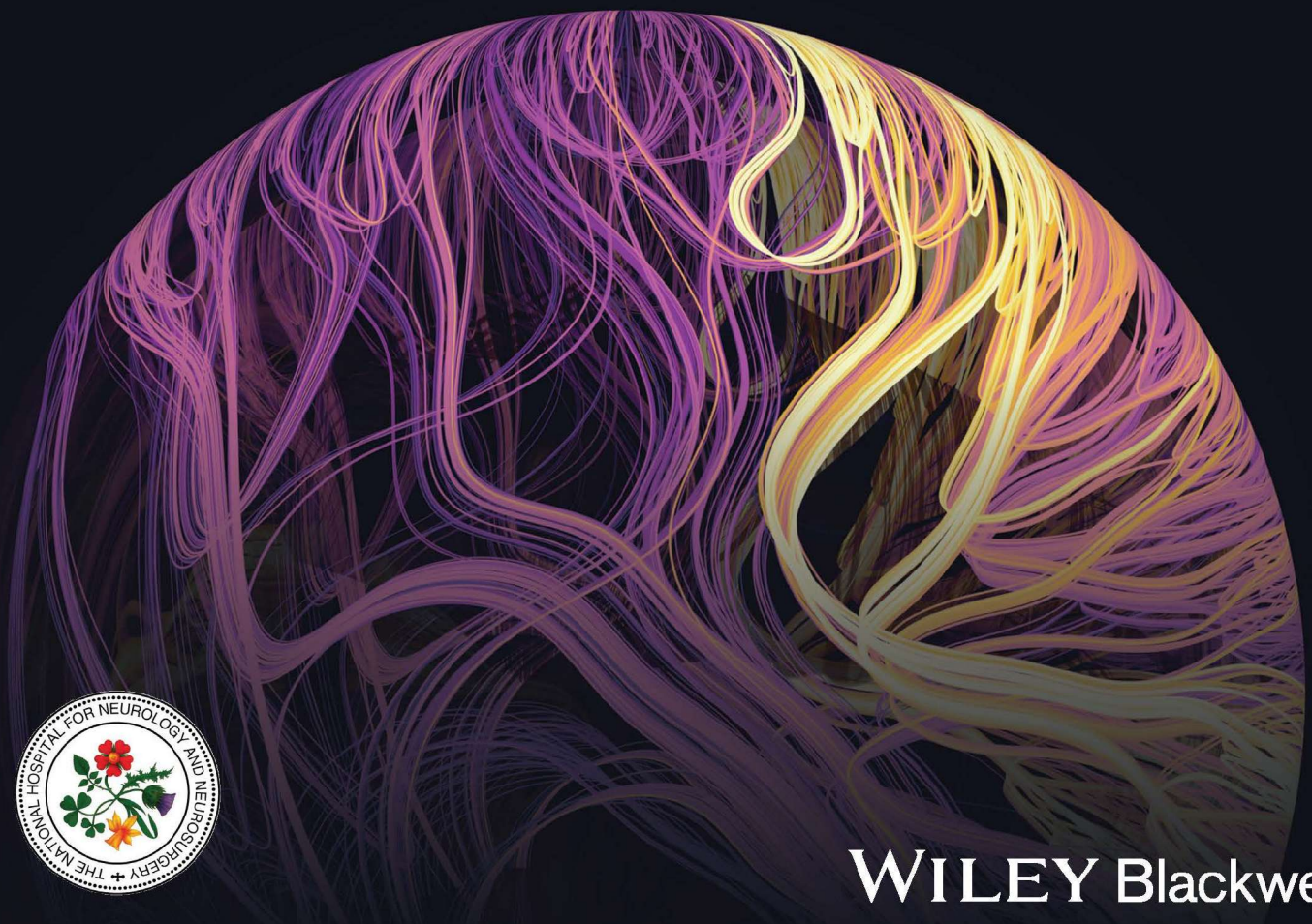
neurology

A QUEEN SQUARE TEXTBOOK

third edition

edited by

ROBIN HOWARD | DIMITRI KULLMANN | DAVID WERRING | MICHAEL ZANDI



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Neurology
A Queen Square Textbook

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Third Edition

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He was head of service for a large general neurological practice at St. Thomas' Hospital and neurologist to three intensive care units. He was senior neurologist to specialist units for the care of patients with myasthenia gravis, motor neuron disease, Duchenne muscular dystrophy and post-polio syndrome at both Queen Square and St Thomas' hospitals and has written and lectured extensively on each of the subjects. He has been a senior editor and contributor to all three editions of *Neurology: A Queen Square Textbook*.

Dimitri Kullmann FRCP FMedSci FRS

Dimitri Kullmann trained in medicine in Oxford and London and completed a DPhil in Oxford. Following a postdoctoral fellowship at the University of California San Francisco, he trained in neurology at the National Hospital for Neurology and Neurosurgery, Queen Square, and established a laboratory focusing on synaptic transmission at the Institute of Neurology. He is now a professor of neurology at the UCL Queen Square Institute of Neurology and honorary consultant neurologist at the National Hospital for Neurology and Neurosurgery. His research interests include the fundamental mechanisms of synapse function, neurological channelopathies and gene therapy for epilepsy. He was the Editor of *Brain* from 2014 to 2020 and is on the Editorial Board of *Neuron*. He was made a Fellow of the Academy of Medical Sciences in 2001 and of the Royal Society in 2018.

David Werring PhD FRCP FESO

David Werring trained in medicine at Guy's Hospital Medical School and in neurology in London. He was appointed as a consultant neurologist at the National Hospital for Neurology and Neurosurgery, Queen Square in 2005. He is Professor of Clinical Neurology at the Stroke Research Centre, UCL Queen Square Institute of Neurology, and honorary consultant neurologist at the National Hospital for Neurology and Neurosurgery. He delivers acute and outpatient stroke care and leads a research programme focussed on intracerebral haemorrhage and cerebral small vessel disease. He is head of the Research Department of Brain Repair and Rehabilitation, chair of the Association of British Neurologists Stroke Advisory Group, stroke specialty lead for the National Institute for Health Research North Thames Clinical Research Network, President-Elect of the British and Irish Association of Stroke Physicians, and editorial board member of the *European Journal of Neurology, European Stroke Journal, International Journal of Stroke* and *Practical Neurology*. David Werring chaired the UK Stroke Forum 2020–2022.

Michael Zandi PhD FRCP

Michael Zandi trained in medicine in Cambridge, and completed neurology training in Cambridge, Norwich and London, and a PhD in Cambridge with time in the laboratory of Professor Angela Vincent at the Weatherall Institute of Molecular Medicine in Oxford. He is a consultant neurologist at the National Hospital for Neurology and Neurosurgery and Honorary Associate Professor at the UCL Queen Square Institute of Neurology. His research interests include the mechanisms, natural history and clinical treatments of autoimmune encephalitis, cerebral amyloid angiopathy related inflammation, neuroimmunology broadly, and the role of inflammation and autoimmunity in cognitive and psychiatric disorders. He has advised NHS England, the Royal College of Physicians and the National Institute for Health and Care Excellence.

Foreword to the Third Edition

I am delighted to be asked to introduce the publication of this third edition of *Neurology: A Queen Square Textbook*.

Although the field of neurology continues to become ever more specialised, partly as a result of major progress in neuroscience discoveries, this new third edition continues the tradition of presenting a clear useful coherent text that spans the whole of the field.

Previously, neurologists dealt with all neurological conditions; today, specialisation is the norm and to be a neurologist without a special interest is unusual. However, it remains very important to have a solid grounding in general neurology, even for those who ultimately become highly specialised. It is thus fitting that the four editors combine very broad general neurology clinical experience with specialist academic expertise.

Robin Howard, who works jointly at Guy's and St. Thomas' Hospital in London and the National Hospital, is a highly experienced general neurologist; his specialist interests are intensive care neurology and neuromuscular disease. Dave Werring initially practised mainly generally neurology at Watford Hospital but has developed a major interest in stroke and now has an international reputation in clinical research in stroke based at the UCL Queen Square Institute of Neurology. Dimitri Kullmann clinically specialises in intensive care neurology and has made major contributions to the understanding of synaptic physiology in the central and peripheral nervous system, through his laboratory research at the Institute of Neurology. Michael Zandi is an internationally recognised specialist in clinical and laboratory neuroimmunology based at the National Hospital.

In each carefully constructed chapter, this book continues to epitomise this combination of practical experience and academic specialisation. All aspects of all neurological disorders are dealt with in a very readable and instructive way. Indeed, the teams that have been assembled to write each chapter are colleagues that collaborate between institute and hospital on a daily basis. Together, this whole team of consultants assesses around 200,000 outpatients per year at the National Hospital and are all excellent teachers. Together, they have huge expertise in all aspects of neurological disease and are actively engaged in teaching both as a national centre and internationally to Queen Square postgraduate students from all over the world.

Advances in neuroscience have in part led to a bewildering array of diagnostic tests including specialised MRI, PET imaging, specialised neurophysiology, liquid biomarkers, gene panels and whole genome sequencing but it remains important that careful clinical assessment and examination of the patient by the neurologist is central to good neurological practice. The tendency and ease of reaching for many elaborate tests is no substitute for careful clinical evaluation. Indeed, the neurologist undertaking a careful and detailed history and examination is part of the 'DNA' of Queen Square. This principle is evident throughout the book, highlighting that a careful clinical assessment will avoid over- investigation, enable the correct investigations and, importantly, allow appropriate correlation between the clinical findings and investigation results.

The editors and the authors are experienced and distinguished writers who have devoted time to draw together their practical experience. Each chapter has been very carefully edited, and this is evident in the finished product. One can find here well-illustrated neuroanatomy, detailed assessments of common conditions such as stroke and dementia, up-to-date aspects of neurogenetics and ion channels, the philosophy and practicalities of rehabilitation, and rarities such as metabolic disorders of copper, and even unusual muscle diseases.

I know that this book has been produced within an atmosphere of cordiality and friendship at Queen Square, and am pleased to have been able to make a small contribution myself.

It is clear from this third edition just how large a subject neurology has become and how scientific advances, many pioneered within the UCL Queen Square Institute of Neurology, have become translated into clinical practice. I believe this edition, and indeed future editions, will continue to be essential reading for trainee and indeed trained neurologists!

I am delighted that *Neurology: A Queen Square Textbook* has become a standard text for the UK neurologists in training exit examination – a measure of its standing, quality and usefulness.

I want to sincerely congratulate all the authors on this great achievement and this very important contribution to the clinical practice of neurology globally.

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Preface to First Edition

All Editors, Authors and Specialist Advisory Editors of *Neurology: A Queen Square Textbook* hold or recently held consultant or equivalent posts at the National Hospital for Neurology and Neurosurgery and/or the Institute of Neurology, Queen Square.

The National Hospital is part of University College London Hospitals NHS Foundation Trust, and the Institute of Neurology part of University College London.

The 20 co-ordinating authors organised individual chapters, encouraged and liaised with over 70 contributors and with them wrote this book.

The specialist advisory editors gave invaluable advice and guidance in their respective fields. To ensure a worldwide perspective, the six International Regional Editors, all of whom have had close connections with Queen Square, provided advice and comment.

This book is an attempt to provide a fresh and up-to-date approach to the fascinating subject of neurology. We encouraged each author to relate their own clinical experience but, in order to achieve a degree of consistency, we took a robust overview of the important specialities within neurology and their relevance. Each chapter has been coordinated by an expert in the field, to give the reader an overall grasp of each major subject, indicating where developments within neurosciences fit into a broader picture.

The limited size of this book means that it has not been possible to provide references for all material. With the growth of information technology, a wealth of detailed sources are readily available.

We are most grateful to all those who have helped in this joint venture.

Charles Clarke
Robin Howard
Martin Rossor
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Preface to Second Edition

All editors, authors and specialist advisory editors of *Neurology: A Queen Square Textbook* hold or recently held consultant or equivalent posts at the National Hospital for Neurology and Neurosurgery and/or the UCL Queen Square Institute of Neurology, Queen Square.

The National Hospital is part of University College London Hospitals NHS Foundation Trust, and the Institute of Neurology part of University College London.

Twenty-three co-ordinating authors organised individual chapters, encouraged and liaised with over 70 contributors and with them wrote this book.

The specialist advisory editors gave invaluable advice and guidance in their respective fields. To ensure a worldwide perspective, for the first edition our international regional editors, all of whom had close connections with Queen Square, provided guidance and comment.

This book is an attempt to provide a fresh and up-to-date approach to the fascinating subject of neurology. We encouraged each author to relate their own clinical experience but, in order to achieve a degree of consistency, we took a robust overview of the important specialities within neurology and their relevance. Each chapter has been coordinated by an expert in the field, to give the reader an overall grasp of each major subject, indicating where developments within neurosciences fit into a broader picture.

On spelling and use of the English language, whilst appreciating that as a living, multicultural tongue there are wide varieties, we have opted for British English – the sort of way we write our letters, and continue to spell 'neurone' with its terminal -e. On medical conditions named after famous figures, we appreciate that many publishers no longer use the apostrophe to describe the disease named after Alzheimer, Wilson, Parkinson and so on. Our authors by and large did not follow this; thus we have left matters much as they signed off their chapters.

The limited size of this book means that it has not been possible to provide references for all material. With the growth of information technology, a wealth of detailed sources is readily available.

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Preface to Third Edition

The past five decades have witnessed breathtaking advances in clinical medicine and the medical sciences. This rapid change has been particularly striking in the neurosciences, encompassing advances in genetics, neuroimaging, immunology and the interpretation of the molecular and metabolic processes that underlie neural function. Many of these dramatic developments have been reflected in our understanding of the mechanism of disease and translated into investigation and treatment. The pace of scientific and clinical innovation has posed challenges of increasing complexity and cost, potentially limiting adequate provision of the highest standard of healthcare. Indeed, the downside of rapid technological advance has been that inequalities of care continue to widen the divide between the more and less economically developed nations. Furthermore, increasing healthcare costs mean that good care becomes vulnerable to interference by government, private companies and entrepreneurs in ways that might threaten scientific and medical independence.

The demand for neurological services has also greatly increased in recent years due to ageing populations susceptible to neurodegenerative and cerebrovascular diseases, the burgeoning multiplicity of specific treatments available for neurological diseases and advances in the management of disability. The cost of treating patients has escalated beyond all expectation, leading to a constant demand to balance benefit against the ever-increasing and often unrealistic expenditure necessary to keep pace with scientific advances. These spiralling costs increasingly fall to society as a whole; many debate individual and collective responsibility for ensuring that the most vulnerable receive appropriate care.

There are challenges to neurology that are particular to the more and less economically developed world and many of them have been addressed throughout this book. The newer technologies such as artificial intelligence, machine learning, genetic manipulation and access to large-scale electronic health records, threaten many of the principles and ethical precepts upon which medical care has been based; their successful implementation requires vigilance and oversight. Their development has led to fundamental changes affecting the clinical and scientific practice of the specialty. The burgeoning of protocol-driven care and multiple national and international guidelines is a relatively new phenomenon, which has rapidly come to dominate clinical practice and is dependent upon the globalisation and interconnection of healthcare. Clinical and academic neurologists have been in the forefront of scientific advances throughout the history of modern medicine but it could also be argued that, despite the evolution from diagnosis to the treatment, management of neurological conditions and care of the neurological patient, the fundamental clinical approach and work of the clinical neurologist still resemble the practice of Romberg, Duchenne, Charcot, Hughlings Jackson and Gowers.

Queen Square, together with other centres in the UK, Europe and throughout the world, was (and is) a cradle of neurology and the neurosciences. The hospital and the institute have made extensive contributions to the remarkable development of the specialty in a bewildering array of disparate fields. Nonetheless, it is essential to recognise that our specialty now exists as a global congress of interested parties. Progress in medicine evolves because of the activities of innumerable friends and colleagues working in specialist and general hospitals and academic institutes in all countries.

We will continue to wrestle with the prodigious challenges that face all societies, including the evolution of disease and pandemics, global inequalities of poverty and opportunity, the threat to our environment from climate change and the failings of our politicians. We have tried to address these issues in this book in the context of the extraordinary progress of science and clinical medicine within our specialty. Despite all the developments and challenges of recent decades, it remains self-evident that the patient lies at the heart of all we do and that excellence of care for those with neurological disease extends beyond treatment alone.

Robin Howard
Dimitri Kullmann
David Werring
Michael Zandi
Queen Square, London
December 2023

Acknowledgements

This book reflects the efforts of countless clinicians and scientists, most of whom remain unrecognised throughout the text, although their contributions are huge. The editors and authors wish to make it clear that they have only been able to reference a minimal number of those upon whom they have lent heavily and they hope that no offence will be taken where reference to work has not been fully cited because of the lack of space. The editors apologise for any omissions or misrepresentation of fact. They have each maintained a heavy clinical commitment throughout the preparation of this book and have therefore been grateful for the initiative of the lead and contributing authors, to whom they pay tribute.

The present editors are particularly grateful to the three previous editors who graciously handed over their responsibilities: Dr Charles Clarke, Professor Simon Shorvon and Professor Martin Rossor. Each made an enormous contribution to previous editions of this book.

We would like to thank all those who have taught, advised, guided and inspired us to develop our clinical, academic and research studies in neurology and the neurosciences. As noted in previous editions, the list of these individuals is vast and we are unable to mention them all by name. We can simply hope to pass on their wisdom to our own students and colleagues. The authors and editors were distressed to learn of the passing of Linda Luxon. She was an inspiration to patients, students and colleagues. We will miss her wisdom.

We thank those who contributed to the second edition and have moved on, reflecting retirement or promotion.

We thank our publishers, Wiley, and especially Sophie Bradwell, Bhavya Boopathi, Ella Elliott, Katherine King and Adalfin Jayasingh all the team who were involved in production. We are particularly grateful to our freelance copyeditor, Jane Moody.

The authors have been unstinting in their support of the project throughout the extremely difficult times we experienced during the preparation of this book. Many were redeployed to acute services during the worst of the COVID-19 pandemic, when the demands on their expertise were beyond anything previously experienced. Despite these challenges, they were all entirely supportive and remained patient throughout the numerous and burdensome requests from the editors.

The Rockefeller Library provided its valuable resources, both historical and current. The Audio Visual Services Unit was most helpful with the sourcing of some figures and photographs.

Royalties from *Neurology: A Queen Square Textbook* are passed directly to the National Brain Appeal (National Hospital Development Foundation), the registered UK charity (No. 290173) that supports projects at Queen Square.

We lost many of our vulnerable and disabled patients to the ravages of COVID-19 through successive waves of the disease and we remember those who died and those whose lives were changed forever.

Robin Howard wishes to put on record his immense gratitude to his many friends and colleagues both past and present at Guy's and St Thomas' Hospitals.

Robin Howard
Dimitri Kullmann
David Werring
Michael Zandi
November 2023

Cover illustration (Courtesy of Professor Paraskev Nachev) – Ray-traced projection onto a glass sphere of the graph hierarchical community structure of the neural determinants of impaired performance on Advanced Progressive Matrices as derived from graph lesion-deficit mapping of patients with focal brain injury. The spherical projection onto a glass surface is intended to convey the challenge of obtaining a perspicuous representation of the neural basis of fluid intelligence (Cipolotti L, Ruffle JK, Mole J, Xu T, Hyare H, Shallice T, Chan E, Nachev P. Graph lesion-deficit mapping of fluid intelligence. Brain. 2023 Jan;146(1):167-81.)

CHAPTER 1

Global Burden of Neurological Disease and the Neurology of Climate Change

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Introduction

The global population continues to grow, albeit at a slower pace than previously. According to data from the United Nations (UN) Department of Economic and Social Affairs, it is estimated that population numbers will peak in the 2080s at around 10.4 billion. However, the asymmetry in population growth between different areas of the world is striking: more than half of the projected increase to 2050 will be concentrated in eight low-income countries: the Democratic Republic of the Congo, Egypt, Ethiopia, India, Nigeria, Pakistan, the Philippines and Tanzania. In contrast, 61 countries and areas with ageing populations, resulting from increased lifespans and reduced fertility rates, the population is projected to decrease by 1% between 2022 and 2050. India is expected to surpass China as the world's most populous country in 2023 and will have an estimated population of 1.09 billion by 2100. Japan's population, in contrast, will decline from 128 million in 2017 to 60 million over the same period (Figure 1.1).

The other well-recognised demographic is that the share of the global population aged 65 years and over is projected to rise from 9.7% in 2022 to 16.4% in 2050 (Figures 1.2 and 1.3). In Europe and North America, by 2050 one in four (26.9%, up from 18.7% in 2022) will be aged over 65 years. In Eastern and Southeast Asia, the proportion aged 65 years or older could increase from 13% in 2022 to 26% in 2050. By 2100, the over 60s age group will outnumber the under 5 years age group by two to one. In parallel with the increase of ageing populations there will be an increased incidence and prevalence in age-related neurological disorders including stroke, neurodegenerative conditions such as Alzheimer's and Parkinson's diseases, for which there is no prospect of a cure in the immediate future. Governments and planners will need to provide for the long-term care of individuals living with cognitive and motor impairment.

The COVID-19 pandemic has highlighted the importance of epidemiological studies for governments, healthcare policy makers, funders and other stake holders in planning and resource allocation. The global unpreparedness for a pandemic resulted in confusing messages from 'experts' (mask wearing/no mask wearing; lockdown/no lock down) with the resulting unnecessary loss of life. However, this pandemic has also shown how the medical and scientific community can harness global talents with cooperation and good will to overcome such a once in a lifetime pandemic. The same commitment is required for healthcare planning, resource allocation and public health education to deal with the global burden of diseases and, in particular, the massive implications of the increasing incidence of neurological disorders.

The essential elements of good public health and healthcare are well rehearsed – an adequate health work force; effective, affordable, safe and high-quality service delivery, access to medicines and diagnostics, health education, good governance and adequate funding. However, *health* is not simply a question of healthcare provision but must include a broader remit including improving socioeconomic status, gender equality and, most importantly, education, which underpins all these issues. More recently, it has become apparent that topics such as migration, climate change and pollution must also be addressed under the broader heading of health.

Gains in life expectancy have not been matched by increases in healthy life expectancy (the number of years a person can expect to live in good health). To improve health, policy makers need up to date data on the challenges faced in their individual countries. Apart from identifying incidence, prevalence and mortality, it is also necessary to identify modifiable risk factors such as smoking, alcohol intake, hypertension and diet.

The definition of terms used in epidemiological discussion are listed in Table 1.1.

The Global Burden of Neurological Diseases

The Global Burden of Diseases Injuries and Risk Factors (GBD) study was inaugurated in 1990 with funding from the World Bank. In 2007, the Institute of Health Measurement and Evaluation was established at the University of Washington, Seattle, funded by the Bill and Melinda Gates Foundation, and has continued the study. This iterative process aims to provide a systemic, rigorous and scientific assessment of published, publicly available and contributed data on disease incidence, prevalence and mortality. A study of this vast scope and ambition has many limitations. However, a major strength has been to overcome the inclination of 'no data, no problem' by producing a best estimate with an estimate of the degree of uncertainty when data are unavailable or inconsistent. The most recent publication, GBD study 2019, describes 369 diseases and injuries in 204 countries and territories (GBD 2019 Diseases and Injuries Collaborators 2020).

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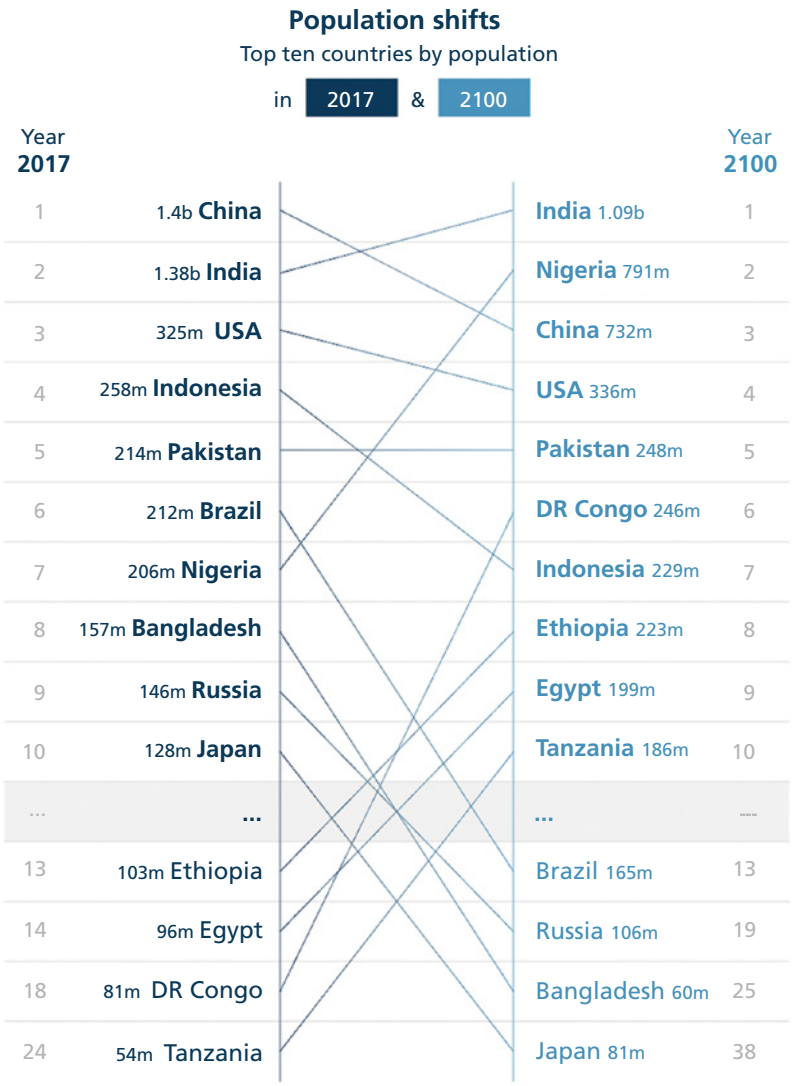

Figure 1.1 Population shifts; top 10 countries by population. Source: reproduced with permission from Vollset et al. (2020).

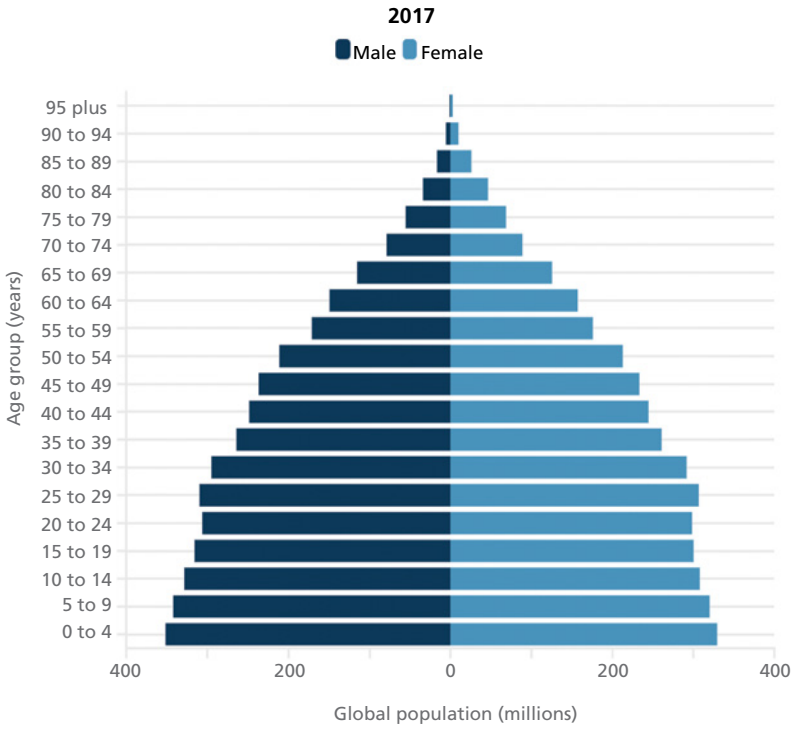

Figure 1.2 Global population age distribution 2017. Source: reproduced with permission from Vollset et al. 2020).

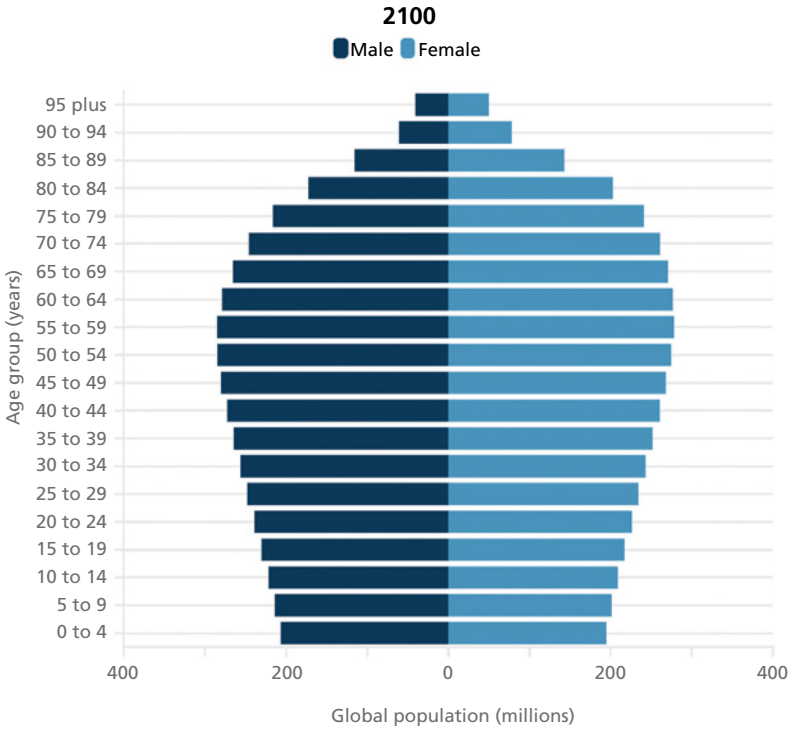

Figure 1.3 Predicted global population age distribution for 2100. Source: reproduced with permission from Vollset et al. (2020).

Table 1.1 Definitions.

Term	Definition
Age standardisation	Statistical technique to compare populations with differing age structures in which the characteristics of populations are statistically transformed to match those of a reference population. This is a useful measurement because relative under- or overrepresentations of different age groups can obscure comparisons of age-dependent differences across populations
Disability-adjusted life-year (DALY)	A measure combining years of life lost due to premature mortality with years of life lost due to time lived in poor health DALY = years of life lost + years lived with disability 1 DALY is a year of perfect health lost Diseases that cause long-term disability, such as mental health or migraine, may lead to a large proportion of DALYs without being a major cause of mortality The advantage of DALY is that it provides a composite, internally consistent measure of population health, which can be used to evaluate the relative burden of different diseases and injuries and compare population health by geographical region and over time
Incidence	The number of new cases of the disease in a defined population over a defined period
Prevalence	The proportion of people with a disease at any point (point prevalence) or period (period prevalence) in time
Quality-adjusted life-year (QALY)	A measure of the state of health of a person or group in which the benefits, in terms of length of life, are adjusted to reflect the quality of life. 1 QALY is equal to 1 year of life in perfect health. QALYs are calculated by estimating the years of life remaining for a patient following a particular treatment or intervention and weighing each year with a quality-of-life score (on a scale of 0–1). It is often measured in terms of a person's ability to carry out the activities of daily life and freedom from pain and mental disturbance
Sociodemographic index	A composite indicator of a country's lag distributed income per capita, average years of schooling and the fertility rate in females under the age of 25 years
Years lived with disability	Can also be described as years lived in less than ideal health. This includes conditions such as influenza, which may last for only a few days, or epilepsy, which can be lifelong. It is measured by taking the prevalence of the condition, multiplied by the disability weight for that condition. Disability weights reflect the severity of the different conditions and are developed through surveys of the general public. 1 year lived with disability represents the equivalent of 1 full year of healthy life lost due to disability or ill-health
Years of life lost (YLL)	Years lost due to premature mortality. YLLs are calculated by subtracting the age at death from the longest possible life expectancy for a person at that age. For example, if the longest life expectancy for men in a country is 75 years, but the man dies at 65 years of cancer, this would be 10 years of life lost due to cancer

Health loss is classified into three broad categories:

- Communicable diseases (including HIV, tuberculosis, malaria), maternal, neonatal, nutritional diseases.
- Non-communicable diseases (NCD; heart disease, stroke, diabetes, cancer, depression).
- Injuries (including self-harm, animal bites and vehicle accidents).

The overall health of the world's population has improved; global life expectancy at birth increased from 67.2 years in 2000 to 73.5 years in 2019. The estimated number of deaths in children under the age of 5 years decreased from 9.6 million in 2000 to 5 million in 2019.

Analysis of more granular data from the GBD study 2019, between 1990 and 2019, after correcting for the effects of population growth and ageing, shows a decline in the rate of disability-adjusted life-years (DALYs) confirming improvements in overall health. There has also been a shift towards a greater proportion of years lived with disability from NCDs and injuries. In the past decade, the rate of decline of age-standardised DALY rates was greatest in those younger than 50 years and this was most apparent in the 0- to 9-years age group. In those aged 50 years and older, the rate of change was slower from 2010 to 2019 compared with earlier time periods. The most important contributors to the declining burden include nine that predominantly affect children: lower respiratory tract infections, diarrhoeal diseases, neonatal disorders, measles, protein-energy malnutrition, congenital birth defects, drowning, tetanus and malaria. For example, the age-standardised DALY rates for measles showed a 90.4% decline (uncertainty interval 87.5–92.8%) between 1990 and 2019. In addition to these conditions, there was also a decline in tuberculosis, which affects mainly adults.

The 10 most important drivers of increasing burden (causing the largest increase in numbers of DALYs) were those affecting mainly older individuals: ischaemic heart disease, diabetes, stroke, chronic kidney disease, lung cancer and age-related hearing loss. The remaining four conditions were HIV/AIDS, other musculoskeletal disorders, low back pain and depression. HIV/AIDS peaked in 2004 and dropped significantly after global antiretroviral drug rollout programmes were initiated.

The GBD 2019 study analysed the burden for all ages (Figure 1.4); the leading neurological or related disorders were stroke (3rd, 5.7 % of DALYs), road injuries (7th, 2.9%), low back pain (9th, 2.5%), HIV/AIDS (11th, 1.9%), tuberculosis (12th, 1.9%), depressive disorders (13th, 1.8%), headache disorders (15th, 1.8%), age-related hearing loss (20th, 1.6%), falls (21st, 1.5%), self-harm (22nd, 1.3%), anxiety disorders (24th, 1.1%), interpersonal violence (26th, 1.1%) and meningitis (40th, 0.6%). Significant increases in the number of DALYs between 1990 and 2019 were noted for all the above disorders except tuberculosis, self-harm, interpersonal violence and meningitis, which declined.

The burden of disease for children under the age of 10 years declined significantly between 1990 and 2019 by 57.5%. This was primarily due to the decline in infectious diseases, including meningitis. Nevertheless, it remains important to realise that from the neurological perspective both short and long term, neonatal disorders were responsible for 1.88 million deaths, comprising 37.3% of deaths in children under the age of five years. Conditions included under this umbrella term include preterm birth complications (with contributing risk factors such as malnutrition, household air pollution from solid fuels and ambient environmental pollution). In 2019, neonatal disorders were still the highest cause of DALYs (32.4%) in this age group, increasing from 23% in 1990. Meningitis accounted for 2.1% of DALYs and, astonishingly, sexually transmitted infections, accounted for by congenital syphilis in 10th place with 1.4% of DALYs, an increase from 0.7% in 1990. Idiopathic epilepsy was 23rd, accounting of for 0.5% of DALYs. Sub-Saharan Africa experienced nearly half of the total DALYs in this age group and, once again, this is a stark reminder of the extent of existing global health inequities.

In the adolescents aged 10–24 years, DALYs for NCDs increased by 13.1% with declines in both infectious diseases and injuries. Injuries were more common in adolescent males and accounted for 13.8% of DALYs: road injuries (ranked 1st), self-harm (3rd) and interpersonal violence (5th). Headache disorders ranked second (5%) followed by depressive and anxiety disorders, which rank 4th and 6th, respectively, were more common in females and accounted for 7% of DALYs. HIV/AIDS ranked 9th (2.6% DALYs), having increased dramatically after 1990 (ranked 33rd, 0.9%) owing to the rapid increase in incidence in the first half of the study period, which was followed by a decline after antiretroviral therapy became more available, especially in sub-Saharan Africa. This was made possible by the development of highly active antiretroviral drugs in the mid-1990s and also by the US Presidents Plan for AIDS Relief for developing countries introduced by George W. Bush in 2003.

Five causes in the top ten for the 10–24 age group also featured in the 25–49 age group top ten: road injuries (ranked 1st), HIV/AIDS (now ranked 2nd), low back pain (4th), headache disorders (5th) and depressive disorders (6th). Stroke was ranked ninth in this group, which may partly be related to HIV/AIDS as a significant predisposing risk factor.

Within the 50–years and the 75 years and older groups (Figure 1.5), there was significant overlap, with ischaemic heart disease and stroke being the leading causes of disease burden. Low back pain (as a symptom but no specific aetiology), age-related hearing loss, falls, blindness and visual loss also overlapped in the top 20 conditions. In the over 75s, Alzheimer's disease now ranked fourth and Parkinson's disease twentieth. Lung cancer and colorectal cancer were also a feature in both age groups, whereas headache disorders, injuries, depression and anxiety were now much lower down the list or not featured at all in the list of most common DALYs.

Overall, the 2019 study emphasises both the transition towards NCDs and also the extent to which disability contributes to the overall burden of disease. Low- and middle-income countries (LMICs) with significant increases in life expectancy now face the double challenge of communicable diseases (albeit reducing) and a rapid rise in the incidence of NCDs. In the past, most of the focus of global health programmes has been directed towards reducing mortality. The recent change in population demographics and disease burden mean that disability management will demand greater health expenditure and research to identify new effective strategies.

National Global Burden of Neurological diseases

United Kingdom

In 2019, the most frequent cause of death in the UK was ischaemic heart disease, with stroke the second most common and Alzheimer's disease the sixth (Figure 1.6). When comparing the top 10 causes of death and disability to other countries similar in terms of socioeconomic status, the incidence of ischaemic heart disease, neurological and psychiatric conditions including low back pain (2nd), depression (3rd), headache disorders (4th), stroke (8th) and falls (10th) was similar. In the United States, drug use disorders were the highest cause of DALYs, while this was ranked ninth in the UK.

In terms of risk factors underlying the most common causes of DALY (Figure 1.7), tobacco use remained the most important despite the reduction in consumption between 2009 and 2019. Other risk factors included high fasting plasma glucose, high body