world population, the total numbers of newly diagnosed cancer cases and deaths have continued to increase. The best strategy to control non-cardia gastric cancer is through screening and the eradication of *H. pylori* using a combination of antibiotics and a proton-pump inhibitor (Ford et al., 2005; Herrero et al., 2014). Implementation studies of such strategies are currently in progress in several countries, and are being carefully monitored with the aim of helping others to develop their own guidelines (Bae et al., 2018).

HPV infection

Persistent infection of the genital tract with high-risk HPV types is a

known, necessary cause of pre-invasive and invasive cancer of the cervix. HPV is also associated with cancer of the vagina, vulva, anus, oropharynx, and penis (De Vuyst et al., 2009; Miralles-Guri et al., 2009). HPV prevalence varies substantially by country and is highest in sub-Saharan Africa; however, like sexual habits, it is not clearly correlated with poverty. The strong excess risk of cervical cancer observed in less affluent individuals and in LMICs is due to the limited availability of and access to organized, or even opportunistic, screening. The contribution of other cofactors linked to low SES, such as smoking, multiparity, and coinfection with HIV, may also play a role (Bosch and de Sanjosé, 2007).

Effective vaccination against HPV infection is now available; more details are provided in Example 2.

HBV infection

In total, 56% of liver cancer cases worldwide are attributable to chronic HBV infection (Maucort-Boulch et al., 2018). In 2015, WHO estimated that 257 million people were chronic carriers of HBV worldwide, including 9 million children younger than 5 years. In children, transmission of the virus may occur perinatally or horizontally (from siblings or close family members), whereas in adults, the virus is transmitted mainly through the reuse of needles and syringes in health-care settings or among people who inject drugs. Countries with high HBV endemicity (5–10%) are mainly located in sub-Saharan Africa and eastern Asia. Intermediate rates of chronic infections (2–5%) are found in populations of the Amazon countries, the southern parts of eastern and central Europe, and the Middle East (Fig. 7.4).

Since the initial recommendation of universal HBV immunization by WHO in 1992, and the subsequent endorsements of the use of a monovalent birth dose given within the first 24 hours of life, the number of countries that include HBV vaccine in their national vaccination schedules has been constantly increasing, and temporal trends indicate a decrease in the prevalence of chronic carriers in many areas (Ott et al., 2017). However, access to a safe and efficient health-care system is difficult in the poorest countries and for deprived population groups, in which the virus is most prevalent (WHO, 2017). In the near future, the reservoir of people living with chronic HBV and the resulting disease burden may increase in highly industrialized, low-endemicity countries that receive migrants from areas with high HBV endemicity (Sharma et al., 2015).

HCV infection

HCV is one of the major risk factors for hepatocellular cancer, accounting for about 20% of cases of the disease globally (Maucort-Boulch et al., 2018). In 2015, WHO estimated that 71 million people were living with

Fig. 7.4. Global endemicity of hepatitis B virus (HBV) infection (1990–2013). The estimated prevalence of chronic HBV infection (HBsAg seroprevalence) is based on pooled data from all eligible studies for each country from 1990–2013. Source: reprinted from Schweitzer et al. (2015), copyright 2015, with permission from Elsevier.
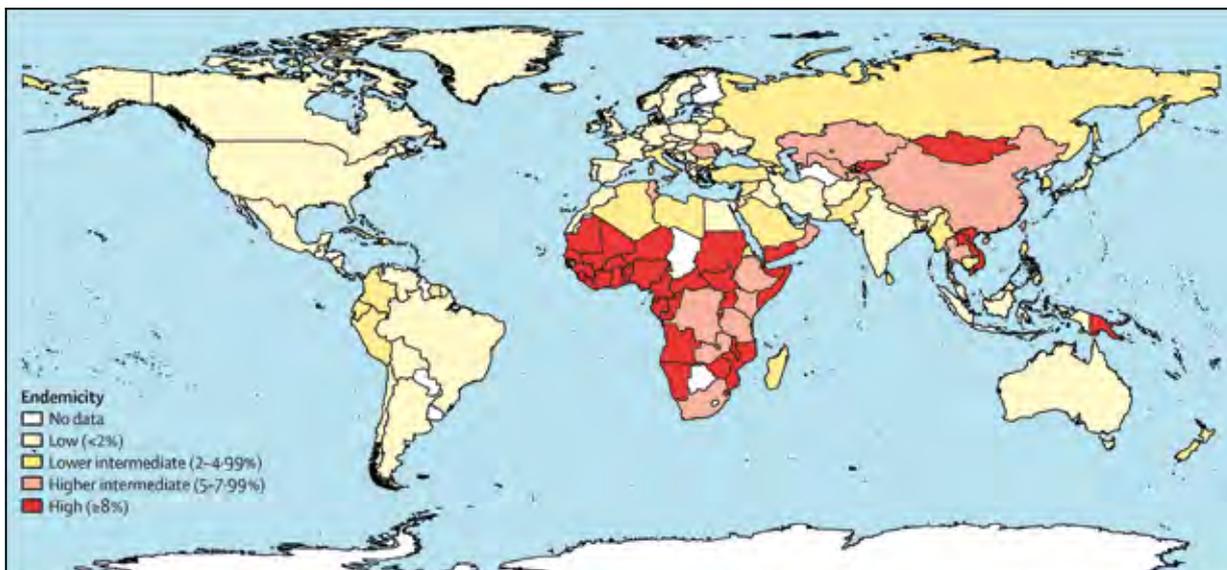
chronic HCV infection, with the prevalence varying between countries. HCV infection is concentrated in certain populations at higher risk and/or in the general population of certain HCV-endemic countries (e.g. Egypt and Mongolia). Higher-risk groups include people who inject drugs, recipients of contaminated blood products or unsafe injections in health-care settings, people with HIV infection, prisoners or previously incarcerated people, and people who have had tattoos or piercings. As a result, in countries with a low prevalence of HCV infection (e.g. the Netherlands), the infection is more prevalent in groups with lower SES (Vriend et al., 2013); in countries with high prevalence and long-established endemicity, the infection is common in groups with all levels of SES.

Access to the new, efficient, but very expensive HCV treatment is improving but remains limited. According to WHO, of the 71 million people living with HCV infection in 2015, only 20% (14 million) knew their diagnosis and only 1.1 million were receiving treatment (WHO, 2017). In addition to effective screening, the main barrier to receipt of treatment and subsequent cure is the cost, but prices have dropped dramatically in some countries (primarily low-income countries) as a result of the introduction of generic versions of antiviral medicines (Aggarwal et al., 2017).

Early diagnosis and screening

Differences in cancer outcomes between social groups may be partially related to differences in access to care. Stage at diagnosis is a critical factor that determines not only the types of treatment available but also the chances of survival. However, early diagnosis of cancer requires access to screening and diagnostic services. Individuals in underserved populations face practical, geographical, and economic barriers to accessing services. In addition, factors relating to social distance between individuals and their health-care practitioner, cultural alienation, and previous negative experiences within health-care systems also act as barriers to access (Dixon-Woods et al., 2006). These barriers vary in scope and magnitude in different settings, and collectively are important drivers for social disparities in cancer survival in HICs and LMICs. Multiple strategies are therefore required that consider information about those affected and their practical needs to improve access to and progress through the health system (Legler et al., 2002; Institute of Medicine, 2003; Niksic et al., 2015).

Screening programmes can either diminish or widen disparities, depending on how they are designed, implemented, and monitored (von Wagner et al., 2009; Chiou et al., 2014; Kim et al., 2015; Douglas et al., 2016; Kelly et al., 2017). Typically, uptake of screening is higher among those in more advantaged groups, but there are examples of programmes that have succeeded in reducing unequal uptake by focusing on reducing barriers for underserved populations (Legler et al., 2002; von Wagner et al., 2009; Palència et al., 2010). For many countries, however, effective screening is still not being implemented, even for cancers that have been found suitable for early detection in LMICs; this is due to the substantial costs needed to provide the infrastructure, human resources, consumables, follow-up, and surveillance for screening, not to mention competing health demands. As an example, screening to prevent cervical cancer has not been initiated or sustained in the majority of LMICs because of the complexity of cytology-based screening algorithms and the need for: functional and quality-assured laboratories, technicians, and pathologists; strong health-care systems; and reliable referral pathways. However, a lack of cervical cancer screening and high rates of cervical cancer also affect countries in eastern Europe and the Baltic region with very high HDI, for example, Estonia (Vaccarella et al., 2016).

Treatment

In HICs, there is compelling evidence that individuals in less privileged groups receive lower-quality treatment for cancer than those in more privileged groups (Shavers and Brown, 2002; Institute of Medicine, 2003; Hill et al., 2013). The drivers behind these differences are likely to be multifactorial, relating to patient factors including comorbidity, accessibility of health services, and the quality of care received within those services. Globally, there are enormous inequalities in cancer treatment in both quantity and quality (IAEA, 2011). For example, on average, one radiotherapy unit is available for every 120 000 inhabitants in HICs, one radiotherapy unit is available for every 1 million individuals in middle-income countries, and no radiotherapy services are available in 51 countries, independent territories, and islands (IAEA, 2017). The use of cytotoxic drugs is similarly imbalanced worldwide, largely because of the need for adequate hospital, diagnostic, and clinical laboratory facilities and qualified human resources, which are strongly influenced by educational and social factors.

There are also considerable variations across countries in the financing of cancer treatments, in terms of

public contributions, out-of-pocket expenses, and drug costs (Prager et al., 2018). Such financial toxicity of cancer care, particularly in countries with inadequate safeguards, either pushes individuals into poverty or forces them to make difficult decisions in terms of cancer treatment. These barriers to effective, acceptable, and timely cancer care result in poorer survival outcomes and quality of life, with the most vulnerable individuals disproportionately affected. Provision of universal health coverage is therefore essential to achieve equity (Andrulis, 1998; Asaria et al., 2016); however, even in countries which have implemented universal health coverage, monitoring of health system performance is required because some vulnerable populations can receive lower standards of care (Institute of Medicine, 2003; Wrigley et al., 2003; Woods et al., 2006; Hill et al., 2013).

Palliative care

Studies on palliative care have only been taken up recently, mainly in HICs despite the greater need for, and lack of, palliative care in LMICs. Social and cultural beliefs, local regulations, and support in obtaining palliative care all highly influence the use of palliative and hospice care. In HICs, provision of, access to, and use of palliative care have been reported to be lower among less advantaged groups and among older cancer cases and cases without informal care provider. In addition to improved public funds and legal access to opioid drugs, price regulation of such drugs, and better education to tackle false beliefs, innovating palliative care methods such as home-based care could greatly improve quality of life and reduce the marked inequality between many cancer patients at the end of life.

Key points

- Several factors underlie the large inequalities in cancer outcomes and cancer profiles observed between and within countries.
- Lifestyle factors such as tobacco use, unhealthy diet, and excessive alcohol consumption are generally more prevalent among low-income populations.
- Cancer risks are unequally distributed across occupational groups; as a consequence of exposure to carcinogenic agents specific to their employment and other risk factors associated with their typically lower socioeconomic status, manual workers are most severely affected. Inequalities in cancer from environmental exposures may arise from many causes.
- Infection-related cancers and most carcinogenic infections are also characterized by a strong socioeconomic gradient.
- Differences in cancer outcomes between groups of different socioeconomic status are likely to relate to differences in access to high-quality care.

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Introduction to Part 2

Nancy Krieger

Part 2 contains six chapters concerned with mechanisms and context underlying social inequalities in cancer. The foci of these chapters range from theoretical frameworks engaging with biological embodiment of injustice across the life-course to global and national economics, policies, and law. To understand what unifies these diverse chapters, and also where they differ, it is worth stepping back to consider the meanings of the words *mechanism* and *context.*

Start with *mechanism*. The word conjures up images of machines with many interacting complex parts, in which the movement or action of one component causes the movement or action of another. These series of actions – mecha-nisms – are intended to produce desired effects, via processes engineered to be precise and consistent. Deeply anchored in human design, this notion of mechanism system-atically ties together structure and function, the relationships among parts and purpose in space and time, and hence cause and effect (OED, 2018). Yet, curiously, mecha-nism can equally refer to causal re-lationships occurring in natural sys-tems that exist (and, in the case of biological organisms, have evolved) without human design, constituting "an ordered sequence of events involved in biological, chemical, or physical processes" (OED, 2018). Despite starkly different teleological assumptions (i.e. effects produced for a human-made purpose versus produced without human conscious design) – and as testament to the ever-important role of metaphor in both description and scientific ex-planation (Soskice and Harré, 1995; Ziman, 2000; Krieger, 2011) – the word *mechanism* nevertheless man-ages to elide these differences, and invites people to think of both hu-man-designed mechanisms and nat-ural complex systems as "a system of mutually adapted parts working together in a machine or in a man-ner analogous to that of a machine" (OED, 2018). Left unmentioned is the possibility that components of sys-tems can work against each other, in antagonistic relationships.

Context has an equally provoc-ative etymology. It is derived from the Latin word "contextus", meaning

connection, and originally referred to that which was "woven together" and thus "connected" (OED, 2018). First framed in literary terms, context referred to "the part[s] which immediately precede or follow any particular passage or 'text' and determine its meaning" (OED, 2018). Usage has since expanded to refer, abstractly, to the circumstances in which events occur (OED, 2018).

In the case of social inequalities in cancer, the issues of mechanism and context thus necessarily confront questions of agency and accountability, referring to both who and what are responsible for these mechanisms and contexts that produce inequalities, and who needs to do what to rectify them. If, however, context is akin to a web that is woven, and mechanisms are the causal processes comprising the strands of the web, then – revisiting the question I posed back in 1994 about epidemiology and the web of causation, that is, has anyone seen the spider? (Krieger, 1994) – it is fair to ask: who is (are) the weaver(s), and to what end? Could alternative patterns be created? And, in both cases, at what costs to whom? I urge you, the reader, to keep these questions in mind as you critically engage with the chapters in this part. Whether the mechanisms involve societal or biophysical systems or both, in the case of social inequalities, past and present actions by people shape the societal context. Stated another way, injustice is produced by people: there is no *deus ex machina*. The fundamental question remains: is it acceptable for some to thrive at the expense of others?

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CHAPTER 8.

Theoretical frameworks and cancer inequities

Nancy Krieger

Introduction

Cancer inequities: this short phrase encompasses a plethora of ideas. It requires us to think about social injustice, populations, biology, the risk of disease and its treatment, survival, and death. To understand what makes population distributions of cancer inequitable, within and across populations and the places and time periods they inhabit, it is imperative to use theory, specifically, theories of disease distribution (Krieger, 2011). Such theory is critical to defining, analysing, and remedying health inequities, that is, social group differences in health that are unfair, unnecessary, and, in principle, preventable (Whitehead, 1991; Braveman and Gruskin, 2003). This

is because in the case of science, it is theory that structures understanding of causal processes (Ziman, 2002; Krieger, 2011). Without theory, observation, explanation, and interventions are compromised and critical evaluation of the strengths and limitations of extant empirical evidence is undermined.

Although the centrality of theory to scientific observation and causal inference has been recognized for centuries (Ziman, 2002), until recently population health research on cancer and other outcomes has rarely been forthright about the theories of disease distribution informing study hypotheses, the interpretation of findings, and recommendations for action (Krieger, 1994, 2005, 2011, 2014; Wemrell et al., 2016). The cen-

tral argument of this chapter is that theoretical blindfolds can lead to needless suffering and preventable deaths, and to the neglect or worsening of cancer and other health inequities. In this chapter, I deliberately refer to health inequities as opposed to health inequalities to underscore that theorizing is concerned with causal processes, agency, and accountability, and not solely empirical observation of differences.

The problematic dominant disregard for explicit theories of disease distribution and conceptualizing the societal causes of health inequities

For the past century the dominant approach to research and teaching in epidemiology, including cancer

epidemiology, has been to treat the discipline as a theory-free set of methods applied to health data (Krieger, 1994, 2011). The sources of the hypotheses being tested were seen as a matter of either common sense or inspiration, motivated by the available facts at hand.

What went without comment, and perhaps without recognition, was the pervasive theoretical orientation structuring the available facts and ways of thinking about them: that of the biomedical model (Table 8.1). Prioritizing the micro over the macro, both ideologically and technically, the biomedical model simultaneously (i) focuses on the physical, chemical, and biological causes of disease, and (ii) renders invisible how the societal context simultaneously shapes disease rates and the way their causes are conceptualized and analysed, and by whom (Tesh, 1988; Krieger, 1994, 2011; Greene and Loscalzo, 2017). If any social variables appear, they do so as individual risk factors and behavioural choices, framed by the complementary and equally individualistic lifestyle theory (Table 8.1) (Tesh, 1988; Krieger, 1994, 2011; Wemrell et al., 2016). Health inequities receive scant attention. Instead, observed physiological or other biological differences between social groups are largely recast as a matter of intrinsic (also known as genetic) difference, especially for race or ethnicity (Krieger, 1994, 2011).

Biomedical research fosters an aura of being more objective, precise, and potentially actionable, not to mention more scientific and prestigious, compared with the presumptively messier and more subjective research that addresses macro social phenomena that scientists by themselves cannot directly manipulate (even as scientists can contrib-

ute to and evaluate policy-relevant evidence) (Ziman, 2002; Krieger, 2011). There is an undeniable allure to use new tools of –omics, systems, and network biology to peer into cells, identify biomarkers of exposure and disease, and elucidate mechanisms involving biological development and pathological processes. New and exciting opportunities exist to study DNA expression and its regulation, the life-cycle of cells, and the functioning of and interactions between tissues (Gilbert and Epel, 2015; Greene and Loscalzo, 2017), and also to collect and analyse terabytes of health-relevant sensor, cell phone, Internet, and electronic medical record data (Mooney and Pejaver, 2018).

However, technological advances notwithstanding, in both biomedical and lifestyle research the individual remains entrenched as the unit of analysis (Krieger, 2011, 2014). Selection bias remains a potent problem; studies often lack sufficient social and economic diversity to encompass the etiologically relevant range of exposures and outcomes (O'Neil, 2016). Causal agents identified using older methods continue to wreak havoc on population health and health inequities, as exemplified by smoking-related diseases such as lung, oesophageal, and cervical cancer (Proctor, 2011). These persistent problems have spurred vigorous debate about the limits of biomedical and lifestyle theories, and have brought new prominence to theorizing about the societal determination of health and health inequities (Krieger, 1994, 2011, 2014; Berkman and Kawachi, 2000; Solar and Irwin, 2010; Wemrell et al., 2016). A central insight is that all science, whether at the micro or macro level, is conducted by people and incorporates peo-

ple's value-laden (and often simplifying) assumptions about the world; it is explicit use of theory that enables these assumptions to become visible to and testable by independent investigators (Tesh, 1988; Ziman, 2002; Krieger, 2011).

Epidemiological theories of disease distribution for analysing health inequities

Table 8.1 lists key conceptual features of the three major sets of complementary theories of disease distribution in use in contemporary social epidemiology: sociopolitical, psychosocial, and ecosocial (Krieger, 1994, 2011, 2014; Solar and Irwin, 2010; Wemrell et al., 2016). All of these theories are concerned with the causal processes that give rise to health inequities. All reject the individualistic and decontextualized premises of the dominant biomedical and lifestyle theories, and all seek to promote health equity. Nevertheless, their emphases differ.

Sociopolitical theories

The common thread of the six sociopolitical theories listed in Table 8.1 is that they focus on analysing patterns of disease distribution in relation to power, politics, economics, and rights, and pay less (or no) attention to the biology involved in embodying social inequality. Among these theories, the three most explicit in terms of the political and economic drivers of health inequities are: social production of disease or political economy of health, Latin American social medicine or collective health, and critical epidemiology (also from Latin America) (Breilh, 2008; Krieger, 2011 [pp. 167–180, 187–190], 2014; Birn et al., 2017). By providing a frank analysis of who gains from and who

Table 8.1. Epidemiological theories of disease distribution: explicit theoretical focus

Theory	Disease mechanism	Health behaviour	Political economy and social production or reproduction of society	Politics, polities, and social movements	Social determinants (as factors)	Psychosocial exposures	Biological pathways of embodiment	Life-course	Levels	Place	Spatio-temporal scale	History and historical contingency	Eco-system	Reflexivity: of theory and theorists
Dominant: decontextualized														
Biomedical	X	X												
Lifestyle		X												
Social epidemiology alternatives: contextualized														
Sociopolitical														
Social production of disease or political economy of health		X	X	X	X	X			X	X				X
Latin American social medicine or collective health		X	X	X	X	X			X	X		X		X
Critical epidemiology		X	X	X	X	X		X	X	X		X	X	X
Health and human rights		X		X	X				X					X
Population health or social determinants of health	X	X			X	X	X	X	X	X				
Fundamental cause		X			X	X			X					
Psychosocial	X	X			X	X	X	X	X					
Ecosocial and other ecologically oriented theories														
Eco-epidemiology	X	X			X	X	X	X	X	X			X	
Ecosocial	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Source: reprinted from Krieger (2014) by permission from Springer Nature and adapted from Krieger (2011) by permission of Oxford University Press, USA.

is harmed by inequities involving power, wealth, and material resources, all three theories are rooted in European critiques of 19th and 20th century capitalism and imperialism and their imperative to maximize private profit. Intended to be applicable to any type of political economy, they also engage with "how political-economic systems and priorities that value social justice can produce health equity" (Krieger, 2011 [p. 167]). Forged under conditions of middle–late 20th century military dictatorships, the two Latin American theories have more similarities than differences. However, they focus more on the role of collectivities and popular movements in promoting health equity, as opposed to theories from the Global North that focus more on analysing and promoting state-led public health policies and actions (of a type not feasible under military dictatorship).

Another three of the sociopolitical theories – social determinants of health, population health, and fundamental cause – are also concerned with how social conditions shape population health profiles, but with little or no attention paid to the political economy of who gains from the status quo and at whose expense (Solar and Irwin, 2010; Krieger, 2011 [pp. 180–184], 2014; Birn et al., 2017). All three theories focus on finely calibrated social gradients in health, on social and status hierarchies, and on institutional policies and practices that affect the social and physical quality of where people live and work; none, however, explicitly name who benefits from injustice. For example, although the theories are concerned with the adverse impact of low income, they do not specify whose interests are served by low wages, reduced benefits, and

austerity budgets. Of the three, theories on social determinants of health and on population health pay the most attention to biology, primarily in relation to the type and timing of exposures across the life-course from conception onwards. Fundamental cause, by contrast, treats specific exposures as superficial causes; its focus is the flexible resources people can use, such as knowledge, power, prestige, and interpersonal networks, to minimize health-related risks (Link and Phelan, 1995).

Also a sociopolitical theory, the health and human rights framework engages with how both promotion and violation of human rights by governments (and, increasingly, non-state actors) can affect individual and population health (Gruskin et al., 2007; Krieger, 2011 [pp. 190–191]). Based on the Universal Declaration of Human Rights issued by the United Nations in 1948 and aspects subsequently codified in international human rights laws, this theory analyses health inequities in relation to a range of social, political, civic, economic, and cultural rights held to be universal, interrelated, and indivisible. Accordingly, it offers unique tools to analyse the health impacts of government policies and hold governments accountable, including legally, for those impacts.

Psychosocial theories

The central focus of psychosocial theories is, as their name suggests, the health consequences of people's psychological perceptions of – and emotional and behavioural responses to – their social status, social interactions, and social conditions (Krieger, 2011 [pp. 191–201], 2014; Kubzansky et al., 2014). Building on a century of research on the biological responses of organisms to fear and

other psychological stimuli, a major emphasis has been on the brain-mediated biology of stress and its physiological consequences across the life-course (and also intergenerationally, across the placenta). Attention is also given to stress-related health behaviours (e.g. eating, smoking, alcohol consumption, and use of other psychoactive substances). More recently, the scope of theorizing has expanded beyond the biology of stress to consider intersections between psychology, behavioural economics, and neuroscience, albeit without tackling political economy. The aim is to promote policies and institutional practices that can increase the likelihood that all people, not just those with resources (e.g. education and income), can engage in and maintain healthy behaviours (Kawachi, 2014).

Ecosocial theory

The ecosocial theory of disease distribution, first proposed in 1994 and elaborated upon since (Krieger, 1994, 2011, 2014), is an integrative social epidemiological theory that explicitly pays heed to: societal and ecological context; life-course and historical generation; spatiotemporal scales and levels of analysis; pathogenesis; and diverse forms of inequitable relationships within and between countries, including in relation to political economy, racism, class, sex, and sexuality. As illustrated in Fig. 8.1, a central focus is embodiment, referring to how we literally embody, biologically, our lived experience in a societal and ecological context, thereby creating population patterns of health and disease.

Another focus is accountability and agency, both for social inequalities in health and for ways they are (or are not) monitored, analysed,

and addressed. Ecosocial theory shares with other social epidemiological theories of disease distribution a theoretical focus on political economy and the structural determination of material, social, and psychological exposures (both beneficial and adverse). In its ecological orientation, ecosocial theory expands beyond ecoepidemiology (which mainly theorizes about levels) (Susser and Susser, 1996; Lau et al., 2018) by explicitly including concepts and insights from fields such as political ecology, ecolog-

ical evolutionary developmental biology, Indigenous traditional knowledge, and the history and philosophy of science. The point is not a theory of everything but rather a coherent set of conceptual principles and questions about causal processes to guide research. A starting point is recognition that all biological phenomena – including development, health, and evolution (Gilbert and Epel, 2015) – are necessarily expressions of biological embodiment in historical, societal, and ecological context.

Cancer inequities: why theories of disease distribution matter

Why do theories of disease distribution matter? They should spark their users to step back from the current roster of so-called facts and instead promote critical and creative causal thinking, to see who and what is missing (Krieger, 2011).

Selected examples are provided here to illustrate why theory, and choice of theory, matters for cancer inequities.

Fig. 8.1. Ecosocial theory and embodying inequality: core constructs, referring to processes conditional upon extant political economy and political ecology. Source: Krieger (2018).
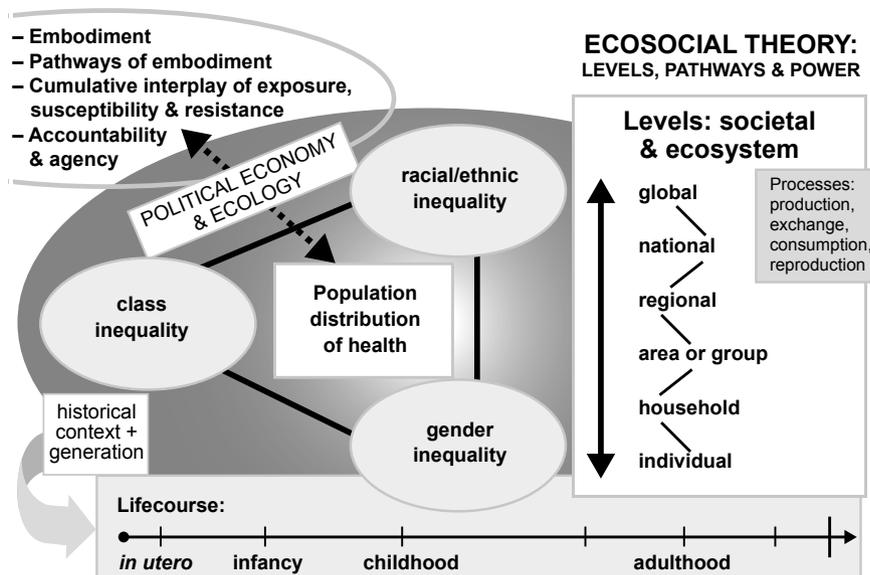
1. *Embodiment*, referring to how we literally incorporate, biologically, in societal and ecological context, the material and social world in which we live.

2. *Pathways of embodiment*, via diverse, concurrent, and interacting pathways, involving: adverse exposure to social and economic deprivation; exogenous hazards (e.g. toxic substances, pathogens, and hazardous conditions); social trauma (e.g. discrimination and

other forms of mental, physical, and sexual trauma); targeted marketing of harmful commodities (e.g. tobacco, alcohol, other licit and illicit drugs); inadequate or degrading health care; and degradation of ecosystems, including alienation of Indigenous populations from their lands.

3. *Cumulative interplay of exposure, susceptibility, and resistance across the life-course*, referring to the importance of timing and accumulation of, plus

responses to, embodied exposures, involving gene expression and not simply gene frequency.

4. *Accountability and agency*, both for social disparities in health and research to explain these inequities.

Table 8.2. Cancer inequities: conceptual grid (Krieger, 2005 [p. 11]) for systematically reviewing evidence availability and gaps, using example of cervical cancer (Newmann and Garner, 2005 [p. 64]). The literature search identified only 45 articles with relevant data; the numbers in the table cells refers to the number of studies with relevant data for each cell (note that one study might have data relevant to more than one cell), and blank cells indicate that the literature review yielded no studies with relevant data.

Domains of social inequality	Prevention	Etiology	Screening	Diagnosis	Access to clinical trials	Treatment	Survival	Morbidity	Mortality
Race or ethnicity and racism	3		5[a]	4		2	4[a]	1	2
Socioeconomic position	1		4	3			1		1
Sex			3						
Sexuality		1	1						
Age				3		2			
Language			1						
Literacy	1								
Disability			2	1					
Immigrant status	4		9	1					
Insurance status			1	4			1		
Geography							1	1	1
Housing status			1						

[a] Contradictory evidence.

Source: reprinted from Newmann and Garner (2014) by permission from Springer Nature and adapted from Krieger (2005) by permission from Springer Nature.

Theory makes the invisible visible

To see theory in action, consider the conceptual grid (applied to cervical cancer) shown in Table 8.2. This grid was developed for a Dana Farber/Harvard Cancer Center interdisciplinary working group on cancer disparities (Krieger, 2005). Analytically informed by the ecosocial theory of disease distribution, the intent of the grid was to identify gaps in knowledge about cancer inequities across the cancer continuum by systematically addressing a specified set of "Domains of Social Inequality: singly & combined, involving adverse conditions & discrimination at multiple levels (person, place, institutional, societal), across the lifecourse" (Krieger, 2005). Used in relation to breast, prostate, colorectal, and cervical cancers (Bigby and Holmes, 2005; Gilligan, 2005; Newmann and Garner, 2005; Palmer and Schneider, 2005), the grid systematically reveals where evidence exists and where it is sparse, thereby helping to guide the next generation of research on cancer inequities (Koh, 2009).

Using social epidemiological theories to see data gaps is nothing new. In the early 1970s, such theories enabled researchers from Howard University, a historically Black university in Washington, DC, to shock the United States cancer establishment by reporting that cancer mortality among Black Americans since 1954 had grown by 32% compared with only 3% among White Americans (Fontaine et al., 1972; Henschke et al., 1973), a fact obscured by the then-routine reporting of solely non-White versus White data. The fallout galvanized the newly formed United States Surveillance, Epidemiology, and End Results Program for cancer statistics, launched in 1972, to ensure that its catchment sites could include and report data for "diverse ethnic subgroups" (Wailoo, 2011 [pp. 120–145]).

Theory guides choices of metrics for monitoring

Theory can also be useful for identifying the kinds of variables needed to monitor health inequities. For example, theories that explicitly address structural racism, such as ecosocial theory and political economy of health, point to the utility of monitoring economic and racial or ethnic cancer inequities using not only conventional individual- and

household-level socioeconomic measures but also measures of economic and racial or ethnic polarization at the neighbourhood, city, or town, and regional levels; these latter measures keep in view the privileged who benefit from inequitable relations, and not just those harmed by these inequities.

One such metric is the Index of Concentration at the Extremes (ICE), which quantifies the extent to which an area's residents are concentrated into groups of extreme levels of high versus low economic or social privilege (Massey, 2001; Krieger et al., 2016). For example, the recently developed ICE for racialized economic segregation quantifies the extent to which an area's residents are concentrated into the extremes of affluent racially privileged groups versus impoverished racially oppressed groups; it can also be used to quantify solely economic or racial polarization (Krieger et al., 2016). Notably, these ICE measures can be meaningfully used at multiple geographical sociopolitical levels, from residential neighbourhood to city or town to region to state. This is in contrast to the more widely used Gini index for income inequality and the Index of Dissimilarity for racial segregation, which are uninformative for small areas precisely because of how segregation reduces inequality within such areas by increasing spatial social polarization (Massey, 2001; Krieger et al., 2016). In an era of growing economic, social, and spatial polarization within and between countries, measures that keep in focus the full range of privilege and deprivation will be crucial to global monitoring and analysis of cancer and other health inequities (Galster and Sharkey, 2017; Krieger, 2017).

Theory illuminates spatiotemporal scale and level in a historical context

Theory can also spark research to improve understanding of the historical, place-based, and sociopolitical dimensions of current cancer inequities in biomarkers and molecular phenotypes. For example, the ecosocial theory of disease distribution prompts the following four questions (source: Krieger, 2013 [p. 23]).

- **"Question 1: Societal history.** What data exist on historical trends in the average population rates of—and health inequities in—the embodied biomarker or outcome? (For example, between and within countries and regions, defined geopolitically and in relation to societal divisions involving property, power, resources, and discrimination, including socioeconomic position, race/ethnicity, Indigenous status, gender, sexuality, disability, nativity, and immigrant status.)
- **"Question 2: Individual (life course) history.** What is the "natural"—and "unnatural"—history of the embodied biomarker or outcome across a person's life course? Does its expression change over time for a given course of illness, or across repeat bouts of an illness? Does its expression vary by the societal groups considered in Question 1 (i.e., display health inequities)?
- **"Question 3: Pathological/cellular history.** What is the "natural"— and "unnatural"—history of the embodied biomarker analyzed at the level of the tissue(s) involved? Does its expression change over the course of the disease? Or vary by the societal groups considered in Question 1 (i.e., display health inequities)?

- **"Question 4: Evolutionary history.** What is known—and debated—about the evolutionary history of the embodied biomarker or outcome under analysis? What insight does this history provide regarding the likely dynamics of expression, within and across individuals, historical generations, and societal groups?"

In the case of the estrogen receptor (ER), which plays an important role in breast cancer, research motivated by such questions readily reveals the fallacies of prevalent biomedical assumptions about alleged innate racial differences underlying observed Black (or African) versus White (or European or Euro-American) differences (Iqbal et al., 2015; Newman, 2015). The scant data on population distributions of this biomarker in a handful of African countries show wildly divergent prevalences of ER-positive and -negative tumours (Eng et al., 2014). Within the USA, Black versus White patterns of breast cancer ER status (and their pace of change, by biological generation) have been shown to vary by historical period, place of birth (states with vs without legal racial discrimination ["Jim Crow"]), socioeconomic position, and both access to and quality of medical care (Krieger et al., 2011, 2018, 2017; Krieger, 2013; Kohler et al., 2015; Rauscher et al., 2016). The evolutionary history of ER further suggests that its expression would be highly sensitive to extracellular signals, for example, hormonal medications, or exposure to periods of famine and great destitution (Krieger, 2013; Krieger et al., 2017). Theory makes the distinction between seeing a difference as fixed and an inequity that can be modified.

Theory pinpoints accountability and agency

Finally, in a period of mounting conservative and corporate-led attacks on public health, on environmental regulations that limit exposure to carcinogens and other adverse substances, and on the science of global climate change (Freudenberg, 2014; Birn et al., 2017), social epidemiological theories that identify the culprits and their motives are crucial for building alliances to protect the health of the people and that of this planet (Birn et al., 2017; Klein, 2017).

Conclusions

In conclusion, the rationale for explicit use of social epidemiological theories of disease distribution for the analysis of cancer inequities is not a faddish concern with conducting politically correct science; it is, instead, a concern to conduct correct science (Krieger, 2011). The ultimate test of the knowledge produced is whether it aids the collective tasks of (i) imagining a world free of health inequities; (ii) identifying the obstacles to health equity; and (iii) equitably engaging all who must work together to bring about a kinder, healthier, more equitable, and more sustainable human world, informed by deep recognition of our interconnection with, and dependence on, our wondrous and threatened planet.

Key points

- Explicit use of social epidemiological theories of disease distribution is critical for defining, analysing, and remedying health inequities, that is, social group differences in health that are unfair, unnecessary, and, in principle, preventable.

- The three major sets of complementary theories of disease distribution used in contemporary social epidemiology are: sociopolitical, psychosocial, and ecosocial.

- Rigorous use of social epidemiological theories that identify the obstacles to health equity are crucial for building alliances to protect the health of people and that of this planet.

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CHAPTER 9.

Recent trends in income inequality

Joe Hasell, Salvatore Morelli, and Max Roser

Introduction

This chapter provides the global context of economic inequalities related to income, which is important to understand health and cancer inequalities. In recent years there has been something of a renaissance in the study of economic inequality, simultaneously responding to, and feeding, the emergence of a public and political consciousness of the issue. Today, social scientists find themselves equipped with a wealth of easily accessible data on inequalities, much of which was unavailable to them 20 years ago.

The purpose of this chapter is to briefly summarize this body of evidence. The focus is on income inequality within countries across three dimensions: overall inequality, the share of income received by the top 1% of the income distribution (referred to here as the "top 1%"), and relative poverty rates. Some context is first provided by a brief look at recent changes in the global distribution of income.

Among advanced industrial economies, the availability of comparable long-term data reveals a general increase in income inequality in the final decades of the 20th century, after substantial declines earlier in the century. However, even among this relatively homogeneous group of countries there are significant and noteworthy differences in terms of the timing and extent of the increase. When global trends are considered, the picture is much more complex.

Inequality has evolved very differently in different countries, with falling or constant levels of inequality in many countries and rising levels in others. No single narrative serves to capture this heterogeneity adequately, but some clear regional patterns do emerge.

Important provisos about the coverage and quality of available data become increasingly pertinent the broader the range of countries and the longer the time period being considered. However, the interpretation of all inequality data requires some care. Unlike the measurement of height or weight, trends and comparisons of inequality data may appear quite different depending on the particular measure chosen. In this chapter these issues are highlighted,

including a brief discussion of some particular limitations that should be considered when linking inequality data to health outcomes.

Global income inequality

Global income inequality simply reflects the combination of inequality between countries and within countries. Between-country inequality is basically due to relative rates of economic growth. Rapid growth in many developing countries, most notably in Asia, and a relative slowing of growth in high-income countries have brought about a convergence in average per capita incomes between countries in recent decades; after two centuries of divergence, this development is of historical significance (Pomeranz, 2000). At the same time, some of the processes driving this catch-up, such as globalization or technological development, have been charged with contributing to the rising inequality seen within many countries, both rich and poor, since the 1980s (Freeman, 1995; Bourguignon, 2015; Basu, 2016). Studying changes in the global income distribution enables these movements to be considered jointly.

Lakner and Milanovic (2016) provided estimates for global inequality decomposed into separate within-country and between-country components (Fig. 9.1). The estimates show that although between-country inequalities are diminishing, they still vastly outweigh within-country inequalities. The increase in within-country inequality visible throughout the 1980s and 1990s, although significant, has been outpaced by the convergence in average incomes between countries, translating into a reduction in overall global inequality.

Note that in Fig. 9.1 there is evidence of a flattening-out in the

Fig. 9.1. Global inequality decomposed into inequalities between countries and within countries. The estimates were constructed by combining national household surveys, some of which referred to consumption and others to (disposable) income, at 2011 purchasing power parity exchange rates. Where surveys in the reference year were unavailable, adjacent years were also used. The inequality metric here is of the Generalized Entropy family. GE(0) (or Theil-L index) is a decomposable measure of overall inequality equal to the mean log deviation. The top horizontal line shows the evolution of overall inequality and the lower horizontal line that of within-country inequality, both in population-weighted terms. The proportions of the between-country and within-country component of global inequality are given as percentages of total inequality for each reference year. Source: compiled from Lakner and Milanovic (2016 [Table A.3]).
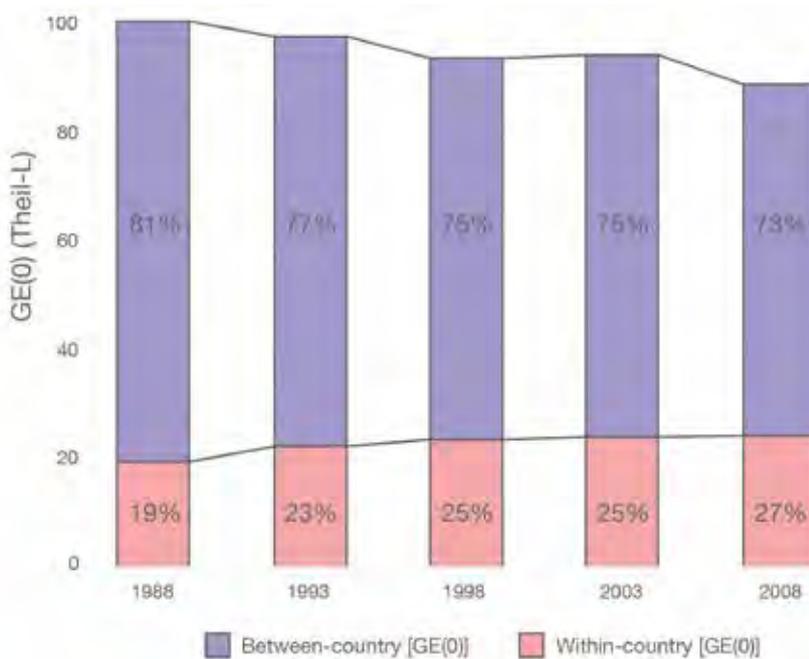
within-country component in recent years. However, it should be noted that this trend, as well as that for overall global inequality, is sensitive to how incomes at the very top of the distribution are accounted for and, indeed, to the measure of inequality chosen. (Ravallion (2018), for instance, reported a range of Atkinson indices that yield rising global income inequality over this period.) In focusing on the share of income received by top-earning percentiles of the population (as captured in administrative tax data), the *World Inequality Report* painted a rather different picture of the evolution of global inequality: between 1988 and 2016 the global top 1% pulled away, with average income growing 100% compared with 60% growth in the world average (WIL, 2018). (Lakner and Milanovic (2016) checked their global inequality estimates for robustness to making some allowance for these missing top incomes. In this case, a far smaller fall was reported over the period 1988–2008, and inequality was only observed to decline after 2000.)

Within-country income inequality

Overall income inequality

Focusing on the within-country inequality, we first consider overall inequality as captured by the most commonly used inequality indicator: the Gini index.

The Gini index is an indicator that attempts to summarize, in a single number, the degree of dispersion across the entire distribution.

It is most easily understood in terms of mean difference: a Gini index of G% means that, if we take any two households from the population at random, the expected difference is $2G$% of the mean.

Global picture since 1990

Fig. 9.2 compares the Gini index for about 2015 with that for about 1990. The estimates are based on household surveys conducted at the national level, drawing primarily from the World Bank's Povcal database (World Bank, 2018), with additional figures from *The Chartbook of*

Fig. 9.2. Gini index for about 2015 plotted against that for about 1990, including both income and consumption survey data. Only countries for which estimates of the Gini index were based on broadly comparable surveys for the two reference years were included. The closest survey to the reference year was selected, up to a maximum of 5 years difference. The size of the circles is in proportion to population size. Data for China are from Kanbur et al. (2017 [Table 1.B]). Source: compiled from Atkinson et al. (2017), Kanbur et al. (2017), and World Bank (2018).
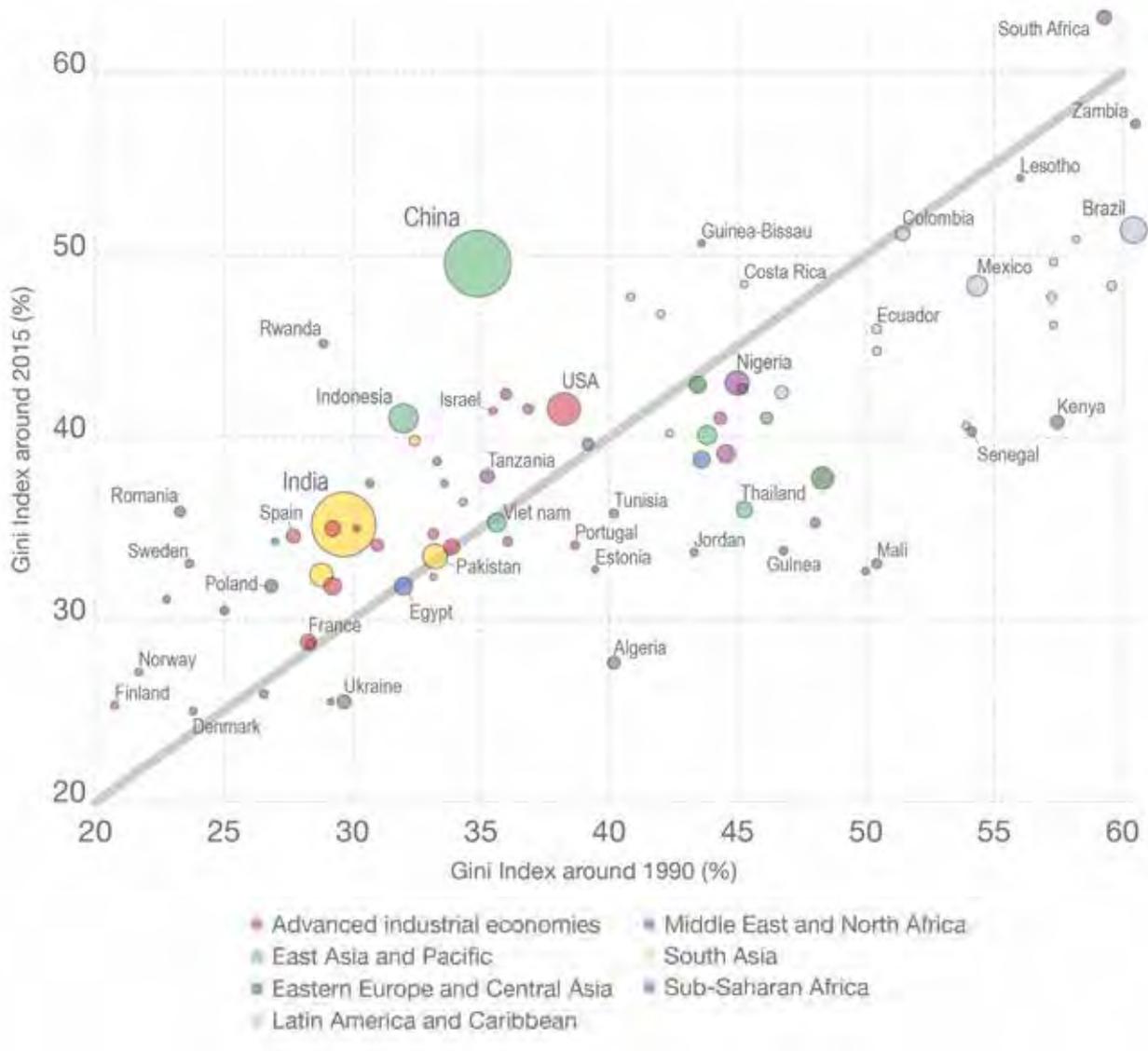
Economic Inequality (Atkinson et al., 2017). Given that surveys are often not conducted on a regular annual basis, estimates for the year closest to each reference year were selected up to a maximum time difference of 5 years. On the basis of this rule, the shortest admissible time between surveys was 15 years, from 1995 to 2010. In practice, Mali had the shortest such time span, with surveys taken from 1994 and 2010; it is only for 6 out of 84 countries that the selected surveys fell less than 20 years apart.

It is important to stress that Fig. 9.2 includes a rather heterogeneous mix of data points that are based on a broad range of survey methodologies and concepts. This introduces significant comparability issues (Alvaredo and Gasparini, 2014; Lakner and Milanovic, 2016). Of these, the most acute divergence is between the use of consumption versus income as the measure of welfare within the survey. Generally speaking, lower-income countries use consumption measures and higher-income countries use income measures. Crucially, the level of consumption is, as a rule, more equally distributed across households than is income, with the gap increasing with average incomes (World Bank, 2016 [pp. 78–79]). (This gap reflects (i) the increasing propensity to save at higher incomes and (ii) a more general tendency for households to smooth consumption levels over time.) The more level distribution of consumption implies a downwards bias in consumption surveys relative to income surveys. This is particularly true for countries with higher average incomes that are represented in Fig. 9.2 on the basis of consumption surveys, such as the Russian Federation. In contrast, surveys in Latin American countries are pre-

dominantly based on income, thereby exaggerating somewhat their position relative to other low- and middle-income countries. (To address this issue, Alvaredo and Gasparini (2014), in their analysis of the Povcal data, choose to apply a downwards adjustment of about 15% to Latin American and Caribbean estimates, so that a Gini index of 50% is reduced to about 43%. This option is not taken here.) Moreover, even among surveys that measure household income, there are a range of income concepts that may be used, relating to which kinds of income are counted and how taxes and transfers are considered.

Such heterogeneity is unavoidable if one wishes to take a global view. However, to attempt to manage this issue, only countries for which the Gini index estimates for the two reference years were based on broadly comparable surveys are included in Fig. 9.2. This restricts the sample to 83 countries.

The colours of the bubbles refer to world region, with advanced industrial economies (as defined by the World Bank, 2016) presented as a separate group. Overall, inequality tends to be higher in Caribbean, Latin American, and sub-Saharan African countries. The Scandinavian countries, and several eastern European and central Asian countries, are positioned at the opposite end of the spectrum. Most advanced industrial economies have a Gini index clustered at about 30–35%, and the USA shows the highest inequality during both periods.

In the figure a 45-degree line is plotted. Those countries lying above the line in Fig. 9.2 show higher inequality in (or around) 2015 than 1990, and those below the line lower inequality. Across all countries, we see a roughly equal split between countries with higher or lower inequality

across the two periods. However, comparing high- and low-inequality countries, we see different patterns. Among those countries with a Gini index below 40% in 1990, there were substantial declines in very few during the period until 2015. Above this threshold, however, the inverse holds. Fig. 9.2 therefore suggests a modest convergence in the Gini index across countries between 1990 and 2015. The pattern, however, works in large part through regional dynamics. There was an increase in inequality in most southern Asian countries, in most advanced industrial economies, and in several transitioning countries in eastern Europe. Across the Caribbean and Latin America, as well as North Africa and the Middle East, the Gini index decreased for almost all countries. Countries in sub-Saharan Africa and the eastern Asia and Pacific regions had more mixed results, with falling inequality among countries with higher inequality in 1990 and rising inequality among countries with lower inequality in 1990.

In terms of the average Gini index, these contrasting trends largely cancelled themselves out during the period; the mean index across all countries in the sample was more or less the same in about 2015 (38.6%) as it was in about 2015 (39.6%), a fall of 1 percentage point being small compared with the large variation in the data. However, sizeable increases in inequality in several populous countries, including China, India, Indonesia, and the USA, yielded a population-weighted average that increased by four percentage points (from 36.7% to 40.8%), in line with the rise seen in the within-country component of global inequality in Fig. 9.1. Therefore, although in the average country in the sample there

was no significant change in the Gini index between 1990 and 2015, the average person lived in a country that had meaningful rises in inequality. (The sample covers less than half of the countries in the world but represents about 85% of the global population; although better global coverage might be expected to affect the unweighted mean reported here, the population-weighted mean would be unlikely to change much.)

Fig. 9.2 does not enable us to trace the different paths taken by countries over the 25 years between the observations; repeating the exercise for the period after 2000 yields some additional information (Fig. 9.3). In this example, surveys were selected with a maximum period of 3 years between each reference year; this increased the number of countries plotted to 93, but India was excluded because of the absence of survey data for about 2000. In terms of additional information, we see that the fall among Caribbean and Latin American countries was concentrated after 2000 (as confirmed in Fig. 9.4), whereas the rises in eastern Europe seen in Fig. 9.2 occurred in the post-Soviet period during the 1990s. Among advanced industrial economies, the rise seen over the full period from 1990 was still continuing into the new millennium.

Fig. 9.3. Gini index for about 2015 plotted against that for about 2000. Both income and consumption survey data were included. Only countries for which estimates of the Gini index were based on broadly comparable surveys for the two reference years were included. The closest survey to the reference year was selected, up to a maximum of 3 years difference. The size of the circles is in proportion to population size. Data for China are from Kanbur et al. (2017 [Table 1.B]). Source: compiled from Atkinson et al. (2017), Kanbur et al. (2017), and World Bank (2018).
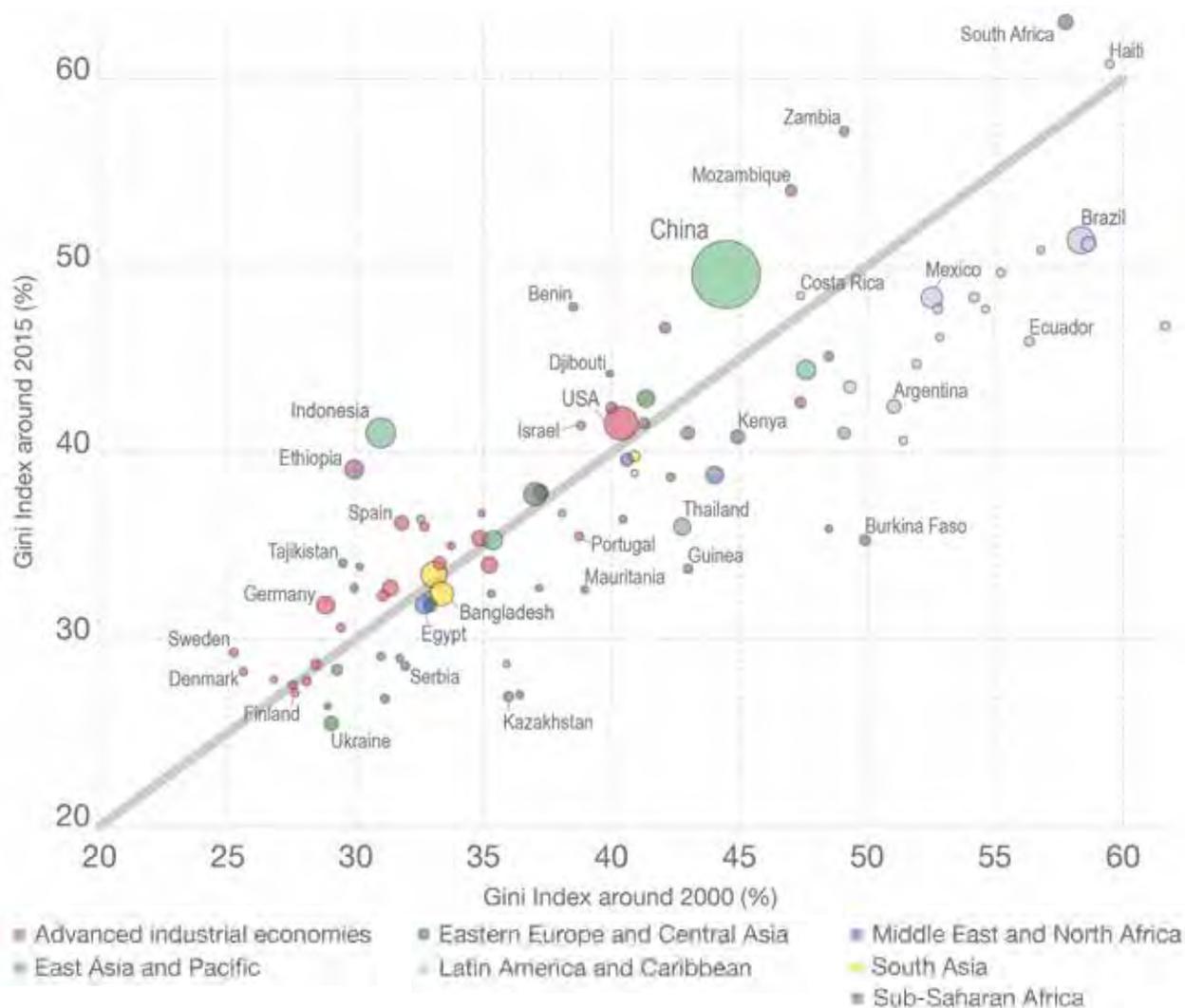
Fig. 9.4. Gini index in selected Latin American countries for the period 1981–2012. Figures refer to equivalized household income, defined as market income plus transfers, less taxes on wage income. Source: SEDLAC (CEDLAS and the World Bank) (2018).
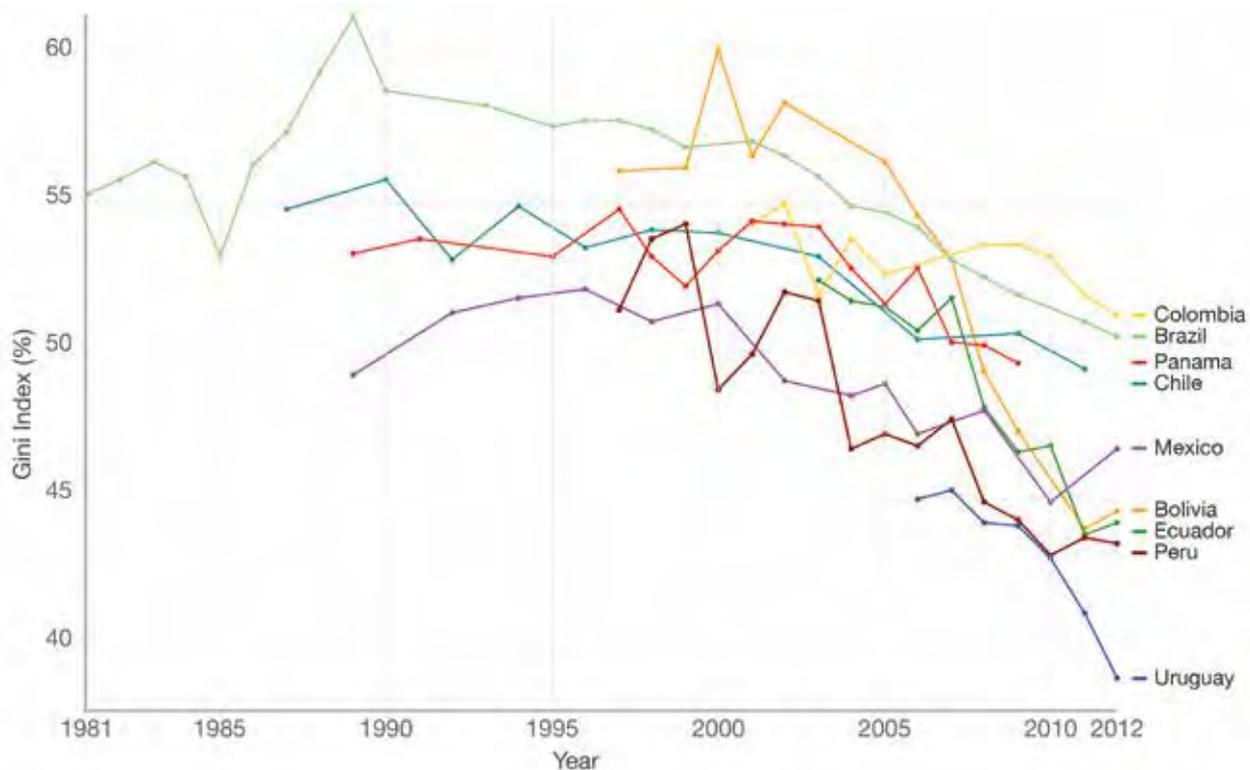
Long-term picture in advanced industrial economies

For several advanced industrial economies, we can benefit from longer-term Gini index series conforming to a more homogeneous set of definitions. In this section we refer to inequality of equivalized disposable household income, that is, income after taxes and transfers have been paid, measured at the household level, but adjusted to account for the size and composition of the household. We primarily draw on data presented in *The Chartbook of Economic Inequality* (Atkinson et al., 2017). Fig. 9.5 demonstrates a general rise in overall income inequality among advanced industrial economies since the 1980s. However, the extent and timing of any increase differed significantly between countries. To highlight these differences, we group countries into those following loosely similar trends over this period. Several countries underwent a more or less continuous increase in inequality between the 1980s and the 2010s (Fig. 9.5a). Another cluster is formed by several Nordic countries, which began their climb somewhat later in the 1990s, and from a lower starting point (Fig. 9.5d).

Indeed, a geographical distinction is often made between high-inequality English-speaking countries, the more moderate continental European countries, and low-inequality Nordic countries. Although it is informative, even this very loose typology masks important differences. For example, Sweden (Fig. 9.5a) stands out in terms of the extent of the rise in inequality seen there, following a different trend from its Nordic neighbours and joining the ranks of countries such as New Zealand and the United Kingdom. More modest, but still significant, increases in inequality in Denmark, Finland, and Norway contrast with the steady levels in France and the Netherlands (Fig. 9.5c), which contribute to a relative convergence between continental European and Nordic countries from the 1980s. The step increase in inequality seen at a greater magnitude in Canada, New Zealand, and the United Kingdom, and at a lower magnitude in Finland and Germany

Fig. 9.5. Gini index in high-income countries for the period 1960–2015. In most cases figures refer to disposable (after taxes and transfers) household income, equivalized for household composition. For Canada, the unit of analysis is the family; for Italy, figures are per capita. Data for Denmark and the USA are from LIS (2018). Source: LIS (2018).

Inequality before and after taxes and transfers
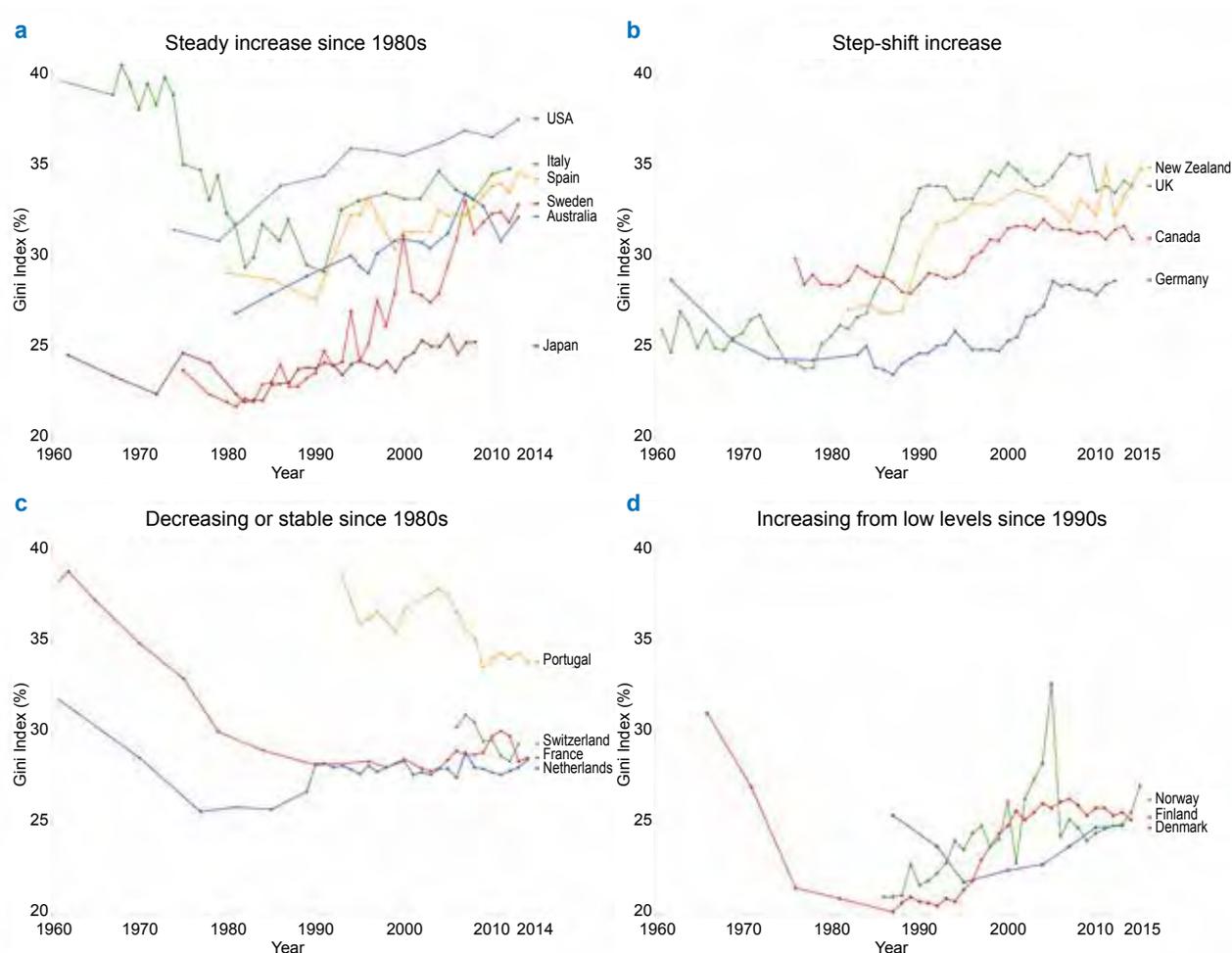
(Fig. 9.5b), also merits attention; the recent levelling out in these countries increasingly serves to accentuate the exceptionality of the USA among high-income countries.

Taken together, advanced industrial economies are today considerably more unequal places than they were in the 1980s. In very recent years, however, the trend is less clear, with the Gini index rising, falling, and levelling out in roughly equal proportions among advanced industrial economies in the post-2008 period (World Bank, 2016 [Table 4.1]).

Using Organisation for Economic Co-operation and Development (OECD) data from 2014 (OECD, 2018), Fig. 9.6 shows the Gini index for market income in red and that for disposable income in blue. The size of the gap between the two measures captures the effect of the system of taxes and transfers (both public and private) on reducing overall inequality. (As noted by Morelli et al. (2015), this difference captures the effect of redistribution rather imprecisely. Between the countries there are important differences in what is counted as a transfer, particularly in relation to pension systems. Moreover, any market responses to tax policy are already included in market income inequality.)

The large variation in the redistributive effect of taxes and transfers systems in different countries means that the resulting level of overall inequality of disposable income has a large degree of independence from market incomes. For instance, inequality

Fig. 9.6. Gini index of market and disposable income, where figures refer to equivalized household income. Most observations are from 2014, but if data from 2014 were not available earlier observations are shown (the earliest is 2011, for China, India, and the Russian Federation). Estimates for the Netherlands are provisional, according to the OECD. *, market income Gini index for China, Hungary, Mexico, and Turkey refers to income after taxes and before transfers. Source: OECD (2018).
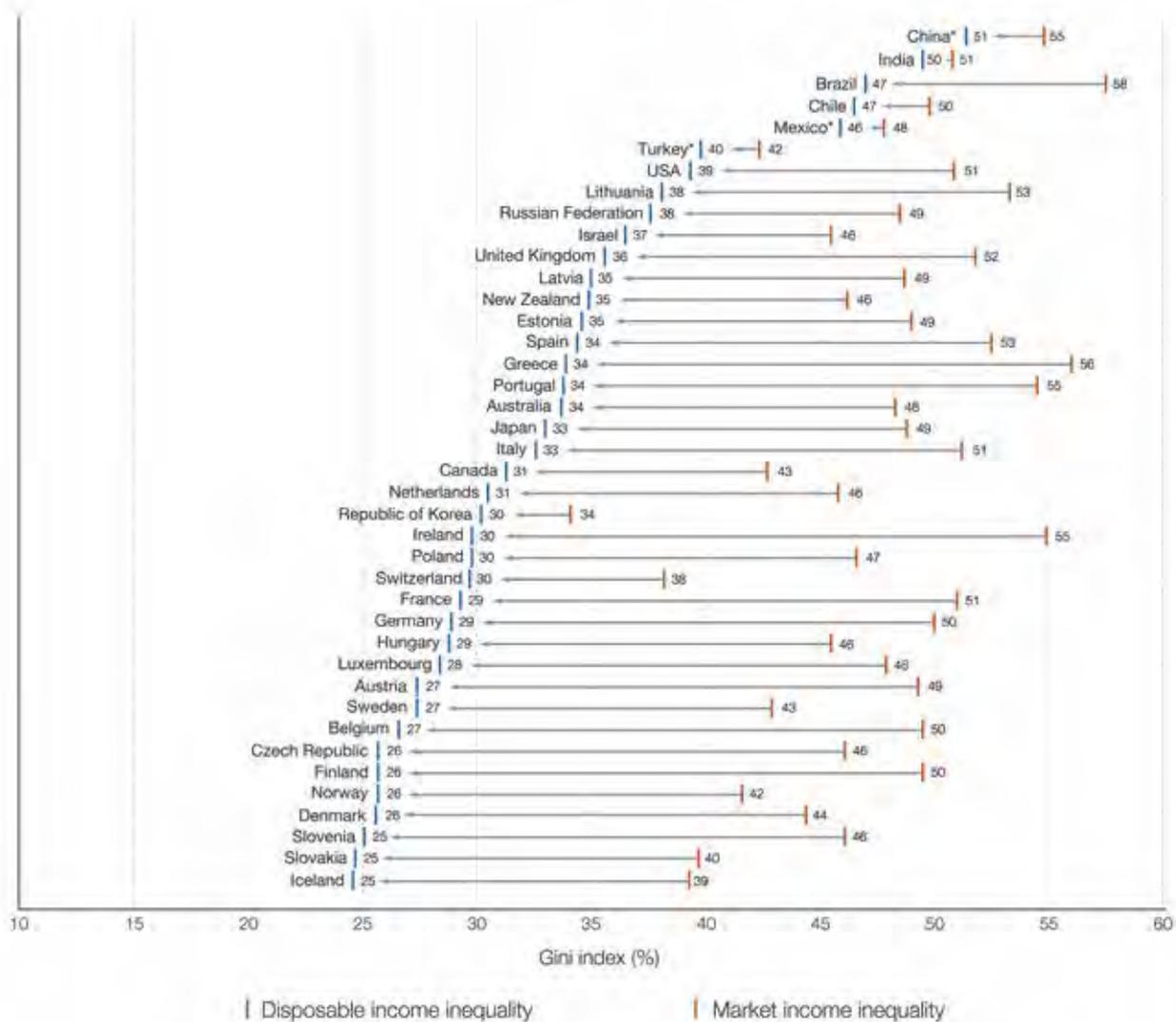
in Chile, India, and Mexico is comparable to that in Finland if we consider incomes before taxes and transfers. However, these countries contrast sharply in terms of their levels of disposable income inequality. Despite starting out with the least equal distribution of market income among OECD countries, Ireland achieves a level of income inequality after taxes and transfers that is considerably lower than that of the United Kingdom.

This is, however, not to downplay the role of market incomes in shaping disposable income inequality. The Republic of Korea is a case in point here: despite minimal redistribution, it lies towards the middle of the rankings in terms of disposable income inequality because of its very low level of inequality in incomes before taxes and transfers (e.g. lower than inequality after taxes and transfers in both the United Kingdom and the USA). More generally, increasing concerns about the political or economic limits to redistributive taxation have brought attention to the level of inequality of market incomes as an important issue in its own right, as well as to

the potential role of predistribution policies to encourage a more equal spread of incomes, assets, and opportunities before the operation of the taxes and transfers system (Atkinson, 2015).

Top income shares

In recent years, increasing attention has been paid to the share of income received by the highest-earning proportions of the population (referred to here as "top income shares") (Atkinson and Piketty, 2007, 2010). This approach has several advantages. First, it addresses a lack of sensitivity in the Gini index to shifts at the extremes of the distribution (Osberg, 2017; WIL, 2018). Second, in practice, the use of the top income shares measure has gone hand in hand with the use of administrative tax data and national accounts aggregates, as opposed to household survey data alone. (Alvaredo et al. (2016) set out a methodology for incorporating both survey and tax data to impute an income distribution consistent with total household income as reported in national accounts. Some of the top income shares series in the World Inequality Database (WID, 2018) are derived in accordance with this distributional national account (DINA) approach.) Such fiscal data avoids one major shortcoming of survey data: that of underreporting of incomes or non-response by those at the very top of the income distribution, and the underestimation of inequality that this may imply.

The Gini indexes reported in the previous section were based exclusively on household surveys. (Analysis by Atkinson et al. (2011) shows that a combination of survey data and administrative tax data for top incomes in the USA implies that

standard Gini index estimates for the country based on survey data alone underestimate the increase in inequality between 1970 and 2006 by more than one half.) As well as affecting levels, this may potentially also understate inequality trends over time, as demonstrated by Atkinson et al. (2011), for instance, in the case of the USA. Top income shares therefore serve as an important counterpart to the foregoing observations using Gini index estimates based on survey data alone.

Another benefit of tax data is that they are often available over far longer timeframes than household survey data are. Consequently, for many countries a much longer-term view of inequality trends is available with top income shares than with the Gini index calculated from household surveys. The downside is that, at present, long-term data are available for a limited range of countries, somewhat skewed towards advanced industrial economies, and this makes summary statements of global scope difficult. Fig. 9.7 shows the share of (pre-tax) income received by the top 1% across three groups of high-income countries: English-speaking countries, central Europe (plus Japan), and Nordic countries. Fig. 9.8 shows the same series for the so-called BRICS grouping of countries (Brazil, the Russian Federation, India, China, and South Africa). In both cases the data are drawn from the World Inequality Database (WID, 2018).

Many of the general observations noted for the Gini index (Figs. 9.2–9.4) still hold. English-speaking countries have, in general, seen a prominent rise in the top 1% share in recent decades, with more muted increases in continental European and Nordic countries. This rise came after a fall,

such that most European countries today remain much more equal places than in the early 20th century. After strong rises in inequality since the 1980s, the BRICS group of countries (Fig. 9.8) today displays levels of top 1% shares that are generally higher than that of high-income countries, in parallel with the Gini index.

The correlation between top income shares and Gini index is, however, far from perfect; indeed, the correlation has weakened somewhat since 2000 (Morelli et al., 2015). The persistently high top 1% share in Brazil, for instance, contrasts with the falling Gini index seen in Fig. 9.4. In the Russian Federation, large declines in the Gini index based on consumption surveys during the 1990s (coinciding with the post-Soviet economic collapse) directly contrast with the rocketing top 1% share over the same period.

Overall, the picture of recent inequality trends painted by top income shares is somewhat less benign than that given by standard Gini index estimates. Among the 22 countries for which top 1% share estimates were available in the World Inequality Database (WID, 2018) about both 2000 and 2015, more countries saw meaningful increases than falls; this is in direct contrast to the change in the Gini index over the same period (Fig. 9.3). This disparity is at least partly due to selection, however, with those countries that have rising Gini index values in Fig. 9.3 overrepresented within this small sample. Nevertheless, given the acknowledged weaknesses of Gini index estimates based on household survey data to capture movements at the extremes of the distribution, data on top income shares, where available, provide an indispensable additional perspective.

Fig. 9.7. Top 1% share of pre-tax income (all income received by individual owners of capital and labour, before tax/transfers but after pensions) in high-income countries for the period 1915–2014. The Italian series on top income share was extended to 2014 (provisional estimates) using adjusted council-level data on incomes reported in income tax returns, kindly provided by Demetrio Guzzanti. Source: WID (2018).
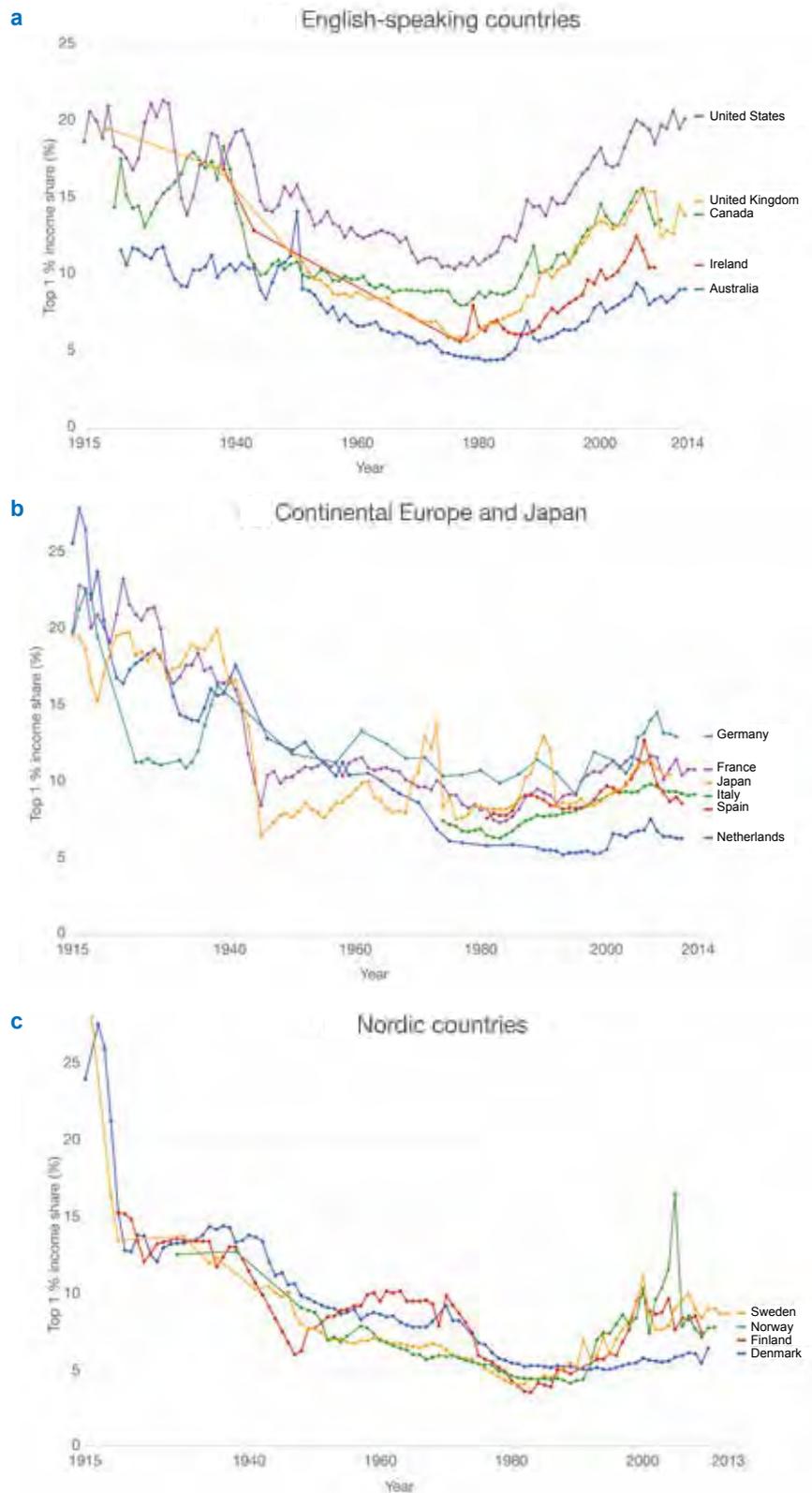
Fig. 9.8. Top 1% share of pre-tax income (defined as for Fig. 9.7) in BRICS countries for the period 1915–2015. BRICS, Brazil, the Russian Federation, India, China, and South Africa. Source: WID (2018).
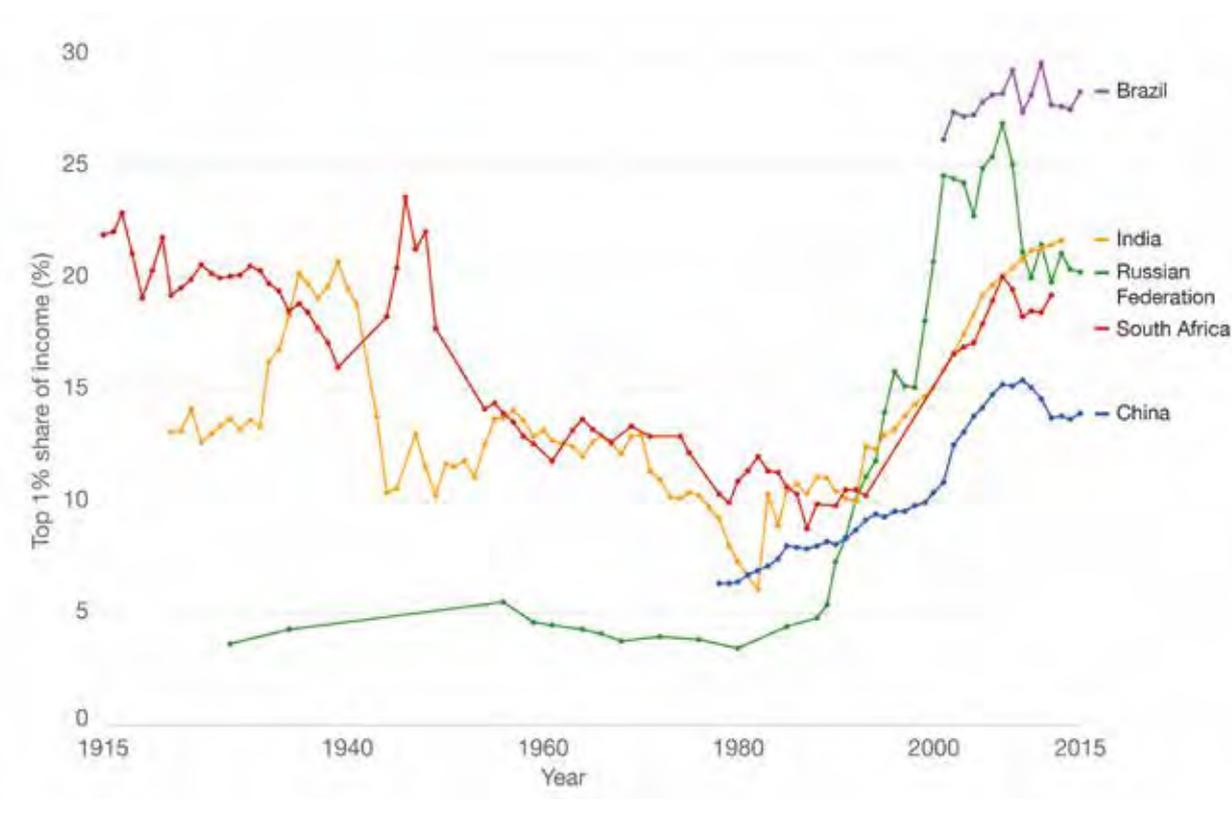
Relative poverty rates

Whereas top income shares track the incomes of a fixed (upper) proportion of the population, poverty rates do the reverse: they fix a level of income (a poverty line) and track the proportion of the population that falls beneath that level. In the case of an absolute poverty rate, that poverty line is set so as to maintain a constant purchasing power over time, at a level considered necessary to achieve a certain minimum standard of living. Relative poverty rates instead refer to a poverty line that is tied in some way to the average standard of living of the time. In real terms, that threshold may rise and fall with the overall fortunes of the population in question. It is this comparative feature that makes the measure an indicator of inequality.

In practice, relative poverty lines are typically defined as some fraction of the contemporaneous median income. We now consider the percentage of individuals with disposable incomes less than 60% of the national median, adopted by the European Union (among others) as its headline poverty indicator. When those countries with estimates available between 2012 and 2014 are considered (Fig. 9.9), poverty rates range from 11% in Czechia to almost 30% in Peru and South Africa. As with other dimensions of income inequality, lower-income countries generally feature more heavily at the top end of the rankings. Again, English-speaking and southern European countries have generally higher levels of inequality than their continental European counterparts, which in turn are more unequal than Nordic countries.

In terms of trends over time (Fig. 9.10), few generalizations are possible, with the exception that, when the most recent observations are compared with those about 1980, no country with available data for this period has seen a meaningful fall in poverty rates. However, some countries stand out for the increase that has occurred over this period; Israel is particularly notable in this respect, and Germany, Spain, and Taiwan, China also had increases of several percentage points. There was also a significant jump in Finland from the

Fig. 9.9. Relative poverty rates (percentage of the total population living in households with equivalized disposable income < 60% of the median) for about 2014. Source: LIS (2018).
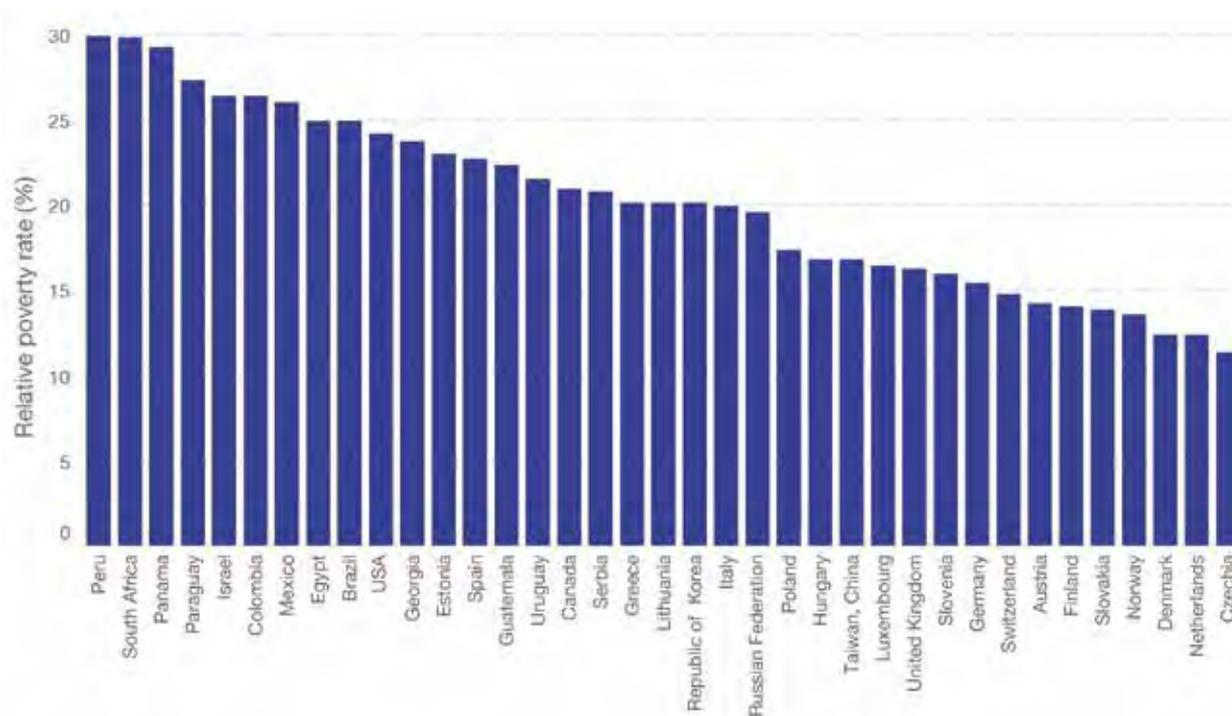
mid-1990s onwards, which moved the poverty rate towards the higher end among Nordic countries, matching the movement seen in the Gini index. After earlier falls in the poverty rate, Canada and France have largely rebounded in recent years. In contrast, in the United Kingdom, a marked increase throughout the 1970s and 1980s has been reversed since 2000, leaving the country with poverty rates more in line with those of the continental European countries. The available data for Ireland extend back long enough to show, at least, that this fall was mirrored there.

Using economic inequality data in health inequalities research

To maintain a meaningfully consistent metric across countries and years, attention must be paid to a number of seemingly technical issues in the definition and measurement of inequality. Following Atkinson and Bourguignon (2015 [p. xxxiv]), we can consider a checklist of questions in assessing the comparability of two inequality data points: (i) inequality of what (pre- or post-tax income, wealth, consumption, other dimensions of well-being); (ii) between whom (individuals, families, or households, with various ways of accounting for household composition); (iii) according to which sources (surveys, tax data); and (iv) according to which measure (Gini index, top shares, etc.).

Such issues, as we have already seen, impinge upon us even in attempting to describe recent inequality trends; they are even more important in attempting to investigate the social impacts of economic ine-

quality, including its relation to health outcomes including cancer. Particular caution has been sounded in the inequality literature against the uncritical use of secondary databases of distributional statistics in econometric studies involving inequality measures as an independent variable (Atkinson and Brandolini, 2001; Jenkins, 2015). Given the facility of sources such as the World Income Inequality Database assembled by the United Nations University World Institute for Development Economics Research (UNU-WIDER, 2018), and its standardized counterpart, it is easy to lose sight of the quality of the ultimate data upon which the sources are constructed, the significant comparability issues between many of the underlying sources that are available, and the interpolation used to fill in for those that are not.

Fig. 9.10. Relative poverty rates (< 60% of the median) for the period 1978–2014. *, including Taiwan, China. Source: LIS (2018).
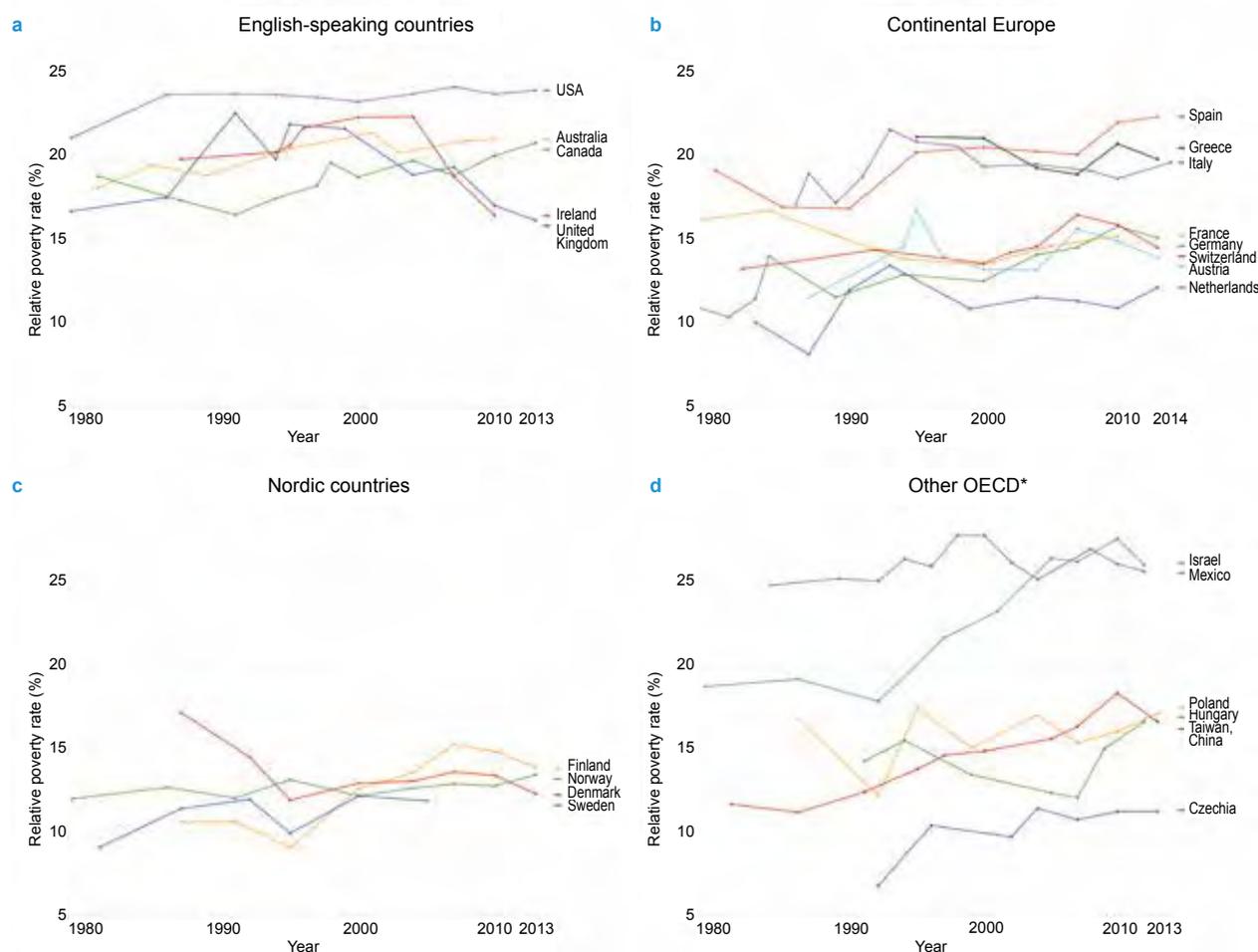
Notwithstanding improvements in recent versions of these sources, Atkinson and Bourguignon (2015 [p. xxxiii]) still advise "careful inspection" before their use.

Clarity about proposed causal mechanisms and how these relate to available distributional data is also needed. In discussing health inequality, Deaton (2013) made a strong case for the position that "facts and correlations, without an understanding of causation, are neither sufficient to guide policy nor to make ethical judgments". Even if we view the facts of inequality as of ethical import in and of themselves (Atkinson, 2015), in seeking to connect them to other

social phenomena, such as health, attention to causality is surely warranted. For instance, causal interpretations of the negative cross-country association between population health and income inequality, as observed in several studies, should be informed by the general absence of an effect when moving to panel or time series data, as surveyed in O'Donnell et al. (2015). However, any empirical approach must take into account the strengths and weaknesses of the various inequality data used. Atkinson and Bourguignon (2015 [p. xxxvii]) further remind us that a very noisy regressor – as the foregoing discussion suggests many

inequality series may well be – is unlikely to yield significant results, regardless of the true relationship. Moreover, depending on the causal path being hypothesized, some inequality measures may be more apt than others. If, for instance, extreme economic disparities are thought to pose a threat to health equality via specifically political channels, as Deaton (2013) suggests, then inequality measures that pay particular attention to top income shares may be more relevant.

Conclusions

In recent decades, levels of income inequality have risen in most

advanced industrial economies. Long-term data show that this increase was preceded by a sustained decline from the early 20th century onwards, tracing a broad U-shaped trend (Atkinson and Piketty, 2007, 2010) over the century in English-speaking countries, with more muted increases in continental European countries. These increases continued in many countries into the 21st century, but Gini indexes have been broadly stable since the global financial crisis of 2007–2008.

When the view is broadened to the global level, the picture is much more heterogeneous. Declines in many countries balance out rises in others, at least in terms of the unweighted mean. However, many of the world's most populous countries had significant increases in inequality, resulting in an increasing population-weighted average since 1990. In terms of inequality among all global citizens, this increase in the within-country component was outpaced by convergence in mean incomes of countries, resulting in a decline in global inequality that has gathered pace since 2000.

As we have argued, data on top income shares cast doubts on some of these conclusions, at times con-tradicting trends shown in the Gini index based on household survey data alone. However, the restricted coverage prevents us from making a full like-for-like comparison at present. More generally, it is important to remember that the way we choose to operationalize our common notions of inequality, and how we measure this, may considerably affect the resulting picture of inequality. A focus on wealth inequality, for instance, would paint a far starker picture of the state of economic inequality, with the poorest 40% of households typically owning less than 5% of household net wealth in OECD countries (Balestra and Tonkin, 2018) and top 1% wealth shares far outstripping those of income (WIL, 2018). Available data on wealth inequality are too scarce to enable any confident statements to be made about global trends. Tentative first estimates of the global top 1% share of wealth from the *World Inequality Report* (WIL, 2018) largely mirror those presented for income, however, with rises throughout the 1980s and 1990s before flattening out in the new millennium.

Many would point out the importance of absolute differences in income, particularly in a global context, whereas in this chapter we have exclusively discussed relative inequality (Atkinson and Brandolini, 2010). In analysing survey data, Kharas and Seidel (2018) found that the incomes of those at the 5th percentile of the global distribution in 1993 grew considerably faster until 2013 than the incomes of those at the 99th percentile (see Lakner and Milanovic, 2016). This sounds considerably less progressive, however, when presented in absolute terms; such increases translate to only tens of dollars per year at the bottom of the distribution but to thousands of dollars per year at the top.

In this chapter we have given a summary of recent inequality trends, emphasizing the differences that are seen across countries and regions. We have also tried to indicate some of the limitations of the existing data and indicate where care is needed in their interpretation. Such considerations should form a background to any understanding of inequality trends, and are of particular importance to those seeking to study the interaction between economic inequality and other social phenomena, including health outcomes.

Key points

- In most advanced industrialized economies, within-country income inequality has risen since the 1980s after falling earlier in the 20th century. However, there were significant differences between countries in terms of the timing and extent of the rise.

- Globally, the picture is much more complex, with recent falls in inequality in many high-inequality countries resulting in an average Gini index today that is quite similar to that of about 1990.

- Significant rises in inequality since 1990 in several populous countries, including China, India, and the USA, mean that the average person lived in a country that had meaningful rises in inequality.

- Given several concerns about data quality and interpretation, it is important to consider multiple perspectives on inequality. In particular, figures on top income shares that incorporate tax data and national accounts are a key complement to standard Gini index estimates based on survey data alone and, in some cases, present notably less benign trends in recent years.

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CHAPTER 10.

The role of health systems in addressing inequalities in access to cancer control

Filip Meheus, Rifat Atun, and André Ilbawi

Introduction

Substantial and, in many cases, worsening inequalities exist in cancer incidence and mortality, whereby women, socioeconomically disadvantaged groups, ethnic minorities, Indigenous populations, and other vulnerable groups experience poorer outcomes (see also Chapter 6). The observed inequalities in cancer outcomes reflect the differences in lifetime exposure to risk factors, such as health-related behaviours (e.g. smoking, excessive alcohol consumption, poor diet), infections, and environmental (e.g. radiation, air pollution) and occupational exposures, as well as unequal access to cancer care.

In May 2017, the Seventieth World Health Assembly adopted Resolution 70.12 on cancer prevention and control, emphasizing the importance of addressing inequalities in access to safe, affordable, and high-quality cancer-related health services and in cancer-specific risk factors in the context of strengthening health systems (WHA, 2017). The Resolution followed recommendations by the World Health Organization (WHO) Secretariat that national cancer control programmes should build on an "effective health system, founded on the principles of universal health coverage and strong primary health care" (WHO, 2016b). Universal health coverage (UHC), whereby all people have access to

the health services they need, including preventive, promotive, curative, rehabilitative, or palliative services, of adequate quality to be effective without exposing users to financial hardship, has become an important global goal for countries to attain equitable health outcomes, founded on political commitments made in the United Nations 2030 Agenda for Sustainable Development (WHO, 2010; Kieny et al., 2017). Strong health systems, including a motivated, well-trained health workforce of sufficient capacity, are essential to achieve UHC (Sloan and Gelband, 2007; Evans et al., 2013; Kieny et al., 2017) and to meet Target 3.4 of the United Nations Sustainable Development Goals to reduce

premature mortality from noncommunicable diseases (NCDs) including cancer (UN, 2015).

In this chapter, a health systems analytical framework (Atun et al., 2013) is used to provide an overview of the main health system features that would help to address inequalities in cancer outcomes. The focus is on key issues related to access to affordable and high-quality cancer care in the context of UHC. In this analysis, access is defined as the ability to use cancer care services, and refers to the degree of fit between an individual or community and the health-care system (Penchansky and Thomas, 1981; Gilson, 2007).

First, we briefly present the analytical framework used in this chapter to analyse health systems, and its key functions and goals. We then discuss barriers to access to cancer care in terms of availability (including physical accessibility), acceptability, and affordability. After that, we consider some key features of a health system required to address inequalities in access to cancer care in the context of UHC, before providing some concluding remarks.

Health systems and cancer control

A health system consists of all actors and actions whose primary interest is to promote, restore, or maintain health (WHO, 2007). Health systems include both the delivery of health-care services and broader individual- and population-level public health interventions within the health sector and across sectors (WHO, 2008; Atun et al., 2013; see also Box 10.1). The health system framework depicted in Fig. 10.1 identifies three goals – improving health (both the level and the distribution), promoting financial risk protection, and ensuring user satisfaction (satisfaction of the population with health services) – guided by overarching principles (i.e. intermediate objectives) of equality, effectiveness, efficiency, and responsiveness (Tandon et al., 2000; Atun et al., 2013), and has many commonalities with the WHO health system framework (WHO, 2007). Health

Fig. 10.1. Health system and context. Source: reprinted from Atun et al. (2013), copyright 2013, with permission from Elsevier.

The context

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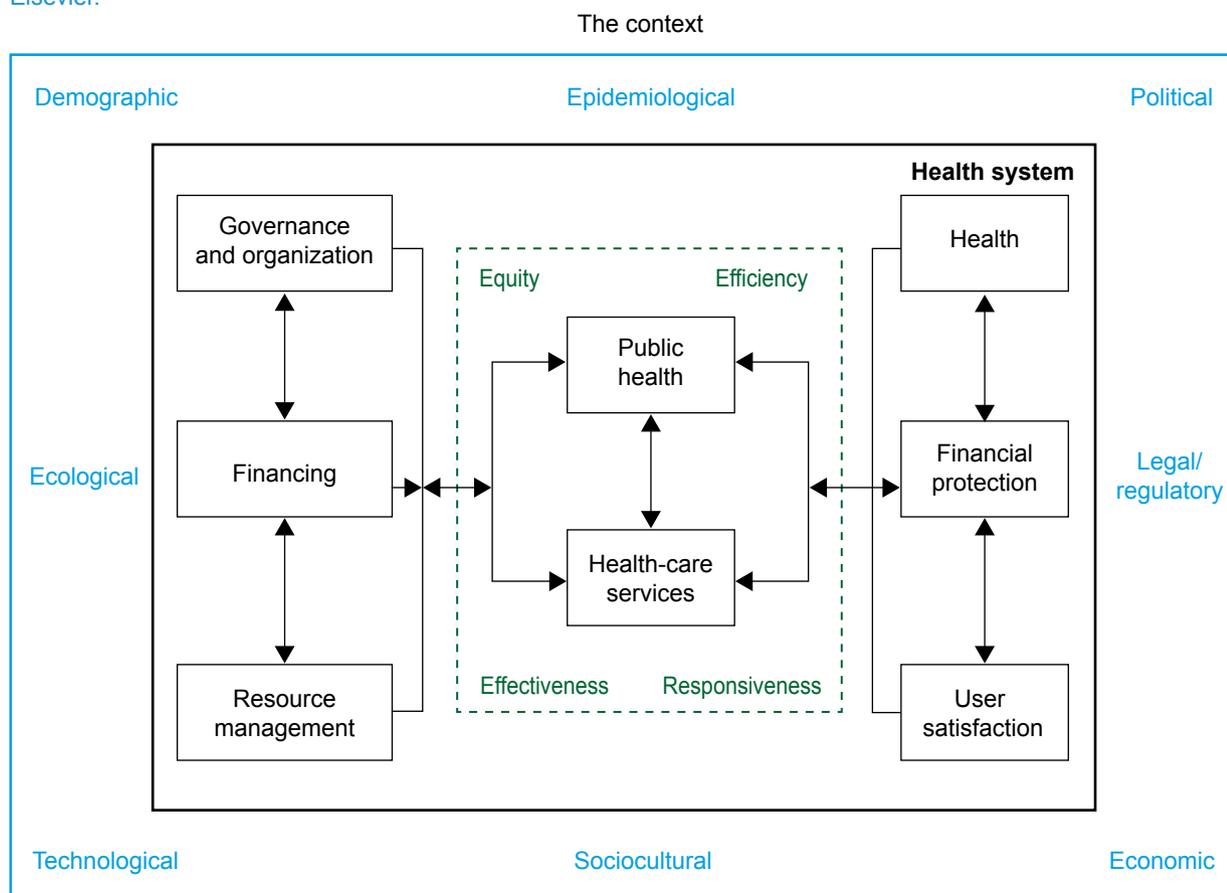
Box 10.1. Health system functions in relation to cancer care. Source: compiled from Atun and Menabde (2008) and Atun et al. (2013).

- *Governance and organization:* governance of cancer care systems and regulatory environment, including national cancer policies, programmes, and targets; development of evidence-based guidelines and quality management for the integrated management of cancers; workforce policies; intersectoral action; community participation and feedback

- *Broader health financing policies:* how funds are collected and pooled; costing (and budgeting) of the national cancer control programme

- *Resource management:* how pooled funds are allocated to health providers (purchasing); what services are provided (priority setting and health technology assessment); development of human resources, capital investments, and equipment

- *Service delivery:* population- and individual-level public health interventions and health-care services provided within the community; primary health care; hospitals and other health institutions

programmes and interventions for cancer are delivered through health systems to achieve these goals, and thereby influence the cancer incidence and mortality of various subgroups within the population (Mills and Ranson, 2006).

To achieve the overall goals of a health system within a given set of contextual factors, it is important to consider the broader political economy context within which it is embedded, as well as demographic, economic, political, legal, social, environmental, and technological factors, which can interact to influence health system functioning and the attainment of these goals (Atun and Menabde, 2008). Health systems are now understood as complex adaptive systems that exhibit properties of self-organization and nonlinearity (Paina and Peters, 2012). This complexity and the broader context may enable or disable efforts to implement and scale up cancer control activities.

Over the past decade, there have been many efforts in the field of

health systems research to develop methods to understand health systems and/or their performance, acknowledging that the health system is a complex system (De Savigny and Adam, 2009; Gilson, 2012). Comparisons of cancer outcomes between settings reveal the significant potential of high-performing health systems to advance the health of an entire population (Barber et al., 2017). Studies have consistently shown the central prominence of a highly functional health system in the attainment of cancer-related goals. For example, a report produced by the Organisation for Economic Cooperation and Development (OECD) ("Cancer care: assuring quality to improve survival") found an almost 4-fold difference in cancer survival rates among OECD countries, attributed to differences in health system capacity, functions, or governance (OECD, 2013). The performance of the health system can explain differences in health outcomes between countries and subpopulations, and should be examined to strengthen

the scientific foundations of health policy at the international and national levels (Barber et al., 2017).

Why are health systems relevant to cancer prevention and control? Historically, health systems interventions in cancer prevention and control have focused on population health, that is, strategies to mitigate cancer risk factors. The objective of these interventions has been to realize the potential of cancer prevention to avoid 30–50% of incident cancer cases through population health interventions, such as tobacco control measures, and general improvements in living conditions that can reduce the burden of select infection-related cancers (Fitzmaurice et al., 2017). Successful population health interventions generally mandate intersectoral action with shared objectives.

In addition to public health, a core function of health systems is health service provision, that is, to care for individuals who develop cancer or precancerous lesions by providing high-quality services across the care continuum in an effective, efficient, equitable, and responsive way to improve their health while ensuring financial protection and user satisfaction. However, all too often, in most health systems current service provision for cancer care is inefficient, inequitable, and fragmented, resulting in a substantial number of avoidable deaths and disability, especially in low- and middle-income countries (LMICs) (Farmer et al., 2010; Knaul et al., 2013; Atun et al., 2015). Indeed, in LMICs services are often unavailable, population coverage is low, and financial catastrophe is all too common. A fundamental shift in the way health services are funded, managed, and delivered is needed to progress towards UHC,

which can help protect outcomes for those with cancer even in times of economic downturns (Maruthappu et al., 2016).

Impact of health system performance on cancer outcomes

Karanikolos et al. (2013) identified three mechanisms through which health systems influence cancer outcomes: coverage and access to cancer care, innovation, and quality of care. Innovation or access to technology is discussed in detail in Chapters 16 and 18; here, we focus on issues related to access to and quality of cancer care.

Inequalities in access to cancer care between and within countries are well demonstrated. Individuals with low incomes, ethnic minorities, Indigenous populations, and other socioeconomically disadvantaged groups face considerable barriers to accessing needed cancer services in LMICs as well as in high-income countries (HICs) (see Focus 5 and Focus 7). The ability to obtain and use the needed health services is associated with both demand-side barriers, which deter individuals, households, and communities from accessing services, and supply-side barriers, with services that are either not available or not of sufficient quality to be effective (e.g. because of shortages in the health workforce and in the supply of medicines). Inequalities in accessing cancer care begin at the earliest stage, from the onset of symptoms, and exist throughout the care continuum, from symptom awareness to accessing treatment and receiving palliative care (Knaul et al., 2018).

Delays in diagnosis, resulting from prolonged duration in the presentation, diagnosis, and/or treatment in-tervals, are often associated with education level, socioeconomic status (SES), ethnicity, rural residence, and other risk factors (Freitas and Weller, 2015; WHO, 2017a; McKenzie et al., 2018). In LMICs, the stigma and discrimination that is still associated with cancer may further delay care-seeking, diagnosis, and treatment (Knaul et al. 2012a). Studies in multiple settings have reproduced these findings, which highlight the failures in health systems to promote health and early diagnosis for certain populations. A systematic review of delays in breast cancer diagnosis in LMICs found consistent evidence that certain demographic, sociocultural, and economic factors contribute to presentation delays (Sharma et al., 2012). Failure to diagnose cancer in a timely manner is generally associated with lower survival rates and worse overall outcomes (Neal et al., 2015).

Disadvantaged groups are also less likely to access any type of treatment; the geographical accessibility and availability, affordability, and acceptability of health services contribute to low rates of effective coverage for cancer patients (Fig. 10.2) (OECD, 2013; Ambroggi et al., 2015; Niessen et al., 2018). Geographical accessibility is particularly relevant in cancer care; across many settings and countries, it has been noted that the further a patient lives from a cancer treatment centre, the greater the delay in diagnosis and/or the more advanced the stage of disease at diagnosis (Galukande et al., 2014). In South Africa, a study of the association between distance to a hospital and stage of breast cancer at diagnosis showed that women living

Fig. 10.2. Common factors that influence equitable access to cancer care. The barriers to access are categorized according to typology proposed by McIntyre et al. (2009). Source: compiled from McIntyre et al. (2009).

Broader health system factors such as the political and economic context as well as individual and household characteristics (poverty, vulnerability, marginalization)	
Availability	Physical accessibility of cancer treatment centres
	Weakness of referral systems
	Shortage of cancer specialists and inadequate geographical distribution
	Lack of equipment and infrastructure
	Lack and shortage of drugs and medical supplies
	Poor communication between providers and patients
Affordability	Inability to pay for the costs of care
	Transportation costs
	Income and productivity losses
	High co-payments and inadequate coverage from the costs of care among insured
Acceptability	Beliefs and perceptions about effectiveness of cancer services
	Respectful treatment by health providers
	Inappropriate training of health workers adapted to social and cultural needs of people
Access to cancer services	

more than 20 km from the hospital were more likely to present with late-stage cancer at diagnosis (Dickens et al., 2014). Longer distances to health-care facilities have also been shown to affect the appropriateness of and adherence to treatment, and to negatively affect quality of life (Ambroggi et al., 2015).

Poor geographical accessibility is compounded by a general lack of available services, particularly in LMICs. Data from the WHO NCD Country Capacity Survey have shown that, in approximately three quarters of low-income countries and half of lower-middle-income countries, basic cancer diagnostic and treatment services are not generally available (WHO, 2016a). An insufficient number of available diagnostic and treatment centres results in long waiting times and is often compounded by low-quality care (Dare et al., 2015). Poorly delivered cancer care results in worse overall outcomes for those affected, thereby subjecting vulnerable subpopulations to the costs and harms of cancer care without the benefits. The underlying causes of low-quality services vary between settings but have been attributed to shortages of human resources, poorly trained or low-volume providers, an inadequate supply of drugs, and a lack of equipment, among other factors (Sullivan et al., 2015). For cancer, as with many other conditions, there is a volume–outcome correlation for both providers and facilities: the higher the volume of services, the more likely a cancer patient is to have a successful outcome (generally until a threshold is reached) (de Cruppé et al., 2015; Sullivan et al., 2015). Accordingly, health systems are generally organized to achieve efficiencies; recognizing that centralizing services can

also improve outcomes must be balanced against over-centralization, which can negatively affect other desirable outcomes, such as equality and user preferences. Inequalities then arise when certain subgroups, generally those living in urban centres or those with higher SES, have access to high-volume centres with highly trained providers and appropriate equipment (Massarweh et al., 2011; Yun et al., 2012; Sun et al., 2014; Wasif et al., 2016).

In addition to ensuring equality, efficiency, and effectiveness, health-care services must also be person-centred and acceptable. In practice, however, and in most settings, cancer treatment decisions are not sufficiently informed by user preferences or oriented around the person. Effective communication with patients plays a particularly important role in cancer management, because of the complexity of decisions about the risks, benefits, and uncertainties of treatment. The conversation-recall and critical-thinking ability of patients may be further affected by the general fear and anxiety that accompanies a cancer diagnosis (Sanders et al., 2018). Studies have consistently shown failure in communications (Miller et al., 2014), whereby sociodemographic factors, such as income, education level, and race, influence the amount of time that physicians spend communicating with patients (Siminoff et al., 2006). For example, in the USA, most patients who receive cancer treatment for metastatic cancer believe that the treatment is being given with curative intent; in reality, however, it is being given to extend the quality and quantity of life or for palliative care (Weeks et al., 2012). Communication between cancer patients and their health-care pro-

viders is further compromised by the fragmentation of services and the number of providers. In one study in Canada, a cancer patient saw a median of 32 providers over the course of their treatment (Smith et al., 1999).

Cultural factors and the attitudes of health providers and patients have consequences for the type of care and support that patients receive. Substantive research has shown that, compared with groups with high SES, groups with low SES are more likely to receive more aggressive treatment, for example, mastectomy rather than breast conservation (Liu et al., 2012), permanent stoma without reconstruction (Averyt and Nishimoto, 2014), and laryngectomy rather than larynx preservation therapy (Hou et al., 2012), without post-treatment survivorship care or psychosocial support. Sociodemographic characteristics also influence the likelihood of initiating and completing therapies, and these characteristics of both patients and health-care professionals can have a profound effect on the acceptability of cancer services (Chaturvedi et al., 2014). Social exclusion and marginalization can further negatively affect both the care received and the decision to pursue care (Quinn et al., 2015).

Beyond accessibility, effectiveness, efficiency, equality, and patient-centredness of services, which can all affect health outcomes, lack of financial accessibility or affordability has been found to be a major barrier to accessing cancer care services. The costs of cancer care can have a considerable economic impact on individuals (and their health, because of barriers to access and interruption to treatment) and their households, leading to catastrophic health expenditures that either push families

into poverty or lead to further impoverishment. There is ample evidence showing the profound impact of out-of-pocket payments for medical expenses. For example, using data from 553 household surveys covering 133 countries, Wagstaff et al. (2018a) found that about 12% of the world's population (nearly 810 million people) incurred catastrophic health expenditures in 2010, with out-of-pocket payments exceeding 10% of total household expenditure. In 2010, nearly 100 million people were impoverished as a result of out-of-pocket spending on health (Wagstaff et al., 2018b). The evidence is more limited for cancer specifically, in particular in LMICs. A recent systematic review by Jan et al. (2018) examined the economic burden of NCDs, including cancer, in LMICs. They found that the incidence of catastrophic health expenditures was highest for cardiovascular diseases, followed by cancer, and "consistently higher" in low-income groups. Being uninsured was associated with a 2–7-fold higher odds of catastrophic out-of-pocket expenditures (Jan et al., 2018). In the Association of Southeast Asian Nations region, a cohort study that followed up newly diagnosed cancer patients for 12 months showed that after 1 year, 48% of households had incurred catastrophic expenditures, with a much higher odds of catastrophic expenditure among those in lower-income groups (Kimman et al., 2015).

The economic burden of cancer is not limited to payments for direct medical costs; direct non-medical costs, such as transportation costs, as well as indirect costs, such as loss of income and costs associated with various coping strategies (e.g. borrowing money to cover the costs of care), negatively affect the economic well-being of a household. For example, in the Democratic Republic of the Congo, Guinea, and Madagascar, not having to pay for the costs of transportation reduced the proportion of patients not attending for surgery by 45% (Shrime et al., 2017). In addition to out-of-pocket costs, financial barriers to cancer care have also been found to lead to a lower uptake of preventive health services, delays in diagnosis or seeking treatment (Freitas and Weller, 2015; McKenzie et al., 2018), and failure to initiate treatment or the premature discontinuation of treatment (e.g. Arora et al., 2007; Israëls et al., 2008; Jan et al., 2015).

Within the wider context of global equality in cancer care, there are also major disparities between countries. Less than 25% of the global population has access to basic, high-quality cancer surgery (Sullivan et al., 2015). Similarly, only 40–60% of patients with cancer are estimated to have access to radiotherapy services (Atun et al., 2015). In approximately three quarters of all low-income countries, the majority of the population generally has no access to basic cancer diagnostic and treatment services or palliative care (WHO, 2016b). It is from these profound disparities in health system capacity that greater inequalities emerge. The few people who are able to receive cancer care in LMICs are typically from the most privileged subpopulations; for most people, services are inaccessible. This global inequality is far too great and cannot be ignored. For specific cancer types, such as childhood cancers, survival can be greater than 80% in high-resource settings and less than 20% in low-resource settings (Gupta et al., 2015; Howard et al., 2018). This cancer di-vide in outcomes is one of the largest inequalities known in health service provisions (Knaul et al., 2012a).

Which health system strategies promote equality in cancer care? An overview of key policy issues

The response to cancer requires an integrated and coordinated effort across the continuum of care, from prevention and early detection to diagnosis, treatment, survivorship, and palliative care; effective action is needed across the different functions of the health system to reduce inequalities and achieve UHC. Several middle-income countries, such as Mexico, Thailand, and Turkey, have demonstrated that progress towards UHC with the inclusion of cancer interventions in their health benefits package is possible (Knaul et al., 2012b; Atun et al., 2013). Generally, to move towards UHC, countries need to consider three interrelated elements corresponding to the three dimensions of coverage depicted in the UHC cube and used in the *World Health Report 2010* (Fig. 10.3): (i) financial protection, by reducing the reliance on out-of-pocket payments in favour of mandatory pre-payment mechanisms; (ii) service coverage, by gradually expanding services from pooled resources, starting with essential services that are of good quality; and (iii) population coverage, by ensuring equality in access to services whereby everyone is covered (WHO, 2010, 2014). To ensure an equitable approach towards UHC, progressive realization of UHC should be adopted whereby the poor and disadvantaged are prioritized or benefit as much as others as countries progress towards UHC (Gwatkin and Ergo, 2011; Jamison et al., 2013).

Fig. 10.3. Dimensions to consider when moving towards universal health coverage. Source: reproduced from WHO (2010).

of their income compared with higher-income groups (Whitehead et al., 2001; Mills et al., 2012). In the few countries where out-of-pocket payments were found to be progressive (e.g. some countries in the Asia-Pacific region), this was likely due to lower-income groups not using services because they could not afford them (O'Donnell et al., 2008).

To improve access to health services while providing financial protection, countries need to expand mandatory pre-payment financing mechanisms based on ability to pay, pool risks to the greatest extent possible, and eliminate out-of-pocket payments at the point of service use. Both mandatory pre-payment and risk pooling are essential to provide financial protection and ensure cross-subsidization of risks (between high- and low-risk individuals) and income (between rich and poor), and can be achieved by increasing domestic resource mobilization through taxation or other government revenue, and/or by introducing mandatory health insurance. These are also the most progressive ways of financing the health system and increasing population coverage (Fig. 10.5) (Mills et al., 2012). Generally, most LMICs are not spending enough on

Countries face several challenges in their quest to achieve UHC and to provide effective, efficient, equitable, and responsive cancer services. Five health system strategies are proposed to promote equality in cancer care while advancing attainment of UHC (Fig. 10.4). The first strategy relates to the financing of health services. How the health system is financed will be different between countries, but recent contributions have shown the importance of progressive domestic public resources, in particular tax-based funding, to progress towards UHC (Moreno-Serra and Smith, 2015; Reeves et al., 2015). In many countries, in particular LMICs, out-of-pocket payments are still a large share of total health-care expenditure and are an important source of financing for the health system. For example, out-of-pocket payments in low-income countries are twice as high as those in HICs (40% vs 20%) (WHO, 2018). Generally, out-of-pocket payments are a regressive source of financing, with lower-income groups contributing a disproportionately higher share

Fig. 10.4. Sample health system strategies to improve access to cancer prevention and control programmes through universal health coverage.
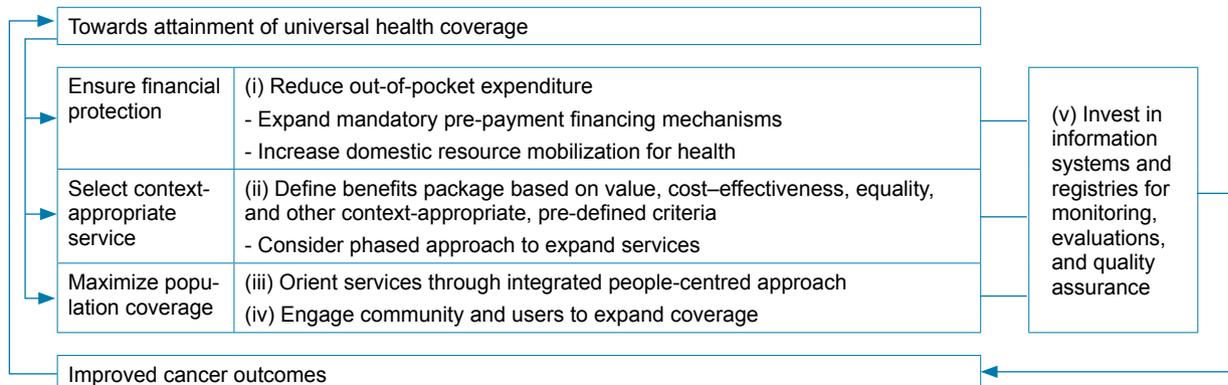
health. The Centre on Global Health Security Working Group on Health Financing suggested that countries should strive for domestic government funding for health services to be at least 5% of gross domestic product (Chatham House, 2014; Mcintyre et al., 2017); in 2015, funding for health services amounted to 1.3% in low-income countries, 2.9% in middle-income countries, and 7.8% in HICs (WHO, 2018). However, these or other proposed spending targets (such as the estimates of the High Level Task Force on Innovative Financing for Health Systems) will not raise sufficient resources in low-income countries, and external support will still be needed to finance an essential package of interventions, including cancer care (Gelband et al., 2016).

The second important strategy relates to which services should be included in the benefit package. This should be informed by transparent priority-setting processes based on considerations of cost–effectiveness, budget impact, and equality that maximize population health but also include vulnerable and underserved populations from the start (Gwatkin and Ergo, 2011; WHO, 2014). The benefit package should be sufficiently comprehensive with no or limited co-payments to minimize out-of-pocket expenses relative to income. This is even a concern in

HICs, where the financial burden of cancer can still be severe because of limited coverage, high co-payments, and/or high deductibles for insured individuals (Ubel et al., 2013; Zafar et al., 2013). For low-resource settings, a phased approach to the expansion of cancer services will be needed; priority should initially be given to essential, cost-effective, and good-quality cancer services. Several countries have established systems of health interventions and technology assessment to inform the setting of priorities and the formulation of sustainable benefit packages, such as the Health Information and Technology Assessment Programme in Thailand. Several other initiatives have also provided guidance on essential packages of health services for NCDs and cancer that countries can implement according to their level of resources, including the WHO list of "best buys" (WHO, 2017b) and the Disease Control Priorities Project (Gelband et al., 2016).

The third strategy relates to the delivery of responsive and person-centred cancer services and the use of evidence-based standards of care. When UHC policies are implemented, strong emphasis should be placed on an integrated approach, with a particular emphasis on the primary health care level. For most cancer patients, primary health care is the first point of entry to the entire

health system. Primary health care therefore has an essential role in organizing health services, in promoting prevention and early diagnosis, improving cancer screening uptake, informing treatment decision-making, and providing end-of-life care (Rubin et al., 2015). Providers must be enabled to identify cancer symptoms, have established referral mechanisms for diagnosis and treatment, and remain engaged to promote continuity of care and support decision-making. Countries need a sufficient and appropriately trained health workforce to ensure delivery of health services in general and of cancer care in particular, a major resource constraint in LMICs. However, having the required health workforce capacity and simply providing access to cancer services is not sufficient; these services also need to be effective and of good quality. It has been estimated that improving the quality of existing health services could prevent millions of deaths from cancer, and it is essential to improve cancer outcomes (Dare et al., 2015). Health systems must therefore be enabled, though governance, organization, and resource management, to provide the highest attainable quality.

Multiple frameworks exist to define domains of quality and implement quality strategies in health services (WHO, 2006). Fundamentally, approaches should be tailored to a specific context and health system; there is no one-size-fits-all approach. Wide variations in standards of health-care delivery exist within and between health-care systems. However, quality strategies are relevant in all settings and should be prioritized to include national policies and quality assurance programmes, regulatory or administrative agencies, clinical guidelines and

Fig. 10.5. Progressivity of financing mechanisms.

Source of funding	Extent of pooling	Progressivity
General tax	+++	
Hypothecated tax (flat)	++	
Social insurance	++	
Private insurance	+	
Out-of-pocket payments	−	

standards, health workforce training and certification programmes, and strengthening information systems and monitoring outcomes with a focus on equality by disaggregating relevant data (Dare et al., 2015; Ghebreyesus, 2018). For example, the development of evidence-based standards in cancer has resulted in significant improvements in cancer outcomes. Data from HICs have demonstrated that centres that have cancer treatment guidelines and that adhere to these guidelines deliver better care, resulting in improved outcomes for the populations served (Boland et al., 2013; Kuehnle et al., 2017). Multidisciplinary tumour board services also have the potential to improve cancer outcomes, but there is variable participation, particularly among vulnerable subpopulations (Lawrenson et al., 2016). In settings where cancer and other health-care services are less well developed, an emphasis on quality is particularly relevant to rapidly scale up capacity, optimize resource use, and expand population coverage (WHO, 2006). Centralization of services must be balanced against equality, enabling people to receive care closer to their homes and thereby reducing indirect costs and facilitating timely care. Community outreach and engagement can help to reduce barriers to care, improve health literacy, and empower patients in decision-making (Hahlweg et al., 2017).

The fourth strategy relates to effective user engagement in the design and delivery of person-centred cancer services. For improved equality in cancer care, the health system must be oriented around the individual rather than around the disease (WHA, 2016). Communities should be empowered and engaged through interventions such as peer support groups and patient navigators, who can facilitate access to and reduce delays in receiving care, particularly for marginalized communities (Gervès-Pinquié et al., 2018). Promoting participatory decision-making is an important principle of integrated, people-centred health services. Treatment guidelines are important to inform health-care providers about the best available treatment, but they generally fail to consider patient preference and are often not designed for informed, participatory decision-making (Chong et al., 2009; OECD, 2010; Institute of Medicine, 2011; Mead et al., 2013). Care planning across the service delivery continuum, from primary care to specialty care, should be prioritized, particularly for subpopulations who are non-native speakers or with lower SES and/or lower education level. To achieve patient-centred health systems, mechanisms to incorporate patient preferences and to assess health-care quality should be established, such as the use of patient-reported outcomes (Kruk et al., 2018; National Academies of Sciences, Engineering, and Medicine, 2018) as recently recommended by OECD (2017).

The fifth strategy relates to the availability and use of data for decision-making. Most health systems have limited data on cancer, especially in relation to outcomes. For example, in a recent global study on cancer survival, only 71 countries and territories had cancer registries that could be used to estimate 5-year net cancer survival. Of these, only 47 could provide data with 100% population coverage (Allemani et al., 2018). Few data exist in LMICs on the equality, efficiency, effectiveness, and responsiveness of the cancer services provided; this critical information is necessary to inform not only what services are provided but also how these services should be provided and to whom, and would enable health systems to truly fulfil their potential to improve cancer outcomes and reduce inequalities.

Conclusions

The effective implementation and expansion of cancer prevention and control interventions require an appropriate understanding of health systems and their interrelated functions. In this chapter we have briefly summarized some of the barriers that countries face and methods to address these, including raising appropriate financing of health systems, ensuring financial protection, providing person-centred cancer services, and improving infrastructure and information and data systems. Health systems have an important role to play in promoting health equality by ensuring that every patient has access to high-quality cancer services throughout the care continuum from prevention and early detection to diagnosis, treatment, survivorship, and palliative care. Equality is also a crucial dimension of UHC, in terms of both financial protection and service coverage. When moving towards UHC, it is essential that service coverage is provided across the social gradient. This may involve initially focusing on a limited number of high-priority health services (including cancer-related health services), for which high coverage of the entire population at risk can be achieved.

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CHAPTER 11.

The economics and control of tobacco, alcohol, food products, and sugar-sweetened beverages

Evan Blecher and Melanie Bertram

Introduction

Tobacco use, alcohol consumption, and high body mass index (BMI) are major risk factors for many noncommunicable diseases (NCDs) and injuries, including cancers.

Tobacco use is responsible for 7 million deaths per year (WHO, 2017b), including 1.5 million from cancer (Lim et al., 2012). Of the 1 billion smokers worldwide, 80% are located in low- and middle-income countries (LMICs), where often the health system does not have the capacity to treat smoking-related diseases. Alcohol consumption is responsible for 3.3 million deaths per year (GBD 2016 DALYs and HALE Collaborators, 2018), including 337 000 from cancer (Stewart and

Wild, 2014). Mortality due to alcohol is affected both by the total volume consumed and by the pattern of drinking, and higher levels of harm are seen in men than in women. Excess calorie intake, including through consumption of sugar-sweetened beverages (SSBs) and calorie-dense foods, combined with low levels of physical activity, contribute to a high BMI. Overweight and obesity are responsible for 2.8 million deaths per year; currently, 1.9 billion adults and almost 400 million children are overweight or obese. The prevalence of overweight and obesity is rapidly increasing in LMICs.

In 2016, tobacco use, alcohol consumption, and high BMI were responsible for 7%, 4%, and 6%, respectively, of all disability-adjusted

life years lost (GBD 2016 Risk Factors Collaborators, 2017). Of all disability-adjusted life years lost due to cancer, tobacco use was responsible for 20%, alcohol consumption for 7%, and high BMI for 5%. Given that 40% of all disability-adjusted life years lost due to cancer were explained by the sum of the most important known risk factors, these three risk factors are by far the most important modifiable risk factors to modulate to prevent cancer (GBD 2016 Risk Factors Collaborators, 2017).

The use of tobacco and consumption of alcohol and SSBs generate costs that are not borne by the consumer but rather by others. These negative externalities include exposure to second-hand smoke and injuries and deaths as a result of

alcohol-related road traffic accidents, violence, and fetal alcohol syndrome. Because of these externalities, the market price paid by the consumer does not reflect the true cost and thus a market failure occurs, which creates an economic motivation for intervention in the market. In addition to the market failure related to price, there are also information market failures in that consumers often poorly understand the health consequences of the use of tobacco or consumption of alcohol or SSBs, which are exacerbated when use or consumption is initiated at a young age or if the product is addictive. Furthermore, in many places where there is significant public funding for health care, a financial externality occurs as public finances are applied to treat illnesses resulting from the use of tobacco or consumption of alcohol or SSBs.

The most common and powerful economic policy intervention used to correct negative externalities is taxes. Taxes increase prices so that the price paid by consumers internalizes these costs, thereby ensuring the price paid by consumers fully accounts for externalities. Such a tax is referred to as a Pigouvian tax. Furthermore, increased prices reduce consumption and also raise revenue for the government. Historically, the role of taxes on these commodities has been to generate revenues because they are relatively price inelastic (see the "Price elasticity of demand" section below), have a small number of substitutes, and are produced by a small number of firms.

Economists consider the demand for a product to be a function of price (of the product itself as well as of substitutes and complements

in consumption), income, tastes, and preferences. Demand is modifiable through policies that influence these variables. For example, increases in taxes that increase the price of the product reduce demand, as does banning advertising. Increasing knowledge of the health effects through warning labels adjusts preferences and therefore reduces demand.

Between- and within-country variations in use

Various definitions of smoking prevalence exist, including current or daily tobacco smoking or cigarette-only smoking. Adult prevalence generally relates to those 15 years and older. Fig. 11.1 shows the current prevalence of smoking of all tobacco products, that is, the broadest definition,

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Fig. 11.1. Adult smoking prevalence by World Bank income group. Red, high-income countries; blue, low- and middle-income countries. Source: compiled from WHO (2014b).
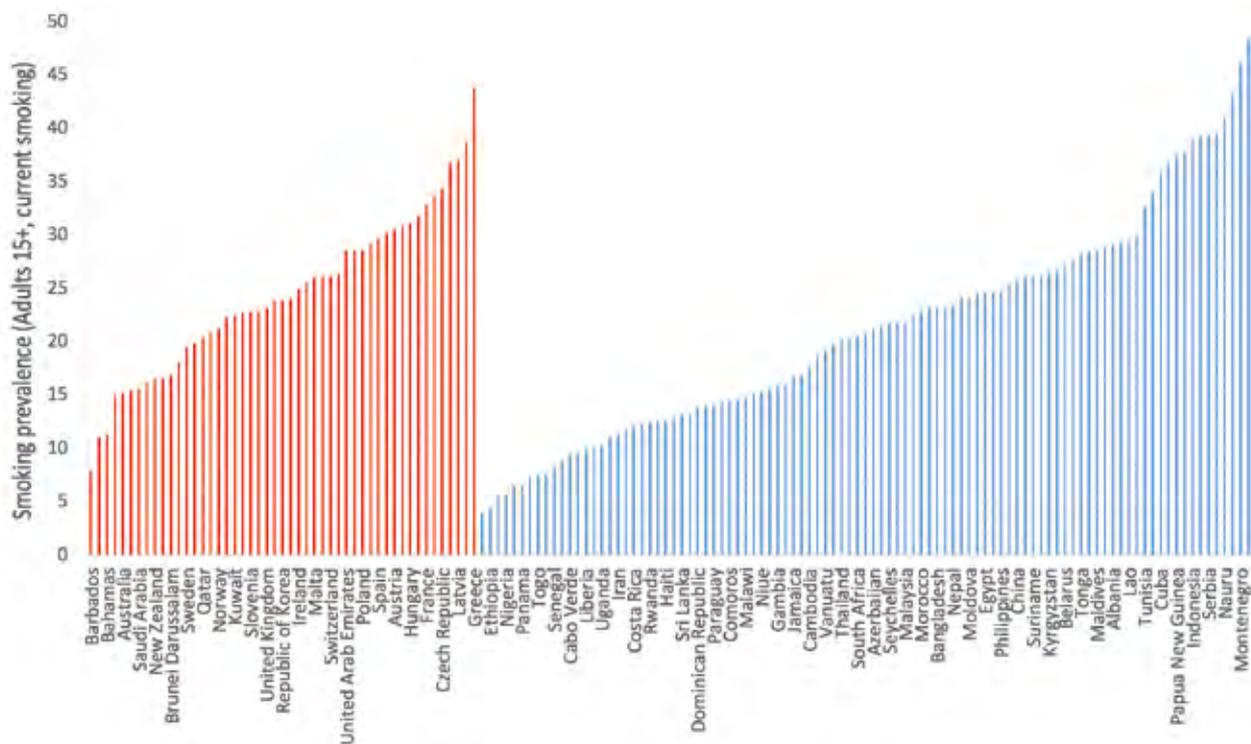
for the most recent year. Large between-country variations in smoking prevalence exist, but without a clear gradient between countries at different levels of socioeconomic development; being a high-income country (HIC) or LMIC is a poor predictor of whether a country has a low or high prevalence of smoking. However, significant variation in tobacco use and a strong socioeconomic gradient exist within countries. For example, Hosseinpoor et al. (2012) found that the poorest men were more than 2.5 times as likely to smoke as the richest men, and, in 42 of 48 countries, the poorest men had a higher smoking prevalence than the richest men. Results among women were more mixed; the poorest women had a higher smoking prevalence than the richest women in only 31 of 48

countries. Using similar data but a different methodology, Harper and McKinnon (2012) found that wealthier men were less likely to be current smokers in 47 of 50 countries (see also Example 1). Results for women also showed greater variation.

This link to income extends to poverty. John et al. (2012a) reported that tobacco use was significantly higher among those living in regions of higher poverty and lower education in Ghana, and higher tobacco use was associated with a lower probability of purchasing health insurance. In Cambodia, expenditure on tobacco was found to crowd-out expenditure on education. Because a higher education level was associated with a reduced frequency of daily smoking, a vicious circle was created: a lower education level led to increased

smoking, which, in turn, led to lower spending on education (John et al., 2012b).

Wide variation in alcohol intake is also seen across countries, with the highest consumption levels seen in the World Health Organization (WHO) European Region (average, 10.9 L per person per year) and the lowest in the Eastern Mediterranean Region (average, 0.7 L per person per year) (WHO, 2014a). Across all settings, men are more likely to consume alcohol than women are, and the amount of alcohol consumed by those who drink is higher for men than for women.

Alcohol intake is generally associated with increased national wealth; the population in more developed economies is more likely to consume alcohol, is at risk of a higher prevalence

Fig. 11.2. Proportion of population who have abstained from the consumption of alcohol within the past 12 months, by World Bank income group. Red, high-income countries; blue, low- and middle-income countries. Source: compiled from WHO (2014b).
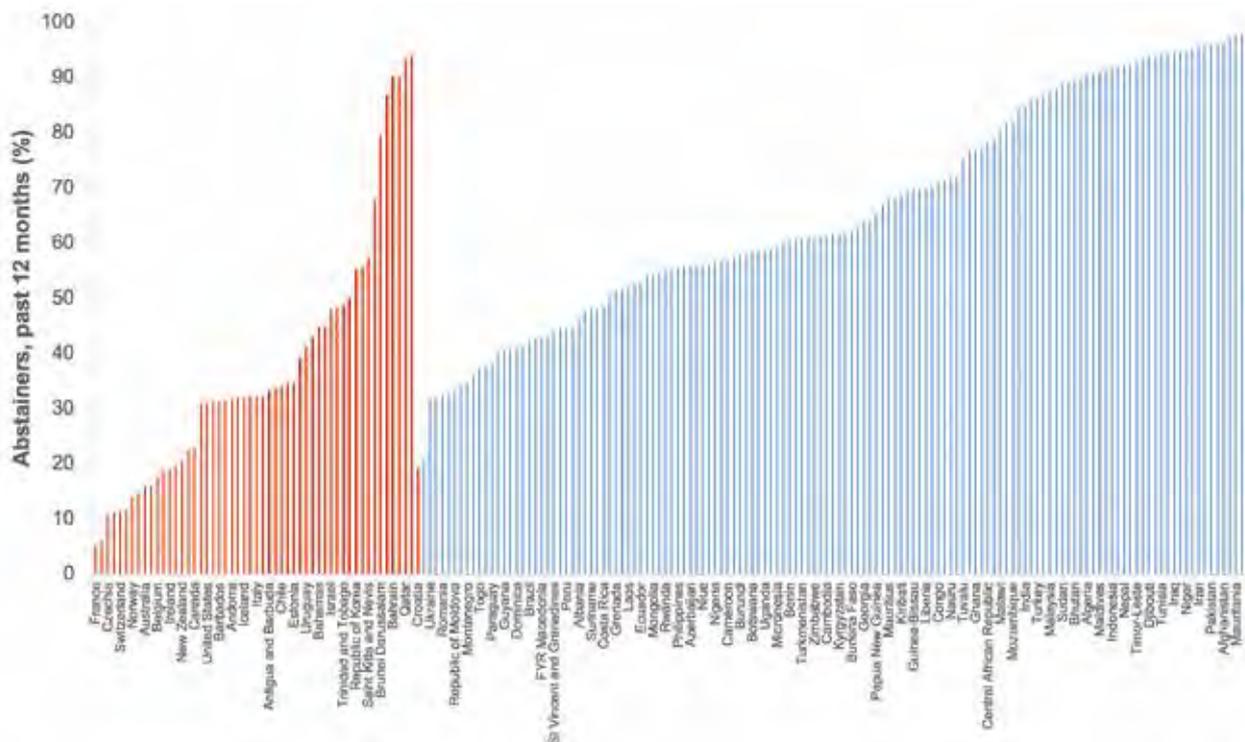
Fig. 11.3. Proportion of population who have undergone periods of heavy episodic drinking within the past 12 months, by World Bank income group. Red, high-income countries; blue, low- and middle-income countries. Source: compiled from WHO (2014b).
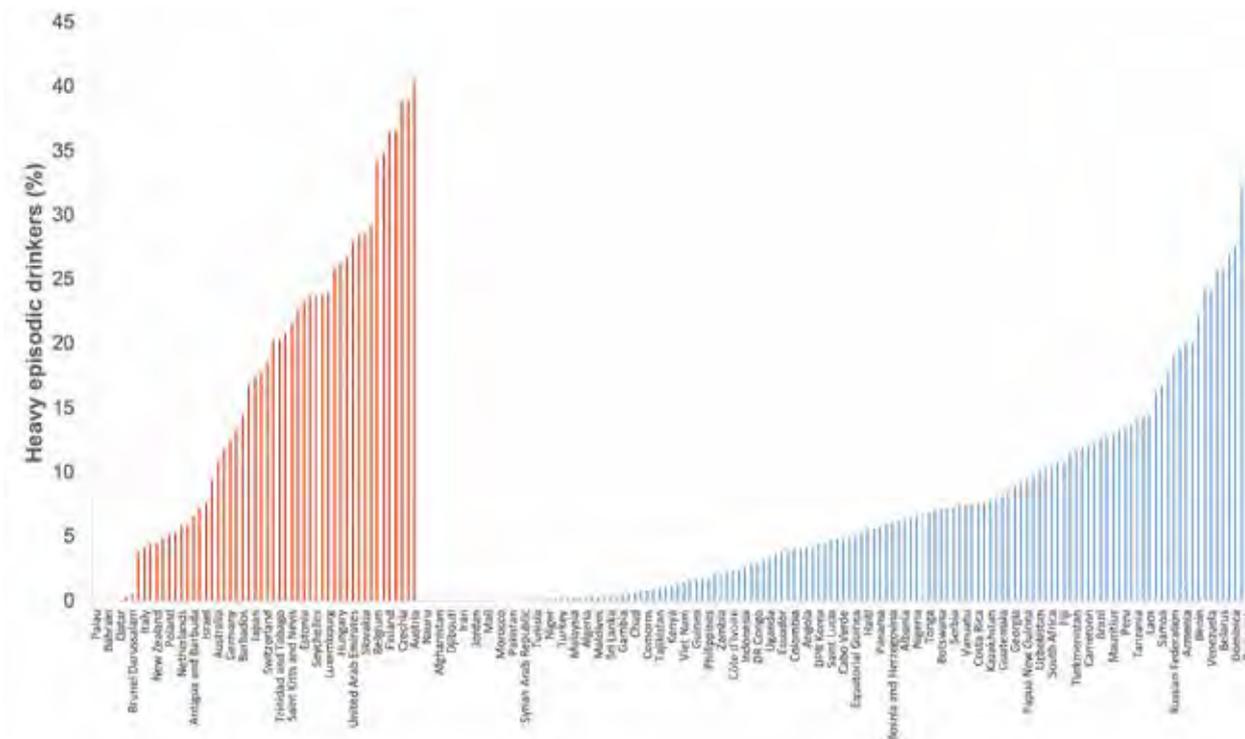
of heavy episodic drinking, and has the lowest numbers of abstainers. Fig. 11.2 displays the proportions of populations who abstain from alcohol consumption, and Fig. 11.3 depicts the proportions who partake in heavy episodic drinking (WHO, 2014b). Although significant within-group variation exists, abstinence is higher in LMICs and declines as gross domestic product (GDP) increases.

Within countries, differences in drinking patterns by socioeconomic status (SES) are complex. People with higher SES are more likely to participate in heavy episodic drinking (the intensity of drinking is important because there is a dose–response association between alcohol consumption and health consequences, including cancer; Stewart and Wild, 2014). However, those with lower SES who engage in heavy episod-

ic drinking do so more frequently than those with higher SES (Collins, 2016), meaning that those with lower SES are more vulnerable to the health consequences of alcohol consumption (Grittner et al., 2012). In addition, adult unemployment has been associated with increased alcohol use, with higher levels of alcohol misuse diagnosed in people who have experienced unemployment within the previous year (Bryden et al., 2013; Popovici and French, 2013).

Having low SES is a risk factor for alcohol-related mortality; lower SES leads to a 1.5–2-fold increase in mortality for alcohol-attributable causes compared with all causes (Probst et al., 2014; see also Chapter 7).

For the purposes of this chapter, SSBs are defined as all types of beverages that contain free sugars (monosaccharides and disaccharides

added to foods and beverages by the manufacturer, cook, or consumer, and sugars naturally present in honey, syrups, fruit juices, and fruit juice concentrates) (WHO, 2015). SSBs include carbonated or non-carbonated soft drinks, fruit or vegetable juices and drinks, liquid and powder concentrates, flavoured water, energy and sports drinks, ready-to-drink tea and coffee, and flavoured milk drinks. Unlike for tobacco use and alcohol consumption, no global database exists on SSB consumption. Individual countries are able to estimate SSB consumption from food intake surveys, but at the global level sales data or modelled estimates, such as those from the Global Burden of Disease Study, are the best sources available (GBD 2016 DALYs and HALE Collaborators, 2018). There is some indication that SSB consumption increases

with the wealth of a country; however, consumption can be very high even at very low per capita GDP values (Euromonitor International, 2018). Limited information exists with which to accurately assess within-country variations in SSB consumption.

Affordability

Tax policy has long been considered the most effective tool to reduce the demand for a product through increases in prices. However, as attention has shifted to rapidly growing LMICs, increasing prices may not be sufficient to reduce demand; incomes are growing more rapidly than prices are increasing. As a result, attention has been shifting to the affordability of products. Affordability is most commonly defined as the ratio of price to income, and several different measures of affordability – based on the narrowest to the broadest measures of income – are described in the following.

Blecher and van Walbeek (2009) have published the longest (1990–2006) analysis of between-country affordability of cigarettes. They used the relative income price, defined as the percentage of GDP required to purchase 100 packs of the cheapest brand of cigarettes. Although this method used a broad measure of income, it was nevertheless able to measure affordability annually in the largest number of countries, particularly LMICs, over the longest period of time. However, relative income price is unable to take into account within-country inequalities in income and price variation. They found that although cigarettes are more affordable in HICs, they have become less affordable since 1990, and at an ever increasing rate since 2000. In nearly all countries where cigarettes have become less affordable, this has

occurred because increases in prices have been greater than increases in incomes.

Recent data on the affordability of beer and SSBs have shown different results. Blecher et al. (2018) reported that beer has similar levels of prices in HICs and LMICs but is significantly more affordable in HICs. They found that beer became more affordable in 81% of HICs and in 95% of LMICs between 1990 and 2016. In another study, Blecher et al. (2017) found that SSBs, proxied by a best-selling cola-flavoured soft drink, became more affordable in 79 of 82 countries between 1990 and 2016.

Price elasticity of demand

The relationship between price and consumption is defined by the price elasticity of demand (PED), or the percentage change in consumption as a result of the percentage change in price. For example, a PED of −0.6 means that a 6% decline in consumption has resulted from a 10% increase in real prices, all else being held constant. If the percentage change in consumption is less than

the percentage change in price, the product is considered price inelastic; if the percentage change in consumption is greater than the percentage change in price, it is considered price elastic.

The price elasticity of tobacco, particularly of cigarettes, has been widely estimated. Although tobacco is universally found to be price inelastic, meaning that the percentage decline in consumption is less than the percentage increase in price, consumption nevertheless has declined. PED has been estimated to be about −0.4 for HICs and between −0.6 and −0.2 for LMICs (IARC, 2011). Younger and poorer smokers are more responsive (i.e. less inelastic) than older and richer smokers. Alcohol is also price inelastic; however, results vary substantially because of the greater product heterogeneity. An important consideration in addition to the price elasticity of an individual product is the cross-price elasticities between different alcohol products. Furthermore, price elasticity also varies substantially by intensity of use; heavier drinkers are

Fig. 11.4. Real taxes levied on, and prices and consumption of, cigarettes in South Africa, 1961–2016 (constant 2016 prices). GST, goods and services tax; VAT, value-added tax. Source: UCT (2018), courtesy of Corné van Walbeek.
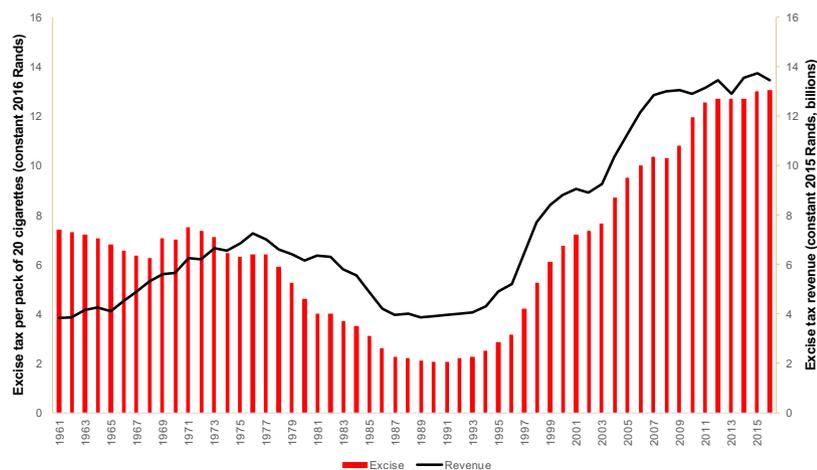
more inelastic. The prices of non-alcoholic beverages are found to be less inelastic than those of alcohol and tobacco; the subset of SSBs is sometimes even elastic because of the large number of substitutes available, particularly those with less or no calories.

Price elasticity has two important implications. The less inelastic, or the more elastic, a product is, the more effective is a tax-induced price increase in reducing consumption. However, the more inelastic a product is, the more efficient a revenue generator it becomes because the percentage decline in consumption is less than the percentage increase in price.

One of the best examples of price elasticity occurred in sales of cigarettes in South Africa. Between 1961 and 1991, cigarette excise taxes declined in real terms by 72%, which led to a 45% decline in real prices (see Fig. 11.4). As a result, consumption increased by 245%. However, since 1991, taxes have increased by 535% and prices by 245%, causing a 43% decline in consumption. Furthermore, because of the price inelastic nature of the product, the decline in consumption coincided with an increase in tax revenues. The increase in tax revenues from 1991 to 2016 was 238% in real terms (see Fig. 11.5).

Tax structure

The policy tool used to increase the price is to increase the excise tax. An excise tax is a consumption tax levied early in the supply chain. It is discriminatory, in that it is applied to a very narrow range of goods. It is applied equally to domestically produced and imported products. Excise taxes are preferred to sales taxes (e.g. goods and services tax, or value-added tax) because sales taxes are non-discriminatory and increasing the rate of tax would not change relative prices. Excise taxes are also preferred to import tariffs or duties, because increasing the tariff or duty would only change relative prices between domestically produced and imported products.

Excise taxes can be levied as specific taxes (per unit of volume) or ad valorem taxes (percentage of value), or a combination of these (mixed system). Taxes can be applied uniformly or in tiers based on product characteristics or value.

There is a consensus that uniform specific taxes represent the optimal tax structure for cigarettes. They result in the least variation in prices, thereby reducing the possibility of smokers trading down to cheaper brands to avoid tax increases, and result in higher prices. Furthermore, they are significantly easier to administer and result in more predictable and stable revenue streams for government.

Uniform specific taxes are not necessarily optimal for alcohol, where significantly greater price variation may warrant the use of ad valorem systems. However, large specific components will result in higher prices and ensure the effectiveness of tax increases. A particularly innovative option, which is equally applicable to SSBs, is targeting the dose of alcohol or sugar when setting the tax. Given that the magnitude of negative externalities is directly related to the dose of alcohol or sugar, taxing the volume of alcohol or sugar rather than the volume of the beverage can generate incentives for producers to reformulate their products to reduce the alcohol or sugar content to reduce their tax burden or, alternatively, to shift spending on advertising to lower-alcohol or lower-sugar beverages.

South Africa began to implement a dose-based tax system on beer in the late 1990s. The rate of tax was also increased each year, thereby increasing the incentives for producers to avoid the tax by shifting the market to lower-alcohol beers. This shift occurred not by the producers lowering alcohol levels in existing beer, but by shifting spending on advertising from higher-alcohol to lower-alcohol beers. Blecher (2015) showed

Fig. 11.6. Advertising expenditure on major South African beer brands and volume of alcohol in beer. ABV, alcohol by volume; LAAV, litres of absolute alcohol by volume. Source: reprinted from Blecher (2015), copyright 2015, with permission from Elsevier.
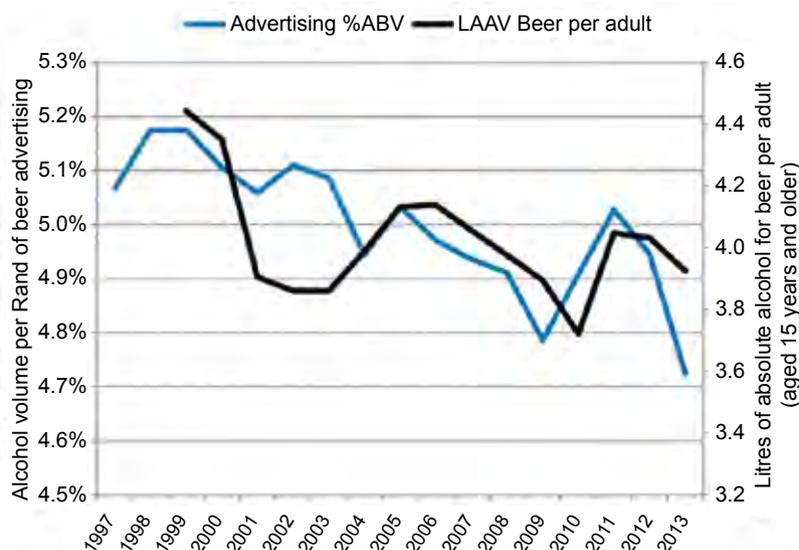
how the average alcohol content by volume of advertised beer fell from 5.2% in 1999 to 4.7% in 2013, which coincided with a 12% reduction in the number of litres of alcohol consumed per adult (from beer) during the same period (see Fig. 11.6).

The most prominent SSB tax was levied in Mexico in 2014, on both carbonated and non-carbonated beverages with sugar. Mexico implemented a uniform specific tax of 1 peso per litre, which equated to approximately 10% of the retail price. Evaluations conducted so far have shown declines in consumption of SSBs (Colchero et al., 2016), with larger declines among the households with low SES.

South Africa and the United Kingdom are the first countries to propose more innovative tax structures to target the dose of sugar. South Africa will impose a tax per gram of sugar from 2018, with an exemption for the first 4 g of sugar. The United Kingdom will impose the tax through tiers rather than a linear model.

Distributional consequences and use of revenues

As indicated earlier, in many countries smoking is more prevalent among the poor than the rich. As a result, the poor are likely to spend a greater proportion of their income on tobacco than the rich. Tax increases are therefore argued to be regressive, because the poor will pay a greater proportion of their income on the tax increase. Taking a more comprehensive approach to considering regressivity, recent studies have indicated that although price policies do create a higher financial burden in lower-income populations, they will have a greater health impact because disease burdens are concentrated in these groups. By preventing diseases, including cancer, price policies therefore have the potential to prevent catastrophic out-of-pocket expenditure incurred because of poor health (Sassi et al., 2018).

The first point to note from the above is that it considers only the

distributional impact of taxes and not that of government expenditure, which is likely to be progressive. For example, South Africa has increased taxes on tobacco and alcohol significantly since the early 1990s; Inchauste et al. (2015) have shown that although excise taxes in South Africa are, on average, regressive, the expenditure that they have enabled was overwhelmingly progressive and the net effects were progressive.

The second point is that one should consider not only the average impact but also the marginal impact. Research shows that the poor are more responsive to tax or price increases than are the rich. This is supported by economic theory, because the poor spend a larger proportion of their income on these commodities. One should expect the poor to reduce their consumption in response to tax or price increases more than the rich. Again, data from South Africa support this. van Walbeek (2002) showed that between 1990 and 1995 cigarette excise taxes became less regressive as the tax increased, as poor households reduced expenditure on tobacco at a faster rate than rich households did.

Third, tobacco tax receipts can be directed to specifically reduce the regressivity of taxes through earmarking. This may include earmarking revenues to assist low-income smokers to quit smoking (Warner, 2000).

Different tobacco and non-tobacco products

In most countries, cigarettes overwhelmingly remain the most-used tobacco product. Some countries have a greater diversity of tobacco products, for example, bidis and chewing tobaccos in South Asia, waterpipe smoking in the Middle East, and snus in Scandinavia. The recent

growth in the popularity of electronic nicotine delivery systems, including electronic cigarettes, which contain nicotine but not tobacco, has added to product variation. Combustible tobacco products are considered to be of highest risk; non-combustible products such as snus have been shown to reduce tobacco-attributable mortality (Ramström and Wikmans, 2014). Electronic nicotine delivery systems show promise in being substantially less harmful than combustible tobacco, although the long-term risk has not yet been established (McNeill et al., 2018; National Academies of Sciences, Engineering, and Medicine, 2018).

The guidelines for implementation of Article 6 of the WHO Framework Convention on Tobacco Control provide countries with a set of best practices for tobacco taxation (WHO, 2018). One of the key recommendations is that countries should tax tobacco products in a comparable way to ensure that increases in taxes and prices do not result in the substitution of cheaper categories of products. In the case where products have similar levels of harm, this is an appropriate strategy. However, as less harmful products have become more prevalent, and a continuum of risk or harm is present, it is appropriate to differentiate taxes according to relative risks (Chaloupka et al., 2015). The overriding focus remains the reduction of demand for the most harmful products.

Cost–effectiveness of different interventions

Appendix 3 of the WHO Global Action Plan for the Prevention and Control of NCDs 2013–2020 provides guidance for countries on the cost–effectiveness and feasibility of implementing health interventions to prevent and control NCDs (WHO, 2017a). Approved by the World Health Assembly in 2017, this guidance provides the most up-to-date economic rationale for implementing interventions. A total of 16 interventions, 11 of which correspond to cancer prevention and treatment (Box 11.1), are considered "best buys", meaning that the cost–effectiveness ratio is less than US$ 100 (adjusted for purchasing power) per disability-adjusted life year gained, the financial impact is low, and there are no major feasibility issues.

Several fiscal and regulatory policies are available to reduce the use of tobacco and the consumption of alcohol and food products that contribute to obesity. Taxation of both tobacco and alcohol products are two of the WHO "best buys", meaning that they are highly cost-effective and feasible to implement in all settings. Taxation of SSBs is also a recommended intervention, although it has been conservatively modelled and is not yet considered as cost-effective as other health taxes.

Other regulatory actions to reduce tobacco use, alcohol consumption, and obesity are also included in WHO "best buys". Regulatory actions tend to be low in cost when only public sector contributions are considered, but with high potential to improve health and reduce social inequalities in health (Nugent et al., 2018).

Conclusions

Use of tobacco and consumption of alcohol and SSBs are significant contributors to disease, disability, and death globally, and significant contributors to the cancer burden. Furthermore, the burden is increasingly shifting to LMICs as well as low-income populations within HICs. These risk factors are modifiable, however, and population-level policy interventions are available to successfully reduce the burden associated with them. Such policy interventions are aimed at reducing the demand for tobacco, alcohol, and SSBs through price and non-price interventions. These interventions, referred to as "best buys" because of their cost–effectiveness, are significantly underutilized, particularly by LMICs. Taxes and other fiscal measures are particularly cost-effective and are able to reduce the negative externalities associated with their use.

Box 11.1. "Best buys" related to cancer prevention and treatment, from the World Health Organization Global Action Plan for the Prevention and Control of NCDs 2013–2020 (WHO, 2017a).

- Increase excise taxes and prices on tobacco products
- Implement plain/standardized packaging and/or large graphic health warnings on all tobacco packages
- Enact and enforce comprehensive bans on tobacco advertising, promotion and sponsorship
- Eliminate exposure to second-hand tobacco smoke in all indoor workplaces, public places, public transport
- Implement effective mass media campaigns that educate the public about the harms of smoking/tobacco use and second hand smoke
- Increase excise taxes on alcoholic beverages
- Enact and enforce bans or comprehensive restrictions on exposure to alcohol advertising (across multiple types of media)
- Enact and enforce restrictions on the physical availability of retailed alcohol (via reduced hours of sale)
- Implement community wide public education and awareness campaign for physical activity which includes a mass media campaign combined with other community based education, motivational and environmental programmes aimed at supporting behavioural change of physical activity levels
- Vaccination against human papillomavirus (two doses) of girls aged 9–13 years
- Prevention of cervical cancer by screening women aged 30–49 years, either through: visual inspection with acetic acid linked with timely treatment of precancerous lesions; pap smear (cervical cytology) every 3–5 years linked with timely treatment of precancerous lesions; human papillomavirus test every 5 years linked with timely treatment of precancerous lesions

Key points

- There is significant between- and within-country variation in tobacco use and alcohol consumption by income and socioeconomic status; within a particular country, low-income populations are more likely to smoke than high-income populations are.

- Smoking and alcohol consumption are the most significant contributors to noncommunicable diseases, but measures to prevent and counter their impact are significantly underfunded within health systems.

- Several tools are available to reduce the demand for tobacco, alcohol, and sugar-sweetened beverages, including taxation.

- Taxation tools are particularly powerful in reducing the use of tobacco and the consumption of alcohol and sugar-sweetened beverages; however, the optimal tax design differs with product type, and careful attention should be paid to the tax structure to ensure maximum impact.

- Attention should also be paid to the distributional impact of taxes to ensure that progressive outcomes are achieved, including the earmarking of revenues to health-related expenditures.

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EXAMPLE 1.

Tobacco-related cancers and taxation of tobacco in low- and middle-income countries

Prabhat Jha, Hellen Gelband, Hyacinth Irving, and Sujata Mishra

Introduction

Tobacco smoking remains the most important avoidable cause of cancer deaths worldwide, accounting for about one third of all cancer deaths in men and about 6% of all cancer deaths in women (Jha, 2009). Smoking will kill about 1 billion people this century if current patterns hold (Jha and Peto, 2014). Chewing tobacco adds to the total, accounting for a substantial proportion of oral cancer deaths in men and women, particularly in South Asia (Gupta and Johnson, 2014; Khan et al., 2014). The toll will be heaviest among groups with lower socioeconomic status (SES) in many countries. Fortunately, both smoking prevalence and its consequences can be reduced by interventions that are feasible in any country (Jha and Peto, 2014; Jha et al., 2015).

In most high-income countries (HICs), such as the USA, smoking prevalence has been declining since the early 1970s. Current smoking prevalence and the rates of smoking-attributable diseases are highest

in groups with lower SES (Singh et al., 2011), with similar smoking prevalence rates in men and women. Historically, however, smoking prevalence rates were higher in groups with higher SES. Over time, the wealthier quit or did not

start, whereas people in groups with lower SES continued to smoke. This has reversed the initial SES gradient in smoking, evident when using smoking rates by education level as an indicator among USA adults (Fig. E1.1).

Fig. E1.1. Trends in prevalence of smoking of those aged 25 years and older by relative education level in the USA, 1940–2000. Smoking histories were constructed from various rounds of the National Health Interview Surveys. Each individual is classified as above or below the average educational achievement in each year for individuals aged 25 years and older in that particular year. Source: reproduced with permission from de Walque (2004).
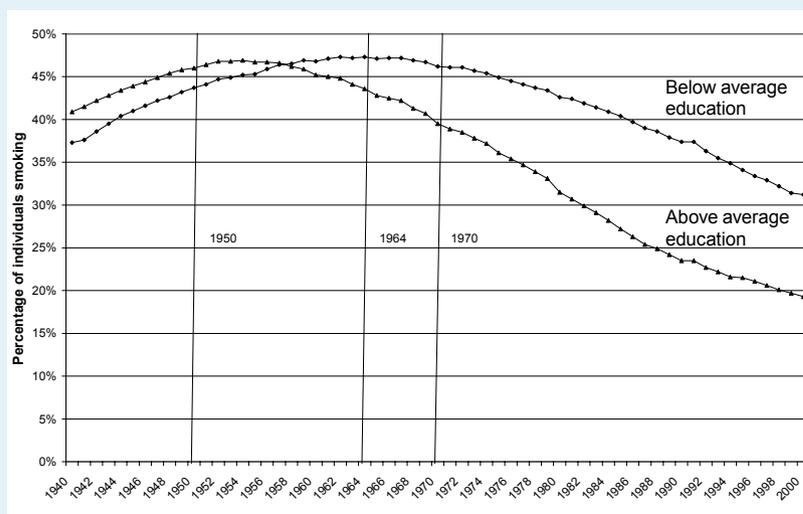
The same transition seems to be taking place in most low- and middle-income countries (LMICs); the decades-long lag in this transition is due to the later start of the smoking epidemic (Palipudi et al., 2012). A major difference is that relatively few women have taken up smoking in LMICs; the smoking epidemic is therefore largely limited to men (Jha, 2009; Jha and Peto, 2014). As a result, tobacco-attributable deaths are still rising among men in LMICs, whereas they have been falling substantially for three decades among men in HICs (Peto et al., 1994).

In this example we review the relationship between tobacco and social inequalities in cancer and overall mortality. We then examine the impact of tobacco control interventions, most notably tobacco taxation, in reducing inequalities in cancer and other diseases, focusing on the evidence in LMICs.

Relationship between smoking and social inequalities, and trends over time

Given that within most countries the poor smoke more than the rich, it follows that the diseases made more common by smoking – including various cancers (notably of the lung and respiratory system, oesophagus, and others) and cardiovascular and respiratory diseases – are also more common among the poor than among the rich (Singh et al., 2011).

A method has been developed (Peto et al., 1994) to crudely estimate the contribution of smoking-attributable deaths by SES (Jha et al., 2006). For example, in 1996 in Canada, England and Wales, Poland, and the USA, there was an approximately 2-fold difference between the highest and the lowest social strata in overall risks of dying among men aged 35–69 years. At least half of the differences in mortality risks be-

tween groups with highest and lowest SES were attributable to deaths from smoking. Smoking therefore accounted for about half of the difference in social inequalities in overall mortality (Fig. E1.2).

The substantial decline in smoking prevalence in many HICs enables us to examine how this change affects social inequalities over time and to quantify the contribution of smoking. Fig. E1.3 shows the trends in mortality in men aged 30–69 years among the poorest and richest quintiles (based on neighbourhood income) in Ontario, Canada, from 1992 to 2012. Ontario has a population of about 12 million and is reasonably representative of the trends among adult men in HICs.

Over this 20-year period, the risk of death from any cancer was about 50% higher among the poorest men than among the richest men, and the risk of premature death from tobacco-attributable cancers in

Fig. E1.2. Social inequalities in mortality in men aged 35–69 years in 1996 from smoking (dark shading) and from any cause. Source: reprinted from Jha et al. (2006), copyright 2006, with permission from Elsevier.
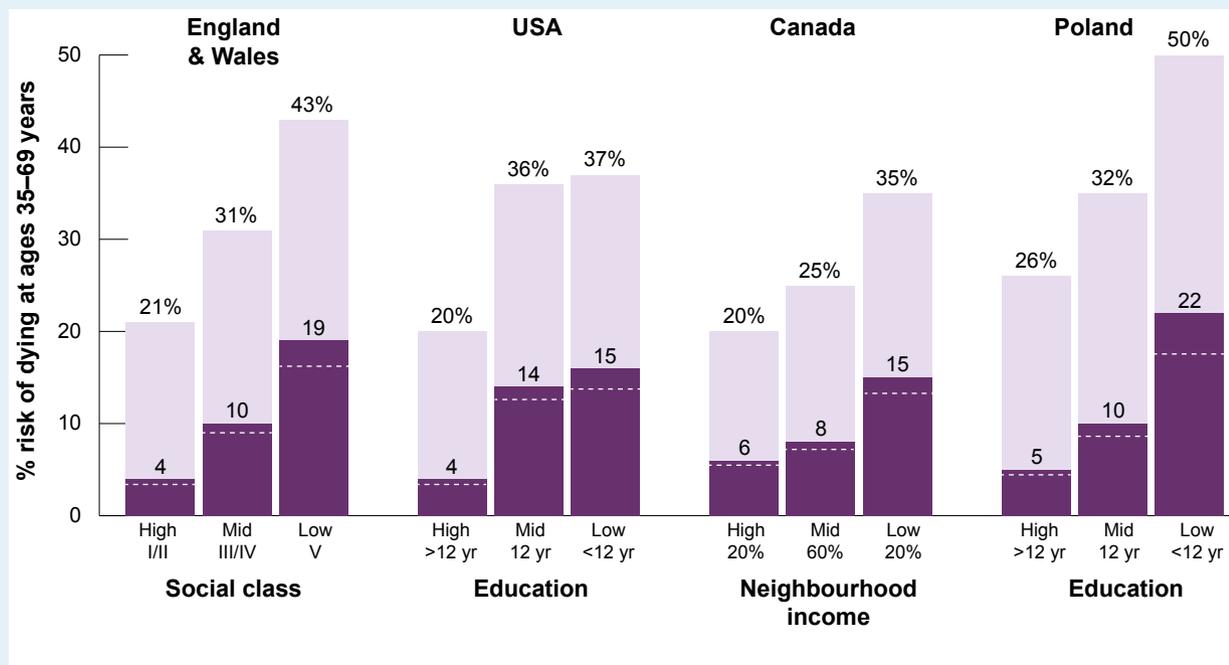
Fig. E1.3. Comparison of mortality rates from cancer in men aged 30–69 years during 1992–2012 from smoking (dark shading) and from any cancer in Ontario, Canada, by income quintile.
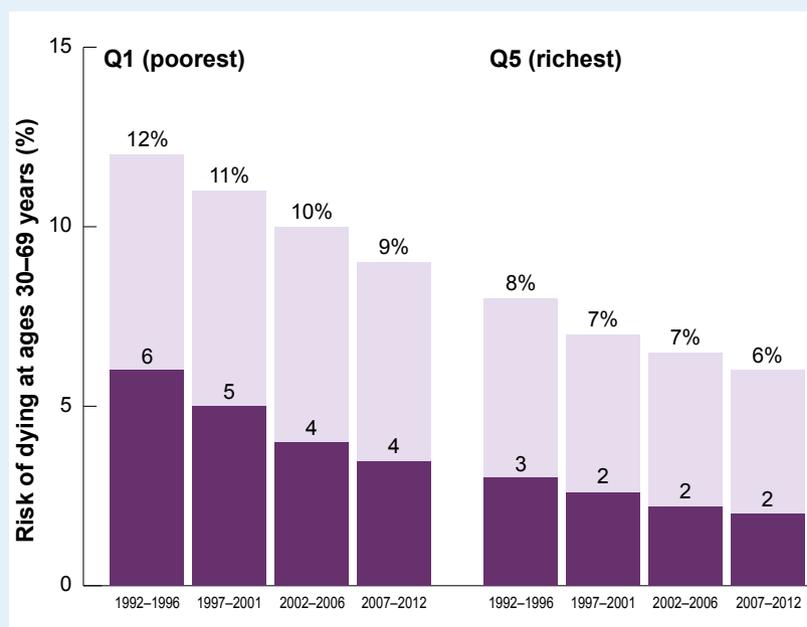
the poorest men was double that in the richest men. The risks have evolved over the period, correlating with previous changes in smoking patterns. During 1992–1996, the beginning of the period, this absolute gap in risk of death from any cancer between poorest and richest was 4% (12% − 8%), and tobacco contributed to about three quarters (6% − 3% = 3%) of this difference. By 2007–2012, the absolute gap had fallen to 3% (9% − 6%), and tobacco contributed to two thirds (4% − 2% = 2%) of the difference. From 1992 to 2012, the risk of death from cancer fell by about one quarter in both the poorest (3%/12%) and the richest (2%/8%) quintile of men. Reduced tobacco-attributable cancer deaths contributed to two thirds of the decline in the poorest men (2%) and half (1%) in the richest men. Thus, in Ontario, declines in tobacco-attributable cancers have reduced the absolute inequal-

ities between the richest and poorest men in cancer mortality.

The main reasons for the declines in smoking-attributable cancer mortality in HICs and the differences by SES have not been extensively studied, but a range of cost-effective interventions have probably contributed to declines. These interventions may be classified into price instruments, which focus on large increases in excise taxes on tobacco, and non-price instruments, which include bans on smoking in public places, bans on advertising and promotion, prominent warning labels or the use of plain packaging, and widespread dissemination of information on tobacco and support for cessation (including pharmacotherapies) (Jha and Peto, 2014; Jha et al., 2015). If these provisions, which are part of the World Health Organization Framework Convention on Tobacco Control (the global treaty to reduce tobacco use), were imple-

mented widely, tobacco consumption in LMICs would also fall (Jha, 2009; Jha and Peto, 2014).

Effects on social inequalities in LMICs from increases in tobacco taxes

Tobacco taxation is the most effective practicable intervention to increase smoking cessation rates and to prevent young people from initiating smoking (Jha, 2009; IARC, 2011; Jha and Peto, 2014; additional information on tobacco taxation in Chapter 11).

In most LMICs, the absolute total of tobacco-related illnesses is still increasing and effective large tobacco tax increases have not yet been widely used. The most relevant evidence for what taxes could accomplish – evidence that could be used to persuade policy-makers of the health and financial benefits of higher taxes – has been generated from robust models. A recent analysis (Global Tobacco Economics Consortium, 2018) examined the health, poverty, and financial consequences of a 50% increase in cigarette price among 500 million male smokers in 13 middle-income countries: six lower-middle-income countries (Armenia, Bangladesh, India, Indonesia, the Philippines, and Viet Nam), and seven upper-middle-income countries (Brazil, Chile, China, Colombia, Mexico, Thailand, and Turkey). The price increase would lead to substantially greater health and financial gains for the lowest-income quintile compared with the highest-income quintile (Fig. E1.4). Some key findings include: the life years gained in the lowest-income quintile were 7 times those in the highest-income quintile, out of 450 million life years gained in the 13 countries; the average life years gained per

Fig. E1.4. Expected value of health and financial benefits gained by the lowest-income and highest-income quintiles of the population in 13 middle-income countries as a result of a 50% increase in cigarette price. PPP, purchasing power parity. *Expected value if no differences exist across bottom and top income groups. Source: reproduced from Global Tobacco Economics Consortium (2018).

highest-income quintile would pay twice as much as the lowest-income quintile of the US$ 122 billion additional tax collected.

The prevailing wisdom among some economists and public health groups has been that higher tobacco taxes hurt the poor more than the rich, based on the observation that low-income smokers spend a disproportionately greater share of their income on tobacco than high-income smokers do. However, at the population level, the health benefits are strongly concentrated in poorer (pre-tax) smokers as a consequence of their reduced tobacco use. Viewed through a public health lens, higher tobacco taxes are pro-poor (Jha and Chaloupka, 1999; Hosseinpoor et al., 2011; Sassi et al., 2018).

Higher taxes generate higher revenues that may be used to improve health and other social services for the poor, such as expanding basic services under universal health coverage (Jha et al., 2015). Tax increases must be implemented with care to avoid substitution effects (see Chapter 11) (Marquez and Moreno-Dodson, 2017).

Effective population tobacco control requires a comprehensive approach, including a set of proven interventions in addition to taxation. Table E1.1 summarizes the impacts of effective non-price interventions and the likely responsiveness to these by groups with lower and higher SES. Groups with lower SES will respond more to excise taxes but are less likely to take up health information. Regulatory interventions, such as bans on tobacco advertising and promotion and bans on public smoking, are likely to be effective across groups with different SES. Cessation interventions are more likely to be taken up by individuals with higher

smoker in the lowest-income quintile were 5 times those in the highest-income quintile; and the cost of treatment averted in the lowest-income quintile was 5 times that in the highest-income quintile, of a total of US$ 157 billion.

If tobacco taxes were increased, about 16 million men (most of whom are in the lowest-income quintile) and their families in the subset of seven countries without universal health coverage would avoid catastrophic health expenditures. The men and their families would also avoid the related income loss from their incapacitation and, for their families, from their death. As result, 8.8 million men, half of whom are in the lowest-income quintile, would avoid falling below the World Bank definition of extreme poverty. In contrast, the

Table E1.1. Interventions to reduce tobacco use, and likely impact among groups with higher and lower socioeconomic status (SES)[a].

Intervention	Low SES	High SES
Higher cigarette taxes	+++	+
Consumer information, prominent warning labels, or plain packaging	+	++
Bans on advertising and promotion and on smoking in public	++	++
Nicotine replacement therapy, electronic nicotine delivery systems (e.g. e-cigarettes), and cessation	+	++

[a] Impact is assessed qualitatively based on the number of + signs assigned.

Source: compiled from Jha and Peto (2014). License: Creative Commons Attribution CC BY 3.0 IGO.

SES (Jha and Peto, 2014; Jha et al., 2015). All of these interventions should be considered in national anti-smoking plans, but large increases in the excise tax have been demonstrated to have the biggest effect. Indeed, as cigarettes are becoming more affordable (Jha, 2009; Jha and Peto, 2014; Chapter 11), it is unlikely that non-price interventions alone will reduce tobacco consumption substantially.

Conclusions

Tobacco use is the root cause of a substantial proportion of social inequalities in the risk of death from cancer and a host of other smoking-related causes. Reductions in tobacco use have helped to reduce the absolute inequalities in cancer mortality in HICs, with reductions in smoking-attributable cancers playing a greater role in the reduced mortality rates among the poorest smokers. A worldwide tripling of the excise tax would reduce consumption by at least one third and avoid about 200 million premature deaths in the first half of this century (Jha and Peto, 2014). Globally, large increases in the excise tax, paired with strategies to reduce substitution to shorter, cheaper cigarettes, could substantially reduce consumption and improve the health of the poor, including reducing social inequalities in cancer mortality.

Acknowledgements

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CHAPTER 12.

The role of law in reducing global cancer inequalities

Jonathan Liberman

Introduction

This IARC Scientific Publication shows that large social inequalities in cancer exist both within and between countries, and that social determinants have an impact across all stages of the cancer continuum. This publication also identifies effective actions necessary for cancer prevention and control generally, and for reducing social inequalities in cancer specifically. As the individual chapters of this book illustrate, law occupies a central place in the prevention and control of cancer, and in the reduction of social inequalities in cancer. The importance of law is evident in each of the major agreed international frameworks for sustainable development, health, noncommunicable disease preven-

tion and control, and cancer prevention and control, including the United Nations Sustainable Development Goals (UN, 2015), the global noncommunicable diseases agenda (WHO, 2018), the World Health Organization Framework Convention on Tobacco Control (WHO, 2003), and the World Health Assembly resolution on cancer prevention and control (WHO, 2017). In each of these instruments, states commit to implementing interventions that can be achieved only through the use of law.

Law is critical both within (at national and subnational levels) and between countries (in the form of international law) to address the shared concerns and activities that cross national borders. Law is sometimes thought of in a narrow way, either at

the domestic level as legislation or in international law as treaties. However, law comes in many shapes and forms, including constitutions, regulations, decrees, ordinances, by-laws, decisions of courts and tribunals, enforcement practices, agreements by states (which are not themselves binding in the manner that treaties are, but may have legal significance) (Zhou and Liberman, 2018), and mechanisms to monitor or enforce compliance with international obligations. This variety and breadth of what represents law highlight both its capacity to affect cancer prevention and control in multiple ways and at multiple levels, and the range of actors it involves.

Law has a particularly powerful role to play in addressing social

inequalities, because of its ability to regulate the environments in which we live; law can modify the structural determinants of social inequalities ("the causes of the causes"; see Chapter 14), both domestically and internationally. However, law is only one of a range of tools that may be used to further the goals of cancer prevention and control, and of reducing inequalities, and is usually used most effectively in coordination with other measures. These may include education and support programmes, medical interventions, financial incentives, professional training and supervision programmes, or non-legally binding forms of international cooperation.

Law in cancer prevention and control

Table 12.1 presents examples of the ways in which law can be used in the areas of cancer prevention and control addressed in this book, and in which social inequalities are identified. Although this chapter focuses on the positive role that law can play, it is important to acknowledge that law can also hinder cancer prevention and control. Law can also exacerbate social inequalities, as demonstrated by: laws that regulate the availability of morphine as a controlled drug in a manner that impedes its availability for palliative care (WHO, 2011); laws that are designed to protect the privacy of personal health information but unreasonably constrain the conduct of essential public health research (Liberman, 2014); protections of

Table 12.1. Examples of the use of law to advance cancer prevention and control

Area of cancer prevention and control	Examples of the use of law
Tobacco use, alcohol consumption, and unhealthy diet	Bans or restrictions on product or company advertising, promotion, and/or sponsorship; regulation of product packaging, including mandatory health warnings, product information, or plain or standardized packaging in the case of tobacco products; bans on smoking in workplaces, in public places, and on public transportation; excise taxes on unhealthy products or other regulations to affect product price, such as minimum pricing; restrictions on when and where products can be sold; and regulation of product content or portion size
Occupational and environmental cancers	Bans on the use of asbestos; various forms of chemical regulation; occupational health and safety law; environmental law; requirements that protective equipment be worn by workers exposed to hazardous materials; protection against sun exposure in the workplace; smoke-free workplaces; housing regulation and building codes; regulation of fuel content; vehicle emissions or efficiency standards; regulation of agricultural practices including burning; and regulation of waste management, including disposal and recycling of end-of-life electrical and electronic equipment (e-waste)
Screening, diagnosis, treatment, and/or care	Regulation of the safety, quality, and efficacy of cancer screening, diagnostics, treatments, and services; measures to increase the availability and affordability of screening, diagnostics, treatments, and services; regulation, qualification, and education of health practitioners, including task-shifting and task-sharing, and prevention of overscreening and overtreatment; responsibilities of health-care professionals to provide meaningful information on treatment options and their implications, including financial; measures to provide or strengthen support for patient and/or family decision-making about treatment; protection of patient privacy and confidentiality; regulation of health insurance, including its coverage; preventing or reducing corruption in the health system; regulation of direct-to-consumer advertising; and regulation of corporate engagement with the clinical community
Life after a cancer diagnosis	Measures to promote the well-being of people who have been diagnosed with cancer throughout their post-diagnosis lives, and to avoid potential negative consequences of having or having had cancer, including protection against discrimination or stigmatization; income protection; protection against misuse of personal health information; protection in employment, including appropriately flexible working arrangements and support; and access to insurance (including health, life, and travel), superannuation/pension funds, and loans
Cancer registries and other collection and maintenance of health information	Providing appropriate legal underpinnings for cancer registries and other relevant data collection and information systems, including notification of individual cases, and specification of details to be provided; providing for sharing of information to enable maintenance of records and to facilitate research; providing for individuals to have appropriate access to their personal health information; and balancing individual rights to privacy (including through protection against inappropriate sharing of information and security breaches, and through de-identification of data) and the need for population-level research

freedom of speech that are extended to corporate expression, limiting the restriction of harmful commercial marketing practices, which are often targeted at less advantaged groups (see Chapter 7); and litigation against health practitioners, which can lead to the practice of "defensive medicine" (O'Dowd, 2015), contributing to problems of overscreening, overdiagnosis, and overtreatment, imposing unnecessary burdens on individuals, families, and already stretched health systems (see Chapter 19).

A matter of human rights

All aspects of cancer prevention and control, including reducing inequalities, are matters of human rights. The right to health is recognized in several international agreements, including the International Covenant on Economic, Social and Cultural Rights (UN, 1966), the Convention on the Rights of the Child (UN, 1989), the International Convention on the Elimination of All Forms of Racial Discrimination (UN, 1965), the Convention on the Elimination of All Forms of Discrimination against Women (UN, 1979), and the United Nations Declaration on the Rights of Indigenous Peoples (UN, 2007). The constitution of the World Health Organization recognizes that "the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being" (International Health Conference, 1946).

The right to "the highest attainable standard of physical and mental health" enshrined in the International Covenant on Economic, Social and Cultural Rights is a right of everyone (UN, 1966). The right – and the corresponding obligations of governments – can only be understood and enjoyed in a social and economic context. The right includes "the right

to a system of health protection which provides equality of opportunity for people to enjoy the highest attainable standard of health". The right applies both to "timely and appropriate health care" and to "the underlying determinants of health, such as access to safe and potable water and adequate sanitation, an adequate supply of safe food, nutrition and housing, healthy occupational and environmental conditions, and access to health-related education and information" (CESCR, 2000). Steps that must be taken by states to achieve the full realization of the right to health include provision for the healthy development of children; the improvement of all aspects of environmental and industrial hygiene; the prevention, treatment, and control of epidemic, endemic, occupational, and other diseases; and the creation of conditions that would ensure medical service and attention in the event of sickness. The right demands "equality of access to health care and health services" (CESCR, 2000).

The right to health includes the four "interrelated and essential elements" of availability, accessibility, acceptability, and quality, as described in Table 12.2 (CESCR, 2000).

Impacts of non-health areas of law and governance

Many areas of law and governance, both domestic and international, have a range of impacts across the spectrum of cancer prevention and control (Liberman, 2017) in terms of the potential both to improve overall cancer outcomes and reduce inequalities, and to worsen outcomes and increase inequalities. These areas of law and governance may pursue worthy goals and objectives and may explicitly provide scope for taking health into account; howev-

er, health goals and objectives may not be prioritized in their design and implementation, and their key actors and stakeholders may overlook or undervalue the health implications of their decisions and actions. For example, although intellectual property laws may be designed to encourage and reward innovation, including in medical products, technologies, and devices, they may in practice make medical treatment unaffordable (WHO, WIPO, and WTO, 2013), particularly for less advantaged groups. Although international trade law and international investment law may be designed to improve economic growth, development, and, in the long run, overall living standards, they inevitably create both winners and losers (Shea et al., 2007). The standards that such laws set for the cross-border flow of goods and services, and the protection of foreign investments, may impose conditions on the regulation of trade in products that cause harm. Trade and investment agreements generally do provide space for bona fide public health regulation, as seen in the comprehensive victories by the governments of Australia (WTO, 2018) and Uruguay (ITALAW, 2016) in defending international trade and investment litigation against their tobacco packaging laws. However, these agreements generally require a range of procedures that may be difficult for some governments to navigate, particularly lower-resourced countries. They may also introduce complexities and constraints in how governments regulate heterogeneous unhealthy products. For example, taxes on unhealthy products (see Chapter 11) such as sugar-sweetened beverages (SSBs), of which there are many kinds (e.g. carbonates, fruit drinks, sports drinks, energy and

Table 12.2. Essential elements of the right to health as relevant to social inequalities in cancer

Essential elements of the right to health[a]	Examples of application to social inequalities in cancer
Availability: functioning public health and health-care facilities, goods, services, and programmes should be available in sufficient quantity within a country	There are enormous disparities in the availability of facilities, goods, services, and programmes across countries. For example, people living in low- and middle-income countries have little or no access to pain relief or palliative care. Of the 298.5 metric tonnes of morphine-equivalent opioids distributed in the world each year, 287.7 metric tonnes (96.4%) are distributed to high-income countries and only 0.1 metric tonnes (0.03%) are distributed to low-income countries (Knaul et al., 2018). Although one radiotherapy unit on average is available for every 120 000 inhabitants in high-income countries, one radiotherapy unit is available for every 1 million individuals in middle-income countries, and 51 countries or independent territories or islands have no radiotherapy services at all (Chapter 7). Less than 25% of the global population has access to basic, high-quality cancer surgery. Many settings have low-quality services, which can be attributed to human resource shortages, poorly trained or low-volume providers, inadequate drug supply, and lack of equipment (see Chapter 10).
Accessibility: health facilities, goods, and services should be accessible to all, "especially the most vulnerable or marginalized sections of the population". This requires: non-discrimination; that facilities, goods, and services be "within safe physical reach for all sections of the population, especially vulnerable or marginalized groups"; affordability, including for socially disadvantaged groups; and the accessibility of information	Individuals with a low income, ethnic minorities, Indigenous populations, and other socioeconomically disadvantaged groups face considerable barriers to accessing needed cancer services in both low- and middle-income countries and high-income countries. This applies throughout the care continuum, from symptom awareness to accessing treatment and receiving palliative care (see Chapter 10). Early diagnosis of cancer requires access to screening and diagnostic services. Individuals in groups of low socioeconomic status and underserved populations may be less likely to recognize the importance of cancer symptoms (see Chapter 7). Geographical accessibility is particularly relevant in cancer care. Generally, the further a patient lives from a cancer treatment centre, the greater the delay and/or the more advanced the stage of the disease upon presentation (see Chapter 10). Across the globe, Indigenous populations experience significant disparities relative to the local non-Indigenous populations, across the cancer continuum. Addressing this excess burden requires culturally appropriate interventions that are developed, implemented, and evaluated in partnership with Indigenous communities, including the development of a culturally competent health-care workforce, and culturally appropriate systems, services, and programmes (see Focus 5). The costs of cancer care can push individuals into poverty or force them to make difficult decisions about their treatment (so-called financial toxicity). These barriers to effective, acceptable, and timely cancer care result in poorer survival outcomes and quality of life, with the most vulnerable individuals disproportionately affected. Without health insurance, the poor are left to fund health care through out-of-pocket expenditure (see Chapter 7). Out-of-pocket payments are twice as high in low-income countries as in high-income countries. The few who are able to receive cancer care in low- and middle-income countries are typically from the most privileged subpopulations (see Chapter 10).
Acceptability: health facilities, goods, and services should be respectful of medical ethics, culturally appropriate (including respectful of the culture of individuals, minorities, people and communities, and sensitive to gender), and designed to respect confidentiality	In most settings, cancer treatment is not sufficiently focused on the individual patient. Decisions are not sufficiently informed by user preferences or oriented around the person. This is particularly important in cancer management, because of the complexity of decisions about risks, benefits, and uncertainties of treatment, and because of the implications of the general fear and anxiety that accompany a cancer diagnosis (see Chapter 10).
Quality: health facilities, goods, and services should be scientifically and medically appropriate, of good quality, and delivered by skilled medical personnel	It has been estimated that improving the quality of existing health services, essential for improving cancer outcomes, can reduce the number of lives lost to cancer by millions. Poor cancer care results in worse overall outcomes for those affected, subjecting vulnerable subpopulations to the costs and harms of cancer care without the benefits (see Chapter 10). In high-income countries, there is compelling evidence that individuals in less privileged groups receive lower-quality treatment for cancer than those in more privileged groups (Chapter 7).

[a] *Source:* CESCR (2000).

vitamin water drinks, sweetened iced tea, and lemonade) (WHO, 2016), must be designed to ensure that they do not unjustifiably discriminate between products (George, 2019). Discrimination between imported and domestic products (whether explicit in law or evident in its practical impacts) that cannot be sufficiently justified on health grounds is likely to breach the obligations that states have undertaken under international trade agreements. This highlights the need to understand and prioritize health and social inequality in "non-health" forums, and to understand "non-health" legal and governance frameworks within health research and practice.

The assertion of rights to health care

As noted above, the right to health includes the right to timely and appropriate health care that meets the requirements of availability, accessibility, acceptability, and quality. States are obliged to take steps to achieve the full realization of the right to health, and are to be held accountable for failing to do so. Methods of accountability may include scrutiny by international human rights bodies, domestic or international criticism, and domestic litigation to enforce compliance. In practice, more advantaged groups will be in better positions to enforce such rights, whether in a formal legal sense through court action or through less formal expectations, requests, or demands that they be provided what they believe they are legally entitled to. This may be because of higher literacy (both health literacy and legal literacy), greater knowledge and access to information, participation in networks of influence, personal or professional connections, greater experience and

confidence in pursuing their rights, or the financial capacity to use legal processes to assert rights and to hold others accountable for failures to provide what is demanded. Creating, clarifying, or strengthening rights and expectations – all of which are generally to be encouraged for improvements in health outcomes – will have the effect of increasing inequalities if only privileged groups are able to do so. For example, if an individual can successfully take a government to court for failure to provide or subsidise a particular treatment for them, their legal action may deliver access to treatment for them that is not available to those who are not in a position to pursue such claims. These are increasing risks (and realities) as we continue to move to more tailored, targeted, and expensive cancer treatments. Chapter 18 describes the ever-increasing research focus on expensive medicines for wealthy patients in wealthy countries and, in emerging economies, the displacement of domestic, affordable innovations by high-end expensive technology. Although commercial interests are driving many of the developments towards so-called precision medicine (Saracci, 2018), the resultant inequalities can be exacerbated by allowing rights to be claimed as legal entitlements in overly individualistic contexts.

Litigation by corporate actors against public health regulation

Table 12.1 includes the kinds of legal interventions that governments can use to regulate exposure to the cancer risk factors of tobacco use, alcohol consumption, and unhealthy diet. All of the interventions listed involve regulation of the behaviour of commercial actors, and inevitably affect

the commercial interests of these actors. Corporate actors whose interests are negatively affected by government regulation may resort to litigation to oppose such regulation, whether under domestic law or regional or international agreements. Such litigation has become common for tobacco control measures over the past decade (e.g. against tobacco plain packaging, graphic health warnings, advertising bans, smoke-free places, product regulation; Zhou et al., 2019), and has also occurred with respect to alcohol (e.g. minimum unit pricing; Scotch Whisky Association, 2017) and diet (SSBs) (Matter of New York Statewide Coalition of Hispanic Chambers of Commerce, 2014). Corporate actors may have various aims in pursuing such litigation, including having laws struck down or amended, receiving compensation, delaying the implementation of laws, tying up government resources and increasing the implementation costs of interventions that may otherwise be inexpensive, or dissuading the litigated-against government from further regulating its behaviour or governments of other countries from doing so (Zhou et al., 2019). Defending litigation of this nature by, or funded by, large multinational companies can be extremely resource-intensive (Crosbie et al., 2018) and may be beyond the capacity of some governments. Such strategic use of litigation by corporate actors can potentially lead to different tiers of regulation, in which higher-resourced governments are able to implement more effective laws than lower-resourced governments because the higher-resourced governments are better able to withstand litigation or legal threats. The more this is the case, the greater the incentive for the corporate actors to dedicate resources to these

less-regulated markets. The implication is that populations in lower-resourced countries face greater exposure to cancer risk factors than populations in higher-resourced countries.

Collaboration in research and the use of evidence in the development and implementation of laws

Across the spectrum of cancer prevention and control, laws (as for all interventions) should be soundly based on evidence, and subject to regular monitoring, evaluation, and improvement. However, the capacity to conduct research varies across countries. Efforts to ensure that the development and implementation of laws are based on evidence should not impose requirements to conduct local research, including duplicating research conducted elsewhere, that are beyond the capacity of lower-resourced governments. Although evidence gathered in one setting should not be unthinkingly applied to other settings, researchers and policy-makers could usefully engage in international collaborations to develop practical guidance on both what kinds of evidence might be usable across settings and on how to reliably extrapolate research findings across settings. Australia – the first country in the world to introduce tobacco plain packaging – has conducted an enormous volume of both pre-implementation research, on which the laws were based, and post-implementation evaluations, to assess their impacts in practice (Cancer Council Victoria, 2018). It would be wholly unreasonable to expect low-resource countries with less capacity, both in government and in the research community, to do the same as Australia, particularly because there is now a valuable body of implementation evidence that can be examined and used by others. The content of such guidance would vary according to subject matter; for example, guidance on how to use implementation research on tobacco control measures (e.g. tobacco plain packaging, graph-ic health warnings) or dietary measures (e.g. nutrition labelling, taxes on SSBs) across settings would be different from guidance on how to use research on different approaches to health workforce regulation, effective ways to engage patients and families in decision-making, or addressing concerns about the collection and use of personal health information.

Conclusions

Law has a vital role to play in reducing social inequalities in cancer, both within and between countries. To maximize its impact, by harnessing the enormous positive effect it can have and by ameliorating its negative effects, legal expertise must be integrated as an essential component of the cancer prevention and control workforce. Interdisciplinary collaborations across all aspects of cancer prevention and control research and practice, across the entire cancer continuum, must be built, nurtured, and maintained.

Key points

- Law occupies a central place in cancer prevention and control generally, and in addressing social inequalities in cancer specifically, including: addressing risk factors (tobacco use, alcohol consumption, unhealthy diet, and occupational and environmental exposures); screening, diagnosis, treatment, and care; life after a cancer diagnosis; and the collection and maintenance of health information.

- All aspects of cancer prevention and control, including reducing inequalities, are matters of human rights. Although creating, clarifying, and strengthening rights related to health are to be encouraged, action is required to ensure that these rights can be availed of in practice by all groups, not only the most advantaged.

- It is essential to understand and manage non-health areas of law and governance, such as international intellectual property, trade and investment regimes, and the strategic use of litigation by corporate actors to resist regulation of their behaviour.

- There is a need for greater international collaboration to establish practical guidance on the use of evidence for the development and implementation of law across settings, particularly to support countries with limited local research capacity.

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CHAPTER 13.

Life-course approach: from socioeconomic determinants to biological embodiment

Michelle Kelly-Irving and Paolo Vineis

Introduction

People with a more disadvantaged socioeconomic position (SEP) have higher rates of mortality at a given age; in other words, they die younger (Gallo et al., 2012). They are also more likely to suffer from worse health, diseases, and disabilities across the life-course, especially in older age. Mechanisms through which SEP may influence health include behaviours (e.g. smoking, unhealthy diets, sedentary lifestyles), availability of and access to health-care services, and chemical and physical exposures (e.g. occupational exposures, pollution). There is increasing evidence that chronic psychosocial stress may exert long-term effects through physiological wear and tear (meaning that

a depletion of biological resources in response to the environment occurs over time; Seeman et al., 1997), involving inflammatory responses, reduced immune function, and biological age acceleration.

The socioeconomic gradient in health outcomes has been referred to as a social fact, given its ubiquitous nature, its persistence across a variety of pathological processes, and the fact that its pattern is replicated with new emerging diseases (Hertzman, 2012). The potential impact of SEP on many pathological processes means that it is considered one of the main determinants of life expectancy and health, occurring upstream of typically identified risk factors such as smoking and sedentary lifestyles (the terms upstream

and downstream are frequently used in epidemiology, although their use has been criticized; Krieger, 2008). The multilayered social environment within which humans exist and live ultimately affects the cells, organs, and biological systems. This concept, known as embodiment, was initially developed by Krieger (2005) and occurs as a dynamic set of social and biological processes and interactions between individuals within a population and their environments over time (Kelly-Irving and Delpierre, 2018). The pervasive nature of the social structures that make up the outer layer of our environments means that an embodiment dynamic occurs differentially across the strata of SEP. Despite this, SEP remains neglected as a public health imperative and is

not clearly identified as a risk factor in public policies.

The life-course approach to health is a conceptual framework that merges social science and epidemiological methods (Kelly-Irving et al., 2015). It originated in the social sciences, where there was a primary interest in assessing the "social organisation of an individual's passage through life" (Backett and Davison, 1995). In this framework, susceptibility to disease is an inevitable interaction between social and biological phenomena. Therefore, using a life-course approach encapsulates not only the objective measurement of ill health and deprivation but also the subjective ideas about the experience of illness or poor social circumstances. It defines the dichotomy whereby individuals actively determine the trajectory of their life-course but are passively subjected to external insults (Giele and Elder, 1998). The term life-course implies the fluid and continuous movement of individuals and populations through time. Time is also an essential component in the development of chronic diseases, which have long induction and latency periods.

The life-course approach to epidemiology broadens the scope and offers a theoretical backdrop to what is largely a methodological discipline, by looking at human disease and well-being holistically. It is based on "social and biological pathways" and "social and biological chains of risk" (Kuh et al. 1997). These concepts were developed in the book *A Life Course Approach to Chronic Disease Epidemiology* (Kuh and Ben-Shlomo, 1997), which helped to establish life-course epidemiology as a bona fide theoretical and methodological approach. The timing of exposures, in other words the stage along the life-course at which an exposure occurs, can be important in understanding its later effects (Lynch and Smith, 2005) and especially pertinent to the study of chronic diseases such as cancers (Kelly-Irving and Delpierre, 2018). Poor socioeconomic circumstances during childhood are particularly important in determining, for example, a higher risk of stomach cancer through exposure to *Helicobacter pylori* infection (Malaty and Graham, 1994).

The aim of this chapter is to summarize research on social to biological processes that occur over the life-course, with an emphasis on processes involved in social inequalities in cancer, using a multidisciplinary approach that integrates information on SEP, environmental exposures, and risk factors with biological measurements (Vineis et al., 2016). Identification of the biological basis of the social determinants from a life-course perspective is demonstrated with examples from the literature, focusing on results from the Lifepath project (https://www.lifepathproject.eu/).

Construction of health inequalities from early life

Obesity is a risk factor for several types of cancer, including cancer of the stomach, endometrium, colon, breast, pancreas, and liver (Lauby-Secretan et al., 2016). Children with lower SEP literally carry a heavier burden of disease from earlier in the life-course, at least in high-income countries. They accrete fat mass at a faster rate and are more likely to be overweight or obese at any age, to change from not being overweight to being overweight or obese, and to maintain a status of overweight or obesity over time (McCrory et al., 2017). These patterns are difficult to change once entrenched. Overweight and obesity have been shown to have a social pattern from early childhood, with more disadvantaged children having a higher body mass index (BMI) from the age of about 3 years. However, little is known about whether social differentials vary after adipose rebound and into adolescence, and whether these trajectories differ by national context. In a large European study (McCrory et al., 2017), the child BMI growth trajectory was greater for children with mothers with a lower education level. Overall, SEP was strongly implicated in the etiology of childhood obesity. In a previous analysis, it was observed that the BMI of parent and child are linked from age 3 years and remain so throughout the early childhood years (Fantin et al., 2016). The association between the overall social environment and a child's BMI becomes significant and increasingly important over the life-course; adjusting for the BMI of parents only partly reduces this link. This suggests that the observed rise in the BMI of children during the past decades in most populations is reversible.

The relationship between higher BMI and risk of cancer is now well documented (Lauby-Secretan et al., 2016; Kyrgiou et al., 2017). Important and still unmeasured biological processes may result from an accumulation of fatty tissue in childhood. A close relationship exists between nutrient excess and dysregulation in the cellular and molecular mediators of immunity and inflammation. So-called lipid spillover from fat promotes metabolic disease by fostering ectopic lipid deposits. Because an estimated excess of 20–30 million macrophages accumulate with each kilogram of excess fat in a human, one could argue that increased adipose tissue mass is a state of increased inflammatory mass (Lumeng

and Saltiel, 2011). This evidence suggests that the etiological backdrop to an association with incidence of cancer begins in early life and may operate through inflammatory and immune system dysregulation.

Beyond examining physiological dysregulation within one system, researchers have also been interested in examining how early-life social conditions may be involved in overall physiological wear and tear across systems. A composite measure of biological health has been developed called allostatic load (Seeman et al. 1997); originally defined as a score based on selected biomarkers, allostatic load measures the lifelong physiological wear and tear (originally mainly related to stress response). Research has demonstrated that socioeconomic adversity, in particular in early life, leads to a higher allostatic load (i.e. higher lifelong stimulation of several key physiological systems), which in turn is related to increased risks of health outcomes and unhealthy ageing. Barboza Solís et al.

(2016) carried out a study in a large British birth cohort to examine the relationship between low SEP at birth (identified by either the mother's low education level or the father's manual occupation) and a higher allostatic load in midlife (age ~45 years). By conducting path analyses (Fig. 13.1), it was discovered that the pathways between maternal education level and paternal occupation and allostatic load were largely the same. They operated through childhood material deprivation level, educational attainment in adulthood, and adult BMI in both men and women. Such physiological wear and tear is only one process among other interrelated processes, such as cellular senescence and functional decline, involved in accelerated biological ageing (Delpierre et al., 2016).

Another set of important social to biological mechanisms involving the immune system may be set up in childhood. A study by Gares et al. (2017) showed that children from more disadvantaged social backgrounds are more likely than advan-

taged children to be infected by a ubiquitous herpesvirus, Epstein–Barr virus (EBV), by the age of 3 years, because of the material conditions to which they were exposed. EBV is involved in certain types of cancers (including nasopharyngeal carcinoma, Burkitt lymphoma, Hodgkin lymphoma, and post-transplant lymphoproliferative disorder). The main interest of this finding is that early acquisition of pathogens affects the maturation of the immune system, in turn affecting its function either positively or negatively. EBV is largely benign, but a social pattern was observed in the timing of exposure and acquisition, which means that immune maturation and function may be modified by these material and social conditions in the early-life environment. Understanding the development and determinants of immune function may be important in explaining why some social groups are more susceptible to certain cancers, because tumour development is determined partly by immune surveillance (Kelly-Irving et al., 2017).

Fig. 13.1. Relationship between maternal educational attainment at birth and allostatic load at age 45 years in the 1958 British birth cohort, highlighting the percentage of the association explained by different pathways. BMI, body mass index. Source: reprinted from Barboza Solís et al. (2016), copyright 2016, with permission from Elsevier.
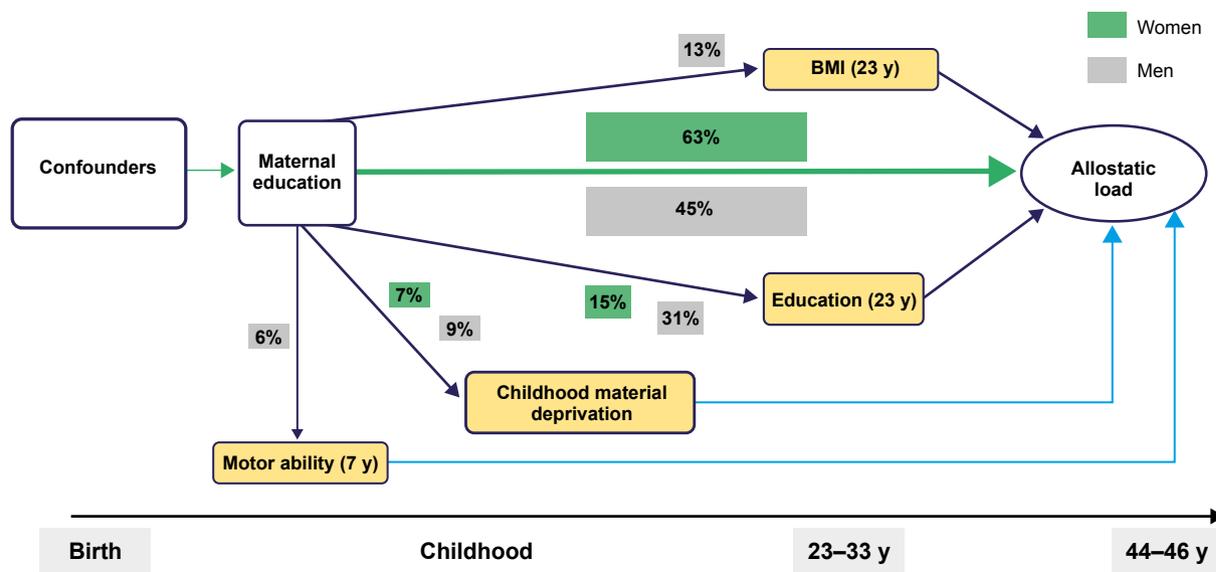
SEP as a risk factor for noncommunicable diseases in adults

There is evidence that SEP is associated with the risk of noncommunicable diseases (NCDs), including cancer. A large multicohort study and meta-analysis was carried out with individual-level data from 48 independent prospective cohort studies. Information about SEP (indexed by occupation), risk factors (high alcohol intake, physical inactivity, current smoking, hypertension, diabetes, and obesity), and mortality for a total population of 1 751 479 (54% women) from seven high-income countries was used.

Participants with low SEP had greater mortality compared with those with high SEP, and this association weakened but remained significant in mutually adjusted models that included the risk factors (Fig. 13.2). The population attributable fraction was highest for smoking, followed by physical inactivity and SEP. Low SEP was associated with a 2.1-year reduction in life expectancy between the ages of 40 years and 85 years; considering the risk factors individually, the corresponding years of life lost were 0.5 years for high alcohol intake, 0.7 years for obesity, 3.9 years for diabetes, 1.6 years for hypertension, 2.4 years for physical inactivity, and 4.8 years for current smoking (Stringhini et al., 2017). For cancer, the hazard ratio associated with low SEP (after adjustment for risk factors) was 1.26 (95% confidence interval [CI], 1.19–1.34), which is comparable with that for other NCDs. This work underlines the importance of considering social circumstances as important determinants of mortality and accelerated ageing in their own right.

Fig. 13.2. Pooled hazard ratios of socioeconomic position (SEP) and 25 × 25 (an initiative to cut mortality due to noncommunicable diseases by 25% by 2025) risk factors for all-cause mortality and cause-specific mortality. The minimally adjusted models were only adjusted for sex, age, and race or ethnicity; in the mutually adjusted models, SEP and the 25 × 25 risk factors are mutually adjusted. BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio. Source: Stringhini et al. (2017) © 2017 Stringhini et al. Published by Elsevier Ltd.

Risk factor and outcomes	Minimally adjusted HR (95% CI)	Mutually adjusted HR (95% CI)
Low SES (reference high SES)		
All-cause	1.46 (1.39–1.53)	1.26 (1.21–1.32)
CVD	1.52 (1.37–1.67)	1.29 (1.16–1.43)
Cancer	1.43 (1.34–1.52)	1.26 (1.19–1.34)
Other	1.45 (1.35–1.56)	1.25 (1.17–1.33)
Current smoking (reference never smoking)		
All-cause	2.27 (2.14–2.39)	2.21 (2.10–2.33)
CVD	2.19 (1.98–2.42)	2.21 (2.00–2.44)
Cancer	2.64 (2.40–2.91)	2.52 (2.32–2.74)
Other	2.05 (1.91–2.20)	1.99 (1.85–2.14)
Diabetes		
All-cause	1.87 (1.72–2.03)	1.73 (1.60–1.88)
CVD	2.18 (1.86–2.55)	1.92 (1.64–2.27)
Cancer	1.21 (1.06–1.38)	1.18 (1.04–1.34)
Other	2.21 (2.01–2.42)	2.08 (1.91–2.26)
Physical inactivity		
All-cause	1.43 (1.34–1.53)	1.28 (1.19–1.37)
CVD	1.54 (1.43–1.65)	1.35 (1.25–1.46)
Cancer	1.25 (1.15–1.36)	1.14 (1.06–1.23)
Other	1.50 (1.37–1.64)	1.34 (1.22–1.47)
High alcohol intake (reference moderate intake)		
All-cause	1.64 (1.44–1.87)	1.36 (1.23–1.51)
CVD	1.45 (1.26–1.66)	1.19 (1.08–1.32)
Cancer	1.70 (1.44–1.99)	1.38 (1.21–1.56)
Other	1.76 (1.52–2.03)	1.46 (1.30–1.65)
Hypertension		
All-cause	1.38 (1.30–1.46)	1.31 (1.24–1.38)
CVD	1.83 (1.66–2.03)	1.69 (1.53–1.88)
Cancer	1.08 (0.98–1.18)	1.07 (0.99–1.16)
Other	1.38 (1.28–1.47)	1.29 (1.21–1.38)
Obesity (reference normal BMI)		
All-cause	1.18 (1.09–1.27)	1.05 (0.97–1.14)
CVD	1.46 (1.28–1.66)	1.22 (1.06–1.40)
Cancer	1.01 (0.92–1.10)	1.02 (0.94–1.11)
Other	1.17 (1.08–1.26)	1.01 (0.92–1.10)

0.5 1.0 1.5 2.0 2.5 3.0

Social and biological mechanisms: pathways towards health inequalities

In a study that used data from the European Prospective Investigation into Cancer and Nutrition (EPIC) Italy cohort, retrospective information was collected about participants' childhood SEP, their highest educational attainment, and their adult occupation (Castagné et al., 2016). The aim was to examine whether SEP over the life-course affected the inflammatory system in adulthood. Early-life manual occupation was linked with a higher inflammatory score (β = 0.29; P = 0.002). When basal inflammation is chronically elevated, it is linked with metabolic and cardiovascular pathologies and cancer. Inflammation is one of the so-called enabling events associated with the hallmarks of cancer described by Hanahan and Weinberg (2011).

In addition to attempts to understand the relationships between social factors and biological factors, the association between these biological factors and subsequent health outcomes has been investigated. For example, a positive association was established between overall physiological wear and tear at the age of 45 years and mortality before the age of 55 years. This relationship was stronger than the association between any individual biomarker and mortality (Castagné et al., 2018).

Another analysis focused more specifically on how the educational attainment of individuals is related to an epigenetic mechanism, DNA methylation, which is used to represent overall biological ageing (Fiorito et al., 2017). Compared with those with high SEP, having low SEP was associated with greater accelerated ageing (β = 0.99 years; 95% CI, 0.39–1.59; P = 0.002). The results

suggested that individuals with a lower education level experienced a higher rate of biological ageing than those with a higher education level, even after controlling for several behavioural factors. Individuals who experienced life-course SEP improvement had intermediate levels of accelerated ageing compared with those with low or high SEP, suggesting a possible reversibility of the effect and supporting the relative importance of the early-life social environment. In a related study, the same age-acceleration DNA-based indicator was able to predict cancer mortality during follow-up (Dugué et al., 2018). Overall, these studies provide evidence for the existence of social to biological processes that go beyond behavioural factors. Socioeconomic adversity may be associated with accelerated epigenetic ageing, implicating biomolecular mechanisms that link SEP to age-related diseases and longevity.

Translating research findings for policy action

Research focused on understanding life-course mechanisms must be translated into meaningful findings for potential policy use, either as interventional research or as policy recommendations. Results so far emphasize the need for primary prevention within the childhood and adolescent environment to slow the trend towards higher BMI and the consequent propensity towards a pro-inflammatory state. Primary prevention involves acting upon social material as well as psychosocial factors. However, mitigating the consequences of adverse social trajectories in adulthood to encourage behaviour change, and limiting the consequences of occupational hazards, is also likely to affect biological

predispositions to chronic diseases at their roots.

Social environments may act on biology through the action of exogenous exposures that encompass chemical and physical exposures (air pollution, pesticides, viral exposures, occupational exposures) or behavioural exposures (tobacco, alcohol, food, etc.). In addition to these material agents, social relationships (e.g. isolation) or life stress events (e.g. adverse childhood experiences [ACEs]) can lead to unhealthy ageing. In this case perception and interpretation are involved, together with internal molecules from the body, mainly linked to stress–perception and stress–response systems.

In our research, we consider primary prevention in terms of the common root of the most prevalent chronic diseases, including cancers, linked with accelerated ageing. There is much evidence for interrelations between obesity, diabetes, cardiovascular diseases, cognitive decline, and cancer (Giovannucci et al., 2010; Fatke et al., 2013; Tolppanen et al., 2013; Vagelatos and Eslick, 2013). Researchers have even proposed a human disease network based on the molecular relationships between phenotypes (Goh et al., 2007; Barabási et al., 2011). In parallel, socioeconomic and psychosocial factors such as ACEs have been identified as important upstream exposures for many of these chronic conditions and their risk factors (see Krieger, 2008 for limitations of the concepts of upstream and downstream). ACEs have been associated with ischaemic heart disease (Dong et al., 2004), obesity (Thomas et al., 2008), perceived health (Dube et al., 2010), self-reported cancer (Kelly-Irving et al., 2013a), psychopathology (Clark et al., 2010), inflammation (Danese et al., 2009),

mortality (Felitti et al., 1998; Kelly-Irving et al., 2013b), health behaviours (Anda et al., 2002; Dube et al., 2002, 2003), and allostatic load (Barboza-Solís et al., 2015) (for a review see also Hughes et al., 2017). Policies targeting socioeconomic and psychosocial factors in childhood may be an effective method of improving the lives of children in the present, and preventing the onset of chronic conditions such as cancer in the future. Such an outcome-wide approach to epidemiology can facil-itate the translation into public health policy (VanderWeele, 2017), and can be carried out in parallel with mechanism-focused approaches.

Conclusions

To reduce the impact of socioeconomic inequalities on health, building a dialogue between researchers, policy-makers, and other stakeholders is key. Life-course evidence of the social to biological embodiment highlights the need for investment in early life to prevent the onset of NCDs, including cancer, in later life.

Key points

- This chapter summarizes life-course approaches to assess socioeconomic inequalities in cancer, providing results from the Lifepath project that are relevant to cancer.

- The life-course approach to health is a conceptual framework where the primary interest is in assessing the "social organisation of an individual's passage through life".

- Social determinants of risk factors associated with cancer begin in early life and persist across the life-course.

- The pathways between social determinants and health outcomes operate as a dynamic set of social and biological processes and interactions between individuals within a population and their environments over time.

- A multidisciplinary approach is needed, integrating information on socioeconomic position, environmental exposures, and risk factors with biological measurements.

- The evidence on social determinants of disease, including cancer, needs to be translated for use by policy-makers.

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Introduction to Part 3

Lynette Denny and Christopher P. Wild

Social inequalities in health refer to differences that are systematic, socially produced, unnecessary, and avoidable. They are considered unjust and unfair.

The World Health Organization (WHO) promotes a life-course approach to health, and emphasizes that people's health and well-being are linked to "poverty reduction, education, access to clean air and water, the realisation of human rights and sustainable livelihoods and environments, all of which are underpinned by good governance" (Kuruvilla et al., 2018).

The WHO Commission on Social Determinants of Health (CSDH, 2008) highlighted the impact of inequalities and how to structure a response. Achieving equality in health, such that no one is left behind, is at the heart of the United Nations Sustainable Development Goals for 2030; more specifically Goal 3 is to "ensure healthy lives and promote well-being at all ages" (UN, 2015). The 2017 World Health Assembly resolution on cancer prevention and control is consistent with these earlier pieces of work in highlighting the need to implement cancer control programmes with a focus on equity and access.

This part of the book moves beyond definitions of social inequalities in cancer and beyond analysis of the current status of those inequalities. Rather, the chapters respond to the overarching objectives described by the broader United Nations and WHO initiatives mentioned above by suggesting actions to tackle inequalities in cancer, through both the implementation of currently available measures and the conduct of research to provide the evidence base to do more.

The areas covered include: (i) the accurate and ongoing measurement of inequalities in cancer, including in vulnerable groups within a population, to ensure that cancer control interventions truly benefit everyone; (ii) the definition of a research agenda to fill the gaps in knowledge to enable a more effective and timely approach to reduce inequalities; (iii) the investment required for the development and adoption of cancer control measures in low- and middle-income countries; (iv) the development of national cancer control plans that

focus on improving systems and better care, rather than primarily investing in technologies that may be of limited impact and serve to increase inequalities; and (v) the avoidance of the increased morbidity and waste of resources associated with overdiagnosis and overtreatment of cancer in some high-income settings.

This part of the book also describes lessons learned from AIDS activism, notably the partnerships and advocacy that can help to accelerate a reduction in social inequalities by effective cooperation and by holding to account those in positions of responsibility.

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PART 3.

TACKLING SOCIAL INEQUALITIES IN CANCER

CHAPTER 14.

Assessing the impact of a public health intervention to reduce social inequalities in cancer

Gwenn Menvielle, Ivana Kulhánová, and Johan P. Mackenbach

Introduction

Reducing social inequalities in health is one of the main public health challenges of our times. However, it is still not well understood which interventions and preventive strategies are the most effective to achieve this goal. Having knowledge of which interventions and strategies are the most effective implies that the target population and the relevant determinants in which to intervene have been identified, and that the types of inequalities that we aim to decrease have been clearly specified. This chapter discusses how these aspects are important considerations when assessing the effect of public health approaches to reducing social inequalities in cancer. Examples in the field of social inequalities in cancer are used to illustrate how the effect of an intervention (its magnitude and direction of change) will depend on how inequalities are measured as well as how the choice of the target population and target determinants will have an impact on the magnitude of health inequalities.

What inequalities do we aim to reduce?

Relative and absolute inequalities

Inequalities can be measured using relative or absolute measures. The most frequently used are described in Chapter 4. An increasing number of studies report that relative and absolute measures of inequalities lead to different conclusions in terms of whether inequalities are increasing or decreasing over time, which population (sex, age groups, ethnic groups, geographical areas, time periods, health status) shows the largest inequalities, and whether interventions widen or narrow inequalities (Mackenbach et al., 2015, 2016a; Platt et al., 2016). Fig. 14.1 illustrates this concept with a schematic example, in which mortality risk is determined for people with both low and high socioeconomic status (SES) over two different periods.

Studies documenting social inequalities in Europe have provided several examples of these discrepancies. For instance, trends in social inequalities in mortality have shown contradictory findings depending on

Fig. 14.1. Schematic illustration of trends in relative and absolute inequalities: mortality rates for two periods and for two different levels of socioeconomic status (SES). In period 1, the relative risk of mortality for people with low versus high SES is 2 and the rate difference is 200; in period 2, the relative risk is 2 and the rate difference is 100. Therefore, relative inequalities have remained the same, whereas absolute inequalities have decreased.
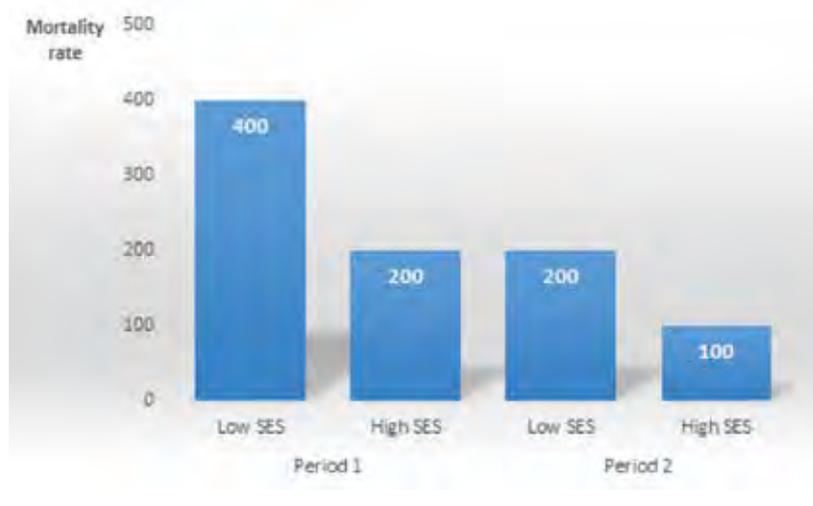
whether relative or absolute inequalities were considered. Relative inequalities are being observed to increase in both men and women in many western European countries, whereas absolute inequalities are decreasing (Mackenbach et al., 2015, 2016a; de Gelder et al., 2017). This situation can be illustrated with measures of both absolute (rate difference) and relative (rate ratio) inequalities in cancer mortality in men with a low versus a high education level over two separate periods in the 1990s and the 2000s in three European populations (Table 14.1). Whereas Norway experienced an increase in both relative and absolute inequalities, the other populations showed contradictory trends in relative and absolute inequalities. More specifically, absolute inequalities between men with a low versus a high education level in France decreased (the difference in age-standardized mortality rates declined from 242.9 deaths per 100 000 in the 1990s to 229.5 deaths per 100 000 in the

2000s), whereas relative inequalities increased (the rate ratio increased from 1.81 in the 1990s to 1.87 in the 2000s). In contrast, in Turin, Italy, absolute inequalities remained stable overall, but relative inequalities were observed to increase. In a context of recent declines in cancer mortality rates in all social strata in these three countries, these opposing trends are the consequence of differences in the speed of the decline in cancer mortality rates among individuals with lower and higher SES.

The need to compute both absolute and relative measures is increasingly stressed in the scientific literature (and discussed in Chapter 4). However, a recent review (King et al., 2012) pointed out that, at the time of its publication, far too many studies were still quantifying social inequalities in health on a relative scale only. Because relative and absolute measures can lead to different conclusions, providing both measures is important to evaluate interventions aimed at reducing social inequalities in health. However, when the types of measures give contradictory conclusions, determining whether inequalities are increasing or decreasing is not only a mathematical but also a normative exercise. More generally, although measurement of the magnitude, direction, and rate of change of health inequalities has long been seen as a value-neutral process, this is not only a mathematical and technical issue but also implies judgements about what is fair or acceptable. Value judgements are closely embedded in inequality measurements (Harper et al., 2010). A relative measure of inequality will quantify inequalities regardless of the absolute level of the health outcome considered. Therefore, a preference for relative measures of inequalities

Table 14.1. Differences between cancer mortality rates by education level in three populations in Europe during the 1990s and the 2000s in men

Location	Rate difference[a]		Rate ratio[b]	
	1990s	2000s	1990s	2000s
Norway	125.4	180.4	1.38	1.67
France	242.9	229.5	1.81	1.87
Turin, Italy	172.6	169.3	1.55	1.70

[a] Difference between the age-standardized mortality rate of men with a low (up to lower secondary) and high (tertiary) education level, per 100 000 person years.

[b] Ratio of the age-standardized mortality rate of men with a low (up to lower secondary) to a high (tertiary) education level.

Source: compiled from de Gelder et al. (2017)

implies that equality matters more than any other consideration, which corresponds to a strictly egalitarian normative position. In contrast, equality is not the only factor that matters for absolute measures of inequalities, because an absolute measure of inequality also takes into account the overall level of the health outcome.

Low and Low (2006) argued that it is better to use relative inequalities when the aim is to assess progress in reducing inequalities in the context of overall health improvement. Indeed, absolute inequalities are likely to decrease, whereas decreasing relative inequalities will be observed only if health is improving faster among the most deprived people (Mackenbach et al., 2016b). Nevertheless, others may argue that a reduction in relative inequalities requires larger relative improvements in health in groups with lower SES than in groups with higher SES, which is a challenging task for policy-makers. However, a relative measure using the most advantaged group as a reference is appropriate for assessing trends in social inequalities when this most advantaged group has already reached the best achievable health outcome. In our opinion, in the general current context of average health improvement, a reduction in absolute but not relative inequalities, although it is not the ideal situation, should be seen as a first and important step towards the elimination of social inequalities in health (Mackenbach, 2015).

Reference point used to assess inequalities

Historically, social epidemiological studies first quantified social inequalities in health using measures that compared two groups (rate difference, rate ratio, or similar measures) and disregarded what was happening in the rest of the population. It was then suggested that measures that account for the entire population would produce a more accurate measure of social inequalities in health, because they would include all socioeconomic groups (Mackenbach and Kunst, 1997). Such measures would also be more adapted to comparisons between different populations (sex, age groups, ethnic groups, geographical areas, time periods, health status), because they would account for possible differences in their distribution by SES. Measures differ not only according to the population groups compared but also according to the reference point used to assess inequalities.

Some measures assess inequalities using a specific group as a reference point, usually the least deprived group or the group with the best health outcomes (which often happens to be the same group). These measures conclude that there is no inequality when everybody has the same level of health as this specific group. Among these types of measures are the rate ratio and the relative version of the population-attributable risk (PAR) (both are relative measures, and the latter includes the entire population), as well as the rate difference and the absolute version of the PAR, or the number of attributable cases (both are absolute measures, and the latter includes the entire population).

Other measures do not use a specific group as a reference point and conclude that there is no inequality when everybody has the same level of health, whatever the level achieved. Among these types of measures are the relative index of inequality (RII), which is a relative measure, and the slope index of inequality (SII), which is an absolute measure; both of these measures include the entire population.

All of these measures (RII, SII, and PAR) are defined in Chapter 4. It is important to note that PAR is different from the population-attributable fraction methodology. When interpreting PAR, a causal effect is not necessarily assumed between SES and health. As mentioned in Chapter 4, the absolute version of PAR corresponds to the number of cases that could be avoided if everybody had the same level of health as a specific group, usually the least deprived. However, this reduction may not be achievable in reality; if it is achievable, it may be by means other than changing the socioeconomic stratification in the population. For instance, when assessing social inequalities in participation in cancer screening, PAR can be decreased by implementing organized screening.

As for relative and absolute inequalities, different conclusions about the magnitude and the trends in social inequalities in health could be observed with measures that used different reference points. In a study that investigated changes in inequalities in cancer mortality by education level in France between 1990–1998 and 1999–2007 (Menvielle et al., 2013), several measures were used to quantify social inequalities in health. Although all of the measures used were relative, they yielded contrasting conclusions. Among women, social inequalities remained stable over time when quantified with RII; RII decreased from 1.45 to 1.28, although the temporal change was not statistically significant. In contrast, an increase in social inequalities was observed when using hazard ratio; compared with women with a tertiary education, hazard ratio was

observed to increase from 0.92 (95% confidence interval [CI], 0.72–1.18) to 1.33 (95% CI, 1.09–1.63) in women with a general secondary education. When quantified with PAR, social inequalities increased strongly, from 9% to 24%. The contradictory results observed when using different measures of inequalities were explained by different trends in cancer mortality between groups of different education level. As shown in Table 14.2, between 1990–1998 and 1999–2007 cancer mortality decreased among women with the lowest and highest education levels, but remained stable or even increased among the largest group, that of women with a medium education level (lower and vocational upper secondary). Cancer mortality was therefore similar between groups of different levels of education during 1999–2007, with the exception of women with a

tertiary education, who had lower cancer mortality. This specific situation explains the decrease in RII, although it was not statistically significant (cancer mortality became similar for the majority of the population), whereas inequalities as assessed by other measures increased (only women with the highest education level experienced a decrease in cancer mortality over time).

When assessing the impact of public health approaches on social inequalities in cancer, researchers and policy-makers should carefully consider the measure used to quantify social inequalities, because different measures provide information on the achievement of different objectives. Measures such as RII provide information on whether the entire population has reached the same level of health, but without providing information on the level of

health achieved, whereas measures such as PAR provide information on whether the entire population has achieved the level of health of a specific group (usually those with the highest SES).

Public health approaches to reducing social inequalities in health can ultimately aim to eliminate social inequalities by improving the level of health of the entire population until it is the same as that of the healthiest group. PAR has several strengths in this approach: it is a measure that uses a specific reference group; it takes into account the entire population; and it enables assessment of the change in inequalities compared with a hypothetical situation, for example, a target goal set by a public health plan. However, PAR is not free from methodological limitations; in particular, unlike RII, it provides no information on the social gradient. For all

Table 14.2. Differences between cancer mortality by education level in women in France during the 1990s and the 2000s

Education level	No. of women (% of total)	No. of deaths	MR	HR (95% CI)	RD
1999–2007: relative version of the PAR[a], 24%; absolute version of the PAR[a], 37; RII, 1.28 (95% CI, 1.08–1.52)					
No diploma	22 741 (16.5)	425	170	1.41 (1.18–1.69)	49
Primary	29 020 (21.1)	621	162	1.36 (1.14–1.61)	41
Lower and vocational upper secondary	46 108 (33.5)	633	162	1.40 (1.19–1.65)	41
General upper secondary	16 618 (12.1)	195	157	1.33 (1.09–1.63)	36
Tertiary	23 346 (16.9)	180	121	1.00	Reference
Total	137 833 (100.0)[b]	2054	154	–	–
1990–1998: relative version of the PAR, 9%; absolute version of the PAR[a], 15; RII, 1.45 (95% CI, 1.23–1.72); P_{trend}[c] = 0.32					
No diploma	32 359 (24.7)	750	190	1.30 (1.07–1.59)	44
Primary	37 449 (28.6)	716	150	1.05 (0.86–1.28)	4
Lower and vocational upper secondary	33 988 (25.9)	425	155	1.08 (0.88–1.33)	9
General upper secondary	14 043 (10.7)	142	134	0.92 (0.72–1.18)	−12[d]
Tertiary	13 141 (10.0)	118	146	1.00	Reference
Total	130 980 (100.0)[b]	2151	161	–	–

CI, confidence interval; HR, hazard ratio; MR, age-standardized mortality rate (per 100 000 person-years); PAR, population-attributable risk; RD, rate difference; RII, relative index of inequality.

[a] Number of deaths attributable to differences in education (per 100 000 person years): the product of MR and relative PAR.

[b] Percentages may not add up to 100, because of rounding errors.

[c] Comparison of the RII for the two periods.

[d] The negative RD value indicates a higher mortality rate among women with a tertiary education.

Source: Menvielle et al. (2013), © Menvielle et al.; licensee BioMed Central Ltd. 2013

these reasons, it is recommended to assess inequalities using both types of measures, to properly evaluate interventions aimed at reducing social inequalities in health. When these types of measures give contradictory conclusions, a value judgement is required to determine whether inequalities are decreasing or increasing. In our opinion, a decrease or a stabilization in the value of RII should be interpreted as progress towards the reduction of inequalities only if measures such as PAR are not increasing. If PAR is observed to be increasing, this would mean that the level of health has equalized within the entire population, but not necessarily to the best possible level.

Target of the intervention

An important aspect of prevention policies is the target population. This discussion started with the well-known article titled "Sick individuals and sick populations" published by Rose in 1985, in which he distinguished between population-based interventions (or a population strategy of prevention) that target the entire population and interventions that target high-risk groups (Rose, 1985). Rose noted that population-based interventions were likely to lead to larger improvements in health in terms of number of health outcomes avoided, because they shifted the risk distribution of the entire population to a lower risk.

More recently, Frohlich and Potvi (2008) discussed the general framework proposed by Rose from a social inequalities perspective, suggesting the replacement of a high-risk-group approach by a vulnerable-group approach (where a vulnerable group is defined as a group that is at higher risk because of shared socioeconomic conditions). Frohlich and Potvin stressed that population-based pre-

vention policies may lead to a widening in health inequalities, because these policies may affect people with different SES in different ways, and may have a stronger effect among the groups with highest SES. This phenomenon is referred to as the inverse prevention law. To be fully effective in improving the health of the population without increasing social inequalities in health, prevention policies should therefore combine a population strategy of prevention with a vulnerable-group approach to create a so-called proportionate universalism approach. This type of intervention targets the entire population, but the scale and the intensity of the intervention are proportionate to the level of disadvantage (Marmot, 2010). A schematic illustration of this concept is given in Fig. 14.2, and an example of a proportionate universalism approach for breast cancer screening is given at the end of this section (Table 14.3). From a theoret-

ical point of view, this approach is without any doubt the most appealing one. However, in the current context of budget restrictions, policy-makers may be tempted either to target only the people most in need or to implement population-based strategies (McLaren et al., 2010).

Interventions differ in their level of action and the targeted factors, and one can distinguish between upstream and downstream interventions. Upstream policies target distal factors and aim to modify the structural determinants of social inequalities, also called "the causes of the causes", through various policies such as fiscal, environmental, social, or health-care policies (CSDH, 2008). Upstream policies also include policies aimed at changing the social stratification. Downstream interventions more narrowly target clinical or behavioural factors, also called proximal factors, usually at an individual level.

Fig. 14.2. Schematic illustration of the proportionate universalism approach: how a reduced gradient in health outcome by socioeconomic status is achieved after the implementation of an intervention that has a greater effect on those at a greater disadvantage. © Queen's Printer for Ontario, 2015. Adapted and reproduced with permission.
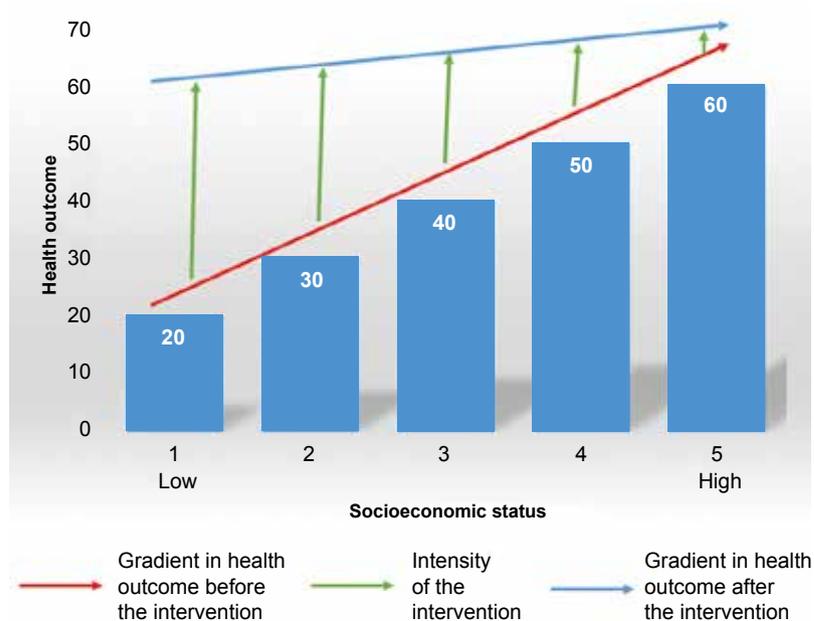
Table 14.3. Individual participation rates[a] in breast cancer screening by deprivation quintile, relative to the least deprived group, for women who could undergo mammography only at radiologists' offices or who had the additional option of being screened at a mobile mammography unit

Deprivation quintile	OR (95% CI)		
	Screening only in radiologists' offices (*n* = 35 804)	Screening in radiologists' offices or in mobile mammography unit (*n* = 28 298)	Total population (*n* = 64 102)
1 (least deprived)	1	1	1
2	0.87 (0.74–1.01)	1.06 (0.90–1.25)	0.92 (0.81–1.04)
3	0.86 (0.71–1.00)	1.11 (0.95–1.30)	0.94 (0.84–1.06)
4	0.83 (0.71–0.96)	1.15 (0.99–1.35)	0.94 (0.84–1.06)
5 (most deprived)	0.81 (0.69–0.95)	1.00 (0.84–1.19)	0.85 (0.75–0.97)

CI, confidence interval; OR, odds ratio.

[a] All models adjusted for age and distance to radiologist's office. ORs for the total population also adjusted for invitation to the mobile mammography unit.

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Midstream policies have been defined by some researchers as area-based initiatives or territorial approaches. These policies concentrate resources in the most disadvantaged areas. The underlying idea is that a concentration of problems may hinder the completion of mainstream programmes, and such policies are an easy method of reaching a large number of deprived people. However, these policies have several limitations. The majority of deprived people do not live in deprived areas. Many of the structural problems faced by deprived people are generated at a national or even higher level and may not be solved by local solutions that only attenuate the effects but do not address the roots of these problems. Finally, it has been argued that these policies shift the responsibility for improving health from the state to the community, and ultimately to the individual (Asthana and Halliday, 2006).

Interventions can also differ in the required level of involvement of the individual: interventions can range from providing information to offering incentives, restricting choices, and

introducing regulations. Some authors have proposed the categorization of interventions into superficial or radical interventions (McLaren et al., 2010). Superficial interventions are fully agent-based; they aim to change people's health by motivating individuals to change their behaviour (e.g. quitting smoking). In contrast, radical interventions use environmental control methods; they aim to change people's health by changing the context in which people live, independent of an individual's action (e.g. a ban on the use of asbestos and, as adopted in Denmark, legislation on the trans-fatty acid content in food). A real-life intervention, whether population-based or targeted at those most in need, will fall somewhere on the continuum from superficial to radical interventions. Superficial interventions directly target proximal factors and are classified as downstream interventions. Radical interventions act on distal factors and are classified as upstream interventions. However, although upstream policies are aimed at changing the context in which people live, thereby creating an environment more favourable to

health, they are not necessarily fully radical interventions, because the outcome may ultimately rely on action taken by a person (e.g. participation in nationwide organized cancer screening).

The effect of an intervention on social inequalities in health depends on its characteristics. We already mentioned that population-based interventions may increase social inequalities in health, because they may have a stronger effect among the least deprived people. This is more likely to be observed if population-based interventions are aimed at modifying social norms through agent-based approaches, instead of changing an individual's exposure through global environmental control methods. More generally, the more the strategy relies on the characteristics and actions of an individual, the more likely it is to increase social inequalities in health. A recent study showed that upstream and/or more radical interventions were more likely to reduce inequalities than are downstream and/or more superficial interventions (Lorenc et al., 2013). The most efficient interventions in

reducing social inequalities in various health outcomes were free provision of resources (e.g. free fruit in schools or free folic acid supplements during routine gynaecological visits), fiscal interventions on tobacco price, and structural workplace interventions. In contrast, media campaigns, which are population-based superficial interventions, led to an increase in inequalities. This finding was supported by many studies on smoking prevention but was also suggested for folic acid intake. However, upstream policies and radical interventions may have unintended consequences that have a greater impact on the least socially disadvantaged groups, thereby increasing social inequalities in health. For instance, although many studies have reported that workplace smoking bans did not have a differential impact across individuals with different SES, several other studies have made the contrasting observation that workplace smoking bans were more effective in reducing smoking among the least disadvantaged, therefore exacerbating social inequalities in smoking (Thomas et al., 2008).

Cancer screening programmes provide an interesting example of the impact of interventions on social inequalities. Such programmes exist for colorectal cancer (men and women) and for breast cancer and cervical cancer (women). Cancer screening can be opportunistic (i.e. based purely on the will of the patient and/or health professional) or organized. Organized screening mostly relies on directly informing (usually through letters) and inviting the population to screening, while removing (at least partially) the out-of-pocket payment. Compared with opportunistic screening, organized screening is associated with increased partici-

pation, smaller inequalities in participation (Palència et al., 2010; Walsh et al., 2011), and, in most settings, reduced inequalities in cancer survival (Louwman et al., 2007; Puliti et al., 2012; Pacelli et al., 2014; Seneviratne et al., 2015). Although organized cancer screening programmes are not fully radical interventions, because the individual must make the decision to attend, well-organized screening programmes can reduce demographic and financial barriers, and therefore address some of the underlying or fundamental causes of non-participation in cancer screening. Although organized cancer screening programmes therefore reduce social inequalities in participation in cancer screening, such programmes do not totally remove social inequalities in cancer screening. This has been illustrated by a study that found that women facing adverse economic conditions (low income, lacking food sometimes or often, financial difficulties) were less likely to participate in breast cancer screening, even when a nationwide organized screening programme exists (Menvielle et al., 2014).

In addition, organized screening programmes can be supplemented by strategies aimed at increasing participation of the most disadvantaged people, such as local interventions in these groups or greater involvement of primary-care physicians. A review compared several interventions implemented to improve participation in breast cancer and cervical cancer screening in the most disadvantaged groups (Spadea et al., 2010), and found that local interventions in disadvantaged populations, in particular interventions aimed at increasing the involvement of health professionals and decreasing geographical and financial barriers, were the most

effective for increasing participation in cancer screening. This review showed that a combination of a population-based and vulnerable-group approach may be the best strategy to improve participation in breast cancer and cervical cancer screening among all women, and therefore decrease social inequalities in cancer screening, supporting the proportionate universalism approach.

An implementation of breast cancer screening provides an example of the proportionate universalism approach (Guillaume et al., 2017). In a rural French region (the Orne department, with an area of 1710 km^2 and 290 015 inhabitants), in addition to the nationwide breast cancer screening programme, a mobile mammography unit has been used since 2003 to increase the participation rate in breast cancer screening. The mobile mammography unit was parked in 109 different places, mostly in rural areas far from radiologists' offices, at different times during each 2-year screening round. Results based on the participation rate in breast cancer screening over the period 2003–2012 are presented in Table 14.3. Socioeconomic differences in participation rates in breast cancer screening were smaller in the group who were offered the additional option of undergoing mammography at the mobile unit compared with those who could only be screened at a radiologist's office. Overall, social inequalities in participation in breast cancer screening were reduced in the total population compared with the population who could only undergo mammography at a radiologist's office. Compared with the least deprived quintile, the odds ratio (OR) in the fourth deprivation quintile increased from 0.83 (95% CI, 0.71–0.96) in the population who could only undergo

mammography at the radiologist's office to 0.94 (95% CI, 0.84–1.06) in the total population. However, the odds ratio in the most deprived quintile remained statistically lower than 1 in the total population (OR, 0.85; 95% CI, 0.75–0.97). The study concluded that a proportionate universalism approach could be beneficial in decreasing social inequalities in health.

Conclusions

This chapter has summarized the important challenges for public health interventions that aim to reduce social inequalities in health. From the examples described, it is clear that it may not be sufficient to improve the average level of health of the population to combat social inequalities. There is no single measure – whether relative or absolute – that is adequate for all public health purposes. The types of measures that are best able to monitor changing social inequalities in health as well as the target population and/or factors differ according to the type of intervention and its policy implications in public health. When interpreting the impact of a public health intervention on health inequalities, clarity is needed about the assumptions made in the use of each measure. The available literature highlights the lack of evaluations that investigate the possible differential effect of interventions according to SES. To advance the fight against social inequalities in health, there is an urgent need for more evaluations of the effect of interventions on social inequalities in health.

Key points

- Determining whether inequalities are increasing or decreasing is not only a mathematical but also a normative exercise.
- Opposing trends can be observed in relative and absolute inequalities as the consequence of differences in the speed of health change among individuals with lower and higher socioeconomic status.
- A decrease in social inequalities in health does not necessarily mean that health has improved in all socioeconomic groups.
- Prevention policies should combine a population-based and a vulnerable-population approach, also known as proportionate universalism.
- The more the strategy relies on the characteristics and actions of an individual, the more likely it is to increase social inequalities in health.

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CHAPTER 15.

Research priorities for social inequalities in cancer in sub-Saharan Africa

Valerie McCormack and Robert Newton

Introduction

As seen in Chapter 6, to date most research on social inequalities in cancer has been conducted in high-income countries despite the fact that, globally, absolute disadvantage is far greater in resource-limited settings. Specifically, perhaps nowhere in the world is inequality more evident than in sub-Saharan Africa, which is home to some of the poorest and most deprived people in the world. By almost any health-related measure, such as the number of doctors per head of population or the availability of radiotherapy or even morphine, sub-Saharan Africa lags behind the rest of the world (Wakeham et al., 2012; Newton et al., 2013). A further challenge to cancer risks and treatment is a large and unique comorbidity profile, including a high prevalence of HIV. This chapter focuses predominantly on this region, but many issues are also relevant in other resource-limited settings.

Cancer in sub-Saharan Africa

There were an estimated 1 055 000 new cases of cancer in Africa and 693 000 deaths from the disease in 2018 (Bray et al., 2018). This burden is increasing rapidly because of demographic expansion and ageing, such that a doubling of incidence and deaths is projected by 2040. This prediction does not take into account the changing risk factor profile in this continent, which is undergoing rapid transition. The prevalence of tobacco use is currently low but is rising in some areas as a result of promotion by the tobacco industry (Nsimba and Sussman, 2006). Urbanization, changing diets, increasing prevalence of obesity, decreasing levels of physical activity, increasing alcohol consumption, and fertility transitions characterized by delayed or less childbearing are expected to increase the incidence of cancers associated with these risk factors (Moultrie et al., 2012; Holmes et al., 2018). Notably, the incidence of breast cancer has risen markedly in Africa; it is now the most common tumour among women in many sub-Saharan African countries, just as it is worldwide (Ginsburg et al., 2017).

In 2018, the most commonly diagnosed cancers in Africa in men, shown in Fig. 15.1, are prostate cancer,

Fig. 15.1. Most common cancer types in men (left) and women (right) in Africa in 2018. Source: reproduced from Ferlay et al. (2018).

Legend (men):
- Prostate (114)
- Lung (38)
- Liver (8)
- Colorectum (7)
- Stomach (6)
- Non-melanoma skin cancer (4)
- Kaposi sarcoma (3)
- Lip, oral cavity (3)
- Oesophagus (1)
- Bladder (1)
- Not applicable
- No data

Legend (women):
- Breast (156)
- Cervix uteri (27)
- Thyroid (1)
- Liver (1)
- Not applicable
- No data
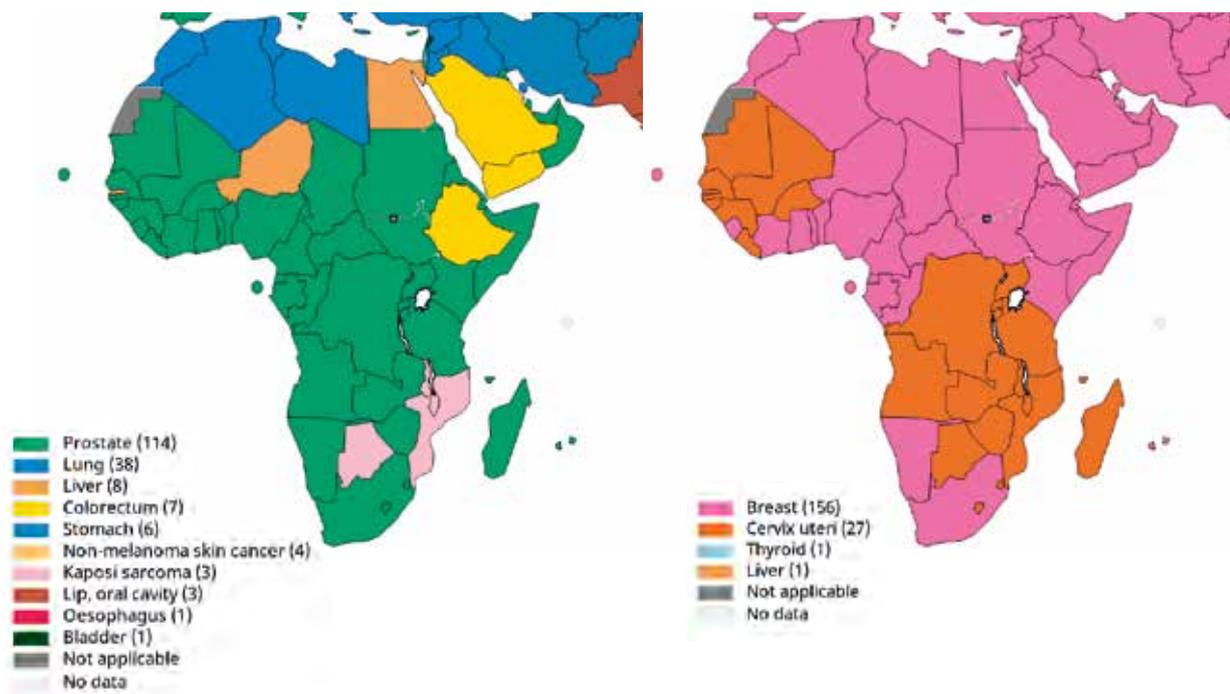
liver cancer, Kaposi sarcoma (KS), non-Hodgkin lymphoma (NHL), lung cancer, colon and rectum cancer, and oesophageal cancer. In women, the most common cancers are breast cancer, cervical cancer, liver cancer, colon and rectum cancer, NHL, ovarian cancer, and KS. Several of these cancers are associated with poverty or infections, namely KS, NHL, liver cancer, cervical cancer, and oesophageal cancer. Among children, the most frequent cancers in many sub-Saharan African countries include Burkitt lymphoma and KS, whereas leukaemia and non-Burkitt lymphomas predominate elsewhere. Currently, at least one third of cancers in Africa are caused by infections, many of which are preventable (Plummer et al., 2016). With the exception of hepatitis B virus in some but not all African countries, efforts to reduce the burden of cancer-causing infections are patchy or absent. Cancer control programmes aimed at the early detection of disease and effective treatment

are few; indeed, there is widespread failure to cure even the curable cancers, the most notable of these being childhood cancers. Effective palliative care is available to only a small minority of those dying from cancer.

In terms of societal inequalities, although economies of some African countries have experienced immense growth, and life expectancy has increased across the continent over the past 20 years, inequalities have also grown. In 2016, the mean Gini index (see Chapter 4) in Africa was higher than the world average, driven by extreme inequalities in just seven countries: Angola, Botswana, the Central African Republic, the Comoros, Namibia, South Africa, and Zambia (UNDP Africa, 2017). Despite a global decline in the number of people living in extreme poverty, Fig. 15.2 illustrates that the absolute number of people living in poverty is increasing in sub-Saharan Africa. Furthermore, despite a reduction in the proportion of populations living in

poverty around the world, Fig. 15.3 shows how this reduction has been substantially less in sub-Saharan Africa (in which > 40% of the population live in poverty). Sustainable Development Goal 1, adopted by the United Nations Member States in 2015, is to end poverty by 2030; however, one in three people in sub-Saharan Africa currently live below the international poverty line. For a family living in poverty on less than 1.90 international dollars per day, if a family member has symptoms of cancer, how does the family attain the know-how, resources, and finances, and overcome logistical and sometimes sociocultural barriers, to reach a cancer diagnostic facility, navigate the health-care system, and support their family member through their treatment, in a hospital located up to several hundred kilometres away?

Such is the situation facing the majority of cancer patients in sub-Saharan Africa. As economic development continues, a levelling-up approach

Fig. 15.2. The number of people living in extreme poverty has declined on a global scale for the past two decades, but not in sub-Saharan Africa. Source: Roser and Ortiz-Ospina (2018).

Total population living in extreme poverty, by world region

Numbers are in millions of people. Extreme poverty is defined as living with per capita household consumption below 1.90 international dollars per day (in 2011 PPP prices). International dollars are adjusted for inflation and for price differences across countries.
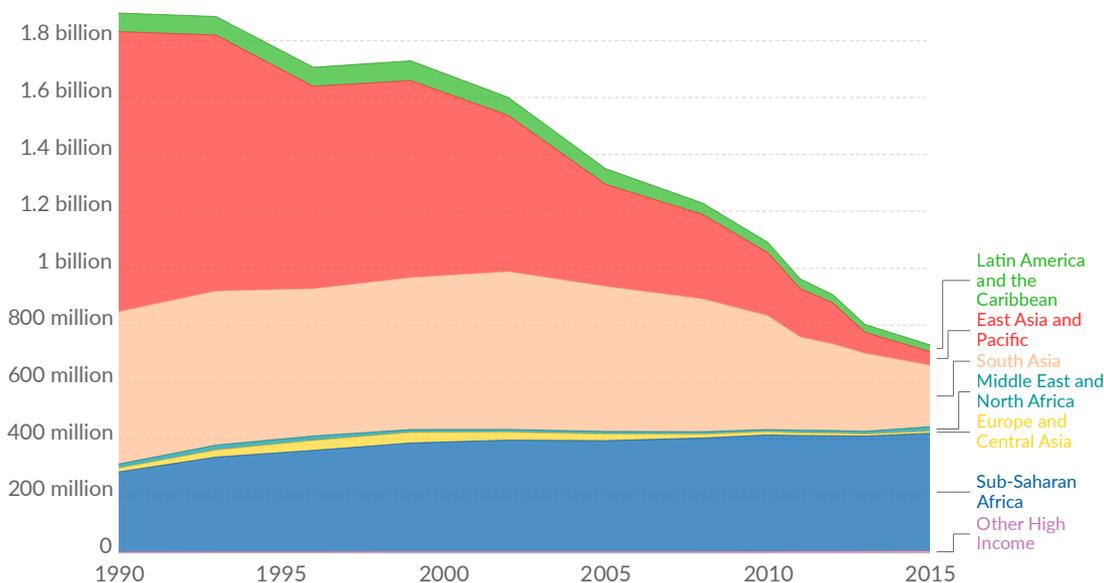
Our World in Data

Source: PovcalNet (World Bank)   OurWorldInData.org/extreme-poverty/   • CC BY

Note: Consumption per capita is the preferred welfare indicator for the World Bank's analysis of global poverty. However, for about 25% of the countries, estimates correspond to income, rather than consumption.

Fig. 15.3. The proportion of the population living in extreme poverty has declined steeply across the world, but in 2015 it remained above 40% in sub-Saharan Africa. Source: Roser and Ortiz-Ospina (2018).

Share of population living in extreme poverty by world region

Extreme poverty is defined as living with less than 1.90$ per day (in 2011 International Dollar). International dollars are adjusted for price differences across countries and across time.
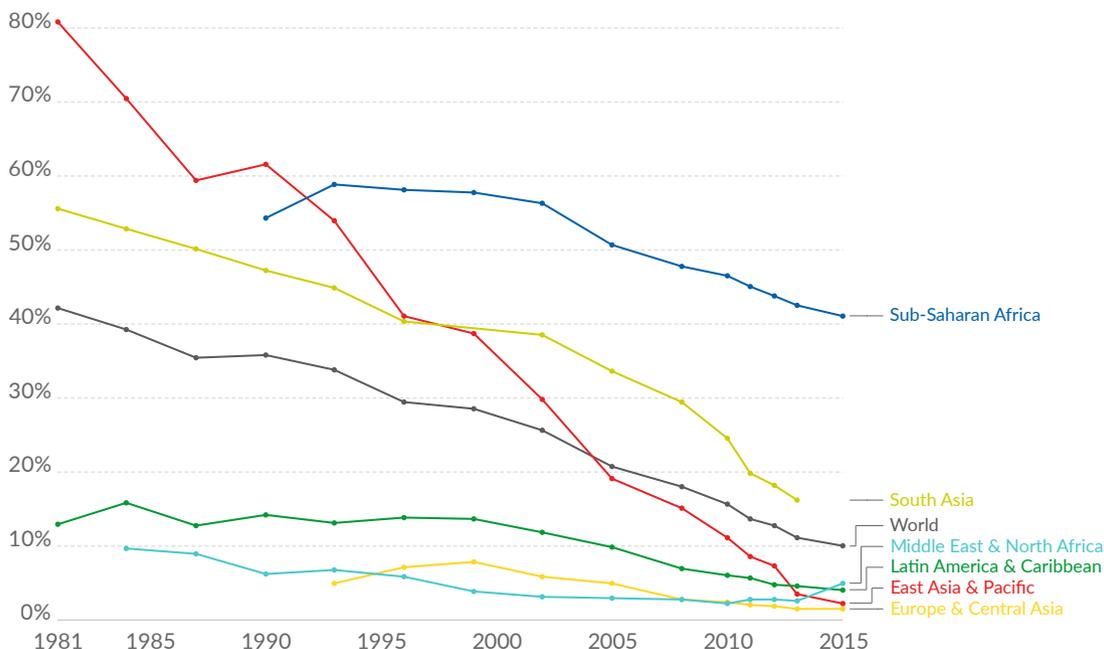
Our World in Data

Source: World Bank   OurWorldInData.org/extreme-poverty/   • CC BY

for cancer prevention and cancer care will be needed to achieve an equitable sharing of progress in improving cancer outcomes (Braveman and Tarimo, 2002).

Research on social inequalities in the occurrence of cancer

Predominantly on the basis of European and North American countries, Whitehead introduced the logic of interventions to tackle health inequalities (Fig. 15.4) and summarized a typology of four categories of actions to tackle them (Whitehead, 2007): strengthening individuals, strengthening communities, improving living and working conditions, and promoting healthy macro-policies.

Impeding the first fundamental task in the logic of intervention (Fig. 15.4) – observing the problem of cancer inequality – are weak health information systems. Cancer intelligence data need to be strengthened across many low-income settings; in Africa this initiative is supported by IARC (http://gicr.iarc.fr/en/) and the African Cancer Registry Network (Gakunga et al., 2015). However, measuring the burden of cancer in Africa is severely restrained by three related problems that may have social gradients and that make population-based cancer registration a challenging yet vital component of cancer control programmes: (i) an inadequate characterization of disease: technologies for diagnosing cancer are unavailable in many countries, particularly in imaging and histopathology for diagnosis; furthermore, poorer individuals may not be able to afford histology and other diagnostic fees and may never be diagnosed within the formal health-care system; (ii) an incomplete ascertainment of cases: there is uncertainty about the scale of this problem, and it affects our understanding of the geographical distribution of specific cancer types; and (iii) an inadequate ascertainment of population denominator data.

With this background, basic cancer registration needs to be strengthened to first gauge the extent of cancer inequalities between and within countries. An ideal situation would be to have one urban and one rural registry in as many countries as possible, because some of the most disadvantaged populations reside in rural settings. Supporting transitions to electronic health information systems, now being adopted in some low- and middle-income countries (LMICs), would greatly facilitate this process (Mutale et al., 2013). In terms of estimating social gradients in cancer incidence, differences have justifiably been well documented for certain population groups at very high risk, including of AIDS-defining and HIV-associated cancers in people living with HIV/AIDS. In terms of socioeconomic indicators, it is often not feasible for cancer registries to routinely collect good-quality data at the individual level; however, expanding area-level indicators based on geographic information systems could be generated from residential origin. Some registries are attempting to capture data on socioeconomic indicators, occupation, actual ethnicity, or predicted race based on analysis of surnames (e.g. in the National Cancer Registry of South Africa), and others are focusing their efforts on the collection of such detailed data for a short period or on a smaller geographical scale. Where this is possible, even if denominator data or cohorts are not available for the calculation of absolute incidence or mortality rates, insights into social or other gradients can be obtained from relative risks for a specific cancer using other cancers as controls. Impressively, the Nairobi Cancer Registry has been able to do this. From an analysis of 22 000 cancers diagnosed during 2000–2014, the relative incidences of individual cancers in White, Asian, and Kenyan ethnicities, and between the different Kenyan tribes, were calculated (Korir et al., 2017).

Social inequalities and primary prevention research

Given the inadequate cancer diagnostic and treatment facilities, for many cancers primary prevention is key to cancer control in LMICs. For established carcinogens, social

Fig. 15.4. The logic of interventions. Source: reproduced from Whitehead (2007), copyright 2007, with permission from BMJ Publishing Group Ltd.

| Observed problem of health inequality | → | Perceived causes of problem | → | Policy goals to address causes | → | Theories about how and why interventions might work to bring about change in causes | → | Design of intervention programme | → | Outcome of programme |
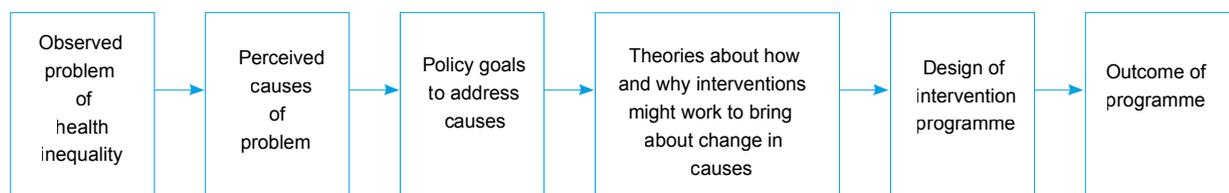
gradients in exposure prevalence, exposure levels, and, importantly, exposure source apportionment can be conducted within cross-sectional or cohort studies to inform later exposure mitigation interventions. As a starting point, a somewhat underutilized resource to assess social gradients in cancer risk factors are Demographic and Health Surveys (DHS); the representativeness and large scale of the repeated standard DHS provide valuable data on household- and individual-level social indicators and environmental and lifestyle risk factors (Corsi et al., 2012). Some risk factors for cancer are now included (see examples in Box 15.1),

Box 15.1. Demographic and Health Surveys data relevant to research on social inequalities in cancer.

Social indicators: education, wealth, education, occupation, marital status, and religion.

Risk factors: tobacco use (and type), alcohol consumption, anthropometry (including being underweight, of normal weight, overweight, obese), diabetes, HIV, fertility (age at first birth, number of children), and household (cooking fuels, water source).

Screening: breast cancer screening and cervical cancer screening.

and socioeconomic indicators are both extensive and relevant to the setting. Indicators that relate to the most disadvantaged groups of society, such as level of literacy, are key and provide essential information in the design of communication strate-

gies for cancer awareness and early presentation. For example, as African countries implement the World Health Organization Framework Convention on Tobacco Control, progress in eliminating social inequalities can be monitored. Analyses of recent DHS

**Fig. 15.5.** Demographic and Health Surveys provide useful data for use in evaluating social inequalities in lifestyle and environmental risk factors for cancer. Here, tobacco use in men is higher in less educated than in more educated men, and this difference is, on average, larger on a relative scale in low-income countries. RII, relative index of inequality; SII, slope index of inequality. Source: reproduced from Sreeramareddy et al. (2018), copyright 2018, with permission from BMJ Publishing Group Ltd.

a — Relative inequality

Country	RII (95% CI)
Low income	
Niger	0.86 (0.60, 1.11)
Ethiopia	2.28 (1.59, 2.98)
Burkina Faso	1.79 (1.44, 2.13)
Kenya	2.09 (1.36, 2.82)
Zimbabwe	2.53 (2.04, 3.01)
Haiti	5.15 (3.75, 6.56)
Liberia	3.95 (2.80, 5.11)
Uganda	4.98 (2.81, 7.15)
Moldova	1.68 (1.32, 2.04)
Benin	11.86 (7.52, 16.20)
Democratic Republic Congo	3.06 (2.50, 3.63)
Malawi	5.38 (3.88, 6.89)
Rwanda	7.18 (5.34, 9.03)
Comoros	4.55 (3.01, 6.09)
Tanzania	5.76 (3.46, 8.05)
Madagascar	2.16 (1.94, 2.39)
Bangladesh	1.78 (1.61, 1.95)
Burundi	8.17 (6.00, 10.34)
Mozambique	7.17 (5.18, 9.16)
Sierra Leone	3.84 (3.01, 4.67)
Nepal	3.34 (2.80, 3.87)
Cambodia	6.53 (5.54, 7.52)
Subtotal	3.61 (2.83, 4.61)
Lower middle income	
Armenia	1.03 (0.84, 1.22)
Senegal	1.44 (1.02, 1.85)
Nigeria	1.76 (1.48, 2.03)
Sao Tome	3.98 (1.12, 6.85)
Cameroon	2.06 (1.59, 2.54)
Cote d'Ivoire	1.66 (1.30, 2.02)
Kyrgyz Republic	0.79 (0.64, 0.94)
Swaziland	2.03 (1.45, 2.60)
Honduras	1.85 (1.41, 2.30)
Lesotho	1.71 (1.35, 2.06)
Ghana	11.86 (6.53, 17.19)
Ukraine	1.60 (1.35, 1.85)
Indonesia	1.42 (1.31, 1.53)
Zambia	2.82 (2.28, 3.36)
Congo	2.99 (2.16, 3.81)
Timor	1.60 (1.44, 1.76)
Pakistan	2.12 (1.69, 2.55)
Guyana	3.14 (2.31, 3.98)
India	2.58 (2.48, 2.67)
Subtotal	1.99 (1.66, 2.38)
Upper middle income	
Namiba	1.48 (1.10, 1.85)
Gabon	1.64 (1.14, 2.14)
Albania	1.50 (1.19, 1.82)
Azerbaijan	1.46 (1.10, 1.83)
Dominican Republic	4.27 (3.42, 5.12)
Maldives	1.58 (1.25, 1.91)
Subtotal	1.82 (1.24, 2.67)

Less use ← → More use for less educated

b — Absolute inequality

Country	SII (95% CI)
Low income	
Niger	-0.03 (-0.08, 0.02)
Ethiopia	0.07 (0.05, 0.09)
Burkina Faso	0.14 (0.09, 0.19)
Kenya	0.15 (0.09, 0.22)
Zimbabwe	0.21 (0.17, 0.25)
Haiti	0.22 (0.19, 0.25)
Liberia	0.22 (0.17, 0.26)
Uganda	0.25 (0.18, 0.32)
Moldova	0.26 (0.16, 0.36)
Benin	0.29 (0.25, 0.33)
Democratic Republic Congo	0.29 (0.24, 0.33)
Malawi	0.30 (0.26, 0.34)
Rwanda	0.31 (0.27, 0.35)
Comoros	0.34 (0.27, 0.41)
Tanzania	0.35 (0.27, 0.43)
Madagascar	0.36 (0.32, 0.40)
Bangladesh	0.38 (0.32, 0.44)
Burundi	0.41 (0.37, 0.45)
Mozambique	0.41 (0.35, 0.47)
Sierra Leone	0.47 (0.41, 0.53)
Nepal	0.56 (0.50, 0.62)
Cambodia	0.58 (0.54, 0.62)
Subtotal	0.30 (0.23, 0.36)
Lower middle income	
Armenia	0.02 (-0.09, 0.14)
Senegal	0.06 (0.01, 0.11)
Nigeria	0.07 (0.05, 0.09)
Sao Tome	0.10 (0.05, 0.16)
Cameroon	0.12 (0.08, 0.16)
Cote d'Ivoire	0.12 (0.06, 0.17)
Kyrgyz Republic	0.12 (0.02, 0.21)
Swaziland	0.12 (0.07, 0.16)
Honduras	0.15 (0.09, 0.21)
Lesotho	0.18 (0.11, 0.25)
Ghana	0.20 (0.16, 0.24)
Ukraine	0.24 (0.16, 0.31)
Indonesia	0.25 (0.20, 0.30)
Zambia	0.25 (0.20, 0.29)
Congo	0.28 (0.22, 0.34)
Timor	0.31 (0.25, 0.37)
Pakistan	0.32 (0.24, 0.40)
Guyana	0.34 (0.27, 0.41)
India	0.50 (0.49, 0.51)
Subtotal	0.20 (0.11, 0.29)
Upper middle income	
Namiba	0.09 (0.03, 0.15)
Gabon	0.11 (0.04, 0.18)
Albania	0.17 (0.09, 0.25)
Azerbaijan	0.19 (0.07, 0.31)
Dominican Republic	0.19 (0.16, 0.22)
Maldives	0.24 (0.14, 0.34)
Subtotal	0.16 (0.11, 0.21)

Less use ← → More use for less educated

data (in about 2015; Fig. 15.5) show greater prevalence of tobacco use in men with a lower versus a higher education level across many African countries and other LMICs (Sreeram-areddy et al., 2018). In contrast, the prevalence of tobacco use in African women is low.

Poverty is also connected to higher risks of exposure to infectious carcinogenic agents and to carcinogens originating from food, occupational, or environmental sources, some of which are depicted in Fig. 15.6. For example, indoor air pollution from the burning of biomass fuels in poorly ventilated kitchens leads to excessive exposure to polycyclic aromatic hydrocarbons in women and young children (Ezzati and Kammen, 2001);

clean-fuel cooking stoves are an attractive remedial solution to reduce the risks of multiple respiratory diseases, including lung cancer. Aflatoxin, a mould that grows on staples such as maize and peanuts kept in poor storage conditions, causes hepatocellular carcinoma, which is particularly common in West Africa. HIV prevalence is higher in groups with lower socioeconomic status (Wabiri and Taffa, 2013). With respect to occupational exposures, LMICs tend to have fewer regulations on the protection of workers from environmental carcinogens (McCormack and Schüz, 2012). Even when such regulations exist, they are difficult to monitor and enforce, especially within the large informal employment

sector. Furthermore, environmental protection measures are often weak, and the disposal of industrial waste may not exclude downstream human exposure.

Human biomonitoring studies, involving analyses of exposure or effect biomarkers, provide the most definitive evidence of exposure to carcinogens. To address social inequality, the sampling frame of such studies needs to be purposefully designed. Without targeted recruitment to enhance participation, socially disadvantaged groups may otherwise be under- or even unrepresented (Morrens et al., 2017). A growing number of cohorts in Africa aim to fill this gap, such as rural and HIV/AIDS cohorts.

Fig. 15.6. Examples of carcinogen exposures that are prevalent among poorer populations in sub-Saharan Africa. (a, top left) Traditional alcohols, such as this kachasu distillation in Malawi, are much cheaper than commercial alcohols and can have ethanol percentages of 60% and higher. (b, top right) Exposure to polycyclic aromatic hydrocarbons is high in women who cook and sleep by a fire that burns biomass; western Kenya. (c, bottom left) *Schistosoma haematobium*, a bladder carcinogen, affects people living on Lake Malawi. (d, bottom right) Aflatoxin-affected maize, a major cause of hepatocellular carcinoma in Africa. Source: (a–c) courtesy of Valerie McCormack and (d) courtesy of Thomas Lumpkin/CIMMYT via Flickr; CC BY-NC-SA 2.0.

The journey to diagnosis and cancer care

Early diagnosis of cancer and timely appropriate treatment are essential components of cancer control. For treatable cancers for which stage at diagnosis is a major prognostic factor, social inequalities in the length of, barriers to, and composition of the cancer journey are important to understand, especially for potentially curable cancers, such as those of the breast, cervix, and endometrium in women, and of the prostate in men. In about 2015, the majority of cancers in sub-Saharan Africa were diagnosed at stages III and IV, limiting treatment and survival prospects even under the best circumstances. Furthermore, within-country social inequalities in this already-late-stage distribution, and thus in survival outcomes, are present. For breast cancer, 75% of patients are diagnosed at stages III and IV (Jedy-Agba et al., 2016); this was higher in 2010 than in Black and White women in the USA diagnosed four decades previously. Unfortunately, the stage distribution may be even worse as many non-tertiary hospitals do not have diagnostic imaging facilities to detect the presence of metastases. This late-stage distribution is amenable to change, however, even over a short time frame. At the Chris Hani Baragwanath Hospital in Soweto, South Africa, a functioning dedicated breast cancer clinic, which can be relied upon by peripheral hospitals and clinics, has achieved a reduction in stage III/IV disease from 70% to 50% in 5 years, in the absence of any form of organized early-detection programme (McCormack et al., 2013). However, when such improvements are made to overall situations, women already at a disadvantage need extra attention. For breast cancer,

sub-Saharan African social groups with more advanced disease at diagnosis are more likely to be unmarried women, women with lower socioeconomic status, less educated women, Christian women compared with Muslim women, and those with less breast cancer awareness, including those who do not believe that the disease is curable (Brinton et al., 2017; Jedy-Agba et al., 2017; McKenzie et al., 2018a). Cancer conceptualization at the community level is important to tackle, notably the prevalent views that cancer is incurable and that taking a biopsy leads to death or a fate too often sadly described as "worse than HIV" (Malambo and Erikson, 2018; McKenzie et al., 2018b).

Beyond identification of groups at risk of late-stage diagnosis, research on social inequalities needs to address how socioeconomic, cultural, health system, and geospatial factors influence different segments of the prolonged journey to diagnosis, a protracted diagnostic period, and a delayed or incomplete treatment regimen (Fig. 15.7). These segments need to be dissected; it is too often assumed that the pre-contact (or patient delay) symptomatic period is where the delay occurs, but increasing evidence suggests that the post-contact (health system) period may in fact be where the greatest delay occurs for most patients. Incorporation of traditional social structures into community sensitization and to the referral process may be an effective way to increase awareness and reach cancer patients at the start of this journey (Kapambwe et al., 2013).

Many factors must be considered in determining which social groups have prolonged journeys to cancer diagnosis. In addition to the socioeconomically disadvantaged with reduced access to health care, pop-

ulations may be inhibited because of lower cancer awareness, cancer stigma, and competing life stressors. Individuals with a lower level of education, including the illiterate, are a substantial patient group, because cancer now affects people who were born in the 1950s and 1960s when global literacy rates were 40%, that is, half of the literacy rates reached by the end of the 20th century (OECD, 2014). In the massive geographical expanses of African countries, with a few or just a single cancer treatment hospital, patients need to overcome barriers associated with time and travel costs to reach a cancer care centre, often without personal transportation. Travel distances are beyond those faced by rural populations in most countries. Despite language barriers, a small proportion of people travel to neighbouring countries in an attempt to seek diagnosis and care. Furthermore, sexual inequalities in who would be taken to a hospital for a potential cancer diagnosis were present in some countries, but appear to have improved. For example, in the 1960s–1970s oesophageal cancer case series reported had male-to-female ratios of more than 30, most likely due to sexual-biased referral, which have since declined to less than 6 (Middleton et al., 2018). Moving to the present day, populations of the growing urban slums of some larger African metropolises are likely to face similar challenges in achieving effective cancer service delivery or benefiting from awareness campaigns as, for example, the populations of the slums of Mumbai. At the other side of the residential spectrum, little is known about what proportion of people with cancer obtain a cancer diagnosis or care among nomadic populations, such as the Maasai, Pokot, and San. Within a

Fig. 15.7. A late-stage cancer diagnosis in sub-Saharan Africa results after a long symptomatic period (P1+P2). Delays and losses from recommended care plans can also occur in the diagnostic (P3) and treatment (P4) phases. Identifying where, why, and how these delays and losses lead to social inequalities is a first step towards reducing inequalities in outcomes.

- Pre-symptomatic period
- P1 Symptomatic period: symptom recognition to first health provider contact
- P2 Symptomatic period: first health provider contact to reaching diagnostic hospital
- P3 Presentation to histology confirmation to treatment start
- P4 Treatment start to completion
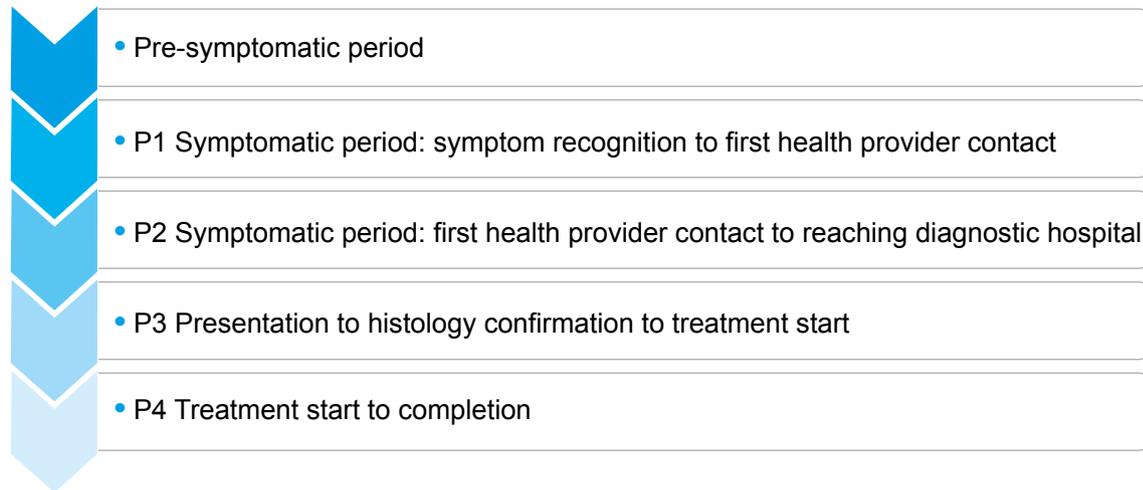
syndemic framework (Mendenhall, 2017), the comorbidities affecting African cancer patients have a distinct profile. People living with HIV (35 million older than 15 years worldwide, the majority in sub-Saharan Africa) have increased cancer risks; in the era of antiretroviral drugs, however, they are now more likely to have non-HIV-associated malignancies. Research on drug–drug interactions, side-effects, and outcomes in Africa for this comorbidity is in its infancy, as it is for other prevalent comorbidities, including diabetes, hypertension, and obesity.

Finally, the cost of cancer treatment is a major barrier to achieving equality in access to cancer care, costs which often lead to a catastrophic financial burden on families. However, initiatives are under way to achieve more efficient and lower-cost resource-appropriate treatments (Gopal, 2017), which should improve access for all. Examples of technological advances to accelerate and streamline diagnosis (Haney et al., 2017) include cytology-free point-of-care diagnosis of cervical cancer, organization of periodic one-stop 24-hour breast cancer diagnostic clinics as piloted in Zambia (Pinder et al., 2018), and mobile-phone-based imaging to detect oral cancers and for molecular cancer diagnostics.

In conclusion, in strengthening sub-Saharan African cancer control programmes for prevention and improvement of outcomes, attention to all social groups is critical because cancer inequalities are already present and are large. While efforts are being made to address these, it is important to keep in mind the care and compassion needed for a terminally ill cancer patient, as highlighted by Singer and Bowman: "If someone is condemned to a premature death because of the injustice of global health inequality, it is doubly unjust for that person to be condemned to an agonising death racked by preventable pain" (Singer and Bowman, 2002).

Key points

- The evidence base for within-country social inequalities in cancer needs strengthening in sub-Saharan Africa; existing evidence suggests that inequalities in prognosis and survival are extremely large.
- Studies of social gradients in risk factors from existing population health surveys and from specific cancer studies, using other cancers as controls, offer useful insights.
- Poverty is linked to vulnerabilities to alcohol, tobacco, infections including HIV, and occupational and environmental carcinogenic exposures, as well as syndemics, that is, multiple related comorbidities, at the time of diagnosis.
- Across all social groups, shortening time to diagnosis and ensuring treatment access and completion are key to reducing the immense social inequalities in cancer outcomes.

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FOCUS 8.

Social inequalities in cancer in Asia

Rengaswamy Sankaranarayanan

Asia has about 60% of the world's population and about one half of the world's poor people. The continent bears one half of the global burden of cancer, with considerable between- and within-country variations in cancer profiles, incidence, survival, and mortality. These disparities reflect the striking socioeconomic differences and the variations in ethnicity, sociocultural practices, diet, government investments in health care, development of public health services, affordability of and access to health care, and health-care finance mechanisms (Sankaranarayanan et al., 2010, 2014; Allemani et al., 2018). On the basis of demographic changes (i.e. no change in cancer risk), the estimated number of new cancer cases in Asia is projected to increase

from 8.8 million in 2018 to 11.5 million in 2030 (Ferlay et al., 2018).

There are huge differences in the incidence of major cancer types across Asia; between Asian countries, there is a 7-fold difference for cervical cancer, a 9-fold difference for breast cancer, a 25-fold difference for colorectal cancer, a 30-fold difference for lung cancer, and a 7-fold difference for non-Hodgkin lymphoma in age-standardized incidence rates, as a result of vast differences in the prevalence of risk factors and in screening and diagnostic practices (Bray et al., 2017). The steadily declining trend in cervical cancer incidence and the increasing trends in the incidence of breast cancer and colorectal cancer in most countries reflect changes in

socioeconomic patterns, delayed childbearing and fewer pregnancies, and changing education and income levels, as well as an increasing adoption of poor-quality dietary patterns and sedentary lifestyles. Cancers associated with chronic infection, such as liver cancer and stomach cancer, predominate in East Asian countries, and cancers associated with tobacco use, such as head and neck cancers, predominate in the Indian subcontinent; these differences highlight the underlying variations in the prevalence of risk factors.

Many low- and lower-middle-income Asian countries have poorly developed, inadequately financed, and overextended government health services, which contribute to advanced-stage clinical presentation

and poor survival outcomes. Cancer health services are either non-existent or highly inadequate in rural and remote locations, leading to vast differences between outcomes in urban and rural areas. Survival outcomes in high-income Asian countries are almost twice those in low-income Asian countries (Sankaranarayanan et al., 2014; Allemani et al., 2018).

The availability of and access to specialized cancer surgical care, radiotherapy, and essential cancer drugs are highly variable in Asia, reflecting the wide gaps in economic development and the focus on vertical investments in government health services. Access to palliative care is poor in many Asian countries, because of legal restrictions on opioids

and a medical culture that undervalues quality of life (Payne et al., 2012). The time-bound implementation of resource-appropriate cancer control measures in Asia, particularly in large countries such as China, India, Indonesia, and the Philippines, has the largest potential to reduce global cancer inequalities.

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CHAPTER 16.

Low-cost approaches to reducing social inequalities in cancer in low- and middle-income countries and disadvantaged populations

Rengaswamy Sankaranarayanan

Introduction

Cancer control has received significantly less attention compared with other public health issues from governments in many low- and middle-income countries (LMICs) despite a significant and increasing disease burden. The striking inequalities in cancer burden and outcomes between high-income countries (HICs) and LMICs are exemplified by the fact that, although 60% of the estimated 14 million new cases and 75% of the estimated 8.8 million cancer deaths per year occur in LMICs, only 5% of global spending on cancer is directed at these countries; most LMICs spend less than 2% of their gross domestic product on health (Prager et al., 2018). Giv-

en these realities, it is not surprising that substantial inequalities exist between countries in terms of cancer occurrence, care, and outcomes.

The health systems in LMICs and in disadvantaged population must be reoriented to adopt proven and cost-effective low-cost technologies and approaches to reduce and eliminate the inequalities in cancer outcomes. Some of the low-cost technologies and approaches that have the potential to reduce inequalities if implemented correctly are discussed in this chapter.

Eliminating cervical cancer

Cervical cancer is a very rare long-term outcome of persistent infection of the lower genital tract with one of

the high-risk human papillomavirus (HPV) types, particularly HPV16 and HPV18 (Bosch et al., 2002; IARC 2007). HPV vaccination and screening for precancerous lesions are two major and highly effective interventions to prevent invasive cervical cancer.

It is possible to eventually eliminate cervical cancer, and to achieve a drastic reduction or elimination in cervical cancer incidence in successive age-specific cohorts, in the foreseeable future if the currently available prevention and early detection interventions are implemented with high coverage and quality assurance.

Of the estimated 528 000 new cervical cancer cases and 266 000 deaths per year, more than 85%

occur, disproportionately, in LMICs. Low-cost technologies and approaches that may be used in LMICs to minimize inequalities in cervical cancer outcomes are listed in Table 16.1.

Vaccination

HPV vaccination is a highly effective primary prevention intervention, which is becoming more affordable for governments to introduce as part of national immunization programmes. The reasons for its increasing affordability include: falling vaccine prices; the scope for negotiated pricing; the possibility of obtaining assistance from donor agencies and Gavi, the Vaccine Alliance, for eligible countries; and the de-escalation from three doses to two doses for the primary target group of girls and boys aged 9–14 years. For girls and boys aged 9–14 years a two-dose schedule is now recommended by the World Health Organization, which has been adapted by several countries (WHO, 2017). For those older than 15 years, three doses are recommended. HPV vaccination at the population level in different national programme settings has consistently been found to be associated with a reduction in the prevalence of vaccine-targeted high-risk HPV types, cross-protection, no HPV type-replacement, and a reduction in the prevalence of anogenital warts, Pap smear abnormalities, and high-grade cervical neoplasia among young vaccinated women; these findings, together with excellent safety indicators, confirm that HPV vaccination can substantially reduce inequalities in cervical cancer risk globally (Drolet et al., 2015; Garland et al., 2016; Saccucci et al., 2018).

Recent results from observational studies indicate that even a single dose of HPV vaccine is immunogenic and has similar effectiveness in preventing vaccine-targeted high-risk HPV as two or three doses of HPV vaccine (Kreimer et al., 2018;

Table 16.1. Strategic low-cost approaches to reducing inequalities in cervical cancer prevention and elimination

Factors contributing to inequalities	Strategic low-cost approaches
Inability to access HPV vaccine because of high costs	Introduce HPV vaccination, targeting girls aged 10–11 years, in national immunization programmes
Misinformation on safety and efficacy of HPV vaccination	Continuous, focused education of the public and stakeholders; prompt documentation and management of adverse events, if any; vaccine delivery supported by efficient cold-chain infrastructure
No access to cervical cytology or HPV screening	Offer VIA screening by nurses or midwives
Loss to follow-up for diagnosis and treatment of precancerous lesions	Use single-visit approach of screening and treating using VIA and cryotherapy and/or thermocoagulation
Erratic cryotherapy service; erratic refrigerant supply chain	Use thermocoagulation for treatment of precancerous lesions
Limited financial resources for screening	Offer screening to women aged 30–39 years
Inability to provide catch-up vaccination to extended age groups (e.g. 13–18 years) and organized screening every 5 years to women aged 30–64 years	Provide HPV vaccination to girls aged 11–12 years and offer a single lifetime screen at age 35–39 years
Lack of radiotherapy services	Offer surgery for early-stage cancer; advocate, lobby, and catalyse national engagement in improving access to surgical care and in establishing radiotherapy infrastructure
Lack of any cancer treatment facilities and/or services	Offer palliative care; advocate, lobby, and catalyse national engagement in establishing and improving access to treatment infrastructure
Insufficient financing of prevention, early detection, and treatment interventions	Advocate, lobby, and obtain national budgetary commitment

HPV, human papillomavirus; VIA, visual inspection with acetic acid

Sankaranarayanan et al., 2018). Further long-term follow-up and evaluation of those receiving a single dose, whether by default in national programmes or in planned studies, in terms of lasting immunity and prevention of persistent infection and of high-grade cervical intraepithelial neoplasia (CIN), is a top research priority to reduce disparities in vaccination coverage and cervical cancer prevention. Another research priority is investigating the value of two doses of HPV vaccine for cervical cancer prevention in those aged 15–18 years. If resources permit additional vaccination of this age group as part of catch-up vaccination, substantial cervical cancer prevention benefits can be obtained. A recent study in India reported similar efficacy of two and three doses in girls aged 15–18 years in generating antibodies and in preventing persistent HPV16 and HPV18 infections (Bhatla et al., 2018). Dosage de-escalation to one dose or two doses for older girls will lead to substantial cost savings, improved vaccine coverage, and significant logistical advantages in vaccine delivery, thereby ultimately reducing inequalities in primary prevention initiatives for cervical cancer. Although sex-neutral vaccination of boys and the use of polyvalent vaccine for both boys and girls are attractive options, these are not recommended in many countries because they are not cost-effective in LMICs.

Screening

Even with the advent of HPV vaccination, screening will be an important complementary intervention for cervical cancer prevention for several years to come. The primary objective of cervical cancer screening is to detect high-grade (grades 2 and 3) CIN, the precursor lesion of

the common squamous cell carcinoma, and adenocarcinoma in situ, the precursor of adenocarcinoma, sufficiently early that they can be treated to prevent the development of cancer. Effective cervical screening tests include conventional cytology (Pap smear), liquid-based cytology, HPV testing, and visual inspection with acetic acid (VIA). Because the risk of HPV16 and HPV18 infections is substantially reduced in vaccinated populations, the approach to cervical cancer screening will be re-evaluated so that the harms and costs associated with screening can be reduced and an optimal screening approach can be developed that is integrated with HPV vaccination.

Although the Pap smear is still the main method of screening and is associated with substantial declines in cervical cancer risk in HICs, it is a challenging and resource-intensive technology and is not feasible in LMICs, where cervical cancer risk is high (Vaccarella, 2016). Cytology-based screening programmes in some middle-income countries have been associated with suboptimal outcomes in reducing the cervical cancer burden because of poor organization, poor coverage, a lack of quality assurance, and inadequate health systems. Cost–effectiveness studies have indicated that cytology-based screening is the least cost-effective screening method (Mezei et al., 2017). Any LMICs without current screening programmes planning to invest in cervical cancer screening should consider screening with HPV testing at prolonged intervals (e.g. 7 or 10 years) rather than cytology-based screening, because HPV testing is a more objective and accurate test than cytology-based screening and has a high negative predictive value.

HPV screening, particularly self-collected HPV testing, linked with treatment has enormous potential to reduce inequalities and is highly cost-effective (Mezei et al., 2017). The average costs of the different screening approaches were calculated (in 2005 dollars) as US$ 13.3 for provider-collected HPV testing, US$ 7.5 for self-collected HPV testing, US$ 6.6 for cytology-based screening, and US$ 2.1 for VIA (Mezei et al., 2017). In the context of declining rates of HPV infection after the introduction of HPV vaccines, HPV testing will be the screening test of choice in the future.

VIA involves detection of acetowhite lesions on the cervix 1 minute after the application of freshly prepared 3–5% acetic acid. Its feasibility of being rapidly introduced in public health services with the least infrastructure means that VIA has been widely implemented in opportunistic settings in many low-income countries in sub-Saharan Africa and in Bangladesh. A single-visit approach (SVA) for screening with rapid diagnosis and treatment improves coverage for all elements of screening, eliminates the need for follow-up visits, and makes screening more time- and cost-efficient in low-resource settings (Parham et al., 2015; Msyamboza et al., 2016; Shiferaw et al., 2016).

Both VIA and HPV testing have been associated with a reduction in high-grade CIN and a reduced incidence of and mortality from cervical cancer in randomized trials, and this evidence provides a solid basis for the introduction of HPV- and VIA-based screening programmes (Denny et al., 2005; Sankaranarayanan et al., 2007, 2009; Ronco et al., 2010; Shastri et al., 2014). However, the infrastructure requirements and

affordability of HPV testing and the subjective nature of VIA testing are major limitations of these screening methods.

VIA screening is particularly suitable for SVA, and WHO has issued guidelines for implementing SVA in public health settings (WHO, 2013). Whether provider-collected HPV testing or VIA is a more efficient alternative depends on the cost of the HPV test, loss to follow-up, and VIA test performance. Self-collected HPV testing is cost-effective when it yields population coverage gains over other screening methods. Major research priorities are how to triage HPV-positive women (both vaccinated and unvaccinated women) and the potential role of VIA in the triage of HPV-positive women in LMICs.

In summary, VIA screening is feasible, simple, safe, accurate, acceptable, and easily accessible to the women at highest risk. Its introduction in health services helps to establish a screening culture and infrastructure that can be used to implement more accurate HPV testing in the future, when affordable, simple, and point-of-care HPV tests become available. In the short term, although it is less optimal relative to HPV testing, VIA screening has the most potential to reduce screening-related disparities. Although it is unlikely that a single screening modality will be appropriate worldwide, with the current knowledge it is possible to adapt a cost-effective means of cervical cancer screening to each country to reduce disparities. A judicious combination of HPV vaccination and screening with HPV testing or VIA has enormous potential to eliminate cervical cancer and substantially reduce inequalities, a potential that remains largely unexploited in many high-

risk countries (Sankaranarayanan et al., 2015; Denny et al., 2017).

Reducing breast cancer disparities

Despite extraordinary progress in basic, translational, and clinical research that has yielded better biological categorization of disease and more effective new treatments, significant disparities exist in breast cancer awareness, early detection, uptake of screening where it is available, diagnosis and treatment, and survival outcomes between HICs and LMICs, between urban and rural populations, and between different ethnicities within countries (Iqbal et al., 2015; Pace et al., 2015; Jedy-Agba et al., 2016; Pace and Shulman, 2016). In recent years there has been substantial progress in early detection and treatment; more than 90% of patients with early-stage breast cancer are cured, provided they are adequately treated. However, this progress has not percolated uniformly between different countries and different populations in the same country, as exemplified by the fact that only 12% of breast cancer patients diagnosed in The Gambia survive beyond 5 years (Sankaranarayanan et al., 2010). Patients with low socioeconomic status (SES) and in LMICs are more likely to be diagnosed with breast cancer at late clinical stages, to experience delays in treatment, and to die from the disease.

A lack of breast cancer awareness, poor availability of and access to public health services, and low participation in mammography screening programmes, where they exist, all lead to delays in diagnosis and treatment, which are responsible for the late-stage diagnoses and poor outcomes in groups with low SES in HICs and in populations of LMICs in general.

Improving breast cancer awareness among women, increasing the skills of primary care physicians to promptly refer women with suspected breast cancer, and increasing access to timely early-stage diagnosis and to comprehensive, good-quality health-care coverage and treatment are important to minimize inequalities in breast cancer outcomes. The approaches that can be used to address inequalities in breast cancer control are outlined in Table 16.2. Whereas measures to improve the participation of women in screening programmes, where they exist, are vital for early detection in HICs, systematic mammography screening or ultrasound screening (USS) of asymptomatic women is not feasible in LMICs because of the inadequacy or even paucity of infrastructure, trained human resources, and health-care funding.

USS with a breast probe is used mostly as a supplementary screening tool to mammography to assess lesions not visible by mammography, such as in dense breasts with a lot of connective and glandular tissue. USS is relatively more affordable, is well tolerated, and does not require intravenous contrast or ionizing radiation. However, a highly experienced provider is required, and USS has less specificity than mammography. USS may be valuable as a potential screening tool for those with dense breasts (Geisel et al., 2018), but it is not widely available in LMICs.

There is sufficient evidence from randomized trials that breast cancer can be diagnosed in its early stages after a clinical breast examination (CBE) (Mittra et al., 2010; Sankaranarayanan et al., 2011; Lauby-Secretan et al., 2015). However, even a CBE-based screening programme will require resources to investigate

Table 16.2. Strategic low-cost approaches to reducing inequalities in breast cancer control

Factors contributing to inequalities	Strategic low-cost approaches
Patients with breast cancer present at advanced clinical stages	Improve breast cancer awareness; increase participation in screening, where such programmes are available; improve access to early diagnosis using CBE, basic imaging, and FNAC for symptomatic women (triple testing)
Mammography screening is not feasible	Improve breast cancer awareness among women; promote opportunistic CBE among asymptomatic women; use triple testing to triage women found to have abnormalities on CBE
Diagnostic mammography is not feasible because of lack of equipment and human resources	Provide ultrasound imaging
Any form of imaging is not feasible	Provide CBE and FNAC; advocate and ensure national commitment to improve infrastructure and human resources
Core biopsy is unaffordable	Offer FNAC
Testing for all three receptors (estrogen receptor, progesterone receptor, and HER2/Neu) is not feasible	At the least, test for estrogen receptor; advocate and ensure national commitment to introduce immunohistochemistry to test for estrogen receptor and progesterone receptor
Radiotherapy services are lacking, and anti-cancer drugs are not available	Offer modified radical mastectomy for early-stage and locally advanced-stage cancer; advocate and ensure national commitment to improve infrastructure and human resources; catalyse national engagement in improving access to anti-cancer drugs and in establishing radiotherapy infrastructure
Branded drugs are not available	Use generic drugs
Providing antiestrogen and/or estrogen receptor modulators is not feasible	Offer bilateral prophylactic salpingo-oophorectomy by surgery or radiotherapy
Cancer treatment facilities and/or services are lacking	Offer palliative care; advocate, lobby, and catalyse national engagement in establishing and improving access to early diagnosis and treatment infrastructure
Patients do not accept treatment or abandon treatment before its completion	Improve awareness of the importance of completing treatment to be cured; improve treatment access and affordability by appropriate health-care financing mechanisms
Financing of prevention, early detection, and treatment interventions is insufficient	Advocate, lobby, and obtain national budgetary commitment

CBE, clinical breast examination; FNAC, fine-needle aspiration cytology; HER2, human epidermal growth factor receptor 2

and treat screen-positive women and follow them up. Although CBE is widely used in the early detection of breast cancer, there are no formal health service programmes that are based on CBE alone; it is therefore difficult to quantify the proportional contribution of CBE in the early detection of breast cancer. Compared with screening, early diagnosis of breast cancer linked with adequate treatment of symptomatic women

therefore seems to be a more feasible approach to reducing disparities in breast cancer outcomes.

Late-stage presentation of breast cancer is attributed largely to modifiable factors; strategies to improve breast cancer awareness in women and in the health system could be highly conducive to reducing inequalities (McKenzie et al., 2018). Improving awareness of breast cancer and access to triple diagnosis – expert

CBE, diagnostic imaging by USS or mammography or both, and tissue diagnosis in the form of fine-needle aspiration cytology (FNAC) or excision biopsy – have been associated with early diagnosis of breast cancer (Gadgil et al., 2017). The combination of mobile health (m-Health, the use of mobile devices in public health practice) to improve awareness and the use of CBE, USS, and FNAC to examine women suspected to have

breast cancer provides an attractive package of low-cost diagnostic interventions for LMICs. It is likely that most of the gains observed in breast cancer survival before the introduction of widespread mammography screening and adjuvant chemotherapy and hormone therapy in developed countries were due to (i) improved awareness of breast cancer symptoms and signs and (ii) the value of locoregional treatment in improving survival outcomes of women with clinically detected early-stage breast cancer (Sankaranarayanan et al., 2010).

To benefit from early-detection initiatives to reduce inequalities in breast cancer outcomes, it is critical that diagnosis of early-stage breast cancer is followed by adequate treatment (Denny et al., 2017). The third edition of the Disease Control Priorities project, a global initiative funded by the Bill & Melinda Gates Foundation, has identified treatment of early-stage breast cancer as part of essential cancer interventions for LMICs that could be "effective, cost-effective, affordable, and feasible", along with tobacco control, HPV and hepatitis B virus vaccinations, cervical cancer screening, and treatment of certain childhood cancers, in reducing inequalities in cancer outcomes in LMICs (Gelband et al., 2016). Guidelines to develop affordable and effective breast cancer treatment programmes tailored to existing resources in LMICs have been proposed by the Breast Health Global Initiative (Anderson et al., 2011). These guidelines may be adapted by LMICs to improve survival outcomes from breast cancer. It is the responsibility of the governments in such countries to strengthen health systems to improve awareness, early diagnosis, and adequate treatment to eliminate current disparities in breast cancer outcomes.

Reducing oral cancer inequalities and improving outcomes

In LMICs where the risk of oral cancer is high, such as Bangladesh, India, Nepal, Pakistan, and Sri Lanka, most patients with oral cancer present at advanced clinical stages. When the disease has spread to the regional lymph nodes and surrounding tissues, 5-year survival rates are less than 30%, even with the most aggressive treatments. Advanced oral cancers contribute to the poor overall cancer outcomes in LMICs compared with HICs. Whereas tobacco and alcohol control measures are of paramount importance in preventing oral cancer, early detection at stage I or II and adequate single-modality treatment, such as surgery or radiotherapy, improves prognosis considerably, with 5-year survival rates exceeding 90%. It has been well documented in a randomized trial that oral visual screening was associated with a significant reduction in oral cancer incidence and mortality among people who use tobacco and/or consume alcohol (Sankaranarayanan et al., 2005, 2013). An atlas for the early detection of oral cancer published by IARC is a useful manual for primary care practitioners to perform oral visual screening and correctly diagnose precancerous lesions and early-stage asymptomatic invasive cancer, enabling the prompt referral of the patient (Ramadas et al., 2008). Because oral cancers are preceded by oral precancerous lesions, such as leukoplakia, erythroplakia, and oral submucous fibrosis, interventions to change habits in such individuals have the potential to prevent oral cancer.

Reducing colorectal cancer inequalities and improving outcomes

Colorectal cancer incidence rates are increasing in most LMICs where long-term incidence data are available. Screening with faecal occult blood tests, most commonly with faecal immunochemical tests, and triaging screen-positive people with colonoscopy are the most widely used prevention and control approaches. Screening for early-stage colorectal cancer and its precursors is highly effective in reducing mortality rates. Although many HICs have initiated population-based screening programmes with faecal occult blood tests and colonoscopy triage, participation in such programmes is low and is highly variable between groups with different levels of education or SES; these differences in screening participation contribute to inequalities in outcomes (Honein-AbouHaidar et al., 2013; Decker and Singh, 2014; Kim and Hwang 2016; Basu et al., 2018). Colorectal cancer screening programmes are still evolving; interventions to raise awareness and increase participation among population subgroups with low participation are needed to reduce disparities in uptake rates. Recently, Thailand introduced faecal immunochemical test screening for colorectal cancer through primary care clinics in public health services in Lampang Province, demonstrating the feasibility of introducing such organized programmes in middle-income countries. The pilot project was associated with increased diagnosis of early-stage colorectal cancer and its precursors (Khuhaprema et al., 2014). As a result of this experience, colorectal cancer screening is being scaled up in phases in Thailand.

Other low-cost approaches to reduce cancer disparities

Strengthening cold-chain infrastructure and delivery systems in national immunization programmes can substantially improve the coverage and efficiency of cancer-preventive vaccination programmes, such as hepatitis B virus and HPV vaccination. Telepathology networks have the potential to substantially improve diagnostic accuracy, patient care, and professional education. Given the substantial penetration rates of mobile phones in LMICs, using m-Health applications can: enhance awareness for the public, patient, and provider; provide health education and promote healthy behaviours; improve early diagnosis; enable better monitoring and evaluation of health-care interventions; and improve adherence to treatment and follow-up care (Eskandar et al., 2015). Health system reforms to improve breast cancer awareness and introduce cervical cancer screening, CBE, oral visual screening, and faecal immunochemical tests, and the shifting of follow-up of treated cancer patients to the primary health care level, have immense potential to reduce disparities. Many LMICs, particularly in sub-Saharan Africa and Central America, will benefit substantially by systematically investing in basic cancer diagnostic tools (e.g. histopathology, FNAC, and basic immunohistochemistry such as estrogen receptor, basic imaging, and tumour markers), treatment infrastructure (e.g. investing in radiotherapy and clinical oncology services, augmenting surgical capacity, and improving the supply chain for essential drugs), and monitoring and evaluation systems (e.g. medical records and population-based cancer registries) in a timely manner. LMICs have the worst cancer outcomes, and such investments can substantially reduce disparities in cancer outcomes.

Conclusions

The disparities in access to cancer care and outcomes between HICs and LMICs, and between population subgroups within countries, are staggering. The reasons for these disparities include fragmented and poorly financed and organized health-care systems, a lack of suitable health-care financing mechanisms, inadequate infrastructure and trained human resources, the poor affordability and accessibility of care for many patients, and a lack of awareness among both the public and medical communities. Addressing these multiple deficiencies at the same time is impossible; however, tackling disparities resulting from major cancer types with low-cost, low-technology methods offers the most pragmatic approach in addressing the inequalities in cancer outcomes in LMICs.

Key points

- A pragmatic approach to reducing social inequalities in cancer is to focus on addressing inequalities in the outcomes of major cancer types.

- A judicious combination of human papillomavirus (HPV) vaccination and screening with HPV testing or visual inspection with acetic acid has enormous potential to eliminate cervical cancer and substantially reduce inequalities.

- Improving breast cancer awareness and access to triple diagnosis, consisting of expert clinical breast examination, diagnostic imaging, and tissue sampling, and improving access to treatment have enormous potential to reduce inequalities in breast cancer outcomes.

- Introducing oral visual screening in public health settings in high-risk countries can improve oral cancer outcomes.

- Systematically introducing faecal immunochemical testing and improving access to colonoscopy triage have large potential to reduce disparities in colorectal cancer outcomes.

- Systematically investing in mobile health, primary health care, and basic cancer care infrastructure has substantial potential to reduce disparities in cancer outcomes.

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Part 3 • Chapter 16. Low-cost approaches to reducing social inequalities in cancer in low- and middle-income countries and disadvantaged populations

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EXAMPLE 2.

HPV vaccination and screening for cervical cancer

Partha Basu

Introduction

Cervical cancer is a classic example of a preventable disease that causes significant morbidity and mortality in socially disadvantaged women, primarily because of inadequate access to universal health care. The disparities are further aggravated by sexual inequalities, which have a strong bearing on the health and rights of women and make them even more vulnerable (Singh et al., 2012). Cervical cancer is therefore a negative consequence of the systematic disadvantages that women experience as a result of social deprivation as well as sexual inequality.

Social inequality and cervical cancer burden

The imbalance in cervical cancer burden between the high-income countries (HICs) and low- and middle-income countries (LMICs) of the world highlights the lopsided access to preventive health care as a result of social and gender inequality. Pre-vention of cervical cancer is one of the great success stories of modern medicine; the two-pronged approach of the vaccination of adolescent girls against human papillomavirus (HPV) and the systematic screening of adult women can potentially eliminate the disease (Tsu and Ginsburg, 2017). Despite this, cervical cancer continues to be the most common cancer in women in 27 countries and is the leading cause of cancer mortality in women in 45 countries, all LMICs (Fitzmaurice et al., 2015). IARC estimated that, in 2012, almost 90% of cervical cancer deaths occurred in LMICs, and there was an 18-fold difference between the highest and lowest mortality rates globally (Ferlay et al., 2013). Women with low socioeconomic status (SES) experience a higher burden of the disease. A pooled analysis based on 57 studies observed a globally increased risk of approximately 2-fold in groups of low versus high social class (by education and income) for the development of invasive cervical cancer (Parikh et al., 2003). The increased risk exceeded 3-fold when the analysis was restricted to LMICs.

The mortality rates of cervical cancer are much higher in LMICs, because of the late-stage diagnosis of the disease and limited access to therapeutic services. A lack of awareness, a cultural preference for traditional healing systems over modern treatment, a lack of female empowerment, and the low priority of women's health in the family unit greatly contribute to delayed access to care (Denny et al., 2017). The plight of women with cervical cancer is worsened by the fact that only 50% of cancer patients in LMICs have access to radiotherapy, a much-needed treatment for cervical cancer (Zubizarreta et al., 2015). There are 28 countries in Africa without a single radiotherapy machine, and it is unlikely that the situation will improve in the near future (Abdel-Wahab et al., 2017). The social differentials that influence cervical cancer incidence and mortality also exist within HICs. Populations of racial and ethnic minorities encounter cultural barriers and prejudices

as well as financial hardship, leading to their underuse of health-care services. In the USA, African-American women experience 100% higher cervical cancer mortality rates compared with White women (10.1 per 100 000 vs 4.7 per 100 000 after correcting for hysterectomies; Beavis et al., 2017). The social costs of losing a wife and a mother at her prime to cervical cancer, and the hardships faced by the entire family because of the catastrophic health expenditure (e.g. children being forced to drop out of school), are greater for populations with low SES.

Indigenous populations and immigrants tend to have poorer access to health care, even in HICs. Their participation in cervical cancer screening programmes is often much lower compared with the rest of the population, for several reasons: poorly organized health services, political and economic marginalization, language barriers, and mistrust in modern health systems (Moore et al., 2014; Bianco et al., 2017). During 2003–2006, the age-standardized cervical cancer mortality rate for Indigenous women aged 20–69 years in certain provinces in Australia was reported as 10.3 per 100 000 women, 5 times as high as the rate of 2.0 per 100 000 for non-Indigenous women of the same age range (Australian Institute of Health and Welfare, 2009). The low participation in screening programmes by Indigenous women is the most significant factor contributing to this disparity.

Access to cervical cancer screening

The effect of social inequality

Many HICs have achieved up to 80% reduction in cervical cancer incidence and mortality rates by systematically implementing population-based screening (Vaccarella et al., 2014; Denny, 2015; Vaccarella et al., 2016). More than 70% of eligible women residing in the 28 Member States of the European Union have access to population-based cervical cancer screening (Basu et al., 2018). The beneficiaries of such programmes undergo a suitable screening test every 3–5 years and have access to appropriate follow-up care. This is in stark contrast to LMICs, including Baltic and eastern European countries, where cervical cancer screening either is non-existent or is provided in a highly sporadic manner, with poor-quality services and/or low coverage of the target population; consequently, cervical cancer rates are still rising in these countries (Vaccarella et al., 2016). The fragmented nature of health services, the lower priority of preventive health care, inefficient governance, inadequate resources, and competing health priorities preclude the implementation of well-organized screening programmes in LMICs (Denny, 2015).

Health-care financing models based on insurance can introduce inequalities within a country, because health-care needs are greater among those with the least ability to pay. Although extreme poverty in China has declined, rural elderly women have limited access to health facilities, especially preventive services, and are therefore victims of inequality (Tsu and Levin, 2008).

Closing the divide

For cervical cancer screening to become a reality in LMICs, an affordable, highly sensitive, robust, and point-of-care screening test is required, so that infrequent screening (once or twice in a lifetime) has a high impact and a minimum number of visits is required to manage screen-positive women. As described in Chapter 16, simple and inexpensive screening algorithms such as screening by visual inspection with acetic acid, followed by immediate treatment of eligible screen-positive women by cryotherapy, have enabled many low-income countries to implement cervical cancer screening and thus reduce inequality.

Cervical cancer screening programmes in LMICs should aim to screen women less frequently and achieve a high coverage of the target population. The test and the management algorithm should be selected depending on the health system capacity and available resources. It is imperative that health authorities address the structural, economic, and cultural barriers that women of remote, Indigenous, and immigrant populations face in accessing screening and treatment services. Some of the strategies to improve screening uptake in marginalized women include working closely with target groups, while involving key religious and community leaders, to develop culturally tailored messages to promote screening that reflect the values and beliefs of the target groups. A randomized controlled study demonstrated significant improvement in screening participation in Indigenous women in Canada by replacing the conventional Pap smear test with HPV self-testing (Zehbe et al., 2016).

Access to HPV vaccination

The effect of social inequality

Administering two doses of the HPV vaccine to preadolescent girls (aged

Fig. E2.1. Global map delineating the status of human papillomavirus (HPV) vaccine introduction in national immunization programmes (WHO, 2018). Partial introductions: Georgia, India, Indonesia, the Philippines, the Russian Federation, and the United Arab Emirates; planned introductions for 2018: Ethiopia, Grenada, Maldives, Mauritania, Saint Kitts and Nevis, and Senegal. Source: compiled from WHO/IVB Database.

■ Introduced (Includes partial introduction) to date (96 countries or 49%)
☐ Not Available, Not Introduced/No Plans (98 countries or 51%)
▨ Not applicable
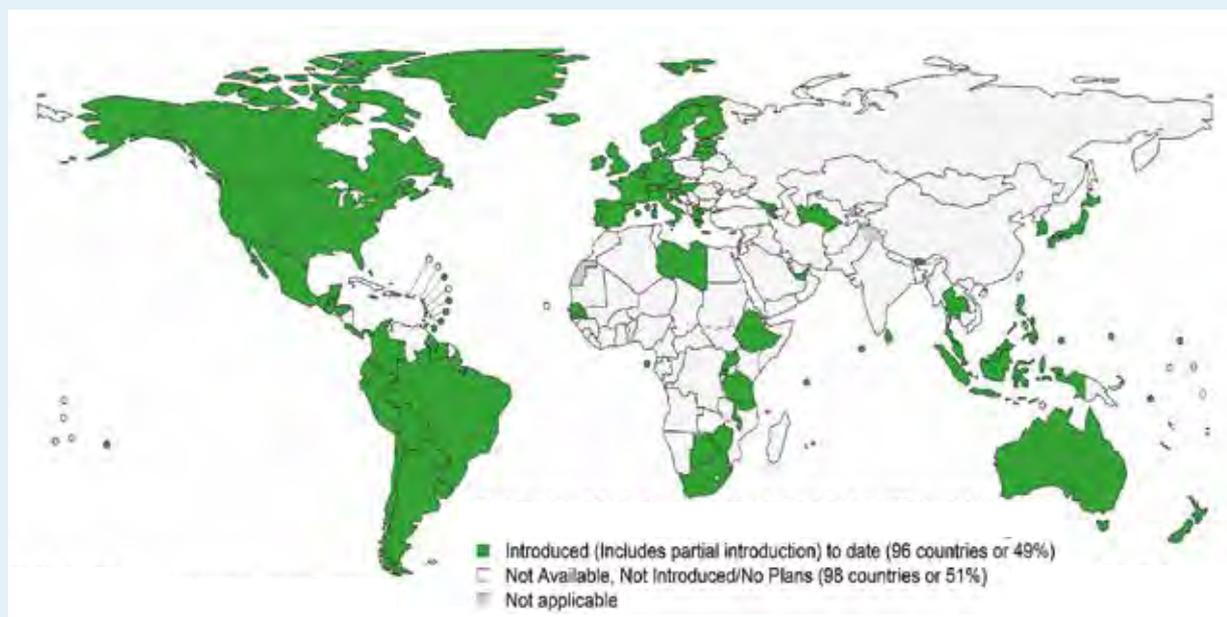
9–13 years), with high coverage of the target population, is the most potent long-term solution to inequality in the cervical cancer burden. Rapid and significant declines in the prevalence of vaccine-targeted HPV infections, as well as in the prevalence of high-grade cervical premalignant lesions, at the population level after the introduction of the vaccine in the national immunization programmes have been reported by several countries (Gertig et al., 2013; Kavanagh et al., 2014). The excellent safety profile of the vaccine has been endorsed by the World Health Organization (WHO) and other vaccine surveillance agencies (WHO, 2017).

However, there remains a huge unmet need for HPV vaccination. According to the WHO database (updated in October 2018), a total of 91 countries (including 6 countries with partial introduction) now include the HPV vaccine in the national immunization programmes (Fig. E2.1) (WHO, 2018). Unfortunately, these include only 20% of the LMICs. Only three low-income countries (Rwanda, Uganda, and Zimbabwe) have included the vaccine in national programmes. It has been estimated that by 2014 only 32.0% of girls aged 10–14 years in HICs had received at least one dose of the vaccine; this proportion was only 15.2% in upper-middle-income countries, 0.2% in lower-middle-income countries, and 1.0% in low-income countries (Bruni, 2017). Because of the very low uptake of HPV vaccination before 2014 in the 72 low-income countries that were eligible to receive vaccine donations from Gavi, the Vaccine Alliance (previously known as the Global Alliance for Vaccines and Immunisation), only 2000 of the 400 000 potentially preventable cases of cervical cancer were averted (Jit et al., 2014). There are several reasons to explain the low uptake of the vaccine, especially in LMICs: its high cost and competing health-care priorities, cultural issues related to a sex-specific vaccine, the logistical challenges of delivering a multidose vaccine and reaching adolescent girls, and the negative campaigns against the vaccine by the anti-vaccine lobbies.

Closing the divide

The high cost of the HPV vaccine has been a major impediment to its widespread introduction in LMICs. Price negotiations with the manufacturers by Gavi, the Vaccine Alliance (which negotiated a price of US$ 4.50 per dose for Gavi-eligible countries), the Pan American Health Organization Revolving Fund (which negotiated a price of US$ 9.58 per dose for Latin American countries), and national governments have drastically reduced the price. Pilot

vaccination projects are under way in 25 LMICs; many of these countries will scale up their programmes in the near future.

It is encouraging to note that the majority of HPV vaccination programmes in LMICs have achieved excellent target population coverage. Coverage was estimated for HPV vaccine demonstration projects and national programmes in 41 LMICs (Gallagher et al., 2017); final-dose (second or third dose, depending on the vaccination protocol) coverage estimates exceeded 50% in all 41 LMICs and exceeded 90% in nearly half of the LMICs. Interestingly, the reported HPV vaccine uptake among Indigenous girls has been high and comparable to that of non-Indigenous girls in countries where the vaccine is available through national immunization programmes (Brotherton et al., 2013; Jacobs-Wingo et al., 2017).

The reason for the success story of HPV vaccination in LMICs was the adequate preparation carried out before the launch of the programmes. Such preparation involved: adequately sensitizing national-level stakeholders, community leaders, and parents of eligible girls; coordinating with the education sector for school-based vaccinations; allowing sufficient time and resources for the planning process; and leveraging the existing logistics of routine immunization programmes. Higher coverage was achieved through school-based vaccination compared with health-facility-based vaccination (Paul and Fabio, 2014). Eligibility criteria based on school grade, rather than age, were more convenient to implement in school settings. However, these school-based programmes excluded girls who did not attend schools, thereby increasing social disparities among girls. A dual approach of school-based and health-facility-based vaccination can reduce this disparity.

Conclusions

The Seventieth World Health Assembly in 2017 endorsed vaccinating girls against HPV and screening women as the "best buy" to prevent cervical cancer. There is no dearth of evidence that a combination of vaccination and screening can potentially eliminate cervical cancer; the crux of the problem remains the socioeconomic disparities that preclude universal access to these preventive interventions. The education and empowerment of women, as well as improved access to reproductive health care and general increase in SES, have resulted in a slow decline in cervical cancer incidence in many LMICs, even in the absence of effective screening programmes. However, the impact of such social vaccination (prevention due to social changes) is limited, and may be offset by changing sexual practices. High coverage of the HPV vaccination and a pragmatic approach to ensure low-frequency but high-quality screening of vaccinated women can, in the long run, significantly reduce the disparity in the disease burden. It is the responsibility of national governments, political leaders, civil societies, and advocates to support the prevention of cervical cancer. Policies aimed at minimizing inequalities in health, reforming primary health care, pragmatically mobilizing resources, and prioritizing evidence-based and resource-appropriate interventions are key to preventing cervical cancer. Support from the global community can help to ensure that LMICs achieve their Sustainable Development Goals by preventing avoidable cervical cancer deaths.

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FOCUS 9.

Social inequalities in cancer in Latin America

Raúl Murillo

Introduction

According to the latest regional human development report for Latin American countries, significantly reduced social inequalities were observed from 2002 to 2013, as indicated by a lower Gini index, which decreased from 0.54 in 2002 to 0.49 in 2013 (UNDP, 2016). The main factor associated with this reduced Gini index was the reduction in poverty; however, other types of exclusion persist, linked to factors such as ethnicity and sex (ECLAC, 2016; UNDP, 2016).

Although the reduction in poverty has been accompanied by improvements in both education and health-related indicators, including increased school access, reduced infant mortality, and increased life expectancy, progress in policies to maintain these achievements has been insufficient; this lack of progress is due particularly to the scant development in social protection (UNDP, 2016). This situation has resulted in demographic and epidemiological transitions in the form of an ageing population and an increased burden of chronic diseases. A large percentage of the population (particularly the elderly population) are experiencing poorer conditions because of limited access to basic social services (including health-care services) and, after the diagnosis of disabling diseases such as cancer, a higher risk of impoverishment (ECLAC, 2016; UNDP, 2016).

Cancer inequalities

Similarly to countries in other world regions, Latin American countries show a positive association between gross domestic product (GDP) or Human Development Index (HDI) and overall cancer incidence (Goss et al., 2013; Fidler et al., 2016); however, cancer mortality does not seem to be strongly associated with GDP or HDI (Rezaeian et al., 2016). In countries that are transitioning towards improved socioeconomic conditions, a decline in cancer types associated with infection and an increase in cancer types associated with so-called westernized lifestyles have been reported (Bray et al., 2012; Rezaeian et al., 2016). Although cervical cancer and breast cancer often

Fig. F9.1. Trends in breast cancer and cervical cancer mortality rates in selected Latin American countries according to the inequality-adjusted Human Development Index (I-HDI; the higher the better). ASR, age-standardized rate; HDI, Human Development Index (a function of life expectancy, education level, and gross national income; the higher the better). The Gini index is used as a measure of inequality (0% indicates complete equality and 100% complete inequality). Orange, breast cancer mortality rates; grey, cervical cancer mortality rates. Source: compiled from the WHO-IARC mortality database, the UNDP human development reports, and the World Bank Open Data.
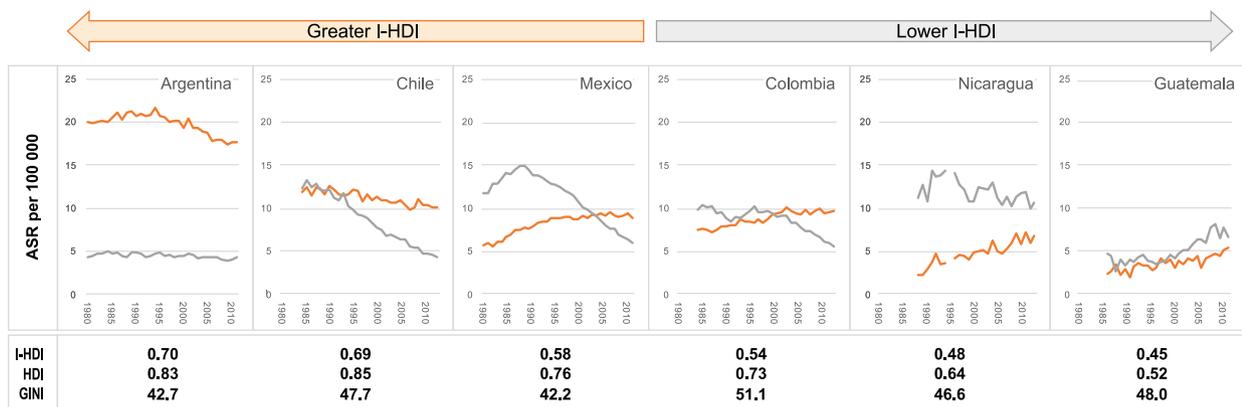
show opposite trends during this transition (i.e. a decrease in cervical cancer and an increase in breast cancer), this is not always the case in Latin American countries, where different patterns are observed by inequality and HDI levels (Fig. F9.1). Countries with the highest inequality-adjusted HDI in the region have decreasing trends for both cervical cancer and breast cancer mortality, with a gradient that depends on initial mortality rates over the observation period; however, countries with the lowest inequality-adjusted HDI in the region have increasing breast cancer mortality rates and variable trends in cervical cancer mortality rates.

Income and education level are major determinants of cervical cancer mortality in Latin American countries, even in the absence of organized screening programmes (McKinnon et al., 2011; Pereira-Scalabrino et al., 2013). Despite observed improvements in both determinants (UNDP, 2016), within-country socioeconomic disparities in cancer mortality have not decreased substantially in the re-

gion. Recent reports from Colombia indicate not only increasing inequalities in cancer mortality with education level for different cancer types but also re-emerging inequalities in cervical cancer mortality, in contrast with previous reports of decreasing trends (de Vries et al., 2016, 2018). In addition, studies in Brazil reported an inverse correlation between breast cancer mortality and social exclusion index (Gonzaga et al., 2015) and a positive association between breast cancer mortality and both inequality indexes and a rural residence (Girianelli et al., 2014; Figueiredo and Adami, 2018).

Despite the fact that disparities in cancer outcomes with ethnicity and sex continue to be major concerns, as previously indicated, information about their specific association with cancer incidence or mortality rates in Latin American countries is scarce. Indigenous groups represent about 10% of the general population in Latin America (Goss et al., 2013), and a review showed higher incidence rates of gallbladder cancer and in-

fection-related cancers for Indigenous populations than for the Latin American general population, suggesting an association with poverty and lower education level (Moore et al., 2014).

The roots of cancer inequalities

In general, a higher mortality burden in low-income populations may be related to reduced access to health care, including both preventive and therapeutic services; however, the burden of poverty-related cancer in Latin American countries cannot be completely explained by this factor, just as decreasing mortality rates cannot be completely explained by improved access to health care.

The association between poverty and the prevalence of infections that cause cancer is well established. Accordingly, data from Latin American countries confirm the relationship between poverty and the prevalence of *Helicobacter pylori* infection (Porras et al., 2013). However, data on the prevalence of human papillomavirus

(HPV) infection do not show a strong socioeconomic gradient (Bruni et al., 2018); the differences observed in cervical cancer incidence rates between groups with different levels of socioeconomic status (SES) are probably explained by the availability of and access to cervical cancer screening. However, it is possible that HPV cofactors associated with determinants of SES play a major role in cervical cancer incidence in Latin American countries; indeed, an inverse correlation between fertility rates and education level in women is observed in the region (UNDP, 2016).

With respect to behavioural risk factors, there is no strong association between cancers associated with tobacco use and GDP in the region; however, a review found an inverse correlation between smoking prevalence and income level in Latin America (Bardach et al., 2016). In addition, other factors that affect the incidence of cancer, such as the prevalence of obesity, do not show robust links with SES; this observation may be due to the transition status, in which some affluent Latin American communities still have a high prevalence of overweight and obesity (Corvalán et al., 2017).

Most research on socioeconomic inequalities and cancer in Latin American countries is focused on access to cancer screening and treatment. As well as income and education level, information from Argentina, Brazil, Colombia, Costa Rica, Mexico, and Peru consistently shows an independent association between health insurance status and cancer screening coverage for both cervical cancer and breast cancer (Brenes-Camacho and Rosero-Bixby, 2009; De Maio et al., 2012; Agudelo-Botero, 2013; Barrionuevo-Rosas et al., 2013; Bermedo-Carrasco et al., 2015; Silva et al., 2017). A pooled analysis from eight Latin American countries highlighted a recent doctor's visit as a factor determining whether a woman had received a Pap smear test, regardless of SES (Soneji and Fukui, 2013), and studies in Brazil and Peru showed reduced coverage of cancer screening among non-White and Indigenous populations, respectively, compared with the general populations in those countries (Barrionuevo-Rosas et al., 2013; Martínez-Mesa et al., 2013).

The few available studies on cancer types for which no screening programmes exist, such as stomach cancer and colorectal cancer, have also shown mortality-associated socioeconomic gradients (de Vries et al., 2015; Parreira et al., 2016). Beyond income or HDI, data indicate the significant role of an individual's health insurance status (stomach cancer in Colombia) and whether an individual has an urban or rural domicile (colorectal cancer in Brazil) in cancer mortality rates.

Avenues to reduce cancer inequalities

Compared with countries with lower GDP and HDI in the region, countries with higher GDP and HDI show not only greater progress towards universal health coverage but also greater progress in the implementation of preventive measures such as vaccinations against HPV and hepatitis B virus (HBV) and tobacco control policies (Bruni et al., 2016; Piñeros et al., 2016). However, the progress of a country in terms of average socioeconomic conditions may mask major social inequalities within the country; disadvantaged populations may be excluded from these benefits.

Although organized screening programmes have been demonstrated to reduce unequal access to early cancer diagnosis, most countries in Latin America provide only opportunistic screening for both cervical cancer and breast cancer. Furthermore, only a few countries have introduced alternative approaches for hard-to-reach populations, such as self-collected HPV tests or screen-and-treat programmes (single-visit approach) for cervical cancer (Di Sibio et al., 2016; Murillo et al., 2016).

Addressing inequalities in cancer by reducing poverty and increasing social protection coverage, especially without losing the significant achievements observed in the reduction of inequality during the past decades, is an enormous challenge for Latin American countries. Greater political commitment is called for, but also innovative approaches to increase health insurance coverage for catastrophic diseases, implement already-proven interventions, and evaluate novel technologies and models of care.

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CHAPTER 17.

Sharing lessons learned from the AIDS response to address social inequalities in cancer

Michel Sidibé

"As long as poverty, injustice, and gross inequality persist in our world, none of us can truly rest."

Nelson Mandela

Introduction

The AIDS epidemic challenged us, not just as a global health community but also as a collective humanity. At the turn of the millennium, the AIDS epidemic was devastating entire countries: in 2000, 27.4 million people were living with HIV and an estimated 1.5 million people died from AIDS-related illnesses. However, only about 611 000 of the people living with HIV were receiving antiretroviral therapy; in sub-Saharan Africa, this figure was only 6800 (UNAIDS, 2018b).

Today, we celebrate tremendous progress. The number of new HIV infections per year has been reduced by 47% since peaking in 1996 and the number of AIDS-related deaths

has fallen by more than 51% since the peak in 2004 (Fig. 17.1). In the span of just a few years, the number of people living with HIV receiving antiretroviral therapy has increased dramatically. At the end of 2017, a record 21.7 million people living with HIV were receiving antiretroviral therapy, a net increase of 2.3 million people since the end of 2016 (Fig. 17.2) (UNAIDS, 2018a).

However, as we celebrate gains it must be recognized that these are not distributed equally. Groups that fear or face discrimination are often left behind, and are less likely to access the services they need. Moreover, the majority of people who are newly infected with HIV live in low-income countries; approximately 66%

of new HIV infections in 2017 occurred in countries in sub-Saharan Africa (UNAIDS, 2017a), where funding for AIDS is stagnating (Fig. 17.3) (UNAIDS, 2018b).

To reach the target set out in the 2030 Agenda for Sustainable Development to end AIDS as a public health threat (UN, 2015) we need to overcome numerous challenges, from tackling HIV-related stigma and discrimination, harmful social and cultural norms that disadvantage both men and women, and economic inequalities to decreasing the cost of expensive health technologies and second- and third-line treatment regimens. Many of these challenges also apply to the prevention and treatment of cancer, and the Joint

Fig. 17.1. The fall in the annual numbers of new HIV infections and of AIDS-related deaths. Source: reproduced from UNAIDS (2018a).

Number of new HIV infections and deaths among the HIV population (all causes), global, 1990–2017

Number people living with HIV, global, 1990–2017

— New HIV infections   — Deaths among people living with HIV

— Number of people living with HIV

Source: UNAIDS 2018 estimates.
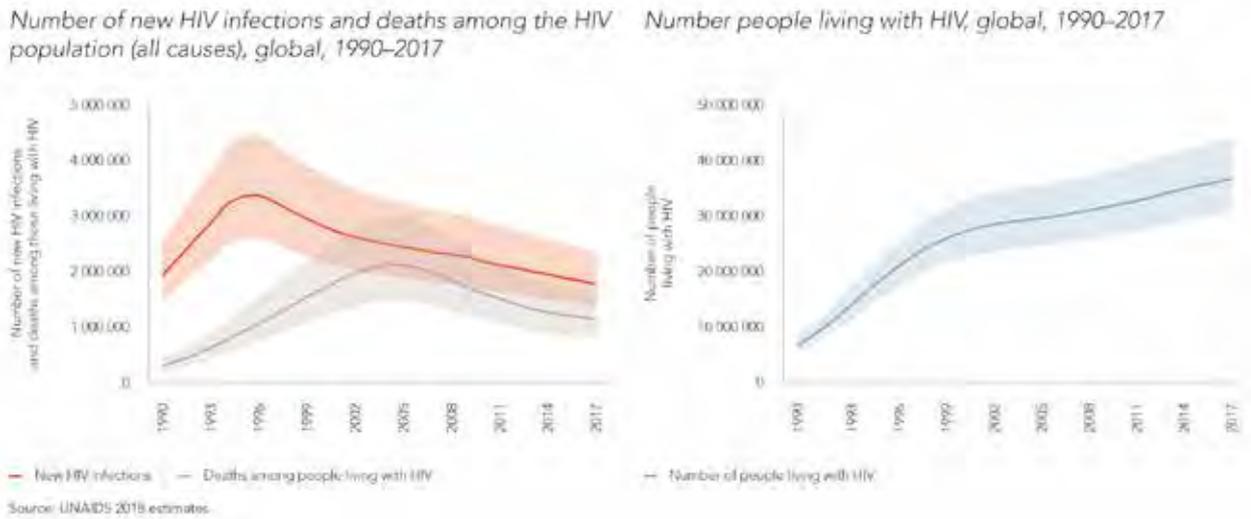
Fig. 17.2. The rising numbers of people living with HIV and receiving antiretroviral therapy during 2000–2017, with the target for 2020. Source: reproduced from UNAIDS (2018a).

*Number of people living with HIV accessing antiretroviral therapy, global, 2000–2017 and 2020 target*

— Number of people living with HIV on antiretroviral therapy   ● Target

Source: UNAIDS 2018 estimates; Global AIDS Monitoring 2018.
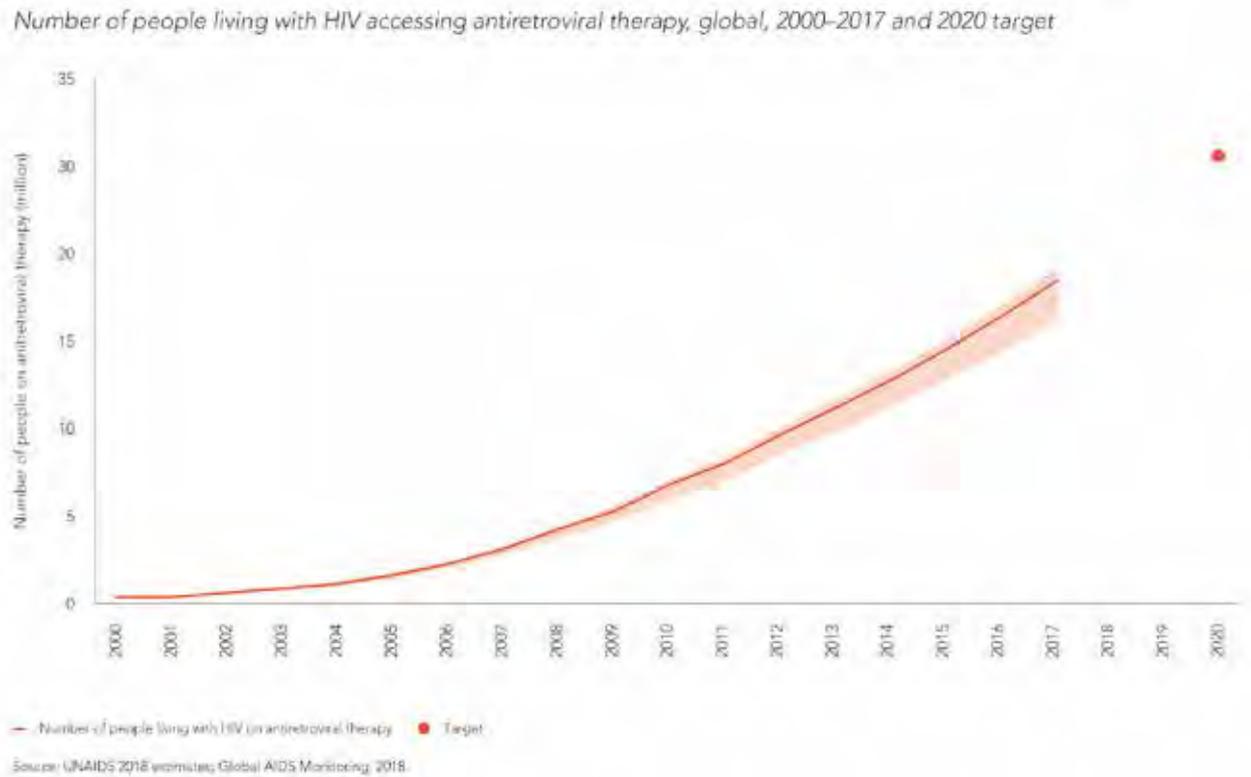
Fig. 17.3. Stagnation in annual increase in donor funding: the annual percentage change in HIV resource availability from all sources (public and private) in low- and middle-income countries during 2000–2017. Source: reproduced from UNAIDS (2018a).

Annual percentage change in HIV resource availability from all sources (public and private), low- and middle-income countries, 2000–2017

Source: UNAIDS resource availability and needs estimates, 2018.
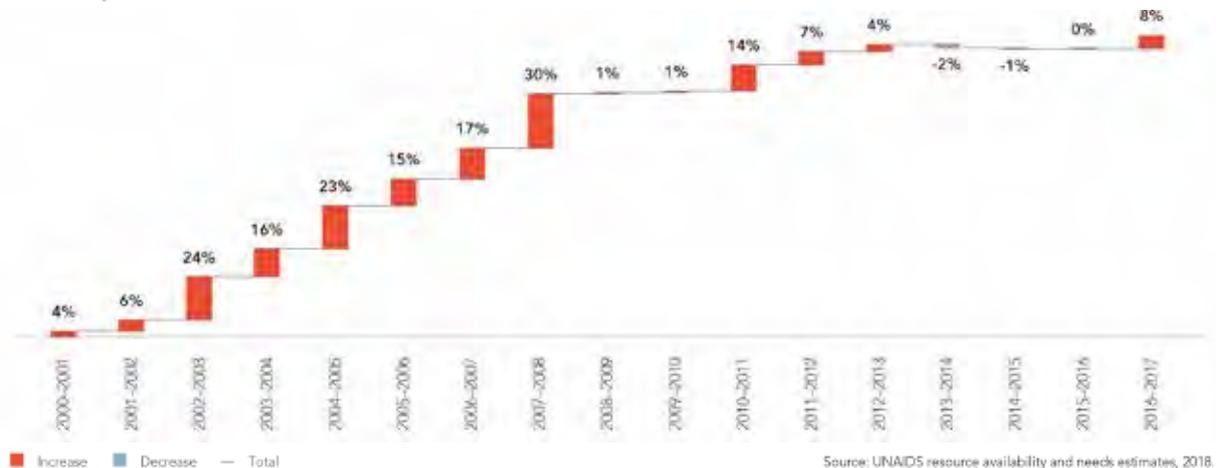
Fig. 17.4. Sharing lessons learned from the AIDS response to address social inequalities in cancer.
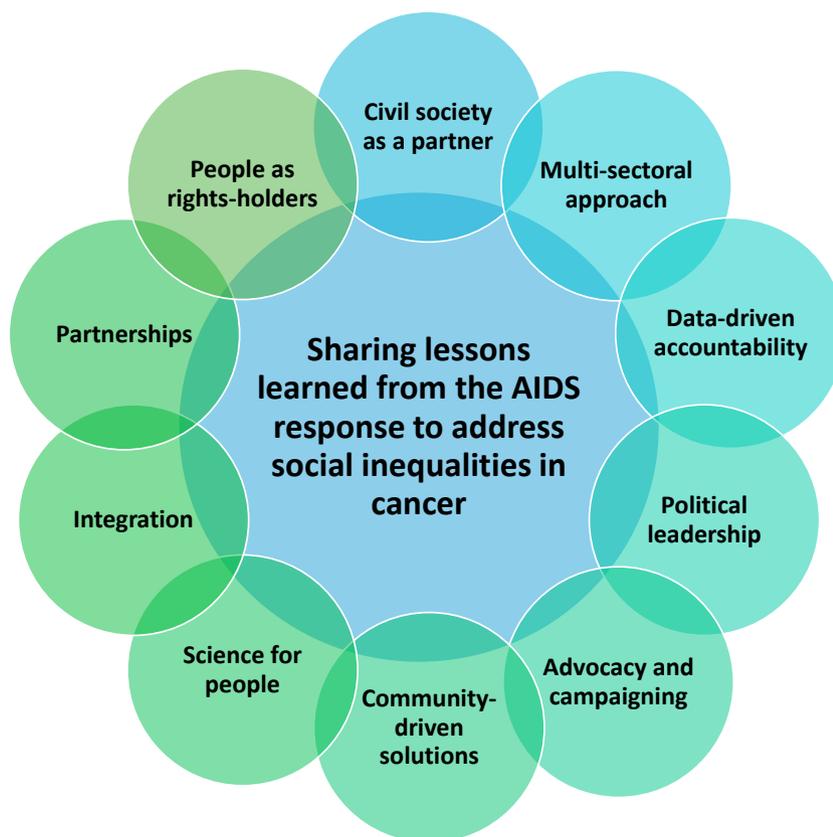
United Nations Programme on HIV and AIDS (UNAIDS) welcomes the opportunity to share lessons learned from the AIDS response with a view to strengthening collaboration with initiatives to address social inequalities in cancer. The 10 key interrelated lessons (Fig. 17.4) are described in the following sections.

Lesson 1: People as rights-holders

From the outset more than 30 years ago, the AIDS response was framed as a human rights imperative and a matter of social justice. The communities affected were at the forefront, caring for loved ones while demanding action. People took to the streets and performed "die-ins" at scientific meetings around the world. They lobbied governments for funding and pharmaceutical companies for better and more affordable medicines, new scientific discoveries, and their wide implementation. They demanded access to leaders at the highest levels and a seat at the decision-making table.

Framing the AIDS response as a rights issue not only helped to generate action but also helped to demonstrate how the ability of affected communities to protect themselves from HIV depends on their ability to exercise their rights. Population health and well-being depend on an enabling social, legal, political, and economic environment. Governments and other powerful actors have obligations and responsibilities to generate such environments by adopting laws, policies, and practices that empower individuals and communities to claim and exercise their rights. These rights include freedom from discrimination and violence as well as rights to equality, participation, information, education, and health. In turn, the right to health encompasses, among other things, sexual and reproductive health, and safe and healthy working conditions (CESCR, 2000).

Lesson 2: Civil society as a partner

From the beginning, civil society has been the engine of the AIDS response, driving funding and research and challenging stigma and discrimination. When treatment first became available, civil society engaged in strategic litigation to ensure equitable access to treatment, lobbied to decrease the prices of medicines, and was essential in ensuring the meaningful engagement of community stakeholders in the development and implementation of public health programmes and policies at the local, regional, and international levels. In particular, the participation of civil society has helped establish more successful implementation of high-quality HIV services, more significant stakeholder input to HIV policy-making, and an increased focus on the human rights of key populations, including people living with HIV (OHCHR, 2015).

When UNAIDS was established, it became the first (and remains the only) United Nations organization where civil society is formally represented on its governing body, the Programme Coordinating Board. The participation of civil society, represented by people living with HIV and other affected communities, provided a unique opportunity to advance human rights issues in a United Nations context and has helped to anchor the global AIDS response in the lived experiences of communities.

Lesson 3: Multisectoral approach

UNAIDS was launched in 1996 as a collective endeavour of several United Nations agencies aimed at ensuring a multisectoral and coordinated global AIDS response (ECOSOC, 1994). It was justified by the epidemic's "urgency and magnitude, its complex socioeconomic and cultural roots, the denial and complacency still surrounding HIV and its routes of transmission, and the discrimination and human rights violations faced by those infected or threatened by HIV" (ECOSOC, 1995).

The cosponsored nature of UNAIDS enables it to address HIV through a multisectoral approach, with a view to generating an overall enabling environment for an effective AIDS response. For example, legal and justice systems play a critical role in shaping social and behavioural norms in society, and the United Nations Development Programme, with its mandate on governance, acts as lead convener of UNAIDS in addressing HIV-related laws, policies, and practices (UNAIDS, 2018c).

Consider sexual inequality, which is a major risk factor for both HIV and human papillomavirus (HPV), the central cause of cervical cancer. Women living with HIV are up to 5 times more likely to develop cervical cancer than HIV-negative women (UNAIDS, 2016a). Where women lack the power to exercise their rights to health, education, and information, they also lack access to lifesaving health interventions (WHO, 2018), including sexual and reproductive health education and services, and access to the HPV vaccine. HPV vaccination programmes are often school-based, but by the time girls reach the age at which they should receive the multidose vaccine (9–12 years), many have dropped out of school or attend irregularly (Wigle et al., 2013; Watson-Jones et al., 2015). Another example is age-of-consent laws, which pose barriers for adolescents to access sexual and reproductive health services, including HIV testing (Fig. 17.5) (UNAIDS, 2016b).

Many of the barriers to reaching people with HIV and cancer are profound and deep, anchored in the

Fig. 17.5. Countries with age-of-consent laws that could discourage adolescents from accessing reproductive and sexual health services. Source: reproduced from UNAIDS (2018a).

Countries with age of consent laws to access sexual and reproductive health services, 2018

| 52% | 53% | 92% | 59% | 90% | 58% | 61% | 57% |

Asia and the Pacific | Eastern and southern Africa | Eastern Europe and central Asia | Latin America | Caribbean | Middle East and North Africa | Western and central Africa | Western and central Europe and North America

Reporting countries
Countries with laws requiring parental consent for adolescents to access sexual and reproductive health services

Source: 2017 and 2018 National Commitments and Policy Instrument.

prevailing power structures within our societies.

Lesson 4: Data-driven accountability

HIV disproportionately affects populations that are already marginalized, stigmatized, discriminated against, and even criminalized across many societies. These groups are critical to actualizing an effective AIDS response, and are often referred to as key populations. They include gay men and men who have sex with men, sex workers, transgender people, and people who inject drugs. UNAIDS acknowledges that prisoners and other incarcerated people are also particularly vulnerable to HIV and frequently lack adequate access to services. UNAIDS encourages countries to "define the specific populations that are key to their epidemic and response, based on the epidemiological and social context" (UNAIDS, 2015b).

HIV is also unequally distributed geographically, both between and within countries. Today, programming takes the information about local epidemiology and local response into account, with programming being designed for specific districts and facilities (UNAIDS, 2018a).

Disaggregated data are critical, not only to ensure that interventions are tailored and targeted to benefit key populations but also as a powerful tool for accountability. For example, data are used to hold United Nations Member States accountable for the ambitious targets set at high-level United Nations General Assembly meetings on AIDS. The most recent United Nations High-Level Meeting on Ending AIDS, held in June 2016, translated the UNAIDS 2016–2021 strategy "On the fast track to ending AIDS" into commitments negotiated and adopted by Member States in a political declaration committing them to these ambitious targets (United Nations General Assembly, 2016).

The Global AIDS Monitoring system, including the National Commitments and Policy Instrument, relies on an online data collection system and supports the monitoring process. It has one of the highest state reporting rates in global health (UNAIDS, 2016c). Importantly, this tool goes beyond epidemiological data collection and includes reporting on laws and policies, with civil society partners completing one part of the instrument to help validate and bring critical perspective to national reports from governments. Disaggregated data also enable UNAIDS to engage in evidence-informed advocacy to highlight social inequalities (Fig. 17.6). For example, in 2014, *The Gap Report* explored why 12 populations (people living with HIV, adolescent girls and young women, prisoners, migrants, people who inject drugs, sex workers, gay men and men who have sex with men, transgender people, children and pregnant women living with HIV, displaced people, people with disabilities, and people aged 50 years and older) are being left behind and what, concretely, must be done to include them in the AIDS response (UNAIDS, 2014).

Lesson 5: Political leadership

The importance of political leadership cannot be overstated, and several lessons have been learned

Fig. 17.6. Key populations at higher risk of HIV infection and their global relative risk, compared with the general population, of HIV acquisition in 2017. Source: reproduced from UNAIDS (2018a).

Relative risk of HIV acquisition, by population group compared to the general population, global, 2017

Female sex workers — **13 times higher**

People who inject drugs — **22 times higher**

Gay men and other men who have sex with men — **28 times higher**

Transgender women — **13 times higher**

HIV incidence rate within the key population
HIV incidence rate within the general population

Source: UNAIDS special analysis, 2018.

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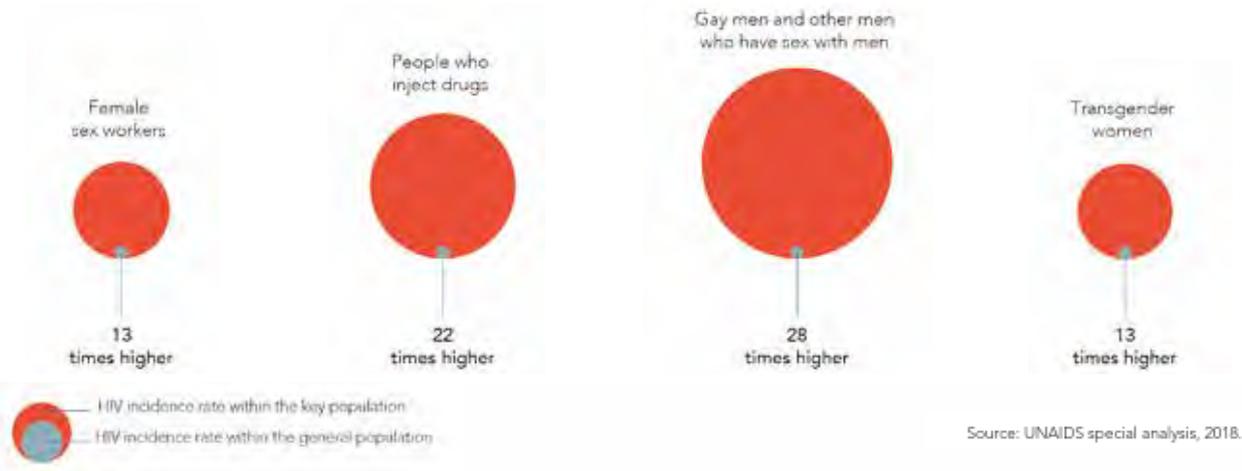
about the need to generate a sense of urgency and leverage attention and resources around AIDS, for example by creating the Global Fund to Fight AIDS, Tuberculosis and Malaria and by commanding the attention of the United Nations Security Council.

The partnership paradigm that is perhaps less known but has demonstrated success is that of shared responsibility and global solidarity promoted by UNAIDS and adopted by the African Union in July 2012 (African Union Commission, NEPAD Agency, and UNAIDS, 2012). The *Roadmap on shared responsibility and global solidarity for AIDS, tuberculosis and malaria responses in Africa (2012–2015)* set out actions to be taken at the national, regional, and global levels to compel high-burden countries to fulfil their mutual obligations in accountable and transparent ways, donors to commit to long-term investment, and countries to dedicate sustainable domestic resources and strong national AIDS responses.

To ensure accountability, global targets were set and benchmarked.

It worked: since the launch of the shared-responsibility Global Compact at the 2011 United Nations General Assembly High-Level Meeting on AIDS (UNAIDS, 2011) and the 2016 "Political declaration on HIV and AIDS: on the fast track to accelerating the fight against HIV and to ending the AIDS epidemic by 2030" High-Level Meeting (United Nations General Assembly, 2016), the share of funding for low- and middle-income countries (LMICs) from domestic resources started climbing, and now represents 56% of their total HIV/AIDS investments (UNAIDS, 2018a). Côte d'Ivoire, Kenya, Malawi, Rwanda, and Seychelles have all increased their domestic HIV expenditures with the aim of paying for the treatment of their citizens from their own budgets.

Lesson 6: Advocacy and campaigning

The AIDS response revolutionized health advocacy and demonstrated how a respect for human rights and the active engagement of affected communities promote public health

aims. It went beyond managing the disease to addressing the issues that confront people living with HIV, including punitive laws, policies, and social norms that accentuate stigma, discrimination, fear, and misinformation. The AIDS movement refused to hold major conferences in countries with punitive laws against people living with HIV. It has been suggested that initiatives to tackle noncommunicable diseases could use a similar tactic by taking a stand against countries that, for example, fail to restrict advertising of junk food to children (Buse and Sprague, 2017).

AIDS advocacy changed the global dynamic of fundraising for health. The success of these efforts has been unprecedented. Total investments to address the AIDS epidemic in LMICs grew from US\$ 4.5 billion in 2000 to US\$ 20.6 billion in 2017, expressed in constant 2016 dollars for comparison (UNAIDS, 2015a, 2018a). AIDS advocacy was no longer the domain of activists but encompassed policy-makers, scientists, celebrities, religious leaders, and people living with HIV. It also used a range of evidence-informed

arguments, including those demonstrating how investing in AIDS is critical for the development, security, and stability of countries.

Lesson 7: Community-driven solutions

In the context of HIV and as recently demonstrated by experiences with Ebola, there is evidence that, in many countries, community-based organizations can reach people who are being left behind because of prejudice, poverty, or punitive laws, or simply because they live in remote areas. Given the scarcity of health personnel, particularly in LMICs, high-quality community health workers are a critical, integral, cost-effective link that needs to be adequately connected to the formal health system.

UNAIDS promotes differentiated care models that simplify and adapt HIV services to better serve the needs of people living with HIV and increase the efficiency of the health system. Differentiated care incorporates concepts such as simplification, task-shifting, and decentralization, all of which facilitate more effective allocation of resources, provide better access to services for underserved populations, and deliver care in ways that improve quality of care and of life (UNAIDS, 2017b).

For example, access to cheap and easy-to-use diagnostic tools (including rapid testing) and good-quality treatment and prevention commodities and technologies has been critical in effective HIV responses in all countries (Wafula et al., 2014).

Lesson 8: Science for people

Access to affordable antiretroviral drugs and other essential medicines lies at the heart of the right to health. From the early days of the AIDS ep-

idemic civil society has been at the forefront, exerting pressure on powerful actors, from governments denying the science behind the epidemic to pharmaceutical companies putting profit before the lives of people. Civil society has also worked closely with the scientific community in seeking solutions that benefit and work for communities, including by simplifying treatment regimes.

On the subject of pricing of medicines, an important development driven by AIDS activism was the Doha Declaration on the Trade-related Aspects of Intellectual Property Rights (TRIPS) Agreement and Public Health, which was adopted by the World Trade Organization Ministerial Conference in 2001. It reaffirmed the right of World Trade Organization members to protect public health and, in particular, to promote access to medicines for all by using the flexibilities in the TRIPS Agreement. The advent of generic HIV drugs turned the tide on access and affordability, reducing the price of antiretroviral drugs per person per year from US$ 10 000 in 2000 to less than US$ 100 in 2011 (UNAIDS, 2015a).

The Medicines Patent Pool, established by Unitaid in 2010 (MPP, 2018a), has become a critical global actor in increasing access to and promoting innovation in the fields of HIV, hepatitis C virus, and tuberculosis treatments through voluntary licensing and patent pooling. To date, it has signed licensing agreements with nine patent holders for 13 HIV antiretroviral drugs, two hepatitis C virus antiviral drugs, and an investigational tuberculosis treatment (MPP, 2018b).

Lesson 9: Integration

An important overarching theme for the 2016 Political Declaration on

Ending AIDS is taking AIDS out of isolation. Among the commitments of the High-Level Meeting is integrating HIV services into universal health coverage, including services to address cervical cancer. In the context of service delivery, for example, sexual and reproductive health services need to integrate both HIV and the prevention and control of cervical cancer.

About 80% of all cases of cervical cancer, which is an AIDS-defining illness, occur in LMICs (Kent, 2010). Linking cervical cancer screening and HIV services can be a cost-effective way of improving cervical cancer screening and treatment. For example, the Cervical Cancer Prevention Program in Zambia integrated a national cervical cancer prevention programme with an existing HIV programme; this led to the implementation of cervical cancer screening, which covered more than 100 000 women (28% of whom were living with HIV) over a period of 5 years (UNAIDS, 2016a).

Lesson 10: Partnerships

Issue-specific coalitions and campaigns work best when they bring together government insiders and outsiders to combine perspectives and expertise. That approach has been taken throughout the AIDS response, with partnerships crossing all boundaries and including governments, civil society, academia, science, the private sector, and groups focused on other disease, including cancer.

An example of synergy between the AIDS response and cancer prevention, treatment, care, and support is the Pink Ribbon Red Ribbon (PRRR) initiative, an innovative partnership between the George W. Bush Institute, the United States

President's Emergency Plan for AIDS Relief, UNAIDS, and the Susan G. Komen Foundation. PRRR works to expand the availability of vital cervical cancer screening and treatment and breast care education, especially for women living with HIV in Africa.

Since 2011, the PRRR partnership has helped to screen nearly 500 000 women for cervical cancer in Botswana, Ethiopia, the United Republic of Tanzania, and Zambia, including 380 000 who were screened for the first time and more than 110 000 women living with HIV. With the support of PRRR and Gavi, the Vaccine Alliance, the PRRR partnership has recently expanded its goal to support vaccination of girls against HPV16 and HPV18 in Africa. So far, 148 000 girls in Botswana, Ethiopia, and Zambia have completed the series of vaccinations (PRRR, 2018).

The lessons learned from the AIDS response have been critical in decreasing the stigma and fear that can prevent women from seeking cervical cancer screening.

Conclusions

The 2030 Agenda for Sustainable Development (UN, 2015) is fundamentally about generating profound structural change and societal transformation. It represents much of what has been practised in the AIDS response: inclusive partnerships, working across sectors, addressing inequalities, empowering communities, and enhancing access to justice. Let us embrace the 2030 Agenda as a springboard for enhanced cooperation within, across, and beyond the global health community, and rally together around its central theme: "leave no one behind".

Indeed, the ultimate measure of our collective success must be whether the poorest, the most marginalized, and the most vulnerable benefit from the goals of the 2030 Agenda for Sustainable Development, including Goal 3: to ensure healthy lives and promote well-being for all at all ages. Quick-fix and vertical solutions will not enable the realization of any of the health targets of the 2030 Agenda. We need to go upstream and address the causes of exclusion and ill health, in specific contexts and for specific populations. Vulnerable and marginalized groups must be engaged every step of the way so that priorities are set by people for people.

It will not be easy. A trend of discontent is fuelling populism and the scapegoating of marginalized populations groups in many parts of the world. Inequalities are widening and are embedded across health systems, where priorities are often skewed towards biomedical interventions. Services are vertical, fragmented, and not reaching deep enough or far enough. Out-of-pocket spending remains high, and corruption is rampant.

In the journey to end AIDS, much has been learned and many successes can be celebrated. Perhaps the most important lesson is the need to forge partnerships and alliances with a shared commitment to people and their rights.

The AIDS response and initiatives to address social inequalities in cancer both need to scale up efforts to address the structural and root causes of ill health, many of which relate to poverty and social inequalities. Let us join forces and build on lessons learned from the AIDS response by building coalitions, sharing good practices, and creating space for civil society at different levels: globally, regionally, nationally, and locally.

Let us approach cancer prevention and treatment as an opportunity to lead a broad coalition demanding health as a fundamental, universal human right.

Key points

- Although there is a long journey ahead to end the AIDS epidemic as a public health threat as set out in the 2030 Agenda for Sustainable Development, tremendous progress has been made, particularly in recent years. It is therefore timely to review lessons learned from the AIDS response with a view to addressing social inequalities in cancer.

- Ten such lessons are: framing the AIDS response as a human rights imperative; recognizing civil society as a critical partner and engine of the response; mobilizing a coordinated, multisectoral global response; prioritizing the critical role of disaggregated data for monitoring and accountability; ensuring strong political leadership; supporting advocacy and campaigning; promoting community-driven solutions; ensuring science for people; integrating the AIDS response with other health areas; and building partnerships.

- Both the AIDS response and initiatives to address social inequalities in cancer need to scale up efforts to address the structural causes of ill health. If these movements work together more closely, efforts can be strengthened and a broader coalition formed to demand health as a fundamental, universal human right.

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CHAPTER 18.

Technology and cancer systems: creating better policy to enhance equality

Richard Sullivan and Ajay Aggarwal

A tsunami of technology

The application of technology – defined as the production or use of advanced or sophisticated tools, whether diagnostic, surgical, radiotherapeutic, or pharmaceutical – in cancer control is a mixed blessing. Its benefit or harm depends on many intrinsic and external factors. In this sense, technology is both a cure for and a cause of global inequalities in cancer. By any metric, cancer is one of the most technocentric global disease domains. Methods developed by Cambrosio et al. (2006) were used to estimate that, of the total number of publications in the field of cancer (~125 000) in 2017, a staggering 72.6% had some form of technology at their core. This percentage is predicted to rise to 82.6% of about 200 000 publications per year by 2027; many of these will be published by major emerging powers, such as China, which has seen the volume of its technocentric research publications experience a massive 23% compound annual growth rate in the past 10 years (Chinese Journal of Cancer, 2017). The research agendas of high-income countries (HICs) and institutions that wish to industrialize their innovation have led to a global cancer research effort that is dominated by high-tech and rapid technology transfer (Kneller, 2001).

For instance, in the latest review of future cancer research innovations in the USA by a *Lancet Oncology* Commission, the list of the top 20 consists of some of the most advanced technologies in biomedicine, never mind cancer care (Jaffee et al., 2017). An example is liquid biopsies, which involve the sampling and analysis of non-solid biological tissue as part of an early detection strategy. In addition, artificial intelligence and advanced analytical methodologies have a wide-ranging role, from predicting how cancers will progress and evolve on the basis of their genetic profiles to optimizing chemotherapeutic treatment delivery schedules to reduce toxicity without compromising tumour control. Other technologies include DNA cages, which enable precise delivery of chemotherapy drugs to tumour cells in vivo in response to ultraviolet light, and the genome-editing tool CRISPR/Cas9, which has been

used to engineer genomes and to activate or repress the expression of genes. CRISPR/Cas9 provides an efficient technology to dissect mechanisms of tumorigenesis and discover new therapeutic targets (Zhan et al., 2018). Next-generation systemic therapeutics will be aimed at the microbiome, immunome, and epigenome.

The traditional hegemony of pharmaceuticals in this technological space is now being augmented by precision surgery, including the intelligent scalpel (which provides instantaneous diagnosis during surgery), nanorobotics (Felfoul et al., 2016), and radical new applications of computing to radiotherapy planning (e.g. deep learning to facilitate automated treatment contouring and planning). Emerging powers are also joining this global technocentric paradigm at a rapid rate. In a recent review of the 150 most important research questions facing Chinese researchers, 149 were concerned with some form of technology (Chinese Journal of Cancer, 2017). For example, the rapid rise in lung-cancer-specific research in China (which in 2016 overtook the USA to become the country producing the most research in this field) has been built mostly on technical innovations (Aggarwal et al., 2016).

Technology for cancer control draws from a wide field, from research tools (e.g. sequencing machines) to the primary modalities of treatment (e.g. medicines, surgery, and radiotherapy), supported by the two further domains of imaging and pathology. In 1970 there were 48 cancer medicines used in 102 different regimens; today, a typical healthcare system in an HIC has about 746 cancer medicines that can be combined into more than 3540 regimens (Arruebo et al., 2011). Surgery has also undergone rapid technological expansion during the same period. In 1970, 289 instruments were used in 37 procedures with three levels of complexity; today, 4899 instruments are used in more than 300 procedures with six levels of complexity (Purushotham et al., 2012; Sullivan et al., 2015).

In addition, many generic technologies, such as mobile phones and the Internet, form a key component of the cancer pathway, whether used to send money to family members to pay for treatment or by doctors to evaluate images and pathology results. By changing the social determinants of health, these technologies undeniably contribute to better outcomes for cancer patients through both earlier diagnosis and direct care (McKenzie et al., 2016).

This rapid expansion has multiple drivers. Cancer has become a platform for innovation across general science and technology; there are few spheres of technology that cannot be applied to cancer care (Sullivan, 2007). Neoliberal policies that favour the private sector above the public sector have also set national policy agendas (Chapman, 2016). The pillar of wealth creation has towered above health as a human right in most national settings, even those traditionally built on the Bismarckian tradition of welfare and solidarity. The commercial imperative, framed by the World Trade Organization Agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS) and national policies such as the 1980 Bayh–Dole Act in the USA, has also created an ecosystem where technological innovation for profit takes primacy (Boettiger and Bennett, 2006). Revenues from the sales of cancer medicines are expected to reach US$ 147 billion by 2020 (compound annual growth rate, 10%). Pharmaceutical product life-cycles have shortened 5-fold since 1997, and new combinations, treatment stacking (i.e. more treatments added into models of care), and increases in off-label prescribing have been major drivers of increased use.

Technological innovation has also changed the meaning of cancer through advances in cytological, morphological, and genotypic phenotyping; this has created an exponentially increasing number of types of cancers, as well as pathways of care, defined by prognostic stratification (Aparicio and Caldas, 2013). The evolving culture of cancer care, and cancer medicine more broadly, has also played a major part in these changes. The biomedical paradigm includes the use of innovative technology and personalized medicine as key determinants of a good cancer care system (as well as perceived high-quality care), despite the many shortcomings of these developments (Davis and Abraham, 2013; Tannock and Hickman, 2017).

Technology: a cure for and a cause of inequality

The most cursory examination of improvements in cancer outcomes since the 1940s reveals the positive impact of innovative technologies across the spectrum (Nathanson, 1943), from new forms of classic chemotherapy, which can now cure many childhood and adult haematological malignancies, to advances in surgical technologies (e.g. total mesorectal excision), which have dramatically improved rectal cancer mortality rates (Heald and Ryall, 1986; Heald et al., 2017). Indeed, technological improvements in surgery, radiotherapy, pathology, and imaging, linked to earlier diagnosis

and better screening (e.g. of cervical cancer), have been the foundations for improved population outcomes. Point-of-care visual inspection with acetic acid (Basu et al., 2015) for cervical cancer screening, targeted at the most vulnerable female populations, is an excellent example of how a technology can directly reduce inequalities in outcomes (Shastri et al., 2014). Other so-called frugal innovations also promise to deliver technological innovations that could, in theory, reduce inequalities by providing diagnostic and pathological tools to rural health centres, thereby improving early diagnosis in these vulnerable populations (Horton et al., 2018; Sayed et al., 2018). For example, a screening device for oral cancer that attaches to a smart phone, lab-on-a-chip devices, and the foldscope (a folding microscope) are all affordable, easy-to-use technologies that can help to deliver pathology services outside major centres (Cybulski et al., 2014; Esfandyarpour et al., 2017).

It is now also clear that many technological developments, such as the ability to transfer funds using mobile phones, have contributed indirectly to better outcomes by enabling patients to access health care. In India, publicly funded second-opinion services such as Navya (https://www.navyanetwork.com/), provided by the National Cancer Grid of India, have been of huge benefit to patients in groups with lower socioeconomic status (SES) in providing improved access to free public cancer care (Pramesh et al., 2014a). Despite issues related to privacy, the system of digital identity of all Indian citizens (the Aadhaar) is also likely to have a significant positive impact on cancer care by providing a dedicated method of linking insurance and patients with public hospitals (Nilekani, 2011).

However, the benefits of these technologies are unevenly distributed between countries and between certain populations (e.g. low-income groups, elderly populations, and ethnic minorities) within countries. Technologies are embedded within models and pathways of care and cultures of clinical practice. It follows that any health system that is based largely on the power of the market, that fails in its national duties to provide access to high-quality cancer care, and that takes inadequate steps to address the underlying socioeconomic causes of late-stage diagnosis cannot deliver equality in access to cancer technologies.

The focus on pharmaceuticals and biomarkers means that nearly all federal, philanthropic, and private cancer research funders are now aligned in their financial support of expensive cancer treatments (Cambrosio et al., 2006; Aggarwal et al., 2017a). In comparison, research domains that are essential to improving equality (e.g. prevention, palliative care, health services research, and even childhood cancer) receive little support or political capital (Pritchard-Jones et al., 2011; Sullivan et al., 2013); for example, the United Kingdom philanthropic funder Cancer Research UK spends less than 2% of its £700 million annual budget on prevention. This imbalance has led to significant inequalities in outcomes with a global research system focused on expensive medicines for wealthy patients in wealthy countries; such innovations have improved outcomes for those patients but not for patients in groups with lower SES, even in HICs (Aggarwal et al., 2017a). This finding is not limited to HICs but is increasingly being observed in emerging economies, where domestic, affordable innovations are being displaced by high-end expensive technology (e.g. cobalt radiotherapy machines are being displaced by linear accelerator technology) (Sullivan et al., 2014).

Pharmaceuticals represent a paradox in the link between technology and inequalities. Many countries lack basic medicines, resulting in poor outcomes for those patients with cancer types for which medicines are the major modality of cure and control; however, the creation of a generation of expensive cancer drugs that are delivering less and less clinically meaningful benefit has created both real and perceived inequalities (Del Paggio et al., 2017a, b). The inequality paradox in cancer medicines is highlighted by emerging economies in Europe that are unable to deliver basic chemotherapeutic drugs but are nevertheless putting increasing resources into newer immunotherapies (Cherny et al., 2017).

High-resolution analysis of direct cancer expenditures across Europe has found significant overspend on low-impact clinical technologies and underspend on basic, high-impact clinical technologies, particularly in countries with lower Human Development Index, leading to a complete disconnection between cancer expenditure and outcomes (Luengo-Fernandez et al., 2013, 2016). Such actions have the potential to deliver more harm to the most vulnerable sectors of society, who experience worse outcomes because of the lack of access to basic cancer care, in addition to facing financial toxicity from low-value high-tech care. An emerging issue in all countries is the perception of inequality by patients who, misled by media hype, believe that the latest technologies (e.g. proton beam therapy) provide

some miraculous route to cure, irrespective of the clinical facts.

In the past two decades, the bellwether non-pharmaceutical technology that epitomizes the increasing socioeconomic inequalities as a result of the introduction of new technologies in cancer care has been the da Vinci robotic surgical system. This device, which enables surgeons sitting at a console to operate remotely controlled arms for minimally invasive surgery, was first granted United States Food and Drug Administration approval in 2000. It was expected that its inherent advantages (i.e. improved visualization of the surgical field, enhanced range of motion of the robotic arms, and improved ergonomics for the surgeon) would translate into improvements in patient outcomes (Wright, 2017). However, in the case of prostate cancer and rectal cancer, no improvements in functional or oncological outcomes have been observed (Ilic et al., 2017; Jayne et al., 2017). Despite the lack of clear evidence for its superiority over open and laparoscopic techniques and its higher associated costs, the robotic surgical system has rapidly been implemented across the USA and Europe, and even in many low- and middle-income countries (Barbash and Glied, 2010; Ramsay et al., 2012). It could now be considered the cornerstone of surgical treatment for prostate cancer in these countries, with increasing use across tumour types, despite the lack of level one evidence (e.g. evidence from at least one properly designed randomized controlled trial) (Kaye et al., 2015; Wright, 2017).

Studies have demonstrated that the uncoordinated adoption of new technologies in health systems has created a socioeconomic differentiation in access to cancer care (Aggarwal et al., 2017b, 2018). In the English National Health Service, where health care is free at the point of use, robotic surgery for prostate cancer has been adopted piecemeal; as a result, a significant number of men who wish to access these treatments have bypassed local centres in favour of alternative centres where the treatment is routinely available. Men who chose preferentially to travel further to centres that offered robotic prostatectomy were on average younger, fitter, and more affluent than those who did not choose to do so (Aggarwal et al., 2018). This tells us that the geographical variation in the availability of new and so-called innovative technologies within health systems means that these are more likely to be accessed by patients with greater financial or physical resources, creating profound inequalities in access and outcomes.

This compounds entrenched socioeconomic differences in care, especially where men with lower SES are unable to attend higher-performing centres because of economic constraints. Furthermore, such patterns of mobility mean that hospitals located in socioeconomically deprived areas with older demographic profiles have to manage far more complex patient cohorts, with subsequent effects on their measured quality and outcomes (Aggarwal et al., 2017c). The substantial levels of patient mobility driven by the differential availability of robotic surgery have led to competition between hospitals to retain their local patients and prevent a loss of income (Aggarwal et al., 2017d). This resulting competition contributed to the closure of 25% of radical prostatectomy centres in the English National Health Service and the widespread adoption of robot-assisted radical prostatectomy.

Technology has a powerful impact in driving patient demand and the configuration of cancer services, not only in unregulated markets in emerging economies but also in HICs with health systems built on equality and solidarity (Pramesh et al., 2014b). Further inequalities in access to treatments and in outcomes may result as the geographical reconfiguration and closure of services is driven by the decisions of fitter, younger, more affluent individuals, rather than by an understanding of the relative needs of the different populations served (Stitzenberg et al., 2009).

Policy interventions to manage technologies

The impact of technology on cancer control depends on industrial and macroeconomic policy, and it remains an open question whether systems and clinical communities have the will or the appetite to embrace different paradigms in relation to national policies. This is especially the case when so much health care is being delivered in pure market economies with unregulated private sectors and underinvested public systems (Bhattacharyya et al., 2017). The impact of this approach is crystal clear: poor, unequal outcomes coupled with catastrophic expenditures, often as a result of accessing unaffordable (and, in many cases, unnecessary) cancer technologies (Kimman et al., 2012).

Current cancer control systems have two intrinsic flaws, which reflect massive political failure at the national and global levels: (i) the failure of policy-makers to ensure universal health coverage or the rational allocation of resources to key modalities and site-specific cancers; and (ii) the ad hoc funding by governments of extensive pharmaceutical technologies or proton beam therapy in the absence of provision of basic radiotherapy or adequate surgical capacity. To

rectify these intrinsic flaws, the following policy interventions, aimed broadly at reducing inequalities in access to affordable and necessary cancer technologies as well as addressing technology-induced inequalities, are strongly recommended.

(i) *Build a culture of funding for affordable technologies:* A reorientation of public funding for research that builds on technology domains that are likely to deliver improvements in outcomes, while minimizing inequalities, is required. Examples of research areas that could reduce price as a barrier to access include: repurposing cancer drugs, using reformulations for childhood cancers, developing new forms of radiotherapy technology that require fewer treatment sessions, and improving surgical outcomes by virtual-reality-enhanced surgical training. This reorientation of funding needs to take place at the same time as building momentum in key non-pharmaceutical technological domains (e.g. pathology, surgery, and radiotherapy) as well as creating a policy dialogue to emphasize that such approaches are not second-class technology and medicine. There is also an urgent need for high-income research funders to more actively fund research in low- and middle-income settings (Rodin et al., 2017). Finally, it is imperative that research funding organizations consider a wider range of research domains beyond pharmaceuticals and biomarkers, such as diagnostics and prevention, to change the epidemiological course of cancer (earlier-stage diagnosis and/or reduced incidence), rather than the continued focus on therapeutics that are delivering ever more marginal gains (Booth et al., 2008; Davis et al., 2017).

(ii) *Governance:* Clinical governance of pathways and models of care built on evidence-based cancer guidelines and even stricter protocols for cancer treatment are necessary. This should also include the regulation of the private-sector technologies, requiring the demonstration of quality and improved outcomes.

(iii) *Pricing and reimbursement:* A wide range of supply- and demand-side policies are needed to manage technologies, with a specific focus on value-based payment systems and health technology assessment programmes for all technologies.

(iv) *Public and patient engagement and regulation of the marketization of cancer care:* A new narrative is necessary to balance the unrelenting mantra calling for personalized medicine and access to everything for everyone. Technology is not a substitute for better governance in the face of clinical and systems failure or a lack of human resources; technology can only enhance, not create, capacity and capability. Framing cancer as a systems problem could help advance the discourse. More radical, however, would be the introduction of policies that legislated against direct-to-consumer and false advertising and regulated the engagement of the clinical community by technology companies.

Conclusions

Fundamentally, weaving clinically meaningful new technologies into cancer care in an affordable and rational manner requires an ethos in national cancer control planning that focuses on systems and better care, not just on innovation and access (Sullivan et al., 2017).

Key points

- The research agendas of high-income countries have led to a global cancer research effort that is dominated by all things high-tech, whether diagnostic, surgical, radiotherapeutic, or pharmaceutical.
- The benefits of technologies are unevenly distributed between countries and between certain populations (e.g. low-income groups, elderly populations, and ethnic minorities) within countries.
- Research domains essential to improving equality (e.g. prevention, palliative care, health services research, and even childhood cancer) receive little financial or political support, compared with technology-driven models and pathways of care and cultures of clinical practice.
- Policy interventions to manage technologies include: creating a research culture that incentivizes the development of affordable technologies; building pathways and models of care according to evidence-based cancer guidelines; controlling pricing and reimbursements; and engaging the public and patients.
- Weaving clinically meaningful new technologies into cancer care in an affordable and rational manner requires an ethos in national cancer control planning that focuses on systems and better care, not just on innovation and access.

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CHAPTER 19.

The inverse care law: overutilization of health services and overdiagnosis

Salvatore Vaccarella and Louise Davies

Introduction

Individuals and populations with lower social conditions (a broad descriptor encompassing access to shelter, warmth, clean water, freedom from war, and education) are known to experience higher mortality rates from cancer, because of limited access or a lack of access to health systems (see Chapters 3, 7, 10, and 15); there is also growing evidence that individuals, populations, and countries with higher social conditions may experience the negative effects of too much medical care (Hart, 1971). Fig. 19.1 depicts how people may be disproportionately subject to overdiagnosis, which is defined as the identification and treatment of cancers that would probably not have gone on to cause symptoms.

A cancer that is overdiagnosed exposes people to the risk of adverse effects of treatment without any benefit, because treatment was not needed. In addition to undergoing unnecessary surgery, radiation, and chemotherapy, all of which carry toxicity, and often lifelong therapies,

Fig. 19.1. A graphical depiction of the inverse care law, as described by Hart (1971). The availability of and access to effective medical services and good social care is inversely related to the needs of the population served. Source: compiled from Hart (1971).
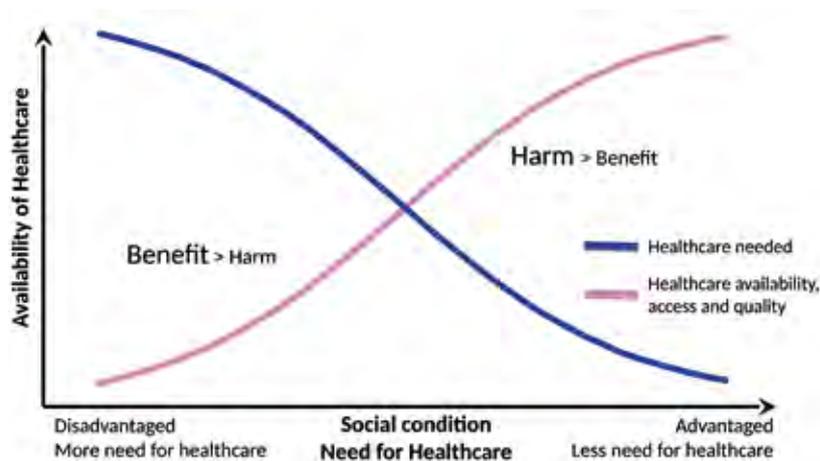
patients can suffer psychological consequences as a result of the diagnosis; there are also financial costs to the individual and the health system associated with treatment. This paradoxical situation occurs in many health systems today, some of which are facing relevant resource constraints. The causes of overdiagnosis are multifactorial. First, compared with less affluent groups, wealthier people generally have greater access to care, because they have greater mobility to get to care locations and the ability to pay (Welch and Fisher, 2017; Brodersen et al., 2018). Second, in some settings, non-indicated screening services are offered to those who can pay, despite the fact that there is no evidence that the benefits outweigh the harms. Third, there is an increasing use of imaging or other advanced technologies in medicine more broadly, for both indicated and non-indicated uses (see Chapter 17). Failure to manage the problem of overdiagnosis affects all users of the health-care system, whether wealthy or not; if resources and efforts are focused on unnecessary practices and potentially harmful treatments, they are not available to invest in the prevention and treatment of more threatening cancers and diseases, therefore precluding the reduction of social inequalities in cancer and threatening the sustainability of health systems.

The impact and magnitude of overdiagnosis in a population can be so large that it visibly affects the incidence rates of a cancer. Among the cancers particularly affected are breast cancer, prostate cancer, melanoma, and thyroid cancer (Lim et al., 2012; Morris et al., 2013). The case of thyroid cancer is used in this chapter as an example of the impact of overdiagnosis in cancer.

In the past decades, several high-income countries (HICs) have reported large increases in the incidence of thyroid cancer, particularly of small papillary carcinomas. Countries where large increases have been observed include France, Italy, and the USA, but it is in the Republic of Korea where the incidence has risen most rapidly: thyroid cancer incidence increased from 12 cases per 100 000 in 1993–1997 to 60 cases per 100 000 in 2003–2007 (Davies and Welch, 2006; Ahn et al., 2014; Vaccarella et al., 2016). Within only a few years, thyroid cancer became the most commonly diagnosed cancer in women in the Republic of Korea. In contrast, thyroid cancer mortality rates have been largely stable at very low levels or even declining in most of the countries where increasing incidence rates of the disease have been reported. There is no evidence of exposure to new thyroid cancer risk factors. The contribution of known and potential risk factors, including radiation exposure before the age of 20 years, excess or deficit intake of iodine, excess body mass, and dietary factors, cannot explain the sudden rise in thyroid cancer incidence rates and the strong variations observed even between neighbouring countries and regions where risk factors are similar (Vaccarella et al., 2016).

This increasing incidence of thyroid cancer was attributed to opportunistic thyroid screening in the setting of nationally sanctioned screening programmes for breast cancer and other cancers in the Republic of Korea, and to the increased medical surveillance and scrutiny of the thyroid gland in other HICs. These activities, particularly the use of ultrasound, have uncovered a substantial amount of subclinical disease existing in the thyroid gland. Asymptomatic papillary thyroid cancer of small dimensions is found in approximately 10% of autopsy series (Harach et al., 1985; Furuya-Kanamori et al., 2016), and incidental thyroid nodules are found in approximately 16% of computed tomography and magnetic resonance scans in the USA (Yoon et al., 2008). The so-called epidemic of thyroid cancer can be largely explained by overdiagnosis, which has been estimated to account for up to 60–90% of the diagnosed thyroid cancer cases in some HICs (Vaccarella et al., 2016).

Although this phenomenon initially concerned HICs, high incidence rates have also recently been observed for the period 2008–2012 in countries transitioning to a higher level of Human Development Index, particularly in some areas of Brazil, China, and Turkey (Bray et al., 2017; Lortet-Tieulent et al., 2019) where surveillance of the thyroid gland and use of advanced diagnostic techniques are becoming increasingly common. At the country level, a strong positive correlation exists between thyroid cancer incidence (but not mortality) and the average level of development. Fig. 19.2 shows that higher thyroid cancer incidence rates are found in countries with higher average levels of socioeconomic development than in those with lower average levels of socioeconomic development. However, thyroid cancer mortality rates are approximately similar between countries, or only slightly lower in countries with higher levels of socioeconomic development than in those with lower average levels of socioeconomic development.

Further evidence of the role of overdiagnosis is provided by the fact that, in both HICs and low-income countries, the highest rates

Fig. 19.2. Age-standardized incidence rates of thyroid cancer, in both sexes, by average level of socioeconomic development in 2012. Socioeconomic development of a country is usually measured by the Human Development Index (UNDP, 2018), which is a function of life expectancy, education, and income. However, life expectancy is not an appropriate marker of socioeconomic development if used as an independent variable when cancer mortality is the dependent variable (although thyroid cancer mortality is generally very low and its inclusion would not substantially change the results). To measure average level of socioeconomic development, we have therefore used only education and income to create an index that we refer to as the education and income index (EDI). EDI is a dimensionless variable of value between 0 and 1 and, for the purpose of this analysis, we defined four categories of socioeconomic development: low (EDI ≤ 0.5), medium (0.5 < EDI ≤ 0.65), high (0.65 < EDI ≤ 0.8), and very high (EDI > 0.8). Circles are proportional to the population size of the country. KOR, Republic of Korea.

The consequences of overdiagnosis and overtreatment are significant for patients, with the majority of them undergoing total thyroidectomy and many also having lymph-node dissection and radioiodine treatment. Hypoparathyroidism and nerve injury are among the most common consequences of unnecessary thyroid surgery. Large geographical differences have been reported in thyroidectomy rates in the USA, suggesting a major role of local customs in the identification and treatment of thyroid cancer (Francis et al., 2017). The economic costs of thyroid cancer overdiagnosis are likely to be very high. A study in the USA (Aschebrook-Kilfoy et al., 2013) estimated the cost for a hypothetical cohort of patients; the lifetime cost to patients with thyroid cancer was approximately US$ 35 000 for those without metastasis and approximately US$ 59 000 for those with metastasis. The annual total cost of thyroid cancer in the USA is expected to reach approximately US$ 2.4 billion by 2019. Similarly, Lubitz et al. (2014) estimated the cost of thyroid cancer to the United States health-care system to be US$ 1.6 billion in 2013. In the Republic of Korea, US$ 1.7 billion was spent on thyroid cancer treatment in 2010.

In summary, there is a growing recognition that a large fraction of the thyroid cancer epidemic is due to overdiagnosis and that, in addition to an unnecessary burden for each of the diagnosed patients, this may represent a major economic cost to the health system. Overdiagnosis is likely to affect other cancers, for example, melanoma and cancers of the breast and prostate, which are subject to intensive surveillance and screening. Unnecessary identification and treatment should be avoided. Human and economic resources should not be

of thyroid cancer incidence are observed where examination of the thyroid gland is easily accessible and unregulated, that is, in countries and urban areas where health services are mainly private and market-oriented, and technologies such as ultrasound and needle biopsy services are available (Brito and Hay, 2017). The great between-country and within-country variability in the incidence of thyroid cancer (Francis et al., 2017) certainly reflects the different intensity of surveillance in the different areas and local practices. A strong correlation between

thyroid cancer incidence and the density of endocrinologists and ultrasound machines has been reported in the USA (Boscoe et al., 2014; Udelsman and Zhang, 2014). Within countries, there is evidence that individuals and populations with higher socioeconomic status (SES) and with greater access to health care have a higher incidence of thyroid cancer and are likely to suffer more from thyroid cancer overdiagnosis and overtreatment compared with groups with lower SES (Lim et al., 2012; Morris et al., 2013; Altekruse et al., 2015).

directed towards the detection and management of low-risk cancers, the treatment of which is likely to provide more harm than benefit; instead, resources should be directed towards the provision of high-quality and equitable health care for all individuals and populations.

Key points

- The inverse care law describes how the availability of and access to effective medical services and good social care is inversely related to the needs of the population served.

- Individuals and populations with lower social conditions are known to experience higher mortality rates from cancer, because of limited access or a lack of access to health systems; there is also growing evidence that individuals, populations, and countries with higher social conditions may experience the negative effects of too much medical care.

- Overdiagnosis of cancer exposes people to the risk of major adverse effects and the health system to substantial financial costs, with minimal, or no, benefits. This paradoxical situation occurs in many health systems today, some of which are facing relevant resource constraints.

- Failure to manage the problem of overdiagnosis affects all citizens. Resources and efforts are focused on unnecessary practices and potentially harmful treatments, instead of being available for the prevention and treatment of more threatening cancers and diseases, therefore precluding the reduction of social inequalities in cancer and the sustainability of health systems.

- The impact and magnitude of overdiagnosis in a population can be so large that it visibly affects the incidence rates of a cancer; the case of thyroid cancer is an example.

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CONCLUSIONS.

Reducing Social Inequalities in Cancer: Setting Priorities for Research

Salvatore Vaccarella, PhD[1]; Joannie Lortet-Tieulent, PhD[2]; Rodolfo Saracci, MD[3]; Miranda M. Fidler, PhD[4];
David I. Conway, PhD[5]; Nadia Vilahur, PhD[6]; Diana Sarfati, MBChB, MPH, PhD[7]; Ahmedin Jemal, DVM, PhD[8];
Johan P. Mackenbach, MD, PhD[9]; Michael G. Marmot, MD, PhD, FRCP[10]; Kurt Straif, MD, PhD[11]; Christopher P. Wild, PhD[12]

[1]Scientist, Infections and Cancer Epidemiology Group, Section of Infections, International Agency for Research on Cancer, Lyon, France; [2]Postdoctoral Scientist, Infections and Cancer Epidemiology Group, Section of Infections, International Agency for Research on Cancer, Lyon, France; [3]Senior Visiting Scientist, International Agency for Research on Cancer, Lyon, France; [4]Postdoctoral Scientist, Section of Cancer Surveillance, International Agency for Research on Cancer, Lyon, France; [5]Professor of Dental Public Health, School of Medicine, Dentistry and Nursing, University of Glasgow, Glasgow, United Kingdom; [6]Scientist, IARC Handbooks Group, Section of Evidence Synthesis and Classification, International Agency for Research on Cancer, Lyon, France; [7]Professor of Public Health, Department of Public Health, University of Otago, Wellington, New Zealand; [8]Scientific Vice President, Surveillance and Health Services Research, American Cancer Society, Atlanta, GA; [9]Professor of Public Health, Department of Public Health, Erasmus MC University Medical Center Rotterdam, Rotterdam, the Netherlands; [10]Professor of Epidemiology and Public Health, Institute of Health Equity, Department of Epidemiology and Public Health, University College London, London, United Kingdom; [11]Section Head, Section of Evidence Synthesis and Classification, International Agency for Research on Cancer, Lyon, France; [12]Director, International Agency for Research on Cancer, Lyon, France.

Corresponding author: Salvatore Vaccarella, PhD, International Agency for Research on Cancer, 150 cours Albert Thomas, 69372 Lyon Cedex 08, France; vaccarellas@iarc.fr

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Social inequalities in cancer are a global problem, as has been well documented in the World Health Organization (WHO)/International Agency for Research on Cancer (IARC) publication *Social Inequalities and Cancer.*[1] Inequalities in income, wealth, education, and power disproportionally impact the most disadvantaged individuals, communities, and countries to produce a social gradient in the incidence, survival, and mortality of many cancers both within and between countries.[2–4] From April 16 to 18, 2018, the IARC convened a workshop to examine the current evidence and identify research priorities for reducing social inequalities in cancer. International and WHO/IARC experts drawn from many different disciplines presented a series of articles to be published in an IARC scientific publication; extensive discussion in subgroups and plenary sessions resulted in participants identifying 3 research priorities.

First Priority: Generating Knowledge and Monitoring Progress

Gathering high-quality scientific evidence on the magnitude of social inequalities in cancer and increasing knowledge regarding the many dimensions of the problem (socioeconomic, ethnic, racial, gender, cultural, historical, political) is necessary to develop research priorities at the global, regional, national, and community levels and to inform public health interventions. In all countries from which high-quality data are available, mainly high-income and middle-income countries, there is clear evidence of a socioeconomic gradient for the risk of overall cancer mortality and survival from high to low socioeconomic status, with strik-

ing differences observed between the lowest and highest socioeconomic status groups. In low-income countries, data are nonexistent or of poor quality and, when available, reveal poor cancer outcomes, including often dramatically low cancer survival, even for preventable or curable cancers (eg, cervical and childhood cancers). These are the consequences of the limited or complete absence of resources and infrastructures at every step of cancer control. Nonetheless, even in the most affluent countries, cancer outcomes among vulnerable populations (eg, those living in poverty[3] and Indigenous[5] and racial minorities[6]) are much worse than outcomes in other groups.

Producing evidence and monitoring progress in reducing social inequalities in cancer require: 1) supporting existing high-quality population-based cancer registries, enabling them to expand surveillance and research on social determinants of cancer incidence, survival, and mortality, particularly through linkage of selected, informative social indicators and data sources; 2) establishing de novo population-based cancer registries where information is missing, including in low-income countries and rural areas, that would collect at least some basic social indicators; and 3) conducting regular population-based surveillance of inequalities in risk factors (eg, surveys to collect information on risk behaviors and access to health care).

Second Priority: Expanding Research Focused on Prevention

If social inequalities affect all stages of the cancer continuum, from prevention to end-of-life care, prevention has the largest potential for

reducing cancer inequalities in all settings. Yet this area remains largely underfunded, especially relative to the huge financial investments in other cancer-related areas, like basic science and treatment. The grant budget for cancer research in high-income countries specifically allocated to prevention hardly reaches 10%.[7] Understanding both how interventions affect inequalities and how these interventions, or packages of interventions, can be best designed to reduce such inequalities is critical. Interventions can be wide-reaching, aiming to create equal living conditions (through, for example, fiscal policies and regulation of air quality, food, clean water, healthy housing, and occupational exposures) as well as to reduce inequalities in exposure to risk factors for cancer and to increase access to early detection (including price polices; the regulation of cancer-causing products, such as tobacco and alcohol; vaccination against cancer-causing agents such as human papillomavirus and hepatitis B virus; and cervical cancer screening). By nature, the solutions require interdisciplinary approaches across a broad research spectrum and can certainly benefit from the engagement of affected communities and other stakeholders.

The scientific evidence for reducing social inequalities in cancer globally calls for an expansion of both research focus and investments in prevention.

Third Priority: Focus on Equality When Implementing and Assessing Cancer Control Measures

The workshop emphasized the importance of the broad and equitable application of known beneficial interventions directed at every stage

of the cancer continuum to all populations, driven by social goals. This requires innovative strategies, political commitment, and public policies to deliver measures supporting a reduction in inequalities, enabling everyone access to "preventive and curative health care services, without falling into poverty"; this is the goal of universal health coverage.[8] Countries, communities, and individuals with lower socioeconomic conditions; minorities; and Indigenous populations are at risk of benefitting only indirectly (and with a considerable delay) from relevant advances in medicine,[9] likely leading to widening social inequality in cancer care and outcomes. Furthermore, a particular danger is that research emphasis and investments are increasingly (and disproportionately) directed toward "expensive" research or practices. Such practices involve high-tech medical devices; immunotherapy drugs; or, more generally, precision

medicine approaches for which the benefits in terms of cancer control, with few exceptions, are often marginal or, in some cases, are even offset by harms, such as overdiagnosis and overtreatment.[10]

All interventions and cancer control programs, from prevention to treatment measures, should account for their overall effect and should be explicitly designed, at a minimum, to avoid exacerbating social inequalities in cancer and ideally to decrease or eliminate them. Furthermore, for every intervention, progress in reducing social inequalities in cancer outcomes should be monitored, regularly reported on, and used to introduce improvements.

A Commitment

In a world submerged by massive data flows,[11] some fundamental social facts (such as poverty) are more likely than other phenomena to be obscured, misconstrued, or simply

set aside and neglected. Social determinants of and social inequalities in health are no exception: for this reason, the WHO committed in 2008 to keep them high in the global agenda with the landmark report of the Commission on Social Determinants of Health.[12] Research can be used to effectively decrease social inequalities in cancer.[13,14] Through this expert workshop, and its wider role in convening international cancer leaders and promoting cooperation in research, the IARC today renews and reinforces the WHO commitment through its special mission of developing cancer research for cancer prevention. This endeavor will more broadly contribute to meeting the objectives of the noncommunicable diseases strategy as part of the United Nations Sustainable Development Goals, provided an enhanced engagement in the agenda for tackling social inequalities in cancer is given the priority it deserves.

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Disclosures of interests

Professor David I. Conway reports being a member of the Socialist Health Association Scotland.

Dr Lynette Denny reports having received personal consultancy fees from Merck Sharp and Dohme and from GlaxoSmithKline Pharmaceuticals.

Dr Alastair H. Leyland reports holding stocks in AstraZeneca and GlaxoSmithKline.