NEUROLOGICAL DISORDERS

public health challenges

World Health Organization

Alzheimer's Disease International

EPDA

IBE

International Headache Society

multiple sclerosis international federation

WFN

WORLDHEADACHE

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contents

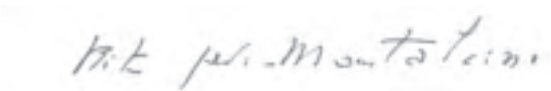
foreword

In the 19th century and at the beginning of the 20th, brain research belonged to many different areas that differed in methodology and targets: the morphological, the physiological and the psychological. The latter used to consider the brain as a black box where only the input and output were known but not at all the neuronal components and the way they interact with each other.

At the beginning of the third millennium, due to prolonged ageing, neurodevelopmental disorders are growing and a much deeper knowledge of the brain is necessary. Scientific and technological research, from molecular to behavioural levels, have been carried out in many different places but they have not been developed in a really interdisciplinary way. Research should be based on the convergence of different interconnected scientific sectors, not in isolation, as was the case in the past.

As this report demonstrates, the burden of neurological disorders is reaching a significant proportion in countries with a growing percentage of the population over 65 years old.

With this report go my best wishes that it be disseminated worldwide and that it receive the deserved attention of the Global Health Community in all the countries of the world.



Rita Levi-Montalcini
1986 Nobel Prize in Medicine

preface

Within its remit to provide leadership on all matters concerning health, one of the core functions of the World Health Organization (WHO) is to engage in partnerships where joint action is needed. WHO plays an important role in bringing crucial health-related topics to the agenda of policy-makers and health planners and in raising awareness of them among health-care professionals and all who have an interest in health matters.

WHO's Department of Mental Health and Substance Abuse carries out this role for the three different sets of issues for which it is responsible: mental disorders, substance abuse and alcohol-related issues, and neurological disorders. Two recent publications have focused attention on its work. *The world health report 2001 – Mental health: new understanding, new hope* is an advocacy instrument to shed light on the public health aspects of mental disorders, and the report *Neuroscience of psychoactive substance use and dependence* produced by the department in 2004 tackles the area of substance abuse and alcohol. We realized a similar exercise is needed in the field of neurological disorders.

The Global Burden of Disease study, the ongoing international collaborative project between WHO, the World Bank and the Harvard School of Public Health, has produced evidence that pinpoints neurological disorders as one of the greatest threats to public health. A clear message emerges that unless immediate action is taken globally, the neurological burden is expected to become an even more serious and unmanageable problem in all countries. There are several gaps in understanding the many issues related to neurological disorders, but we already know enough about their nature and treatment to be able to shape effective policy responses to some of the most prevalent among them.

To fill the vast gap in the knowledge concerning the public health aspects of neurological disorders, this document *Neurological disorders: public health challenges* fulfils two roles. On one hand, it provides comprehensive information to the policy-makers and on the other hand, it can also be used as an awareness-raising tool. The document has unique aspects that should be stressed. It is the result of a huge effort bringing together the most significant international nongovernmental organizations working in the areas of various neurological disorders, both in a professional capacity and in caring for people affected by the conditions. It is the fruit of healthy interaction and collaboration between these organizations and WHO, with its network of country and regional offices: health experts on

one hand working together with the extensive and competent world of professionals and researchers on the other. Some of these organizations have also contributed financially to this endeavour. This exercise thus demonstrates that such collaboration is not only possible but can also be very productive.

The document is distinctive in its presentation as it provides the public health perspective for neurological disorders in general and presents fresh and updated estimates and predictions of the global burden borne by them. Separate sections discuss some of the most important disorders in detail: dementia, epilepsy, headache disorders, multiple sclerosis, neuroinfections, neurological disorders associated with malnutrition, pain associated with neurological disorders, Parkinson's disease, stroke and traumatic brain injuries.

The document makes a significant contribution to the furthering of knowledge about neurological disorders. We hope it will facilitate increased cooperation and innovation and inspire commitment to preventing these debilitating disorders and providing the best possible care for people who suffer from them.

Benedetto Saraceno
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acknowledgements

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abbreviations

AD	Alzheimer's disease
ADI	Alzheimer's Disease International
AED	antiepileptic drug
AIDS	acquired immunodeficiency syndrome
ART	antiretroviral therapy
BPSD	behavioural and psychological symptoms of dementia
CNS	central nervous system
CRPS	complex regional pain syndrome
CSF	cerebrospinal fluid
CT	computerized tomography
DALY	disability-adjusted life year
FAO	Food and Agriculture Organization of the United Nations
EEG	electroencephalography
EMSP	European Multiple Sclerosis Platform
EPDA	European Parkinson's Disease Association
EUREPA	European Epilepsy Academy
GBD	Global Burden of Disease
GDP	gross domestic product
GNI	gross national income
HAART	highly active antiretroviral therapy
HIV	human immunodeficiency virus
IBE	International Bureau for Epilepsy
IASP	International Association for the Study of Pain
ICF	International Classification of Functioning, Disability and Health
ICH	intracerebral haemorrhage
IHS	International Headache Society
ILAE	International League Against Epilepsy
MRI	magnetic resonance imaging
MS	multiple sclerosis
MSIF	Multiple Sclerosis International Federation
PD	Parkinson's disease
PET	positron emission tomography
RTA	road traffic accident
SAH	subarachnoid haemorrhage
SMR	standardized mortality ratio
TBI	traumatic brain injury
TIA	transient ischaemic attack
UNESCO	United Nations Educational, Scientific and Cultural Organization
UNICEF	United Nations Children's Fund
UNFPA	United Nations Population Fund
VaD	vascular dementia
WFN	World Federation of Neurology
WFNS	World Federation of Neurosurgical Societies
WHA	World Headache Alliance
WHO	World Health Organization
YLD	years of healthy life lost as a result of disability
YLL	years of life lost because of premature mortality

introduction

One of the key constitutional responsibilities of the World Health Organization (WHO) is to foster partnership and collaboration among scientific and professional groups in order to contribute to the advancement of global health. To help prioritize health needs and design evidence-based health programmes globally, WHO initiates a large number of international projects and activities involving numerous governmental and non-governmental organizations, health professionals and policy-makers.

The Global Burden of Disease (GBD) study, a collaborative endeavour of the World Health Organization (WHO), the World Bank and the Harvard School of Public Health, drew the attention of the international health community to the burden of neurological disorders and many other chronic conditions. This study found that the burden of neurological disorders was seriously underestimated by traditional epidemiological and health statistical methods that take into account only mortality rates but not disability rates. The GBD study showed that over the years the global health impact of neurological disorders had been underestimated (*1*).

With awareness of the massive burden associated with neurological disorders came the recognition that neurological services and resources were disproportionately scarce, especially in low income and developing countries. Furthermore, a large body of evidence shows that policy-makers and health-care providers may be unprepared to cope with the predicted rise in the prevalence of neurological and other chronic disorders and the disability resulting from the extension of life expectancy and ageing of populations globally (*2, 3*).

In response to the challenge posed by neurological disorders, WHO launched a number of global public health projects, including the Global Initiative on Neurology and Public Health whose purpose is to increase professional and public awareness of the frequency, severity and costs of neurological disorders and to emphasize the need to provide neurological care at all levels including primary health care. This global initiative has revealed a paucity of information on the burden of neurological disorders and a lack of policies, programmes and resources for their management (*4–6*).

In response to these findings, WHO and the World Federation of Neurology (WFN) recently collaborated in an international Survey of Country Resources for Neurological Disorders involving 109 countries and covering over 90% of the world's population. The survey collected information from experts on several aspects of the provision of neurological care around the world, ranging from frequency of neurological disorders to the availability of neurological services across countries and settings. The findings show that resources are clearly inadequate for patients with neurological disorders in most parts of the world; they highlight inequalities in the access to neurological care across different populations, especially in those living in low income countries and in the developing regions of the world (*7*). The results of the survey, which include numerous tables, graphs and commentaries, have been published in the WHO/WFN Atlas of Country Resources for Neurological Disorders (*8*). The atlas is available at http://www.who.int/mental health/neurology/ or on request from WHO.

This report takes the collaboration with nongovernmental organizations and the Atlas Project one step further. It aims to inform governments, public health institutions, nongovernmental organizations and others so as to help formulate public health policies directed at neurological disorders and to guide informed advocacy. WHO has produced this report in collaboration with several nongovernmental organizations, including (in alphabetical order) Alzheimer's Disease International, European Parkinson's Disease Association, International Association for the Study of Pain, International Bureau for Epilepsy, International Headache Society, International League Against Epilepsy, Multiple Sclerosis International Federation, World Federation of Neurology, World Federation of Neurosurgical Societies and World Headache Alliance. It addresses the most important public health aspects of the following neurological disorders: dementia, epilepsy, headache disorders, multiple sclerosis, neuroinfections, neurological disorders associated with malnutrition, pain associated with neurological disorders, Parkinson's disease, stroke and traumatic brain injuries. These common disorders were selected after discussion with several experts and nongovernmental organizations and represent a substantial component of the global burden of neurological disorders.

The report is based on significant contributions by many individuals and organizations spanning all continents. Their names are indicated in the Acknowledgements section, and their input is acknowledged with thanks.

OUTLINE OF THE REPORT

Chapter 1 provides an overview of basic public health concepts and general principles as they apply to neurological disorders, including epidemiology and burden, health promotion, disease prevention, health policy, service provision and delivery of care, disability and rehabilitation, stigma, and education and training. Public health is defined as the science and practice of protecting and improving the health of the population through prevention, promotion, health education, and management of communicable and noncommunicable diseases including neurological disorders. In other words, public health is viewed as a comprehensive approach concerned with the health of the community as a whole rather than with *medical* health care that deals primarily with treatment of individuals. The focus of public health interventions could be primary, secondary or tertiary prevention. The above-mentioned concepts are illustrated by examples from the field of neurological disorders. Public health aspects of individual neurological disorders covered by the report are discussed in greater detail in Chapter 3.

Each chapter contains a numerical list of references to works that are cited in the text. A second list, arranged alphabetically, suggests reading material that is recommended to give an overview of the subject matter of the section or chapter; some of the key references may be repeated in the reading list.

Chapter 2 contains a series of tables and graphs that provide projected estimates of the global burden of neurological disorders for 2005, 2015 and 2030. The illustrations are accompanied by a summary of the GBD methodology, observations on its limitations and brief commentaries on the findings of the GBD study. The results are presented according to WHO regions, epidemiological subregions and World Bank income categories. Annex 1 lists WHO Member States and Annex 2 presents countries according to World Bank categories. Annex 3 provides the list of GBD cause categories, sequelae and case definitions used for calculation of estimates for neurological disorders. Annex 4 contains the GBD estimates for neurological disorders for 2005, 2015 and 2030.

Chapter 3 consists of 10 sections that focus on the public heath aspects of the specific neurological disorders covered by the report. Although notable differences exist between relevant public health issues for each neurological disorder, most sections cover the following topics: diagnosis and classification; etiology and risk factors; course and outcome; magnitude (prevalence, incidence, distribution by age and sex, global and regional distribution); disability and mortality; burden on patients' families and communities; treatment, management and rehabilitation; delivery and cost of care; gaps in treatment and other services; policies;

research; and education and training. Accompanying tables, graphs, boxes and other graphic material illustrate specific points made in the text. Details of relevant nongovernmental organizations, including their objectives, are given in Annex 5.

Chapter 4 gives the conclusions and recommendations of the report, which are based on the following findings. Neurological disorders are a significant and increasing public health problem. Many of them can be either prevented or treated at a relatively low cost. Resources for neurological disorders are grossly inadequate in most parts of the world. Significant inequalities in provision of neurological treatment and care exist between developing and developed countries. Stigma and discrimination against people with neurological disorders are ubiquitous and need to be eliminated through public education and global campaigns. Dignity of people with neurological disorders needs to be preserved and their quality of life improved. Long-term treatment and care of patients with chronic neurological disorders and conditions should be incorporated into primary care. Public health aspects of neurological disorders should be incorporated into undergraduate and postgraduate teaching and training curricula in neurology. More research on neurological disorders is needed and it should be facilitated through better funding, multidisciplinary approaches and international collaboration.

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CHAPTER 1

public health *principles* *and* neurological disorders

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9	Epidemiology and burden
9	Health promotion and disease prevention
12	Health policy
14	Service provision and delivery of care
16	Disability and rehabilitation
20	Stigma
22	Education and training
23	Conclusions

This chapter explains briefly the principles of public health, epidemiology and the burden of disease, and the ways in which health promotion and disease prevention are achieved. It looks at risks to health and prevention strategies, and explains what health policy means. It then describes the goals and functions of health systems and in particular considers service provision for neurological disorders. As many neurological disorders result in considerable morbidity, special attention is paid to disability and rehabilitation. The all-important part played by stigma in neurological disorders is assessed and, finally, education and training in neurology are discussed.

Many distinctions can be made between the practice of public health and that of clinical neurology. Public health professionals approach neurology more broadly than neurologists by monitoring neurological disorders and related health concerns of entire communities and promoting healthy practices and behaviours among them to ensure that populations stay healthy. Public health specialists focus on health and disease of entire populations rather than on individual patients, whereas neurologists usually treat one patient at a time for a specific neurological condition. These two approaches could be seen as being almost at the opposite ends of the health-care spectrum. What this chapter aims to do is to help build bridges between these two approaches and serve as a useful guide to the chapter that follows — on the public health aspects of specific neurological disorders.

PRINCIPLES OF PUBLIC HEALTH

Public health is the science and art of disease prevention, prolonging life and promoting health and well-being through organized community effort for the sanitation of the environment, the control of communicable diseases, the organization of medical and nursing services for the early diagnosis and prevention of disease, the education of the individual in personal health and the development of the social machinery to ensure for everyone a standard of living adequate for the maintenance or improvement of health (*1*). The goal of public health is to fulfil every society's ambition to create conditions in which all people can be healthy. Public health addresses the health of the population as a whole rather than the treatment of individuals. WHO defines health as *"a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"* (*2*). "Healthy people in healthy communities" is the ultimate goal of all public health interventions, which are aimed at promoting physical and mental health and preventing disease, injury and disability (*3*). Public health is particularly concerned with threats to the overall health of the community. As interventions are aimed primarily at prevention, monitoring the health of the community through surveillance of cases assumes great importance as does the promotion of a healthy lifestyle and healthy behaviour. In many cases, however, treating a disease can be vital to preventing it in other people, such as during an outbreak of a communicable disease. Another way of describing public health is "collective action for sustained population-wide health improvement" (*4*). This definition highlights the focus on actions and interventions that need collaborative actions, sustainability (i.e. the need to embed policies within supportive systems) and the goals of public health (population-wide health improvement and the reduction of health inequalities).

Since the 1980s, the focus of public health interventions has broadened towards population-level issues such as inequity, poverty and education and has moved away from advocating for change in the behaviour of individuals. The health of people is affected by many elements ranging from genetics to socioeconomic factors such as where they live, their income, education and social relationships. These are the social determinants of health, and they pervade every society in the world. Predictably, poor people have more health problems and worse health than the better-off sections of populations (*5*). Today public health seeks to correct these inequalities by advocating policies and initiatives that aim to improve the health of populations in an equitable manner.

The extension of life expectancy and the ageing of populations globally are predicted to increase the prevalence of many noncommunicable, chronic, progressive conditions including neurological disorders. The increasing capacity of modern medicine to prevent death has also increased the frequency and severity of impairment attributable to neurological disorders. This has raised the issue of restoring or creating a life of acceptable quality for people who suffer from the sequelae of neurological disorders.

Public health plays an important role in both the developed and developing parts of the world through either the local health systems or the national and international nongovernmental organizations. Though all developed and most developing countries have their own government health agencies such as ministries or departments of health to respond to domestic health issues, a discrepancy exists between governments' public health initiatives and access to health care in the developed and developing world. Many public health infrastructures are non-existent or are being formed in the developing world. Often, trained health workers lack the financial resources to provide even basic medical care and prevent disease. As a result, much of the morbidity and mortality in the developing world results from and contributes to extreme poverty.

Though most governments recognize the importance of public health programmes in reducing disease and disability, public health generally receives much less government funding compared with other areas of medicine. In recent years, large public health initiatives and vaccination programmes have made great progress in eradicating or reducing the incidence of a number of communicable diseases such as smallpox and poliomyelitis. One of the most important public

health issues facing the world nowadays is HIV/AIDS. Tuberculosis is also re-emerging and is a major concern because of the rise of HIV/AIDS-related infections and the development of strains resistant to standard antibiotics.

As the rate of communicable diseases in the developed world decreased throughout the 20th century, public health began to put more focus on chronic diseases such as cancer, heart disease and mental and neurological disorders. Much ill-health is preventable through simple, non-medical methods: for example, improving the quality of roads and enforcing regulations about speed and protective measures such as helmet use help to reduce disability as a result of head injuries.

To increase the awareness of professionals and people in general about the public health aspects of neurological disorders, and to emphasize the need for the prevention of these disorders and the necessity to provide neurological care at all levels including primary health care, WHO launched a number of international public health projects including the Global Initiative on Neurology and Public Health. The outcome of this large collaborative endeavour, which involved many health professionals from all parts the world, clearly indicated that there was a paucity of information about the prevalence and burden of neurological disorders and a lack of policies, programmes and resources for their treatment and management (*6*–*8*).

EPIDEMIOLOGY AND BURDEN

In general, health statistics focus primarily on quantifying the health status of populations and suffer from several limitations that reduce their practical value to policy-makers. The statistical information is partial and fragmented and in many countries even the most basic data (e.g. the annual number of deaths from particular causes) are not available. Further, the simple "head count" approach does not allow policy-makers to compare the relative cost–effectiveness of different interventions, for example the treatment of conditions such as acute stroke versus the long-term care of patients with chronic disorders such as Parkinson's disease or multiple sclerosis. At a time when people's expectations of health services are growing and funds are constrained, such information is essential for the rational allocation of resources.

To address these limitations, a large collaborative project called the Global Burden of Disease (GBD) Study was undertaken by WHO, the World Bank and the Harvard School of Public Health (*9*). The objectives of this unique international undertaking were as follows: to incorporate nonfatal conditions in the assessments of health status; to disentangle epidemiology from advocacy and produce objective, independent and demographically plausible assessments and projections of the burden of health conditions and diseases; and to measure disease and injury burden by developing a novel method that can also be used to assess the cost–effectiveness of interventions, in terms of the cost per unit of disease burden averted. The GBD study developed an internationally standardized and nowadays widely accepted single measurement index: the disability-adjusted life year (DALY). For neurological disorders, perhaps the most important dimension of the GBD study is the attention given to the total morbidity of populations by quantifying the contribution of nonfatal, chronic disorders to the reduction of health status. The GBD study is discussed in detail in Chapter 2, with its methodology and limitations and projected estimates for neurological disorders for 2005, 2015 and 2030.

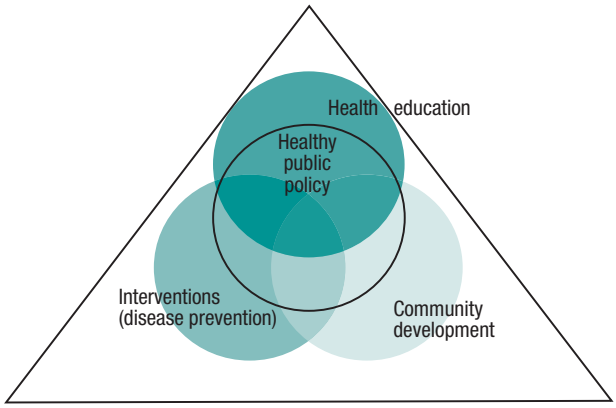
HEALTH PROMOTION AND DISEASE PREVENTION

Health promotion

Historically, the concepts of health promotion and disease prevention have been closely related. According to WHO, health promotion is a process of enabling people to increase control over their health and improve it. It refers to any activity destined to help people to change their lifestyle and move towards a state of optimal health. Health promotion can be facilitated through a combination

of efforts aimed at raising awareness, changing behaviours, and creating environments that support good health practices, healthy public policies and community development (*10*). The nature and scope of health promotion is illustrated in Figure 1.1.

Figure 1.1 Nature and scope of health promotion



Successful health promotion demands a coordinated action by governments, the health sector and other social and economic sectors, nongovernmental and voluntary organizations, local authorities, industry and the media. A list of required health promotion strategies across sectors and settings is contained in the Bangkok Charter for Health Promotion in a Globalized World (*11*) (see Box 1.1). For neurological disorders, health promotion is particularly important. In the case of traumatic brain injuries, development of policies in countries to prevent road traffic accidents and legislation to wear helmets are examples of health promotion strategies.

Disease prevention

The concept of disease prevention is more specific and comprises primary, secondary and tertiary prevention (*12*). *Primary prevention* is defined as preventing the disease or stopping individuals from becoming at high risk. Universal and selective preventive interventions are included in primary prevention. Universal primary prevention targets the general public or a whole population group without an identified specific risk (e.g. iodine supplementation programmes to prevent neurological and other disorders caused by iodine deficiency). Selective primary prevention targets individuals or subgroups of the population whose risk of developing disease is significantly higher than average, as evidenced by biological, psychological or social risk factors (e.g. prevention of stroke through adequate management of hypertension, diabetes and hypercholesterolemia). *Secondary prevention* aims at decreasing the severity of disease or reducing risk level or halting progression of disease through early detection and treatment of diagnosable cases (e.g. ensuring drug compliance in the treatment of epilepsy). *Tertiary prevention* includes interventions that reduce premature death and disability, enhance rehabilitation and prevent relapses and recurrence of the illness. Rehabilitation may mitigate the effects of disease and thereby prevent it from resulting in impaired social and occupational functioning; it is an important public health intervention that has long been neglected by decision-makers. Moreover, rehabilitation is an essential aspect of any public health strategy for chronic diseases, including a number of neurological disorders and conditions such as multiple sclerosis, Parkinson's disease and the consequences of stroke or traumatic brain injury. Box 1.2 describes some examples illustrating the role of primary, secondary and tertiary preventive strategies for the neurological disorders discussed in this document.

Box 1.1 Bangkok Charter for Health Promotion in a Globalized World

To make advances in implementing health promotion strategies, all sectors and settings must act to:

- *advocate* for health based on human rights and solidarity;
- *invest* in sustainable policies, actions and infrastructure to address the determinants of health;
- *build capacity* for policy development, leadership, health promotion practice, knowledge transfer and research, and health literacy;
- *regulate and legislate* to ensure a high level of protection from harm and enable equal opportunities for health and well-being for all people;
- *establish partnerships and build alliances* with public, private, nongovernmental and international organizations and civil society to create sustainable actions.

Source: *(11)*.

Health risks

Focusing on risks to health is a key to preventing any disease or injury. Many factors are relevant in prioritizing strategies to reduce risks to health. These include the extent of the threat posed by different risk factors, the availability of cost-effective interventions, and societal values and preferences. Risk assessment and estimates of the burden of disease resulting from different risk factors may be altered by many different strategies (*13*).

The chain of events leading to an adverse health outcome includes proximal (or direct) causes and distal causes that are further back in the causal chain and act through a number of intermediary causal factors. It is therefore essential that the whole of the causal chain is considered in the assessment of risks to health. Trade-offs also exist between assessments of proximal and distal causes. As one moves further away from the direct causes of disease, there can be a decrease in causal certainty and diagnostic consistency, which is often accompanied by an increase in complexity of treatment. Distal causes, however, are likely to have an amplifying effect in that they can affect many different sets of proximal causes and so can potentially make large differences (*14*).

Prevention strategies

Prevention strategies and interventions designed to reduce or prevent a particular disease are of two types. In population or mass approaches, a whole population is asked to be involved in modifying their behaviour in some way (e.g. being immunized against poliomyelitis). In targeted or high-risk approaches, only high-risk individuals are involved, which necessitates some form of screening to identify those who are at high risk (e.g. HIV testing) (*13*).

The distribution and determinants of risks in a population have major implications for strategies of prevention. A large number of people exposed to a small risk may generate many more cases than a small number exposed to a high risk. Thus, a preventive strategy focusing on high-risk individuals will deal only with the margin of the problem and will not have any impact on the considerable amount of disease occurring in the large proportion of people who are at moderate risk.

Box 1.2 Examples of preventive strategies for neurological disorders

PRIMARY PREVENTION
(Measures to prevent the onset of disease or avoid a targeted condition)

- Use of vaccine against poliomyelitis within the Global Polio Eradication Initiative has led to elimination of indigenous polioviruses from all but four countries.
- Measures to control blood pressure, cholesterol levels and diabetes mellitus, to reduce tobacco use, and to promote overall healthy eating patterns and physical activity are advocated for primary prevention of stroke. In Japan, government-led health education campaigns and increased treatment of high blood pressure have reduced blood pressure levels in the populations: stroke rates have fallen by more than 70%.
- Wearing a helmet is the single most effective way to reduce head injuries and fatalities resulting from motorcycle and cycle crashes. For example, wearing a helmet has been shown to decrease the risk and severity of injuries among motorcyclists by about 70%, the likelihood of death by almost 40%, and to substantially reduce the costs of health care associated with such crashes.

SECONDARY PREVENTION
(Early and accurate diagnosis, appropriate treatment, management of risk factors, compliance)

- Medical treatment of epilepsy with first-line antiepileptic drugs can render up to 70% of patients seizure-free when adequately treated.
- Management of patients with stroke by an organized unit significantly reduces mortality and disability in comparison with standard care on a general medical ward.

TERTIARY PREVENTION
(Rehabilitation, palliative care, treatment of complications, patient and caregiver education, self-support groups, reduction of stigma and discrimination, social integration)

- Interventions targeting stress and depression among carers of patients with dementia, including training, counselling and support for caregivers, have shown positive results for the management of dementia.
- The strategy of community-based rehabilitation has been implemented in many low-income countries around the world; where it is practised, it has successfully influenced the quality of life and participation of persons with disabilities in their societies.
- Methods to reduce stigma related to epilepsy in an African community successfully changed attitudes to epilepsy: traditional beliefs were weakened, fears were diminished, and community acceptance of people with epilepsy increased.

In contrast, population-based strategies that seek to shift the whole distribution of risk factors have the potential to control the incidence of a disorder in an entire population (*14*).

With targeted approaches, efforts are concentrated on those who are most at risk of contracting a disease (e.g. HIV-positive individuals). This has two benefits: first, it avoids the waste of the mass approach and, second, people who are identified as being at high risk are more likely to comply with behaviour change. However, such an approach could increase the costs because of the need to identify the high-risk group of people most likely to benefit. Which prevention approach is the most cost effective in a particular setting will depend on the prevalence of high-risk people in the population and the cost of identifying them compared with the cost of intervention.

Some areas of behavioural change benefit from active government intervention through legislation or financial incentives. For example, road traffic safety is one area where government action can make a big difference in preventing traumatic brain injuries. This can be achieved through control and legislation on alcohol and drug use, better roads, speed control, better motor vehicle design, and requirements to use seatbelts and helmets (see Table 1.1).

Table 1.1 Benefits of wearing a motorcycle helmet

Not wearing a helmet	Wearing a helmet
• increases the risk of sustaining a head injury • increases the severity of head injuries • increases the time spent in hospital • increases the likelihood of dying from a head injury	• decreases the risk and severity of injuries by about 72% • decreases the likelihood of death by up to 39%, the probability depending on the speed involved • decreases the costs of health care associated with a crash

Source: (*15*).

A different set of interventions can be used to achieve the same goal, and some interventions will reduce the burden associated with multiple risk factors and diseases. For example, interventions to reduce blood pressure, cigarette smoking and cholesterol levels reduce cerebrovascular and cardiovascular diseases and a number of others. The effect of using multiple interventions at the same time might be more than would be expected by summing the benefits of carrying out the interventions singly. Risk reduction strategies are therefore generally based on a combination of interventions. For example, a CVD Risk Management Package has been developed by WHO for managing cardiovascular events (heart attacks and stroke). For cardiovascular disease prevention and control activities to achieve the greatest impact, a paradigm shift is required from the "treatment of risk factors in isolation" to "comprehensive cardiovascular risk management". The risk management package facilitates this shift. It has been designed primarily for the management of cardiovascular risk in individuals found by opportunistic screening to have hypertension. It could be adapted, however, to be used with diabetes or smoking as entry points. The package is meant to be implemented in a range of health-care facilities in low and medium resource settings, in both developed and developing countries. For this reason it has been designed for three scenarios that reflect the commonly encountered resource availability strata in such settings (*16*). The minimum conditions that characterize the three scenarios, in terms of the skill level of the health worker, the diagnostic and therapeutic facilities and the health services available, are described in Table 1.2.

HEALTH POLICY

Health policy usually refers to formal statements or procedures within institutions and governments that define health priorities and actions aimed at improving people's health. It can have a number of other goals in addition to preventing illness and promoting population health. In choos-

Table 1.2 Characteristics of three scenarios in the WHO CVD Risk Management Package

Resource availability	Scenario one	Scenario two	Scenario three
Human resources	Non physician health worker	Medical doctor or specially trained nurse	Medical doctor with access to full specialist care
Equipment	Stethoscope Blood pressure measurement device Measuring tape or weighing scale Optional: test tubes, holder, burner, solution or test strips for checking urine glucose	Stethoscope Blood pressure measurement device Measuring tape or weighing scale Test tubes, holder, burner, solutions or test strips for checking urine glucose and albumin	Stethoscope Blood pressure measurement device Measuring tape or weighing scale Electrocardiograph Ophthalmoscope Urine analysis: fasting blood, sugar, electrolytes, creatinine, cholesterol and lipoproteins
General drugs	Essential: thiazide diuretics Optional: metformin (for refill)	Thiazide diuretics Beta blockers Angiotensin converting enzyme inhibitors Calcium channel blockers (sustained release formulations) (Reserpine and methyldopa if the above antihypertensives are unavailable) Aspirin Metformin (for refill)	Thiazide diuretics Beta blockers Angiotensin converting enzyme inhibitors Calcium channel blockers (sustained release formulations) (Reserpine and methyldopa if the above antihypertensives are unavailable) Aspirin Insulin Metformin Glibenclamide Statins (if affordable) Angiotensin receptor blocker (if affordable)
Other facilities	Referral facilities Maintenance and calibration of blood pressure measurement devices	Referral facilities Maintenance and calibration of equipment	Access to full specialist care Maintenance and calibration of equipment

Source: (*16*).

ing appropriate combinations of interventions, governments are also concerned with reducing poverty and other inequalities, with questions of human rights, acceptance by the community and political needs. They must also consider how different types of interventions can be incorporated into the health infrastructure available in the country, or how the infrastructure could be expanded or adapted to accommodate the desired strategies. This section discusses only health policy issues related to health promotion and disease prevention.

A health policy paradox shows that preventive interventions can achieve large overall health gains for whole populations but might offer only small advantages to each individual. This leads to a misperception of the benefits of preventive advice and services by people who are apparently in good health. In general, population-wide interventions have the greatest potential for prevention. For instance, in reducing risks from high blood pressure and cholesterol, shifting the mean values of whole populations will be more cost effective in avoiding future heart attacks and strokes than screening programmes that aim to identify and treat only those people with defined hypertension or raised cholesterol levels. Often both approaches are combined in one successful strategy.

A critical health policy issue, especially for developing and resource-poor countries, concerns the appropriate balance between primary and secondary prevention and between population and high-risk approaches to primary prevention. If the goal is to increase the proportion of the population at low risk and to ensure that all groups benefit, the strategy with the greatest potential is the one directed at the whole population, not just at people with high levels of risk factors or established disease. The ultimate goal of a health policy is the reduction of population risk; since most of the population in most countries is not at the optimal risk level, it follows that the majority of prevention and control resources should be directed towards the goal of reducing the entire population's risk. For example, policies for prevention of traumatic brain injuries such as wearing of helmets need to be directed at the whole population. Thus, risk reduction through primary prevention is clearly the preferred health policy approach, as it actually lowers future exposures and the incidence of new disease episodes over time.

The choice may well be different, however, for different risks, depending to a large extent on how common and how widely distributed is the risk and the availability and costs of effective interventions. Large gains in health can be achieved through inexpensive treatments when primary prevention measures have not been effective. An example is the treatment of epilepsy with a cheap first-line antiepileptic drug such as phenobarbital.

One risk factor can lead to many outcomes, and one outcome can be caused by many risk factors. When two risks influence the same disease or injury outcomes, then the net effects may be less or more than the sum of their separate effects. The size of these joint effects depends principally on the amount of prevalence overlap and the biological results of joint exposures (*13*). For example, in the case of neuroinfections such as HIV, one risk factor (i.e. HIV infection) leads to many outcomes, as explained in Chapter 3.5. For some other neurological disorders, one outcome can result from many risk factors: in the case of epilepsy, for example, from factors such as birth injury, head trauma, central nervous system infections and infestations, as explained in Chapter 3.2.

SERVICE PROVISION AND DELIVERY OF CARE

Health systems

Health systems comprise all the organizations, institutions and resources that devote their efforts and activities to promote, restore and maintain population health. These activities include formal health care such as the professional delivery of personal medical attention, actions by traditional practitioners, home care and self-care, public health activities such as health promotion and disease prevention, and other health-enhancing interventions such as the improvement of environmental safety.

Beyond the boundaries of this definition, health systems also include activities whose primary purpose is something other than health — education, for example — if they have a secondary, health-enhancing benefit. Hence, while general education falls outside the definition of health systems, health-related education is included. In this sense, every country has a health system, no matter how fragmented or unsystematic it may seem to be.

The World Health Report 2000 outlines three overall goals of health systems: good health, responsiveness to the expectations of the population, and fairness of financial contribution (*17*). All three goals matter in every country, and much improvement in how a health system performs with respect to these responsibilities is possible at little cost. Even if we concentrate on the narrow definition of reducing excess mortality and morbidity — the major battleground — the impact will be slight unless activities are undertaken to strengthen health systems for delivery of personal and public health interventions.

Progress towards the above goals depends crucially on how well systems carry out four vital functions: service provision, resource generation, financing and stewardship (*17*). The provision of

services is the most common function of a health-care system, and in fact the entire health system is often identified and judged by its service delivery.

The provision of health services should be affordable, equitable, accessible, sustainable and of good quality. Failure in any of these objectives adversely affects the care that is delivered. Not much information is forthcoming from countries on these aspects of their health systems, however. Based on available information, serious imbalances appear to exist in many countries in terms of human and physical resources, technology and pharmaceuticals. Many countries have too few qualified health personnel, while others have too many. Staff in health systems in many low income countries are inadequately trained, poorly paid and work in obsolete facilities with chronic shortages of equipment. One result is a "brain drain" of demoralized health professionals who go abroad or move into private practice. The poorer sectors of society are most severely affected by any constraints in the provision of health services.

Service delivery

Organization of services for delivery of neurological care has an important bearing on their effectiveness. Because of their different social, cultural, political and economic contexts, countries have various forms of service organization and delivery strategies. The differing availability of financial and human resources also affects the organization of services. Certain key issues, however, need to be taken into account for structuring services to provide effective care to people with neurological disorders. Depending upon the health system in the country, there is a variable mix of private and public provision of neurological care.

The three traditional levels of service delivery are primary, secondary and tertiary care. *Primary care* includes treatment and preventive and promotional interventions conducted by primary care professionals. These vary from a general practitioner, nurse, other health-care staff and non-medical staff to primary care workers based in rural areas. Primary care represents the point of entry for most people seeking care and is the logical setting where neurological disorders should begin to be addressed. Many potential benefits exist for providing services through primary care. Users of primary care are more likely to seek early help because of the wide availability of facilities, their easy accessibility, cultural acceptability and reduced cost, thus leading to early detection of neurological disorders and better clinical outcome.

Integration of neurological services into the primary care system needs to be a significant policy objective in both developing and developed countries. Providing neurological care through primary care requires significant investment in training primary care professionals to detect and treat neurological disorders. Such training should meet the specific practical training needs of different groups of primary care professionals such as doctors, nurses and community health workers. Preferably, ongoing training is needed to provide subsequent support for reinforcing new skills. In many countries, this has not been possible and thus suboptimal care is provided (*18*).

Primary care centres are limited in their ability to adequately diagnose and treat certain neurological disorders. For the management of severe cases and patients requiring access to diagnostic and technological expertise, a *secondary level of care* is necessary. A number of neurological services may be offered in district or regional hospitals that form part of the general health system. Common facilities include inpatient beds in general medicine, specialist beds, emergency departments and outpatient clinics. The various types of services include consultation/liaison services, diagnostic facilities such as electroencephalography (EEG) and computerized tomography (CT), planned outpatient programmes, emergency care, inpatient care, intensive care, respite care, referral facilities for primary care services, multidisciplinary neurological care and rehabilitation programmes. These services require adequate numbers of general as well as specialist professionals who can also provide supervision and training in neurology to primary care staff.

Tertiary care is the most specialized form of neurological diagnosis, treatment and rehabilitation, and is often delivered in teaching hospitals. In some countries, there are also other public or private facilities offering various types of neurological services in inpatient wards and outpatient clinics. These facilities are not expected to deliver primary neurological care but act as secondary and tertiary referral services. They also serve as facilities for clinical research, collection of epidemiological data, and the creation and distribution of health educational materials. Neurological specialist services require a large complement of trained specialist staff. Shortages of such staff are a serious problem in low income countries, as are the lack of financial resources and infrastructure.

Very few countries have an optimal mix of primary, secondary and tertiary care. Even within countries, significant geographical disparities usually exist between regions. Little concerted effort has been made to use primary care as the principal vehicle of delivery of neurological services. Some countries have good examples of intersectoral collaboration between nongovernmental organizations, academic institutions, public sector health services and informal community-based health services. At present, such activities are limited to small populations in urban areas; most rural populations have no access to such services. Even in developed countries, more emphasis is placed on providing specialist services than on approaches to integrate neurological services into primary care.

Many neurological disorders run a chronic, relapsing or remitting course. Such disorders are better managed by services that adopt a continuing care approach, emphasizing the long-term nature of these neurological disorders and the need for ongoing care. The emphasis is on an integrated system of service delivery that attempts to respond to the needs of people with neurological disorders. Integrated and coordinated systems of service delivery need to be developed where services based in primary, secondary and tertiary care complement each other. In order to address the needs of persons with neurological disorders for health care and social support, a clear referral and linkage system needs to be in place. The key principles for organizing such services include accessibility, comprehensiveness, coordination and continuity of care, effectiveness, and equity within the local social, economic and cultural contexts.

DISABILITY AND REHABILITATION

Disability

Many neurological disorders and conditions affect an individual's functioning and result in disabilities or limit activities and restrict participation. According to the International Classification of Functioning, Disability and Health (ICF), the medical model views disability as a problem of the person, directly caused by disease, trauma or other health condition that requires medical care provided in the form of individual treatment by professionals (*19*). Management of the disability is aimed at cure or the individual's adjustment and behaviour change. The social model of disability sees the issue mainly as a socially created problem and a matter related to the full integration of individuals into society. According to the social model, disability is not an attribute of the individual, but rather a complex collection of conditions, many of which are created by the social environment: the approach to disability requires social action and is a responsibility of society.

Rehabilitation

WHO defines rehabilitation as an active process by which those affected by injury or disease achieve a full recovery or, if a full recovery is not possible, realize their optimal physical, mental and social potential and are integrated into their most appropriate environment (*19*). Rehabilitation is one of the key components of the primary health-care strategy, along with promotion, prevention and treatment. While promotion and prevention primarily target risk factors of disease and

treatment targets ill-health, rehabilitation targets human functioning. As with other key health strategies, it is of varying importance and is relevant to all other medical specialities and health professions. Though rooted in the health sector, rehabilitation is also relevant to other sectors including education, labour and social affairs. For example, building of ramps and other facilities to improve access by disabled people falls beyond the purview of the health sector but is nevertheless very important for the comprehensive management of a person with a disability.

As a health-care strategy, rehabilitation aims to enable people who experience or are at risk of disability to achieve optimal functioning, autonomy and self-determination in the interaction with the larger physical, social and economic environment. It is based on the integrative model of human functioning, disability and health, which understands human functioning and disability both as an experience in relation to health conditions and impairments and as a result of interaction with the environment.

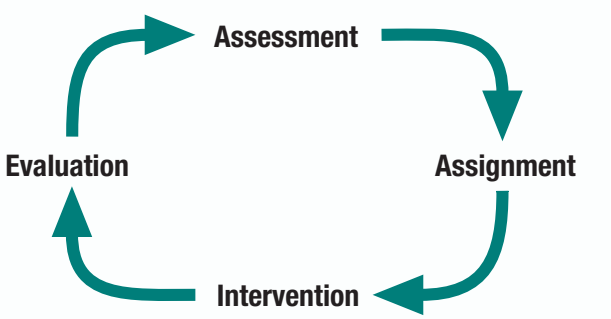
Rehabilitation involves a coordinated and iterative problem-solving process along the continuum of care from the acute hospital to the community. It is based on four key approaches integrating a wide spectrum of interventions: 1) biomedical and engineering approaches; 2) approaches that build on and strengthen the resources of the person; 3) approaches that provide for a facilitating environment; and 4) approaches that provide guidance across services, sectors and payers. Specific rehabilitation interventions include those related to physical medicine, pharmacology and nutrition, psychology and behaviour, education and counselling, occupational and vocational advice, social and supportive services, architecture and engineering and other interventions.

Rehabilitation services are like a bridge between isolation and exclusion — often the first step towards achieving fundamental rights. Health is a fundamental right, and rehabilitation is a powerful tool to provide personal empowerment.

Rehabilitation strategy

Because of the complexity of rehabilitation based on the above-mentioned integrative model, rehabilitation services and interventions applying the rehabilitation strategy need to be coordinated along the continuum of care across specialized and non-specialized services, sectors and payers. Figure 1.2 illustrates the iterative problem-solving process sometimes called Rehab-CYCLE (*20*). The Rehab-CYCLE involves four steps: assess, assign, intervene and evaluate. The process is applied on two levels. The first refers to the guidance along the continuum of care and the second to the provision of a specific service.

Figure 1.2 The Rehab-CYCLE



From the *guidance perspective*, the assessment step includes the identification of the person's problems and needs, the valuation of rehabilitation potential and prognosis and the definition of long-term service and goals of the intervention programme. The assignment step refers to the assignment to a service and an intervention programme. From the guidance perspective, the intervention step is not further specified. The evaluation step refers to service and the achievement of the intervention goal.

From the *service perspective*, the assessment step includes the identification of a person's problems, the review and potential modification of the service or goals of the intervention programme and the definition of the first Rehab-CYCLE goals and intervention targets. The assignment step refers to the assignment of health professionals and interventions to the intervention targets. The intervention step refers to the specification of the intervention techniques, the definition of indicator measures to follow the progress of the intervention, and the definition of target values to be achieved within a

predetermined time period. The evaluation step refers to the evaluation of the achievement of the goal with respect to the specified target values of the indicator measures, the Rehab-CYCLE goals and ultimately the goals of the intervention programme. It also includes the decision regarding the need for another intervention cycle based on a reassessment.

Rehabilitation of neurological disorders

Rehabilitation should start as soon as possible after the diagnosis of a neurological disorder or condition and should focus on the community rehabilitation perspective. The type and provision of services is largely dependent on the individual health-care system. Therefore no generally agreed principles currently exist regarding the provision of rehabilitation and related services.

Rehabilitation is often exclusively associated with well-established and coordinated multidisciplinary efforts by specialized rehabilitation services. While availability and access to these specialized inpatient or outpatient services are at the core of successful rehabilitation, a need also exists for rehabilitation service provision, from the acute settings through the district hospital and the community, often by health professionals not specialized in rehabilitation but working closely with the rehabilitation professionals. It is important to recognize that rehabilitation efforts in the community can be delivered by professionals outside the health sector, ideally in collaboration with rehabilitation professionals.

Rehabilitation services are limited or nonexistent in many developing countries for people with disabilities attributable to neurological disorders or other causes. This means that many individuals with disabilities will depend totally on other people, usually family members, for help with daily activities, and this situation enhances poverty. Impoverished communities throughout the world are affected by a disproportionate number of disabilities and, in turn, people with disabilities become more vulnerable to poverty because of a lack of access to, or availability of, health care, social care and rehabilitation services. When rehabilitation services are available, the lack of human resources limits considerably the transfer of knowledge from specialized centres to district and community settings.

To address this situation, a community-based rehabilitation strategy has been introduced by WHO as a complement to existing rehabilitation models and to look beyond the medical needs. The strategy of community-based rehabilitation has been implemented in many low income countries around the world and has successfully influenced the quality of life and participation of persons with disabilities in societies where it is in practice.

The philosophy of rehabilitation emphasizes patient education and self-management and is well suited for a number of neurological conditions. The basis for successful neurorehabilitation is the in-depth understanding and sound measurement of functioning and the application of effective interventions, intervention programmes and services. A wide range of rehabilitation interventions, intervention programmes and services has been shown to contribute effectively to the optimal functioning of people with neurological conditions.

Effective neurorehabilitation is based on the involvement of expert and multidisciplinary assessment, realistic and goal-oriented programmes, and evaluation of the impact on the patient's rehabilitation achievements; evaluation using scientifically sound and clinically appropriate out-

Box 1.3 Case-study: Giovanni

Giovanni is a 20-year-old man who was beaten by a mob two years ago after a football game and suffered traumatic brain injury. He was slow to recover with severe physical limitations, fully conscious but with severe communication problems. He needs an assistive communication device which is not provided by the health system and is not possible for his family to purchase, so his family made a basic communication table he uses to spell out words by pointing letter by letter with a finger, the only part of his body he controls partially. Giovanni is totally dependent in all daily activities and needs assistance 24 hours a day. He has a standard wheelchair (though he requires an electrical one); he has no way of leaving his house to access community facilities, he cannot return to his previous job, and he has no relocation option in view.

come measures should also incorporate the patient's and the family's perspectives. There are a number of complexities in the process of neurorehabilitation, as patients can present with diverse sequelae, including the following:

- *Physical functioning limitations* can be evident in many ways — such as paralysis of the left or right side of the body, or both sides — which limit severely the person's capacity for many daily living activities, as well as mobility in the community and, eventually, the capacity to return to work or school. Patients can also present with rigidity, uncoordinated movements, and/or weakness. This is evident in the case-studies of Giovanni and Juan given below in Box 1.3 and Box 1.4, respectively. In developing countries, people with disabilities have very limited access not only to rehabilitation services but also to appropriate assistive technology, such as adequate wheelchairs: persons with head injury who require wheelchairs for adequate positioning and mobility may be severely impaired in their possibility to leave their house and participate in community activities, access educational facilities, or work.
- *Cognitive impairments* can manifest in the form of memory and attention problems, mild to severe intellectual deficiency, lack of perseverance and a limited ability to learn, all of which can make it impossible to return to work, may affect emotional stability, and limit performance at work or at home. All of these problems will affect the person's emotional status, as well as that of the family and friends. It can also mean social isolation in the long term, aggravating depression.
- *Behavioural problems* such as poor impulse control, uncontrolled anger and sexual impulses, lack of insight and perseverance, and the impossibility to learn from past errors are only some of the behavioural sequelae that affect the person's capacity to get involved and be accepted socially, and further limit the possibility of returning to educational or vocational services. Behavioural problems can also become evident when the person affected realizes the severity of his or her limitations, and the fact that they may be permanent.
- *Communication impairments* in the form of speech problems, poor vocalization or stomas, in combination with lack of access to augmentative or alternative communication devices in developing countries, as in Giovanni's case (Box 1.3), are a sure means of social isolation.
- *Basic daily living activities* are affected by functional and cognitive limitations. For a man like Giovanni (Box 1.3), such things as getting dressed or getting a spoonful of food to his mouth can be impossible.
- *Psychosocial limitations*, such as limited access to education, the impossibility to return to vocational status or be relocated vocationally, are consequences of previously mentioned limitations, all of which further impact on the behavioural, physical and cognitive aspects of the person affected by a neurological disorder that causes disability.

Costs of rehabilitation services

The National Head and Spinal Cord Injury Survey (*21*) divided costs into direct and indirect. Direct costs were associated with the monetary values of real goods and services that were provided for health care, while indirect costs were the monetary loss incurred by society because of interrupted productivity by the injured person. In 1974, the total cost for all head injuries studied was

Box 1.4 Case-study: Juan

Juan is a 32-year-old man, a former alcohol and drug addict who sustained a car accident eight years ago. He recovered well from his physical limitations, except for a total paralysis of his right arm and uncoordinated movements of his left arm and legs. He was depressed for years, refusing medical treatment for his former addiction problem. He could not return to his former job as an agricultural labourer and was supported by his mother, who had to find a job to maintain them both. Finally, on his own, Juan adapted his tools to be able to function as a shoe-shiner in a park. At his last appointment, he was newly wed and attended with his wife and child. He was finally happy with himself and his life, although conscious of his deficits.

US$ 2384 million, of which 29% was related to the direct costs of care and 71% to indirect costs. The largest annual cost was found to be in the 25–44-year age group, where the loss incurred due to productivity was maximal. Payments for indirect costs are by far the greatest share, and legal charges are only slightly less than the cost for the entire medical, hospital and rehabilitation services provided.

STIGMA

Stigma has been defined as a deeply discrediting attribute that reduces a person to one who is in some way tainted and can therefore be denigrated. It is a pervasive problem that affects health globally, threatening an individual's psychological and physical well-being. It prevents individuals from coming forward for diagnosis and impairs their ability to access care or participate in research studies designed to find solutions.

Stigmatization of certain diseases and conditions is a universal phenomenon that can be seen across all countries, societies and populations. It refers to the relation between "the differentness of an individual and the devaluation society places on that particular differentness". For stigmatization to be consistently effective, however, the stigmatized person must acquiesce to society's devaluation. When people with "differentness" internalize society's devaluation, they do not feel empowered to change the situation and the negative stereotypes become an accepted part of their concept of the disorder. The labelling, stereotyping, separation from others and consequent loss of status highlight the role of power relations in the social construction of stigma (*22*).

People differentiate and label socially important human differences according to certain patterns that include: negative stereotypes, for example that people with epilepsy or other brain disease are a danger to others; and pejorative labelling, including terms such as "crippled", "disabled" and "epileptic".

In neurology, stigma primarily refers to a mark or characteristic indicative of a history of neurological disorder or condition and the consequent physical or mental abnormality. For most chronic neurological disorders, the stigma is associated with the disability rather than the disorder per se. Important exceptions are epilepsy and dementia: stigma plays an important role in forming the social prognosis of people with these disorders. The amount of stigma associated with chronic neurological illness is determined by two separate and distinct components: the attribution of responsibility for the stigmatizing illness and the degree to which it creates discomfort in social interactions. An additional perspective is the socially structured one, which indicates that stigma is part of chronic illness because individuals who are chronically ill have less "social value" than healthy individuals. Some additional aspects and dimensions of stigma are given in Box 1.5.

Stigma leads to direct and indirect discriminatory behaviour and factual choices by others that can substantially reduce the opportunities for people who are stigmatized. Whatever the mechanisms involved, stigma is an important public health problem. Stigma increases the toll of illness for many people with brain disorders and their families; it is a cause of disease, as people

Box 1.5 Dimensions of stigma

Concealability	The extent to which the condition becomes obvious or can be hidden from others.
Course of the mark	The way the condition changes over time and its ultimate outcome.
Disruptiveness	The degree of strain and difficulty stigma adds to interpersonal relationships.
Aesthetics	How much the attribute makes the character repellant or upsetting to others.
Origin	Who was responsible for the acquired stigmatizing condition and how.
Peril	Perceived dangers, both real and symbolic, of the stigmatizing condition to others.

Source: (*23*).

who are stigmatized have high exposure to health risks and low access to protective factors and treatment.

Sometimes coping with stigma surrounding the disorder is more difficult than living with any limitations imposed by the disorder itself. Stigmatized individuals are often rejected by neighbours and the community, and as a result suffer loneliness and depression. The psychological effect of stigma is a general feeling of unease or of "not fitting in", loss of confidence, increasing self-doubt leading to depreciated self-esteem, and a general alienation from the society. Moreover, stigmatization is frequently irreversible so that, even when the behaviour or physical attributes disappear, individuals continue to be stigmatized by others and by their own self-perception.

People with some neurological disorders (e.g. epilepsy) and their families may also be subjected to other forms of social sanction, such as being excluded from community activities or from societal opportunities such as education or work. One of the most damaging results of stigmatization is that affected individuals or those responsible for their care may not seek treatment, hoping to avoid the negative social consequences of diagnosis. This leads in turn to delayed or lost opportunities for treatment and recovery. Underreporting of stigmatizing conditions can also reduce efforts to develop appropriate strategies for their prevention and treatment.

Epilepsy carries a particularly severe stigma because of misconceptions, myths and stereotypes related to the illness. In some communities, children who do not receive treatment for this disorder are removed from school. Lacking basic education, they may not be able to support themselves as adults. In some African countries, people believe that saliva can spread epilepsy or that the "epileptic spirit" can be transferred to anyone who witnesses a seizure. These misconceptions cause people to retreat in fear from someone having a seizure, leaving that person unprotected from open fires and other dangers they might encounter in cramped living conditions. Recent research has shown that the stigma people with epilepsy feel contributes to increased rates of psychopathology, fewer social interactions, reduced social capital, and lower quality of life in both developed and developing countries (*22*).

Efforts are needed to reduce stigma but, more importantly, to tackle the discriminatory attitudes and prejudicial behaviour that give rise to it. Fighting stigma and discrimination requires a multilevel approach involving education of health professionals and public information campaigns to educate and inform the community about neurological disorders in order to avoid common myths and promote positive attitudes. Methods to reduce stigma related to epilepsy in an African community by a parallel operation of public education and comprehensive treatment programmes successfully changed attitudes: traditional beliefs about epilepsy were weakened, fears were diminished, and community acceptance of people with epilepsy increased (*24*).

The provision of services in the community and the implementation of legislation to protect the rights of the patients are also important issues. Legislation represents an important means of dealing with the problems and challenges caused by stigmatization. Governments can reinforce efforts with laws that protect people with brain disorders and their families from abusive practices and prevent discrimination in education, employment, housing and other opportunities. Legislation can help, but ample evidence exists to show that this alone is not enough.

The emphasis on the issue of prejudice and discrimination also links to another concept where the need is to focus less on the person who is stigmatized and more on those who do the stigmatizing. The role of the media in perpetrating misconceptions also needs to be taken into account. Stigmatization and rejection can be reduced by providing factual information on the causes and treatment of brain disorder; by talking openly and respectfully about the disorder and its effects; and by providing and protecting access to appropriate health care.

EDUCATION AND TRAINING

Education in neurology contains important aspects of quality assurance and continuing improvement in the delivery of the best care to people with neurological disorders. Training in neurology does not refer only to postgraduate specialization but also the component of training offered to undergraduates, general physicians and primary health-care workers. To reduce the global burden of neurological disorders, an adequate focus is needed on training, especially of primary health workers in countries where neurologists are few or nonexistent.

Training of primary care providers

As front line caregivers in many resource-poor countries, primary care providers need to receive basic training and regular continuing education in basic diagnostic skills and in treatment and rehabilitation protocols. Such training should cover general skills (such as interviewing the patient and recording the information), diagnosis and management of specific disorders (including the use of medications and monitoring of side-effects) and referral guidelines. Training manuals tailored to the needs of specific countries or regions must be developed. Primary care providers need to be trained to recognize the need for referral to more specialized treatment rather than trying to make a diagnosis.

Training of nurses is particularly important globally. In low income countries, where few physicians exist, nurses may be involved in making diagnostic and treatment decisions. They are also an important source of advice on promoting health and preventing disease, such as providing information on diet and immunization.

Training of physicians

The points to be taken into consideration in relation to education in neurology for physicians include:

- core curricula (undergraduate, postgraduate and others);
- continuous medical education;
- accreditation of training courses;
- open facilities and international exchange programmes;
- use of innovative teaching methods;
- training in the public health aspects of neurology.

Teaching of neurology at undergraduate level is important because 20–30% of the population are susceptible to neurological disorders (*25*). The postgraduate period of training is the most active and important for the development of a fully accredited neurologist. The following issues need consideration: mode of entry, core training programmes, evaluation of the training institutions, access to current literature, rotation of trainees between departments, and evaluation of the trainees during training and by a final examination. The central idea is to build both the curriculum and an examination system that ensure the achievement of professional competence and social values and not merely the retention and recall of information.

Neurological curricula vary considerably across countries. This is not necessarily undesirable because the curriculum must take into account local differences in the prevalence of neurological disorders. Some standardization in the core neurological teaching and training curricula and methods of demonstrating competency is desirable, however. The core curriculum should be designed to cover the practical aspects of neurological disorders and the range of educational settings should include all health resources in the community. The core curriculum also needs to reflect national health priorities and the availability of affordable resources.

Continuous medical education is an important way of updating the knowledge of specialists on an ongoing basis and providing specialist courses to primary care physicians. Specialist neurolo-

gists could be involved in training of primary care doctors, especially in those countries where few specialists in neurology exist. Regional and international neurological societies and organizations have an important role to play in providing training programmes: the emphasis should be on active problem-based learning. Guidelines for continuous medical education need to be set up to ensure that educational events and materials meet a high educational standard, remain free of the influence of the pharmaceutical industry and go through a peer review system. Linkage of continuous medical education programmes to promotion or other incentives could be a strategy for increasing the number of people attending such courses.

Neurologists play an increasingly important part in providing advice to government and advocating better resources for people with neurological disorders. Therefore training in public health, service delivery and economic aspects of neurological care need to be stressed in their curricula.

Most postgraduate neurology training programmes, especially those in developed countries, are resource intensive and lengthy — usually taking about six years to complete. Whether adequate specialist training in neurology might be undergone in less time in certain countries or regions would be a useful subject for study. The use of modern technology facilities and strategies such as distance-learning courses and telemedicine could be one way of decreasing the cost of training.

An important issue, as for other human health-care resources, is the "brain drain", where graduates sent abroad for training do not return to practise in their countries of origin. This public health challenge still needs to be faced with innovative means.

CONCLUSIONS

Public health is the science and practice of protecting and improving the population's health through prevention, promotion, health education, control of communicable and noncommunicable diseases and monitoring of environmental hazards. It is a comprehensive approach that is concerned with the health of the community as a whole. Public health is community health: "Health care is vital to all of us some of the time, but public health is vital to all of us all of the time" (*3*).

The mission of public health is to fulfil society's interest in assuring conditions in which people can be healthy. The three core public health functions are:

- the assessment and monitoring of the health of communities and populations at risk to identify health problems and priorities;
- the formulation of public policies designed to solve identified local and national health problems and priorities;
- ensuring that all populations have access to appropriate and cost-effective care, including health promotion and disease prevention services, and evaluation of the effectiveness of that care.

Public health comprises many professional disciplines such as medicine, nutrition, social work, environmental sciences, health education, health services administration and the behavioural sciences. In other words, public health activities focus on entire populations rather than on individual patients. Specialist neurologists usually treat individual patients for a specific neurological disorder or condition; public health professionals approach neurology more broadly by monitoring neurological disorders and related health concerns in entire communities and promoting healthy practices and behaviours so as to ensure that populations stay healthy. Although these approaches could be seen as two sides of the same coin, it is hoped that this chapter contributes to the process of building the bridges between public health and neurology and thus serves as a useful guide for the chapters to come.

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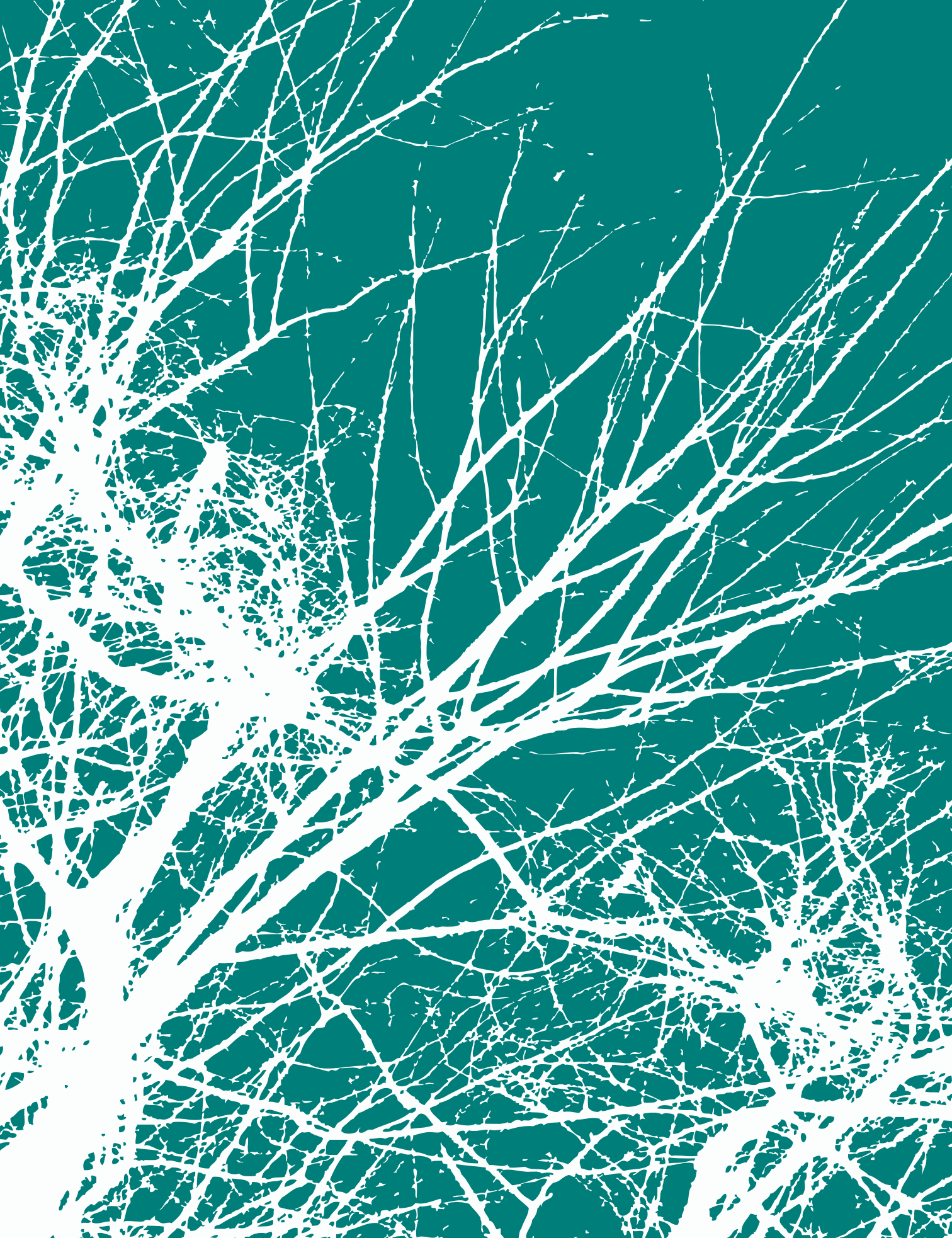


CHAPTER 2

global burden of neurological disorders
estimates and projections

in this chapter

Ever-increasing demand for health services forces health planners to make choices about resource allocation. Information on relative burden of various health conditions and risks to health is an important element in strategic health planning. What is needed to provide this information is a framework for integrating, validating, analysing, and disseminating the fragmentary, and at times contradictory, data that are available on a population's health, along with some understanding of how that population's health is changing over time.

The Global Burden of Disease (GBD) approach is one of the most widely used frameworks for information on summary measures of population health across disease and risk categories. The GBD framework is based on the use of a common metric to summarize the disease burden from diagnostic categories of the International Classification of Diseases and the major risk factors that cause those health outcomes.

GBD STUDIES AND THEIR KEY RESULTS

In 1993, the World Bank, WHO and the Harvard School of Public Health carried out a study to assess the global burden of disease for the year 1990. The methods and findings of the 1990 GBD study have been widely published (*1–3*). To prepare internally consistent estimates of incidence, prevalence, duration and mortality for almost 500 sequelae of the diseases and injuries under consideration, a mathematical model, DisMod, was developed (*4*). The main purpose was to convert partial, often nonspecific, data on disease and injury occurrence into a consistent description of the basic epidemiological parameters.

Many conditions including neuropsychiatric disorders and injuries cause considerable ill-health but no or few direct deaths. Therefore separate measures of survival and of health status among survivors needed to be combined to provide a single, holistic measure of overall population health. To assess the burden of disease, the 1990 GBD study used a time-based metric that measures both premature mortality (years of life lost because of premature mortality or YLL) and disability (years of healthy life lost as a result of disability or YLD, weighted by the severity of the disability). The sum of these two components,

disability-adjusted life years (DALYs), provides a measure of the future stream of healthy life (years expected to be lived in full health) lost as a result of the incidence of specific diseases and injuries (*2*). One DALY can be thought of as one lost year of healthy life and the burden of disease as a measure of the gap between current health status and an ideal situation where everyone lives into old age free from disease and disability.

The results of the 1990 GBD study confirmed that noncommunicable diseases and injuries were a significant cause of health burden in all regions of the world. Neuropsychiatric disorders and injuries in particular were major causes of lost years of healthy life as measured by DALYs, and were significantly underestimated when measured by mortality alone (*2*).

The 1990 GBD study represented a major advance in the quantification of the impact of diseases, injuries and risk factors on population health globally and by region. Government and nongovernmental agencies alike have used these results to argue for more strategic allocations of health resources to disease prevention and control programmes that are likely to yield the greatest gains in terms of population health. Following publication of the initial results of the GBD study, several national applications of its methods were used, which led to substantially more data in the area of descriptive epidemiology of diseases and injuries.

As a follow-up to the 1990 GBD study, WHO undertook a new global assessment of the burden of disease for the year 2000 and subsequent years in 2002. The GBD 2000 study drew on a wide range of data sources to develop internally consistent estimates of incidence, health state prevalence, severity and duration, and mortality for over 130 major causes, for 14 epidemiological subregions of the world (*5*).

Projections of global mortality and burden of disease

In order to address the need for updated projections of mortality and burden of disease by region and cause, updated projections of future trends for mortality and burden of disease between 2002 and 2030 have also been prepared by WHO (*6*). These have been based on methods similar to those used in the original GBD 1990 study, but use the latest available estimates for 2002 and the latest available projections for HIV/AIDS, income, human capital and other inputs (*7*). Relatively simple models were used to project future health trends under various scenarios, based largely on projections of economic and social development, and using the historically observed relationships of these with cause-specific mortality rates.

Rather than attempt to model the effects of the many separate direct determinants or risk factors for diseases from the limited data that are available, the GBD methodology considered a certain number of socioeconomic variables including: average income per capita, measured as gross domestic product (GDP) per capita; average number of years of schooling in adults, referred to as "human capital"; and time, a proxy measure for the impact of technological change on health status. This latter variable captures the effects of accumulating knowledge and technological development, allowing the implementation of more cost-effective health interventions, both preventive and curative, at constant levels of income and human capital. These socioeconomic variables show clear historical relationships with mortality rates, and may be regarded as indirect, or distal, determinants of health. In addition, a fourth variable, tobacco use, was included in the projections for cancer, cardiovascular diseases and chronic respiratory diseases, because of its overwhelming importance in determining trends for these causes.

Projections were carried out at country level, but aggregated into regional or income groups for presentation of results. Baseline estimates at country level for 2002 were derived from the GBD analyses published in *The world health report 2004* (*8*). Mortality estimates were based on analysis of latest available national information on levels of mortality and cause distributions as at late 2003. Incidence, prevalence, duration and severity estimates for conditions were based on the GBD analyses for the relevant epidemiological subregion, together with national and sub-national

level information available to WHO. These baseline estimates represent the best estimates of WHO, based on the evidence available in mid-2004, and have been computed using standard categories and methods to maximize cross-national comparability.

Limitations of the Global Burden of Disease framework

By their very nature, projections of the future are highly uncertain and need to be interpreted with caution. Three limitations are briefly discussed: uncertainties in the baseline data on levels and trends in cause-specific mortality, the "business as usual" assumptions, and the use of a relatively simple model based largely on projections of economic and social development (*9*).

For regions with limited death registration data, such as the Eastern Mediterranean Region, sub-Saharan Africa and parts of Asia and the Pacific, there is considerable uncertainty in estimates of deaths by cause associated with the use of partial information on levels of mortality from sources such as the Demographic and Health Surveys, and from the use of cause-specific mortality estimates for causes such as HIV/AIDS, malaria, tuberculosis and vaccine-preventable diseases. The GBD analyses have attempted to use all available sources of information, together with an explicit emphasis on internal consistency, to develop consistent and comprehensive estimates of deaths and disease burden by cause, age, sex and region.

The projections of burden are not intended as forecasts of what will happen in the future but as projections of current and past trends, based on certain explicit assumptions and on observed historical relationships between development and mortality levels and patterns. The methods used base the disease burden projections largely on broad mortality projections driven to a large extent by World Bank projections of future growth in income per capita in different regions of the world. As a result, it is important to interpret the projections with a degree of caution commensurate with their uncertainty, and to remember that they represent a view of the future explicitly resulting from the baseline data, choice of models and the assumptions made. Uncertainty in projections has been addressed not through an attempt to estimate uncertainty ranges, but through preparation of pessimistic and optimistic projections under alternative sets of input assumptions.

The results depend strongly on the assumption that future mortality trends in poor countries will have the same relationship to economic and social development as has occurred in higher income countries in the recent past. If this assumption is not correct, then the projections for low income countries will be over-optimistic in the rate of decline of communicable and noncommunicable diseases. The projections have also not taken explicit account of trends in major risk factors apart from tobacco smoking and, to a limited extent, overweight and obesity. If broad trends in risk factors are towards worsening of risk exposures with development, rather than the improvements observed in recent decades in many high income countries, then again the projections for low and middle income countries presented here will be too optimistic.

ESTIMATES AND PROJECTIONS FOR NEUROLOGICAL DISORDERS

This document presents the GBD estimates for neurological disorders from the projected estimates for 2005, 2015 and 2030. The complete set of tables is contained in Annex 4.

Cause categories

The cause categories used in the GBD study have four levels of disaggregation and include 135 specific diseases and injuries. At the first level, overall mortality is divided into three broad groups of causes: Group I consists of communicable diseases, maternal causes, conditions arising in the perinatal period and nutritional deficiencies; Group II encompasses the noncommunicable diseases (including neuropsychiatric conditions); and Group III comprises intentional and unintentional injuries. Deaths and health states are categorically attributed to one underlying cause using

the rules and conventions of the International Classification of Diseases. In some cases these rules are ambiguous, in which event the GBD 2000 followed the conventions used in the GBD 1990. It also lists the sequelae analysed for each cause category and provides relevant case definitions.

Methodology

For the purpose of calculation of estimates of the global burden of disease, the neurological disorders are included from two categories: neurological disorders within the neuropsychiatric category, and neurological disorders from other categories. Neurological disorders within the neuropsychiatric category refer to the cause category listed in Group II under neuropsychiatric disorders and include epilepsy, Alzheimer and other dementias, Parkinson's disease, multiple sclerosis and migraine. Neurological disorders from other categories include diseases and injuries which have neurological sequelae and are listed elsewhere in cause category Groups I, II and III (*10*). The complete list used for calculation of GBD estimates for neurological disorders is given in Annex 3. Among the various neurological disorders discussed in this report, please note that for headache disorders, GBD includes migraine only (see Chapter 3.3). Also, GBD does not describe separately the burden associated with pain (see Chapter 3.7). There are also some diseases and injuries, which have neurological sequelae that have not been separately identified by the GBD study, and are not presented in this report; these include tuberculosis, HIV/AIDS, measles, low birth weight, birth asphyxia and birth trauma. The burden estimates for these conditions include the impact of neurological and other sequelae which are not separately estimated.

DATA PRESENTATION

This chapter summarizes data with the important findings presented as charts and maps for DALYs, deaths, YLDs and prevalence as estimated for neurological disorders in the GBD study. The complete set of tables is given in Annex 4. The data are presented for the following variables.

DALYs	Absolute numbers Percentage of total DALYs DALYs per 100 000 population
Deaths	Absolute numbers Percentage of total deaths Deaths per 100 000 population
YLDs	Absolute numbers Percentage of total YLDs YLDs per 100 000 population
Point prevalence	Total number of cases with different neurological disorders Prevalence per 1000 population of individual neurological disorders

Please note that prevalence and YLDs are available for the neurological cause – sequela combinations. These data are therefore provided for all neurological disorders within the neuropsychiatric category, cerebrovascular disease, combined for neuroinfections and neurological sequelae of infections (poliomyelitis, tetanus, meningitis, Japanese encephalitis, syphilis, pertussis, diphtheria, malaria), neurological sequelae associated with nutritional deficiencies and neuropathies (protein–energy malnutrition, iodine deficiency, leprosy, and diabetes mellitus), and neurological sequelae associated with injuries (road traffic accidents, poisonings, falls, fires, drownings, other unintentional injuries, self-inflicted injuries, violence, war, and other intentional injuries) (see Table 2.1).

While YLDs are separately estimated for each sequela, death (and hence YLLs and DALYs) are only estimated at the cause level, and for many causes it is not possible to describe sequela-specific deaths. The tables for DALYs and deaths therefore only describe data for neurological cause categories (Table 2.2).

Table 2.1 Neurological disorder groupings used for YLDs and prevalence data

Neurological disorders in neuropsychiatric category	Disorders/injuries with neurological sequelae in other categories
Epilepsy Alzheimer and other dementias Parkinson's disease Multiple sclerosis Migraine	Cerebrovascular disease Neuroinfections Nutritional deficiencies and neuropathies Neurological injuries

Table 2.2 Neurological disorder groupings used for DALYs and deaths data

Neurological disorders in neuropsychiatric category	Disorders/injuries with neurological sequelae in other categories
Epilepsy Alzheimer and other dementias Parkinson's disease Multiple sclerosis Migraine	Cerebrovascular disease Poliomyelitis Tetanus Meningitis Japanese encephalitis

Regional and income categories

Projections of mortality and burden of disease are summarized according to two groupings of countries, as follows.

- **WHO regions**. WHO Member States are grouped into six regions (Africa, the Americas, South-East Asia, Europe, Eastern Mediterranean and Western Pacific, see http://www.who.int/about/regions/en/index.html). WHO regions are organizational groupings and, while they are largely based on geographical terms, are not synonymous with geographical areas. For further disaggregation of the global burden of disease, the regions have been further divided into 14 epidemiological subregions, based on levels of child (under five years of age) and adult (aged 15–59 years) mortality for WHO Member States (Table 2.3). When these mortality strata are applied to the six WHO regions, they produce 14 mortality subregions. These are listed in Annex 1, together with the WHO Member States in each group.

Table 2.3 Definitions of mortality strata used to define subregions

Mortality stratum	Child mortality	Adult mortality
A	Very low	Very low
B	Low	Low
C	Low	High
D	High	High
E	High	Very high

- **Income categories**. The income categories are based on World Bank estimates of gross national income (GNI) per capita in 2001 (*11*). Each country is classified as low income (GNI US$ 745 or less), lower middle income (GNI US$ 746–2975), upper middle income (GNI US$ 2976–9205), and high income (GNI $ 9206 or more). Annex 2 lists countries according to the World Bank income categories.

The following tables and text describe the estimates for DALYs, deaths and YLDs for neurological disorders as estimated and projected for 2005, 2015 and 2030.

Estimates of disability-adjusted life years (DALYs)

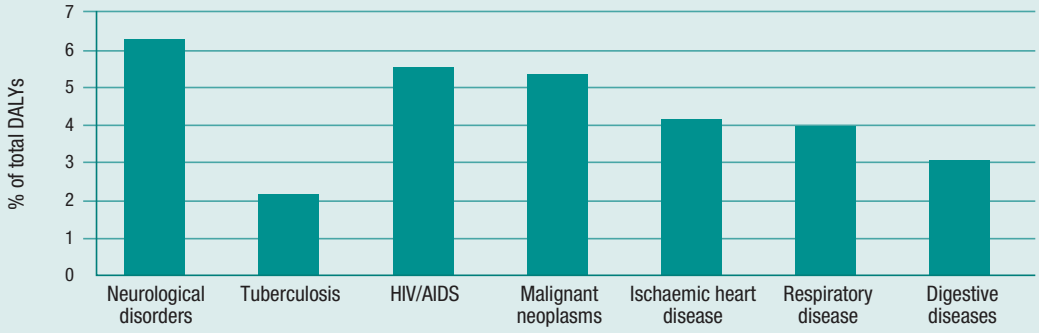
Neurological disorders included in the neuropsychiatric category contribute to 2% of the global burden of disease, while cerebrovascular disease and some of the neuroinfections (poliomyelitis, tetanus, meningitis and Japanese encephalitis) contribute to 4.3% of the global burden of disease in 2005. Thus neurological disorders constitute 6.3% of the global burden of disease (see Table 2.4). The term "neurological disorders" henceforth used in this chapter includes those conditions in the neuropsychiatric category as well as in other categories. Figure 2.1 presents selected diseases as a percentage of total DALYs, in order to compare the burden constituted by them with that of neurological disorders. For example, HIV/AIDS and malignant neoplasm each constitute slightly over 5% of total burden.

Table 2.4 presents the total number of DALYs in thousands associated with neurological disorders and as percentage of total DALYs for 2005, 2015 and 2030. Neurological disorders contribute to 92 million DALYs in 2005 projected to increase to 103 million in 2030 (approximately a 12% increase). While Alzheimer and other dementias are projected to show a 66% increase from 2005 to 2030, there is an estimated 57% decrease in DALYs associated with poliomyelitis, tetanus, meningitis and Japanese encephalitis combined.

Table 2.4 Number of DALYs for neurological disorders and as percentage of global DALYs projected for 2005, 2015 and 2030

Cause category	2005		2015		2030	
	No. of DALYs (000)	Percentage of total DALYs	No. of DALYs (000)	Percentage of total DALYs	No. of DALYs (000)	Percentage of total DALYs
Epilepsy	7308	0.50	7419	0.50	7442	0.49
Alzheimer and other dementias	11078	0.75	13540	0.91	18394	1.20
Parkinson's disease	1617	0.11	1762	0.12	2015	0.13
Multiple sclerosis	1510	0.10	1586	0.11	1648	0.11
Migraine	7660	0.52	7736	0.52	7596	0.50
Cerebrovascular disease	50785	3.46	53815	3.63	60864	3.99
Poliomyelitis	115	0.01	47	0.00	13	0.00
Tetanus	6423	0.44	4871	0.33	3174	0.21
Meningitis	5337	0.36	3528	0.24	2039	0.13
Japanese encephalitis	561	0.04	304	0.02	150	0.01
Total	**92392**	**6.29**	**94608**	**6.39**	**103335**	**6.77**

Figure 2.1 Percentage of total DALYs for selected diseases[a] and neurological disorders[b]



[a] GBD cause categories
[b] Neuropsychiatric plus other categories

Among neurological disorders, more than half of the burden in DALYs is contributed by cerebrovascular disease, 12% by Alzheimer and other dementias and 8% each by epilepsy and migraine (see Figure 2.2).

Neurological disorders contribute to 10.9%, 6.7%, 8.7% and 4.5% of the global burden of disease in high, upper middle, lower middle and low income countries, respectively, in 2005 (see Figure 2.3). The higher burden in the lower middle category reflects the double burden of communicable diseases and noncommunicable diseases. DALYs per 100 000 population for neurological disorders are highest for lower middle and low income countries (1514 and 1448, respectively) as estimated for 2005 (see Table 2.5).

Table 2.5 DALYs per 100 000 population for neurological disorders globally and by World Bank income category, 2005

Cause category	World (100 000 population)	Income category			
		Low	Lower middle	Upper middle	High
Epilepsy	113.4	158.3	80	139.2	51.3
Alzheimer and other dementias	172	90.7	150.7	166.9	457.3
Parkinson's disease	25.1	15.1	19.7	17.5	70.8
Multiple sclerosis	23.4	20.1	23.3	24.9	32.5
Migraine	118.9	114	106.8	147.1	146.3
Cerebrovascular disease	788.4	662.5	1 061.2	612.2	592
Poliomyelitis	1.8	2.6	1.6	0.9	0.6
Tetanus	99.7	228.6	10.8	1.3	0.1
Meningitis	82.9	143.2	51.2	39.7	10.7
Japanese encephalitis	8.7	13	9	0.4	0.6
Total	**1 434.3**	**1 448.1**	**1 514.3**	**1 150.1**	**1 362.2**

As shown in Table 2.6, neurological disorders contribute most to the global burden of disease in the European Region (11.2%) and the Western Pacific Region (10%) compared with 2.9% in the African Region in 2005. DALYs per 100 000 population as estimated for 2005 are highest for Eur-C epidemiological subregion (2920) and lowest for Emr-B (751) (see Figure 2.4).

Figure 2.2 DALYs for individual neurological disorders as percentage of total neurological disorders

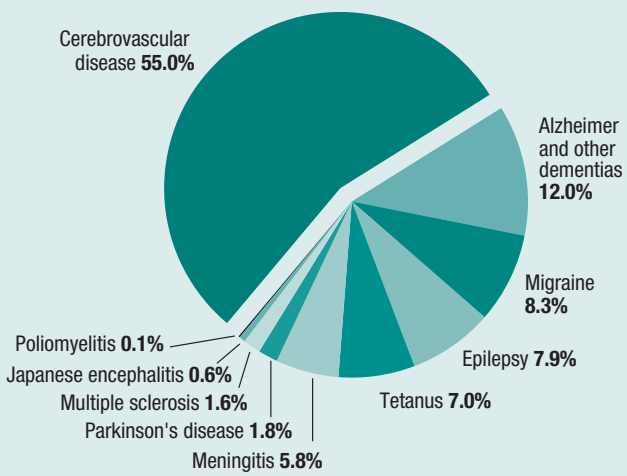


Figure 2.3 Neurological disorders as percentage of total DALYs for 2005, 2015 and 2030 across World Bank income category

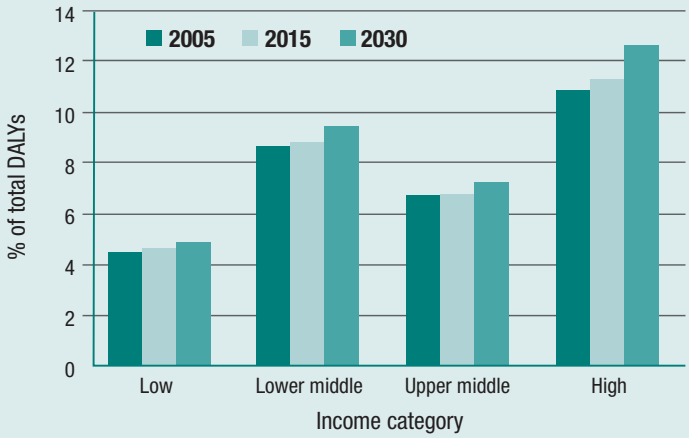
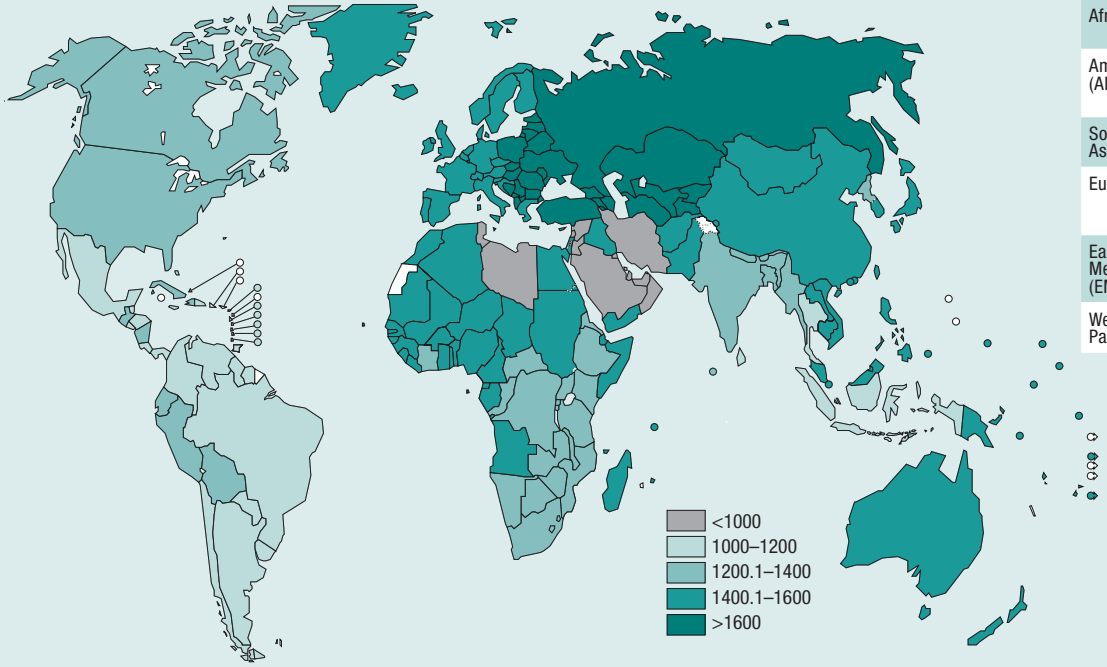


Figure 2.4 DALYs per 100 000 population associated with neurological disorders by WHO region and mortality stratum, 2005



The designations employed and the presentation of material on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dashed lines represent approximate border lines for which there may not yet be full agreement.

WHO 06.154

Region	Mortality stratum	DALYS per 100 000 population for neurological disorders
Africa (AFR)	Afr-D Afr-E	1 536.73 1 361.41
Americas (AMR)	Amr-A Amr-B Amr-D	1 214.18 1 135.56 1 251.09
South-East Asia (SEAR)	Sear-B Sear-D	750.50 1 480.39
Europe (EUR)	Eur-A Eur-B Eur-C	1 463.53 1 665.33 2 920.22
Eastern Mediterranean (EMR)	Emr-B Emr-D	1 089.68 1 377.09
Western Pacific (WPR)	Wpr-A Wpr-B	1 543.28 1 470.80

Table 2.6 Neurological disorders as percentage of total DALYs by WHO region, 2005

Cause category	World (%)	WHO region					
		AFR (%)	AMR (%)	SEAR (%)	EUR (%)	EMR (%)	WPR (%)
Epilepsy	0.50	0.46	0.73	0.46	0.40	0.54	0.44
Alzheimer and other dementias	0.75	0.10	1.47	0.26	2.04	0.42	1.32
Parkinson's disease	0.11	0.02	0.22	0.07	0.30	0.06	0.15
Multiple sclerosis	0.10	0.03	0.17	0.08	0.20	0.09	0.15
Migraine	0.52	0.13	0.97	0.41	0.80	0.51	0.73
Cerebrovascular disease	3.46	1.11	3.10	1.93	7.23	2.69	6.81
Poliomyelitis	0.01	0.00	0.00	0.01	0.00	0.01	0.01
Tetanus	0.44	0.77	0.01	0.81	0.00	0.54	0.10
Meningitis	0.36	0.24	0.39	0.81	0.24	0.43	0.24
Japanese encephalitis	0.04	0.00	0.00	0.05	0.00	0.06	0.09
Total	**6.29**	**2.86**	**7.06**	**4.90**	**11.23**	**5.34**	**10.04**

Estimates of deaths

Neurological disorders are an important cause of mortality and constitute 12% of total deaths globally (see Table 2.7). Within these, cerebrovascular diseases are responsible for 85% of the deaths due to neurological disorders (see Figure 2.5). Neurological disorders constitute 16.8% of the total deaths in lower middle income countries compared with 13.2% of the total deaths in high income countries (Figure 2.6). Among the neurological disorders, Alzheimer and other dementias are estimated to constitute 2.84% of the total deaths in high income countries in 2005. Cerebrovascular disease constitute 15.8%, 9.6%, 9.5% and 6.4% of the total deaths in lower middle, upper middle, high and low income countries respectively (Table 2.8).

Table 2.7 Deaths attributable to neurological disorders as percentage of total deaths, 2005, 2015 and 2030

Cause category	2005 (%)	2015 (%)	2030 (%)
Epilepsy	0.22	0.21	0.19
Alzheimer and other dementias	0.73	0.81	0.92
Parkinson's disease	0.18	0.20	0.23
Multiple sclerosis	0.03	0.03	0.02
Migraine	0.00	0.00	0.00
Cerebrovascular disease	9.90	10.19	10.63
Poliomyelitis	0.00	0.00	0.00
Tetanus	0.33	0.23	0.13
Meningitis	0.26	0.17	0.10
Japanese encephalitis	0.02	0.01	0.01
Total	**11.67**	**11.84**	**12.22**

Figure 2.5 Deaths from selected neurological disorders as percentage of total neurological disorders

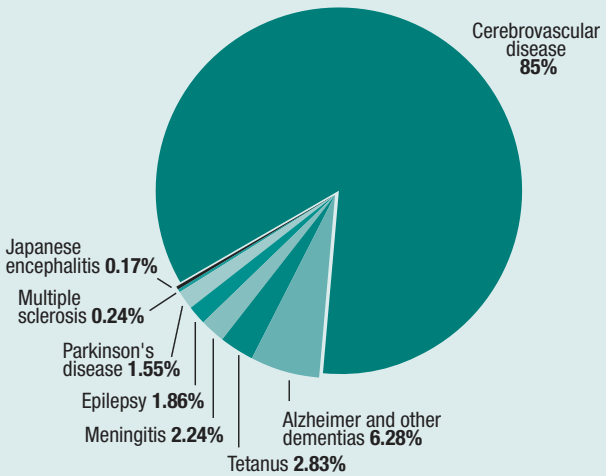


Figure 2.6 Neurological disorders as percentage of total deaths for 2005, 2015 and 2030 across World Bank income category

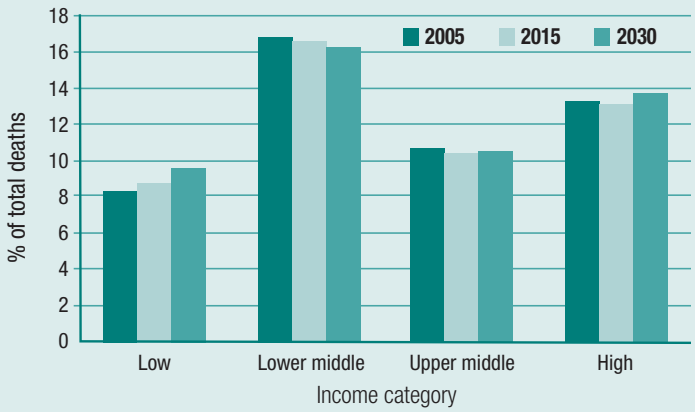


Table 2.8 Deaths attributable to neurological disorders as percentage of total deaths by World Bank income category, 2005

Cause category	World (%)	Income category			
		Low (%)	Lower middle (%)	Upper middle (%)	High (%)
Epilepsy	0.22	0.28	0.17	0.20	0.11
Alzheimer and other dementias	0.73	0.41	0.34	0.46	2.84
Parkinson's disease	0.18	0.06	0.18	0.15	0.60
Multiple sclerosis	0.03	0.01	0.02	0.05	0.10
Migraine	0.00	0.00	0.00	0.00	0.00
Cerebrovascular disease	9.90	6.41	15.81	9.64	9.48
Poliomyelitis	0.00	0.00	0.00	0.00	0.01
Tetanus	0.33	0.64	0.04	0.01	0.00
Meningitis	0.26	0.39	0.18	0.16	0.04
Japanese encephalitis	0.02	0.03	0.01	0.00	0.00
Total	**11.67**	**8.23**	**16.77**	**10.67**	**13.18**

Table 2.9 YLDs per 100 000 population associated with neurological disorders and other diseases and injuries with neurological sequelae and as percentage of total YLDs projected for 2005, 2015 and 2030

Cause category/sequelae	2005		2015		2030	
	YLDs (100 000 population)	Percentage of total YLDs	YLDs (100 000 population)	Percentage of total YLDs	YLDs (100 000 population)	Percentage of total YLDs
Epilepsy	64.7	0.73	60.9	0.73	55.6	0.71
Alzheimer and other dementias	147.4	1.66	165.4	1.98	203.9	2.60
Parkinson's disease	17.7	0.20	17.3	0.21	17.1	0.22
Multiple sclerosis	20	0.23	19.3	0.23	18.4	0.23
Migraine	118.9	1.34	108.9	1.31	96	1.22
Cerebrovascular disease	176.8	2.00	174.9	2.10	177.8	2.27
Neuroinfections	98.4	1.11	71.8	0.86	45.6	0.58
Nutritional deficiencies and neuropathies	194.9	2.20	174.3	2.09	133.9	1.71
Neurological injuries	425.4	4.80	393.5	4.72	360.8	4.60
Total	**1264.2**	**14.27**	**1186.3**	**14.23**	**1109.1**	**14.14**

Estimates of years of healthy life lost as a result of disability (YLDs)

Table 2.9 describes the estimates for YLDs per 100 000 population associated with neurological disorders and other diseases and injuries with neurological sequelae and as percentage of totals projected for 2005, 2015 and 2030 in the world. The number of YLDs per 100 000 population

associated with neurological disorders and other diseases and injuries with neurological sequelae is projected to decline from 1264 in 2005 to 1109 in 2030. This decline is expected to be attributable to a decrease in YLDs associated with cerebrovascular disease, neuroinfections, nutritional deficiencies and neuropathies, and neurological injuries. YLDs associated with Alzheimer and other dementias, however, are projected to increase by 38%. When expressed as a percentage of the total, YLDs associated with neurological disorders and other diseases and injuries with neurological sequelae comprise 14% of the total in 2005 and are projected to remain the same by 2030.

Figure 2.7 presents the top five categories of YLDs per 100 000 population globally and for World Bank income categories. YLDs per 100 000 population for neuroinfections, and the nutritional deficiencies and neuropathies category are highest for low income countries, while for neurological injuries, epilepsy and migraine, they are highest in upper middle income countries. For Alzheimer and other dementias, they are highest for high income countries. For cerebrovascular disease, YLDs are similar in lower middle and high income countries, demonstrating the epidemiological transition taking place in the lower middle income group of countries. Figure 2.8 demonstrates that almost half of the burden in terms of YLDs attributable to neurological disorders is in low income countries followed by lower middle income countries (31.7%). The higher burden is also a reflection of a higher percentage of population in low and lower middle income countries.

CONCLUSIONS

Burden of disease analyses as presented above are useful for informing health policy. They help in identifying not only the fatal but also the nonfatal outcomes for diseases that are especially important for neurological disorders. The above analyses demonstrate that neurological disorders cause a substantial burden because of noncommunicable conditions such as cerebrovascular disease, Alzheimer and other dementias as well as communicable conditions such as meningitis and Japanese encephalitis. As a group they cause a much higher burden than digestive diseases, respiratory diseases and malignant neoplasms.

The GBD framework provides a common denominator that can be used to judge progress over time within a single country or region or relative performance across countries and regions. It is clearly demonstrated, by comparing 2005 data with the previous GBD study (*2*), that neurological disorders continue to represent a significant burden. The GBD framework, for all its limitations,

Figure 2.7 Top five causes of YLDs among neurological disorders, by World Bank income category, 2005

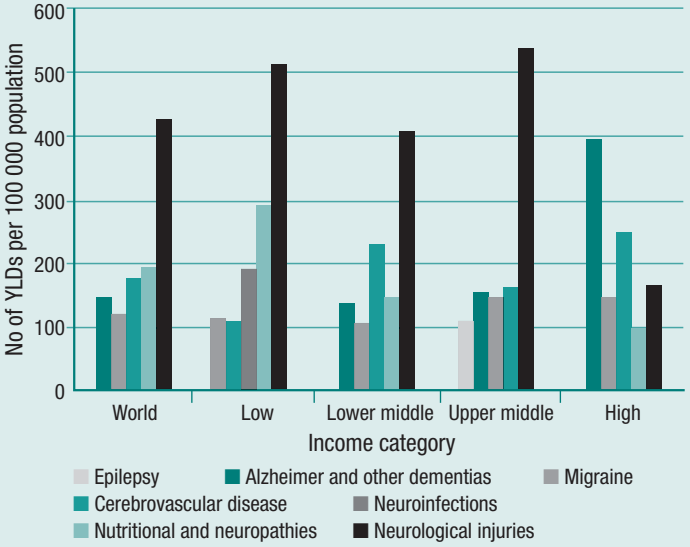
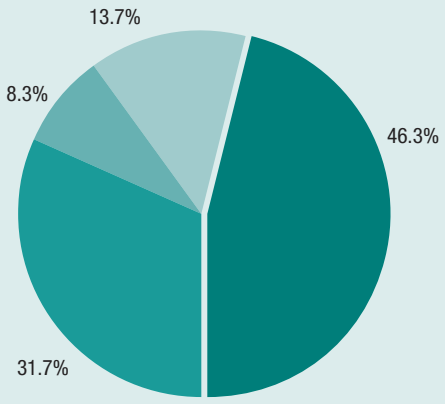


Figure 2.8 YLDs associated with neurological disorders by World Bank income category, 2005



Income category	World population (%)
Low	41.9
Lower middle	35.2
Upper middle	8.2
High	14.7

is a useful approach for projecting future trends of mortality and burden of disease, which help in planning the strategy for control and prevention of diseases. A clear message emerges from the projections discussed in this chapter that — unless immediate action is taken globally — the neurological burden will continue to remain a serious threat to public health.

The double burden of communicable and noncommunicable neurological disorders in low and middle income countries needs to be kept in mind when formulating the policy for neurological disorders in these countries. In absolute terms, since most of the burden attributable to neurological disorders is in low and lower middle income countries, international efforts need to concentrate on these countries for maximum impact. Also the burden is particularly devastating in poor populations. Some of the impact on poor people includes the loss of gainful employment, with the attendant loss of family income; the requirement for caregiving, with further potential loss of wages; the cost of medications; and the need for other medical services.

The above analysis is useful in identifying priorities for global, regional and national attention. Some form of priority setting is necessary as there are more claims on resources than there are resources available. Traditionally, the allocation of resources in health organizations tends to be conducted on the basis of historical patterns, which often do not take into account recent changes in epidemiology and relative burden as well as recent information on the effectiveness of interventions. This can lead to suboptimal use of the limited resources. Economic evaluations consider marginal costs and benefits and use outcome measures such as DALYs to inform decisions. For example, phenobarbital is by far the most cost-effective intervention for managing epilepsy and therefore needs to be recommended for widespread use in public health campaigns against epilepsy in low and middle income countries. A population-level analysis of cost-effectiveness of first-line antiepileptic drug treatment is illustrated in the discussion on epilepsy (Chapter 3.2). Aspirin is the most cost-effective intervention both for treating acute stroke and for preventing a recurrence. It is easily available in developing countries, even in rural areas (*12*). The disease-specific sections discuss in detail the various public health issues associated with neurological disorders. This chapter strengthens the evidence provided earlier that increased resources are needed to improve services for people with neurological disorders. It is also hoped that analyses such as the above will be adopted as an essential component of decision-making and will be adapted to planning processes at global, regional and national levels, so as to utilize the available resources more efficiently.

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RECOMMENDED READING

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CHAPTER 3

neurological disorders
a public health approach

in this chapter	
42	3.1 Dementia
56	3.2 Epilepsy
70	3.3 Headache disorders
85	3.4 Multiple sclerosis
95	3.5 Neuroinfections
111	3.6 Neurological disorders associated with malnutrition
127	3.7 Pain associated with neurological disorders
140	3.8 Parkinson's disease
151	3.9 Stroke
164	3.10 Traumatic brain injuries

This chapter consists of 10 sections that focus on the public health aspects of the common neurological disorders as outlined in the box. Although notable differences exist between relevant public health issues for each neurological disorder, most sections cover the following topics: diagnosis and classification; etiology and risk factors; course and outcome; magnitude (prevalence, incidence, distribution by age and sex, global and regional distribution); disability and mortality; burden on patients' families and communities; treatment, management and rehabilitation; delivery and cost of care; gaps in treatment and other services; policies; research; and education and training.

3.1 Dementia

Dementia is a syndrome caused by disease of the brain, usually of a chronic or progressive nature, in which there is disturbance of multiple higher cortical functions, including memory, thinking, orientation, comprehension, calculation, learning capacity, language and judgement. Consciousness is not clouded. Dementia mainly affects older people: only 2% of cases start before the age of 65 years. After this the prevalence doubles with every five-year increment in age. Dementia is one of the major causes of disability in later life.

There are very many underlying causes of dementia. Alzheimer's disease (AD), characterized by cortical amyloid plaques and neurofibrillary tangles is the most common, accounting for one half to three quarters of all cases. Vascular dementia (VaD) is diagnosed when the brain's supply of oxygenated blood is repeatedly disrupted by strokes or other blood vessel pathology, leading to significant accumulated damage to brain tissue and function. The distinction between AD and VaD has been called into question, given that mixed pathologies are very common. Perhaps vascular damage is no more than a cofactor accelerating the onset of clinically significant symptoms in people with AD. There are a few rare causes of dementia that may be treated effectively by timely medical or surgical intervention— these include hypercalcaemia, subdural haematoma, normal pressure hydrocephalus, and deficiencies of thyroid hormone, vitamin B12 and folic acid. For the most part, altering the progressive course of the disorder is unfortunately not possible. Symptomatic treatments and support can, however, transform the outcome for people with dementia and their caregivers.

Alzheimer and other dementias have been reliably identified in all countries, cultures and races in which systematic research has been carried out, though levels of awareness vary enormously. In India, for example, while the syndrome is widely recognized and named, it is not seen as a medical condition. Indeed, it is often regarded as part of normal ageing (*1*).

For the purpose of making a diagnosis, clinicians focus in their assessments upon impairment in memory and other cognitive functions, and loss of independent living skills. For carers and, arguably, for people with dementia, it is the behavioural and psychological symptoms of dementia (BPSD) that are most relevant. Nearly all studies indicate that BPSD are an important cause of caregiver strain. They are a common reason for institutionalization as the family's coping reserves become exhausted. Problem behaviours may include agitation, aggression, calling out repeatedly, sleep disturbance (day–night reversal), wandering and apathy. Common psychological symptoms include anxiety, depression, delusions and hallucinations. BPSD occur most commonly in the middle stage of dementia (see also the section on Course and outcome, below). Despite their significance, there has been relatively little research into BPSD across cultures. One might anticipate that cultural and environmental factors could have a strong influence upon both the expression

of BPSD and their perception by caregivers as problematic (*2*). Behavioural and psychological symptoms appear to be just as common in dementia sufferers in developing countries (*3*). In some respects the developing country caregivers were more disadvantaged. Given the generally low levels of awareness about dementia as an organic brain condition, family members could not understand their relative's behaviour, and others tended to blame the carers for the distress and disturbance of the person they were looking after.

ETIOLOGY AND RISK FACTORS

The main risk factor for most forms of dementia is advanced age, with prevalence roughly doubling every five years over the age of 65 years. Onset before this age is very unusual and, in the case of AD, often suggests a genetic cause. Single gene mutations at one of three loci (beta amyloid precursor protein, presenilin1 and presenilin2) account for most of these cases. For late-onset AD both environmental (lifestyle) and genetic factors are important. A common genetic polymorphism, the apolipoprotein E (apoE) gene e4 allele greatly increases risk of going on to suffer from dementia; up to 25% of the population have one or two copies (*4, 5*). However, it is not uncommon for one identical twin to suffer from dementia and the other not. This implies a strong influence of the environment (*6*). Evidence from cross-sectional and case–control studies suggests associations between AD and limited education (*7*) and head injury (*8, 9*), which, however, are only partly supported by longitudinal (follow-up) studies (*10*). Depression is a risk factor in short-term longitudinal studies, but this may be because depression is an early presenting symptom rather than a cause of dementia (*11*). Recent research suggests that vascular disease predisposes to AD as well as to VaD (*12*). Smoking seems to increase the risk for AD as well as VaD (*13*). Long-term follow-up studies show that high blood pressure (*14, 15*) and high cholesterol levels (*15*) in middle age each increase the risk of going on to develop AD in later life.

Reports from epidemiological studies of protective effects of certain prescribed medication, non-steroidal anti-inflammatory drugs, hormone replacement therapy (HRT) and cholesterol-lowering therapies are now being investigated in randomized controlled trials. The randomized controlled trial of HRT in postmenopausal women indicated, against expectation, that it increased rather than lowered the incidence of dementia.

Despite many investigations, far too little is still understood about the environmental and lifestyle factors linked to AD and other dementias. It may be that the focus on research in developed countries has limited possibilities to identify risk factors. Prevalence and incidence of AD seem to be much lower in some developing regions (see the section on Epidemiology and burden, below). This may be because some environmental risk factors are much less prevalent in these settings. For example, African men tend to be very healthy from a cardiovascular point of view with low cholesterol, low blood pressure and low incidence of heart disease and stroke. Conversely, some risk factors may only be apparent in developing countries, as they are too infrequent in the developed economies for their effects to be detected; for example, anaemia has been identified as a risk factor in India (*16*).

COURSE AND OUTCOME

Dementia is usually a progressive disease and can be cured only if a reversible condition is identified as a cause and treated effectively. This happens in a small number of cases in the developed world, but could be more common in developing countries, where relevant underlying physical conditions (including marked nutritional and hormonal deficiencies) are more common.

Dementia affects every person in a different way. Its impact can depend on what the individuals were like before the disease: their personality, lifestyle, significant relationships and physical health.

The problems linked to dementia can be best understood in three stages (see Box 3.1.1).

Times are given as guidelines only — sometimes people can deteriorate more quickly and sometimes more slowly. Dementia reduces the lifespan of affected persons. In the developed, high income countries, a person with dementia can expect to live for approximately 5–7 years after diagnosis. In low and middle income countries, diagnosis is often much delayed, and survival in any case may be shorter. Again, of course, there is much individual variation — some may live for longer, and some may live for shorter times because of interacting health conditions.

Symptoms of dementia in early, middle and late stage of the disease are given in Box 3.1.1. It should be noted that not all persons with dementia will display all the symptoms. Nevertheless, a summary of this kind can help caregivers to be aware of potential problems and can allow them to think about future care needs. At the same time, one must not alarm people in the early stages of the disease by giving them too much information.

EPIDEMIOLOGY AND BURDEN

In 2005, Alzheimer's Disease International commissioned a panel of experts to review all available epidemiological data and reach a consensus estimate of prevalence in each region and the numbers of people affected. Evidence from well-conducted, representative epidemiological surveys was lacking in many regions. The panel estimated that, globally, 24.3 million people have dementia today, with 4.6 million new cases annually. Numbers of people affected will double every 20 years to 81.1 million by 2040. Most people with dementia live in developing countries: 60% in 2001 rising to an estimated 71% by 2040. Rates of increase are not uniform; numbers in developed countries are forecast to increase by 100% between 2001 and 2040, but by more than 300% in China, India and neighbouring countries in South-East Asia and the Western Pacific. The detailed estimates contained

Box 3.1.1 Stages and symptoms of dementia (Alzheimer's disease)

Early stage

The early stage is often overlooked. Relatives and friends (and sometimes professionals as well) see it as "old age", just a normal part of the ageing process. Because the onset of the disease is gradual, it is difficult to be sure exactly when it begins. The person may:

- have problems talking properly (language problems)
- have significant memory loss — particularly for things that have just happened
- not know the time of day or the day of the week
- become lost in familiar places
- have difficulty in making decisions
- become inactive and unmotivated
- show mood changes, depression or anxiety
- react unusually angrily or aggressively on occasion
- show a loss of interest in hobbies and activities

Middle stage

As the disease progresses, limitations become clearer and more restricting. The person with dementia has difficulty with day-to-day living and:

- may become very forgetful, especially of recent events and people's names
- can no longer manage to live alone without problems
- is unable to cook, clean or shop
- may become extremely dependent on family members and caregivers
- needs help with personal hygiene, i.e. washing and dressing
- has increased difficulty with speech
- shows problems with wandering and other behaviour problems such as repeated questioning and calling out, clinging and disturbed sleeping
- becomes lost at home as well as outside
- may have hallucinations (seeing or hearing things that are not there)

Late stage

The late stage is one of nearly total dependence and inactivity. Memory disturbances are very serious and the physical side of the disease becomes more obvious. The person may:

- have difficulty eating
- be incapable of communicating
- not recognize relatives, friends and familiar objects
- have difficulty understanding what is going on around them
- be unable to find his or her way around in the home
- have difficulty walking
- have difficulty swallowing
- have bladder and bowel incontinence
- display inappropriate behaviour in public
- be confined to a wheelchair or bed

in this document (*17*) constitute the best available basis for policy-making, planning and allocation of health and welfare resources.

There is a clear and general tendency for prevalence to be somewhat lower in developing countries than in the industrialized world (*18*), strikingly so in some studies (*19, 20*). This trend was supported by the consensus judgement of the expert panel convened by Alzheimer's Disease International, reviewing all available evidence (*17*). It does not seem to be explained merely by differences in survival, as estimates of incidence are also much lower than those reported in developed countries (*21, 22*). It may be that mild dementia is underdetected in developing countries because of difficulties in establishing the criterion of social and occupational impairment. Differences in level of exposure to environmental risk factors might also have contributed. The strikingly different patterns of mortality in early life might also be implicated; older people in very poor countries are exceptional survivors — this characteristic may also confer protection against AD and other dementias.

Long-term studies from Sweden and the United States of America suggest that the age-specific prevalence of dementia has not changed over the last 30 or 40 years (*23*). Whatever the explanation for the current discrepancy between prevalence in developed and developing countries, it seems probable that, as patterns of morbidity and mortality converge with those of the richer countries, dementia prevalence levels will do likewise, leading to an increased burden of dementia in poorer countries.

Studies in developed countries have consistently reported AD to be more prevalent than VaD. Early surveys from South-East Asia provided an exception, though more recent work suggests this situation has now reversed. This may be due to increasing longevity and better physical health: AD, whose onset is in general later than that of VaD, increases as the number of very old people increases, while better physical health reduces the number of stroke sufferers and thus the number with VaD. This change also affects the sex distribution among dementia sufferers, increasing the number of females and reducing the number of males.

Disability, burden and cost

Dementia is one of the main causes of disability in later life. In a wide consensus consultation for the Global Burden of Disease (GBD) report, disability from dementia was accorded a higher weight than that for almost any other condition, with the exception of spinal cord injury and terminal cancer. Of course, older people are particularly likely to have multiple health conditions — chronic physical diseases affecting different organ systems, coexisting with mental and cognitive disorders. Dementia, however, has a disproportionate impact on capacity for independent living, yet its global public health significance continues to be underappreciated and misunderstood. According to the GBD estimates in *The world health report 2003*, dementia contributed 11.2% of all years lived with disability among people aged 60 years and over: more than stroke (9.5%), musculoskeletal disorders (8.9%), cardiovascular disease (5.0%) and all forms of cancer (2.4%). However, the research papers (since 2002) devoted to these chronic disorders reveal a starkly different ordering of priorities: cancer 23.5%, cardiovascular disease 17.6%, musculoskeletal disorders 6.9%, stroke 3.1% and dementia 1.4%.

The economic costs of dementia are enormous. These can include the costs of "formal care" (health care, social and community care, respite care and long-term residential or nursing-home care) and "informal care" (unpaid care by family members, including their lost opportunity to earn income).

In the United Kingdom, direct formal care costs alone have been estimated at US$ 8 billion, or US$ 13 000 per patient. In the United States, costs have been estimated at US$ 100 billion per year, with patients with severe dementia costing US$ 36 794 each (1998 prices) (*23, 24*). A more recent estimate is of US$ 18 billion annually in the United States for informal costs alone. In developed

countries, costs tend to rise as dementia progresses. When people with dementia are cared for at home, informal care costs may exceed direct formal care costs. As the disease progresses, and the need for medical staff involvement increases, formal care costs will increase. Institutionalization is generally the biggest single contributor to costs of care.

Very little work has been done on evaluating the economic costs of dementia in developing countries. Shah et al. (*25*) list five reasons for this: the absence of trained health economists, the low priority given to mental health, the poorly developed state of mental health services, the lack of justification for such services, and the absence of data sets. Given the inevitability that the needs of frail older persons will come to dominate health and social care budgets in these regions, more data are urgently needed.

Detailed studies of informal costs outside western Europe and North America are rare, but a careful study of a sample of 42 AD patients in Denizli, Turkey, provides interesting data (*26*). Formal care for the elderly was rare: only 1% of old people in Turkey live in residential care. Families therefore provide most of the care. The average annual cost of care (excluding hospitalization) was US$ 4930 for severe cases and US$ 1766 for mild ones. Most costs increased with the severity of the disease, though outpatient costs declined. Carers spent three hours a day looking after the most severely affected patients.

The 10/66 Dementia Research Group also examined the economic impact of dementia in its pilot study of 706 persons with dementia and their caregivers living in China, India, Latin America and Nigeria (*27*). The key findings from this study are summarized in Box 3.1.2.

TREATMENT AND CARE

Early diagnosis is helpful so that the caregiver can be better equipped to deal with the disease and to know what to expect. A diagnosis is the first step towards planning for the future. There is no simple test to make a diagnosis. The diagnosis of AD is made by taking a careful account of the person's problems from a close relative or friend, together with an examination of the person's physical and mental state. It is important to exclude other conditions or illnesses that cause memory loss, including depression, alcohol problems and some physical illnesses with organic brain effects.

Currently there are no treatments that cure dementia. There is, however, evidence that drugs (cholinesterase inhibitors), in some cases but not all, temporarily decelerate the progressive cognitive decline that occurs in AD, and maybe in other forms of neurodegenerative dementia. These drugs act on the symptoms but not on the disease itself; they make only a small contribution to maintaining function. Evidence-based drug therapies are available for psychological symptoms such as depression, anxiety, agitation, delusions and hallucinations that can occur in people with dementia. There are modestly effective drugs (neuroleptics) available for the treatment of associated behavioural problems such as agitation. All of these drugs should be used with caution (the doctrine being "start low, go slow"), particularly tricyclic antidepressants (because of anticholinergic side-effects, therefore SSRI antidepressants — selective serotonin reuptake inhibitors — should always be preferred) and neuroleptics (because of anticholinergic side-effects, sedation, and an increased risk of stroke and higher all-cause mortality).

It is important to recognize that non-drug interventions are often highly effective, and should generally be the first choice when managing behavioural problems. The first step is to try to identify and treat the cause, which could be physical, psychological or environmental. Psychosocial interventions, particularly the provision of information and support to carers, have been shown to reduce the severe psychological distress often experienced by carers. Carers are also greatly assisted by a network of community health and social services; self-help organizations, especially Alzheimer associations, can also help them to find appropriate help. Carers can be educated about

dementia, countering lack of understanding and awareness about the nature of the problems faced. They can also be trained to manage better most of the common behavioural symptoms, in such a way that the frequency of the symptoms and/or the strain experienced by the carer is reduced. Above all, the person with dementia and the family carers need to be supported over the longer term. People with dementia need to be treated at all times with patience and respect for their dignity and personhood; carers needs unconditional support and understanding — their needs should also be determined and attended to.

Resources and prevention

Developing-country health services are generally ill-equipped to meet the needs of older persons. Health care, even at the primary care level, is clinic-based; the older person must attend the clinic, often involving a long journey and waiting time in the clinic, to receive care. Even if they can get to the clinic the assessment and treatment that they receive are orientated towards acute rather than chronic conditions. The perception is that the former are treatable, the latter intractable and not within the realm of responsibility of health services. The 10/66 Dementia Research Group's caregiver pilot study in 2004 indicated that people with dementia were using primary and secondary care health services. Only 33% of people with dementia in India, 11% in China and South-East Asia and 18% in Latin America had used no health services at all in the previous three months. In all centres, particularly in India and Latin America, there was heavy use of private medical services. One may speculate that this reflects the caregivers' perception of the relative unresponsiveness of the cheaper government medical services.

The gross disparities in resources within and between developed and developing countries are leading to serious concerns regarding the flouting of the central ethical principle of distributive justice. New drug treatments are very expensive. Anticholinesterase therapies for AD are beyond the reach of all but the richest families in most developing countries. The same would be true for most SSRI antidepressants and "atypical" antipsychotic drugs, both of which are generally favoured in the West for use in older patients over the older and cheaper tricyclic antidepressants and "typical" antipsychotic drugs because of their better safety and side-effect profiles. The advent of a disease-modifying, as opposed to symptomatic, treatment for AD would introduce similar ethical concerns regarding accessibility to those that have arisen in relation to the management of HIV/AIDS in low income countries. Equity is also an important issue within developing countries. Access to care is often entirely dependent upon means to pay. Quite apart from economic constraints, health-care resources are grossly unevenly distributed between rural and urban districts. Most specialists, indeed most doctors, work in cities. Provision of even basic services to far-flung rural communities is an enormous challenge.

Box 3.1.2 The 10/66 Dementia Research Group: key findings

From the development perspective, one of the key findings from the study was that caregiving in the developing world is associated with substantial economic disadvantage. A high proportion of caregivers had to cut back on their paid work in order to care. Many caregivers needed and obtained additional support, and while this was often informal unpaid care from friends and other family members, paid caregivers were also relatively common.

People with dementia were heavy users of health services, and associated direct costs were high. Compensatory financial support was negligible; few older people in developing countries receive government or occupational pensions, and virtually none of the people with dementia in the 10/66 study received disability pensions.

Caregivers were commonly in paid employment, and almost none received any form of caring allowance. The combination of reduced family incomes and increased family expenditure on care is obviously particularly stressful in lower income countries where so many households exist at or near subsistence level. While health-care services are cheaper in low income countries, in relative terms families from the poorer countries spend a greater proportion of their income on health care for the person with dementia. They also appear to be more likely to use the more expensive services of private doctors, in preference to government-funded primary care, presumably because this fails to meet their needs.

Source: (*1*).

Future development of services for older people needs to be tailored to suit the health systems context. "Health systems" here can be taken to include macroeconomic factors, social structures, cultural values and norms, and existing health and welfare policy and provision.

Specialists — neurologists, psychiatrists, psychologists and geriatricians — are far too scarce a resource to take on any substantial role in the first-line care for people with dementia. The focus must be upon primary care. Many developing countries have in place comprehensive community-based primary care systems staffed by doctors, nurses and generic multipurpose health workers. The need is for:

- more training in the basic curriculum regarding diagnostic and needs-based assessments;
- a paradigm shift beyond the current preoccupation with prevention and simple curative interventions to encompass long-term support and chronic disease management;
- outreach care, assessing and managing patients in their own homes.

For many low income countries, the most cost-effective way to manage people with dementia will be through supporting, educating and advising family caregivers. This may be supplemented by home nursing or paid home-care workers; however, to date most of the growth in this area has been that of untrained paid carers operating in the private sector. The direct and indirect costs of care in this model therefore tend to fall upon the family. Some governmental input, whether in terms of allowances for people with dementia and/or caregivers or subsidized care would be desirable and equitable. The next level of care to be prioritized would be respite care, both in day centres and (for longer periods) in residential or nursing homes. Such facilities (as envisaged in Goa, for example) could act also as training resource centres for caregivers. Day care and residential respite care are more expensive than home care, but nevertheless basic to a community's needs, particularly for people with more advanced dementia.

Residential care for older people is unlikely to be a priority for government investment, when the housing conditions of the general population remain poor, with homelessness, overcrowding and poor sanitation. Nevertheless, even in some of the poorest developing countries (e.g. China and India), nursing and residential care homes are opening up in the private sector to meet the demand from the growing affluent middle class. Good quality, well-regulated residential care has a role to play in all societies, for those with no family support or whose family support capacity is exhausted, both as temporary respite and for provision of longer-term care. Absence of regulation, staff training and quality assurance is a serious concern in developed and developing countries alike.

Similarly, low income countries lack the economic and human capital to contemplate widespread introduction of more sophisticated services; specialist multidisciplinary staff and community services backed up with memory clinics and outpatient, inpatient and day care facilities. Nevertheless, services comprising some of these elements are being established as demonstration projects. The ethics of health care require that governments take initial planning steps, now. The one certainty is that "in the absence of clear strategies and policies, the old will absorb increasing proportions of the resources devoted to health care in developing countries" (*28*). This shift in resource expenditure is, of course, likely to occur regardless. At least, if policies are well formulated, its consequences can be predicted and mitigated.

Prevention, where it can be achieved, is clearly the best option, with enormous potential benefits for the quality of life of the individual, the family and carers, and for society as a whole. Primary preventive interventions can be highly cost effective, given the enormous costs associated with the care and treatment of those with dementia (see the section on Disability, burden and cost, above). The primary prevention of dementia is therefore a relatively neglected area. Evidence from the developed world suggests that risk factors for vascular disease, including hypertension, smoking, type II diabetes, and hypercholesterolaemia may all be risk factors for AD as well as VaD. The epidemic of smoking in developing countries (with 13% of African teenagers currently

smoking), and the high and rising prevalence of type II diabetes in South-East Asia (a forecast 57% increase in prevalence between 2000 and 2010, compared with a 24% increase in Europe) should therefore be particular causes of concern. It is as yet unclear whether the improvements in control of hypertension, diet and exercise, and particularly the decline in smoking seen in developed Western countries that has led to rapid declines in mortality from ischaemic heart disease and stroke, will lead to a later decline in the age-specific incidence of AD and other dementias. Many of these preventive measures are also likely to improve general health (*29*).

Delivery of care

All over the world the family remains the cornerstone of care for older people who have lost the capacity for independent living, whether as a result of dementia or other mental disorder. However, stereotypes abound and have the potential to mislead. Thus, in developed countries with their comprehensive health and social care systems, the vital caring role of families, and their need for support, is often overlooked. This is true for example in the United Kingdom, where despite nuclear family structures and contrary to supposition, there is a strong tradition that persists today for local children to provide support for their infirm parents. Conversely, in developing countries the reliability and universality of the family care system is often overestimated. Older people are among the most vulnerable groups in the developing world, in part because of the continuing myths that surround their place in society (*30*). It is often assumed that their welfare is assured by the existence of the extended family. Arguably, the greatest obstacle to providing effective support and care for older persons is the lack of awareness of the problem among policy-makers, health-care providers and the community. Mythologizing the caring role of the family evidently carries the risk of perpetuating complacency.

The previously mentioned 10/66 Dementia Research Group's multicentre pilot study was the first systematic, comprehensive assessment of care arrangements for people with dementia in the developing world, and of the impacts upon their family caregivers (*27*). As in the EUROCARE study with data from 14 European countries (*31*), most caregivers in developing countries were older women caring for their husbands or younger women caring for a parent. Caring was associated with substantial psychological strain as evidenced by high rates of psychiatric morbidity and high levels of caregiver strain. These parameters were again very similar to those reported in the EUROCARE study. Some aspects, however, were radically different. People with dementia in developing countries typically live in large households, with extended families. Larger families were associated with lower caregiver strain; however, this effect was small and applied only where the principal caregiver was co-resident. Indeed, it seemed to operate in the opposite direction where the caregiver was non-resident, perhaps because of the increased potential for family conflict.

In many developing countries, traditional family and kinship structures are widely perceived as under threat from the social and economic changes that accompany economic development and globalization (*30*). Some of the contributing factors include the following:

- Changing attitudes towards older people.
- The education of women and their increasing participation in the workforce (generally seen as key positive development indicators); tending to reduce both their availability for caregiving and their willingness to take on this additional role.
- Migration. Populations are increasingly mobile as education, cheap travel and flexible labour markets induce young people to migrate to cities and abroad to seek work. In India, Venkoba Rao has coined an acronym to describe this growing social phenomenon: PICA — parents in India, children abroad. "Push factors" are also important. In the economic catastrophe of the 1980s, two million Ghanaians left the country in search of economic betterment; 63% of older persons have lost the support of one or more of their children who have migrated to distant places in Ghana or abroad. Older people are particularly vulnerable after displacement as a result of war or natural disaster.

- Declining fertility in the course of the final demographic transition. Its effects are perhaps most evident in China, where the one-child family law leaves increasing numbers of older people, particularly those with a daughter, bereft of family support.
- In sub-Saharan Africa, changing patterns of morbidity and mortality are more relevant; the ravages of the HIV/AIDS epidemic have "orphaned" parents as well as children, as bereaved older persons are robbed of the expectation of economic and practical support into later life.

A PUBLIC HEALTH FRAMEWORK

At its 20th annual conference held in Kyoto, Japan, Alzheimer's Disease International released a Kyoto Declaration, benchmarking progress in ten key areas using a public health framework developed by WHO (see Table 3.1.1). The framework addresses treatment gaps, policies, research and training and identifies three levels of attainment for countries with low, medium and high levels of resources, hence suggesting a feasible, pragmatic series of actions and objectives for health systems at all levels of development.

Table 3.1.1 Minimum actions required for dementia care[a]

Ten overall recommendations	Scenario A Low level of resources	Scenario B Medium level of resources	Scenario C High level of resources
1. Provide treatment in primary care	Recognize dementia care as a component of primary health care Include the recognition and treatment of dementia in training curricula of all health personnel Provide refresher training to primary care physicians (at least 50% coverage in five years)	Develop locally relevant training materials Provide refresher training to primary care physicians (100% coverage in five years)	Improve effectiveness of management of dementia in primary health care Improve referral patterns
2. Make appropriate treatments available	Increase availability of essential drugs for the treatment of dementia and associated psychological and behavioural symptoms Develop and evaluate basic educational and training interventions for caregivers	Ensure availability of essential drugs in all health-care settings Make effective caregiver interventions generally available	Provide easier access to newer drugs (e.g. anticholinesterase agents) under public or private treatment plans
3. Give care in the community	Establish the principle that people with dementia are best assessed and treated in their own homes Develop and promote standard needs assessments for use in primary and secondary care Initiate pilot projects on development of multidisciplinary community care teams, day care and short-term respite care Move people with dementia out of inappropriate institutional settings	Initiate pilot projects on integration of dementia care with general health care Provide community care facilities (at least 50% coverage with multidisciplinary community teams, day care, respite and inpatient units for acute assessment and treatment) According to need, encourage the development of residential and nursing-home facilities, including regulatory framework and system for staff training and accreditation	Develop alternative residential facilities Provide community care facilities (100% coverage) Give individualized care in the community to people with dementia

Ten overall recommendations	Scenario A Low level of resources	Scenario B Medium level of resources	Scenario C High level of resources
4. Educate the public	Promote public campaigns against stigma and discrimination Support nongovernmental organizations in public education	Use the mass media to promote awareness of dementia, foster positive attitudes, and help prevent cognitive impairment and dementia	Launch public campaigns for early help-seeking, recognition and appropriate management of dementia
5. Involve communities, families and consumers	Support the formation of self-help groups Fund schemes for nongovernmental organizations	Ensure representation of communities, families, and consumers in policy-making, service development and implementation	Foster advocacy initiatives
6. Establish national policies, programmes and legislation	Revise legislation based on current knowledge and human rights considerations Formulate dementia care programmes and policies: – Legal framework to support and protect those with impaired mental capacity – Inclusion of people with dementia in disability benefit schemes – Inclusion of caregivers in compensatory benefit schemes Establish health and social care budgets for older persons	Implement dementia care policies at national and subnational levels Establish health and social care budgets for dementia care Increase the budget for mental health care	Ensure fairness in access to primary and secondary health care services, and to social welfare programmes and benefits
7. Develop human resources	Train primary health-care workers Initiate higher professional training programmes for doctors and nurses in geriatric psychiatry and medicine Develop training and resource centres	Create a network of national training centres for physicians, psychiatrists, nurses, psychologists and social workers	Train specialists in advanced treatment skills
8. Link with other sectors	Initiate community, school and workplace dementia awareness programmes Encourage the activities of nongovernmental organizations	Strengthen community programmes	Extend occupational health services to people with early dementia Provide special facilities in the workplace for caregivers of people with dementia Initiate evidence-based mental health promotion programmes in collaboration with other sectors
9. Monitor community health	Include dementia in basic health information systems Survey high-risk population groups	Institute surveillance for early dementia in the community	Develop advanced monitoring systems Monitor effectiveness of preventive programmes
10. Support more research	Conduct studies in primary health-care settings on the prevalence, course, outcome and impact of dementia in the community	Institute effectiveness and cost–effectiveness studies for community management of dementia	Extend research on the causes of dementia Carry out research on service delivery Investigate evidence on the prevention of dementia

[a] Based on overall recommendations from *The world health report 2001* (*32*).

CONCLUSIONS AND RECOMMENDATIONS	
1	Dementia is a disease and not a part of normal ageing.
2	Dementia affects some 24 million people, most of them elderly, worldwide. Up to two thirds live in low and middle income countries.
3	Awareness of dementia is very low in all world regions, a problem leading to stigmatization and inefficient help-seeking.
4	No cure is currently available for the most common causes of dementia, but much can and should be done to improve the quality of life of people with dementia and their carers.
5	Governments should be urged to take account of the needs of people with dementia, as an integral part of a comprehensive programme of health and welfare services for older people.
6	The priority should be to strengthen primary care services, through training and reorientation from clinic-based acute treatment services to provision of outreach and long-term support.
7	Governments, nongovernmental organizations working in the area of Alzheimer and other dementias, professionals and carers need to work together to raise awareness, counter stigma and improve the quality and coverage of care services.

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RECOMMENDED READING

For professionals

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- Draper B, Melding P, Brodaty H, eds. *Psychogeriatric service delivery: an international perspective*. New York, Oxford University Press, 2004.

For carers and non-medical readers

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Box 3.1.3 Case-study: Brazil

Brazil has among the 11 largest populations of elderly people in the world; eight of these populations are in developing countries. According to the Brazilian 2000 census, there are 10 million people aged 65 years and over, corresponding to about 6% of the whole population. It is predicted that by 2050 the elderly population will have increased by over 300%, whereas the population as a whole will have increased only by over 30%. Brazil has also one of the highest rates of urbanization in the world with almost one third of the whole population living in only three metropolitan areas (São Paulo, Rio de Janeiro and Belo Horizonte), as well as one of the highest levels of inequality between the rich and the poor with almost 50% of the national income concentrated among the richest 10% of the population. Most elderly people live in large cities in poverty.

According to a recent consensus on the global prevalence of dementia, Brazil has today 729 000 people with dementia; this number is estimated to increase to 1.4 million by 2020 and to 3.2 million by 2040. Dementia in Brazil is still a hidden problem and there is little awareness of it.

Most elderly people live with their spouses or extended family (only 15% live alone and fewer than 1% live in institutions). Families with one or more elderly members are relatively advantaged because of the means-tested non-contributory pension benefits for older Brazilians, introduced in the 1990s. However, the informal support that family caregivers can offer to their relations in more need is still difficult because of impoverishment.

The majority of Brazilians (75%) are cared for by the federal programme SUS (Unified Health System) while the remainder are in the hands of a private system. Primary care is provided primarily by the Family Health Programme, in which health professionals go to the patient's home for periodic health evaluation and management; however, this programme covers only 40% of the population. Specialists (geriatricians, psychiatrists and neurologists) see referred patients as outpatients and inpatients. Long-term care is scarce and is mostly provided by religious organizations for those with severe disability and limited family support. Community care is generally available in metropolitan areas, but only from private providers for those who can afford the charges. Home care provided by SUS is being introduced but still covers only a small proportion of the elderly population.

While the current health system does not meet the needs of older people, there are encouraging developments. The Brazilian Psychiatric Association has a Geriatric Psychiatry section promoting training in dementia assessment and care; the geriatricians and neurologists have similar initiatives. Four universities have research programmes in dementia. Several regional nongovernmental organizations work to support people with dementia and their caregivers; these are united in a federation — Federação Brasileira de Associaçãoes de Alzheimer (FEBRAZ) — which is a member of Alzheimer's Disease International.

Box 3.1.4 Case-study: India

In India, life expectancy has gone up from 20 years at the beginning of the 20th century to 62 years at present. Better medical care and low fertility have made the elderly population the fastest growing section of society. India has over one billion people, 16% of the world's population: it is estimated that the growth in the elderly population is 5–8% higher than growth in the total population. The consequence is that, while in 2001 there were 70 million people aged over 60 years, by 2025 there will be an estimated 177 million.

According to a recent consensus, the prevalence of dementia in India is 1.9% over the age of 60 years. In the context of the large population and demographic transition, the total numbers are estimated to more than treble in the next 35 years, reaching over six million by 2040. The public health and socioeconomic implications are enormous.

The joint family system — the traditional support system for frail elderly people — is crumbling because of the migration of the younger generation to the cities in search of better prospects. The women who traditionally took on the role of caregivers are also working and cannot spend as much time caring for the elderly. Dementia is considered as a normal part of ageing and is not perceived as requiring medical care. Thus primary health-care physicians rarely see this condition in their clinical work. Private medical care (which includes home visits) is preferred and this leads to a higher out-of-pocket cost for dementia care. Carers experience significant burdens and health strain. More than 80% of carers are female and around 50% are spouses who are themselves quite old. People with dementia are often neglected, ridiculed and abused. Old-age homes do not admit people with dementia.

These research findings led to the implementation of the Dementia Home Care Project which was supported by WHO. In this project, a flexible, stepped-care intervention was adopted to empower the carers with knowledge and skills to manage the person with dementia at home. The intervention was implemented by locally trained home care advisers under supervision. This not only helped in decreasing the stress of looking after a person with dementia, but also helped the caregivers to manage behavioural problems and thus reduced the number of deaths in the intervention group.

Evidence from research has helped the advocacy campaign in India. There is a need to make dementia a public health priority and create a network of home care advisers to provide supportive and educational interventions for the family caregivers through the primary health-care system in India.

Box 3.1.5 Case-study: Nigeria

Nigeria is the most populous African country, with about 130 million inhabitants. According to United Nations estimates, it is likely that the figure of 0.5 million (4.7% of the whole population) people over 60 years of age in 2000 will have more than trebled by 2040 (1.8 million people, i.e. 7.5% of the population). Old people have traditionally been cared for within the extended family. Social and economic changes have disrupted this system, however, especially by young people moving into the towns and leaving the old people to cope on their own. No effective alternatives have been provided for their care.

Specialist health services are in short supply. In 2005 there were only about 77 psychiatrists and three occupational therapists in the country. Industrial therapy was not offered anywhere. Specialist social workers are few and work under severe limitations. There are no specialist services for the elderly (geriatric or psychogeriatric services, meals on wheels, respite care or drop-in centres) and few nursing homes. There is no insurance cover for medical services for elderly people.

Usually record-keeping, accountability and political will are poor, so that many elderly people who retire do not receive their benefits. Recently the Federal Government has introduced a contributory pension scheme, but in the past elderly people found it difficult to learn about and access their entitlements. Elderly Nigerians are among the poorest groups in the country.

A national policy on elderly care was published in 2003, and a National Implementation Plan is now under way, but is being piloted only among certain Federal civil servants.

Assessing the extent of dementia among this huge, varied and shifting population is not easy, but what little research has been done suggests prevalence rates for dementia may be low. Interest in the mental health of elderly Nigerians is only just beginning: for example in the past three years, old-age mental health clinics have been established at two universities. There is no formal training for geriatric medicine and psychiatry. Anti-dementia drugs are rarely available.

3.2 Epilepsy

Epilepsy is a chronic neurological disorder affecting both sexes and all ages, with worldwide distribution. The term is also applied to a large group of conditions characterized by common symptoms called "epileptic seizures", which may occur in the context of a brain insult that can be systemic, toxic or metabolic. These events (called provoked or acute symptomatic seizures) are presumed to be an acute manifestation of the insult and may not recur when the underlying cause has been removed or the acute phase has elapsed.

Epilepsy has been defined as "a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiological, cognitive, psychological and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure" (*1*). An epileptic seizure is defined as "a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain" (*1*). These definitions recognize that a diagnosis of epilepsy implies the existence of a persistent epileptogenic abnormality that is present whether seizures occur or not, as well as that there may be consequences of this persistent abnormality other than the occurrence of seizures that can cause continuous disability between seizure occurrence (interictally). Because it is often difficult to identify definitively an enduring predisposition to generate epileptic seizures, a common operational definition of epilepsy is the occurrence of two or more non-provoked epileptic seizures more than 24 hours apart.

Differential diagnosis of transient events that could represent epileptic seizures involves first determining that the events are epileptic, then distinguishing between provoked epileptic seizures and a chronic epileptic condition. Febrile seizures in infants and young children and withdrawal seizures in alcoholics are common examples of provoked seizures that do not require a diagnosis of epilepsy. If seizures are recurrent, it is next necessary to search for an underlying treatable cause. If such a cause cannot be found, or if it is treated and seizures persist, then treatment of seizures is guided by diagnosis of the specific seizure type(s), and syndrome if present (see Box 3.2.1).

Etiology and risk factors

Epileptic conditions are multifactorial disorders, and it is useful to discuss three important factors. The first factor is predisposition, or threshold. Anyone with a functioning brain is capable of having a seizure; however, seizures occur more easily in some people than in others. The ease with which a seizure can be provoked, or an epileptic condition can be induced, is referred to as a threshold. Individual differences in threshold are largely attributable to genetic variations but could also be acquired, such as certain types of perinatal injuries, which can alter threshold. Threshold is a dynamic phenomenon; it varies throughout the day, it also changes in relation to hormonal influences

during the menstrual cycle in women. Stimulant drugs lower seizure threshold and sedative drugs increase it; however, withdrawal from sedative drugs can lower threshold and provoke seizures. Antiepileptic drugs work by increasing seizure threshold.

The second important factor for epilepsy is the epileptogenic abnormality itself. Epilepsies attributable to identifiable brain defects are referred to as symptomatic epilepsies. Symptomatic epilepsies can be caused by a variety of disorders, including brain malformations, infections, vascular disturbances, neoplasms, scars from trauma, including strokes, and disorders of cerebral metabolism. Treatment for symptomatic epilepsy is most effective if it is directed at the underlying cause. The most common symptomatic epilepsy is temporal lobe epilepsy, usually associated with a characteristic lesion called "hippocampal sclerosis". Hippocampal sclerosis appears to be caused by cerebral injury within the first few years of life in individuals with a genetic predisposition to this condition. Some forms of epilepsy are unassociated with identifiable structural lesions or diseases and are usually unassociated with other neurological or mental deficits. These are genetically transmitted, generally easily treated with medications without sequelae, and referred to as idiopathic epilepsies.

The third important factor is the precipitating condition, which determines when seizures occur. Common precipitating factors include fever for children with febrile seizures, alcohol and sedative drug withdrawal, sleep deprivation, stimulant drugs and — in some patients — stress. Reflex seizures are precipitated by specific sensory stimuli. The most common are photosensitive seizures induced by flickering light, but some patients have very specific reflex epilepsy with seizures precipitated by such stimuli as being startled, particular types of music, certain visual patterns, reading, eating and hot-water baths. Identification of precipitating factors is helpful if they can be avoided, but in most patients specific precipitating factors are not apparent, and may not exist at all.

Patients with a high seizure threshold can experience severe epileptogenic brain injuries and precipitating factors but never have seizures, while those with low seizure thresholds can develop epilepsy with minimal insults and, in many, from precipitating factors alone (provoked seizures).

COURSE AND OUTCOME

Because there are many types of seizures and epilepsy, there is no single course or outcome. Prognosis depends on the seizure type, the underlying cause, and the syndrome when this can be determined. Approximately one in 10 individuals will experience at least one epileptic seizure in their lifetime, but only one third of these will go on to have epilepsy. There are a number of idiopathic epilepsy syndromes characterized by onset at a certain age, and specific seizure types. Those that begin in infancy and childhood, such as benign familial neonatal seizures, benign childhood epilepsy with centrotemporal spikes, and childhood absence epilepsy, usually remit spontaneously, while those that begin in adolescence, the juvenile idiopathic epilepsies, are often lifelong. Most of these are easily treated with antiepileptic drugs (AEDs), with no neurological or

Box 3.2.1 Types of epileptic seizure

I. Generalized onset	II. Focal onset	III. Neonatal
A. Clonic and tonic seizures B Absences C Myoclonic seizure types D Epileptic spasms E Atonic seizures	A Local 1 Neocortical 2 Limbic B With ipsilateral propagation C With contralateral spread D Secondarily generalized	

Source: adapted from (*2*).

mental sequelae. Slowly, the genetic basis of these idiopathic epilepsies is being revealed, and there appears to be considerable diversity in that single-gene mutations can give rise to more than one syndrome, while single syndromes can be caused by more than one gene mutation.

The prognosis of symptomatic epilepsies depends on the nature of the underlying cause. Epilepsies attributable to diffuse brain damage, such as West syndrome and Lennox–Gastaut syndrome, are characterized by severely disabling medically refractory "generalized" seizures, mental retardation and often other neurological deficits. Epilepsies resulting from smaller lesions may be associated with "focal" seizures that are more easily treated with drugs and can remit spontaneously as well. When pharmacoresistant focal seizures are due to localized structural abnormalities in one hemisphere, such as hippocampal sclerosis in temporal lobe epilepsy, they can often be successfully treated by localized resective surgery. Some patients with more diffuse underlying structural lesions that are limited to one hemisphere can also be treated surgically with hemispherectomy or hemispherotomy.

Whereas 80–90% of patients with idiopathic epilepsies can expect to become seizure free, and many will undergo spontaneous remission, the figure is much lower for patients with symptomatic epilepsy, and perhaps only 5–10% of patients with temporal lobe epilepsy and hippocampal sclerosis will have seizures that can be controlled by pharmacotherapy. Of these patients, however, 60–80% can become free of disabling seizures with surgery. Advances in neurodiagnostics, particularly neuroimaging, are greatly facilitating our ability to determine the underlying causes of seizures in patients with symptomatic epilepsies and to design more effective treatments, including surgical interventions.

EPIDEMIOLOGY

Incidence of epilepsy and unprovoked seizures

The annual incidence of unprovoked seizures is 33–198 per 100 000, and the incidence of epilepsy is 23–190 per 100 000 (*3*). The overall incidence of epilepsy in Europe and North America ranges from 24 and 53 per 100 000 per year, respectively (*4–6*). The incidence in children is eventually higher and even more variable, ranging from 25 to 840 per 100 000 per year, most of the differences being explained by the differing populations at risk and by the study design (*3*). In developing countries, the incidence of the disease is higher than that in industrialized countries and is up to 190 per 100 000 (*3, 7*). Although one might expect a higher exposure to perinatal risk factors, infections and traumas in developing countries, the higher incidence of epilepsy may be also explained by the different structure of the populations at risk, which is characterized by a predominant distribution of young individuals and a short life expectancy.

Incidence by age, sex and socioeconomic status

In industrialized countries, epilepsy tends to affect mostly the individuals at the two extremes of the age spectrum. The peak in the elderly is not detected in developing countries, where the disease peaks in the 10–20-year age group (*8*). This may depend on the age structure of the population and on a relative under-ascertainment of the disease in older individuals.

The incidence of epilepsy and unprovoked seizures has been mostly reported to be higher in men than in women in both industrialized and developing countries, though this finding has rarely attained statistical significance. The different distribution of epilepsy in men and women can be mostly explained by the differing genetic background, the different prevalence of the commonest risk factors in the two sexes, and the concealment of the disease in women for sociocultural reasons.

The incidence of epilepsy is higher in the lower socioeconomic classes. This assumption is supported by the comparison between industrialized and developing countries and by the comparison, within the same population, of people of different ethnic origin (*9*).

Prevalence of epilepsy

The overall prevalence of epilepsy ranges from 2.7 to 41 per 1000 population, though in the majority of reports the rate of active epilepsy (i.e. at least one seizure in the preceding five years) is in the range 4–8 per 1000 (*5, 10*). The prevalence of active epilepsy is generally lower in industrialized countries than in developing countries, which may reflect a lower prevalence of selected risk factors (mostly infections and traumas), a more stringent case verification, and the exclusion of provoked and unprovoked isolated seizures.

Prevalence by age, sex and socioeconomic status

In industrialized countries, the prevalence of epilepsy is lower in infancy and tends to increase thereafter, with the highest rate occurring in elderly people (*10*). Where available, age-specific prevalence rates of lifetime and active epilepsy from developing countries tend to be higher in the second (254 vs 148 per 1000) and third decades of life (94 vs 145 per 1000) (*8*). The differences between industrialized and developing countries may be mostly explained by the differing distribution of the risk factors and by the shorter life expectancy in the latter.

As with incidence, prevalence of epilepsy tends to be higher in men. However, this finding is not consistent across studies and, with few exceptions, is not statistically significant.

Socioeconomic background has been found to affect the frequency of epilepsy reports in both industrialized and developing countries. In developing countries, prevalence rates have been shown to be greater in the rural compared with the urban context (*11, 12*) or in the lower compared with the higher socioeconomic classes. However, opposite figures were reported in a meta-analysis of epidemiological studies from India (*13*), which suggests that rural and urban environments should not be invariably used as proxies of lower vs higher socioeconomic conditions.

Mortality

The mortality rate of epilepsy ranges from 1 to 8 per 100 000 population per year, but international vital statistics give annual mortality rates of 1–2 per 100 000 (*14*). Based on a meta-analysis of studies investigating mortality in the past 100 years, the standardized mortality ratio (SMR) for epilepsy, which is the ratio between the deaths observed among patients with epilepsy and the deaths expected in a reference population with a similar age distribution, was found to range from 1.3 to 9.3 (*15*). The SMR for epilepsy ranges from 1.6 to 5.3 in children and adults and is inversely correlated with age (*16*). The higher SMRs may be partly explained by the inclusion of provoked seizures. The highest mortality risk in the youngest age groups can be interpreted in part in the light of the underlying epileptogenic conditions and the lower number of competing causes of death.

It is extremely difficult to analyse the epilepsy death rate in the general population of a developing country because incidence studies of epilepsy are difficult to perform, death certificates are unreliable and often unavailable, and the cause of death is difficult to determine. Based on available data, it seems that the mortality rate of epilepsy in developing countries is generally higher than that reported in developed countries. These data cannot be generalized, however, as they have been obtained from selected populations (*17*).

BURDEN ON PATIENTS, FAMILIES AND COMMUNITIES

Worldwide, 50 million people have epilepsy. Many more people, however — an estimated 200 000 000 — are also affected by this disorder, as they are the family members and friends of those who are living with epilepsy. Around 85% of people with epilepsy live in developing countries. There are two million new cases occurring in the world every year. Up to 70% of people with epilepsy could lead normal lives if properly treated, but for an overwhelming majority of patients this is not the case (*18*).

Epilepsy is among the disorders that are strongly associated with significant psychological and social consequences for everyday living (*19*). People with hidden disabilities such as epilepsy are among the most vulnerable in any society. While their vulnerability may be partly attributed to the disorder itself, the particular stigma associated with epilepsy brings a susceptibility of its own. Stigmatization leads to discrimination, and people with epilepsy experience prejudicial and discriminatory behaviour in many spheres of life and across many cultures (*20*).

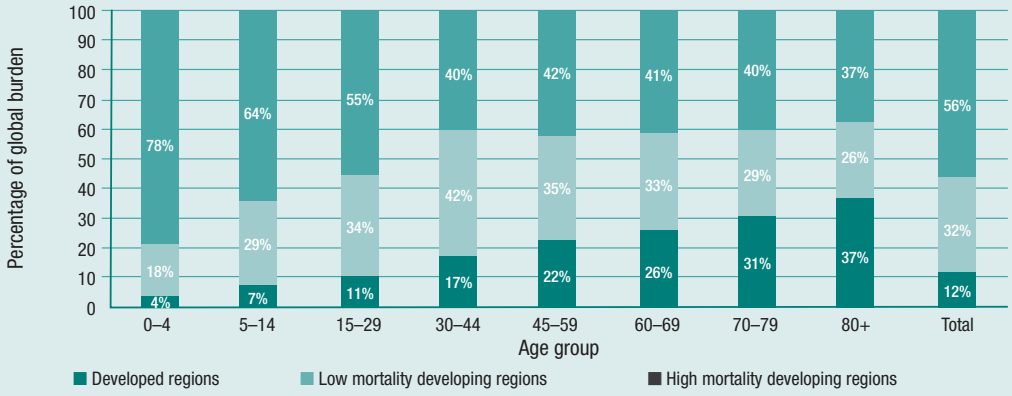
People with epilepsy experience violations and restrictions of both their civil and human rights. Civil rights violations such as unequal access to health and life insurance or prejudicial weighting of health insurance provisions, withholding of the right to obtain a driving licence, limitations to the right to enter particular occupations and the right to enter into certain legal agreements, in some parts of the world even marriage, are severely aggravated by epilepsy. Discrimination against people with epilepsy in the workplace and in respect of access to education is not uncommon for many people affected by the condition. Violations of human rights are often more subtle and include social ostracism, being overlooked for promotion at work, and denial of the right to participate in many of the social activities taken for granted by others in the community. For example, ineligibility for a driving licence frequently imposes restrictions on social participation and choice of employment.

Informing people with epilepsy of their rights and recourse is an essential activity. Considering the frequency of rights violations, the number of successful legal actions is very small. People are often reluctant to be brought into the public eye, so a number of cases are settled out of court. The successful defence of cases of rights abuse against people with epilepsy will serve as precedents, however, and will be helpful in countries where there are actions afoot to review and amend legislation.

Epidemiological assessment of the global burden of epilepsy

Overall, epilepsy contributed more than seven million DALYs (0.5%) to the global burden of disease in 2000 (*21, 22*). Figure 3.2.1 shows the distribution of DALYs or lost years of healthy life attributable to epilepsy, both by age group and by level of economic development. It is apparent that close to 90% of the worldwide burden of epilepsy is to be found in developing regions, with more than half occurring in the 39% of the global population living in countries with the highest levels of premature mortality (and lowest levels of income). An age gradient is also apparent, with the vast majority of epilepsy-related deaths and disability in childhood and adolescence occurring in developing regions, while later on in the life-course the proportion drops on account of relatively greater survival rates into older age by people living in more economically developed regions.

Figure 3.2.1 Distribution of the global burden of epilepsy, by age group and level of economic development



Source (*22*).

Economic assessment of the national burden of epilepsy

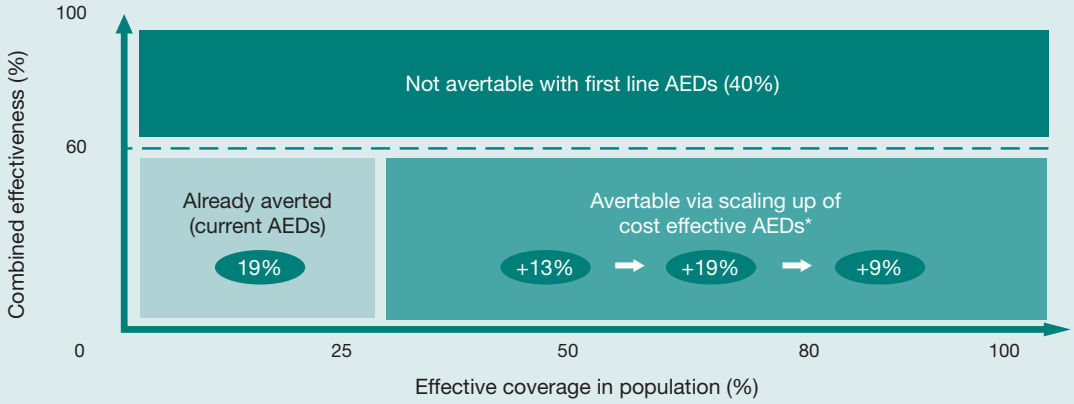
Economic assessments of the national burden of epilepsy have been conducted in a number of high income countries (e.g. *23, 24*) and more recently in India (*25*), all of which have clearly shown the significant economic implications the disorder has in terms of health-care service needs, premature mortality and lost work productivity. For example, the Indian study calculated that the total cost per case of these disease consequences for epilepsy amounted to US$ 344 per year (equivalent to 88% of average income per capita), and that the total cost for the estimated five million cases resident in India was equivalent to 0.5% of gross national product. Since such studies differ with respect to the exact methods used, as well as underlying cost structures within the health system, they are currently of most use at the level of individual countries, where they can serve to draw attention to the wide-ranging resource implications and needs of people living with epilepsy.

The avertable burden of epilepsy

Having established the attributable burden of epilepsy, two subsequent questions for decision-making and priority setting relate to avertable burden (the proportion of attributable burden that is averted currently or could be avoided via scaled-up use of proven efficacious treatments) and resource efficiency (determination of the most cost-effective ways of reducing burden). Figure 3.2.2 provides a schematic overview of these concepts.

As part of a wider WHO cost–effectiveness work programme (*26*), information has been generated concerning the amount of burden averted by the current or scaled-up use of treatment with AEDs, together with estimates of cost and cost–effectiveness (*27*). Effectiveness was expressed in terms of DALYs averted and costs were expressed in international dollars. Compared with a "do nothing" scenario (i.e. the untreated natural history of epilepsy), results from nine developing epidemiological subregions suggest that extending AED treatment coverage to 50% of primary epilepsy cases would avert 150–650 DALYs per million population (equivalent to 13–40% of the current burden), at an annual cost per case of International $ 55–192. Older first-line AEDs (phenobarbitone, phenytoin) were most cost effective on account of their similar efficacy but lower acquisition cost (International $ 800–2000 for each DALY averted). In all nine developing regions, the cost of securing one extra healthy year of life was less than average per capita income. Extending coverage further to 80% or even 95% of the target population would evidently avert more of the burden still, and would remain an efficient strategy despite the large-scale investment in manpower, training and drug supply/distribution that would be required to implement such a programme. The results for one developing subregion in Africa — consisting of 20 countries with a high rate of child mortality and a very high level of adult mortality — are depicted in Figure 3.2.2

Figure 3.2.2 Attributable and avertable burden of epilepsy in an epidemiological subregion of Africa



* Each DALY averted costs less than average per capita income.

Source: schema (*28*); data (*27*).

(*27, 28*), which divides the total attributable burden of epilepsy into three categories: burden that is averted by AEDs at current levels of effective treatment coverage (19%); burden that is avertable via the scaling-up of AEDs (to a further 41% if complete coverage is reached); and burden that is not avertable via AEDs (estimated to be 40%, though this assumes that the current level of drug compliance would prevail).

TREATMENT, REHABILITATION AND COST

The primary focus of care for patients with epilepsy is the prevention of further seizures, which may, after all, lead to additional morbidity or even mortality (*29*). The goal of treatment should be the maintenance of a normal lifestyle, preferably free of seizures and with minimal side-effects of the medication. Up to 70% of people with epilepsy could become seizure free with AED treatment.

In 25–30% of people with epilepsy the seizures cannot be controlled with drugs. Epilepsy surgery is a safe and effective alternative treatment in selected cases. Investment in epilepsy surgery centres, even in the poorest regions, could greatly reduce the economic and human burden of epilepsy. There is a marked treatment gap with respect to epilepsy surgery, however, even in industrialized countries.

Attention to the psychosocial, cognitive, educational and vocational aspects is an important part of comprehensive epilepsy care (*30*). Epilepsy imposes an economic burden both on the affected individual and on society, e.g. the disorder commonly affects young people in the most productive years of their lives, often leading to avoidable unemployment.

Over the past years, it has become increasingly obvious that severe epilepsy-related difficulties can be seen in people who have become seizure free as well as in those with difficult-to-treat epilepsies. The outcome of rehabilitation programmes would be a better quality of life, improved general social functioning and better functioning in, for instance, performance at work and improved social contacts (*31*).

In 1990, WHO identified that the average cost of medication (phenobarbitone) could be as low as US$ 5 per person per year (*32*). From an economic point of view also, therefore, it is an urgent public health challenge to make effective epilepsy care available to all who need it, regardless of national and economic boundaries.

Prevention

Currently, epilepsy tends to be treated once the condition is established, and little is done in terms of prevention. In a number of people with epilepsy the cause for the condition is unknown; prevention of this type of epilepsy is therefore currently not possible (*33, 34*). A sizeable number of people with epilepsy will have known risk factors, but some of these are not currently amenable to preventive measures. These include cases of epilepsy attributable to cerebral tumours or cortical malformations and many of the idiopathic forms of epilepsy.

One of the most common causes of epilepsy is head injury, particularly penetrating injury. Prevention of the trauma is clearly the most effective way of preventing post-traumatic epilepsy, with use of head protection where appropriate (for example, for horse riding and motorcycling) (*34*).

Epilepsy can be caused by birth injury, and the incidence should be reduced by adequate perinatal care. Fetal alcohol syndrome may also cause epilepsy, so advice on alcohol use before and during pregnancy is important. Reduction of childhood infections by improved public hygiene and immunization can lessen the risk of cerebral damage and the subsequent risk of epilepsy (*33, 34*).

Febrile seizures are common in children under five years of age and in most cases are benign, though a small proportion of patients will develop subsequent epilepsy. The use of drugs and other methods to lower the body temperature of a feverish child may reduce the chance of having a febrile convulsion and subsequent epilepsy, but this remains to be seen.

Epilepsy may be a complication of various infections of the central nervous system (CNS), such as cysticercosis and malaria (*35, 36*). These conditions are more prevalent in the tropical belt, where low income countries are concentrated. Elimination of the parasite in the environment would be the most effective way to reduce the burden of epilepsy worldwide, but education concerning how to avoid infection can also be effective.

To sum up, currently the prevention of epilepsy may be possible in cases caused by head trauma and by infections and infestations of the CNS, but would require intensive efforts to improve basic sanitation, education and practice. Most cases of epilepsy at the current state of knowledge are probably not preventable but, as research improves our understanding of genetics and structural abnormalities of the brain, this may change.

Treatment gap

Worldwide, the proportion of patients with epilepsy who at any given time remain untreated is large, and is greater than 80% in most low income countries (*33, 34*). The size of this treatment gap reflects either a failure to identify cases or a failure to deliver treatment. In most situations, however, both factors will apply. Inadequate case-finding and treatment have various causes, some of which are specific to low income countries. They include people's attitudes and beliefs, government health policies and priorities (or the lack of them), treatment costs and drug availability, as well as the attitude, knowledge and practice of health workers. In addition, there is clear scarcity of epilepsy-trained health workers in many low income countries. The lack of trained personnel and a proper health delivery infrastructure are major problems, which contribute to the overall burden of epilepsy. For instance, in most sub-Saharan countries there is no resident neurologist and there are no scanning facilities using magnetic resonance imaging (MRI) (*35*). This situation is found in many other resource-poor countries and is usually more acute in rural areas. The lack of trained specialists and medical facilities needs to be seen in the context of severe deficiencies in health delivery that apply not only to epilepsy but also to the whole gamut of medical conditions. Training medical and paramedical personnel and providing the necessary investigatory and treatment facilities will require tremendous effort and financial expenditure and will take time to achieve. The aim should be to provide high standards of epilepsy care with equitable access to all who need them throughout the world.

There is a dearth of epilepsy services, trained personnel and AEDs, which contributes to a massive diagnostic and treatment gap in epilepsy that is more pronounced in low income countries. A huge effort is required to equalize care for people with epilepsy around the world. Improvement of the care delivery system and infrastructure alone are not a sufficient strategy but need to be supplemented by education of patients, their families and the general public.

RESEARCH

Despite the significant advances in understanding epileptogenic mechanisms and in counteracting their pathological consequences, the problem still has to be faced of treating more effectively the severe epilepsies and of preventing their unfavourable evolution (*37*). So far, research has been unsuccessful in developing effective strategies capable of preventing the development of the pathogenic process, set in motion by different etiological factors, that leads ultimately to chronic epilepsies (*38*). To do so, it is important to take advantage of the results that are continuously being made available to the scientific community thanks to the synergy of basic and clinical multidisciplinary research. This means that the clinical applicability of neurobiological results should be evaluated, the way in which the new information can be translated into diagnostic and therapeutic terms should be assessed, and ad hoc guidelines and recommendations should be produced accordingly.

In elaborating their health-care strategies, regional and national communities should not simply refer to the available scientific information, but should also contribute to it by means of their own

original investigations. This is mandatory if they are to meet specific local requirements taking into account the socioeconomic situations in which health-care policy is to be formulated. Important actions have been undertaken by the International League Against Epilepsy (ILAE) through its various commissions (on genetics, neurobiology, psychobiology, epidemiology, therapeutic strategies, diagnostic methods and health-care policy) to help developing countries in establishing research projects oriented to their specific problems. Moreover, ILAE is active in promoting international collaborative research networks, facilitating partnerships between developed and developing countries, promoting fellowships and grant programmes and in sensitizing the relevant international institutions such as the World Bank, WHO and the United Nations Educational, Scientific and Cultural Organization (UNESCO) to epilepsy research (*39*). A specific project for collaborative studies involving developed and developing countries is part of the triennial action plan of the Global Campaign Against Epilepsy. The project aims to stimulate and facilitate the synergy between countries in different economic situations that is particularly important for epidemiological and genetic studies and clinical trials of new AEDs.

The main point here is that research is not a matter of technology; rather, it is the result of an intellectual attitude aimed at understanding and improving the principles upon which every medical activity should be based. Therefore, everybody whose work concerns epilepsy can and should contribute to the advancement of epileptology to the benefit of the millions of human beings suffering from epilepsy, no matter how advanced the technological context of his or her current work.

EDUCATION AND TRAINING

Education and training programmes aimed at improving the expertise of health-care providers play an essential role in fostering epilepsy care throughout the world. The need for an integrated, multidisciplinary approach to epilepsy care prompted several countries to organize annual epilepsy courses for neurologists, general practitioners, technicians and nurses at national level.

Multinational programmes are being implemented on the basis of the pioneering experience of ILAE's European Epilepsy Academy (EUREPA), which has developed two innovative educational models: train-the-trainers courses and European Epileptology Certification. The aim of the train-the-trainers courses is to turn experienced personnel into qualified teachers of epileptology. It significantly contributes to raising the profile of epilepsy care across Europe and is now being implemented in other regions. European Epileptology Certification can be obtained by completing an 18-month educational programme based on periods of training in selected institutions that allow the accumulation of credits.

EUREPA is also developing an important project of distance education in epileptology. Some modules have been completed and successfully tested: the course on genetics of epilepsy has already been evaluated (*40*). An annual residential Epilepsy Summer School for young epileptologists from all over the world exists at Venice's International School of Neurological Sciences; since 2002, it has trained students from 64 countries. The interaction between students and teachers and among the students themselves resulted in several ongoing international collaborative projects that are further contributing to raising the profile of epilepsy care in several developing areas (*41*).

The philosophy on which the educational initiatives of ILAE and EUREPA are based is an interactive relationship that stimulates the active participation of students. The theoretical teaching, based either on residential courses or distance education systems, includes an interactive discussion of clinical cases and practical training programmes in qualified epilepsy centres. A further effort is needed to expand exchange programmes for visiting students from economically disadvantaged countries.

PARTNERSHIPS WITHIN AND BEYOND THE HEALTH SYSTEM

Partnerships within and beyond the health system are essential in order to achieve a world in which no person's life is limited by epilepsy. As the President of ILAE put it, "we all have a shared interest in that we want to improve epilepsy care throughout the world". Such partnerships include:

- nongovernmental organizations, which are themselves partnerships as they are made up of individuals who have common goals and interests;
- patients and professionals at national, regional and global levels, in order to raise awareness of epilepsy and stimulate research;
- patient and professional nongovernmental organizations and WHO, in order to decrease the treatment gap;
- patients, professionals and politicians, for example to develop national health-care programmes;
- foundations and charitable organizations, who support the work of the nongovernmental organizations both financially and with human resources;
- health-care providers, to try to improve the availability, accessibility and affordability of treatment;
- the private sector, especially the pharmaceutical industry.

ILAE/IBE/WHO Global Campaign Against Epilepsy

The problems related to provision of care and treatment to people with epilepsy are too complex to be solved by individual organizations, therefore the three leading international organizations working in the field of epilepsy (ILAE, the International Bureau for Epilepsy (IBE) and WHO) joined forces to create the Global Campaign Against Epilepsy. The Campaign aims to provide better information about epilepsy and its consequences and to assist governments and those concerned with epilepsy to reduce the burden of the disorder. Its strategy, specific objectives and activities are summarized in Box 3.2.2.

To date, over 90 countries are involved in the Campaign. As part of general awareness-raising, regional conferences on public health aspects of epilepsy have been organized in all six regions of WHO with the participation of over 1300 delegates from the epilepsy organizations (IBE and

Box 3.2.2 ILAE/IBE/WHO Global Campaign Against Epilepsy

Objectives	Strategy	Activities
■ To increase public and professional awareness of epilepsy as a universal and treatable brain disorder ■ To raise epilepsy to a new plane of acceptability in the public domain ■ To promote public and professional education about epilepsy ■ To identify the needs of people with epilepsy at national and regional levels ■ To encourage governments and departments of health to address the needs of people with epilepsy, including awareness, education, diagnosis, treatment, care, services and prevention	■ To provide a platform for general awareness ■ To assist departments of health in the development of national programmes on epilepsy	■ Organization of regional conferences followed by Regional Declarations ■ Assessment of country resources for epilepsy worldwide ■ Assistance with the development of regional reports ■ Development of educational materials ■ Coordination of demonstration projects

ILAE), public health experts from governments and universities and representatives from WHO headquarters and regions.

The goals of the conferences were to review the present situation of epilepsy care in the region, to identify the country's needs and resources to control epilepsy at a community level, and to discuss the involvement of countries in the Campaign. As a result of these consultations, Regional Declarations summarizing perceived needs and proposing actions to be taken were developed and adopted by the conference participants.

In order to make an inventory of country resources for epilepsy worldwide, a questionnaire was developed by an international group of experts in the field. On the basis of the data collected through this questionnaire, regional reports were developed. These reports provide a panoramic view of the epilepsy situation in each region, outline the various initiatives that were taken to address the problems, define the current challenges and offer appropriate recommendations (*32, 42*).

The next logical step in the assessment of country resources was the comprehensive analysis of the data. Within the framework of the WHO Atlas Project, launched by WHO in 2002 to provide information about health resources in different countries, the analysis was summarized in the Atlas of Epilepsy Care in the World (*30*). The epilepsy atlas has been produced in collaboration with the ILAE/IBE/WHO Global Campaign Against Epilepsy using ILAE and IBE chapters and WHO networks. The atlas provides global and regional analyses on epilepsy resources and is another result of the fruitful collaboration between ILAE, IBE and WHO (*43*).

One of the main activities aiming to assist countries in the development of their national programmes on epilepsy is the initiation and implementation of demonstration projects. The ultimate goal of these projects is the development of a variety of successful models of epilepsy control that may be integrated into the health-care systems of the participating countries and regions. In general terms, each demonstration project has four aspects:

- assessing whether knowledge and attitudes of the population are adequate, correcting misinformation and increasing awareness of epilepsy and how it can be treated;
- assessing the number of people with epilepsy and estimating how many of them are appropriately treated;
- ensuring that people with epilepsy are properly served by health personnel equipped for their task;
- analysing the outcome and preparing recommendations for those who wish to apply the findings to the improvement of epilepsy care in their own and other countries.

In summary, it may be concluded that the collaboration of ILAE, IBE and WHO within the frame of the Global Campaign has been very successful and led to significant achievements in various areas such as raising public and professional awareness and education, development of effective modules for epilepsy control, and assessment and analysis of epilepsy resources in all countries of the world.

CONCLUSIONS AND RECOMMENDATIONS	
1	Epilepsy is one of the most common serious neurological disorders worldwide with no age, racial, social class, national or geographic boundaries.
2	Worldwide, 50 million people have epilepsy. Around 85% of these live in developing countries.
3	Up to 70% of people with epilepsy could lead normal lives if properly treated, but for an overwhelming majority of patients this is not the case.
4	The worldwide incidence, prevalence and mortality of epilepsy are not uniform and depend on several factors, which include the structure of the local population, the basic knowledge of the disease, the socioeconomic and cultural background, the presence of environmental risk factors, and the distribution of infrastructure, financial, human and material resources.
5	Some forms of epilepsy, particularly those associated with CNS infections and trauma, may be preventable.
6	As epileptic seizures respond to drug treatment, the outcome of the disease depends on the early initiation and continuity of treatment. Difficulties with availability of or access to treatment (the treatment gap) may seriously impair the prognosis of epilepsy and aggravate the social and medical consequences of the disease.
7	In low income countries the treatment gap needs to be seen in the context of the local situation, with inadequate resources for all forms of health delivery as well as education and sanitation.
8	The treatment gap is not only a matter of the lack of availability of AEDs, but encompasses the lack of infrastructure, training and public awareness of the condition. All these areas need to be confronted.
9	Integration of epilepsy care in national health systems needs to be promoted by developing models for epilepsy control worldwide.

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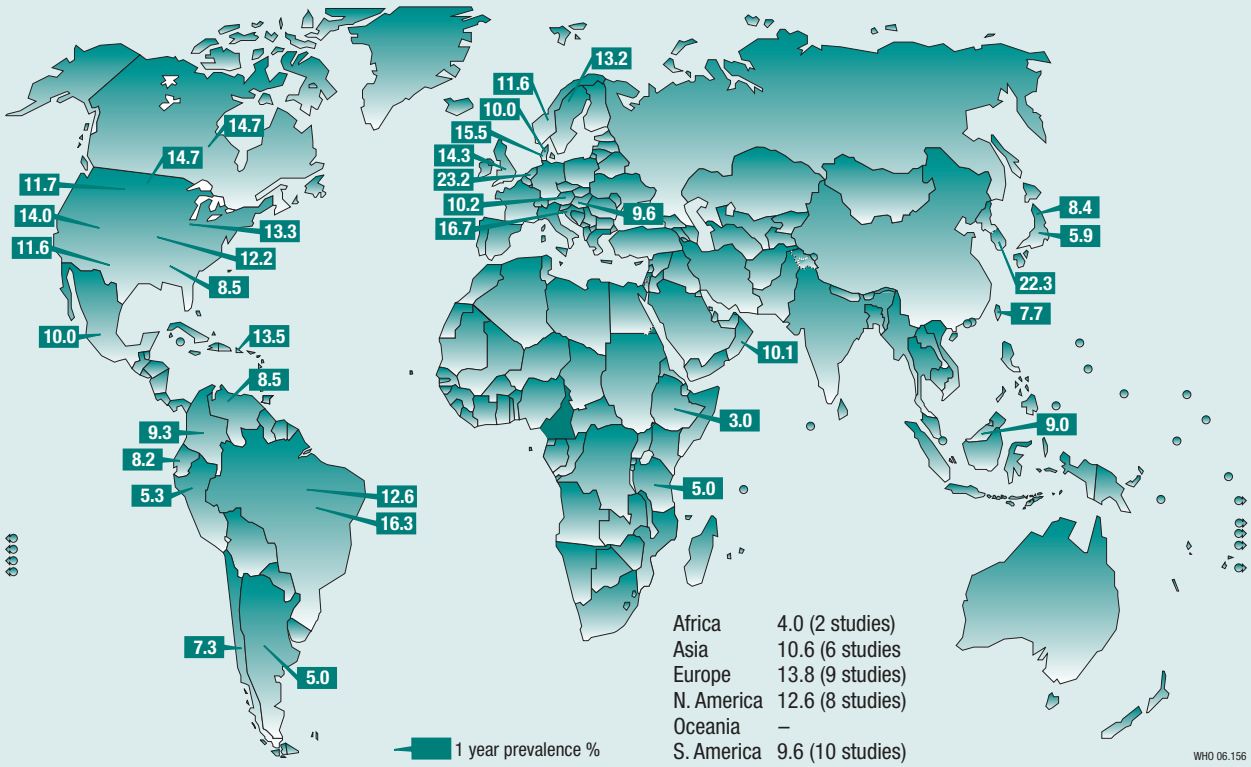
3.3 Headache disorders

Headache is a painful feature of a relatively small number of primary headache disorders, some of which are widespread and are often life-long conditions. Headache also occurs as a characteristic symptom of many other conditions; these are termed secondary headache disorders. Collectively, headache disorders are among the most common disorders of the nervous system, causing substantial disability in populations throughout the world.

Figure 3.3.1 Population-based epidemiological studies of migraine



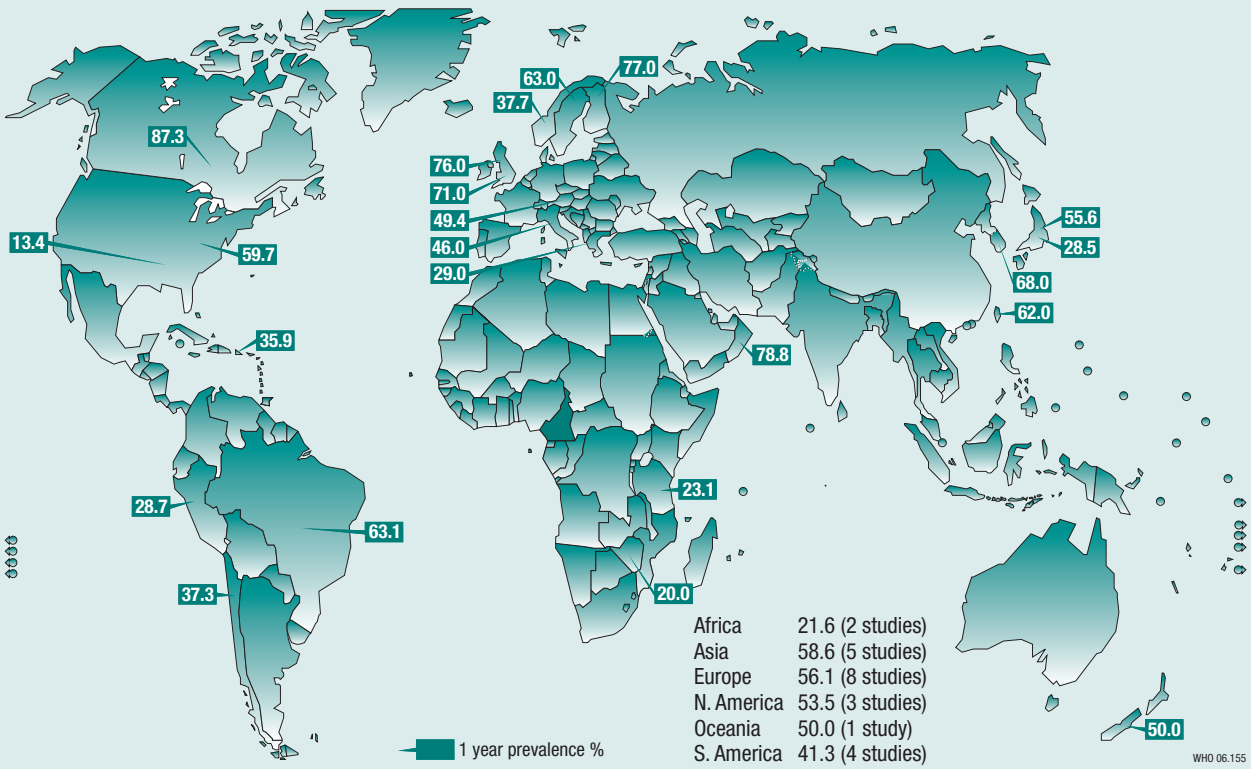
Note: All studies used International Headache Society criteria (or reasonable modifications of these criteria) for diagnosing migraine and were conducted in general population or community-based adult samples of at least 500 participants. Numbers are estimated 1-year prevalences.
Source: (*3*).

Despite the widespread and incapacitating nature of headache, it is underestimated in scope and scale, and headache disorders remain under-recognized and under-treated everywhere (*1*). Table 3.3.1 classifies headache disorders into primary, secondary, and neuralgias and other headaches, with their symptoms (*2*).

The worldwide epidemiology of headache disorders is only partly documented. Population-based studies have mostly focused on migraine (Figure 3.3.1) which, though the most frequently studied, is not the most common headache disorder. Others, such as the more prevalent tension-type headache and the more disabling so-called chronic daily headache syndromes, have received less attention. Furthermore, few population-based studies exist for developing countries, where limited funding and large and often rural (and therefore less accessible) populations, coupled with the low profile of headache disorders compared with communicable diseases, prevent the systematic collection of information.

Nevertheless, despite regional variations, headache disorders are thought to be highly prevalent throughout the world, and recent surveys add support to this belief. Sufficient studies have been conducted to establish that headache disorders affect people of all ages, races, income levels and geographical areas (Figure 3.3.2). Four of them — three primary headache disorders and one secondary — have particular public health importance.

Figure 3.3.2 Population-based epidemiological studies of headache disorders[a]



[a]all headache disorders or unspecified headache.
Note: All studies were conducted in general population or community-based adult samples of at least 500 participants. Numbers are estimated 1-year prevalences.
Source: (*3*).

Table 3.3.1 Classification of headache disorders

Type	Symptoms
Primary	1. Migraine 2. Tension-type headache 3. Cluster headache and other trigeminal autonomic cephalalgias 4. Other primary headaches
Secondary	5. Headache attributed to head and/or neck trauma 6. Headache attributed to cranial or cervical vascular disorder 7. Headache attributed to non-vascular intracranial disorder 8. Headache attributed to a substance or its withdrawal 9. Headache attributed to infection 10. Headache attributed to disorder of homoeostasis 11. Headache or facial pain attributed to disorder of cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cranial structures 12. Headache attributed to psychiatric disorder
Neuralgias and other headaches	13. Cranial neuralgias, central and primary facial pain and other headaches 14. Other headache, cranial neuralgia, central or primary facial pain

Source: (*1*).

TYPES OF HEADACHE DISORDERS

Migraine

Migraine is a primary headache disorder. It almost certainly has a genetic basis (*4*), but environmental factors play a significant role in how the disorder affects those who suffer from it. Pathophysiologically, activation of a mechanism deep in the brain causes release of pain-producing inflammatory substances around the nerves and blood vessels of the head. Why this happens periodically, and what brings the process to an end in spontaneous resolution of attacks, are uncertain.

Usually starting at puberty, migraine is recurrent throughout life in many cases. Adults with migraine describe episodic disabling attacks in which headache and nausea are the most characteristic features; others are vomiting and dislike or intolerance of normal levels of light and sound. Headaches are typically moderate or severe in intensity, one-sided and pulsating, aggravated by routine physical activity; they usually last from several hours to 2–3 days. In children, attacks tend to be of shorter duration and abdominal symptoms more prominent. Attack frequency is typically once or twice a month but can be anywhere between once a year and once a week, often subject to lifestyle and environmental factors that suggest people with migraine react adversely to change in routine.

Migraine is most disabling to people aged 35–45 years, but it can trouble much younger people, including children. Studies in Europe and the United States have shown that migraine affects 6–8% of men and 15–18% of women (*5, 6*). A similar pattern probably exists in Central America: in Puerto Rico, for example, 6% of men and 17% of women were found to have migraine (*7*). In South America, prevalences appear only slightly lower (*8*).

A recent survey in Turkey suggested even greater prevalence in that country: 9% in men and 29% in women (*9*). Similarly, in India, although major studies are still to be conducted, anecdotal evidence suggests migraine is very common. High temperatures and high light levels for more than eight months of the year, heavy noise pollution and the Indian habits of omitting breakfast, fasting frequently and eating rich, spicy and fermented food are thought to be common triggers (*10*). Migraine appears less prevalent, but still common, elsewhere in Asia (around 8%) and in Africa (3–7% in community-based studies) (*3*). In these areas also, major studies have yet to be carried out.

The higher rates in women everywhere (2–3 times those in men) are hormonally driven.

Tension-type headache

The mechanism of tension-type headache is poorly understood, though it has long been regarded as a headache with muscular origins (*11*). It may be stress related or associated with musculoskeletal problems in the neck.

Tension-type headache has distinct subtypes. As experienced by very large numbers of people, *episodic tension-type headache* occurs, like migraine, in attack-like episodes. These usually last no more than a few hours but can persist for several days. *Chronic tension-type headache*, one of the chronic daily headache syndromes, is less common than episodic tension-type headache but is present most of the time: it can be unremitting over long periods. This variant is much more disabling.

Headache in either case is usually mild or moderate and generalized, though it can be one-sided. It is described as pressure or tightness, like a band around the head, sometimes spreading into or from the neck. It lacks the specific features and associated symptoms of migraine.

Tension-type headache pursues a highly variable course, often beginning during the teenage years and reaching peak levels around the age of 30–40 years. It affects three women to every two men. Episodic tension-type headache is the most common headache disorder, reported by over 70% of some populations (*12*), though its prevalence appears to vary greatly worldwide (*3*). In Japan, for example, Takeshima et al. (*13*) found 22% of the population to be affected, while Abduljabbar et al. (*14*) recorded only 3.1% with tension-type headache in a rural population of Saudi Arabia (though it was still the most common headache type). Lack of reporting and underdiagnosis were thought to be factors here, and it may be that cultural attitudes to reporting a relatively minor complaint explain at least part of the variation elsewhere. Chronic tension-type headache affects 1–3% of adults (*3*).

Cluster headache

Cluster headache is one of a group of primary headache disorders (trigeminal autonomic cephalalgias) of uncertain mechanism that are characterized by frequently recurring, short-lasting but extremely severe headache (*1*).

Cluster headache also has episodic and chronic forms. *Episodic cluster headache* occurs in bouts (clusters), typically of 6–12 weeks' duration once a year or two years and at the same time of year. Strictly one-sided intense pain develops around the eye once or more daily, mostly at night. Unable to stay in bed, the affected person agitatedly paces the room, even going outdoors, until the pain diminishes after 30–60 minutes. The eye is red and watery, the nose runs or is blocked on the affected side and the eyelid may droop. In the less common *chronic cluster headache* there are no remissions between clusters. The episodic form can become chronic, and vice versa.

Though relatively uncommon, probably affecting no more than 3 per 1000 adults, cluster headache is clearly highly recognizable. It is unusual among primary headache disorders in affecting six men to each woman. Most people developing cluster headache are 20–30 years of age or older; once present, the condition may persist intermittently for 40 years or more.

Medication-overuse headache

Chronic excessive use of medication to treat headache is the cause of medication-overuse headache (*15*), another of the chronic daily headache syndromes.

Medication-overuse headache is oppressive, persistent and often at its worst on awakening in the morning. A typical history begins with episodic headache — migraine or tension-type headache. The condition is treated with an analgesic or other medication for each attack. Over time, headache episodes become more frequent, as does medication intake. In the end-stage, which not all patients reach, headache persists all day, fluctuating with medication use repeated every few hours. This evolution occurs over a few weeks or much, much longer. A common and

probably key factor at some stage in the development of medication-overuse headache is a switch to pre-emptive use of medication, in anticipation of the headache.

All medications for the acute or symptomatic treatment of headache, in overuse, are associated with this problem, but what constitutes overuse is not clear in individual cases. Suggested limits are the regular intake of simple analgesics on 15 or more days per month or of codeine- or barbiturate-containing combination analgesics, ergotamine or triptans on more than 10 days a month (*1*). Frequency of use is important: even when the total quantities are similar, low daily doses carry greater risk than larger weekly doses.

In terms of prevalence, medication-overuse headache far outweighs all other secondary headaches (*16*). It affects more than 1% of some populations (*17*), women more than men, and children also. In others for whom there are no published data, in Saudi Arabia for example, clinical experience suggests this disorder is not uncommon, with a tendency to be more evident in affluent communities.

Serious secondary headaches

Some headaches signal serious underlying disorders that may demand immediate intervention (see Box 3.3.1). Although they are relatively uncommon, such headaches worry nonspecialists because they are in the differential diagnosis of primary headache disorders. The reality is that intracranial lesions give rise to histories and physical signs that should bring them to mind.

Over-diagnosed headaches

Headache should not be attributed to sinus disease in the absence of other symptoms indicative of it. Many patients with headache visit an optician, but errors of refraction are overestimated as a cause of headache. Dental problems may cause jaw or facial pain but rarely headache.

EPIDEMIOLOGY AND BURDEN

Taken together, headache disorders are extraordinarily common. In developed countries, tension-type headache alone affects two thirds of adult males and over 80% of females (*12*). Extrapolation from figures for migraine prevalence and attack incidence suggests that 3000 migraine attacks occur every day for each million of the general population (*6*). Less well recognized is the toll of chronic daily headache: up to one adult in 20 has headache on more days than not (*17, 18*). Fur-

Box 3.3.1 Serious secondary headaches (headaches to worry about)

Intracranial tumours rarely produce headache until quite large, when raised intracranial pressure is apparent in the history and, in all likelihood, focal neurological signs are present. Because of the infrequency of intracranial tumours, brain scanning is not justified as a routine investigation in patients with headache *(18)*.

Meningitis, and its associated headache, occur in an obviously ill patient. The signs of fever and neck stiffness, later accompanied by nausea and disturbed consciousness, reveal the cause.

The headache of **subarachnoid haemorrhage**, commonly but not always of sudden onset, is often described as the worst ever. Neck stiffness may take some hours to develop. Unless there is a clear history of similar uncomplicated episodes, these characteristics demand urgent investigation.

New headache in any patient over 50 years of age should raise the suspicion of **giant cell (temporal) arteritis**. Headache can be severe. The patient, who does not feel entirely well, may complain of marked scalp tenderness. Jaw claudication is highly suggestive.

Primary angle-closure glaucoma, rare before middle age, may present dramatically with acute ocular hypertension, a painful red eye with the pupil mid-dilated and fixed, and, essentially, impaired vision. In other cases headache or eye pain may be episodic and mild.

Idiopathic intracranial hypertension is a rare cause of headache not readily diagnosed on the history alone. Papilloedema indicates the diagnosis in adults, but is not seen invariably in children with the condition.

More commonly encountered in the tropics are the acute infections, **viral encephalitis**, malaria and **dengue haemorrhagic fever**, all of which can present with sudden severe headache with or without a neurological deficit. These infections need to be recognized wherever they are likely to occur.

Other disorders seen more in the tropics that may present with subacute or chronic headache are **tuberculosis, neurocysticercosis, neurosarcoidosis** and **HIV-related infections**. These are often diagnosed only on imaging or by specific laboratory tests.

thermore, several (though not all) follow-up studies in developed countries suggest that headache prevalence and burden are increasing (*19*).

No significant mortality is associated with headache disorders, which is one reason why they are so poorly acknowledged. Nevertheless, among the recognizable burdens imposed on people affected by headache disorders are pain and personal suffering, which may be substantial, impaired quality of life and financial cost. Above all, headache disorders are disabling: worldwide, WHO ranks migraine alone at 19th among all causes of years of life lost to disability (YLDs) (*20*). Collectively, all headache disorders probably account for double this burden (*3*), which would put them among the top ten causes of disability. Repeated headache attacks, and often the constant fear of the next, damage family life, social life and employment (*21*). For example, social activity and work capacity are reduced in almost all people with migraine and in 60% of those with tension-type headache. Headache often results in the cancellation of social activities while, at work, people who suffer frequent attacks are likely to be seen as unreliable — which they may be — or unable to cope. This can reduce the likelihood of promotion and undermine career and financial prospects.

While people actually affected by headache disorders bear much of their burden, they do not carry it all: employers, fellow workers, family and friends may be required to take on work and duties abandoned by headache sufferers. Because headache disorders are most troublesome in the productive years (late teens to 60 years of age), estimates of their financial cost to society are massive — principally from lost working hours and reduced productivity because of impaired working effectiveness (*22*). In the United Kingdom, for example, some 25 million working or school days are lost every year because of migraine alone (*6*). Tension-type headache, less disabling but more common, and chronic daily headache, less common but more disabling, together cause losses that are almost certainly of similar magnitude.

Therefore, while headache rarely signals serious underlying illness, its public health importance lies in its causal association with these personal and societal burdens of pain, disability, damaged quality of life and financial cost. Not surprisingly, headache is high among causes of consulting both general practitioners and neurologists (*23, 24*). One in six patients aged 16–65 years in a large general practice in the United Kingdom consulted at least once because of headache over an observed period of five years, and almost 10% of them were referred to secondary care (*25*). A survey of neurologists found that up to a third of all their patients consulted because of headache — more than for any other single complaint (*26*).

Far less is known about the public health aspects of headache disorders in developing and resource-poor countries. Indirect financial costs to society may not be so dominant where labour costs are lower but the consequences to individuals of being unable to work or to care for children may be severe. There is no reason to believe that the burden of headache in its personal elements weighs any less heavily where resources are limited, or where other diseases are also prevalent.

BARRIERS TO CARE

Headache ought to be a public health concern, yet there is good evidence that very large numbers of people troubled, even disabled, by headache do not receive effective health care (*2*). For example, in representative samples of the general populations of the United States and the United Kingdom, only half the people identified with migraine had seen a doctor for headache-related reasons in the last 12 months and only two thirds had been correctly diagnosed (*27*). Most were solely reliant on over-the-counter medications, without access to prescription drugs. In a separate general-population questionnaire survey in the United Kingdom, two thirds of respondents with migraine were searching for better treatment than their current medication (*28*). In Japan, awareness of migraine and rates of consultation by those with migraine are noticeably lower (*29*). Over

80% of Danish tension-type headache sufferers had never consulted a doctor for headache (*30*). It is highly unlikely that people with headache fare any better in developing countries.

The barriers responsible for this lack of care doubtless vary throughout the world, but they may be classified as clinical, social, or political and economic.

Clinical barriers

Lack of knowledge among health-care providers is the principal clinical barrier to effective headache management. This problem begins in medical schools where there is limited teaching on the subject, a consequence of the low priority accorded to it. It is likely to be even more pronounced in countries with fewer resources and, as a result, more limited access generally to doctors and effective treatments.

Social barriers

Poor awareness of headache extends similarly to the general public. Headache disorders are not perceived by the public as serious since they are mostly episodic, do not cause death and are not contagious. In fact, headaches are often trivialized as "normal", a minor annoyance or an excuse to avoid responsibility. These important social barriers inhibit people who might otherwise seek help from doctors, despite what may be high levels of pain and disability. Surprisingly, poor awareness of headache disorders exists among people who are directly affected by them. A Japanese study found, for example, that many patients were unaware that their headaches were migraine, or that this was a specific illness requiring medical care (*31*). The low consultation rates in developed countries may indicate that many headache sufferers are unaware that effective treatments exist. Again, the situation is unlikely to be better where resources are more limited.

Political and economic barriers

Many governments, seeking to constrain health-care costs, do not acknowledge the substantial burden of headache on society. They fail to recognize that the direct costs of treating headache are small in comparison with the huge indirect cost savings that might be made (for example by reducing lost working days) if resources were allocated to treat headache disorders appropriately.

MANAGEMENT AND PREVENTION

Successful management of headache disorders follows five essential steps:

- the sufferer must seek medical treatment;
- a correct diagnosis should be made;
- the treatment offered must be appropriate to the diagnosis;
- the treatment should be taken as directed;
- the patient should be followed up to assess the outcome of treatment, which should be changed if necessary.

Therefore the key to successful health care for headache is education (*31*), which first should create awareness that headache disorders are a medical problem requiring treatment. Education of health-care providers should encompass both the elements of good management (see Box 3.3.2) and the avoidance of mismanagement.

Diagnosis

Committing sufficient time to taking a systematic history of a patient presenting with headache is the key to getting the diagnosis right. The history-taking must highlight or elicit description of the characteristic features of the important headache disorders described above. The correct diagnosis is not always evident initially, especially when more than one headache disorder is present, but the history should awaken suspicion of the important secondary headaches. Once it is established that there is no serious secondary headache, a diary kept for a few weeks to record

the pattern of attacks, symptoms and medication use will usually clarify the diagnosis. Physical examination rarely reveals unexpected signs after an adequately taken history, but should include blood pressure measurement and a brief but comprehensive neurological examination including the optic fundi; more is not required unless the history is suggestive. Examination of the head and neck may find muscle tenderness, limited range of movement or crepitation, which suggest a need for physical forms of treatment but do not necessarily elucidate headache causation.

Investigations, including neuroimaging, rarely contribute to the diagnosis of headache when the history and examination have not suggested an underlying cause.

Realistic objectives

There are few patients troubled by headache whose lives cannot be improved by the right medical intervention with the objective of minimizing impairment of life and lifestyle (*32*). Cure is rarely a realistic aim in primary headache disorders, but people disabled by headache should not have unduly low expectations of what is achievable through optimum management.

Medication-overuse headache and other secondary headaches are, at least in theory, resolved through treatment of the underlying cause.

Predisposing and trigger factors

Migraine, in particular, is said to be subject to certain physiological and external environmental factors. While predisposing factors increase susceptibility to attacks, trigger factors may initiate them. The two may combine. Attempts to control migraine by managing either are often disappointing. A few predisposing factors (stress, depression, anxiety, menopause, and head or neck trauma) are well recognized but not always avoidable or treatable. Trigger factors are important and their influence is real in some patients, but generally less so than is commonly supposed. Dietary triggers are rarely the cause of attacks: lack of food is a more prominent trigger. Many attacks have no obvious trigger and, again, those that are identified are not always avoidable. Diaries may be useful in detecting triggers but the process is complicated as triggers appear to be cumulative, jointly overflowing the "threshold" above which attacks are initiated. Too much effort in seeking triggers causes introspection and can be counter-productive. Enforced lifestyle change to avoid triggers can itself adversely affect quality of life.

In tension-type headache, stress may be obvious and likely to be etiologically implicated. Musculoskeletal involvement may be evident in the history or on examination. Sometimes, neither of these factors is apparent. An interesting variation in the Muslim world is the marked rise, observed in people ordinarily susceptible to headache, in tension-type headache incidence on the first day of fasting (*33*).

Box 3.3.2 Seven elements of good headache management

1	Evident interest and investment of time to inform, explain, reassure and educate
2	Correct and timely diagnosis
3	Agreed high but realistic objectives
4	Identification of predisposing and/or trigger factors and their avoidance through appropriate lifestyle modifications
5	Intervention (optimal management of most primary headaches combines adequate but not excessive use of effective and cost-effective pharmaceutical remedies with non-pharmacological approaches; secondary headaches generally require treatment of the underlying cause)
6	Follow-up to ensure optimum treatment has been established
7	Referral to specialist care when these measures fail

Cluster headache is usually but not always a disease of smokers, many of them heavy consumers of tobacco. However, patients with cluster headache who still smoke cannot be promised that giving up will end or even improve their headaches. Alcohol potently triggers cluster headache and most patients have learnt to avoid it during cluster periods.

THERAPEUTIC INTERVENTIONS

The purpose of pharmacotherapy of primary headache, once non-drug measures have been fully exploited, is to control symptoms so that the impact of the disorder on each individual patient's life and lifestyle is minimized. This requires a therapeutic plan tailored for each patient, and patients with two or more coexisting headache disorders are likely to require separate plans for each disorder.

Migraine

Most people with migraine require drugs for the acute attack. These may be symptomatic or specific. The desirable goal of acute therapy with drugs currently available — resolution of symptoms and full return of function within two hours — is not attainable by all. When symptom control with best acute therapy is inadequate, it can be supplemented with prophylactic medication (*34*), usually for 4–6 months, aiming to reduce the number of attacks.

General population surveys indicate that large numbers of people with migraine manage themselves, with no more than symptomatic over-the-counter remedies (*27*). For many this appears adequate. Simple oral analgesia — acetylsalicylic acid or ibuprofen — is used to best advantage in soluble formulations taken early because gastric stasis develops as the migraine attack progresses and this impedes absorption. A prokinetic antiemetic — metoclopramide or domperidone — enhances the analgesic effect by promoting gastric emptying and is most suitable for nausea and vomiting. When oral symptomatic therapy fails, it is logical to bypass the gut using a non-steroidal anti-inflammatory drug such as diclofenac, with or without domperidone, given as rectal suppositories (*35*).

Specific drugs — triptans and, in certain circumstances, ergotamine tartrate — should not be withheld from those who need them. There are specific contraindications to these drugs, particularly coronary disease (and multiple risk factors thereof) and uncontrolled hypertension, but triptans as a class show higher efficacy rates than symptomatic treatments. Population-based needs assessments suggest many more people with migraine should receive triptans than currently do. Cost has much to do with this, and this constraint must be more evident in resource-poor countries where triptans are unlikely to be available. Denial of the best treatment available is difficult to justify for patients generally, however, and therefore for individuals: unnecessary pain and disability are the result. In addition, increasingly it is being demonstrated in developed countries that under-treatment of migraine is not cost effective: the time lost by sufferers and their carers is expensive, as are repeated consultations in the search for better therapy. On this basis some specialists believe that disability assessment should be the means to select patients to receive triptans. Where disability is the basis of choice, however, it should be noted that over 80% of people with migraine report disability because of it (*36*).

Which triptan to choose is an individual matter because different patients respond differently to them: one may work where another does not. In countries where more than one is available, patients may reasonably try each in turn to discover which suits them best. Relapse (return of headache within 6–48 hours) in 20–50% of patients who have initially responded is a troublesome limitation of triptans. A second dose is usually effective for relapse but, occasionally in some patients and often in a few, induces further relapse. This problem may underlie medication-overuse headache attributable to triptan overuse (*37*).

Drugs in a range of pharmacological classes have limited but often useful prophylactic efficacy against migraine through mechanisms that are presumably not identical but are unclear. The choice

of agent is guided by comorbidities and contraindications. Because poor compliance is a major factor impairing effectiveness, drugs given once daily are preferable, all else being equal. Beta-blockers without partial agonism (such as atenolol, metoprolol, and propranolol in a long-acting formulation) are likely to be first-line prophylactics in many countries. Cardioselectivity and hydrophilicity do not affect efficacy but both improve the side-effect profile, so atenolol may be preferred. Certain antiepileptic drugs (AEDs), notably divalproex or sodium valproate and topiramate, have good evidence of efficacy. Amitriptyline is useful especially when migraine and tension-type headache occur together. Relatively low doses are often sufficient. Among calcium channel blockers, only flunarizine has efficacy. Methysergide, a synthetic ergot alkaloid, is effective but recommended for use only under specialist supervision, and not for more than six months continuously.

In some women, hormonal influences are important in driving attack frequency, and a special approach may be taken to menstruation-related migraine (*38*).

Tension-type headache

Reassurance and over-the-counter analgesics (acetylsalicylic acid or ibuprofen rather than paracetamol) (*39*) are sufficient for infrequent episodic tension-type headache. Most people with this condition manage themselves: episodic tension-type headache is self-limiting and, though it may be temporarily disabling, it rarely raises anxieties. If medication usage is on fewer than two days per week there is little risk of escalating consumption.

People consult doctors because of episodic tension-type headache when it is becoming frequent and, in all likelihood, is no longer responding to painkillers. Long-term remission is then the objective of management, as it is for chronic tension-type headache. Symptomatic medication is contraindicated for tension-type headache occurring on more than two days per week: where it is already being taken at high frequency a diagnosis of chronic tension-type headache rather than medication-overuse headache cannot be made with confidence. Whichever condition is present (and it can be both), frequently taken symptomatic medication must be withdrawn as the first step (see below).

Physiotherapy is the treatment of choice for musculoskeletal symptoms accompanying frequent episodic or chronic tension-type headache. In stress-related illness, lifestyle changes to reduce stress, and relaxation and/or cognitive therapy to develop stress-coping strategies, are the treatment mainstays. Prophylactic medication has a limited role. Amitriptyline is first-line in most cases, withdrawn after improvement has been maintained for 4–6 months. Long-term remission is not always achievable, especially in long-standing chronic tension-type headache. A pain management clinic may be the final option.

Cluster headache

Because of its relative rarity, cluster headache has a tendency to be misdiagnosed, sometimes for years. It is the one primary headache that may not be best managed in primary care, but the primary care physician has an important role not only in recognizing it at once but also in discouraging inappropriate "treatments" (tooth extraction is not infrequent).

Medication-overuse headache

Prevention is the ideal management of medication-overuse headache, which means avoidance of acute medication for headache on more than 2–3 days per week on a regular basis. Education is the key factor: many patients with medication-overuse headache are unaware of it as a medical condition (*40*). Once this disorder has developed, early intervention is important since the long-term prognosis depends on the duration of medication overuse (*41*).

Treatment is withdrawal of the suspected medication(s). Although this will lead initially to worsening headache and sometimes nausea, vomiting and sleep disturbances, with forewarning and explanation it is probably most successful when done abruptly (*42*).

Serious secondary headaches

All the serious secondary headaches described above require specialist referral. In most cases, this should be immediate or urgent.

FOLLOW-UP AND REFERRAL

Neither the first diagnosis, nor the first proposed treatment plan, may be correct. Follow-up is essential, at intervals balanced on the one hand to allow time for treatment interventions to achieve observable effect and on the other to meet patients' natural desires for a quick solution to a painful and often debilitating problem.

For migraine and episodic tension-type headache, attack frequency is likely to be the principal determinant. For chronic tension-type headache, follow-up provides the psychological support that is often needed while recovery is slow.

In medication-overuse headache, early review is essential once withdrawal from medication has begun, in order to check that it is being achieved: nothing is less helpful than discovering, three months later, that the patient ran into difficulties and gave up the attempt. During later follow-up, the underlying primary headache condition is likely to re-emerge and require re-evaluation and a new therapeutic plan. Most patients with medication-overuse headache require extended support: the relapse rate is around 40% within five years (*41*).

Urgent referral for specialist management is recommended at each onset of cluster headache. Weekly review is unlikely to be too frequent and allows dosage incrementation of potentially toxic drugs to be as rapid as possible. Patients commencing lithium therapy, or changing their dose, need levels checked within one week.

In all other cases, specialist referral is appropriate when the diagnosis remains (or becomes) unclear or these standard management options fail.

HEALTH-CARE POLICY

The volume of headache referrals to neurologists seen in developed countries is difficult to justify, and should not be repeated in countries where headache-related health services are being developed. The common headache disorders require no special investigation and they are diagnosed and managed with skills that should be generally available to physicians. Management of headache disorders therefore belongs in primary care for all but a very small minority of patients. Models of health care vary but, in most countries, primary care has an acknowledged and important role. It is a role founded on recognition that decisions in primary care take account of patient-related factors — family medical history and patients' individual expectations and values — of which the continuity and long-term relationships of primary care generate awareness (*43*) while promoting trust and satisfaction among patients (*44*).

Even in primary care, however, the needs of the headache patient are not met in the time usually allocated to a physician consultation in many health systems. Nurses and pharmacists can complement the delivery of health care.

- The evident burden of headache disorders on individuals and on society is sufficient to justify a strategic change in the approach to headache management (*31, 45*). In order to implement beneficial change, public health policy in all countries must embrace the following elements.
- The prevalence of the common headache disorders in each region of the world needs to be known, through further epidemiological research where necessary, in order to gain a complete picture of headache disorders and their clinical, social and economic implications locally.
- This information, as it is accumulated, should be employed to combat stigma and increase public awareness of headache as a real and substantial health problem.

- Education, as the key to effective headache management, needs improving at all levels. In the case of the medical profession, this should begin in medical schools by giving headache disorders a place in the undergraduate curriculum that matches their clinical importance as one of the most common causes of consultation. Nowhere is this the case at present.
- The health economics of headache disorders and their effective treatment generally support investment of health-care resources in headache management programmes, set up in collaboration with key stakeholders to create services appropriate to local systems and local needs. Their outcomes should be evaluated in terms of measurable reductions in population burden attributable to headache disorders.

PARTNERSHIPS WITHIN AND BEYOND THE HEALTH SYSTEM

The elements listed above form the framework of WHO's Global Campaign to Reduce the Burden of Headache Worldwide (*45*). Launched in March 2004, this campaign — known as "Lifting the Burden" — is a formal partnership between WHO and the international nongovernmental organizations for headache: the lay World Headache Alliance and the professional International Headache Society and European Headache Federation. The objectives of *Lifting the Burden* are, region by region throughout the world, to:

- measure the burden of headache disorders;
- raise awareness of headache disorders among local health policy-makers;
- work with people and agencies locally to plan locally appropriate health-care solutions;
- put these solutions in place, providing clinical management supports;
- test them, and modify and re-test if necessary, for optimal beneficial change.

Aside from this partnership, lay and professional groups in countries around the world play important, though often less formal, roles in education and in sharing information and experience.

RESEARCH

Five research fronts are currently important in the field of headache medicine.

- Basic research concentrates on elucidating disease mechanisms, particularly those that respond to environmental influences and those with a genetic basis. The findings will guide the development of new treatments.
- Pharmaceutical research and clinical trials support the translation of new discoveries into better treatments for people with headache disorders.
- Epidemiological research will establish the scope and scale of headache-related burden of illness around the world. The results will guide appropriate allocation of health-care resources by policy-makers. Epidemiological studies may also identify preventable risk factors for headache disorders.
- Health services research, backed by health economics studies, may show that the reallocation of resources towards improving health-care delivery offers greater benefits for people with headache disorders — by more effectively using treatments already available — than the search for new pharmacological interventions. This is particularly so given the prevalence of medication misuse (both underuse and overuse). Community intervention studies may lead to better prevention of headache disorders.
- Outcomes research is needed to guide optimal health care and its delivery through organized health services.

The importance of patient and public involvement in defining research objectives should be emphasized: lay people have experience and skills that complement those of researchers.

CONCLUSIONS AND RECOMMENDATIONS	
1	Headache disorders are common and ubiquitous. They have a neurological basis, but headache rarely signals serious underlying illness. The huge public health importance of headache disorders arises from their causal association with personal and societal burdens of pain, disability, damaged quality of life and financial cost.
2	Headache disorders have many types and subtypes, but a very small number of them impose almost all of these burdens. They are diagnosed clinically, requiring no special investigations in most of the cases.
3	Although headache disorders can be treated effectively, globally they are not, because health-care systems fail to make treatment available.
4	Management of headache disorders everywhere in the world has low priority, which abjectly fails to match headache-related health-care provision and delivery to people's needs.
5	Effective management of headache disorders can be provided in primary care for all but a very small minority of patients. Nurses and pharmacists can complement the delivery of health care by primary care physicians.
6	Good management, at whatever level, requires education of doctors and of people affected by headache disorders. Mismanagement, and overuse of medications to treat acute headache, are major risk factors for disease aggravation.
7	Every government should acknowledge the humanitarian arguments for effective health care for headache disorders.
8	Every government should be aware of the financial cost to the country of headache disorders in its population. Cost-of-illness studies will create awareness of the potential savings that better health care for headache disorders may achieve through mitigated productivity losses.
9	Partnerships between health policy-makers, health-care providers and people affected by headache disorders and their advocacy groups may be the best vehicle for determining, and bringing about, the changes that people with headache need.

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3.4 Multiple sclerosis

Multiple sclerosis affects around 2.5 million people worldwide: it is one of the most common neurological disorders and cause of disability of young adults, especially in Europe and North America. There is a lack of epidemiological studies from Asia where the prevalence is reported to be low, though, with the availability of more neurologists and magnetic resonance imaging, a larger number of patients are being diagnosed. Although some people experience little disability during their lifetime, up to 60% are no longer fully ambulatory 20 years after onset, with significant implications for their quality of life and the financial cost to society.

Multiple sclerosis (MS) is an inflammatory demyelinating condition of the central nervous system (CNS) that is generally considered to be autoimmune in nature. In people with MS, the immune trigger is unknown, but the targets are myelinated CNS tracts. In regions of inflammation, breakdown of the blood–brain barrier occurs and destruction of myelin ensues, with axonal damage, gliosis and the formation of sclerotic plaques.

Plaques (MS lesions) may form in the CNS white matter in any location (and also in grey matter); thus, clinical presentations may be diverse. Continuing lesion formation in MS often leads to physical disability and, not infrequently, to cognitive decline.

DIAGNOSIS AND CLASSIFICATION

As the above definition suggests, MS can lead to a wide variety of symptoms, affecting different parts of the body and with varying severity. Diagnosis of MS has always been clinically based, but many tests — notably magnetic resonance imaging (MRI) and more specific diagnostic criteria — are now available to assist the clinician. MRI, the examination of the cerebrospinal fluid (CSF) and visual evoked potentials are helpful in confirming the clinical suspicion of MS. In Asia, where the prevalence is reported to be low (1–5 per 100 000), the clinical presentation may be similar to that seen in Europe and North America, with manifestations suggesting cerebral, brainstem, cerebellar, optic nerve and spinal cord involvement (western type of MS) or may present with more restricted recurrent optic nerve and spinal cord involvement (opticospinal form or the Asian variant). The reason for this variation is not known.

Typically, the clinician takes a detailed neurological history and carries out a neurological examination to assess how the nervous system has been affected. To establish the diagnosis of MS, a neurologist must demonstrate that involvement of the CNS is disseminated in time and space and exclude any other diagnostic possibility. Defined criteria are used to conclude whether the features fulfil the clinical diagnosis and allow for more precision, thus lessening the likelihood of an incorrect diagnosis. Currently, the most widely accepted guidelines to the diagnosis of MS are the "McDonald criteria" (*1*). These criteria incorporate MRI to provide evidence of dissemination in

time and space and enable the clinician to make an early diagnosis of MS. They also facilitate the diagnosis of MS after a first attack (a clinically isolated syndrome) and in disease with insidious progression (the primary progressive form of MS), see below.

While these criteria have proved to be useful in a typical adult Caucasian population of western European ethnic origin, their validity remains to be proven in other regions such as Asia where some studies still use Poser's criteria. As the experience with MRI in MS builds up, it is expected that the McDonald criteria with minor modifications will become applicable worldwide. It is always essential that other conditions mimicking MS (such as vascular disorders, Sjogren's disease and sarcoid) are excluded.

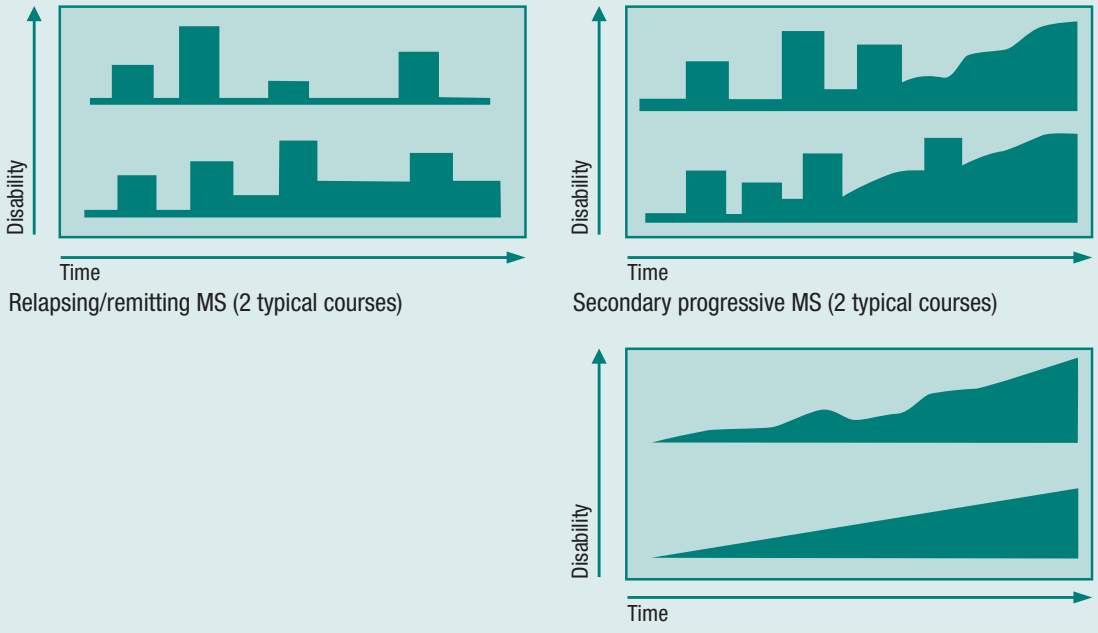
COURSE AND OUTCOME

Just as the symptoms of MS are varied, so too is the course of the disease. Although some people with MS experience little disability during their lifetime, up to 60% are no longer fully ambulatory 20 years after onset. In rare cases MS is so malignantly progressive it is terminal, but most people with MS have a normal or near-normal life expectancy.

Typical patterns of progression, illustrated in Figure 3.4.1, are explained below.

- **Relapsing/remitting MS**. Approximately 80% of patients will initially present this form of MS, in which there are unpredictable attacks (relapses) during which new symptoms appear or existing symptoms become more severe. The relapses can last for varying periods (days or months) and there is partial or total recovery (remission). The disease may appear to be clinically inactive for months or years, though MRI studies show that asymptomatic inflammatory activity is usually more frequent. Over time, however, symptoms may become more severe with less complete recovery of function after each attack, possibly because of gliosis and axonal loss in repeatedly affected plaques. People with MS may then enter a progressive phase, characterized by a step-like downhill course.

Figure 3.4.1 Patterns of progression of multiple sclerosis



Source (*2*).

- **Secondary progressive MS** is characterized by progression that is not relapse related. Approximately 50% of patients with relapsing/remitting MS will develop secondary progressive MS within 10 years, and 80% will have developed this form of MS within 20 years of disease onset.
- **Primary progressive MS**, which affects around 10–15% of all MS patients, is characterized by a lack of distinct attacks, but with slow onset and then steadily worsening symptoms. There is an accumulation of deficits and disability which may level off at some point or continue over years.
- **Benign MS**. A diagnosis of benign MS is retrospective, when the accumulated disability from relapsing/remitting MS is either mild or non-existent after a long period (usually considered to be 15–20 years). Given that follow-up studies show that most patients of this type will eventually enter a disabling secondary progressive phase, the term "benign" is somewhat misleading.

Prognostic factor

Although MS is an unpredictable condition, some studies have suggested that onset with sensory symptoms or optic neuritis may have a better outlook. It has also been shown that multisite presentations and poor recovery from an initial episode may indicate a worse outcome. Studies that have observed a difference by sex usually indicate that males experience a more severe course than females.

EPIDEMIOLOGY AND BURDEN

The incidence and prevalence of MS have been studied extensively (*3*). Some features of the disease are generally accepted and are discussed further in this section.

- The frequency of MS varies by geographical region throughout the world, apparently increasing with distance from the equator in both hemispheres.
- The disease is more common among women than men.
- Peak onset is at around 30 years of age.
- The disease is less common among non-white individuals than whites.

Etiology and risk factors

The distributions of MS by geography, sex, age, and race or ethnicity have all been explored for clues to etiology. Most early research focused on the possible role of an environmental factor that varied with latitude. To date no such risk factor for the disease has been unequivocally identified, though researchers continue to believe that one exists. There is substantial evidence of a genetic predisposition to the disease based on familial aggregation, and some debate over whether genetics or exposure to an environmental trigger primarily accounts for its geographical distribution. Relatively little is known about factors that predict the course of MS.

The worldwide distribution of MS can be only an indirect reflection of its cause, implicating some environmental factor that varies with latitude, and can be interpreted in at least three different ways in the search for clues to a specific etiology. First, an environmental risk factor may be more common in temperate than tropical climates. Second, such a factor may be more common in tropical climates, where it is acquired at an earlier age and consequently has less impact. Third, this factor may be equally common in all regions, but the chance of its acquisition or of the manifestation of symptoms is either increased by some enhancing factor present in temperate climates or reduced by a protective factor present in tropical areas.

Among those factors that have been most closely scrutinized are:

- infections, including a number of viral infections such as measles and Epstein–Barr virus;
- climate and solar conditions;
- living conditions;
- diet and trace elements.

It is now generally accepted that the etiology of MS involves some interplay of genetic and environmental factors. Evidence of racial or ethnic resistance, the increased risk among MS family members, and elevated monozygotic twin concordance rate all favour a genetic contribution to acquisition of the disease. The studies from which this evidence is derived, however, also indicate that heredity cannot entirely explain the occurrence of MS. This is underlined by the fact that no population-based study of monozygotic twins has found a concordance rate in excess of 30%. Some environmental factor, such as a virus or toxin, must still play a role.

Global and regional distribution

The fact that there is an uneven geographical distribution of MS has been known since early in the 20th century. The prevalence of MS has been shown to vary with latitude, with rates broadly rising as distance from the equator increases, in both the northern and southern hemispheres. While there is some truth to this, it belies the complex interaction of geography, genes and environment that larger scale epidemiological studies have uncovered.

As a recent meta-analysis of the epidemiology of MS put it "The updated distribution of MS [in Europe], showing many exceptions to the previously described north-south gradient, requires more explanation than simply a prevalence-latitude relationship. Prevalence data imply that racial and ethnic differences are important in influencing the worldwide distribution of MS and that its geography must be interpreted in terms of the probable discontinuous distribution of genetic susceptibility alleles, which can however be modified by environment. Because the environmental and genetic determinants of geographic gradients are by no means mutually exclusive, the race versus place controversy is, to some extent, a useless and sterile debate" (*4*).

There is substantial literature on the relationship between migration and the prevalence and incidence of MS. Studies both between and within countries invariably show that immigrants moving from high-risk to low-risk areas have a higher rate than that in their new homeland, but often somewhat lower than that in their place of origin. (Note that if this observation were based only on prevalence data, it might simply reflect the fact that sick and disabled people are less likely to move, rather than less frequent exposure to a risk factor or more frequent exposure to a protective factor in the new place of residence. However, data for the United States are based primarily on incidence and document the same decline in risk as found in prevalence studies.)

There are fewer studies of immigrants from low-risk to high-risk areas, but most findings indicate that immigrants retain the same risk as in their countries of origin. This may be because they carry some protective factor with them, but these studies frequently involve non-white immigrants in whom the disease is known to be rare and who may be genetically resistant.

All areas at medium to high risk for MS throughout the world have predominantly white populations. In countries with both white and non-white populations, MS rates are lower among non-whites. For example, the disease is virtually non-existent among Australian Aborigines, New Zealand Maoris and Black people in South Africa. In the United States, incidence and prevalence rates are twice as high among whites as among African Americans regardless of latitude. Furthermore, MS is also less frequent among North American Indians, Latin Americans, and people of the Western Pacific Region than among whites.

Childhood multiple sclerosis

While MS is predominantly an illness of young to middle-aged adults, it is also increasingly apparent that the disease can occur in children. Interest in, and knowledge of, paediatric MS has been increasing, and as a consequence the number of children diagnosed has also risen considerably over the last 10 years. At least 2.5–5% of all patients with MS experience their first clinical attack prior to their 16th birthday, though this may be an underestimate.

Typically, with paediatric MS, the sex difference is not as marked as it is with adults, the ratio of female to male being closer to 1:1 than the 2:1 that is normally cited for adults. This suggests

that, while the genetic implication of being female may influence MS risk, it appears to do so much more after puberty.

Further evidence of the role that environmental factors play comes from the studies of children of migrants. For example, the prevalence rates among the British-born children of immigrants from India, Pakistan, and parts of Africa and the West Indies were very much higher than those recorded for their parents and approximately equal to the expected rate for England.

IMPACT

Multiple sclerosis has a profound impact on patients' social roles and the well-being of their families. Varying degrees of functional decline typically accompany MS. Because the onset is usually at about 30 years of age, the loss in productivity of people with MS can be substantial. Such functional decline will often interfere with the opportunities for people with MS to perform their customary roles. For example, physical disability — complicated by fatigue, depression and possibly cognitive impairment — contributes to an unemployment rate as high as 70% among people with MS; to replace lost earnings, they frequently collect disability benefits and social welfare. People with MS use more health-care resources than the general population (*5*). Together with their family members, they may also bear a financial burden related to home and transport modifications and the need for additional personal services.

The socioeconomic impact of MS on the individual is well illustrated by a recent United Kingdom study (*6*). In this population-based survey of all known patients with MS and their relatives in the county of Hampshire, England, about 53% of those who were employed at the time of diagnosis gave up their jobs, and the standard of living of 37% of patients and their families declined as a direct result of the disease. The ability to continue in gainful employment or to maintain social contacts and leisure activities correlates with the course and severity of the disease and cognitive function. Most carers reported symptoms that clearly related to organic pathologies, anxiety and symptoms of depression. The occurrence of these symptoms was associated with disease severity. The professional careers of 57% of relatives were also adversely affected by the patient's illness.

The economic cost to society is also great (*7*). A recent economic analysis for the Australian MS Society (Acting Positively) illustrated the impact of the disease, which is considered typical (so far no global economic impact studies have been published). The Australian study found that the burden of the disease is likely to grow. Prevalence is expected to grow by 6.7% in the next five years, faster than population growth attributable to demographic ageing. The total financial costs of MS in 2005 are estimated at more than US$ 450 m (0.07% of GDP) and US$ 29 070 per person with MS, or US$ 23 per Australian per year. Lost productive capacity and the replacement value of informal community care are the two largest cost components (*8*). The following key economic factors were highlighted by the Australian study.

- Informal care for people with MS in the community represents 43% of total costs, with an average of 12.3 hours per week of informal care required per person with MS.
- Aids and modifications for people with physical disability were estimated to represent a further 4.6% of total financial costs.
- Production losses stemming from reduced work hours, temporary absences, early retirement and premature death are responsible for around 26% of total economic costs.
- Pharmaceuticals for people with MS, mainly beta-interferons, are estimated to represent 14% of total costs.
- Nursing home accommodation accounts for around 4.3% of total economic costs. Of the estimated 730 people with MS in (high care) nursing homes 37% are under 65 years of age.
- Other health-care costs — including hospitalizations, specialist and primary care and allied health expenses — account for 4.4%. Research is 1.9% of health expenditure, below the aver-

age of 2.4%. Deadweight losses arising from taxation revenue foregone and welfare payment transfers are estimated as US$ 10.5 million or 2.3% of total costs in 2005.

- The burden of disease — the suffering and premature death experienced by people with MS — is estimated to cost an additional 8968 DALYs (years of healthy life lost), with two thirds attributable to disability and one third to premature death.
- Last but not least, in Australia MS causes more disability and loss of life than all chronic back pain, slipped discs, machinery accidents, rheumatic heart disease or mental retardation.

PREVENTION AND TREATMENT

Uncertainty over the cause or development of MS implies that prevention is not currently a realistic option. Furthermore, there are no curative treatments available for MS (*9*). A number of disease-modifying drugs have been developed in the past 20 years, however, which reduce the number of attacks in the relapsing/remitting form of the disease. The extent to which eventual disease burden and disability are limited by use of the drugs is less clear. The most widely used disease-modifying drugs for MS are the beta-interferons (1a and 1b) and glatiramer acetate, which reduce the frequency and perhaps the severity of relapses. Although these drugs have been introduced in the developing regions, their high cost means many patients are unable to have access to them. The United States National MS Society also has developed several guidelines and recommendations, mainly for medical treatment (such as changing therapy and early intervention). To date, no medical treatments for the progressive forms of the disease exist, and results from studies focusing on neuroprotection and repair are eagerly awaited.

Corticosteroids are the medications of choice for treating exacerbations and can be administered in the hospital or community setting (the latter is usually preferred) (*10*). In addition to strategies aimed at the impact of the disease, drugs to ameliorate common MS symptoms — such as urinary dysfunction, spasticity and neuropathic pain — are relatively well established and widely used. European guidelines have been developed for both the use of the established disease-modifying drugs and the treatment of symptoms (*11, 12*).

Even though drug treatment options are relatively limited, significant improvements in the quality of life of people with MS can be supported by improved rehabilitation approaches. For patients with relatively moderate disability, exercise (both aerobic and non-aerobic) has been found to be useful, as has physiotherapy. There have been few, if any, studies evaluating the rehabilitation needs of those with more severe disability.

Neurorehabilitation

The philosophy of neurorehabilitation, which emphasizes patient education and self-management, is well suited to meet the complex and variable needs of MS (*13*). Neurorehabilitation aims to improve independence and quality of life by maximizing ability and participation. It has been defined by WHO as "an active process by which those disabled by injury or disease achieve a full recovery or, if a full recovery is not possible, realize their optimal physical, mental and social potential and are integrated into their most appropriate environment". Together with Rehabilitation in Multiple Sclerosis, the European Multiple Sclerosis Platform (EMSP) developed useful guidance on this issue in their recommendations on MS rehabilitation services (*14*), one of the reference guidelines for their European Code of Good Practice in MS.

The essential components of successful neurorehabilitation include expert multidisciplinary assessment, goal-oriented programmes and evaluation of impact on patient and goal achievement through the use of clinically appropriate, scientifically sound outcome measures incorporating the patient's perspective (*14*).

While these principles are intuitively sound, the evidence underpinning multidisciplinary assessment and goal-orientated programmes is weak. Fundamental to the provision of robust

evidence of the benefits of rehabilitation interventions is the use of scientifically sound outcome measures. In the field of MS, the limitations of the Expanded Disability Status Scale have been well aired and it can be argued that the scale is even less relevant to neurorehabilitation as it fails to incorporate the views of the patient.

The issues relating to the management of symptoms that affect people with MS are identical to those concerning neurorehabilitation: the need for robust clinical trials based on scientifically sound outcome measures, multidisciplinary expertise and the involvement of patients. The frequency with which these symptoms affect people with MS has been documented for a range of symptoms including fatigue, spasticity, pain and cognitive impairment. The need for a multidisciplinary and multimodal approach to symptom management is described in a recent review (*15*) and is exemplified in the case of spasticity (*16*).

Service delivery

Evaluating service delivery may be considered the most important and relevant issue in the management of MS. This is because it incorporates acute hospital and neurorehabilitation services with community-based activities and has to bring together medical and social services in a way that meets the complex and ever-changing needs of the person with MS.

Ideally, most services should be community-based with supporting expertise from the acute hospital or rehabilitation centre at times of particular need (such as at diagnosis or during a severe relapse) or complexity (when multiple symptoms interact and intensive inpatient rehabilitation is required). The optimum method of service delivery has not yet been defined, and little comparison has been made of existing services.

A recently published study (*17*) compared two forms of service delivery in a randomized controlled trial. One group received what was described as "hospital home care", in which patients remained in the community but had immediate access to the hospital-based multidisciplinary team when required, while the other group received routine care. No difference was seen in the level of disability between the two groups after 12 months, but the "hospital home care" patients, who were more intensely treated, had significantly less depression and improved quality of life.

There continue to be major problems worldwide in delivering a model of care that provides truly coordinated services. There is serious inequity of service provision both within and across countries, and an inordinate and unacceptable reliance on family and friends to provide essential care. Establishing guidance, such as has been done by the National Institute for Clinical Excellence (*18*), is a step forward but a global initiative such as that of the Multiple Sclerosis International Federation (MSIF) to promote the quality of life of people with MS may be more effective (*19*). The key challenge will be ensuring the translation of these guidelines into practice.

Delivery of care to people with MS varies significantly around the world. In part this reflects the differences in incidence and therefore the relative importance afforded to the disease within a country's health system. Given the importance of expensive diagnostic equipment (scanners) and the cost of the existing treatments, however, the variation also reflects different national income levels. In the developed countries, the cost of the treatment is borne by the government or insurance companies but in some regions the patients have to pay for drugs, making it difficult for them to take advantage of emerging new treatments.

The delivery of care for people with long-term illnesses is becoming increasingly "patient centred", and a culture of treatment by interdisciplinary teams is emerging. Within this model, the aim is to offer patients a seamless service, which typically involves bringing together various health professionals including doctors, nurses, physiotherapists, occupational therapists, speech and language therapists, clinical psychologists and social workers. Other professionals with expertise in treating neurologically disabled people cover dietetics, continence advisory and management services, pain management, chiropody, podiatry and ophthalmology services.

Quality of life issues

MS will usually have a substantial adverse effect on a person's quality of life. Improving quality of life should be a key goal for policy-makers as well as those who advocate on behalf of people with MS. A recent key step has been the publication by MSIF of its quality of life principles (*19*), as mentioned above. The development of these principles was based on a series of interviews, a literature review, the clinical, programmatic, and research experience of the authors, and review by a work group and a technical oversight group organized by MSIF.

The principles are designed to be used by international organizations, national MS societies, people with MS and their families, governments, health, social and continuing care providers, employers, researchers, businesses and others to evaluate existing and proposed services and programmes and to advocate for improvements. The areas covered include:

- independence and empowerment;
- medical care;
- continuing care (long-term or social);
- health promotion and disease prevention;
- support for family members;
- transport;
- employment and volunteer activities;
- disability benefits and cash assistance;
- education;
- housing and accessibility of buildings in the community.

Treatment gap

There is no doubt that a significant treatment gap exists in approaches to MS between countries (and possibly within countries). Until a cure is found, people with MS have to rely on reducing the inflammation during an acute phase by the use of corticosteroids and providing symptomatic relief. The disease-modifying agents such as beta-interferon and glatiramer acetate can be offered to decrease the relapses and disease burden. Ideally, this treatment programme requires early diagnosis and adequate human resources and equipment. The situation is especially problematic in the developing countries, as often equipment such as an MRI scanner is not available or is too expensive. The disease-modifying agents are also costly and beyond the reach of many patients. In addition, rehabilitation centres for people with MS are not available.

A further illustration of the treatment gap between rich and less developed countries in their treatment of MS is apparent from data currently being collected by WHO, the MSIF and the EMSP. These data, which will in time be integrated into an international comparative and interactive database (MSIF/WHO Atlas of MS and European Map of MS), have been sourced by surveying neurologists and patient organizations across 98 geographically and economically diverse countries.

For example, in response to the key treatment question "What percentage of people with MS who fulfil the clinical prescription criteria for disease-modifying drugs [in your country] receive treatment?" the average answer from 15 responding members of the European Union was 64%. This compares with (for example) 45% for Brazil, 50% for the Russian Federation, 10–15% for Turkey and less than 5% for India.

RESEARCH

As with many neurological diseases, MS is extremely difficult to study. Even after several decades of intense research activity, it remains a mysterious condition with no known pathogen or accepted determinants of its severity or course. Nonetheless, optimism amongst the MS research community is high. Advances in non-invasive investigative techniques, particularly MRI, have led

to significant improvements in the ability to create images and track the course of the disease. Key areas of current research encompass immunology, genetics, virology/bacteriology, and the biology of the cells that make, maintain and repair myelin in the CNS (including developments in neural stem cells). The key outcome of the research effort to date has been an improved understanding of the pathology and the evolution of the disease and, as a consequence, new approaches to treatment including repair and neuroprotection.

In addition to the advances being made at the therapeutic level, significant improvements are being made in the management of the disease. In large part this has been stimulated by researchers adopting a more patient-centred approach. Whereas MS research used to be conducted by physicians on behalf of people with MS, today's research protocols are more likely to be driven by patient perspectives. This is leading to research being carried out into factors determining the quality of life of people with MS, such as health-care policy, employment and welfare matters and the wider familial impact of the disease. Fortunately, there are active multiple sclerosis support groups in several regions of the world that are involved in improving the quality of life of people with MS.

TRAINING

There is a specific lack of public and professional awareness of the dimension of MS in the domains of epidemiology and impact of disease on individuals, carers and society, including impact on individual loss of independence, and cost of long-term care. In particular, the chronic progressive nature of the condition must be better conveyed to all. MSIF, through its member organizations, has proven very effective and capable of concerted action in the field of patient and lay public education.

CONCLUSIONS AND RECOMMENDATIONS	
1	MS is the most prevalent inflammatory demyelinating disease of the central nervous system in young adults.
2	The cause is (as yet) unknown.
3	Initially, MS most often runs a relapsing/remitting course, later becoming progressive.
4	Depending on the site and extent of the lesions, a variety of symptoms may occur, often in parallel.
5	Many of the symptoms may be treated effectively with drugs and rehabilitation measures.
6	Immunomodulating therapies may reduce relapse frequency and progression of MRI abnormalities.
7	Rehabilitation is most important and aims at leading individuals to adapt their lifestyle.
8	Burden and costs, including the costs of treatment, are considerable for the persons affected, their relatives and society.

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3.5 Neuroinfections

Infectious diseases that involve the nervous system affect millions of people around the world. They constitute the sixth cause of neurological consultation in primary care services and are reported globally by a quarter of WHO's Member States and by half the countries in some parts of Africa and South-East Asia. Neuroinfections are of major importance since ancient times and, even with the advent of effective antibiotics and vaccines, still remain a major challenge in many parts of the world, especially in developing nations.

Approximately 75% of the world population live in developing countries where the worst health indicators are found. Their major health problems are generally related to warm climate, overcrowding, severe poverty, illiteracy and high infant mortality which induce a burden of illness from communicable diseases that differs drastically from the rest of the world. Added to these problems, the health budgets are low and opportunities for community interventions very small. A demographic transition is under way throughout the world: as populations age, the burden of noncommunicable diseases (cardiovascular illnesses, stroke and cancer) increases, particularly in the least favoured regions. Thus, the majority of least-developed countries are facing a double burden from communicable and noncommunicable diseases. The global public health community is now faced with a more complex and diverse pattern of adult disease than previously expected and proposes a "double response" that integrates prevention and control of both communicable and noncommunicable diseases within a comprehensive health-care system (*1*).

Some diseases that used to be found in the developed world but have virtually disappeared, such as poliomyelitis, leprosy and neurosyphilis, are still taking their toll in developing regions. In addition, some of the protozoan and helminthic infections that are so characteristic of the tropics are now being seen with increasing frequency in developed countries owing to migration, large-scale military ventures and rapid means of transport that have the undesirable potential to introduce disease vectors. Although some infectious diseases have been nearly wiped out, the vast majority of them will not be eliminated in the foreseeable future. Indeed, WHO reports that at least 30 new diseases have been scientifically recognized around the world in the last 20 years (*2*). These *emerging diseases* include hantavirus (first identified in the United States in 1993), cryptosporidiosis (a waterborne cause of diarrhoea that recently affected more than 400 000 people in a single outbreak in the United States), the Ebola virus from Africa and the human immunodeficiency virus (HIV), among others. *Re-emerging diseases* are the infections once thought

under control and that re-emerge: diseases such as tuberculosis, malaria, cholera and even diphtheria are making a comeback.

Other main concerns are the development of drug-resistant organisms, the increasing number of immunocompromised populations such as those affected by the acquired immunodeficiency syndrome (AIDS) and malnutrition, and the rising number of diseases previously considered rare (Lyme disease, rickettsioses, Creutzfeldt–Jakob disease and Ebola). Most of these diseases can cause high mortality rates in some populations and produce severe complications, disability and economic burden for individuals, families and health systems. Education, surveillance, development of new drugs and vaccines, and other policies are in constant evolution to fight against old and emerging infectious diseases of the nervous system.

This chapter covers some of the more frequent neuroinfections that have a major impact on health systems, especially in the developing world. Infectious diseases that involve the nervous system are reported globally by 26.5% of WHO's Member States and by 50% of countries in some parts of Africa and South-East Asia (*3*).

- Viral diseases: HIV/AIDS, viral encephalitis, poliomyelitis and rabies.
- Mycobacterial and other bacterial diseases: tuberculosis, leprosy neuropathy, bacterial meningitis and tetanus.
- Parasitic diseases: neurocysticercosis, cerebral malaria, toxoplasmosis, American trypanosomiasis (Chagas disease), African trypanosomiasis (sleeping sickness), schistosomiasis and hydatidosis.

VIRAL DISEASES

HIV/AIDS

The acquired immunodeficiency syndrome (AIDS) is caused by a retrovirus known as the human immunodeficiency virus (HIV), which attacks and impairs the body's natural defence system against disease and infection. HIV is a slow-acting virus that may take years to produce illness in a person. During this period, an HIV-infected person's defence system is impaired, and other viruses, bacteria and parasites take advantage of this "opportunity" to further weaken the body and cause various illnesses, such as pneumonia, tuberculosis and mycosis. When a person starts having such opportunistic infections, he or she has AIDS. The amount of time it takes for HIV infection to become full-blown AIDS depends on the person's general health and nutritional status before and during the time of HIV infection. The average time for an adult is approximately 10 years without antiretroviral therapy (ART). Women are more likely to be infected with HIV than men. Children are also at risk (*4*).

The number of people living with HIV globally has reached its highest level with an estimated 40.3 million people, rising from an estimated 37.5 million in 2003. More than three million people died of AIDS-related illnesses in 2005; more than 500 000 of them were children. Sub-Saharan Africa continues to be the most affected region globally, with 64% of new infections occurring there. HIV treatment has improved markedly, however, and hundreds of thousands of people are now living longer in better health because they are receiving ART: an estimated 250–350 000 deaths were averted in 2005 because of expanded access to HIV treatment (*5*).

Neurological complications occur in 39–70% of patients with AIDS and significantly impact on functional capacity, quality of life and survival. Neuropathological examination identifies abnormal neurological conditions in more than 90% of autopsies but is not always demonstrated clinically (*6*). The main etiological considerations include primary HIV-related syndromes, opportunistic conditions, inflammatory conditions, and medications (*7*) (see Table 3.5.1).

Table 3.5.1 Neurological diseases in the HIV-infected individual

Type of condition	Examples
Primary HIV-related syndromes	HIV-associated cognitive–motor complex HIV-associated myelopathy HIV-associated polyneuropathy HIV-associated myopathy
Opportunistic conditions	Toxoplasma encephalitis Cryptococcal meningitis Cytomegalovirus encephalitis/polyradiculitis Progressive multifocal leukoencephalopathy Primary central nervous system lymphoma
Inflammatory conditions	Acquired demyelinating neuropathies Aseptic meningitis
Treatment-associated conditions	Zidovudine-induced myopathy Nucleoside analog-induced neuropathy

Source: (*7*).

Multiple investigations in recent years suggest that the effects of neurological complications and opportunistic infections related to HIV have a clear trend to diminish since the introduction of new and more powerful antiretroviral agents. Nevertheless, prolonging the life of patients infected by the virus, attributable to therapeutic success, paradoxically favours the emergence of some neurological affections as treatment-associated neuropathy/myopathy; these affections can be more important than the benefits of therapy to achieve viral suppression.

Accurately diagnosing neurological disease in the HIV-infected individual is crucial for several reasons. First, many complications are treatable and their treatment can lead to either increased survival or improved quality of life. Second, identifying currently untreatable conditions provides the patient with the opportunity to participate in a growing number of therapeutic trials. Further, an accurate and focused diagnostic assessment and treatment plan will limit therapeutic misadventures and lead to cost-effective care delivery.

The worldwide use of highly active antiretroviral therapy (HAART) has played an important role in changing the incidence of neurological complications in AIDS patients. Recent studies have shown that HAART has produced both quantitative and qualitative changes in the pattern of HIV neuropathology: an overall decrease in the incidence of some cerebral opportunistic infections such as toxoplasmosis and cytomegalovirus encephalitis, for which successful treatment is available, whereas other uncommon types and new variants of brain infections, such as varicella-zoster encephalitis, herpes simplex virus encephalitis or HIV encephalitis, are being reported more frequently as ART promotes some immune recovery and increases survival (*8*). In developing countries, some endemic infections such as tuberculosis and Chagas disease have re-emerged in direct association with the spreading of HIV, and are now being considered as markers of AIDS.

Unfortunately, some patients may develop paradoxical clinical outcomes after starting treatment with HAART, known as neurological immune restoration inflammatory syndrome (NIRIS). Some treatment-related neurological disorders, like zidovudine-induced myopathy, nucleoside analog-induced neuropathy and efavirenz-induced neuropsychiatric disorders, can be more important than the benefits of the therapy of viral suppression (*9*).

Some therapies can prevent, treat or even cure many of the opportunistic infections and relieve the symptoms associated with them, but there is no cure for HIV/AIDS. The core benefit of HAART lies in its ability to reduce the rate of opportunistic infections by enhancing immune function,

slowing viral replication in the body and thereby improving patients' quality of life and diminishing mortality. The cost of antiretroviral drugs is declining but, unfortunately, the treatments are still not affordable or accessible for most people.

Nevertheless, these important advances over the last decade have transformed HIV infection from a short-term, inevitably fatal disease to a chronic condition amenable to medical management, similar to diabetes or congestive heart failure.

It is important to integrate HIV prevention and care, and the challenges are immense: worldwide, fewer than one in five people at risk of becoming infected with HIV has access to basic prevention services. Of people living with HIV, only one in ten has been tested and is aware of the infection. For prevention interventions to achieve the results necessary to get ahead of the epidemic, projects with short-term horizons must translate into long-term programmatic strategies. In settings in which HIV is largely sexually transmitted, information and education campaigns can save lives. For example, intensive prevention programmes in the Mbeya region of the United Republic of Tanzania led to an increase in the use of condoms and the treatment of sexually transmitted infections between 1994 and 2000; those changes were accompanied by a decline in HIV prevalence among 15–24-year-old women from 21% to 15% in the same period (*10*). In settings in which HIV transmission is linked more closely to injecting drug use, harm-reduction strategies (for example, the provision of clean injecting equipment as well as adequate therapy for drug dependence) have proved to be effective. Other measures include voluntary counselling and testing, and improving women's health — including access to family planning and safe childbirth — in order to prevent HIV transmission from mother to infant. There is no cure for HIV/AIDS.

Viral encephalitis

Acute viral encephalitis is often an unusual manifestation of common viral infections and most commonly affects children and young adults. Every day, more types of viruses are being associated with encephalitis (see Box 3.5.1), and its variable presence depends on the age group, geographical zone, season of the year and the state of health of patients. In the United States, epidemiological studies calculate the incidence of viral encephalitis approximately at 3.5–7.4 per 100 000 population. Estimates have been given for some causes of viral encephalitis: for example, it has been estimated that herpes simplex encephalitis (HSE) has an annual incidence of about one per million.

Herpes simplex encephalitis is the most important and common cause of *fatal sporadic viral encephalitis* in the industrialized world. At a global level, it seems that the most common cause of epidemic encephalitis is actually Japanese B encephalitis, with 10–15 000 deaths per year, markedly more than for herpes simplex encephalitis. It must be considered, however, that in up to about 50% of cases of viral encephalitis no specific cause can be found, so the predominant type is difficult to determine (*11*).

Box 3.5.1 Causes of viral encephalitis

- Herpes simplex virus (HSV-1, HSV-2)
- Other herpes viruses:
  - varicella zoster vírus (VZV)
  - cytomegalovirus (CMV)
  - Epstein–Barr vírus (EBV)
  - human herpes vírus 6 (HHV6)
- Adenoviruses
- Influenza A
- Enteroviruses, poliovirus
- Measles, mumps and rubella viruses
- Rabies
- Arboviruses, e.g.
  - Japanese B encephalitis virus
  - St Louis encephalitis virus
  - West Nile encephalitis virus
  - Eastern, Western, and Venezuelan equine encephalitis virus
  - Tick-borne encephalitis viruses
- Bunyoviruses, e.g. La Crosse strain of California virus
- Reoviruses, e.g. Colorado tick fever virus
- Arenaviruses, e.g. lymphocytic choriomeningitis virus
- Retroviruses, e.g. HIV-1
- Papovavirus, e.g. JC virus

Source: adapted from (*11*).

Viruses enter the central nervous system (CNS) through two distinct routes: hematogenous dissemination or neuronal retrograde dissemination. Hematogenous spread is the most common path. Humans are usually incidental terminal hosts of many viral encephalitides. Arbovirus encephalitides are zoonoses, with the virus surviving in infection cycles involving biting arthropods and various vertebrates, especially birds and rodents. The virus can be transmitted by an insect bite and then undergoes local replication in the skin.

Patients with viral encephalitis are marked by acute onset of a febrile illness and can experience signs and symptoms of meningeal irritation, focal neurological signs, seizures, alteration of consciousness and behavioural and speech disturbances. The diagnosis is made by immunological tests, neuroimaging techniques, electroencephalography and, sometimes, brain biopsy. No specific treatment is available for every encephalitis, and the illness often requires only medical support. The mortality rate and severity of sequelae depend largely on the etiological agent. Herpes virus encephalitis carries a mortality rate of 70% in untreated patients, with severe sequelae among survivors. Pharmacotherapy for herpes virus encephalitis consists of acyclovir and vidarabine. Effective preventive measures include control of vectors by removing water-holding containers and discarded tyres. Vaccines are available for eastern equine encephalitis, western equine encephalitis, and Venezuelan equine encephalitis in horses. Despite control efforts and disease surveillance, the 1999 outbreak of West Nile virus in New York with subsequent spread to other states showed that different viruses may spread because of increased international travel and trade (*12*).

Japanese encephalitis is a leading cause of viral encephalitis in Asia, with 30–50 000 clinical cases reported annually. It occurs from the islands of the Western Pacific in the east to the Pakistan border in the west, and from the Democratic People's Republic of Korea in the north to Papua New Guinea in the south. Japanese encephalitis virus is transmitted by mosquitoes, which breed particularly in flooded rice fields. Pigs are the amplifying hosts. Distribution of the infection is thus very significantly linked to irrigated rice production combined with pig-rearing. An effective killed vaccine is available, but it is expensive and requires one primary vaccination followed by two boosters. It provides adequate protection for travellers but has limited public health value in areas where health service resources are scarce.

Poliomyelitis

Poliomyelitis is a crippling disease caused by any one of three related viruses, poliovirus types 1, 2 or 3. The primary way to spread poliovirus is through the faecal–oral route: the virus enters the body through the mouth when people eat food or drink water that is contaminated with faeces. The virus then multiplies in the intestine, enters the bloodstream, and may invade certain types of nerve cells which it can damage or destroy. Polioviruses spread very easily in areas with poor hygiene. In any child under 15 years of age with acute flaccid paralysis or any person of any age with paralytic illness, poliomyelitis always has to be suspected.

In 1963, Cuba began using an oral vaccine in a series of nationwide polio campaigns. Shortly thereafter, indigenous wild poliovirus transmission was interrupted. Through an extraordinary international effort that begun 18 years ago, indigenous polioviruses have now been eliminated from all but four countries of the world, down from over 125 when the collaboration started (*13*). This progress is the result of a unique partnership forged between governments and the spearheading partners of the Global Polio Eradication Initiative — WHO, Rotary International, the United States Centers for Disease Control and Prevention (CDC) and UNICEF — to take up key challenges to reach all children, everywhere. The most visible element of the polio eradication initiative has been the National Immunization Days, as they require the immunization of every child under five years of age (nearly 20% of a country's population) several times a year for a number of years in a row. As the result of an aggressive, deliberate and internationally coordinated effort, endemic

poliomyelitis has changed from being a devastating disease with a global distribution to one that is now endemic in four countries. In 2005, 1951 cases were reported worldwide.

Rabies

Rabies is one of the oldest and most feared diseases reported in medical literature. Rabies is a viral zoonosis (an animal disease transmissible to humans) caused by rhabdoviruses of the genus *Lyssavirus*. The disease is maintained in nature by several domestic and wild animal reservoir species, including dogs, foxes, mongooses, raccoons, skunks and many species of bat. Human infection is incidental to the epidemiology of rabies. In terms of risks to human health, dogs are the most dangerous reservoir: more than 99.9 % of human deaths from rabies worldwide result from the bite of a rabid dog. It is estimated that 50 000 persons die of rabies each year, mainly in Africa and Asia.

Human infection occurs when the virus, contained in the saliva of a rabid animal, is transmitted through penetrating bite wounds, open cuts in the skin, or contact with mucous membranes. The severity of the bite determines the risk of infection. The virus slowly travels up the nerve to reach the CNS where it replicates and then travels down nerves to the salivary glands where there is further replication. Man is occasionally infected, and once infection is established in the CNS the outcome is almost invariably fatal.

Second-generation vaccines consisting of highly purified vaccines prepared on primary and continuous cell lines and in embryonating eggs are available, though expensive, to prevent the occurrence of the disease in persons exposed to an animal suspected of rabies. The vaccines are usually administered according to regimens involving fewer doses (usually five or six) than those used for brain tissue vaccines. The regimens most commonly applied in the world are those recommended by WHO.

Control of rabies depends on education, vaccination of dogs, cats and farm animals and notification of suspected cases to local authorities (*14*).

MYCOBACTERIAL AND OTHER BACTERIAL DISEASES

Tuberculosis

With nine million new cases in 2004, resulting in 1.7 million deaths, tuberculosis is a leading infectious cause of morbidity and mortality worldwide (*15*). The resurgence of tuberculosis in many countries is attributable to its interaction with HIV infection, which has pernicious effects. Tuberculosis is the leading cause of death among people with HIV, while infection with HIV is the most potent risk factor for a latent tuberculosis infection to convert to active disease (*16*). Although tuberculosis most commonly affects the lungs (the usual site of primary infection), it can cause disease in any part of the body as a consequence of haematogenous spread from the lung. The proportion of all cases of tuberculosis that are extrapulmonary (i.e. in sites other than the lungs) varies between countries but is typically about 10–20%. Among extrapulmonary cases, the most common sites involved are the lymph nodes and the pleura, but the sites of tuberculosis associated with neurological disorders (meninges, brain and vertebrae) also constitute an important group. Meningeal tuberculosis has a high case-fatality rate, and neurological sequelae are common among survivors. Cerebral tuberculoma usually presents as a space-occupying lesion with focal signs depending on the location in the brain. Vertebral tuberculosis usually presents with local pain, swelling and deformity, and there is risk of neurological impairment because of spinal cord or cauda equina compression.

The diagnosis of nervous system tuberculosis is often difficult, because of its nature of great simulator and also because of limited access to methods to confirm it (*17*). Diagnosis depends on epidemiological and clinical data and findings during cerebrospinal fluid (CSF), neuroimaging and

bacteriological studies. Although not a direct consequence of tuberculosis, peripheral neuropathy can occur in tuberculosis patients as a side-effect of treatment with isoniazid, especially among patients who are malnourished, abuse alcohol, or are infected with HIV.

There are important public health approaches to the primary prevention of these tuberculosis-related conditions and to the secondary prevention of their adverse consequences. The most important overall approach to primary prevention consists of cutting the chain of transmission by case-finding and treatment. This approach is the basis of the international tuberculosis control strategy known as DOTS, which forms a central pillar of WHO's new strategy for its Stop TB campaign (*16*). Although BCG vaccination has little impact in reducing the number of adults with infectious pulmonary tuberculosis, it is of crucial importance in preventing disseminated and severe cases of disease (including tuberculosis meningitis) in children. Therefore, in countries with high tuberculosis prevalence, WHO recommends a policy of routine BCG immunization for all neonates as part of the Expanded Programme on Immunization (EPI). It is estimated that the 100 million BCG vaccinations given to infants worldwide in 2002 will have prevented 30 000 cases of tuberculosis meningitis in children during their first five years of life (*18*). The primary prevention of isoniazid-induced peripheral neuropathy is by routine administration of pyridoxine to tuberculosis patients.

The main public health approach to the secondary prevention of the adverse consequences of tuberculosis disease of the meninges, brain and vertebrae is through promoting the application of the International Standards for Tuberculosis Care (*19*) to ensure prompt diagnosis and effective treatment. High-quality tuberculosis care will result not only in patients having the best possible outcome of treatment, but also in the public health benefit of decreased tuberculosis transmission by infectious cases and thereby, ultimately, an impact on the global burden of all tuberculosis cases, including those associated with neurological disorder. The key steps in diminishing the global burden of neurological disorder associated with tuberculosis are to promote: investment in full implementation of the Stop TB strategy and International Standards for Tuberculosis Care; full immunization coverage so that all neonates are protected by BCG from risk of disseminated and severe tuberculosis; and better understanding of the epidemiology of tuberculosis disease associated with neurological disorder through improved surveillance in countries with high tuberculosis prevalence.

Leprosy neuropathy

Leprosy is the cause of the most common treatable neuropathy in the world, caused by *Mycobacterium leprae*. The incubation period of the disease is about five years: symptoms, however, can take as long as 20 years to appear. The infection could affect nerves by direct invasion or during immunological reactions. In rare instances, the diagnosis can be missed, because leprosy neuropathy may present without skin lesions (neuritic form of leprosy). Patients with this form of disease display only signs and symptoms of sensory impairment and muscle weakness, posing difficulties for diagnosis, particularly in services where diagnostic facilities such as bacilloscopy, electroneuromyography and nerve biopsy are not available.

Delay in treatment is a major problem, because the disease usually progresses and the resulting disability if untreated may be severe, even though mycobacteria may be eliminated. Delay in treatment is, however, usually a result of delayed presentation because of the associated stigma. People with long-term leprosy may lose the use of their hands or feet because of repeated injury resulting from lack of sensation. Early diagnosis and treatment with the WHO-recommended multidrug therapy (MDT) is essential in order to prevent the disease from progressing and resulting in disability.

Bacterial meningitis

Bacterial meningitis is a very common cause of morbidity, mortality and neurological complications in both children and adults, especially in children. It has an annual incidence of 4–6

cases per 100 000 adults (defined as patients older than 16 years of age), and *Streptococcus pneumoniae* and *Neisseria meningitidis* are responsible for 80% of all cases (*20*). In developing countries, overall case-fatality rates of 33–44% have been reported, rising to over 60% in adult groups (*21*). Bacterial meningitis can occur in epidemics that can have a serious impact on large populations.

The highest burden of meningococcal disease occurs in sub-Saharan Africa, which is known as the "meningitis belt", an area that stretches from Senegal in the west to Ethiopia in the east, with an estimated total population of 300 million people. The hyperendemicity in this area is attributable to the particular climate (dry season between December and June, with dust winds) and social habits: overcrowded housing at family level and large population displacements for pilgrimages and traditional markets at regional level. Because of herd immunity (whereby transmission is blocked when a critical percentage of the population had been immunized, thus extending protection to the unvaccinated), the epidemics occur in a cyclical fashion.

Meningitis is characterized by acute onset of fever and headache, together with neck stiffness, altered consciousness and seizures. The diagnosis can be confirmed by its clinical characteristics and bacteriological and immunological analyses of the CSF. Antibiotic treatment is effective in most cases but several neurological complications can remain, such as cognitive difficulties, motor disabilities, hypoacusia and epilepsy. In a recent review, treatment with corticosteroids was associated with a significant reduction in neurological sequelae and mortality (*22*).

Progress is more likely to come from investigations into preventive measures, especially the use of available vaccines and the development of new vaccines. Meningitis caused by *Haemophilus influenzae* type B has been nearly eliminated in developed countries since routine vaccination with the *H. influenzae* type B conjugate vaccine was initiated. The introduction of conjugate vaccines against *S. pneumoniae* may substantially reduce the burden of childhood pneumococcal meningitis and may even produce herd immunity among adults. The approval in 2005 of a conjugate meningococcal vaccine against serogroups A, C, Y and W135 is also an important advance that may decrease the incidence of this devastating infection. Local and nationwide surveillance, including the laboratory investigation of suspected cases, is critical for early detection of epidemics and the formulation of appropriate responses.

Tetanus

Tetanus is acquired through exposure to the spores of the bacterium *Clostridium tetani* which are universally present in the soil. The disease is caused by the action of a potent neurotoxin produced during the growth of the bacteria in dead tissues, e.g. dirty wounds or — for neonatal tetanus — in the umbilicus following non-sterile delivery. Tetanus is not transmitted from person to person: infection usually occurs when dirt enters a wound or cut. At the end of the 1980s, neonatal tetanus was considered a major public health problem. WHO estimated that, in 1988, 787 000 newborn children died of neonatal tetanus, a rate of 6.5 cases per 1000 live births. In 2004 the number of reported cases was 13 448. A worldwide total of 213 000 deaths were estimated to have occurred in 2002, 198 000 of them concerning children younger than five years of age (*23*).

Unlike poliomyelitis and smallpox, the disease cannot be eradicated because tetanus spores are present in the environment. Once infection occurs, mortality rates are extremely high, especially in areas where appropriate medical care is not available. However, this death toll can be prevented. Neonatal tetanus can be prevented by immunizing pregnant women and improving the hygienic conditions of delivery. Adult tetanus can be prevented by immunizing people at risk, such as workers manipulating soil; others at risk of cuts should be also included in the prevention measures. Some forms of toxoid are available (DTP, DT, TT or Td) and at least three primary doses should be given by the intramuscular route. Vaccination coverage with three doses of DTP is more than 80% for most countries around the world. The Maternal and Neonatal Tetanus elimination initiative was

launched by UNICEF, WHO and the United Nations Population Fund (UNFPA) in 1999, revitalizing the goal of elimination of maternal and neonatal tetanus as a public health problem, defined as less than one case of neonatal tetanus per 1000 live births in every district of every country.

PARASITIC DISEASES

Neurocysticercosis

Cysticercosis is infection by the larvae of the pork tapeworm *Taenia solium*. The adult tapeworm (flat, ribbon-like, approximately 2–4 m long) lives only in the small intestine of humans, who acquire it (taeniasis) by eating undercooked pork containing the viable larvae or cysticerci. A tapeworm carrier passes microscopic *Taenia* eggs with the faeces, contaminating the close environment and contacts and causing cysticercosis to pigs and humans. Human beings therefore acquire cysticercosis through faecal–oral contamination with *T. solium* eggs (*24*). Thus, vegetarians and other people who do not eat pork can acquire cysticercosis. Recent epidemiological evidence suggests that the most common source of infective eggs is a symptom-free tapeworm carrier in the household. Therefore, cysticercosis should be seen as a disease mostly transmitted from person to person (*25*). In the CNS, the larvae or cysticerci can cause epilepsy, hydrocephalus, spinal cord involvement, stroke, etc. (*24, 26*).

Cysticercosis is the parasitic disease that most frequently affects the CNS and is one of the major health problems of developing countries in Africa, Asia and Latin America. In addition, because of high immigration rates from endemic to non-endemic areas and tourism, neurocysticercosis is now commonly seen in countries that were previously free of the disease. Despite the advances in diagnosis and therapy, neurocysticercosis remains endemic in most low income countries, where it represents one of the most common causes of acquired epilepsy (*27*). Almost 50 000 deaths attributable to neurocysticercosis occur every year. Many more patients survive but are left with irreversible brain damage — with all the social and economic consequences that this implies (*28*). Seizures occur in up to 70% of patients. Several articles from different countries in Latin America consistently showed an association between around 30% of all seizures and cysticercosis (*29*).

Accurate diagnosis of neurocysticercosis is based on assessment of the clinical and epidemiological data and the results of neuroimaging studies and immunological tests (*30*). Therapy must be individualized according to the location of parasites and the degree of disease activity: this implies symptomatic therapy, anticysticidal drugs (albendazole/praziquantel), antiepileptic drugs and surgical treatment of complications such as hydrocephalus.

Neurocysticercosis is one of a few conditions included in a list of potentially eradicable infectious diseases of public health importance (*31*). The control strategy that seems promising at the moment is a combination of different available tools in order to interrupt or reduce the cycle of direct person-to-person transmission: mass human chemotherapy to eliminate the tapeworm stage, enforced meat inspection and control, improvement of pig husbandry and inspection, treatment of infected animals, surveillance, identification and treatment of individuals who are direct sources of contagion (human carriers of adult tapeworm) and their close contacts, combined with hygiene education and better sanitation. Animal vaccines are under development. Major obstacles include the lack of basic sanitary facilities in endemic areas, the extent of domestic pig-rearing, the costs of the interventions, and their cultural acceptability. Multiple genotypes of *T. solium* ramifications have been discovered in different regions, which could explain some of the possible differences in pathology of *T. solium* worldwide. Recently, a proposal was published to declare neurocysticercosis an international reportable disease (*32*). WHO suggests that all endemic countries should recognize the importance of taeniasis and cysticercosis, collect epidemiological data and adopt policies and strategies for their control. So far, the infection has not been eliminated from any

region by a specific programme and no national control programmes are yet in place. Successful pilot demonstrations of control measures have been or are being conducted in Cameroon, Ecuador, Mexico and Peru, and a regional action plan developed in 2002 for eastern and southern Africa is now under way.

Cerebral malaria

Malaria remains a serious public health problem in the tropics, mostly in Africa. There exist four *Plasmodium* species that affect humans; of these, only *Plasmodium falciparum* can sequester in capillaries of the CNS and cause cerebral malaria. The infection is acquired when the parasite is inoculated through the skin during the sting of an infected *Anopheles* mosquito. Some patients with cerebral malaria present with diffuse cerebral oedema, small haemorrhages and occlusion of cerebral vessels by parasitized red cells. The burden of falciparum malaria is not only because of infection and mortality: the neurocognitive sequelae add significantly to this burden (*33*).

P. falciparum is identified by examination of blood smears with Giemsa stain. Since parasitaemia is cyclical, repeated examinations may be required. The CSF is normal in cerebral malaria. Neuroimaging studies may demonstrate brain swelling, cerebral infarcts, or small haemorrhages in severe cases. Artemisinin derivatives and quinine are the drugs of choice for cerebral malaria. Despite therapy, mortality remains high in severe or complicated malaria (*34*).

Preventive strategies relied upon are: the early treatment of malaria infections with effective medicines (artemisinin-based combination therapies) to prevent the progression of the disease to severe malaria; and vector control through different practices to reduce the rate of infection (use of insecticide-treated nets, bednets, insecticide sprays and mosquito coils). All these methods have been found to be highly cost effective. At present, multiple studies are under way to modify *Plasmodium* genes in order to diminish parasite virulence and consequently the morbidity and mortality attributable to malaria.

Toxoplasmosis

Toxoplasmosis is a disease caused by an obligate intracellular protozoal parasite termed *Toxoplasma gondii*. Human infection usually occurs via the oral or transplacental route. Consumption of raw or undercooked meat containing viable tissue cysts (principally lamb and pork) and direct ingestion of infective oocysts in other foods (including vegetables contaminated by feline faeces) are common sources of infection. Transplacental infection may occur if the mother acquires an acute infection or if a latent infection is reactivated during immunosuppression. In immunocompetent women a primary infection during early pregnancy may lead to fetal infection, with death of the fetus or severe postnatal manifestations. Later in pregnancy, maternal infection results in mild or subclinical fetal disease. In adults, most *T. gondii* infections are subclinical, but severe infection can occur in patients who are immunocompromised, such as those with AIDS and malignancies. Affected organs include both the grey and white matter of the brain, retina, alveolar lining of the lungs, heart, and skeletal muscle.

Patients with AIDS are at particular risk for developing disseminated toxoplasmosis, which more often manifests as CNS abnormalities. As many as 50% of patients with AIDS who are seropositive for *T. gondii* develop encephalitis. Toxoplasmosis is the most common cause of a focal brain lesion in patients with AIDS. The disease commonly localizes to the basal ganglia, though other sites in the brain and spinal cord may be affected. A solitary focus may be seen in one third of patients, but multiple foci are more common. In AIDS-related *Toxoplasma* encephalitis, a well-circumscribed indolent granulomatous process or features of diffuse necrotizing encephalitis occur.

For most people, prevention of toxoplasmosis is not a serious concern, as infection generally causes no symptoms or mild symptoms. High-risk groups, however, should consider being tested for *Toxoplasma* infection. HIV-infected individuals who test positive should receive drugs to prevent

development of toxoplasmosis when their CD4 count falls below 100 (*35*). Pregnant women, women who plan to become pregnant, and immunocompromised individuals who test negative for *Toxoplasma* infection should take precautions against becoming infected. Precautions consist in measures such as consuming only properly frozen or cooked meats, avoiding cleaning cats' litter pans and avoiding contact with cats of unknown feeding history.

American trypanosomiasis: Chagas disease

Chagas disease is a serious problem of public health in Latin America, and is becoming more important in developed nations owing to the high flow of immigrants from endemic areas. Chagas disease is caused by *Trypanosoma cruzi*, a protozoan that it is transmitted by means of triatomine insects. Up to 8% of the population in Latin America are seropositive, but only 10–30% of them develop symptomatic disease (*36*).

The disease is a major cause of congestive heart failure, sudden death related to chronic Chagas disease, and cerebral embolism (stroke). Chagas disease can be diagnosed by demonstration of *T. cruzi* in blood smears and CSF samples or by serological testing. Neuroimaging usually demonstrates the location and extent of the cerebral infarct. Secondary prevention of stroke with long-term anticoagulation is recommended for all chagasic patients with stroke and heart failure, cardiac arrhythmias or ventricular aneurisms.

Traditional control programmes in Latin American countries have focused on the spraying of insecticides on houses, household annexes and other buildings. National programmes aimed at the interruption of the domestic and peridomestic cycles of transmission involving vectors, animal reservoirs and humans are feasible and have proved to be very effective. A prime example is the programme that has been operating in Brazil since 1975, when 711 municipalities had triatomine-infested dwellings: 10 years later only 186 municipalities remained infested, representing a successful accomplishment of the programme's objectives in 74% of the originally infested areas (*37*).

African trypanosomiasis: sleeping sickness

African trypanosomiasis, also known as sleeping sickness, is a severe disease that is fatal if left untreated. The causative agents are protozoan parasites of the genus *Trypanosoma*, which enter the bloodstream via the bite of blood-feeding tsetse flies (Glossina spp.). The acute form of the disease attributable to *Trypanosoma brucei rhodesiense*, widespread in eastern and southern Africa, is closely related to a common infection of cattle known as N'gana, which restricts cattle-rearing in many prime areas of Africa. The chronic form caused by *T.b. gambiense* is found in western and central Africa.

Cattle and other wild mammals act as reservoir hosts of the parasites. Tsetse flies can acquire parasites by feeding on these animals or on an infected person. Incubation time usually varies from three days to a few weeks for *T.b. rhodesiense*, and several weeks to months for *T.b. gambiense*. Inside the human host, trypanosomes multiply and invade most tissues. Infection leads to malaise, lassitude and irregular fevers. Early symptoms, which include fever and enlarged lymph glands and spleen, are more severe and acute in *T.b. rhodesiense* infections. Advanced symptoms include neurological and endocrine disorders. As the parasites invade the CNS, mental deterioration begins, leading to coma and death.

Sleeping sickness claims comparatively few lives annually, but the risk of major epidemics means that surveillance and ongoing control measures must be maintained, especially in sub-Saharan Africa where 36 countries have epidemiological risk. Control relies mainly on systematic surveillance of at-risk populations, coupled with treatment of infected people. In addition, reduction of tsetse fly numbers plays a significant role, especially against the rhodesiense form of the disease. In the past, this has involved extensive clearance of bush to destroy tsetse fly breeding

and resting sites, and widespread application of insecticides. More recently, efficient traps and screens have been developed that, usually with community participation, can keep tsetse populations at low levels in a cost-effective manner (*38*).

Schistosomiasis

Schistosomiasis is an infection with a relatively low mortality rate but a high morbidity rate; it is endemic in 74 developing countries, with more than 80% of infected people living in sub-Saharan Africa. Infection is caused by trematode flatworms (flukes) of the genus *Schistosoma*: in freshwater, intermediate snail hosts release infective forms of the parasite. There are five species of schistosomes able to infect humans: *Schistosoma haematobium* (the urinary form) and *S. japonicum, S. mekongi, S. mansoni* and *S. intercalatum* (the "intestinal" forms).

If people are in contact with water where infected snails live, they become infected when larval forms of the parasites penetrate their skin. Later, adult male and female schistosomes pair and live together in human blood vessels. The females release eggs, some of which are passed out in the urine (in *S. haematobium* infection) or stools (*S. mansoni* and *S. japonicum*), but some eggs are trapped in body tissues. Immune reactions to eggs lodged in tissues are the cause of disease. Systemic complications are bladder cancer, progressive enlargement of the liver and spleen, intestinal damage due to fibrotic lesions around eggs lodged in these tissues, and hypertension of the abdominal blood vessels. Most cases of cerebral schistosomiasis are observed with *S. japonicum*, constituting 2–4% of all *S. japonicum* infections. However, CNS schistosomiasis also can occur with other species and involves seizures, headache, back pain, bladder dysfunction, paresthesias and lower limb weakness. Death is most often caused by bladder cancer associated with urinary schistosomiasis and by bleeding from varicose veins in the oesophagus associated with intestinal schistosomiasis. Children are especially vulnerable to infection, which develops into chronic disease if not treated. Diagnosis is made by using urine filtration and faecal smear techniques, antigen detection in endemic areas and antibody tests in non-endemic areas.

The disease is controlled through an integrated approach: drug treatment with praziquantel or oxamniquine (effective only against *S. mansoni*), provision of an adequate safe water supply, sanitation and health education (*39*).

Hydatidosis

Cystic hydatidosis/echinococcosis is an important zoonosis caused by the tapeworm *Echinococcus granulosus*. At present, four species of *Echinococcus* are recognized: *E. granulosus, E. multilocularis, E. oligarthrus* and *E. vogeli*. The parasite is distributed worldwide and about 2–3 million patients are estimated in the world (*40*). It causes serious human suffering and considerable losses in agricultural and human productivity. General lack of awareness of transmission factors and prevention measures among the population at risk, abundance of stray dogs, poor meat inspection in abattoirs, improper disposal of offal and home slaughtering practices play a role in the persistence of the disease.

The incidence of surgical cases ranges from 0.1 to 45 cases per 100 000 people. The real prevalence ranges between 0.22% and 24% in endemic areas. Ultrasounds have been very useful in large-scale prevalence surveys. Large prevalence studies have been conducted in many countries: in the Libyan Arab Jamahiriya, Morocco and Tunisia, the prevalence ranged from 1% to 2%.

In the normal life-cycle of *Echinococcus* species, adult tapeworms (3–6 mm long) inhabit the small intestine of carnivorous definitive hosts, such as dogs, coyotes or wolves, and echinococcal cyst stages occur in herbivorous intermediate hosts, such as sheep, cattle and goats. In most infected countries there is a dog–sheep cycle in which grazing sheep ingest tapeworm eggs passed in the faeces of an infected dog. Dogs ingest infected sheep viscera, mainly liver and lungs,

containing larval hydatid cysts in which numerous tapeworm heads are produced. These attach to the dog's intestinal lining and develop into mature adult tapeworms. Humans become infected by ingesting food or drink contaminated with faecal material containing tapeworm eggs passed from infected carnivores, or when they handle or pet infected dogs. Oncospheres released from the eggs penetrate the intestinal mucosa and lodge in the liver, lungs, muscle, brain and other organs, where the hydatid cysts form. In the CNS, hydatidosis produces spinal disease and also is a potential cause of intracranial hypertension.

To control the parasite, a number of antihelminthic drugs have proved to be effective against adult stages of *E. granulosus* in the final host. The best drug currently available is praziquantel which exterminates all juvenile and adult echinococci from dogs. Several of the benzimidazole compounds have been shown to have efficacy against the hydatid cyst in the intermediate host. Echinococcosis can be controlled through preventive measures that break the cycle between the definitive and the intermediate host. These measures include dosing dogs, inspecting meat and educating the public on the risk to humans and the necessity to avoid feeding offal to dogs.

IMPLICATIONS AND PREVENTION

Infectious diseases that involve the nervous system affect millions of people around the world, especially in some regions in Africa and South-East Asia. Most of these diseases can cause high mortality rates in some populations and produce severe complications, disability and economic burden for individuals, families and health systems. Even with the advent of effective antibiotics and vaccines, they still remain a major challenge in many parts of the world, especially in developing countries where the worst health indicators are found. Some diseases that had been found in the developed world but have virtually disappeared, such as poliomyelitis, leprosy and neurosyphilis, are still taking their toll in developing regions. Conversely, some of the protozoan and helminthic infections that are so characteristic of the tropics are now being seen with increasing frequency in developed countries. Other major concerns are the development of drug-resistant organisms, the increasing number of immunocompromised populations and the rising number of diseases previously considered rare. Education, surveillance, development of new drugs and vaccines, and other policies are in constant evolution to fight against old and emerging infectious diseases of the nervous system.

Some preventive measures have a more rapid impact and are more cost effective than others. Regular, large-scale treatment to prevent disease is cheap, by treating carriers (i.e. humans or dogs) to prevent humans from getting infected as an intermediate host, or to regularly lower the worm load so that the person does not suffer from infection. Large-scale treatment in humans can be combined for several diseases (the "preventive chemotherapy" concept), and can be packaged in domestic animals — such as dogs — with other interventions such as rabies vaccination. The basic idea is to deliver such public health treatment packages regularly, to enable people to avoid the worst effects of infection, even with an ongoing lack of water, sanitation and hygiene. It has to be said that environmental measures would eventually solve the problem, but require a much more substantial investment and commitment. Some diseases are easily controlled and prevented with basic, inexpensive measures that are available worldwide, but their effectiveness entails a massive education effort and steady surveillance.

CONCLUSIONS AND RECOMMENDATIONS	
1	Neuroinfections constitute the sixth cause of neurological consultation in primary care services worldwide and, even with the advent of effective antibiotics and vaccines, still remain a major challenge in many parts of the world.
2	The global public health community is now faced with a more complex and diverse pattern of adult disease than previously expected and proposes a double response that integrates prevention and control of both communicable diseases and noncommunicable diseases within a comprehensive health-care system.
3	Some diseases that had virtually disappeared from the developed world are still taking their toll in developing regions. Conversely, some of the protozoan and helminthic infections that are so characteristic of the tropics are now being seen with increasing frequency in developed countries.
4	Other major concerns are the development of drug-resistant organisms, the increasing number of immunocompromised populations and the rising number of diseases previously considered rare.
5	Education, surveillance, development of new drugs and vaccines and other public policies are in constant evolution to fight against old and emerging infectious diseases of the nervous system.

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3.6 Neurological disorders associated with malnutrition

In low income countries, inadequate amounts of food (causing conditions such as child malnutrition and retarded growth) and inadequate diversity of food (causing deficiency of vital micronutrients such as vitamins, minerals or trace elements) continue to be priority health problems. Malnutrition in all its forms increases the risk of disease and early death. Nearly 800 million people in the world do not have enough to eat. Malnutrition affects all age groups, but it is especially common among poor people and those with inadequate access to health education, clean water and good sanitation. Most of the malnutrition-related neurological disorders are preventable.

Chronic food deficits affect about 792 million people in the world (*1*). Malnutrition directly or indirectly affects a variety of organ systems including the central nervous system (CNS). A number of nutritional conditions are included in the Global Burden of Disease (GBD) study, such as protein–energy malnutrition, iodine deficiency, vitamin A deficiency, and iron deficiency anaemia. Over 15% of the disability-adjusted life years (DALYs) lost globally are estimated to be from malnutrition (*2*).

This section focuses on neurological disorders associated with malnutrition. In addition, it touches briefly on the ingestion of toxic substances in food or alcohol, as these also contribute to neurological disorders.

Most of the malnutrition-related neurological disorders can be prevented and therefore they are of public health concern. Raising awareness in the population, among leaders and decision-makers and in the international community is important in order to adopt an appropriate health policy.

ETIOLOGY, RISK FACTORS AND BURDEN

The major dietary nutrients needed by living organisms, especially human beings, can be grouped into macronutrients and micronutrients. The macronutrients are the energy-yielding nutrients — proteins, carbohydrates and fat — and micronutrients are the vitamins and minerals. The macronutrients have a double function, being both "firewood" and "building blocks" for the body, whereas the micronutrients are special building items, mostly for enzymes to function well. The term "malnutrition" is used for both macronutrient and micronutrient deficiencies. Macronutrient and micronutrient problems often occur together, so that the results in humans are often confounded and impossible to separate out. Table 3.6.1 outlines which of the nutrients may contribute to neurological disorders if not provided in sufficient amounts, together with their recommended daily allowances. Table 3.6.2 outlines some of the

neurological consequences attributable, in certain circumstances, to ingestion of toxic substances in food and alcohol.

Table 3.6.1 Neurological disorders caused by nutrient deficiency

Nutrient	RDA[a]	Neurological disorder when deficient
Macronutrients		
Total energy	2200 (kcal)	In childhood: long-term mental deficit
Vitamins		
Vitamin B1 Thiamine	1.1 mg	Beri-beri, polyneuropathy, Wernicke's encephalopathy
Vitamin B3 Niacin	15 mg NE	Pellagra including dementia and depression
Vitamin B6 Pyridoxine	1.6 mg	Polyneuropathy
Vitamin B12 Cobalamine	2.0 µg	Progressive myelopathy with sensory disturbances in the legs
Folate	180 µg	Neural tube defects (myelomeningocele) of the fetus, cognitive dysfunction in children and elderly?
Minerals		
Iodine	150 µg	Iodine deficiency disorders
Iron	15 mg	Delayed mental development in children
Zinc	12 mg	Delayed motor development in children, depression
Selenium	55 mg	Adverse mood states

[a] Recommended daily allowance for an adult.

Table 3.6.2 Potentially toxic food compounds that may contribute to neurological disorders

Food compound	Potential neurological disorder when ingested
Alcohol	Fetal alcohol syndrome, retarded mental development in childhood, Wernicke's encephalopathy, visual problems (amblyopia), peripheral neuropathy
Lathyrus sativus	Spastic paraparesis (lathyrism)
Cyanogenic glucosides from insufficiently processed cassava roots	Konzo, tropic ataxic neuropathy

MAIN NEUROLOGICAL COMPLICATIONS OF MALNUTRITION

Macronutrient deficiency (general malnutrition)

The nervous system develops in utero and during infancy and childhood, and in these periods it is vulnerable to macronutrient deficiencies. As a rule, general malnutrition among adults does not cause specific neurological damage, whereas among children it does.

Undernutrition can be assessed most commonly by measurement of the body weight and the body height. With these two measurements, together with age and sex, it will be possible to evaluate the energy stores of the individual. The aims of the anthropometric examination are:

- to assess the shape of the body and identify if the subject is thin, ordinary or obese;

- to assess the growth performance (this applies only to growing subjects, i.e. children).

A person who is too thin is said to be "wasted" and the phenomenon is generally called "wasting". Children with impaired growth are said to be "stunted" and the phenomenon is called "stunting". Both these conditions may cause neurological disturbances in children.

The percentage of wasted children in low income countries is 8%, ranging from 15% in Bangladesh and India down to 2% in Latin America (*3*). Different kinds of disasters may raise the figures dramatically in affected areas. This presents a disturbing picture of malnutrition among children under five years of age in underprivileged populations. These children should be an important target group for any kind of nutritional intervention to be undertaken in these countries.

Stunting is also widespread among children in low income countries. Its prevalence ranges from 45% in Bangladesh and India to 16% in Latin America. The global average for stunting among children in low income countries is 32% (*3*). Increasing evidence shows that stunting is associated with poor developmental achievement in young children and poor school achievement or intelligence levels in older children. "The causes of this growth retardation are deeply rooted in poverty and lack of education. To continue to allow underprivileged environments to affect children's development not only perpetuates the vicious cycle of poverty but also leads to an enormous waste of human potential. … Efforts to accelerate economic development in any significant long-term sense will be unsuccessful until optimal child growth and development are ensured for the majority" (*3*).

Long-term effects of malnutrition

Apart from the risk of developing coronary heart disease, diabetes and high blood pressure later in life owing to malnutrition in early life, there is now accumulating evidence of long-term adverse effects on the intellectual capacity of previously malnourished children. It is methodologically difficult, however, to differentiate the biological effects of general malnutrition and those of the deprived environment on a child's cognitive abilities. It is also methodologically difficult to differentiate the effect of general malnutrition from the effect of micronutrient deficiencies, such as iodine deficiency during pregnancy and iron deficiency in childhood, which also cause mental and physical impairments. Malnourished children lack energy, so they become less curious and playful and communicate less with the people around them, which impairs their physical, mental and cognitive development.

Two recent reviews highlight the evidence of general malnutrition per se causing long-term neurological deficits (*4, 5*). An increasing number of studies consistently show that stunting at a young age leads to a long-term deficit in cognitive development and school achievement up to adolescence. Such studies include a wide range of tests including IQ, reading, arithmetic, reasoning, vocabulary, verbal analogies, visual-spatial working memory, simple and complex auditory working memory, sustained attention and information processing. Episodes in young childhood of acute malnutrition (wasting) also seem to lead to similar impairments. The studies also indicate that the period in utero and up to two years of age represents a particularly vulnerable time for general malnutrition (*4*).

In addition to food supplementation, it has been nicely demonstrated that stimulation of the child has long-term beneficial effects on later performance. One such study is from Jamaica, where stunted children who were both supplemented and stimulated had an almost complete catch-up with non-stunted children (*6*), see Figure 3.6.1.

Treatment of severe malnutrition

If a child becomes seriously wasted, this in itself is a life-threatening condition. Even if the child is brought to hospital, the risk of dying still remains very high. WHO has issued a manual for the management of severe malnutrition that is available on its web site (*7*). An important element, in

addition to initial treatment similar to intensive care, is to stimulate the child in order to prevent the negative long-term effect on the cognitive capacity of the child.

Micronutrient deficiencies

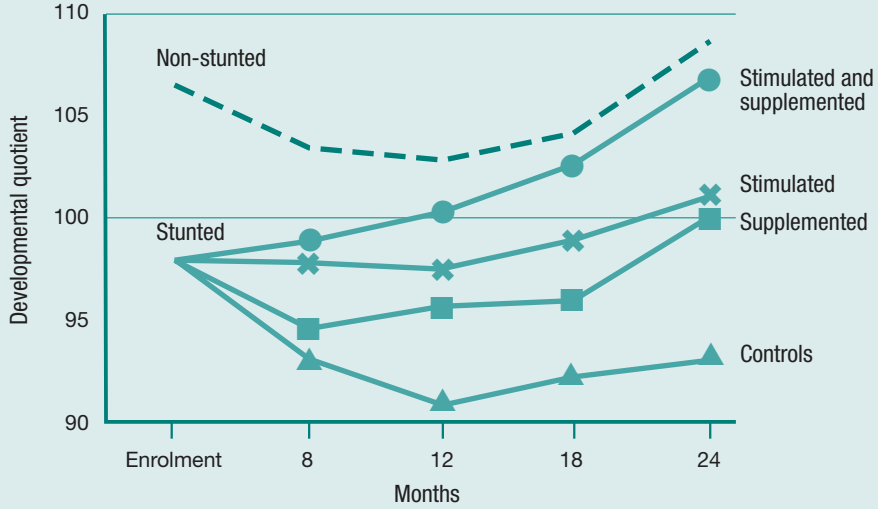
Micronutrients is the term used for those essential nutrients that are needed in small amounts for human growth and functioning. They are essentially used as cofactors for enzymes engaged in various biochemical reactions. They comprise vitamins, fat-soluble as well as water-soluble, and trace elements (= minerals). Iron, vitamin A, zinc and iodine are most discussed today, but other important micronutrients are vitamin C and the vitamin B complex. Diets that supply adequate energy and have an acceptable nutrient density will usually also cover the needs for micronutrients. When the diet is otherwise monotonous, however, it is recommended to supplement it with micronutrient-rich foods. Food preservation methods, high temperature and exposure to sunlight can reduce the activity of many vitamins. Most of these deficiencies are strongly linked to poverty and human deprivation. Some of these conditions are much more significant with regard to their global occurrence and their impact on the nervous system than other micronutrient deficiencies, so this section focuses on deficiencies of vitamin A, vitamin B complex, iodine and iron.

Vitamin A deficiency

Vitamin A assumes two types of function in the body: systemic functions (in the whole body) and local functions in the eye.

Vitamin A is very important for the mucous membranes as it is needed for the proper production of mucopolysaccharides, which help to protect against infections. If vitamin A is deficient, the wetness of the mucous membranes will decrease and the membranes will become more like skin than mucous membranes. This can be seen in the eye as xerophthalmia (dry eye in Greek). Inside the eye, vitamin A is used in the rods (the receptors for low intensities of light). If there is too little vitamin A, the person will not be able to see in low light intensity: he or she will become night-blind. Vitamin A deficiency has long been identified as the major cause of nutritional blindness. This is still an important problem around the world: it is estimated that 250–500 000 children are blinded each year because of eye damage brought about by severe vitamin A deficiency. It is the single most important cause of blindness in low and middle income countries.

Figure 3.6.1 Mean developmental quotients of stunted[a] and non-stunted[b] children: results of intervention over two years



[a] Adjusted for initial age and score.
[b] Adjusted for age only.
Source: (*6*).

Vitamin A deficiency does not only cause eye damage: it also increases mortality owing to increased vulnerability and impaired immune function, especially to diarrhoeal diseases and measles. Vitamin A deficiency develops quite quickly in children with measles, as infections make the body consume its vitamin A stores much more quickly. Children between six months and four years old are most vulnerable to vitamin A deficiency. An estimated 100 million pre-school children globally are estimated to have vitamin A deficiency and 300 000 are estimated to die each year because of vitamin A deficiency.

In order to prevent child deaths and childhood blindness, many low income countries have integrated vitamin A supplementation into their immunization programmes. Children at risk are given vitamin A capsules every six months. The cost of the capsules is low (currently US$ 0.05 each).

Vitamin B complex deficiencies

The B vitamins generally are coenzymes in the energy metabolism in the body. Vitamin B deficiencies have occurred in extreme situations in the past, such as in the 19th century when the steam mills in South-East Asia started to provide polished rice. Suddenly, people had enough energy but insufficient supply of B vitamins and developed beri-beri, a Sinhalese word for "I cannot". It may also occur today in refugee populations, if they are provided with a very limited choice of food items with enough energy but deficient in B vitamins. Similarly, it may also happen to alcoholics and people with other types of very monotonous diets.

The different deficiency syndromes of vitamin B overlap and are sometimes very difficult to distinguish from one another. A recent example is the Cuban neuropathy in the mid-1990s, in which over 50 000 people suffered from a gait and visual disturbance, technically a polyneuropathy (*8, 9*). Massive research resources were put in to find the exact cause. It is now known that the population that experienced the epidemic had an extreme diet (tea with sugar as the main source of energy; which is likely to generate a vitamin B deficiency) and the epidemic stopped as soon as universal distribution was made of tablets with vitamin B complex. This led the scientists to conclude that it was a vitamin B complex deficiency, without being able to distinguish the vitamins from each other. From a public health perspective, therefore, the B vitamins may as well be treated together, the only exceptions being vitamin B12 and folate.

Vitamin B1 (*thiamine*). Beri-beri is one form of vitamin B1 deficiency, and the main symptom is a polyneuropathy in the legs (*10*). In severe cases, one can suffer from cardiovascular complications, tremor, and gait and visual disturbances. An acute form of the syndrome seen in alcoholics is Wernicke's encephalopathy (discussed in the section on alcohol). It is characterized by a serious confusion, unsteadiness and eye movement disorders. It can be rapidly reversed if correctly diagnosed and immediately treated with high-dose thiamine.

Vitamin B3 (*niacin*). Deficiency of niacin leads to "pellagra", an Italian word for "rough skin", which was common in Italy and Spain in the 19th century when large populations were sustained on a maize diet. In its classic form it appears with three Ds: dermatitis, diarrhoea and dementia; that is with cutaneous signs, erythema, pigmentation disorders, diarrhoea and neuropsychiatric disturbances such as confusion and psychomotor agitation.

Vitamin B6 (*pyridoxine*). Vitamin B6 is involved in the regulation of mental function and mood. Neuropsychiatric disorders including seizures, migraine, chronic pain and depression have been linked to vitamin B6 deficiency (*11*). Some studies have suggested that neurological development in newborns could be improved by supplementation in pregnancy, but this is still a hypothesis (*12*). Vitamin B6 deficiency may occur especially during intake of some drugs which antagonize with the vitamin (i.e. isoniazid, penicillamine).

Folate. Folate (or folic acid) plays an important role for rapidly dividing cells such as the blood cells, and a folate deficiency causes a special type of anaemia called megaloblastic anaemia which is reversible when folate is given. In recent years, it has been found that folate deficiency during

pregnancy increases the risk of fetal malformation in the form of neural tube defects (NTDs = myelo-meningocele) (*13*). Folate supplementation for women at the time of conception protects against neural tube defects (*13*). Supplementation of folate in wheat flour is therefore common in Europe and North America, with the objective of reducing the risk of neural tube defect (*14–16*). In Canada, Chile and the United States, mandatory fortification of flour substantially improved folate and homocysteine status, and neural tube defect rates fell by between 31% and 78% (*17*). Nevertheless, many countries do not choose mandatory folic acid fortification, in part because expected additional health benefits are not yet scientifically proven in clinical trials, in part because of feared health risks, and because of the issue of freedom of choice. Thus additional creative public health approaches need to be developed to prevent neural tube defects and improve the folate status of the general population.

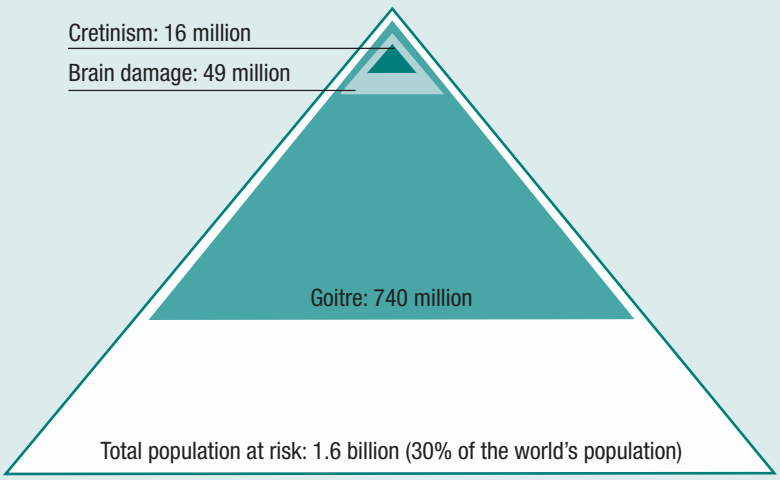
Vitamin B12 (*cobalamine*). The vitamin B12 or cobalamine is — like folate — important in the formation of blood cells, particularly the red blood cells. Vitamin B12 is different from the other B vitamins because it needs an "intrinsic factor" produced by the gut in order to be absorbed. This means that people with gut disorders and also elderly people may experience vitamin B12 deficiency. Vitamin B12 deficiency also causes a megaloblastic anaemia which is reversible when vitamin B12 is given. What is worse is an insidious irreversible damage to the central and peripheral nervous systems. In a severe form it may also cause a psychiatric disorder with irritability, aggressiveness and confusion. It has been suggested that vitamin B12 deficiency might contribute to age-related cognitive impairment; low serum B12 concentrations are found in more than 10% of older people (*18*) but so far there is insufficient proof of beneficial effects of supplementation. The most serious problem with vitamin B12 deficiency still seems to be the irreversible progressive myeloneuropathy, which is difficult to diagnose.

Iodine deficiency disorders

Iodine deficiency does not cause one single disease, but many disturbances in the body. These are denoted by the term iodine deficiency disorders: their effects range from increased mortality of fetuses and children, constrained mental development — in its worst form, cretinism — to impaired school performance and socioeconomic development, as detailed in Table 3.6.3.

WHO has estimated that 1.6 billion people in 130 countries live in areas where they are at risk of being deficient in iodine. Goitre — indicated by a swelling of the thyroid gland — is present in 740 million people, and some 300 million suffer from lowered mental ability as a result of a lack of iodine. Iodine deficiency disorders today constitute the single greatest cause of preventable brain damage in the fetus and infant and retarded psychomotor development in young children. At least 120 000 children every year are born cretins — mentally retarded, physically stunted, deaf-mute or paralysed — as a result of iodine deficiency. In addition, an estimated annual total of at least 60 000 miscarriages, stillbirths and neonatal deaths stem from severe iodine deficiency in early pregnancy, as shown in Figure 3.6.2 (*19*).

Figure 3.6.2 Toll of iodine deficiency worldwide



Source: adapted from (*19*).

Table 3.6.3 Spectrum of disorders caused by iodine deficiency

Iodine deficiency disorder	Effect
Goitre	Enlargement of the thyroid gland
Hypothyroidism	Decreased production of thyroid hormones
Miscarriages	Early death of fetuses in the womb
Stillbirths	Late death of fetuses (the child is dead at birth)
Perinatal mortality	Increased number of deaths among newborn children
Congenital abnormalities	Abnormalities of the newborn child
Cretinism	Severe mental retardation, growth retardation, deaf-mutism and physical disability
Decrease in IQ	
Impaired educability	Lower school performance
Impaired social and human development	

At the World Summit for Children in 1990, the problem of iodine deficiency disorders was highlighted and a strong political will to eliminate them was demonstrated. At that time, the scale and severity of the iodine problem was only just being realized. Since then, several surveys have shown even more severe damage than was estimated from this deficiency in many regions of the world. Work to eliminate iodine deficiency disorders has made enormous progress and is becoming a success story in the prevention of a nutritional deficiency. WHO has issued a useful guide to help programme managers assess the problem and monitor progress towards its elimination (*20*).

The main intervention strategy for control of iodine deficiency disorders is universal salt iodization. Salt was chosen as the commodity to be fortified for a number of reasons: it is widely consumed in fairly equal amounts by most people in a population, it is usually produced centrally or in a few factories, and the cost of iodizing is low (about US$ 0.05 per person per year). Over the last decade, extraordinary progress has been made in increasing the number of people consuming iodized salt. In 1998, more than 90 countries had salt iodization programmes. Now, more than two thirds of households living in countries affected by iodine deficiency disorders consume iodized salt. Universal salt iodization ranges from 63–90% in Africa, the Americas, South-East Asia and the Western Pacific, whereas in Europe it is only 27%, thus leaving Europeans at risk of iodine deficiency disorders. Because of active programmes of salt fortification, iodine deficiency disorders are rapidly declining in the world. In 1990, 40 million children were born with mental impairment attributable to iodine deficiency and 120 000 cretins were born, which was substantially more than just seven years later. WHO has estimated that the number of people with goitre will decrease to 350 million by the year 2025 as a result of iodine enrichment and supplementation programmes. A challenge is to enforce the legislation that has been passed in all but seven of the countries of the world with a recognized iodine-deficiency public health problem. All the salt producers, from large industries to small-scale producers, need to be encouraged to use the more expensive procedure to fortify their salt production, and the consumers also need to be informed. Quality control and monitoring of the impact of the procedures are other continuing tasks related to the world's most widespread preventable cause of mental impairment (*20*).

Iron deficiency anaemia

Iron deficiency anaemia affects more than 3.5 billion people globally, making it the most frequent micronutrient deficiency in the world. Iron deficiency seems to be the only micronutrient deficiency that high income and low income countries have in common. Of the total burden of disease in

DALYs, over 2% is attributable to anaemia. Iron deficiency anaemia depresses human productivity by tiredness, breathlessness, decreased immune function and impaired learning in children. The effect of iron deficiency on learning is difficult to study because iron deficiency is also closely related to poverty and socioeconomic disadvantage. The indirect productivity effects of improved iron status are on cognitive ability and achievement, through impact on mental and motor skills in infants and on cognition, learning and behaviour in children and adolescents. An early severe chronic iron deficiency leads to poorer overall cognitive functioning and lower school achievements (*21, 22*). Thus, macronutrient, iodine and iron deficiencies all have a substantial negative effect on cognition, behaviour and achievement; in all three cases, the effects produced by chronic deficiencies in the early years are manifested later in life (*23*). The estimated losses of GDP attributable to iron deficiency in three countries are considerable (Figure 3.6.3).

The most affected populations are children in the pre-school years and pregnant women in low and middle income countries. In these populations, deficiencies of dietary iron are aggravated by repeated episodes of parasitic diseases such as malaria, hookworm infestation or schistosomiasis in children, and by menstruation, repeated pregnancies or blood loss at delivery in women. A low dietary intake of iron and the influence of factors affecting absorption also contribute to iron deficiency. About 40% of the women in low and middle income countries and up to 15% in high income countries suffer from anaemia.

Better nutrition, iron supplementation or fortification, child spacing and the prevention and treatment of malaria and hookworms can all prevent iron deficiency. Iron is found naturally in meat, fish, liver and breastmilk. Vitamin C increases iron absorption, and coffee and tea decrease absorption. Correction of iron deficiency anaemia is cheap, but a functioning health service is needed to promote the measures among the most vulnerable groups. There is, however, some evidence to suggest that iron supplementation at levels recommended for otherwise healthy children carries the risk of increased severity of infectious disease in the presence of malaria and/or undernutrition. It is therefore advised that iron and folic acid supplementation be targeted to those who are anaemic and at risk of iron deficiency. They should receive concurrent protection from malaria and other infectious diseases through prevention and effective case management (*25*).

Zinc deficiency

There is a close connection between zinc deficiency and stunting. In addition, zinc supplementation of young children in low income countries improves their neurophysiological performance (*26*), also in combination with iron supplements (*27*). Some behavioural abnormalities in adults also seem to respond favourably to zinc supplementation, such as mood changes, emotional lability, anorexia, irritability and depression (*28*).

Selenium deficiency

Selenium deficiency has been linked to adverse mood states (*29*). Selenium supplementation together with other vitamins has been found beneficial in the treatment of mood lability (*30*). Generally, the scientific information about selenium and neurological disorders remains scarce.

TOXICONUTRITIONAL DISORDERS

In the 19th century, medical science successfully revealed the causation of several neurological disorders that occurred in localized epidemics or endemic foci. There are, however, still a number of obscure neurological disorders occurring in localized epidemics or endemic foci in tropical countries. Most of these syndromes consist of various combinations of peripheral polyneuropathy and signs of spinal cord involvement. The term “tropical myeloneuropathies” has been used to group these disorders of unknown etiology; to reduce the confused clinical terminology, Román distinguishes two clinical groups which he calls tropical ataxic neuropathy, with prominent sensory

ataxia, and tropical spastic paraparesis, with predominantly spastic paraparesis with minimal sensory deficit (*31*).

Syndromes of ataxic polyneuropathy

Reports on a form of ataxic polyneuropathy described by Strachan and later by Scott led to the recognition of a tropical neurological syndrome characterized by painful polyneuropathy, orogenital dermatitis and amblyopia, known as Strachan's syndrome. It was linked with malnutrition and reported from Africa. During the Second World War, prisoners of war in tropical and subtropical regions suffered from similar syndromes with "burning feet", numbness and loss of vision with pallor of the temporal border of the optic disks. Spastic paraplegia was also seen in these highly variable conditions (*32*). Since the Second World War, ataxic polyneuropathies have been reported from many tropical and subtropical areas (*31*).

In the 1930s, Moore described, in an institution in Nigeria, a syndrome of visual loss, sore tongue, stomatitis and eczema of the scrotum in adolescent boys. Their cassava-based diet was suggested to be the cause, as the students improved during holidays. The cyanide-yielding capacity of bitter cassava and its toxic effects were described at that time. This syndrome of painful polyneuropathy, ataxia and blurred vision was extensively studied in Nigeria by Osuntokun (*33*). The diagnostic criteria used for this tropical ataxic neuropathy were the presence of two of the following: myelopathy, bilateral optic atrophy, bilateral sensorineural deafness, and symmetrical peripheral polyneuropathy. Men and women were equally affected, with a peak incidence in the fifth and sixth decades of life. The prevalence in certain areas of Nigeria ranged from 1.8% to 2.6% in the general population. When discussing the neurological syndromes resembling Nigerian ataxic neuropathy described from different parts of the world, Osuntokun pointed out that it is unlikely that the same specific etiological factor is involved in all places. In Nigeria, tropical ataxic neuropathy has been shown to persist also into this millennium (*34*).

Syndromes of spastic paraparesis

The second clinical group of tropical myeloneuropathies proposed by Román (*31*) is comprised of syndromes with spastic paraparesis as the main feature. Besides paraparesis as a sequel of extrinsic cord compression resulting from trauma or tuberculosis, several syndromes with spastic paraparesis have been reported in epidemics or endemic foci throughout the world.

The classic form of locally occurring spastic paraparesis, mentioned already by Hippocrates, is lathyrism (*35*), caused by excessive consumption of grass pea, *Lathyrus sativus* (*36*). The clinical picture is an acute or sub-acute onset of an isolated spastic paraparesis, with increased muscle tone, brisk reflexes, extensor plantar responses and no sensory signs. It has been known since ancient times and has occurred in Europe (*37*) and North Africa but is today known as a public health problem in only Bangladesh, India (*38*) and Ethiopia (*39*). An excitotoxic amino acid in the grass pea, beta-N-oxalylamino-L-alanine is held responsible for the disease (*36*).

Figure 3.6.3 Loss of gross domestic product (GDP) attributable to iron deficiency

Source: (*24*).

A second form of spastic paraparesis, nowadays called HTLV-I associated myelopathy/tropical spastic paraparesis, has been found in geographical isolates in different parts of the world (40). It is now proved to be caused by the human T-lymphotropic virus type I (HTLV–I) and is unrelated to nutrition.

A third form of spastic paraparesis with abrupt onset has been reported in epidemic outbreaks in Africa. Clinically and epidemiologically it is similar to lathyrism but without any association with consumption of *L. sativus*. This disease is now called konzo (*41*). Konzo has been reported only from poor rural communities in Africa; it is characterized by the abrupt onset of an isolated and symmetric spastic paraparesis which is permanent but non-progressive. The name derives from the local designation used by the Congolese population affected by the first reported outbreak in 1936. Konzo means "tied legs", and is a good description of the resulting spastic gait. Outbreaks of konzo are described from Cameroon, the Central African Republic, the Democratic Republic of the Congo, northern Mozambique and the United Republic of Tanzania. Konzo has been associated with exclusive consumption of insufficiently processed bitter cassava in epidemiological studies (*42*).

Toxic optic neuropathy

Toxic optic neuropathy, also called nutritional amblyopia, is a complex, multifactorial disease, potentially affecting individuals of all ages, races, places and economic strata (*43*). It may be precipitated by poor nutrition and toxins (especially smoking and alcohol) but genetic predisposal is also an important factor. Most cases of nutritional amblyopia are encountered in disadvantaged countries (*9*). Typically, toxic and nutritional optic neuropathy is progressive, with bilateral symmetrical painless visual loss causing central or cecocentral scotoma. There is no specific treatment for this disorder. Nevertheless, early detection and prompt management may ameliorate and even prevent severe visual deficit.

Alcohol-related neurological disorders

Alcohol and other drugs play a significant role in the onset and course of neurological disorders. As toxic agents, these substances directly affect nerve cells and muscles, and therefore have an impact on the structure and functioning of both the central and peripheral nervous systems. For example, long-term use of ethanol is associated with damage to brain structures which are responsible for cognitive abilities (e.g. memory, problem-solving) and emotional functioning. In people with a history of chronic alcohol consumption the following abnormalities have been observed: cerebral atrophy or a reduction in the size of the cerebral cortex, reduced supply of blood to this section of the brain which is responsible for higher functions, and disruptions in the functioning of neurotransmitters or chemical messengers. These changes may account for deficits in higher cortical functioning and other abnormalities which are often symptoms of alcohol-related neurological disorders.

Fetal alcohol syndrome

The role of alcohol in fetal alcohol syndrome has been known for many years: the condition affects some children born to women who drank heavily during pregnancy. The symptoms of fetal alcohol syndrome include facial abnormalities, neurological and cognitive impairments, and deficient growth with a wide variation in the clinical features (*44*). Not much is known about the prevalence in most countries but, in the United States, available data show that the prevalence is between 0.5 and 2 cases per 1000 births (*45*). Though there is little doubt about the role of alcohol in this condition, it is not clear at what level of drinking and during what stage of pregnancy it is most likely to occur. Hence the best advice to pregnant women or those contemplating pregnancy seems to be to abstain from drinking, because without alcohol the disorder will not occur.

Alcohol-related polyneuropathy

A typical example of a toxiconutritional disorder, alcohol-related polyneuropathy is elicited by a combination of the direct toxicity of alcohol on the peripheral nerve and a relative deficiency of vitamin B1 and folate. In its usual form it starts in an insidious, progressive way with signs located at the distal ends of the lower limbs: night cramps, bizarre sensations of the feet and the sufferer is quickly fatigued when walking. Examination reveals pain at the pressure of the muscular masses. This polyneuropathy evolves to a complete form with permanent pain in the feet and legs. The signs of evolution of alcoholic polyneuropathy are represented by the deficit of the leg muscles leading to abnormal walk, exaggerated pain (compared to burning, at any contact) and skin changes. At the latest stage, ulcers may occur (*46*). The onset of the peripheral neuropathy depends on the age of the patient, the duration of the abuse and also the amount of alcohol consumed. The excessive abuse of this substance determines the central and/or peripheral nervous lesions.

Wernicke's encephalopathy

Wernicke's encephalopathy is the acute consequence of a vitamin B1 deficiency in people with severe alcohol abuse. It is due to very poor diet, intestinal malabsorption and loss of liver thiamine stores. The onset may coincide with an abstinence period and is generally marked by somnolence and mental confusion; which gradually worsens, together with cerebellar signs, hypertonia, paralysis and/or ocular signs. The prognosis depends on how quickly the patient is given high-dose vitamin B1 (by intravenous route, preferably). A delay or an absence of treatment increases the risk of psychiatric sequelae (memory disorders and/or intellectual deterioration). If the treatment is too late, the consequences could be an evolution to a Wernicke–Korsakoff syndrome, a dementia.

Alcohol and epilepsy

Alcohol is associated with different aspects of epilepsy, ranging from the development of the condition in chronic heavy drinkers and dependent individuals to an increased number of seizures in people already with the condition. Alcohol aggravates seizures in people undergoing withdrawal and seizure medicines might interfere with tolerance for alcohol, thereby increasing its effect. Though small amounts of alcohol might be safe, people suffering from epilepsy should be advised to abstain from consuming this agent.

After an episode of weeks of uninterrupted drinking, sudden abstinence may lead to epileptic seizures and severe coma, "delirium tremens". Detoxification should be under medical supervision and possibly with medication to decrease the risk of this potentially life-threatening condition.

In terms of relative risk, much more is known about alcohol and epilepsy than other conditions. There is little difference between abstainers and light drinkers in the risk for chronic harmful alcohol-related epilepsy. Risk is highest at levels of consumption which exceed 20 g of pure alcohol (or two drinks) per day for women and 40 g for men. For example, the WHO project on comparative risk assessment has shown more than a sevenfold increase in risk among those who consume these high volumes or are dependent on alcohol when compared with abstainers for both male and female drinkers (*47*).

PREVENTION OF NUTRITIONAL DEFICIENCIES

The neurological disorders discussed in this chapter stem from three main causes:

- general malnutrition in childhood leading to macronutrient deficiency;
- micronutrient deficiencies caused by insufficient supply or increased consumption (sometimes called "hidden hunger");
- ingestion of toxic compounds.

The prevention of neurological complications attributable to the first two causes is, in theory, very simple: achieve Millennium Development Goal No. 1 by eradicating extreme poverty and hunger. Most people encountering a nutritional deficiency do so because of poverty. Acknowledging that eradicating poverty is easier said than done, there are some strategies that can be used to prevent some of the micronutrient deficiencies. There are three principal ways of approaching a potentially micronutrient-deficient diet:

- Diversification — include other micronutrient-rich food items in the diet.
- Supplementation — add a supplement of the micronutrient, for instance as a pill. This method is used with vitamin A in a large number of low income countries, linked to the immunization programme.
- Fortification — add more of the micronutrient to a common food commodity. Universal salt iodization is an example where this strategy has been used.

Worldwide efforts to cope with the most appalling micronutrient deficiencies are ongoing. Adding iodine to all salt has been a very successful way of preventing neurological complications caused by iodine deficiency. Supplementation of vitamin A for children under five years of age is another successful strategy to prevent blindness as a result of vitamin A deficiency. In societies with more resources and more centralized food distribution, fortification of flour with folate has been shown to decrease the occurrence of neural tube defects. In populations with restricted food choice, such as refugee populations in camps surviving on food rations, surveillance is needed to detect and correct vitamin deficiencies.

The toxic exposures need different approaches. For *L. sativus*, supplementation of cereals during acute food shortages in lathyrism-endemic areas can reduce its consumption. Another possibility is the development of a genetically modified atoxic variety that could prevent the problem. In the case of insufficiently processed toxic cassava, this solution does not seem so attractive, as low-toxic varieties are not as reliable in producing food for the family; the approach should concentrate on the proper processing of cassava. For alcohol, the focus needs to be on restricting alcohol consumption, at least during pregnancy.

The large majority of the malnutrition-related neurological disorders can be avoided by simple measures, such as the following recommended actions for policy-makers.

- Support efforts towards universal salt iodization.
- Support vitamin A supplementation among children under five years of age, if judged necessary.
- Consider strategies to decrease childhood malnutrition.
- Consider folate fortification of flour, if affordable and possible.
- Oversee the distribution of food rations to refugee populations, in order to detect and correct vitamin deficiencies.
- Promote the proper processing of toxic cassava.
- Restrict alcohol consumption, especially during pregnancy.

A preventive approach should include adapted communication with the aim of changing behaviour, strengthening capacities and reducing the incidence of some chronic diseases such as frequent neurological complications. The following activities are possible examples:

- specific nutritional programmes for children and pregnant and nursing women;
- rapid diagnosis of nutritional deficiencies in vitamins and minerals that could have a severe impact on mother and child and alter their mental and physical status and development;
- nationwide measures such as those for the prevention of iodine deficiency and its consequences.

Early interventions could reverse the deleterious tendencies. In many countries, the mass interventions against iron, vitamin A and iodine deficiencies among children (those under five years of age and older ones as well) and pregnant and nursing women, must be reinforced. At the other end of the scale, much remains to be done for adults and elderly people.

A PUBLIC HEALTH FRAMEWORK

Political aspects

Within the context of the fight against poverty, malnutrition would benefit from strong political commitment to improve and develop an integrated approach of various ministries. Improving the dialogue between public and private sectors should be an important approach to emphasize in every country. Efforts remain to be made for a comprehensive salt iodization as recommended by international organizations. This implicates obligatory reinforcement of policies for legislation, standards, application and control. Regulations on the advertising of beers, wines, other alcoholic drinks and tobacco must be reinforced, especially during sports and cultural events. Nigerian President Olusegun Obasanjo has lent his support to the goal of reducing death from chronic disease: "Governments have a responsibility to support their citizens in their pursuit of a healthy, long life. It is not enough to say: 'we have told them not to smoke, we have told them to eat fruit and vegetables, we have told them to take regular exercise'. We must create communities, schools, workplaces and markets that make these healthy choices possible."

Management and provision of care

The management of neurological disorders related to malnutrition — attributable to direct causes or secondary induced effects of metabolic diseases — is a challenge that requires a pragmatic approach in order to be effective. Setting up pilot interventions that are feasible and realistic would be a useful demonstration to WHO Member States concerned by this public health problem. Lessons learnt from other integrated programmes (for both noncommunicable and communicable diseases) could serve as a model for neurological disorders associated with malnutrition.

It is essential to set up a multidisciplinary task force surrounding neurologists and nutritionists. This team should be supplemented by clinicians who are concerned with the secondary causes of neurological diseases related to nutrition, i.e. cardiologists, endocrinologists, specialists in internal medicine and paediatricians. Social scientists would also have an important role, for a better understanding of knowledge, attitudes and practices. Specialists in communication would be involved in the initiative, so as to reach, educate and sensitize the population. Other sectors such as education, private and public sectors, civil society, community leaders and nongovernmental organizations will all have a part to play to contribute to the concretization and reinforcement of the strategies and interventions.

CONCLUSIONS AND RECOMMENDATIONS	
1	Malnutrition, micronutrient deficiencies and ingestion of toxic compounds continue to be priority public health problems. Most of the neurological disorders associated with them are preventable.
2	Priorities need to be identified for the actions needed to deal with neurological disorders associated with malnutrition, micronutrient deficiencies, or the ingestion of toxic compounds.
3	The strategy of communication should use appropriate and diversified channels for better sensitization and social mobilization. It should target the general population, health professionals and social workers. Schools constitute a favourable environment because they provide access to teachers and pupils who can carry the message home at household level.
4	The interrelationship between neurological disorders and nutrition must be stressed in the training of general practitioners, paramedical staff and social workers. The capacities of nongovernmental organizations, community organizations and the education sector must be reinforced and developed so as to target the prevention of nutritional problems.
5	Development and review of training manuals, counselling guidelines and training curricula is a necessary part of capacity-strengthening whose contents need to be centred on specific subjects in accordance with needs assessment, the gaps to be filled and the interventions to be implemented in the community.
6	Educative support to the health services must be elaborated to develop tools of education and counselling for primary and secondary prevention and to develop guidelines and support to facilitate management of the targeted diseases and secondary complications, including disabilities and rehabilitation.

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- The Micronutrient Initiative web site (http://www.micronutrient.org/) includes links to the most important Internet sites regarding the individual micronutrients discussed in this chapter.

3.7 Pain associated with neurological disorders

Pain can be a direct or an indirect consequence of a neurological disorder, with physical and psychological dimensions that are both essential for its correct diagnosis and treatment. Pain — acute and chronic — is a major public health problem that poses significant challenges to health professionals involved in its treatment. Chronic pain may persist long after initial tissue damage has healed: in such cases, it becomes a specific health-care problem and a recognized disease. Adequate pain treatment is a human right, and it is the duty of any health-care system to provide it.

The current and most widely used definition of pain was published by the International Association for the Study of Pain (IASP) in 1979, which states that pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or, is described in terms of such damage" (*1*). This definition was qualified by the Taxonomy Task Force of the association in 1994 (*2*): "Pain is always subjective. Each individual learns the applications of the word through experiences relating to injuries in early life".

The physiological effect of pain is to warn of tissue damage and so to protect life. Pain is classified as nociceptive if it is caused by the activation of nociceptors (primary sensory neurons for pain). Nociceptive pain can be somatic (pain originating from the skin or musculoskeletal system) or visceral (pain originating from visceral organs). The sensory system itself can be damaged and become the source of continuous pain. This type of pain is classified as neuropathic. Chronic neuropathic pain has no physical protective role as it continues without obvious ongoing tissue damage. Pain without any recognizable tissue or nerve damage has its cause classified as idiopathic pain. Any individual pain state may be a combination of different pains. A clinician's duty is to diagnose, treat and support pain patients, which means the identification of pain type(s) and their causative disease(s). It is also to provide adequate treatment aimed at the cause of the pain and symptomatic relief which should include psychosocial support. As the definition of pain reveals, pain has both a physical and a psychological element. The latter plays an important part in chronic pain disorders and their management. Adequate pain treatment is a human right and organization of it involving all its dimensions is the ethical and legal duty of society, health-care professionals and health-care policy-makers.

TYPES OF PAIN ASSOCIATED WITH NEUROLOGICAL DISORDERS

Pain can be a direct or an indirect consequence of a neurological disorder. The former is seen in neurological conditions where there has been a lesion or disease of pathways that normally transmit information about painful stimuli either in the peripheral or in the central nervous system (CNS). These types of pain are termed neuropathic pains. Pain can also be an indirect consequence of a nervous disease when it causes secondary activation of pain pathways. Examples of these types of pain include musculoskeletal pain in extrapyramidal diseases such as Parkinson's disease, or deformity of joints and limbs due to neuropathies or infections.

It is useful to distinguish between acute and chronic pain. Pain begins frequently as an acute experience but, for a variety of reasons — some physical and often some psychological — it becomes a long-term or chronic problem. According to the IASP classification of chronic pain, this term refers to any pain exceeding three months in duration.

Pain directly caused by diseases or abnormalities of the nervous system

Neuropathic pain

In contrast to nociceptive pain which is the result of stimulation of primary sensory nerves for pain, neuropathic pain results when a lesion or disruption of function occurs in the nervous system. Neuropathic pain is often associated with marked emotional changes, especially depression, and disability in activities of daily life. If the cause is located in the peripheral nervous system, it gives rise to peripheral neuropathic pain and if it is located in the CNS (brain or spinal cord) it gives rise to central neuropathic pain.

Peripheral neuropathic pain. Painful diabetic neuropathy and the neuralgia that develops after herpes zoster are the most frequently studied peripheral neuropathic pain conditions. Diabetic neuropathy has been estimated to afflict 45–75% of patients with diabetes mellitus. About 10% of these develop painful diabetic neuropathy, in particular when the function of small nerve fibres is impaired. Pain is a normal symptom of acute herpes zoster, but disappears in most cases with the healing of the rash. In 9–14% of patients, pain persists chronically beyond the healing process (postherpetic neuralgia). Neuropathic pain may develop also after peripheral nerve trauma as in the condition of chemotherapy-induced neuropathy.

The frequencies of many types of peripheral neuropathic pain are not known in detail but vary considerably because of differences in the frequency of underlying diseases in different parts of the world. While pain caused by leprosy is common in Brazil and parts of Asia, such pains are exceedingly rare in Western parts of the world. Because of an explosion in the frequency of diabetes as a result of obesity in many industrialized countries and in South-East Asia, the likely result of this will be an increase in painful diabetic neuropathy within the next decade.

Central neuropathic pain, including pain associated with diseases of the spinal cord. Central post-stroke pain is the most frequently studied central neuropathic pain condition. It occurs in about 8% of patients who suffer an infarction of the brain. The incidence is higher for infarctions of the brainstem. Two thirds of patients with multiple sclerosis have chronic pain, half of which is central neuropathic pain (*3*).

Damage to tissues of the spinal cord and, at times, nerve roots, carries an even higher risk of leading to central neuropathic pain (myelopathic pain). The cause may lie within the cord and be intrinsic, or alternatively, be extrinsic outside the cord. Intrinsic causes include multiple sclerosis and acute transverse myelitis, both of which may result in paraplegia and pain. In certain developing countries, for example in sub-Saharan Africa, intrinsic damage may be attributable to neurotoxins — as in the case of incorrectly prepared cassava, which leads to tropical spastic

paresis. Lathyrism resulting from consumption of the grass pea (*Lathyrus sativus*) may cause a spinal disorder and, in both cases, pain is a significant symptom (see also Chapter 3.6).

Extrinsic causes of cord damage and pain are numerous. Spinal cord injuries result in pain in about two thirds of all patients (*4*). Other causes include compressive lesions, for example tumours and infections, especially tuberculosis and brucellosis. The former group comprises both primary CNS tumours (e.g. neurofibroma and meningioma) and secondary tumours from breast, lung, prostate and other organs, together with lymphomas and leukaemias.

Pain indirectly caused by diseases or abnormalities of the nervous system

Pain arises as a result of several distinct abnormalities of the musculoskeletal system, secondary to neurological disorders. These can be grouped into the following categories:

- musculoskeletal pain resulting from spasticity of muscles;
- musculoskeletal pain caused by muscle rigidity;
- joint deformities and other abnormalities secondary to altered musculoskeletal function and their effects on peripheral nerves.

Pain caused by spasticity

Pain caused by spasticity is characterized by phasic increases in muscle tone with an easy predisposition to contractures and disuse atrophy if unrelieved or improperly managed. In developed countries, the main causes of painful spasticity are strokes, demyelinating diseases such as multiple sclerosis, and spinal cord injuries. With an ageing population, especially in the industrialized countries, and rising numbers of road traffic accidents, an increase in these conditions, and therefore pain, is to be expected in the future.

Strokes and spinal cord disease are also major causes of spasticity in developing countries, for example stroke is the most common cause of neurological admissions in Nigeria.

Pain caused by muscle rigidity

Pain can be one of the first manifestations of rigidity and is typically seen in Parkinson's disease, dystonia and tetanus. Apart from muscle pain in the early stages of Parkinson's disease, it may also occur after a long period of treatment and the use of high doses of L-Dopa causing painful dystonia and freezing episodes. Poverty of movement and tremors may also contribute to the pain in this disorder.

Tetanus infection, common in developing countries, is characterized by intense and painful muscle spasms and the development of generalized muscle rigidity, which is extremely painful. During intense spasm, fractures of spinal vertebrae may occur, adding further pain.

Pain caused by joint deformities

A range of neurological disorders give rise to abnormal stresses on joints and, at times, cause deformity, subluxation or even dislocation. For example "frozen shoulder" or pericapsulitis occurs in 5–8% of stroke patients. Disuse results in the atrophy of muscles around joints and various abnormalities giving rise to pain, the source of which are the tissues lining the joint. In addition, deformities may result in damage to nerves in close proximity resulting in neuropathic pain of the "evoked" or spontaneous type.

The literature does not give data for the prevalence and incidence of the pain associated with the disorders mentioned.

Complex painful disorders

Complex regional pain syndrome (CRPS) refers to several painful disorders associated with damage to the nervous system including the autonomic nervous system. CRPS Type I was previously

known as reflex sympathetic dystrophy, with the cause or preceding event being a minor injury or limb fracture. CRPS II, formerly known as causalgia, develops after injury to a major peripheral nerve. The symptoms exceed both in magnitude and duration those which might be expected clinically given the nature of the causative event. Also, patients often experience a significant reduction in motor function. The pain is spontaneous in type with allodynia and hyperalgesia. Other features of the syndrome include local oedema or swelling of tissues, abnormalities of local blood flow, sweating (autonomic changes) and local trophic changes. Both conditions tend to become chronic. They are a cause of significant psychological and psychiatric disturbance, and treatment is a major problem.

Headache and facial pain

Any discussion of pain arising from disorders of the nervous system must include headache and facial pains: these conditions are discussed in Chapter 3.3. They have been the subject of considerable research and been carefully classified by the International Headache Society. Epidemiological studies have focused primarily on migraine and tension-type headaches (primary headache disorders). Secondary headache disorders are also described (see Box 3.3.1).

ASSESSMENT OF PAIN

Pain has physical and psychological dimensions, both of which may be measured; they form an important aspect of the diagnosis of painful disorders and are essential for the correct application of treatment and its assessment. Pain is a subjective experience but physiological changes that accompany it may be measured: they include changes in heart rate, muscle tension, skin conductivity and electrical and metabolic activity in the brain. These measures are most consistent in acute rather than chronic pain and they are used primarily in laboratory studies. Clinically, pain assessment includes a full history of the development, nature, intensity, location and duration of pain. In addition to clinical examination, self-report measures of pain are often used.

The use of words as descriptors of pain have permitted the development of graded descriptions of pain severity. For example, mild pain, moderate pain, severe pain and very severe pain, to which numerical values may be attached (*1–4*), may be graded on a numerical scale from 0 to 4 indicating the level of pain being experienced. In clinical practice, however, there is widespread use of a 0–10 scale, a visual analogue scale, which is easy to understand and use and is not affected by differences in language. Such measures are often repeated at intervals to gain information about the levels of pain throughout the day, after a given procedure or as a consequence of treatment. More sophisticated verbal measures use groups of words to describe the three dimensions of pain, namely its sensory component, the mood-related dimension and its evaluative aspect. This technique was devised by Melzack and others and is best seen in the Short-Form McGill Pain Questionnaire (*5*). The questionnaire requires the patient to be well acquainted with the words used. Often because of age, not having English as a first language or as a result of some form of mental impairment, the scale cannot be used. In its place it is possible to use a "faces scale" in which recognizable facial images representing a range of pain experiences from no pain to very severe pain are readily understood. Such scales are often used with children. In the case of patients with pain generated as a result of a lesion within the nervous system (neuropathic pain) specific measures have been devised to distinguish between that type of pain and pain arising outside the nervous system (*6*). In the assessment of a patient with neuropathic pain, the evaluation of sensory function is crucial and can be carried out at the bedside with simple equipment.

Another technique used in clinical assessment includes pain drawings, which allow the patient to mark the location of pain and its qualities using a code on a diagram of the body. A pain diary is used by patients to record levels of pain throughout the day, using a visual analogue scale. This reveals the pattern of pain severity in relation to drug therapy and activity levels. Finally, pain behaviour is

often used to aid diagnosis. It is especially useful for determining the extent to which psychological factors influence pain. For example, a wide discrepancy between the behaviour exhibited in the clinic and what might be expected, given the nature of the disorder, is a valuable clue to a person's emotional state, ability to cope with pain and conscious or unconscious desire to communicate distress non-verbally to the clinician. Pain assessment should take account of the patient's sex and ethnic and cultural background, all of which tend to influence the clinical presentation.

PUBLIC HEALTH ASPECTS OF PAIN DISORDERS

Pain — acute and chronic — is a ubiquitous experience and it is also a major public health problem that poses significant challenges to health professionals involved in its treatment. Reliable data about the prevalence and incidence of pain, however, are limited, with available studies being based on either regional surveys of a broad spectrum of painful disorders, or specific pain states.

In a collaborative study of pain in a primary care setting, WHO revealed that persistent pain afflicted between 5.3% and 33% of individuals resident in both developing and developed countries. The lowest frequency was reported in Nigeria and the highest in Santiago, Chile. The study revealed that persistent pain was associated with depression, which affected the quality of life and reduced the level of daily activity of the sufferers (*7*). It was concluded that the essential need to work and to earn income might be a reason why many people in developing countries tolerate pain rather than reporting to doctors or hospitals. Therefore, lack of an adequate social and health-care support network, cost implications and job security must influence the extent to which people living in developing countries and suffer pain fail to seek help.

A detailed study of the prevalence, severity, treatment and social impact of chronic pain in 15 European countries was carried out recently (*8*). The prevalence of chronic pain ranged between 12% and 30%, figures similar to those in the WHO study. The most common sites for pain were the head and neck, knees and lower back. Of the respondents, 25% had head or neck pains (migraine headaches, 4%; nerve injury from whiplash injuries, 4%). Although back pain may have a neurological cause, the likelihood was that in the great majority pain was the result of musculoskeletal disorders or back strain. The authors concluded that one in five Europeans suffer from chronic pain which is of moderate severity in two thirds and severe in the remainder. The study also reveals that, in the opinion of 40% of the respondents, their pain had not been treated satisfactorily and 20% reported that they were depressed. In economic terms, 61% were less able or unable to work outside their homes, 19% had lost their jobs because of pain and another 13% had changed their jobs for the same reason.

A large-scale survey in Australia (*9*) of just over 17 000 adults with pain daily for at least three months (chronic pain) yielded a prevalence rate of 18.5%; in a comparable survey in Denmark, a prevalence rate of 19% was obtained (*10*). It is therefore evident from the three surveys that a prevalence rate for chronic pain of 18–20% is to be expected in adult populations selected at random from developed countries. Unfortunately, these figures do not give any detail about pain arising from the nervous system, except for the information about head and neck pain in the European survey.

Certain neurological disorders causing pain have been examined in terms of the incidence of pain. For example Kurtzke (*11*) estimated that the annual incidence of herpes zoster infection in the United States was 400 per 100 000 of the population. A study of the incidence of post-herpetic neuralgia in 1982 revealed a figure of 40 per 100 000 (*12*). Further information from Bowsher (*13*) indicated that the number of individuals with post-herpetic neuralgia increases with age so that 40% of people over 80 years of age who acquire acute herpes zoster will suffer from chronic post-herpetic neuralgia. In populations in which ever greater numbers are living to 80 years and more, there is likely to be a significant increase in individuals suffering from post-herpetic neuralgia.

The earlier study by Ragozzino et al. (*12*) gave figures for the anatomical distribution of the neuralgia that was present in 56% in the thoracic region, 13% in the face and 13% in the lumbar regions; 11% had pain in the cervical region. One third of patients with multiple sclerosis develop neuropathic pain states, of whom trigeminal neuralgia occurs in 5%, and another one third develop other forms of chronic pain (*3*). There is an increase in the incidence of trigeminal neuralgia in patients with cancer and other diseases that impair the immunological systems.

It is significant that one third of cancer patients have a neuropathic component to their pain as do a similar proportion of patients with prolonged low back pain (*14*).

It should be noted that stump pain arises from a severed nerve in the limb and may be caused by a local neuroma or by tethering of the severed nerve to local tissues. In either case the pain is of the peripheral neuropathic type. In contrast, phantom limb pain is central neuropathic pain and more difficult to treat.

Central stroke pain is defined as neuropathic pain that follows an unequivocal episode of stroke. It is associated with partial sensory loss in all but a few cases. A prospective study by Andersen et al. (*15*) revealed a one-year incidence of 8%, with symptoms being severe in 5% and mild in 3%. For most patients the pain develops gradually during the first month but delays of many months have been recorded. The pain is incapacitating, distressing and often even more so than other symptoms.

Headache disorders have also been the subject of intensive epidemiological research (see Chapter 3.3).

Poor relief of acute pain is a recognized risk factor for the development of chronic pain after various forms of surgery, for example herniotomy, mastectomy, thoracotomy, dental surgery and other forms of trauma. In part, this is the result of nerve injury which presents as acute neuropathic pain in 1–3% of patients. The majority of such patients experience persistent pain one year after the causative event, indicating that acute neuropathic pain is a very definite risk factor for chronic pain. Prompt treatment of early nerve pain is therefore important (*16*).

Hernia repair is followed by moderate to severe pain in 12% of patients one year postoperatively and is of the somatic or neuropathic type (*17*). Breast surgery of various types gives rise to the experience of phantom breast and pain with or without a phantom.

Information about the incidence and prevalence of pain generally, and neurologically related pain in particular, is almost totally lacking for developing countries, although there is no reason to believe that conditions that give rise to pain such as stroke, multiple sclerosis, various forms of headache and other disorders vary in nature. There may well be differences, however, in the extent to which some disorders are present, for example multiple sclerosis is less common in developing countries, whereas others are not encountered in the Western world, such as certain forms of poisoning by neurotoxins from foods, and leprosy which is a cause of neuropathic pain.

HIV/AIDS is a major cause of neuropathic pain in the later stages of the disease: 70% of AIDS sufferers develop this form of pain, which is severe and comparable with the severe pain experienced in cases of advanced cancer. The incidence of severe pain must, therefore, be high in countries where AIDS is a major health problem.

Box 3.7.1 Signs and symptoms of chronic pain

- Immobility and consequent wasting of muscle, joints, etc.
- Depression of the immune system causing increased susceptibility to disease
- Disturbed sleep
- Poor appetite and nutrition
- Dependence on medication
- Overdependence on family and other caregivers
- Overuse and inappropriate use of health-care providers and systems
- Poor performance on the job, or disability
- Isolation from society and family
- Anxiety and fear
- Bitterness, frustration, depression and suicide

The figures quoted in this section show that a significant number of individuals suffer from chronic and incapacitating pain as a result of diseases of the nervous system, or as a result of damage to peripheral nerves at the time of surgery and other forms of trauma. The nature of the pain, which is often neuropathic in type, means that the sufferer has a disabling condition that in time may be primarily the result of pain, which is difficult to relieve. As such, it poses a significant health problem in terms of its personal, social and economic consequences.

DISABILITY AND BURDEN

Anyone involved primarily in the management of chronic pain is aware that it may persist long after the initial tissue damage has healed. Pain reflects pathophysiological changes in the nervous system and they, together with changes that usually occur in patients' emotions and behaviour, have led to the conclusion that, in such cases, chronic pain is a specific health-care problem and a disease in its own right. This diagnostic category is not fully accepted among clinicians because many continue to believe that pain must be a symptom of an ongoing disease or injury. Current research reveals, however, that the pathophysiological changes mentioned persist when signs of the original cause for pain have disappeared. The signs and symptoms of chronic pain, once it has evolved into a disease, are listed in Box 3.7.1. The combination of these features of the condition reveal the potential for physical impairment, disability and handicap which collectively form the basis of significant degrees of burden for both the patient and the family.

TREATMENT AND CARE

Barriers to effective pain relief

Educational barriers

Despite the wide availability of teaching aids for educating professional groups who are heavily engaged in pain management (*18*), relatively little attention has been given to their use in developed countries. They are used to an even lesser extent in developing countries. Therefore many doctors, nurses and others dealing with patients in pain enter their professional careers inadequately equipped to deal with the most common symptom and cause of considerable suffering worldwide.

Politicoeconomic barriers

The availability of drugs for the treatment of pain is a problem in over 150 countries. Frequently, pain management has a low priority, because the chief focus of attention is infectious diseases and, often, there are exaggerated fears of dependence with very restrictive drug control policies. In addition, in developing countries, the cost of medicines generally and therefore problems in their procurement, manufacture and distribution, add further barriers to their use.

A treatment gap

In many countries, therefore, there is a treatment gap, meaning that there is a difference between what could be done to relieve pain and what is being done. That gap exists in a number of developed countries, primarily because of poor pain education and the often limited and patchy nature of specialized facilities for pain treatment. Additionally, in developing countries these problems are far greater and the gap is far wider because of the lack of education, access to appropriate drugs for pain relief and facilities for pain management.

The treatment gap can be reduced worldwide by improving pain education, increasing facilities for pain treatment and access to pain-relieving drugs. In the case of opioid analgesics, an increase in their availability and the employment of correct protocols is a matter of urgency. Improvements of this kind are possible if use is made of the guidelines published by WHO, together with the

International Narcotics Control Board, on achieving balance in a national opioids control policy, which are available in 22 languages on the web site of the WHO Collaborating Centre for Policy and Communications in Cancer Care (*19*). Also, no stricter measures should be enacted than those requested by the international drug conventions and international recommendations (*20*) on the use of opioid medicines. WHO is developing a programme to assist countries in improving access to medications controlled under the drug conventions (see Box 3.7.2) (*19*).

Management of pain of neurological origin

The range of treatments available for pain directly caused by diseases of the nervous system includes pharmacological, physical, interventional (nerve blocks, etc.) and psychological therapies. Treatments for pain are used in association with other forms of treatment for the primary condition, unless of course pain is itself the primary disorder. IASP definitions of pain treatment facilities and services are given in Box 3.7.3.

There are many studies of the medical treatment of peripheral neuropathic pain (*21*). There are far fewer studies published on the treatment of central neuropathic pain, for example post-stroke pain. Neuropathic pain does not respond well to non-opioid analgesics such as paracetamol, acetylsalicylic acid and ibuprofen — a non-steroidal anti-inflammatory drug. Opioids have been shown to have some efficacy in neuropathic pain but there are specific contraindications for their use.

Topical agents may give local relief with relatively little toxicity; they include lidocaine and, to a lesser extent, capsaicin cream, particularly in the treatment of post-herpetic neuralgia. In selected cases, electrical stimulation techniques such as transcutaneous electrical stimulation or dorsal column stimulation may be used, but the latter in particular is expensive which clearly limits its use. Pain associated with spasticity and rigidity is treated with muscle relaxants. In the case of baclofen, it can be administered systemically or intrathecally. However, the latter route requires administration by a trained specialist and therefore is unlikely to be freely available in developing countries.

Pain arising from joints secondarily damaged by the effects of neurological disorders is usually controlled using simple analgesics, for example paracetamol or a non-steroidal anti-inflammatory drug (NSAID).

Box 3.7.2 Access to Controlled Medications Programme

In many parts of the world, patients suffering severe pain face immense challenges in obtaining pain relief, because the opioids that could provide such relief have been categorized as "controlled substances". They are therefore subject to stringent international control and rendered inaccessible.

Severe under-treatment is reported in more than 150 countries, both developing and industrialized. They account for about 80% of the world population. Annually, up to 10 million people suffer from lack of access to controlled medications. Nearly one billion of the people living today will encounter this problem sooner or later. Most of them are pain patients.

The future Access to Controlled Medications Programme, initiated by WHO, will address the main causes for impaired access. These causes stem essentially from an imbalance between the prevention of abuse of controlled substances and the use of such substances for legitimate medical purposes.

For almost 50 years the focus was on the prevention of abuse, which led to too strict rules in many countries that do not allow medical use. In relation to that, prejudice has developed consisting of an unjustified fear of psychological dependence of patients on opioid medication and an unjustified fear of death caused by opioids. Many countries have neglected their obligation to provide sufficient analgesia given in the United Nations drug conventions and as called for by many international bodies (the International Narcotics Control Board, the United Nations Economic and Social Council, the World Health Assembly, etc.)

The programme, as proposed, will focus on regulatory barriers, the functioning of the estimate system for importing/exporting by the countries, and the education of health-care professionals and others involved. It will organize regional workshops where health-care providers, legislators and law enforcers will exchange their views and the problems they encounter. It will train civil servants responsible for submitting estimates and, in doing so, train health-care providers in the rational use of opioids. Furthermore, it will develop other activities, including advocacy.

Psychological techniques — and cognitive/behaviour therapy in particular — are used to help patients cope with pain and maximize their social, family and occupational activities. Research reveals that such therapies are effective in the reduction of chronic pain and absenteeism from work (*22*).

Physical therapy carried out by physiotherapists and nurses is an important part of the management of many patients with neurological diseases, painful or not, including strokes, multiple sclerosis and Parkinson's disease, to name but a few. Relaxation techniques, hydrotherapy and exercise are helpful in the management of painful conditions that have a musculoskeletal component. In fact, in the case of CRPS type I and II they form the first line of treatment when used together with analgesics. There is good evidence that multimodal treatment and rehabilitation programmes are effective in the treatment of chronic pain (*23, 24*).

All health-care workers who treat pain, especially chronic pain, whatever its cause, can expect about 20% of patients to develop symptoms of a depressive disorder. Among patients attending pain clinics, 18% have moderate to severe depression when pain is chronic and persistent. It is known that the presence of depression is associated with an increased experience of pain whatever its origin and also reduced tolerance for pain. Therefore the quality of life of the patient is significantly reduced, and active treatment for depression is an important aspect of the management of the chronic pain disorder.

Service delivery

The management of neurological diseases is primarily a matter for specialist medical and nursing staff, both in developed and developing countries. In contrast, specific facilities for pain management, especially chronic pain management outside neurological centres, are much less well organized and are often absent, especially in developing countries. The relief of pain should be one of the fundamental objectives of any health service. Good practice should ensure provision of evidence-based, high quality, adequately resourced services dedicated to the care of patients and to the continuing education and development of staff. In 1991, an IASP Taskforce on Guidelines for Desirable Characteristics for Pain Treatment Facilities issued definitions of the various types of service in existence for the management of pain by pain clinicians (*25*). They are given in Box 3.7.3.

Box 3.7.3 Definitions of pain treatment services

Pain treatment facility	A generic term describing all forms of pain treatment facilities without regard to personnel involved or types of patient served.
Multidisciplinary pain centre	The centre comprises a team of professionals from several disciplines (e.g. medicine, nursing, physiotherapy, psychology) devoted to the analysis and management of pain, both acute and chronic. The work of the centre includes teaching and research. The centre may have both inpatient and outpatient facilities.
Multidisciplinary pain clinic	The clinic is a health-care delivery facility with a team of trained professionals who are devoted to the analysis and treatment of pain. The clinic may have both inpatient and outpatient facilities.
Pain clinic	Pain clinics vary in size and staffing complements but should not be run single-handed by a clinician. The clinic may specialize in specific diagnoses (e.g. neuropathic pain) or pains related to a specific area of the body (e.g. headache).
Modality-orientated clinic	The clinic offers a specific type of treatment and does not conduct comprehensive assessment or management. Examples include clinics dealing with nerve block, transcutaneous electrical nerve stimulation (TENS), acupuncture and hypnosis.

Source: (*25*).

During the past 15–20 years, the ideals for pain management in general, and services in particular, have increasingly been met in developed countries. They are met to a much lesser extent in developing countries, where other health priorities, costs of treatment and availability of trained personnel are all contributing factors to the relative lack of resources. Nevertheless, strenuous efforts to improve services for people in pain are being made in many developing countries. Even though services for neurological disorders are better provided, many patients with pain of neurological origin may never reach such centres. There is therefore a great need for health-care providers to devote more resources to pain relief in general, which in turn will bring about an improvement in the treatment facilities available for neurological patients with pain.

RESEARCH

Worldwide, research on pain takes place within the disciplines of experimental neurosciences (molecular biology, anatomy, physiology), clinical neurosciences (neurology, neurosurgery, psychiatry), psychology and psychosomatic medicine, anaesthesiology, orthopaedic surgery, public health and community medicine, physical therapy and nursing. The IASP is an interdisciplinary scientific society that fosters interactions between these diverse lines of research via its triennial World Pain Congresses, its scientific journal *Pain*, and books published by IASP Press (*18*). Its Special Interest Group on Neuropathic Pain provides a forum for scientific exchange on neuropathic pain and other types of pain that are related to neurological disorders (*26*).

TRAINING

At present, pain medicine and algesiology are recognized as medical specialties in only a small number of countries (for example Finland, Germany, Turkey and the United Kingdom). Therefore, most medical doctors interested in treating patients for pain spend their residency in one of the existing medical disciplines — particularly anaesthesiology but also orthopaedic surgery, neurology or, more rarely, psychiatry or psychosomatic medicine.

Pain treatment fellowships are offered by some countries, and IASP has postgraduate training positions. In Germany, a medical subspecialty, specialized pain therapy, is supervised by a licensed training centre and carried out after finishing a residency in one of the traditional medical specialties. More general training in pain management does exist but it is very variable within and between specialist medical areas and between countries.

Training programmes for nurses who will specialize in pain management are growing steadily. Such programmes exist mainly in relation to palliative care, post-operative pain management and the work of pain clinics in developed countries but, increasingly, also in countries in the developing world.

Physiotherapy is a discipline in which pain management is an integral part of the working day and therefore should be a major aspect of the training of all physiotherapists.

Clinical psychologists have a major role in the treatment of chronic pain patients. Usually they specialize in pain management after a period of postgraduate training in general clinical psychology and practise either independently or in specialist pain centres. Very few clinical psychologists are available for work with patients in pain, whether attributable to neurological conditions or not, in developing countries. However, specialist training in pain management for medical practitioners who work in hospitals or the community in developing countries is spreading gradually. IASP has provided a core curriculum for professional education in pain that forms the basis for growing numbers of pain education programmes and is available via open access (*27*).

CONCLUSIONS AND RECOMMENDATIONS	
1	Pain is associated with neurological disorders in three ways: as neuropathic pain resulting from diseases, infections or injuries of the central and peripheral nervous system, as musculoskeletal pain secondary to neurological disorders, and as complex regional syndromes in which both the somatic and autonomic nervous systems are involved.
2	Chronic pain may develop from poorly treated or neglected acute pain as a result of changes in the function of the CNS: the pain persists and as such has become a disorder of the nervous system.
3	Pain is a significant symptom in several neurological disorders or after injuries to the nervous system, adding significantly to physical and emotional suffering and often to disability. Neurologists and non-neurologists who have responsibility for patients with neurological disorders should ensure that pain is assessed carefully and recorded in terms of its origins, nature and severity as part of an overall clinical assessment prior to diagnosis and management.
4	There is an urgent need for the inclusion of specific pain education programmes in undergraduate curricula for doctors, nurses and other health professionals likely to deal with pain problems. Postgraduate training is also neglected in many countries, though specialization in pain management is increasing steadily, particularly in developed countries. There is a need to continue and expand postgraduate training in pain management and to develop specialized pain management centres.
5	A treatment gap, which is greatest in developing countries, results from inadequate pain education, the low priority given to pain relief compared with other medical problems such as infectious diseases, and poor access to the most powerful analgesics.
6	A fear of addiction, coupled with unnecessarily restrictive legal controls and limitation of access by cost and availability of other pain-relieving drugs, significantly reduces the potential for pain relief. Recognized international guidelines for the use of powerful analgesics should be observed and unduly restrictive regulations should be suitably modified to ensure availability on a reasonable basis. Guidelines should be made available on the use of co-analgesic drugs and other treatments used to relieve or control very severe pain.
7	There is an urgent need for more research into chronic pain of neurological origin.

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3.8 Parkinson's disease

Parkinson's disease is a chronic progressive neurodegenerative disorder of insidious onset, characterized by the presence of predominantly motor symptomatology (bradykinesia, rest tremor, rigidity, and postural disturbances). It is also associated with a diversity of non-motor symptoms, which, together with late-onset motor symptoms (such as postural instability and falls, freezing of gait, speech and swallowing difficulties), are presently one of the most difficult challenges the treating physician is faced with when dealing with patients with a long duration of the disease.

In addition to the motor symptomatology of Parkinson's disease (PD) (*1*), some non-motor symptoms such as hyposmia, rapid eye movements, sleep behaviour disorder, personality changes, pain, paresthesias and depression may be present and may even manifest before the motor symptoms (*2*). Urinary disturbances, orthostatic hypotension and neuropsychiatric disturbances (dementia, hallucinations and delirium) usually become evident and troublesome after several years in the course of the disease (*3*). Overt dementia is a late complication that most frequently affects older patients with prolonged disease duration (*4*). Late-onset motor symptoms include postural instability and falls, freezing of gait, speech and swallowing difficulties.

The pathophysiology of PD involves the progressive loss of dopamine-containing neurons of the pars compacta of the substantia nigra leading to denervation of the nigrostriatal tract and significant reduction of dopamine at the striatal level. The consequence of this denervation process is an imbalance in the striato-pallidal and pallido-thalamic output pathways, which is responsible for the major motor deficits (*5*). Genetic predisposing factors in combination with environmental factors are thought to be responsible for the cellular changes leading to progressive neuronal degeneration in which mitochondrial dysfunction, oxidative mechanisms and failure of the protein degradation machinery at the cellular level are probably involved (*6*). The presence of Lewy bodies (cytoplasmic proteinaceous inclusions) in surviving dopaminergic neurons is the pathological hallmark of PD.

DIAGNOSIS

As there are no definitive biological or imaging markers, diagnosis is at present made through the use of stringent clinical criteria such as those developed by the Brain Bank of the Parkinson's Disease Society in the United Kingdom (*7*). These criteria are used worldwide and provide for a definite

diagnosis with a high degree of accuracy. Clinicopathological studies based on brain bank material from Canada and the United Kingdom have shown that clinicians diagnose the disease incorrectly in about 25% of patients. In these studies, the most common reasons for misdiagnosis were presence of essential tremor, vascular parkinsonism and atypical parkinsonian syndromes (*8*).

Although, as previously mentioned, the diagnosis is made exclusively on a clinical basis, there are new diagnostic tools that can be used to confirm the presence of dopaminergic denervation at the striatal level, thus lending support to the clinical diagnosis. These include fluorodopa positron emission tomography (FDOPA-PET) and dopamine transporter imaging with radionucleide tracers by means of single photon emission tomography (DAT-SPECT). Both methods are still used as investigational tools and not for the routine diagnosis of PD.

Most cases of Parkinsonism are attributable to primary Lewy body PD. "Parkinsonism-plus" syndromes (which include progressive supranuclear palsy, multisystem atrophy, corticobasal degeneration) and secondary parkinsonisms (mainly drug induced, flunarizine and cinarizine still being important culprits particularly in Latin American countries where these drugs are misused frequently for the prevention of cerebrovascular disorders) account for a small proportion of cases of parkinsonism seen in clinical practice.

ETIOLOGY AND RISK FACTORS

Current theories on the etiology and pathogenesis of PD consider this disorder to be multifactorial and the result of a genetic predisposition possibly interacting with environmental factors. That genes play a role in the etiology of PD is supported at present by the discovery of at least 11 forms of genetic parkinsonism that share clinical features and possibly pathogenetic mechanisms with the more common, as yet, sporadic form of the disease (*9*). The quest for environmental exogenous triggering factors has remained elusive and supported only through indirect evidence gathered from numerous and extensive epidemiological studies. Age, sex, dietary habits, infections, environmental toxins and trauma are among the factors considered by these studies (*10*).

EPIDEMIOLOGY AND MAGNITUDE

Parkinson's disease is a universal disorder, with a crude incidence rate of 4.5–19 per 100 000 population per year. The wide variation in incidence estimates probably reflects differences in methodology and case ascertainment as well as age distribution of the sample population. Age-adjusted rates provide a more realistic figure and range from 9.7 to 13.8 per 100 000 population per year. As this is a chronic disorder with a prolonged course, prevalence is much higher than incidence. Crude prevalence estimates vary from 18 per 100 000 persons in a population survey in Shanghai, China, to 328 per 100 000 in a door-to-door survey of the Parsi community in Bombay, India. Age-adjusted rates give a more restricted range of 72–258.8 per 100 000 persons. The majority of studies reporting overall crude prevalence (including males and females across the entire age range) fall between 100 and 200 per 100 000 persons (*11*). Differences in prevalence have been suggested to be related to environmental risk factors or differences in the genetic background of the population under study. There is no evidence that any increase in the number of new patients being diagnosed each year has to do with variations in causative factors, but more probably with increased awareness and earlier recognition of the disease. Although the disease usually begins in the fifth or sixth decade of life, recent evidence shows increased incidence with advancing age (*12*). It has long been recognized that a small proportion of patients develop the disease at an early age. Patients presenting with the disease before 40 years of age are generally designated as having "early-onset" PD. Among them, those beginning between 21 and 40 years are called "young-onset" PD while those beginning before the age of 20 years are called "juvenile Parkinsonism". Contributions from the field of genetics have demonstrated that a large proportion

of "young-onset", and "juvenile" cases are of genetic origin, while the majority of the remaining cases are presently considered to be sporadic. Some of the late-onset PD cases are also found to have a genetic component. Although PD has been traditionally considered to affect individuals from both sexes equally, data recently published show a higher proportion of males to be affected by this disorder, with a male to female ratio of 1.9 (*12*).

Global and regional distribution

Parkinson's disease affects individuals globally. Regional figures showing differences in both incidence and prevalence probably reflect the existence of factors that may be demographic (variations in life expectancy across countries), health-care-related (lack of proper and widespread recognition of the disorder, variations in access to health care), genetic, and environmental, together with methodological differences. Examples of regional variations abound, and some of them were commented upon above. In addition, early studies had shown variations in prevalence at the international level attributed to ethnic differences across regions. Higher rates were reported for Caucasians in Europe and North America, intermediate rates for Asians in China and Japan, and the lowest rates for Blacks in Africa. However, more recent studies from Asia do not show significant differences in prevalence compared with studies in Caucasians (*11*).

COURSE AND OUTCOME

Parkinson's disease runs a chronic slowly progressive course, being extremely variable in patients. During the initial years of the disease, motor disability may not be significant as symptoms are usually unilateral and mild. If left untreated, after several years it causes significant motor deterioration with loss of independence and ambulation. As the disease progresses, the increasing motor disability affects the activities of daily living. This is further complicated by the development of motor fluctuations and dyskinesias (owing to long term levodopa therapy) (*13*). The gait disturbances — especially freezing of gait and postural instability — lead to frequent falls, with increased risk of fractures. Dysarthria and hypophonia lead to difficulties in communication, while deglutition disorders increase the risk of aspiration pneumonia. In the later stages of the disease, patients usually need increased assistance for most activities of daily living such as feeding, personal hygiene, dressing, turning in bed, rising from the sitting position and walking (*2, 14*).

Mortality in PD is increased compared with a control population, though figures vary considerably from one study to another. Before the discovery of levodopa as the rational therapy of PD the observed mortality vs expected mortality ratio was approximately 3:1 (*15*). The introduction of levodopa has resulted in significant improvement in quality of life and reduction in mortality. The standardized mortality ratio for the PD group in a recent study was 1.52 compared with the controls (*16*). The cause of this increased mortality is attributable to incidental complications related to motor disability (immobility, prostration, deglutition disorders) and autonomic dysfunction leading to falls, fractures, pneumonia, urinary tract infections, etc. (*17*). With an increase in life expectancy, the disease, at present, runs a more prolonged course. As a result, long-term motor complications, both attributable to the disease and treatment-related, and a host of non-motor manifestations mentioned earlier are seen more frequently and account for significant morbidity (*18*).

BURDEN ON PATIENTS, FAMILIES AND COMMUNITIES

The definition of burden, in the case of PD as in any other chronic disabling disorder, varies according to whether it is analysed from the perspective of the patient, the family, or the community. In the case of the patient, burden carries the meaning of a heavy, worrisome and emotionally disturbing load. For the family, the burden also takes into account the plight of the caregivers: it involves the caregiver's appraisal of the balance between level of care demands, resources available, and quality

of giver–recipient relationship. For the community, burden entails both the impact related to social responsibility as well as economic costs. Some of these aspects are covered below.

The impact of receiving a diagnosis of a disease such as PD causes an initial emotional burden on the patient and family: they face an uncertain future living with a chronic disabling disorder — for which there is no cure and which entails significant social stigmatization. After the initial impact and with proper counselling, the patient learns to cope with the disease. As the effect of medications initially, and for a considerable time, produces significant benefit, there ensues what is usually called a honeymoon period, during which an acceptable state of health is achieved. Most patients carry on with their activities and lead an almost normal life for several years without the need of special assistance if they complement their pharmacological treatment with proper physical activity and psychological support.

With the progression of the disease, there is increasing motor impairment and disability. The patient may lose significant autonomy as the severity of the symptoms increases. Motor fluctuations and dyskinesias are compounding factors that further add to the patient's disability and interfere with everyday life. Moreover, with advanced disease the increased prevalence of gait and balance disorders reduces the capacity for independent ambulation. In this scenario, patients begin to need increasing help in everyday activities, and the burden on the caregivers increases in parallel (*19*). Depending on the individual patient, the degree of dependence may vary. In instances in which the disease runs a benign course, the need for special care and assistance may be limited, while in those with a more aggressive course, they may become totally dependent on external help. Designing and creating a more apt housing environment is therefore a necessary consequence that adds to the burden of the family.

An additional burden for the family is indirectly related to the functional impact of the disease. Progressive motor impairment and disability leads the majority of patients still in their active years to lose their jobs, therefore causing a significant reduction of the total household income.

In an ideal setting, the burden on the community may be reflected in many aspects. This burden may be absorbed by the private sector, nongovernmental organizations and government institutions if they provide the necessary funds and efforts for:

- removal of architectural barriers to provide for easier accessibility;
- public transport with disabled access;
- institutions and programmes that provide comprehensive care for the patients and family (establishment and ongoing support);
- subsidized medication programmes;
- compensation for loss of employment benefits;
- research support.

TREATMENT, MANAGEMENT AND COST

The discovery of the dopaminergic deficit was the major turning point in the development of rational pharmacotherapeutic approaches to PD leading to the introduction of levodopa and later dopamine agonists. With the exception of anticholinergics and amantadine, all other drugs subsequently developed (dopa-decarboxylase inhibitors, monoamine oxidase inhibitors, catechol-O-methyl transferase inhibitors) act indirectly through dopaminergic mechanisms (*1, 19*). Functional surgery, developed many years ago as a palliative approach to the therapy of PD, has more recently become an important therapeutic option (*19, 20*).

There have been newer developments in the field of PD pharmacotherapy in an attempt to intervene at different levels of the biochemical machinery of the basal ganglia beyond the dopamine agonist receptor. Drugs acting at the adenosine, glutamate, adrenergic, and serotonin receptors are at present under scrutiny as potentially beneficial at different stages of the disease (*21*).

Initiation of therapy depends on the age and mental status of the patient and the severity of the disease. In young patients, there is evidence supporting the postponement of more potent medications such as levodopa to prevent early development of motor complications. In older patients, not only the risk of motor complications is less, but the safety profile of levodopa is better within a higher age range. Initially, patients are generally medicated with a single drug but as disease progresses multiple medications may be required (*22*).

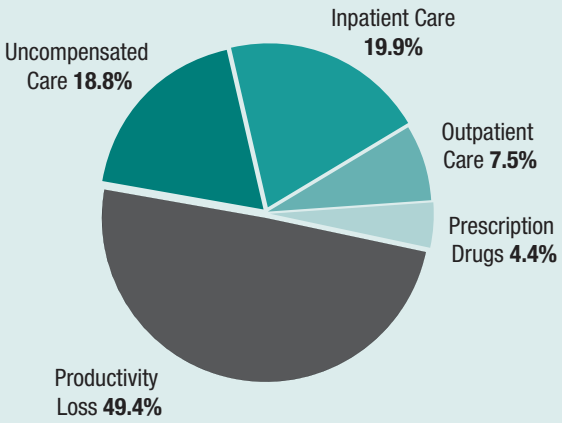
In addition to the primary medications used for symptomatic treatment of the specific motor symptoms of PD, there is also a need for complementary medication to treat the diverse non-motor symptoms (constipation, urinary incontinence, sexual dysfunction, orthostatic hypotension, sleep disorders, psychiatric symptoms such as depression, psychosis and behavioural disorders, and cognitive disturbances) that affect a significant number of patients with PD in the advanced stages.

Functional surgery, both lesional or deep-brain stimulation, also plays an important role in the treatment of the complicated PD patient with drug-refractory disease, as this resource has become increasingly useful in the management of motor complications (motor fluctuations and dyskinesias) (*20*). Three different brain targets for surgery are presently used, depending on the characteristics of the patient.

The comprehensive management of the disease requires, in addition to medical and surgical treatment, the participation of numerous other medical disciplines and health-related professionals, including physical therapist, specialized nurse, occupational therapist, speech and deglutition disorders specialist, psychologist, psychiatrist, urologist and gastroenterologist.

It is also important to deal with the issues related to cost of the disease for the patient, family and society. Unfortunately, available information is limited, and almost restricted to Europe and North America, which makes it difficult to extrapolate it to other regions of the world. It is perhaps better to analyse it in relative terms compared with a control population than to make absolute currency estimates. In a recently published study from the United States, the annual utilization of health services and cost for the PD cohort was significantly higher than for a control population. On an annual basis, PD patients spend approximately two more days in hospital, 43 more days in long-term care institutions, and fill more than 20 more prescriptions than do the controls. The total annual cost is more than double that of the control population, even before adding indirect costs (uncompensated care, productivity loss, etc.). Prescription drugs account for roughly 5% of total costs, followed by outpatient care 7.5%, uncompensated care 19%, and inpatient care 20%, while productivity loss is by far the largest share of the total cost reaching almost 50%. Figure 3.8.1 provides a breakdown of cost distribution in Parkinson's disease according to a study by Huse et al. (*23*).

Figure 3.8.1 Cost distribution in Parkinson's disease



Source: (*23*).

Cost is also relative to accessibility to health delivery and medications, which is quite variable in different regions of the world. An indirect method to estimate cost is to review health spending in absolute terms and relative to the GNP, which will show major differences from one country to another. Of course, different countries have different health priorities, and depending on life expectancy the burden of PD may differ significantly.

PREVENTION

At present there are no proven therapies for prevention of PD (*1*). Although there is evidence of the existence of risk and protective factors, these are not strong enough to warrant specific measures in an attempt to diminish risk or enhance protection.

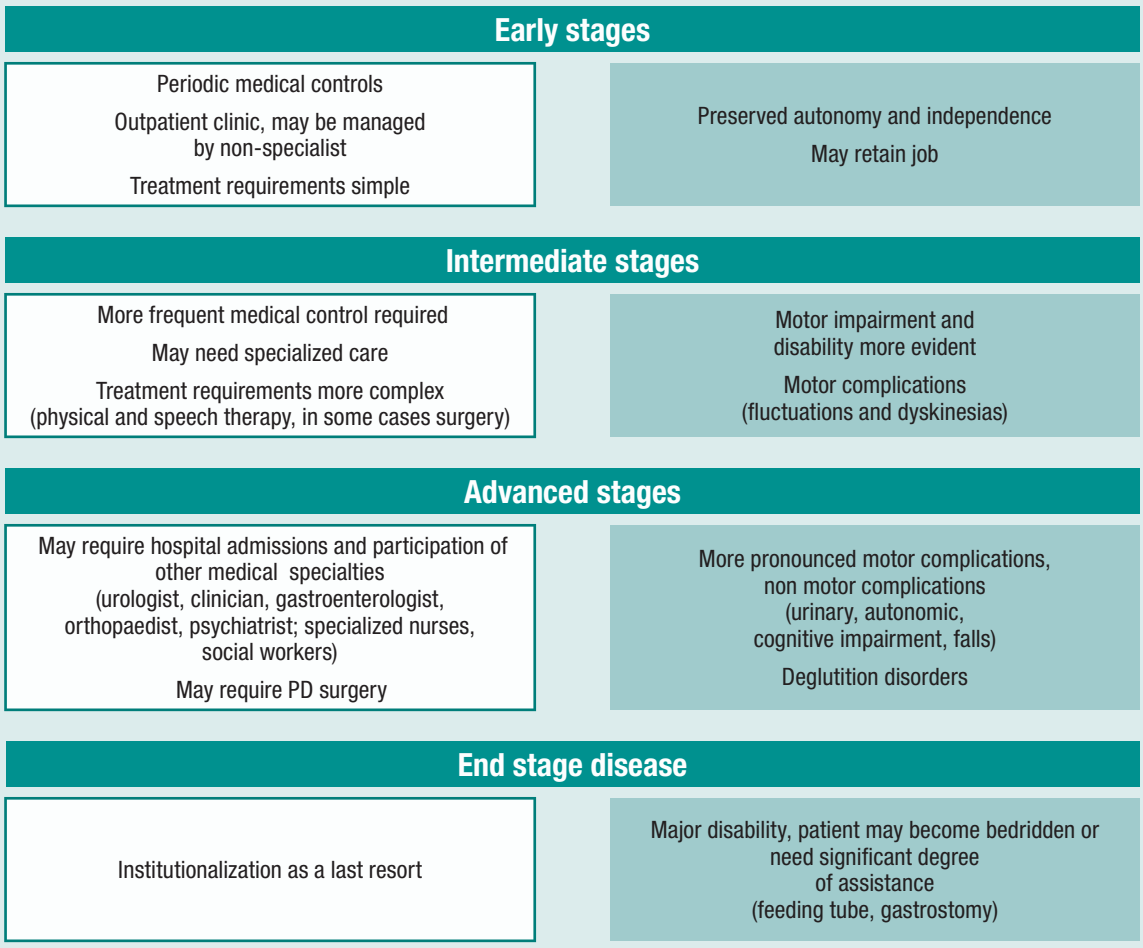
An important part of the present research effort in PD is targeted at understanding the pathogenesis of the disease, in particular the mechanisms involved in cell death. In parallel, drug development programmes, both in the pharmaceutical industry and in non-commercial research laboratories, are engaged in finding neuroprotective and neurorestorative therapies (*21*). If and when these drugs become available, early detection of the disease would be of paramount importance.

INFRASTRUCTURE AND HUMAN RESOURCES

As the disease runs a progressive course going through different stages with changing needs according to each stage, the need for infrastructure and the involvement of human resources varies accordingly. Figure 3.8.2 provides an algorithm on health systems requirement as the disease progresses.

Special mention has to be made of the demand for human resources and infrastructure in the case of patients in whom pharmacological manipulations fail to modify long-term motor complications and who are considered candidates for stereotactic surgery (both lesional or deep-brain stimulation). Although the percentage of patients requiring these procedures is still small, the demand will probably grow until better pharmacological options are available. The cost of these procedures is quite high and the need for specialized personnel, infrastructure, and equipment is significant.

Figure 3.8.2 Progression of Parkinson's disease and health system requirements



DELIVERY OF CARE

Diagnosis and delivery of care for the uncomplicated patient can be performed by the general practitioner or family physician only if they are properly trained in the clinical diagnosis of PD and informed on the critical decisions at initiation of treatment which could affect long-term prognosis. In recent years there has been a shift in different regions of the world, in which PD or movement disorders specialists have become involved with delivery of primary care. This change has taken place for several reasons.

- Initiation of therapy involves crucial therapeutic decisions that may influence the future course of the disease, thus making it necessary for a more experienced physician to make these decisions.
- Awareness and education campaigns have brought PD to the forefront, making the patients more demanding in terms of the quality of medical care they seek.
- The worldwide launching of the Charter for People with Parkinson's Disease in 1997 by the WHO Working Group on Parkinson's Disease (with the support of the European Parkinson's Disease Association), on occasion of the commemoration of World Parkinson's Disease Day. The charter states: "People with PD should have the right to be referred to a doctor with special interest in Parkinson's disease" (*24*).

In the more advanced stages of the disease, it becomes necessary to resort to more specialized care: most patients are referred to a neurologist who can deal more efficiently with the complex issues involved. Depending on the medical customs or organizational aspects of medical care in different countries or regions of the world, consultation with the neurologist is performed at the request of the primary care physician but follow-up rests in the hands of the referring doctor with the occasional assistance of the specialist. In other instances the neurologist, specialized in PD or not, may at this point become the one responsible for the follow-up of the patient.

The complicated PD patient presenting with long term motor complications (fluctuations and/or dyskinesias; gait disturbances, and speech and deglutition disorders; autonomic dysfunction) will need to be referred to specialists working in a centre that has personnel and facilities for special investigation and treatment. It is also necessary at this stage to seek the help of other medical specialties and in some instances admit the patient to hospital, clinic or other health-care institution, either to perform more complex ancillary studies or specialized surgery, or provide for acute inpatient care. According to published data, almost 40% of advanced PD patients (at 15 years into the course of the disease) need to be admitted to long-term care facilities when the need for complex care exceeds the possibilities of the family or primary caregivers at home (*3*).

Treatment gap

There are wide gaps in different aspects of PD care. The first has to do with education and awareness. Knowledge and information about PD is nowhere near as comprehensive as that available for vascular disease or cancer, despite being one of the most frequent neurodegenerative disorders affecting roughly 1% of the population over the age of 65 years. Another very important gap is that related to present limitations of therapy; lack of effective preventive treatments, lack of restorative treatments, and lack of effective therapies to prevent or symptomatically improve long-term complications, both motor and non-motor.

The third aspect has to do with the lack of universal access to the presently available wide range of PD medications, surgery and complementary therapies. This is particularly significant in the poorer or less developed regions of the world, where the lack of properly trained physicians, the high cost of medication and the small number of centres equipped to provide comprehensive management result in inadequate health-care delivery to PD patients.

In WHO's recently published Atlas of Country Resources for Neurological Disorders (*25*), availability of anti-Parkinson drugs in primary care is extremely variable in WHO regions. In the world as a whole, drug availability is only 60.6%, ranging from an extreme of only 12.5% in Africa to 79.1% in Europe. The same is true for rehabilitation, which is an important aspect of the treatment of PD. Worldwide availability of rehabilitation services is of the order of 73.2%, ranging from just 18.8% in Africa to 88.1% in Europe. No less problematic is the lack of neurologists in certain regions; there are 0.03 neurologists per 100 000 population in Africa and 0.07 per 100 000 in South-East Asia as the lowest extremes, compared with 4.84 per 100 000 population in Europe.

Finally, there is a paucity of comprehensive management programmes for PD throughout the world to provide the best standard of care for this disorder. Development of simplified treatment and management guidelines suitable for use in developing countries might be a step forward in closing this treatment gap.

Information on government policy specifically addressing the needs and requirements of PD patients in different regions of the world is scarce. In the majority of cases, wherever information is available, there is no legislation relating to the needs of patients with any type of disability or chronic disorders, including PD. Canada, the European Union and the United States are probably the only countries in the world in which legislation has been passed that consider PD in particular as a medical problem that requires specific policy.

RESEARCH

Research in PD is carried out by different organizations. These include government institutions, government-supported research laboratories at universities and private not-for-profit research facilities, and as part of the research and development programmes of the pharmaceutical industry and private corporations. Even though millions of dollars are invested every year in different areas of research, there are few countries in which significant funds are assigned to research in PD as part of a concerted effort or carefully designed programme with proper supervision and clearly defined goals. Only the European Union and the United States have passed legislation or provided a regulatory framework towards obtaining tangible results in PD within a reasonable time frame.

Multiple areas of research are at present focused on finding the answer to the important questions facing the field of PD. They include research on genetics, pathogenesis, molecular biology and early diagnostic markers (clinical and non-clinical). Therapy is also a main area of research comprising pharmacological therapy as well as non-pharmacological methods (such as surgery, gene therapy, stem cell therapy and trophic factors).

An area of research that has not received proper attention is that related to health systems and service delivery. This subject is crucial in resource-poor countries, where the lack of adequate supervision and guidance in the allocation of funds may cause a distortion — such as being able to provide sophisticated surgical procedures to a minority of PD patients while more than 80% of them are unable to receive the more basic pharmacological agents.

TRAINING

The core medical curricula in most medical schools throughout the world dedicate little time to providing information on PD and the complexities of its treatment and management. Where available, residency training programmes in neurology provide their trainees with more thorough information and training in this regard. In some parts of the world there are PD and movement disorders post-residency fellowships that allow for the development of more comprehensive education in this neurology subspecialty. In their scientific programmes, most local, regional and international neurology meetings have topics related to PD.

Unfortunately the training of health-care professionals towards a more effective health-care delivery for PD patients in resource-poor countries is lacking and constitutes a major challenge. These countries are the ones having the greatest need for trained professionals. Efforts should be made to establish training programmes in these regions to provide for at least:

- proper diagnostic skills for the primary care physician;
- rational use of available pharmacological treatments;
- training of nurses and carers in the complex management issues affecting the long-term complicated PD patient;
- increasing the availability of trained professionals in the areas of physical rehabilitation, speech and deglutition therapy.

PARTNERSHIPS WITHIN AND BEYOND THE HEALTH SYSTEM

Fortunately, the number of nongovernmental organizations, advocacy groups and private foundations with a special interest in PD has grown considerably throughout the world. In the majority of cases these organizations, working together or independently of the health and education systems, provide for training of personnel, disseminate information and organize awareness campaigns for the general population, exert influence on policy-makers and help in the design of specific policy. In addition, many of them fill the gaps wherever and whenever government health organizations fail to respond to the needs of PD patients and their families, providing funds for research and establishing outpatient clinics, rehabilitation centres, long-term care facilities, etc.

CONCLUSIONS AND RECOMMENDATIONS	
1	Diagnosis of PD can be made without the aid of costly resources if clinical criteria are adequately applied.
2	Effective management of PD in its early and intermediate stages can be achieved if available drugs are rationally used.
3	Major challenges from the medical point of view are: a. increasingly complex pharmacological or even surgical requirements in the complicated patient; b. need for a multidisciplinary team approach for the comprehensive management of advanced cases with both motor and non-motor complications.
4	Major challenges from the health system delivery perspective include: a. need for more properly trained professionals (primary care physicians, neurologists, and PD-specialized neurologists, nurses, physiotherapists and speech therapists); b. need for widespread access to current PD medications; c. adequate allocation of resources to establish comprehensive management programmes for PD patients.

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3.9 Stroke

Stroke is one of the main noncommunicable diseases of public health importance. After coronary heart disease and cancer, stroke is the most common cause of death in most industrialized countries. In general terms, stroke is a sudden neurological deficit owing to localized brain ischaemia or haemorrhage. Most strokes are attributed to focal occlusion of the cerebral blood vessel (ischaemic stroke) and the remainder are the result of rupture of a blood vessel (haemorrhagic stroke).

WHO defines stroke as the clinical syndrome of rapid onset of focal (or global, as in subarachnoid haemorrhage) cerebral deficit, lasting more than 24 hours (unless interrupted by surgery or death), with no apparent cause other than a vascular one (*1*). In developed countries up to 75–80% of strokes are attributed to brain ischaemia, while 10–15% of strokes represent primary intracerebral haemorrhage (ICH) and approximately 5–10% are subarachnoid haemorrhage (SAH).

DIAGNOSIS AND CLASSIFICATION

Acute stroke is a medical emergency, and the clinician must diagnose stroke properly and quickly. The diagnosis of stroke is made reasonably accurately on clinical grounds alone by specialists; however, in general medical and emergency-department settings up to 20% of patients with suspected stroke may be misdiagnosed, which indicates that infarction cannot be reliably distinguished from haemorrhage without brain imaging.

In the diagnosis of *haemorrhagic stroke*, computerized tomography (CT) is the most reliable method of demonstrating acute haemorrhage within the first week after stroke onset. Generally, a non-enhanced scan is all that is required. In the diagnosis of ischaemic stroke, CT may or may not show a definite infarct, but a normal scan does not necessarily mean that the patient has not had a stroke. The proportion of visible infarcts also depends on the timing of scanning. Within the first few hours, few infarcts can be seen. It should be noted that less than 50% of infarcts never become visible on CT, especially in patients with milder strokes. In such cases diffusion-weighted magnetic resonance imaging (MRI) would be a preferable method of investigation. In developing countries, patients may not give a clear clinical history, and neuroimaging techniques (CT and MRI) are not widely available, which frequently leads to imprecise diagnosis (*2*).

Subsequently, major advances in the diagnosis have been made with the development of perfusion CT, CT angiography, diffusion-weighted MRI (which permits sensitive imaging of cerebral ischaemia already very early after onset), perfusion MR, MR angiography. Positron emission tomography (PET) and single-photon emission computerized tomography (SPECT) are important research tools to help in better understanding of the intimate pathogenetic aspects of brain ischaemia.

For classification and clinical differentiation of ischaemic stroke subtypes, Oxfordshire Community Stroke Project classification is frequently used. The ICH subtypes are mainly classified and characterized by the means of topographical patterns, namely localization of intracerebral haematomas (clots) in the brain.

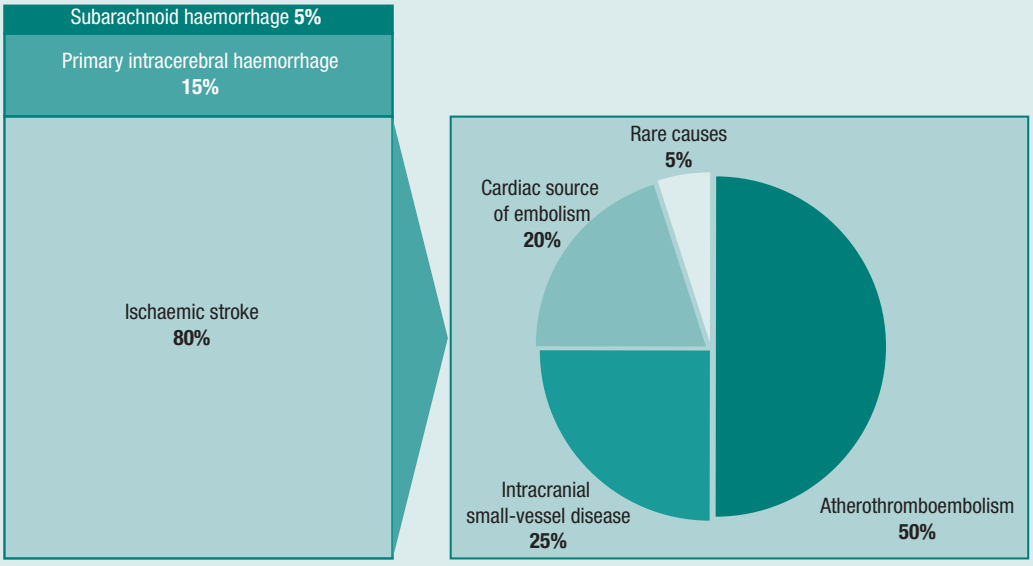
RISK FACTORS AND PREVENTION STRATEGIES

In Caucasians, about 50% of all ischaemic strokes and transient ischaemic attacks (TIAs) are probably attributable to atherothrombotic disease of the extracranial or (less commonly) large intracranial arteries; about 20% of all ischaemic strokes arise from emboli from the heart; about 25% are so-called lacunar infarcts, probably caused by occlusion of one of the small, deep, perforating cerebral arteries; and the remainder are due to a miscellany of much rarer causes (see Figure 3.9.1). In Asian and Afro-Caribbean populations, intracranial small-vessel disease appears to be more common than in Caucasian populations.

Intracerebral haemorrhage occurs as a result of bleeding from an arterial source directly into brain substance. Because hypertension is one of its main causative factors, arterial changes associated with it have been commonly implicated in its pathogenesis. As to SAH, the leading cause — accounting for approximately 80% of cases — is rupture of an intracranial saccular aneurism.

Most conventional vascular risk factors — age, tobacco smoking, diabetes and obesity — are broadly similar for ischaemic stroke and for vascular disease in other parts of the arterial tree. The continuous relationship between stroke and blood pressure, however, is stronger than that for ischaemic heart disease. In contrast to coronary heart disease, initial studies found no overall association between plasma cholesterol concentration and stroke. Several more recent studies have found that plasma lipids and lipoproteins affect the risk of ischaemic stroke, but the exact relationships are still being clarified. Low high-density lipoprotein (HDL) is a risk factor for ischaemic stroke in men, but more data are needed to determine its effect in women (*4*). Potential sources of embolism from the heart are associated with an increased risk of stroke. Atrial fibrillation is by far the most important because it is so common, carries a high relative risk of stroke, and is definitely a causal factor in many cases. Recent years have seen an increasing interest and recognition of new risk factors for vascular disease, including stroke. Most are thought to operate by accelerating atherosclerosis.

Figure 3.9.1 Causes of ischaemic stroke



Source: (*3*).

They include infections, inflammatory and rheological markers, plasma homocysteine concentration and various genetic polymorphisms (*3*). For ICH, age, male sex, low cholesterol, hypertension and excessive alcohol intake were associated with the disease, while only hypertension, smoking and excessive alcohol intake showed their significance as risk factors for SAH.

The importance of any risk factor on a population basis will depend upon both its relative risk and the prevalence of that risk factor in the population. For stroke, five classic risk factors are of main interest in a population perspective: hypertension, smoking, physical inactivity, diabetes and atrial fibrillation. Taken together, these five risk factors account for more than two thirds of all stroke. For hypertension, smoking and atrial fibrillations, studies have convincingly shown that interventions substantially reduce the risk, whereas scientific support for the effect of interventions of physical inactivity and diabetes is weaker.

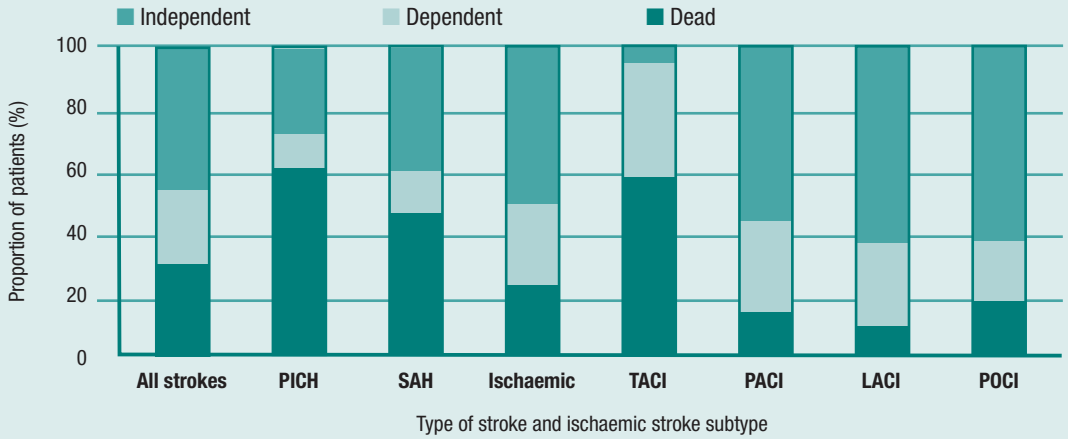
Current knowledge on stroke risk factors clearly indicates that there is a potential to reduce the incidence of stroke considerably: stroke is largely preventable. It remains a challenge, however, to implement effective preventive programmes in the population. One of the success stories has been in Japan, where government-led health education campaigns and increased treatment of high blood pressure have reduced blood pressure levels in the populations: stroke rates have fallen by more than 70% (*5*).

It is also very important that a strategy of comprehensive cardiovascular risk management is followed, rather than treating risk factors in isolation. To make assessment and management of cardiovascular risk feasible and affordable in low and medium resource settings, WHO has developed a CVD risk management package (*6*), see Chapter 1.

COURSE AND OUTCOME

Early death after stroke is generally due to the complications of the brain lesion. Later the complications of dependency (e.g. pulmonary embolism and infection) are a more likely cause. About 30% of patients die within a year of a stroke. Recovery after stroke occurs through several overlapping processes. In the first hours and days these processes may include resolution of the ischaemia, cerebral oedema, and comorbidities (e.g. infection) that exacerbate the functional effects of the stroke itself. Later, neural plasticity by which neurons take on new functions, the acquisition of new skills through training (e.g. physiotherapy and occupational therapy), and modification of the patient's environment lead to further gains in function. Of stroke survivors, nearly half are left dependent. The outcome depends on the pathological type of stroke and the subtype of ischaemic stroke (see Figure 3.9.2) (*3*).

Figure 3.9.2 Outcome patterns in different stroke subtypes



Source: (*3*).

PICH=primary intracerebral haemorrhage; SAH=subarachnoid haemorrhage; TACI=total anterior circulation infarct; PACI=partial anterior circulation infarct; LACI=lacunar infarct; POCI=posterior circulation infarct.

The past few years have changed perception of the prognosis after stroke and TIA. Several studies have shown that the imminent risk of recurrence after TIA or minor stroke is much higher than previously thought, emphasizing the importance that all patients with suspected TIA or stroke are urgently admitted to hospital, adequately diagnosed and appropriately treated. Furthermore, neuroimaging studies have shown that clinically "silent" (but most probably not innocuous) new ischaemic events are at least as common as symptomatic ones. In the long term, the prognosis for recurrence is also grave: after 10 years more than half of patients will experience at least one ischaemic event, indicating a need for better and durable secondary preventive measures and systems for follow-up.

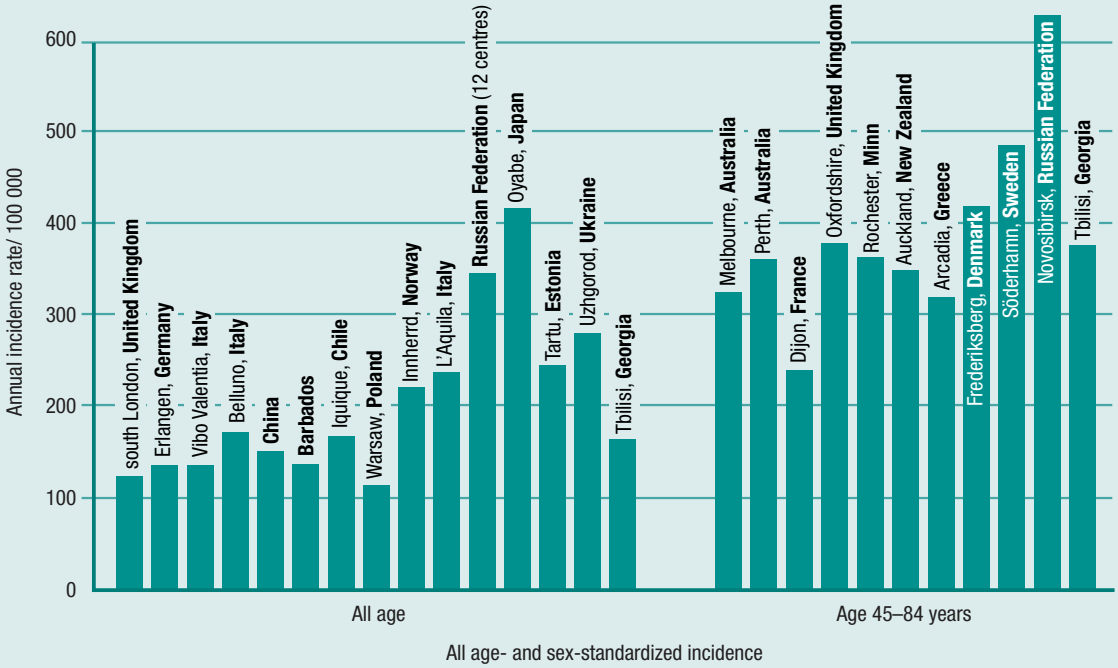
Vascular cognitive impairment and dementia are also common after stroke and at least as frequent as recurrent ischaemic events in a longer perspective. Its development depends on the volume of tissue affected either by infarction and haemorrhage or by their localization. The prevalence of post-stroke dementia in stroke survivors is about 30%, and the incidence of new onset dementia after stroke increases from 7% after one year to 48% after 25 years. Having a stroke doubles the risk of dementia.

EPIDEMIOLOGY AND MAGNITUDE

Stroke prevalence

The best measure of the total burden of stroke in any population is the prevalence, which provides information about the number of people at any one time in that population who have survived a stroke; however, reliable estimates of stroke prevalence are difficult to obtain. The prevalence of stroke among white populations ranges from 500 to 600 per 100 000. Reported rates per 100 000 in New Zealand are 793 crude, 991 men and 700 women; in Finland 1030 men and 580 women; and in France 1445 crude rate in elderly population. Rates per 100 000 from developing countries are also variable and range from 58 in India and 76 in the United Republic of Tanzania to 620 in China and 690 in Thailand. A recent comprehensive review of nine studies of stroke prevalence carried out after 1990 shows far less geographical variation (5–10 per 1000), with the exception

Figure 3.9.3 Stroke incidence in selected countries



of populations in rural Bolivia, in which the prevalence of stroke was as low as 1.7 per 1000, and Papua New Guinea, where no strokes were detected at all (*7*). The study in Bolivia, however, included only patients with stroke-related disability, and the one in Papua New Guinea screened only 213 patients over 20 years of age (the refusal rate in the older age group was 63%). The small variation in age-specific and age-standardized prevalence of stroke across the populations is consistent with the geographical similarity in stroke incidence and case-fatality.

It is uncertain whether the lower prevalence in some developing countries is related to low incidence rates or high mortality rates. It is anticipated that, with time, these populations will have a larger proportion of elderly people, life expectancies will lengthen, disease patterns will shift to patterns in developed countries, and the number of strokes will rise.

Stroke incidence and case-fatality

The first population-based data about stroke incidence in developing countries (India, Nigeria and Sri Lanka) were obtained by WHO in 1971–1974 and showed moderate variations in incidence rates between different parts of the world. A higher prevalence of hypertension but a lower prevalence of diabetes in stroke patients in developing countries compared with developed countries was also reported. In the late 1980s, the WHO Monitoring Trends and Determinants in Cardiovascular Disease (MONICA) stroke project showed relatively large geographical differences in stroke incidence and case-fatality rates, with the rates in less developed countries among the highest in the world (confined to patients 35–64 years old) (*8, 9*). The most recent data, taking into account only so-called "ideal" population-based studies of stroke incidence, show persistent geographical variations (see Figure 3.9.3).

The high incidence of stroke in eastern European countries can be attributed to well-known social and economic changes that have occurred over the past decade, including changes in medical care, access to vascular prevention strategies among those at high risk, and exposure to risk factors such as poor diet and high rates of smoking and alcohol consumption. The marked difference in stroke incidence between genetically similar areas (eastern and western Europe) suggests that potentially modifiable environmental factors are more important than genetic differences in determining stroke susceptibility.

Stroke incidence has shown little or no change over the last 10–20 years in most areas, perhaps owing to unchanged blood pressure levels and unsuccessful hypertension detection and management in the general population. More recently, however, a study from Oxfordshire, United Kingdom, showed that the age-specific incidence of major stroke had declined by over 40% in the last 20 years, while the incidence of minor stroke was similar (*10*), indirectly pointing to the possibility of substantial change being brought about in the rate of stroke by means of primary preventive strategies.

As to the frequency of different stroke subtypes, in some developing countries (Chile, China and Georgia) there is a tendency for haemorrhagic stroke to appear more frequently than ischaemic stroke (see Figure 3.9.4). This may be attributed to the high prevalence of hypertension in these countries as well as genetic, environmental and sociocultural factors.

Case-fatality of total strokes varies little between populations and mostly falls in the range of 20–30%, with the exception of Italy (33%), Georgia (35%) and the Russian Federation (35%) showing higher rates (*7*).

In almost all countries the stroke incidence increases with age, with highest rates in the age group of $\geq$ 85 years (*7*). As to distribution by sex, stroke is slightly more frequent in men than in women.

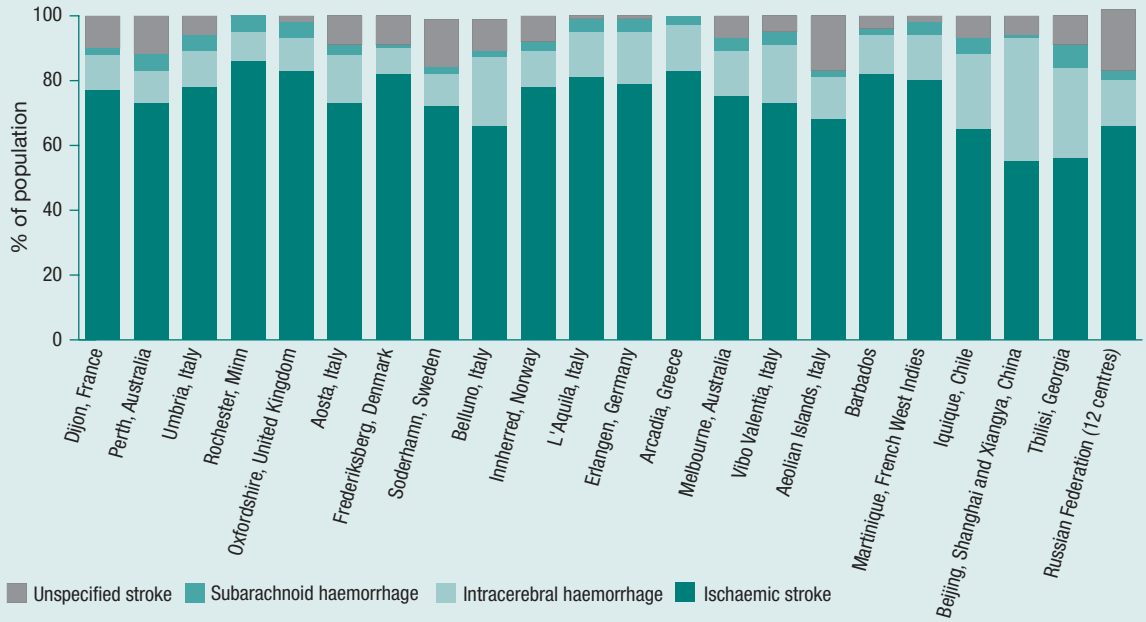
MORTALITY, DISABILITY AND BURDEN

According to the most recent estimates, stroke is the second most common cause of mortality worldwide and the third most common in more developed countries (*9, 11*). Each year, stroke causes about 5.54 million deaths worldwide, with two thirds of these deaths occurring in less developed countries (*12*). Stroke mortality varies widely among countries for which routine death-certificate data are available. In the early 1990s, it was lowest — and had been declining steeply — in Australia, western Europe, Japan and the United States; however, it was two or three times higher in South America. Mortality was up to ten times higher — and increasing — in eastern Europe and the countries of the former Soviet Union. Routine mortality data are, however, limited by the inaccuracies of death certificates and the lack of reliable information about different pathological types of stroke (*13*). Furthermore, mortality depends on both the incidence of stroke and case-fatality and can give no information about strokes that are disabling but not fatal. Without urgent action, deaths from stroke will increase over the next decade by 12% globally and 20% in resource-poor countries (*12*).

Stroke is a major cause of long-term disability. About half of the patients surviving for three months after their stroke will be alive five years later, and one third will survive for 10 years. Approximately 60% of survivors are expected to recover independence with self-care, and 75% are expected to walk independently. It is estimated that 20% will require institutional care. The remainder will need assistance either by family, a close personal friend, or paid attendant. It is noteworthy that psychosocial disabilities (such as difficulties in socialization and vocational functions) are more common than physical disabilities (such as problems with mobility or activities of daily living).

As a major cause of long-term disability, stroke has potentially enormous emotional and socioeconomic impact on patients, their families, and health services. It causes a loss of 49 million disability-adjusted life years (DALYs) worldwide each year (*12*). Lifetime costs per patient are estimated at between US$ 59 800 and US$ 230 000. In the United Kingdom, the cost burden of stroke is estimated to be nearly twice that of coronary heart disease, accounting for about 6% of the total national health and social service expenditure. It is estimated that 41% of all costs for stroke are direct costs and 26% are indirect costs, whereas no less than 34% of expenditure corresponds to informal care. By the year 2020, stroke and coronary artery disease together are expected to be the leading causes of lost healthy life years worldwide. Even these bleak figures do not capture the full burden of stroke: more than a third of people who survive a stroke will have

Figure 3.9.4 Proportional frequency of stroke subtypes in different populations



severe disability. By 2015, over 50 million healthy life years will be lost to stroke, with 90% of this burden in low income and middle income countries (*14*).

TREATMENT, MANAGEMENT AND REHABILITATION

The past decade has witnessed a dramatic change in treatment of acute stroke, leaving the era of an indifferent approach firmly behind. Equally as important as the development of particular emergency treatments, however, is the recognition that the organization of stroke services per se plays a key role in the provision of effective therapies and in improving the overall outcome after stroke.

An important advance in stroke management is the advent and development of specialized stroke services (stroke units) in the majority of developed countries. These services are organized as specialized hospital units focusing exclusively on stroke treatment. Evidence favours all strokes to be treated in stroke units regardless of the age of the patient and the severity and subtype of the stroke. Evidence from randomized trials shows that treatment in stroke units is very effective, especially when compared with treatment in general medical wards, geriatric wards or any other kind of hospital department in which no beds or specialized staff are exclusively dedicated to stroke care. The Stroke Unit Trialist's Collaboration (*15*) has shown that stroke units reduce early fatality (death within 12 weeks) by 28% and death by the end of one year follow-up by 17% (relative risk reduction). Stroke units also decrease disability and result in more discharges to home, rather than having patients institutionalized. In most European countries, the elements of comprehensive stroke unit care outlined by the Stroke Unit Trialists' Collaboration have been adopted, and include assessment and monitoring, physiological management, early mobilization, skilled nursing care, and short-term multidisciplinary team rehabilitation services. Despite proven efficacy and cost–effectiveness, stroke unit care remains underused in almost all parts of the world.

Ischaemic stroke is caused by interruption of the blood supply to a localized area of the brain. This results in cessation of oxygen and glucose supply to the brain with subsequent breakdown of the metabolic processes in the affected territory. The process of infarction may take several hours to complete, creating a time window during which it may be possible to facilitate restoration of blood supply to the ischaemic area and interrupt or reverse the process. Achieving this has been shown to minimize subsequent neurological deficit, disability and secondary complications. Therefore the acute ischaemic stroke should be regarded as a treatable condition that requires urgent attention in the therapeutic window when the hypoxic tissue is still salvageable (*16*). Recent advances in management of ischaemic stroke imply implementation of thrombolytic therapy that restores circulation in zones of critical ischaemia thus allowing minimizing, or even reversing, the neurological deficit. Thrombolysis is effective for strokes caused by acute cerebral ischaemia when given within three hours of symptom onset. Intravenous thrombolysis has been approved by regulatory agencies in many parts of the world and has been established or is in the build-up phase in many areas. The therapy is associated with a small but definitive increase in the risk of haemorrhagic intracerebral complications, which emphasize the need for careful patient selection. Currently less than 5% of all patients with stroke are treated with thrombolysis in most areas where the therapy has been implemented. One half to two thirds of all patients with stroke cannot even be considered for intravenous thrombolytic therapy within a three-hour window because of patient delays in seeking emergency care. Changing the patients' behaviour in the event of acute suspected stroke remains a major challenge. Several studies are currently ongoing on the possibility to extend the current criteria for thrombolysis to larger patient groups including beyond the three-hour window.

In cases of acute stroke, aspirin is given as soon as CT or MRI has excluded intracranial haemorrhage. Immediate aspirin treatment slightly lowers the risk of early recurrent stroke and

increases the chances of survival free of disability: about one fewer patient dies or is left dependent per 100 treated. However, because aspirin is applicable to so many stroke patients, it has the potential to have a substantial public health effect. Aspirin is also likely to reduce the risk of venous thromboembolism.

Heparins or heparinoids lower the risk of arterial and venous thromboembolism, but these benefits are offset by a similar-sized risk of symptomatic intracranial haemorrhage, and such therapy is therefore not generally recommended. For patients at high risk of deep venous thrombosis, low-dose subcutaneous heparin or graded compression stockings are currently being evaluated in clinical trials.

A recent trial did not confirm superiority of surgical treatment over non-surgical management in cases of ICH, though appropriately selected patients with acute, spontaneous ICH may benefit from urgent removal of the clot, particularly in the cerebellum. Selection criteria and choice of surgical procedure vary widely between centres.

Several advances are noted with endovascular treatment of intracranial aneurisms by detachable coils. Recent evidence suggests that endovascular intervention is at least as effective as open surgery, with fewer complications.

Costs of acute stroke treatments

Although limited, the evidence suggests that the cost of organized care in a stroke unit is not any greater than that of care in a conventional general medical ward. Stroke-unit care is therefore likely to be highly cost effective, given that it has an absolute treatment effect similar to that for thrombolysis but is appropriate for so many more acute stroke patients. Although aspirin has only a very modest effect, it is very cost effective (about US$ 58 to prevent one death or dependent stroke survivor) because it is widely applicable and accessible, inexpensive and relatively safe. Thrombolysis is less cost effective, but an accurate analysis requires considerably more data than available (*17*).

Acute stroke management in resource-poor countries

In almost all developed countries, the vast majority of patients with acute stroke are admitted to hospital. By contrast, in the developing world hospital admission is much less frequent and depends mainly on the severity of the stroke — the more severe, the better the chance of being hospitalized. Thus hospital data on stroke admission are usually biased towards the more serious or complicated cases. Home and traditional treatment of stroke is still accepted practice in the most resource-poor countries (*2*).

The aims in the general management of acute stroke are good nursing care, maintenance of pulmonary and cardiovascular functions, fluid, electrolyte and nutritional balance, avoidance of systemic complications, and early rehabilitation, as well as specific stroke treatment (e.g. thrombolysis). All these goals are rarely reached in developing countries, because expert stroke teams and stroke units are rarely available, so patients are unlikely to be treated urgently. The patients are usually cared for by a general practitioner, with only a minority of patients being under the care of a neurologist. Treatment for acute stroke in developing countries is generally symptomatic; thrombolytic and neuroprotective drugs are the exception rather than the rule. Many drugs are delivered by the intravenous route, thus preventing patients from early mobilization. Antiplatelet agents are not used in a systemic manner, and anticoagulants in atrial fibrillation are usually under-prescribed because of poor compliance and the need for frequent monitoring of blood coagulation. Removal of cerebral haematomas and extensive craniotomy for brain decompression are the main neurosurgical procedures for stroke patients in some parts of the developing world; endarterectomy is rarely used though there are few specific data available.

Rehabilitation

Stroke survivors frequently suffer from neurological impairments, functional deficits and handicap. Stroke rehabilitation is the restoration of patients to their previous physical, mental and social capability. Rehabilitation may have an effect upon each level of expression of stroke-related neurological dysfunction. It is of extreme importance to start rehabilitation as soon as possible after stroke onset. In stroke units, in cases of severe stroke with decreased level of consciousness, passive rehabilitation is started and active rehabilitation is initiated in patients with preserved consciousness.

Several organizational models of stroke rehabilitation exist. Rehabilitation is typically started in hospital and followed by short-term rehabilitation in the same unit (comprehensive stroke units), rehabilitation clinics or outpatient settings. A multidisciplinary team approach and involvement and support to carers are key features also in the long term. Several studies have shown that different types of rehabilitation services improve outcome, but less is known about the optimum intensity and duration of specific interventions. The scientific basis for rehabilitation and neural repair has increased considerably, and reorganization of activation patterns in the brain after injury may be monitored by functional imaging studies (PET, functional MRI).

Because of a lack of modern rehabilitation equipment and organization of services in the resource-poor countries, proper and prompt rehabilitation (both passive and active) are often deficient in the majority of developing countries.

SECONDARY PREVENTION

Almost a third of all strokes occur in patients who have previously had a stroke, and about 15% of all strokes are preceded by TIAs. Recurrent cerebrovascular events thus contribute substantially to the global burden of the disease. Recently, an encouraging amount of new information has emerged to modify clinical practice in secondary prevention of ischaemic stroke and TIA.

Lowering of blood pressure has been known for years to reduce the risk of first stroke. The recent trials show that the same applies for secondary stroke prevention, whether ischaemic or haemorrhagic. The relative risk reduction of about a quarter is associated with a decrease in blood pressure of 9 mm Hg systolic and 4 mm Hg diastolic.

Although higher plasma cholesterol concentrations do not seem to be associated with increased stroke risk, it has been suggested that lowering the concentration may decrease the risk. The risk of stroke or myocardial infarction, and the need for vascular procedures, is also reduced by a decrease in cholesterol concentration but it is still debated whether statins are effective in stroke prevention. Aspirin, given to TIA/ischaemic stroke patients, reduces the relative risk of stroke and other important vascular events by about 13%. Compared with aspirin, clopidogrel reduces the risk of stroke and other important vascular events from about 6.0% (aspirin) to 5.4% (clopidogrel) per year. The combination of aspirin and modified-release dipyridamole may also be more effective than aspirin alone.

Long-term oral anticoagulants for TIA/ischaemic stroke patients in atrial fibrillation reduce the annual risk of stroke from 12% to 4%. Anticoagulation may be indicated for about 20% of patients with TIA/ischaemic stroke who have high-risk sources of embolism from the heart to the brain, mostly atrial fibrillation.

Stroke risk ipsilateral to a recently symptomatic carotid stenosis increases with degree of stenosis, and is highest soon after the presenting event. Carotid endarterectomy reduces the risk of stroke substantially in such patients. The recent evidence suggests that the benefit from surgery is also greater in men, patients aged $\geq$75 years, and those randomized and operated upon within two weeks after their last ischaemic event.

Carotid artery stenting is less invasive than carotid endarterectomy but has only been compared with endarterectomy in a few small randomized controlled trials with inconclusive results. Several large studies comparing the two treatments are currently ongoing.

The undoubted effectiveness of medical and surgical interventions must not detract from lifestyle modification, which should provide additional benefits and at lower cost — though with more effort by the patient. In spite of a lack of formal randomized evidence, ceasing to smoke, increasing physical activity, lowering body weight and eating a diet rich in potassium seem to be effective measures to prevent stroke.

All these measures are less achievable in developing countries where there is also a lack of knowledge and information regarding stroke prevention strategies, including lifestyle modification (*18*). Antiplatelet agents are not used systematically and anticoagulants are usually under-prescribed mainly because of difficulties with monitoring. The high-technology preventive measures indicated above are not accessible in the poorest countries. WHO has developed evidence-based recommendations for policy-makers and health professionals for prevention of recurrent heart attacks and strokes in low and middle income populations (*19*).

DELIVERY OF CARE

Developed countries are able to provide accessible health-care services to their people but, even in these countries, services are far from optimal. In developing countries, however, cultural beliefs and failure to recognize stroke symptoms may have an impact on the number of patients seeking medical attention, and those who do come may present after complications have developed. In the United States, approximately 60% of stroke patients present within three hours of stroke onset, while in Europe 40–56% arrive at hospital within six hours. In Turkey, only 40% of stroke patients are seen in the hospital within 12 hours (*2*).

Economic policies of developing countries may not allow large investments in health care, hospitals, brain scanners or rehabilitation facilities. Health care in the acute phase of stroke is the most costly component of the care of stroke patients; in low-resource countries hospital care of even a small proportion of all patients with stroke accounts for a disproportionately high share of total hospital costs. Stroke units, which have been shown to reduce mortality, morbidity and other unfavourable outcomes without necessarily increasing health costs, are available in very few developing countries.

Costs of consultation, investigation, hospitalization and medication may be beyond the means of poor people, especially those who do not have welfare benefits or medical insurance plans. This seriously hampers the provision of care to patients who are otherwise able to seek medical attention.

Although hospital care represents a large proportion of the costs of stroke, institutional care also contributes significantly to overall stroke care costs. Most developing countries do not have well-established facilities for institutional care. The bulk of long-term care of the stroke patient is likely to fall on community services and on family members, who are often ill equipped to handle such issues. There is thus a need for appropriate resource planning and resource allocation to help families cope with a stroke-impaired survivor.

Priorities for stroke care in the developing world

Governments and health planners in developing countries tend to underestimate the importance of stroke. To compound this difficulty, 80% of the population in developing countries live in rural areas, a factor that limits access to specialized services. In these parts of the world, top priority for resource allocation for stroke services should go to primary prevention of stroke, and in particular to the detection and management of hypertension, discouragement of smoking, diabetes control and other lifestyle issues. To achieve this task, stroke prevention awareness must be

raised among health-care planners and governments. Another priority is education of the general public and health-care providers about the preventable nature of stroke, as well as about warning symptoms of the disease and the need for a rapid response. Furthermore, allocation of resources for implementation and delivery of stroke services (e.g. stroke units and stroke teams) should also be a priority. Finally, it is very important to establish key national institutions and organizations that would promote training and education of health professionals and dissemination of stroke-relevant information.

PARTNERSHIPS WITHIN AND BEYOND THE HEALTH SYSTEM

Despite the enormous and growing burden of stroke, the disease does not receive the attention it deserves — including funds for prevention, management and research. In the context of an integrated approach to chronic disease, a Global Stroke Initiative has been formed involving WHO, the International Stroke Society and the World Federation of Neurology. The primary focus of this international collaboration will be to harness the necessary resources for implementing existing knowledge and strategies, especially in the middle and low income countries. The purpose of this strategy is threefold: to increase awareness of stroke; to generate surveillance data on stroke; and to use such data to guide improved strategies for prevention and management of stroke (*20*).

Each of these components is necessary to reduce the global stroke burden. The Global Stroke Initiative is only possible through a strong interaction between governments, national health authorities and society, including two major international nongovernmental organizations.

Increasing awareness and advocacy among policy-makers, health-care providers and the general public of the effect of stroke on society, health-care systems, individuals and families is fundamental to improving stroke prevention and management. Advocacy and awareness are also essential for the development of sustainable and effective responses at local, district and national levels. Policy-makers need to be informed of the major public health and economic threats posed by stroke as well as the availability of cost-effective approaches to both primary and secondary prevention of stroke. Health professionals require appropriate knowledge and skills for evidence-based prevention, acute care and rehabilitation of stroke. Relevant information needs to be provided to the public about the potential for modifying personal risk of strokes, the warning signs of impending strokes, and the need to seek medical advice in a timely manner.

RESEARCH

Stroke research is grossly underfunded even in developed countries (*21*). One of the major problems of stroke epidemiology is the lack of good-quality epidemiological studies in developing countries, where most strokes occur and resources are limited. To address the problem of accurate and comparable data in these countries, an approach to increase the quality of the data collected for stroke surveillance has recently been proposed by WHO. This flexible and sustainable system includes three steps: standard data acquisition (recording of hospital admission rates for stroke), expanded population coverage (calculation of mortality rates by the use of death certificates or verbal autopsy), and comprehensive population-based studies (reports of nonfatal events to calculate incidence and case-fatality). These steps could provide vital basic epidemiological estimates of the burden of stroke in many countries around the world (*20*).

CONCLUSIONS AND RECOMMENDATIONS	
1	Stroke is the second leading cause of mortality worldwide and the major cause of long-term disability in adults.
2	Further increase of stroke mortality is expected, with the majority of deaths from stroke to occur in less developed countries.
3	By 2015, over 50 million healthy life years will be lost from stroke, with 90% of this burden in low and middle income countries.
4	In developed countries, up to 80% of strokes represent ischaemic stroke, while the remaining 20% are attributed to either intracerebral or subarachnoid haemorrhage. In some developing countries the proportion of haemorrhagic strokes is higher.
5	Non-contrast computerized tomography is a reliable diagnostic tool allowing proper differentiation between ischaemic and haemorrhagic stroke and excluding other causes of brain damage.
6	Advent of thrombolytic therapy together with development of stroke units leads to a reduction of mortality and disability caused by stroke.
7	Immediate aspirin treatment of ischaemic stroke is beneficial in terms of reducing early stroke recurrence and increasing disability-free survival.
8	Effective measures to prevent stroke are lifestyle modification (smoking cessation, increased physical activity and the lowering of body weight), control of hypertension and blood sugar, lowering of plasma cholesterol, carotid endarterectomy in selected cases, and long-term antiplatelet or anticoagulant treatment.
9	There is a gap between developed and developing countries in terms of stroke prevention, diagnosis, treatment and rehabilitation caused by the lack of trained specialists and expertise, lack of equipment, inadequate diagnostic evaluation and insufficient funds in resource-poor countries.
10	Stroke research and training are grossly underfunded.

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3.10 Traumatic brain injuries

Traumatic brain injury is the leading cause of death and disability in children and young adults around the world and is involved in nearly half of all trauma deaths. Many years of productive life are lost, and many people have to suffer years of disability after brain injury. In addition, it engenders great economic costs for individuals, families and society. Many lives can be saved and years of disability spared through better prevention.

More and better epidemiological data can help in tailoring effective preventive measures against traumatic brain injury (TBI), with particular emphasis on reducing the impact of road traffic accidents. The world is facing a silent epidemic of road traffic accidents in the developing countries: by 2020, road traffic crashes will have moved from ninth to third place in the world ranking of the burden of disease and will be in second place in developing countries. A lot can be done to reduce the devastating consequences of TBIs.

Systematic triage of patients can lead to important economic savings and better use of scant hospital resources. More standardized pre-hospital and in-hospital care, to minimize secondary brain injury, can improve outcomes substantially.

DEFINITION AND OUTCOME

If the head is hit by an external mechanical force, the brain will be displaced inside the skull and can be injured against the solid meningeal membrane, the dura, or against the inside of the neurocranium. Acceleration and deceleration forces may disrupt the nervous tissue and blood vessels of the brain. All grades of injury can occur, ranging from no visible abnormality of the brain in cases of mild TBI to superficial bruising (contusion), and, in severe cases, dramatic swelling (oedema) as well as large collections of blood (haematomas).

Initial classification of TBI is based mostly upon the clinical examination which is carried out by the physician in the hospital's accident and emergency department. Around 90% of TBIs are classified as "mild", implying that the patient is awake but may have had a loss of consciousness and/or a short amnesia. Only 3–5% are "severe" TBIs, meaning that the patient is unconscious upon admission.

Outcome of TBI, in terms of mortality rates and disability, is related to:

- pre-injury status: age, health and psychosocial function;
- initial clinical grade immediately after injury, reflecting the primary brain damage;

- acute management: pre-hospital and in-hospital;
- complications and secondary brain damage that may develop within minutes of the impact;
- rehabilitation.

In mild TBI, the mortality rate is below 1%, while 20–50% die after suffering a severe TBI. The intermediate category, "moderate" head injury, implies a mortality rate of 2–5%. Disability is a common problem after hospitalization for TBI, even after a mild event (*1*).

DIAGNOSIS AND CLASSIFICATION

The diagnosis of TBI can be obvious in cases where a blow to the head is reported and when superficial wounds can be identified. But some cases are less clear-cut, and TBI may be present without any superficial signs of a head injury.

Further classification of the brain injury is made in order to evaluate prognosis, identify patients at risk for deterioration and choose appropriate observation and treatment. As shown in Table 3.10.1, the Glasgow Coma Scale (GCS) uses a points system to evaluate the best ocular, verbal and motor responses. A normal healthy person will obtain a GCS score (adding up the eye opening score, the verbal score and the motor score) of 15. Someone who opens his eyes only after painful stimulation, utters only incomprehensible sounds and withdraws his hand only after pinching will be given a score of 8. This scale permits the following classification of TBI after clinical examination:

- mild head injury (GCS 13–15);
- moderate head injury (GCS 9–12);
- severe head injury (GCS 3–8).

Table 3.10.1 Glasgow Coma Scale to evaluate brain injury

Points awarded	Eye opening	Verbal response	Motor response
1	None	None	None
2	To pain	Sounds (incomprehensible)	Extends
3	To speech	Words (inappropriate)	Abnormal flexion
4	Spontaneous	Confused	Withdraws
5		Orientated	Localizes pain
6			Obeys commands

Triage

Classification into these categories based on clinical assessment alone must be supported by the results of a computerized tomography (CT) examination in many cases, or a skull X-ray if a CT scanner is not available. A fracture detected on the skull X-ray images indicates an increased risk of deterioration, and the patient will need admission. A CT scan reveals a skull fracture more clearly than an ordinary X-ray examination will do. In addition, it visualizes the bleeding, bruising and swelling of actual brain injury: CT signs of brain damage are present in one third of the mild cases, two thirds of the moderate cases and all the severe cases (*2–4*).

EPIDEMIOLOGY AND BURDEN

There are many scientific reports on TBI, but in view of methodological shortcomings the epidemiological data are not easily comparable (*5*). In spite of these reservations, it can be interesting and informative to compile data from different parts of the world.

Incidence

In Tagliaferri's European study, the TBI incidence rate collected from 23 reports with epidemiological data was found to vary greatly between countries (*5*). Some of the differences could be ascribed to variations in study years, inclusion criteria and research methods. Most rates were in the range 150–300 per 100 000 population per year. The estimated European incidence of TBI was 235 per 100 000 per year, including all hospitalized patients with head injury and those dying of a head injury prior to admission. Admission policies, particularly in cases of mild TBI, will, of course, influence the incidence rates markedly. Therefore, incidence rates such as 546 per 100 000 per year in Sweden and 91 per 100 000 per year in Spain must be interpreted with caution.

Data from many parts of the world consistently show a peak incidence rate in children, young adults and elderly people. Males are injured 2–3 times as often as women.

Prevalence

Prevalence of TBI measures the total number of injuries at a point in time or in a period interval; the calculation should include all those with TBI sequelae such as impairments, disabilities, handicaps or complaints, plus all the newly diagnosed cases at the defined time or time interval.

Estimates from the United States indicate that 1–2% of the population, i.e. around five million people, live with a TBI disability (*6–7*). Many disabled people have neurobehavioural problems. It is therefore no exaggeration to describe TBI disability as an enormous public health problem (*6*).

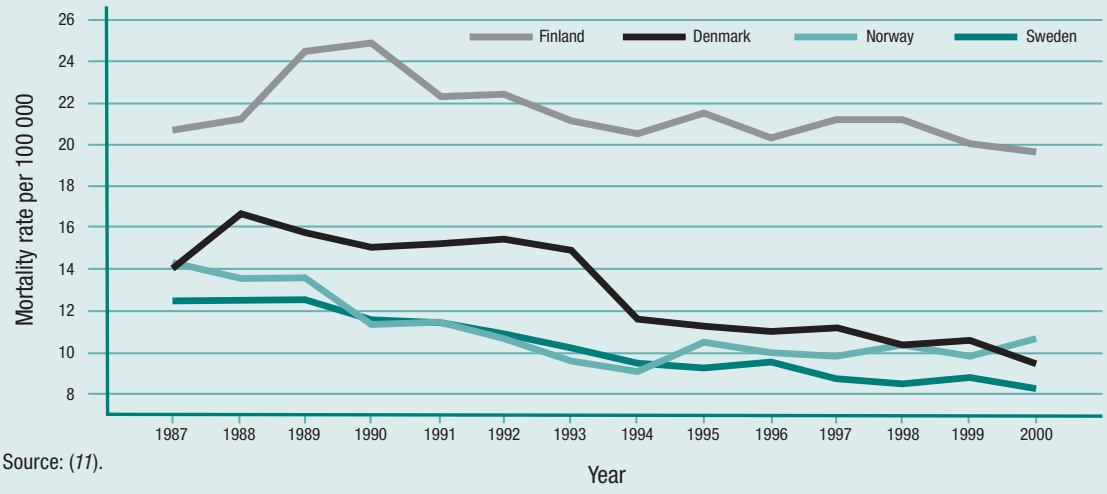
Information on how sequelae develop (diminish or increase) over time is scarce (*8*); better data on prevalence would certainly be useful for improved planning of rehabilitation needs.

Mortality

Case-fatality rate in different parts of the world. The average European pre-hospital case-fatality rate was 8%, while the in-hospital rate was 3%, i.e. a total rate of 11 deaths per 100 cases of TBI, all grades of severity included. The in-hospital rate varies from 2.4 in Australia to 6.2 in the United States and 11 in China, Province of Taiwan (*5*). Admission policies may influence these rates. About one third of the hospitalized patients dying after TBI had talked at some time after the injury: this is an indication that some of them might have been saved (*9*).

Mortality rate per 100 000 population per year is more informative than the case-fatality rate. The average European rate was estimated to be 15 TBI-associated deaths per 100 000 population per year (*5*). The rate is around 10 in Scandinavia, 20 in India, 30 in the United States, 38 in China, Province of Taiwan, 81 in South Africa and 120 in Colombia (*10*). In three of the four Nordic

Figure 3.10.1 Mortality rates associated with traumatic brain injury, Nordic countries, 1987–2000



Source: (*11*).

countries, the TBI mortality rate decreased considerably between 1987 and 2000, as shown in Figure 3.10.1. The decrease is explained by a marked reduction in serious road traffic accidents. It has been suggested that heavy alcohol abuse may explain the persistent and high mortality rate in Finland (*11*).

Disability

Traumatic brain injury is the leading cause of disability in people under 40 years of age. Disability can be classified in a simple fashion using the Glasgow Outcome Scale (see Table 3.10.2):

Table 3.10.2 Glasgow Outcome Scale (GOS)

Classification (GOS level)	Description
Dead	
Persistent vegetative state	Awake but not aware
Severely disabled	Conscious but dependent
Moderately disabled	Independent but disabled
Good recovery	May have minor sequelae

Source: (*10*).

Thornhill and colleagues have recently estimated the annual incidence of disability after TBI (moderate and severe disability together) to be approximately 100 per 100 000 population per year. Their findings revealed a higher incidence than indicated in previous reports, particularly in patients with mild TBI (*1*). Most patients (90%) had sustained a mild head injury, while a few had suffered moderate (5%) or severe (3%) brain injury. Half of the survivors were disabled after mild or moderate TBI, while three quarters of survivors were disabled after a severe injury. Even among young patients with mild injuries and a good pre-injury status, one third failed to achieve a good recovery.

Moderate disability after TBI is 3–4 times more common than severe disability. Severe disability after TBI is reported in 15–20 per 100 000 population per year (*8*). Mostly, patients with severe disability will have a combined mental and physical handicap.

The rarest form of disability after TBI is the vegetative state. It may be transitory, subsiding after a month or so, but may persist in many cases. The persistently vegetative patient needs artificial nutrition and hydration and will have a markedly reduced life span, i.e. 2–5 years. In some cases, complicated ethical and legal discussions arise about the purpose of continuing life-sustaining treatment.

Disability after moderate or severe TBI may take various forms:

- Mental sequelae with personality change, memory disorders, reduced reasoning power and apathy (*9*). A defective recent memory may be particularly incapacitating.
- Disturbed motor function of arm or leg.
- Speech disturbances.
- Epilepsy, which may develop years after the primary injury, is seen in 1–5% of patients.

Recovery

Some patients continue to recover for years after a TBI, but 90% reach their definitive GOS level after six months (*9*).

Elderly patients with TBI are known to have a slower rate of functional recovery, longer stays in rehabilitation and greater levels of disability with comparable injuries.

ETIOLOGY AND RISK FACTORS

The three main causes of TBI are road traffic accidents (RTAs), falls and violence. Their relative importance varies from region to region, see Figure 3.10.2. The graph shows that exposure to hazards varies considerably between regions (*5*). These variations must be taken into account by health planners who design prevention programmes.

Road traffic accidents

As the leading cause of head injury in the world, RTAs account for 40–50% of the cases hospitalized for TBI. The impact of RTAs is even higher in children and young adults with TBI, in cases of moderate or severe TBI and in patients with multiple injuries. Every day about 3000 people die and 30 000 people are seriously injured on the world's roads, nearly half of them with head injuries. Most of the victims are from the low income or middle income countries, with pedestrians, cyclists and bus passengers bearing most of the burden (*12*). Fatality rates among children are six times greater in developing countries than in high income countries.

There has been a steady decrease in RTAs in many industrialized countries during the last two decades, while the problem is increasing in developing countries (*4*). Terms such as "a public health crisis" and "a neglected epidemic" have been used to describe this growing problem (*13*).

Falls and violence

Falls are second in frequency to RTAs, as shown in Figure 3.10.2, and occur more frequently in Australia, India and northern Europe (*5*). In Pakistan, falls from the roof are a common cause of head injury, and account for more than 10% of the injuries in a large neurosurgical series of relatively serious TBIs (*14*).

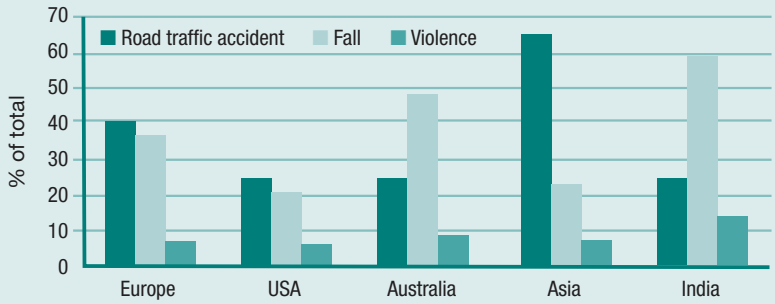
People 70 years or older have a relatively high incidence of head injuries, and in these patients falls are the most common cause. Many factors contribute to the increased risk for falls in elderly people: gait impairment, dizziness, previous stroke, cognitive impairment, postural hypotension, poor visual acuity and multiple medication.

Interpersonal violence is involved in 2–15% of cases (*5*). Most TBIs are the result of blunt trauma, but in some countries there is a high percentage of penetrating injuries, e.g. in the United States where gunshot wounds are the major cause and account for 40% of all head injury deaths, while 34% are secondary to RTAs (*15,16*).

Many factors increase the risk of sustaining a TBI:

- Alcohol and drugs: alcohol is an important contributing factor in TBI from all causes in more than one third of cases (*5*).
- Poverty: living in a low income neighbourhood increases the risk of TBI in children as well as in adults (*17,18*).
- Comorbidity: seizures and being elderly and handicapped aggravate the risk of TBI.

Figure 3.10.2 External causes of traumatic brain injury in selected areas



Note: Variations must be interpreted with caution since case definitions and classification schemes have not been standardized.
Source: (*5*).

ACUTE MANAGEMENT OF TRAUMATIC BRAIN INJURY

Treatment of mild head injuries

Many of the mild cases can be classified as "minor head injuries". These patients can be dismissed after a short clinical examination and adequate information, since their risk of further problems will be very low, i.e. <0.1%. Before dismissal, they deserve brief information, preferably written, about:

- warning signs indicating possible complications;
- how normal and mild symptoms are expected to develop;
- how to resume normal daily activities.

The remaining patients with mild TBI have a 1–6% risk of deterioration (*19*). Therefore, a closer examination may be required to identify the individuals with the highest risk of developing complications. Patients who need special attention are those with:

- decreasing level of consciousness;
- neurological deficit;
- epileptic seizure;
- deficient blood coagulation;
- age >60 years;
- alcohol abuse.

Patients at risk will need a CT examination and/or admission.

- Observation should be maintained for 12–24 hours with repeated examinations to detect a decreasing level of consciousness.
- A CT scan gives excellent information about fractures and brain damage:
- CT scanning of patients with mild TBI has been found very cost effective in Sweden, where scanners are available and manpower in hospitals is expensive (*20*).
- A skull X-ray should be performed if a CT scanner is not available. A fracture will indicate a higher risk of deterioration and admission is necessary for a short time of observation.

The clinical examination, a CT scan and, in some cases, observation in a hospital ward will identify the very few patients in this group requiring treatment by a qualified neurosurgeon.

Treatment of moderate and severe injuries

Patients with moderate or severe TBI represent less than 10% of all the traumatic head injuries. In this category of TBIs, adequate health care can make a difference and substantially improve outcomes. Airway obstruction and falling blood pressure are the acute threats to the vulnerable brain-injured patient. Pre-hospital care with skilled paramedics, early arrival at the scene of the accident, prompt stabilization of the patient's condition in accordance with ABC guidelines, and rapid evacuation reduced overall TBI mortality by 24% in two years in San Diego (*6, 21*).

Well-organized and updated hospital inpatient treatment is equally important. On admission, life-supporting measures should be continued, in accordance with Advanced Trauma Life Support recommendations (*22*). Simultaneously, a rapid diagnostic overview must be carried out: many patients, particularly in RTA cases, will have concomitant injuries of the chest, abdomen, spine or extremities.

In the United Kingdom, the mortality in patients with epidural haematoma declined progressively from 28% to 8% after the introduction of national guidelines for the early management of head injury (*22*). The guidelines clearly indicate how patients at risk should be identified and managed before progressive brain damage occurs.

A study from the United States in patients with severe TBI showed improved outcomes after implementation of evidence-based treatment guidelines. At the same time, reduced hospital costs

were obtained through shortened length of stay, from an average of 21.2 days to an average of 15.8 days (*7*).

Research that focused on identifying the ideal conditions for the extremely vulnerable brain in severe TBIs has resulted in two different approaches in neurointensive care, the Lund model and the perfusion concept. Although they are different in many ways, both have led to improved outcomes in patients with severe TBI (*23*).

REHABILITATION AFTER TRAUMATIC BRAIN INJURY

Although disability after mild TBI may have been underestimated, most patients will make a good recovery with provision of appropriate information and without requiring additional specific interventions (*24, 25*).

Patients with moderate to severe TBI should be routinely followed up to assess their need for rehabilitation. There is strong evidence of benefit from formal interventions, particularly more intensive programmes beginning when the patients are still in the acute ward. The balance between intensity and cost–effectiveness has yet to be determined (*24, 25*).

The importance of rehabilitation is consistently underestimated, not least because of its cost. It is a regrettable truth that this part of the treatment lacks the drama of the primary treatment and is consequently more difficult to fund. It is nonetheless of great importance since TBI damages young lives for whom rehabilitation is as important for the regaining of function as primary treatment is for the saving of life.

Examples of rehabilitation services are shown in Box 3.10.1 and Box 3.10.2.

Neuropsychologists evaluate orientation, attention, intellect, memory, language, visual perception, judgement, personality, mood and executive functions of the patients with TBI. An example of a TBI patient with neuropsychological sequelae is given in Box 3.10.2.

Box 3.10.1 Traumatic brain injury rehabilitation services in Costa Rica

Since 1974, rehabilitation services following TBIs are provided in Costa Rica at the National Rehabilitation Centre (CENARE), San José, which is part of the national health services. This Centre receives patients from all over the country; it is classified as a tertiary care hospital and offers highly specialized medical care to the population on an inpatient and outpatient basis. The neurotrauma unit in the Centre has a 16-bed capacity, and serves an annual average of 50 people through an interdisciplinary team consisting of two physicians (specialized in medical rehabilitation), a head nurse, an occupational therapist, a physical therapist, a psychologist and a social worker. Every week the team makes rounds to the inpatients and meets six outpatients in order to assess them throughout the subacute process of their rehabilitation; active participation of the families is encouraged at all stages of the rehabilitation process. The team counts on the help of a staff respiratory and speech therapist.

The patient population is composed of patients who were over 12 years of age at the moment of the lesion and who sustained severe traumatic head injuries, as well as patients with non-traumatic brain damage. The following services are offered.

Low-level rehabilitation for comatose and slow-to-recover patients, who are referred as soon as their medical condition is stable. They receive structured stimulation, in the form of physical and occupational therapy. Nutritional and feeding requirements are evaluated and installed. Families receive psychological support and advice, orientation in attention protocol, and advice in areas such as feeding, nursing care, positioning, and prevention and care of pressure ulcers. Home visits are scheduled in order to offer advice on eliminating architectural barriers and to give training to family members in their own environment.

Full rehabilitation. Once patients have recovered complete consciousness, cognitive sequelae are evaluated and treated and physical sequelae are further evaluated and treated. Both can be done as inpatients or outpatients, depending on the distance between the Centre and the patient's place of residence. A formal, structured cognitive retraining programme will be implemented in the near future. Patients and their families are supported throughout their subacute and chronic phases of recovery by all team members, and services are offered when needed in an open manner as well as through structured appointments.

COSTS

Any information that is available about the economic consequences of TBI is mostly related to costs of hospitalization, which probably constitute only a relatively small part of the total costs. According to Berg and colleagues (*10*), TBI-associated costs can be subdivided as follows:

- direct costs: hospitalization, outpatient care, rehabilitation;
- indirect costs: lost productivity, in particular after moderate or severe injuries;
- intangible costs to patients, families and friends: related to death or reduced quality of life.

PREVENTION AND EDUCATION

Prevention of road traffic accidents

Road traffic accidents are the major cause of TBIs on a global scale. Although their mortality rates have decreased substantially in many industrialized countries during the past two decades, there is increasing concern about a rising epidemic of RTA injuries in developing countries. By 2020, it is estimated that road traffic crashes will have moved from ninth to third place in the world ranking of the burden of disease and will be in second place in developing countries. To quote an article in the *British Medical Journal*: "… sleepiness among drivers may account for nearly a fifth of road traffic crashes. Similarly, if the international public health community continues to sleep through the global road trauma pandemic it will be accountable for many millions of avoidable deaths and injuries" (*12*).

The frequency and severity of RTAs are related to the following factors:

- The number of cars and motorcycles.
- The design and condition of motor vehicles:
  - use of seat belts lowers risk;
  - functioning brakes and adequate tyres lower the risk of RTAs.
- The quality and design of the road:
  - shared road use by motor vehicles and unprotected road users increases the risk of injury;
  - speed cameras are effective in lowering the risk;
  - speed reduction through road design effectively reduces the risk.

Box 3.10.2 Rehabilitation after traumatic brain injury: a case-study

Vera is a 34-year-old administrator who was head of personnel in a government training office for many years. She sustained a severe head injury in 1999, which did not produce any physical limitation but severely affected her memory and, to a lesser extent, speech. After evaluation it was evident that Vera had important intellectual limitations. She was given memory compensation techniques to use at home and at work, and it was suggested she relocate to a less demanding position. Vera refused to change her job; she asked the team not to visit her superiors and tried in vain to maintain her position at work without letting anybody know her condition. After some months she eventually resigned from her job, very depressed because her staff no longer trusted her and had lost respect for her authority — she constantly made mistakes, could not remember what she had asked for days before, etc. Vera decided to enrol in some of the training courses her office offered to the public, but she failed again and again. Her former subordinates made fun of her failure, which depressed her further. When last seen, Vera was receiving treatment for severe depression, but insisted she wanted to recuperate and could recover her former capacities and employment.

Comment: The consequences of TBI — in the form of memory impairment (as in Vera's case), attention problems, mild to severe intellectual deficiency, lack of concentration and limited ability to learn — can result in impossibility to return to work, affect emotional stability, and limit performance at work and at home. All of these problems will affect the person's emotional status, as well as his or her family and friends. It can also mean social isolation in the long term, further aggravating depression.

- Road safety laws and traffic conditions:
  - poor enforcement of traffic safety regulations increases risk;
  - helmets dramatically reduce the risk of TBI in motorcyclists and cyclists (63–88% reduction of TBI risk in cyclists; 50% reduction of fatalities from motorcycles in the United States from 1982 to 1992);
  - speed is a major killer (5% of pedestrians will die if hit by a car at 32 km/h, while 85% will die if hit at 64 km/h (*26*));
  - alcohol increases the risk of RTA for drivers, pedestrians and cyclists;
  - discouraging the use of cars and heavy vehicles in cities will lower risk;
  - safe public transport incurs fewer deaths per km than travel by private car;
  - dedicated urban spaces for walking and cycling will reduce risk.
- Population density.
- The education of all road users and the general public about safe driving and transport.

A locally relevant evidence base is an urgent requirement for prevention of RTAs. Public health authorities need to acquire more knowledge about the epidemiology of RTAs and the main local causes, especially when injuries are fatal. They should also know that road traffic injuries are preventable and that some measures are very effective. With reliable data about the epidemiology of the "war on the roads", a sense of urgency can be established among policy-makers and effective preventive measures can be designed that are tailored to local traffic conditions and take account of regional data on external causes and risk factors (*12*).

Structural measures have proven to be the most efficient approaches in the prevention of RTAs. Examples are physical measures to separate motor vehicles from pedestrians, speed bumps, speed cameras, strict speed limits and alcohol check-ups.

Educational programmes may be a useful supplement in adults, but there is no evidence that education of pedestrians reduces the risk of motor vehicle collisions involving children on foot (*12*).

Community-based activities (such as American Association of Neurological Surgeons "Think first" and "Group at risk" designed programmes), as well as interaction with motor vehicle companies, are important elements in prevention programmes. Realities in both developed and developing countries must be taken into account to make sure the programmes will be acceptable and efficient.

Prevention of brain injuries from other causes

Prevention of TBIs from falls, violence, sports, work-related accidents, etc. must also be based on a thorough knowledge of regional epidemiology, causes and risk factors. In some countries, for example the United States, the use of firearms accounts for the majority of deaths attributed to TBI. Improved medical treatment would not have much impact in such cases, since most gunshot wounds to the head are fatal. There is a need for more efficient prevention, starting with specific legislation to regulate the use of firearms (*16*).

Education

Educational activities should comprise age-oriented educational programmes including personal computer games, medical and paramedical training in neurotrauma, development of an Advanced Life Support in Brain Injury® (ALSBI), and multimedia educational campaigns on safety of motor vehicles. The creation of foundations for the relatives of victims of injuries or associations for education and the prevention of TBI should be strengthened.

The ALSBI® course objectives could be summarized as follows:

- educate pre-hospital and emergency service physicians in the care of acute neurological patients;

- promote the "time is brain" concept by emphasizing the importance of the initial management of TBI, stroke and other brain disorders;
- avoid secondary neurological damage;
- improve survival and quality of life of head-injured victims;
- spread this knowledge all over the world.

INFRASTRUCTURE AND HUMAN RESOURCES FOR CARE

Taking care of patients with TBI does not differ from any other trauma care. In fact, a large proportion of moderately or severely head-injured patients will have concomitant injuries of the spine, chest, abdomen or extremities.

In densely populated areas of developed countries a complete trauma centre includes:

- a fully staffed and equipped emergencies and admissions unit;
- easy access to radiology services, including an technologically advanced all-body CT scanner;
- operating theatre;
- intensive care unit;
- anesthesiologists, trauma surgeons, neurosurgeons and specialized nurses available 24 hours a day, seven days a week.

In remote areas and in developing countries the situation may be different.

RESEARCH

Research in the field of TBI should cover the following subjects:

- Epidemiology, with particular emphasis on more standardized measures, to allow comparisons between regions and a valid evaluation of care and prevention.
- The management of TBI patients with pre-hospital care, in-hospital care and rehabilitation. Such studies should range from logistics, quality of life studies, pathophysiology, etc. to evaluation of various aspects of multidisciplinary rehabilitation.

CONCLUSIONS AND RECOMMENDATIONS	
1	Research in epidemiology and management has led to better prevention and treatment in some parts of the world during the past two or three decades. Health policy-makers, doctors, nurses and paramedics should be proud of their achievements and join forces to organize a worldwide fight against the silent and neglected epidemic of traumatic brain injury.
2	There is an urgent need for the development of global and national policies in order to minimize the risks and the consequences of road traffic accidents, particularly in the developing countries. This should be a joint effort between different government agencies, medical societies, motor vehicle manufacturers and nongovernmental organizations.
3	Policies to improve the outcome of TBIs and strengthen road traffic safety must aim primarily at improving the research-based knowledge of regional epidemiology, preventive programmes and the acute management of TBI in pre-hospital and inpatient settings.
4	Prevention will have a greater impact if based upon robust data on causes and risk factors involved in TBI and upon knowledge of the efficiency of the various preventive measures.

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CHAPTER 4

conclusions and recommendations

in this chapter

The relationship between neurology and public health has not been adequately explored to date. This report provides considerable detail about the increasing global public health importance of various common neurological disorders. Public health interventions that may be applied in an attempt to reduce their occurrence and consequences have been considered. A clear message emerges: unless immediate action is taken globally, the neurological burden is expected to become an even more serious and unmanageable threat to public health.

This final chapter highlights a number of overall patterns and themes that cut across the neurological disorders discussed in the previous chapters. It reiterates what is known about neurological disorders and makes the case for a public health approach; it then considers what can be done and provides a set of recommendations for decision-makers and health-care providers.

EVIDENCE ON WHICH TO BASE A PUBLIC HEALTH FRAMEWORK FOR NEUROLOGICAL DISORDERS

The burden is already high and is increasing further

Neurological disorders and their sequelae are currently estimated to affect as many as a billion people worldwide. These disorders are found among all age groups and in all geographical regions. Increased life expectancy and reduced fertility have resulted in a demographical transition from predominantly youthful populations to older and ageing ones, causing increases in the neurological disorders such as Alzheimer and other dementias and Parkinson's disease. As a consequence, many low income countries face the double burden of a continuing high level of infections — including some that result in neurological disorders (e.g. HIV and malaria) — and increases in noncommunicable diseases. The number of people with neurological disorders is estimated to increase considerably in years to come. It is forecast that the number of people affected by dementia (already counted in tens of millions) will double every 20 years. While predictions point to higher risk among poor people, children, adolescents and elderly persons, no population group is immune to neurological disorders.

Because most of the neurological disorders result in long-term disability and many have an early age of onset, measures of prevalence and mortality

vastly understate the disability they cause. Pain is a significant symptom in several neurological disorders and adds significantly to emotional suffering and disability. Even burden estimates combining mortality and disability do not take into account the suffering and social and economic losses affecting patients, their families and the community. The socioeconomic demands of care, treatment and rehabilitation put a strain on entire families, seriously diminishing their productivity and quality of life.

A study conducted in Europe estimated that the annual economic cost of neurological diseases (dementia, epilepsy, migraine and other headaches, multiple sclerosis, Parkinson's disease and stroke) amounted to € 139 billion (approximately US$ 180 billion) in 2004. This study only partially included direct non-medical costs (e.g. community care and informal care) and indirect costs and omitted intangible costs. The results also demonstrated that the cost of dementia increases by 25% when informal care is included and the cost of multiple sclerosis increases by at least 50% when intangible costs are included. In the same study, the annual cost of traumatic brain injuries was estimated as € 3 billion; this figure is, however, a gross underestimate as it was based only on hospitalization attributable to trauma and omitted rehabilitation and lost workdays and production, which are substantially higher. Unfortunately, no equivalent estimates are available for developing countries.

Stigma and discrimination are associated with most of these disorders

The stigma often associated with neurological disorders adds to the social and economic burden. One of the most damaging results of stigmatization is that affected individuals or those responsible for their care may not seek treatment, hoping to avoid the negative social consequences of diagnosis. Indeed, in some communities, the stigma leads to the denial of basic human rights. Stigma aggravates the vicious cycle of illness and social negative reaction and leads to social exclusion and discrimination.

Epilepsy, one of the most common neurological conditions, is well understood and accepted in many societies. Yet in many others, particularly in developing countries, epilepsy is considered contagious or the sign of a curse or possession, with blame for the condition attached to the family as well as to the patient. The direct and indirect discriminatory behaviour and factual choices by others cause substantial reduction in societal opportunities such as education, marriage or work, or may result in being excluded from community activities. Fortunately, stigma and its negative effect on quality of life can be substantially reduced by better seizure control, highlighting the need for effective treatment.

Cost-effective interventions are available

For many of the neurological disorders there are inexpensive but effective interventions that could be applied on a large scale through primary care. Phenobarbital for the treatment of epilepsy is one such cost-effective intervention: up to 70% of people with epilepsy could become seizure free with antiepileptic drug treatment, but the proportion who remain untreated at any given time is greater than 80% in most low income countries. This massive treatment gap is attributable to a paucity of epilepsy services, trained personnel and antiepileptic drugs.

Aspirin is by far the most cost-effective intervention both for treating acute stroke and for preventing a recurrence. It is easily available in developing countries, even in rural areas. Nevertheless, the coverage of the affected population with this inexpensive treatment is still extremely low.

Many neurological disorders can be prevented and treated

One of the important actions required by the health sector is an immunization programme for the prevention of neuroinfections, such as poliomyelitis, and the neurological consequences of infections (e.g. *Hemophilus influenzae* type B (Hib)). Meningitis caused by Hib has been nearly eliminated in the industrialized world since routine vaccination with the *H. influenzae* type B con-

jugate vaccine was initiated. BCG vaccination does not prevent transmission of tuberculosis but is still recommended because of its high protective efficacy against serious forms of the disease in children (73% for meningitis and 77% for miliary tuberculosis).

A number of strategies implemented at policy level by governments through legislation, tax or financial incentives can reduce risks to health. For example, in the area of road safety, a significant number of people might not choose to drive safely or to use seatbelts or motorcycle helmets, but government action can encourage them to do so, thereby preventing injuries to themselves and to other people. This would also result in prevention of other disorders secondary to trauma such as epilepsy.

Control of cardiovascular diseases including stroke can be handled through a comprehensive approach taking account of a variety of interrelated risk factors including blood pressure, cholesterol, smoking, body mass index, low levels of physical activity, diet and diabetes. A comprehensive national strategy thus combining prevention, community-based health promotion and access to treatment can substantially decrease the burden associated with cardiovascular diseases, including stroke.

Disability consequent to neurological disorders can be decreased by rehabilitation programmes and policies. For example, building ramps and other facilities to improve access by disabled people falls beyond the purview of the health sector but is nevertheless very important for comprehensive management of people with disability.

Resources are inadequate and inequitably distributed

Despite the huge burden they cause, neurological conditions are largely absent from the international health agenda. Moreover, country health plans frequently do not cover neurological disorders at the same level as other illnesses, creating significant economic difficulties for patients and their families. In all but the least developed countries of the world, poor people are much more likely than the wealthy to develop neurological disorders, and everywhere they are more likely to die as a result. Thus poverty and neurological disorders tend to reinforce each other; this vicious cycle is frequently exacerbated by gender inequalities.

A large survey undertaken by WHO/WFN to collect expert information on aspects of neurological care provision around the world (analysis of which was published as the Atlas of Country Resources for Neurological Disorders) found that, on average, there was one neurologist per 100 000 population worldwide in the reporting countries, ranging from one per 20 000 population in the European Region of WHO to one per three million population in the African Region. Not only are resources inadequately allocated for neurological services, there is also inequity in their distribution across countries and populations. This is particularly true for people living in low and middle income countries as well as for poor population groups in high income countries.

RECOMMENDATIONS FOR ACTION

This report offers health professionals and planners the opportunity to assess the burden caused by neurological disorders in their country and to take appropriate action. All the following recommendations need to be implemented across a wide range of sectors and disciplines if they are to achieve success. They are not a universal blueprint, however, and will have to be adapted to local conditions and capacities. The actions recommended can be beneficial directly — by decreasing the mortality, morbidity and disability caused by neurological disorders — and indirectly by improving the functioning and quality of life of patients and their families.

In certain low income and middle income countries with limited human and financial resources, it may be difficult for governments to apply some of these recommendations on their own. In these circumstances, it is suggested that countries work with international agencies, nongovernmental organizations or other partners to put their plans into practice.

1. Gain commitment from decision-makers

Much of the success of public health efforts in countries ultimately depends upon the degree of political commitment they receive. Support from decision-makers is not only necessary to ensure proper funding and effective legislation and policies, but also to give prevention efforts increased legitimacy and a higher profile in the public consciousness.

Public health professionals have an important contribution to make to the process of gaining political support, by providing decision-makers with solid information on the prevalence, consequences and burden of neurological disorders, and by carefully documenting the proven and promising interventions that can lead to their prevention or management. Information on population needs must be synthesized and disseminated in a way that encourages commitment from decision-makers. Communication methods such as media features and the identification and engagement of community leaders can be used to help build alliances between different stakeholders.

2. Increase public and professional awareness

Public and professional awareness of public health aspects of neurological disorders needs to be raised through the launch of global and local campaigns and initiatives that target health professionals, general practitioners and primary care physicians, specialists in public health, neurologists, health planners, health economists, the media and the general public. Another route of sensitization is the development of educational programmes on the public health aspects of neurology (taking into account local practices and traditions) and including them in the teaching and training curricula of all institutions where neurology is taught.

Self-help groups, patient information programmes and basic educational and training interventions for caregivers need to be encouraged and facilitated. Patients, their families and carers should be represented and fully involved in the development and implementation of policies and services for people with neurological disorders.

3. Minimize stigma and eradicate discrimination

Stigma and discrimination against people with neurological disorders (including epilepsy, dementia, Parkinson's disease, AIDS-related conditions and other neurological disorders) exist globally and need to be eliminated through public education, global and local campaigns and a variety of public health actions involving governments, health professionals, patients, carers and the mass media. The ultimate goal of all such efforts should be to prevent the isolation of patients with neurological disorders and their families and to facilitate their social integration. The dignity of people with neurological disorders needs to be preserved and their quality of life improved. Development of social and health policies for minimizing stigma must take into consideration such key issues as access to care and financing health care, as well as basic human rights. Driving privileges for people with controlled epilepsy indicates practical needs for policy to examine not just personal and public safety, but also how stigma, culture, liability and ethics interact.

Legislation represents an important means of dealing with these problems and challenges. Governments can reinforce the efforts with laws that protect people with brain disorders and their families from abusive practices and prevent discrimination in education, employment, housing and other opportunities. Legislation can help, but ample evidence exists to show that alone it is not enough.

The kind of intervention needed to mitigate stigma varies with the condition. For example, efforts to alleviate the stigma of epilepsy need to be focused on helping individuals acknowledge and adjust to life with treatable disease in a large number of cases. Information, education and communication and social marketing campaigns need to enhance compassion and reduce blame. In the case of other diseases, for example leprosy, the control programme can be made effective by use of a simple message that leprosy can be cured with medicines.

4. Strengthen neurological care within the existing health systems

The most promising approach for reducing the burden of neurological disorders in developing countries is a comprehensive system of primary health care: primary care services supported by secondary and tertiary care facilities, physicians and specialists. Primary care is the point of entry for the vast majority of people seeking medical care — indeed, for many people it is their sole access to medicine. Moreover, because primary care teams work in the community, they are well placed to recognize factors such as stigma, family problems and cultural factors that affect treatment for neurological disorders. Thus, primary care is the logical setting in which neurological disorders need to be dealt with. The important role of primary care is also founded on recognition that decisions in primary care take account of patient-related factors — family medical history and patients' individual expectations and values — of which the continuity and long-term relationships of primary care generate awareness, while promoting trust and satisfaction among patients. For example, effective management of headache disorders can be provided in primary care for all but a very small minority of patients, as the common headache disorders require no special investigation and they can be diagnosed and managed with skills generally available to health-care professionals working in primary care settings.

A careful analysis is required of what is and what is not possible for the treatment and care of neurological disorders at different levels of care. It is thus very important to establish a referral system for management of severe cases and patients requiring access to diagnostic and technological expertise. What is needed is a continuing, seamless care approach to handle the long-term nature of neurological disorders and the call for ongoing care.

5. Incorporate rehabilitation into the key strategies

Rehabilitation complements the other key strategies, promotion, prevention and treatment. While prevention involves targeting risk factors of disease and treatment is dealing with health conditions, rehabilitation targets human functioning. Though rooted in the health sector, rehabilitation is also a relevant strategy that brings together other sectors such as education, labour and social affairs. It is thus a most relevant strategy in the community.

There is a wide range of rehabilitation interventions, programmes and services that have been shown to be effective in contributing to optimal functioning of people with neurological conditions. Rehabilitation services need to be made available to all people with disabilities, and this includes people with disabilities attributable to neurological disorders. Accessible public transport and other facilities must be provided for them.

Multidisciplinary rehabilitation is considered to be beneficial in early recovery of stroke and traumatic brain injury patients. Although options for treatment of multiple sclerosis are relatively limited, sufferers can gain significant improvements in quality of life with neurorehabilitation.

Since community-based rehabilitation programmes are a low-cost way to coordinate medical guidance and community resources in the rehabilitation of disabled people, they need to be encouraged. The programmes should be linked to and supported by institutional and hospital-based care, where appropriate, thus creating a comprehensive rehabilitation service.

6. Develop national capacity and international collaboration

The international implications of dealing with neurological disorders in low and middle income countries are similar to those for a variety of other health concerns. Building capacity in these countries to reduce the burden of neurological disorders will require international contributions of expertise and resources. Examples of such collaboration are the global campaigns against epilepsy (www.who.int/mental_health/management/globalepilepsycampaign/) and headache disorders (www.who.int/mental_health/neurology/headache/), which have been launched by WHO in partnership with leading international nongovernmental organizations working in these areas.

The donor community urgently needs to dedicate more of its resources to help low and middle income countries improve services for the prevention and management of neurological disorders. Nongovernmental organizations have an important role to play in this regard, and they should be encouraged to give greater support to their initiatives. Partnerships between health policy-makers, health-care providers and people affected by neurological disorders and their advocacy groups may be the best vehicle for determining, and bringing about, the changes that people with neurological disorders need.

7. Establish links to other sectors

The risk factors and strategies for prevention for many of the neurological disorders lie beyond the health sector, necessitating the participation of other sectors such as education, transport, welfare, housing and legislation; these sectors need to be fully involved in improving the programmes and services for people with neurological disorders. Partnerships are advantageous in enhancing the effectiveness of interventions, increasing the resources available through joint actions and avoiding a duplication of efforts. Sometimes different sectors may have different and even conflicting priorities; in such situations, the health sector needs the capacity to provide leadership and informed reasoning and to adapt to the agendas and priorities of other sectors.

Road traffic injury prevention and management strategies include the design of vehicles, the design of road networks and roads, urban and rural planning, the introduction and enforcement of road safety legislation and the care and treatment of crash survivors. These are some of the relevant areas for interventions to prevent neurological consequences of road traffic injuries, which are divided among many different sectors and groups.

8. Define priorities for research

The research agenda for developing countries, including operational research, needs to be developed to gain better understanding of the problem so that appropriate responses can be developed and evaluated. Specific areas for research and development could include conducting population-based epidemiological studies in developing countries where insufficient data limit evidence-based planning. It is also necessary to develop and evaluate simple models of care for management of neurological disorders by existing community-based health-care providers. Many currently available medications have significant side-effects and are too expensive for most patients in developing countries. Newer medications need to be developed with lower costs, fewer side-effects, better efficacy, and less frequent dose schedules. Multicentre epidemiological studies and trials of novel treatments should be facilitated through better funding, multidisciplinary approaches and international collaboration.

This report endeavours to contribute to the knowledge base regarding public health aspects of neurological disorders. It is hoped that it will inspire and facilitate increased cooperation, innovation and commitment in preventing neurological disorders and providing the best possible care for people suffering from them.

Annex 1 *List of Member States by WHO region and mortality stratum*

To aid in cause of death and burden of disease analyses, the Member States of the World Health Organization (WHO) have been divided into five mortality strata on the basis of their levels of mortality of children under five years of age (5q0) and of males 15–59 years old (45q15). The classification of WHO Member States into mortality strata was carried out using population estimates for 1999 (from the United Nations Population Division, 1998) and estimates of 5q0 and 45q15 based on WHO analyses of mortality rates for 1999.

Quintiles of the distribution of 5q0 (both sexes combined) were used to define a very low child mortality group (1st quintile), a low child mortality group (2nd and 3rd quintiles) and a high child mortality group (4th and 5th quintiles). Adult mortality 45q15 was regressed on 5q0 and the regression line used to divide countries with high child mortality into high adult mortality (stratum D) and very high adult mortality (stratum E). Stratum E includes the countries in sub-Saharan Africa where HIV/AIDS has had a very substantial impact.

The following table summarizes the five mortality strata. When these mortality strata are applied to the six WHO regions, they produce 14 subregions, which are used throughout this document and its Annexes to present results. The mortality strata to which WHO Member States are classified are listed below. This classification has no official status and is for analytical purposes only.

Definitions of mortality strata used to define subregions

Mortality stratum	Child mortality	Adult mortality
A	Very low	Very low
B	Low	Low
C	Low	High
D	High	High
E	High	Very high

The total number of WHO Member States rose to 193 in 2006 with the addition of the Republic of Montenegro.

WHO Member States, by region and mortality stratum

WHO region	Mortality stratum	Description	Broad group	WHO Member States
Africa (AFR)	Afr-D	Africa with high child and high adult mortality	High mortality developing	Algeria, Angola, Benin, Burkina Faso, Cameroon, Cape Verde, Chad, Comoros, Equatorial Guinea, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Madagascar, Mali, Mauritania, Mauritius, Niger, Nigeria, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone, Togo
	Afr-E	Africa with high child and very high adult mortality	High mortality developing	Botswana, Burundi, Central African Republic, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Eritrea, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Rwanda, South Africa, Swaziland, Uganda, United Republic of Tanzania, Zambia, Zimbabwe
Americas (AMR)	Amr-A	Americas with very low child and very low adult mortality	Developed	Canada, Cuba, United States of America
	Amr-B	Americas with low child and low adult mortality	Low mortality developing	Antigua and Barbuda, Argentina, Bahamas, Barbados, Belize, Brazil, Chile, Colombia, Costa Rica, Dominica, Dominican Republic, El Salvador, Grenada, Guyana, Honduras, Jamaica, Mexico, Panama, Paraguay, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, Uruguay, Venezuela (Bolivarian Republic of)
	Amr-D	Americas with high child and high adult mortality	High mortality developing	Bolivia, Ecuador, Guatemala, Haiti, Nicaragua, Peru
South-East Asia (SEAR)	Sear-B	South-East Asia with low child and low adult mortality	Low mortality developing	Indonesia, Sri Lanka, Thailand
	Sear-D	South-East Asia with high child and high adult mortality	High mortality developing	Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Maldives, Myanmar, Nepal, Timor-Leste
Europe (EUR)	Eur-A	Europe with very low child and very low adult mortality	Developed	Andorra, Austria, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, Netherlands, Norway, Portugal, San Marino, Slovenia, Spain, Sweden, Switzerland, United Kingdom of Great Britain and Northern Ireland
	Eur-B	Europe with low child and low adult mortality	Developed	Albania, Armenia, Azerbaijan, Bosnia and Herzegovina, Bulgaria, Georgia, Kyrgyzstan, Montenegro, Poland, Romania, Serbia, Slovakia, Tajikistan, The former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Uzbekistan
	Eur-C	Europe with low child and high adult mortality	Developed	Belarus, Estonia, Hungary, Kazakhstan, Latvia, Lithuania, Republic of Moldova, Russian Federation, Ukraine
Eastern Mediterranean (EMR)	Emr-B	Eastern Mediterranean with low child and low adult mortality	Low mortality developing	Bahrain, Iran (Islamic Republic of), Jordan, Kuwait, Lebanon, Libyan Arab Jamahiriya, Oman, Qatar, Saudi Arabia, Syrian Arab Republic, Tunisia, United Arab Emirates
	Emr-D	Eastern Mediterranean with high child and high adult mortality	High mortality developing	Afghanistan, Djibouti, Egypt,* Iraq, Morocco, Pakistan, Somalia, Sudan, Yemen
Western Pacific (WPR)	Wpr-A	Western Pacific with very low child and very low adult mortality	Developed	Australia, Brunei Darussalam, Japan, New Zealand, Singapore
	Wpr-B	Western Pacific with low child and low adult mortality	Low mortality developing	Cambodia,** China, Cook Islands, Fiji, Kiribati, Lao People's Democratic Republic,** Malaysia, Marshall Islands, Micronesia (Federated States of), Mongolia, Nauru, Niue, Palau, Papua New Guinea,** Philippines, Republic of Korea, Samoa, Solomon Islands, Tonga, Tuvalu, Vanuatu, Viet Nam

* Following improvements in child mortality over recent years, Egypt meets criteria for inclusion in subregion Emr-B with low child and low adult mortality. Egypt has been included in Emr-D for the presentation of subregional totals for mortality and burden to ensure comparability with *The World Health Report* and other WHO publications.

** Although Cambodia, the Lao People's Democratic Republic and Papua New Guinea meet criteria for high child mortality, they have been included in the Wpr-B subregion with other developing countries of the Western Pacific Region for reporting purposes.

Annex 2 *Country income groups used for reporting estimates and projections*

Income category	Countries
High	Andorra, Aruba, Australia, Austria, Bahamas, Bahrain, Belgium, Bermuda, Brunei Darussalam, Canada, Cayman Islands, Channel Islands, Cyprus, Denmark, Faeroe Islands, Finland, France, French Polynesia, Germany, Greece, Greenland, Guam, Iceland, Ireland, Israel, Italy, Japan, Kuwait, Liechtenstein, Luxembourg, Monaco, Netherlands, Netherlands Antilles, New Caledonia, New Zealand, Northern Mariana Islands, Norway, Portugal, Qatar, Republic of Korea, San Marino, Singapore, Slovenia, Spain, Sweden, Switzerland, United Arab Emirates, United Kingdom, United States of America, United States Virgin Islands
Upper middle	American Samoa, Antigua and Barbuda, Argentina, Barbados, Botswana, Brazil, Chile, Costa Rica, Croatia, Czech Republic, Dominica, Estonia, Gabon, Grenada, Hungary, Isle of Man, Latvia, Lebanon, Libyan Arab Jamahiriya, Lithuania, Malaysia, Malta, Mauritius, Mexico, Oman, Palau, Panama, Poland, Puerto Rico, Saint Kitts and Nevis, Saint Lucia, Saudi Arabia, Seychelles, Slovakia, Trinidad and Tobago, Uruguay, Venezuela (Bolivarian Republic of)
Lower middle	Albania, Algeria, Belarus, Belize, Bolivia, Bosnia and Herzegovina, Bulgaria, Cape Verde, China, Colombia, Cuba, Djibouti, Dominican Republic, Ecuador, Egypt, El Salvador, Fiji, Guatemala, Guyana, Honduras, Iran (Islamic Republic of), Iraq, Jamaica, Jordan, Kazakhstan, Kiribati, Maldives, Marshall Islands, Micronesia (Federated States of), Morocco, Namibia, Occupied Palestinian Territory, Paraguay, Peru, Philippines, Romania, Russian Federation, Saint Vincent and the Grenadines, Samoa, Serbia and Montenegro, South Africa, Sri Lanka, Suriname, Swaziland, Syrian Arab Republic, Thailand, The former Yugoslav Republic of Macedonia, Tonga, Tunisia, Turkey, Turkmenistan, Vanuatu
Low	Afghanistan, Angola, Armenia, Azerbaijan, Bangladesh, Benin, Bhutan, Burkina Faso, Burundi, Cambodia, Cameroon, Central African Republic, Chad, Comoros, Congo, Côte d'Ivoire, Democratic People's Republic of Korea, Democratic Republic of the Congo, Equatorial Guinea, Eritrea, Ethiopia, Gambia, Georgia, Ghana, Guinea, Guinea-Bissau, Haiti, India, Indonesia, Kenya, Kyrgyzstan, Lao People's Democratic Republic, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mongolia, Mozambique, Myanmar, Nepal, Nicaragua, Niger, Nigeria, Pakistan, Papua New Guinea, Republic of Moldova, Rwanda, Sao Tome and Principe, Senegal, Sierra Leone, Solomon Islands, Somalia, Sudan, Tajikistan, Timor-Leste, Togo, Uganda, Ukraine, United Republic of Tanzania, Uzbekistan, Viet Nam, Yemen, Zambia, Zimbabwe
Not included	Anguilla, British Virgin Islands, Cook Islands, Falkland Islands (Malvinas), French Guiana, Gibraltar, Guadeloupe, Holy See, Martinique, Montserrat, Nauru, Niue, Pitcairn, Réunion, Saint Helena, Saint Pierre et Miquelon, Tokelau, Turks and Caicos Islands, Tuvalu, Wallis and Futuna Islands, Western Sahara

Note: Categories are based on the income categories published in *2003 World development indicators* (Washington, DC, The World Bank, 2003). Countries are divided according to 2001 GNI per capita, calculated using the World Bank Atlas method. The groups are: low income, US$ 745 or less; lower middle income, US$ 746–2975; upper middle income, US$ 2976–9205; and high income, US$ 9206 or more. This differs from the list currently available on the World Bank web site because that list has been recently amended.

Annex 3 *Global Burden of Disease cause categories, sequelae and case definitions for neurological disorders*

For the purpose of calculation of global burden of disease (GBD) estimates for this document, the neurological disorders were included from two categories: neurological disorders within the neuropsychiatric category, and neurological disorders from other categories. Neurological disorders within the neuropsychiatric category refer to the cause category listed in Group II under neuropsychiatric disorders and include epilepsy, Alzheimer and other dementias, Parkinson's disease, multiple sclerosis and migraine. Neurological disorders from other categories include diseases and injuries which have neurological sequelae and are listed elsewhere in cause category Groups I, II and III. The table below provides the complete list used for calculation of GBD estimates for neurological disorders.

GBD cause category	Sequelae	Case definition
Neurological disorders in the neuropsychiatric category		
Epilepsy	Cases	Cases meeting ILAE definition Cases meeting ICD-10 criteria for alcohol dependence and harmful use (F10.1 and F10.2), excluding cases with comorbid depressive episode
Alzheimer and other dementias	Cases	Mild, moderate and severe Alzheimer's disease, senile and other dementias
Parkinson's disease	Cases	Cases meeting clinical criteria for Parkinson's disease
Multiple sclerosis	Cases	Cases of chronic or intermittent relapsing multiple sclerosis
Migraine	Cases	Cases meeting IHS definition for migraine
Neurological disorders in other categories		
Cerebrovascular disease	First-ever stroke cases	First-ever stroke according to WHO definition (includes subarachnoid haemorrhage but excludes transient ischaemic attacks, subdural haematoma, and haemorrhage or infarction attributable to infection or tumour).
	Long-term stroke survivors	Persons who survive more than 28 days after first-ever stroke.
Poliomyelitis	Cases: lameness	Viral infection characterized by acute flaccid paralysis and proven by isolation of poliovirus from stool
Tetanus	Episodes	Neonatal: infection with *Clostridium tetani* in infants less than 30 days old with progressive difficulty and inability to feed because of trismus, generalized stiffness, spasms and opisthotonus Non-neonatal: infection with *Clostridium tetani* in non-neonates with initial localized spasms leading to general rigidity, opisthotonus and "risus sardonicus"

GBD cause category	Sequelae	Case definition
Meningitis		Acute bacterial disease with sudden onset and fever, intense headache, nausea, vomiting, neck stiffness and – in meningococcal disease – petechial rash with pink macules; the disease must be accompanied by laboratory evidence (in cerebrospinal fluid or blood) of *Neisseria meningitidis*, *Streptococcus pneumoniae* or *Haemophilus influenzae* type B
	Seizure disorder	Seizures of any type that were present at least six months after hospitalization, RESULTING from meningitis
	Motor deficit	Motor deficit spasticity or paresis of one or more limbs, RESULTING from meningitis
	Mental retardation	IQ of 70 or below RESULTING from meningitis
Japanese encephalitis		Mosquito-borne encephalitis caused by JE virus
	Cognitive impairment	Reduced cognitive function resulting from encephalitis attributable to JE virus
	Neurological sequelae	Neurological deficits resulting from encephalitis attributable to JE virus
Syphilis		Acute and chronic infection with *Treponema pallidum*
	Tertiary – neurological	Late stage of the disease with varied neurological manifestations
Pertussis		Acute bacterial infection of the respiratory tract with *Bordetella pertussis* or parapertussis
	Encephalopathy	Degenerative disease of the brain, which in pertussis is usually a result of hypoxia, leading to mental retardation
Diphtheria		Acute disease caused by toxin-producing *Corynebacterium diphtheriae*
	Neurological complications	Polyneuritis involving both cranial and peripheral nerve palsies, which are largely reversible
Malaria		Infectious disease caused by protozoa of the genus Plasmodium
	Neurological sequelae	Includes hemiplegia, aphasia, ataxia and cortical blindness
Leprosy		Chronic disease resulting from infection with *Mycobacterium leprae*
	Disabling leprosy	Grade 1 and 2 of WHO grades of disability for leprosy
Diabetes mellitus	Neuropathy	Loss of reflexes and of vibration; damage and dysfunction of sensory, motor or autonomic nerves attributable to diabetes
Protein–energy malnutrition	Developmental disability	Limited physical and mental ability to perform most activities in all of the following areas: recreation, education, procreation or occupation
Iodine deficiency	Mild developmental disability	Any of the following attributable to iodine deficiency: bilateral hearing loss, delay of walking ability, mild intellectual impairment
	Cretinoidism	Hypothyroid cretinism: hypothyroidism and stunting as a RESULT of iodine deficiency Neurological cretinism: mental deficiency (IQ below 70), deaf-mutism, and spastic paralysis as a RESULT of iodine deficiency
	Cretinism	Some but not all features of full cretinism as a RESULT of iodine deficiency
Road traffic accidents	Fractured skull – long-term Spinal cord injury – long-term Intracranial injury – long-term Injured nerves – long-term	Includes crashes and pedestrian injuries attributable to motor vehicles
Poisonings	Fractured skull – long-term Spinal cord injury – long-term Intracranial injury – long-term Injured nerves – long-term	Only one outcome is included for poisonings
Falls	Fractured skull – long-term Spinal cord injury – long-term Intracranial injury – long-term Injured nerves – long-term	Includes falls resulting from osteoporotic fractures
Fires	Fractured skull – long-term Spinal cord injury – long-term Intracranial injury – long-term Injured nerves – long-term	Most of the sequelae of fires are the result of burns. Some individuals, however, jump from buildings or are otherwise injured during fires.

GBD cause category	Sequelae	Case definition
Drownings	Fractured skull – long-term Spinal cord injury – long-term Intracranial injury – long-term Injured nerves – long-term	Other than drowning and near-drowning rates, the only other major disabling sequela from near-drowning included is quadriplegia
Other unintentional injuries	Fractured skull – long-term Spinal cord injury – long-term Intracranial injury – long-term Injured nerves – long-term	This is not a residual category, but includes injuries attributable to environmental factors, machinery and electrical equipment, cutting and piercing implements, and various other external causes of unintentional injury
Self-inflicted injuries	Fractured skull – long-term Spinal cord injury – long-term Intracranial injury – long-term Injured nerves – long-term	Suicide attempts, whether or not resulting in death
Violence	Fractured skull – long-term Spinal cord injury – long-term Intracranial injury – long-term Injured nerves – long-term	Interpersonal violence, including assault and homicide
War	Fractured skull – long-term Spinal cord injury – long-term Intracranial injury – long-term Injured nerves – long-term	War injuries and deaths directly attributable to war in combatants and non-combatants; e.g. the estimates of mortality include deaths to children and adults from landmines
Other intentional injuries	Fractured skull – long-term Spinal cord injury – long-term Intracranial injury – long-term Injured nerves – long-term	

Source: Mathers CD et al. *Deaths and disease burden by cause: global burden of disease estimates for 2001 by World Bank country groups*. Washington, DC, World Health Organization/World Bank/Fogarty International Center, United States National Institutes of Health, 2004 (Disease Control Priorities in Developing Countries (DCPP) Working Papers Series, No. 18; http://www.fic.nih.gov/dcpp/wps.html, accessed 25 July 2005).

Annex 4

Table A.4.1 Burden of neurological disorders, in DALYs, by cause, WHO region and mortality stratum, projections for 2005, 2015 and 2030

	DALYs	% total	per 100 000	DALYs	% total	per 100 000	DALYs	% total	per 100 000
WORLD									
	2005			**2015**			**2030**		
Population	**6 441 919 466**			**7 103 297 899**			**7 917 115 397**		
TOTAL DALYs	1 469 610 066			1 481 400 233			1 526 745 574		
Epilepsy	7 307 975	0.50	113.44	7 419 365	0.50	104.45	7 441 536	0.49	93.99
Alzheimer and other dementias	11 077 525	0.75	171.96	13 539 653	0.91	190.61	18 394 267	1.20	232.34
Parkinson's disease	1 616 523	0.11	25.09	1 762 344	0.12	24.81	2 015 065	0.13	25.45
Multiple sclerosis	1 509 696	0.10	23.44	1 585 932	0.11	22.33	1 648 303	0.11	20.82
Migraine	7 659 687	0.52	118.90	7 736 261	0.52	108.91	7 596 089	0.50	95.95
Cerebrovascular disease	50 784 770	3.46	788.35	53 814 944	3.63	757.61	60 864 051	3.99	768.77
Poliomyelitis	115 167	0.01	1.79	46 946	0.00	0.66	13 261	0.00	0.17
Tetanus	6 422 611	0.44	99.70	4 870 770	0.33	68.57	3 173 636	0.21	40.09
Meningitis	5 336 882	0.36	82.85	3 527 560	0.24	49.66	2 038 968	0.13	25.75
Japanese encephalitis	561 038	0.04	8.71	304 123	0.02	4.28	149 931	0.01	1.89
Total	92 391 874	6.29	1 434.23	94 607 898	6.39	1 331.89	103 335 108	6.77	1 305.21
AFRICA (HIGH CHILD, HIGH ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**335 459 111**			**419 571 880**			**550 082 900**		
TOTAL DALYs	162 560 000			177 805 056			193 570 528		
Epilepsy	733 354	0.45	218.61	885 376	0.50	211.02	1 064 481	0.55	193.51
Alzheimer and other dementias	178 867	0.11	53.32	221 661	0.12	52.83	303 739	0.16	55.22
Parkinson's disease	38 555	0.02	11.49	47 146	0.03	11.24	66 606	0.03	12.11
Multiple sclerosis	60 711	0.04	18.10	78 674	0.04	18.75	105 590	0.05	19.20
Migraine	206 278	0.13	61.49	255 460	0.14	60.89	315 904	0.16	57.43
Cerebrovascular disease	1 923 353	1.18	573.35	2 456 636	1.38	585.51	3 520 676	1.82	640.03
Poliomyelitis	8 389	0.01	2.50	3 669	0.00	0.87	1 171	0.00	0.21
Tetanus	1 618 496	1.00	482.47	1 556 776	0.88	371.04	1 205 282	0.62	219.11
Meningitis	387 081	0.24	115.39	380 001	0.21	90.57	316 542	0.16	57.54
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	5 155 084	3.17	1 536.73	5 885 400	3.31	1 402.72	6 899 990	3.56	1 254.35
AFRICA (HIGH CHILD, VERY HIGH ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**382 647 820**			**478 419 411**			**628 734 321**		
TOTAL DALYs	199 234 864			215 301 104			241 062 592		
Epilepsy	913 291	0.46	238.68	1 066 122	0.50	222.84	1 272 664	0.53	202.42
Alzheimer and other dementias	188 677	0.09	49.31	233 292	0.11	48.76	299 644	0.12	47.66
Parkinson's disease	43 020	0.02	11.24	50 089	0.02	10.47	66 823	0.03	10.63
Multiple sclerosis	47 853	0.02	12.51	62 378	0.03	13.04	86 962	0.04	13.83
Migraine	267 571	0.13	69.93	321 413	0.15	67.18	391 515	0.16	62.27
Cerebrovascular disease	2 089 458	1.05	546.05	2 535 342	1.18	529.94	3 443 274	1.43	547.65
Poliomyelitis	2 718	0.00	0.71	1 118	0.00	0.23	253	0.00	0.04
Tetanus	1 176 583	0.59	307.48	1 123 088	0.52	234.75	903 202	0.37	143.65
Meningitis	480 234	0.24	125.50	428 421	0.20	89.55	328 982	0.14	52.32
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	5 209 404	2.61	1 361.41	5 821 262	2.70	1 216.77	6 793 320	2.82	1 080.48

	DALYs	% total	per 100 000	DALYs	% total	per 100 000	DALYs	% total	per 100 000
THE AMERICAS (VERY LOW CHILD, VERY LOW ADULT MORTALITY)									
	2005			2015			2030		
Population	343 363 701			372 395 661			413 323 652		
TOTAL DALYs	47 523 900			49 441 160			49 995 588		
Epilepsy	174 560	0.37	50.84	175 647	0.36	47.17	175 616	0.35	42.49
Alzheimer and other dementias	1 380 277	2.90	401.99	1 634 372	3.31	438.88	2 303 611	4.61	557.34
Parkinson's disease	257 841	0.54	75.09	286 838	0.58	77.03	331 246	0.66	80.14
Multiple sclerosis	121 061	0.25	35.26	123 772	0.25	33.24	124 004	0.25	30.00
Migraine	511 142	1.08	148.86	526 028	1.06	141.26	559 602	1.12	135.39
Cerebrovascular disease	1 684 842	3.55	490.69	1 717 559	3.47	461.22	1 750 879	3.50	423.61
Poliomyelitis	2 539	0.01	0.74	2 225	0.00	0.60	1 886	0.00	0.46
Tetanus	27	0.00	0.01	27	0.00	0.01	28	0.00	0.01
Meningitis	36 770	0.08	10.71	23 206	0.05	6.23	12 285	0.02	2.97
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	4 169 059	8.77	1 214.18	4 489 676	9.08	1 205.62	5 259 157	10.52	1 272.41
THE AMERICAS (LOW CHILD, LOW ADULT MORTALITY)									
	2005			2015			2030		
Population	463 707 779			511 277 519			560 127 320		
TOTAL DALYs	83 157 544			86 918 680			90 204 248		
Epilepsy	752 259	0.90	162.23	765 363	0.88	149.70	735 674	0.82	131.34
Alzheimer and other dementias	705 683	0.85	152.18	916 569	1.05	179.27	1 397 744	1.55	249.54
Parkinson's disease	56 623	0.07	12.21	67 157	0.08	13.14	83 103	0.09	14.84
Multiple sclerosis	107 378	0.13	23.16	114 704	0.13	22.43	117 098	0.13	20.91
Migraine	760 969	0.92	164.11	783 250	0.90	153.19	759 916	0.84	135.67
Cerebrovascular disease	2 577 873	3.10	555.93	2 789 067	3.21	545.51	3 129 619	3.47	558.73
Poliomyelitis	4 184	0.01	0.90	1 656	0.00	0.32	415	0.00	0.07
Tetanus	5 406	0.01	1.17	2 851	0.00	0.56	1 230	0.00	0.22
Meningitis	295 286	0.36	63.68	150 869	0.17	29.51	57 834	0.06	10.33
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	5 265 661	6.33	1 135.56	5 591 485	6.43	1 093.63	6 282 632	6.96	1 121.64
THE AMERICAS (HIGH CHILD, HIGH ADULT MORTALITY)									
	2005			2015			2030		
Population	77 739 657			90 194 020			106 740 220		
TOTAL DALYs	16 806 174			17 120 126			17 995 520		
Epilepsy	147 253	0.88	189.42	161 116	0.94	178.63	168 515	0.94	157.87
Alzheimer and other dementias	82 158	0.49	105.68	103 267	0.60	114.49	155 670	0.87	145.84
Parkinson's disease	7 735	0.05	9.95	9 333	0.05	10.35	13 082	0.07	12.26
Multiple sclerosis	16 503	0.10	21.23	19 298	0.11	21.40	22 093	0.12	20.70
Migraine	155 043	0.92	199.44	165 994	0.97	184.04	171 234	0.95	160.42
Cerebrovascular disease	307 344	1.83	395.35	372 199	2.17	412.66	482 702	2.68	452.22
Poliomyelitis	633	0.00	0.81	256	0.00	0.28	60	0.00	0.06
Tetanus	6 869	0.04	8.84	4 545	0.03	5.04	2 176	0.01	2.04
Meningitis	249 051	1.48	320.37	168 327	0.98	186.63	84 756	0.47	79.40
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	972 590	5.79	1 251.09	1 004 336	5.87	1 113.53	1 100 287	6.11	1 030.81
SOUTH-EAST ASIA (LOW CHILD, LOW ADULT MORTALITY)									
	2005			2015			2030		
Population	308 761 163			336 961 332			364 048 380		
TOTAL DALYs	61 585 292			59 738 224			61 457 480		
Epilepsy	361 414	0.59	117.05	338 893	0.57	100.57	303 458	0.49	83.36
Alzheimer and other dementias	400 013	0.65	129.55	529 452	0.89	157.13	789 056	1.28	216.74
Parkinson's disease	38 298	0.06	12.40	44 291	0.07	13.14	49 351	0.08	13.56
Multiple sclerosis	64 734	0.11	20.97	67 543	0.11	20.04	67 080	0.11	18.43
Migraine	339 628	0.55	110.00	329 367	0.55	97.75	305 781	0.50	83.99
Cerebrovascular disease	1 760 298	2.86	570.12	1 924 622	3.22	571.17	2 165 135	3.52	594.74
Poliomyelitis	6 454	0.01	2.09	2 345	0.00	0.70	479	0.00	0.13
Tetanus	190 414	0.31	61.67	67 754	0.11	20.11	14 159	0.02	3.89
Meningitis	179 622	0.29	58.18	97 609	0.16	28.97	44 339	0.07	12.18
Japanese encephalitis	23 641	0.04	7.66	11 891	0.02	3.53	4 636	0.01	1.27
Total	3 364 516	5.46	1 089.68	3 413 767	5.71	1 013.10	3 743 473	6.09	1 028.29

	DALYs	% total	per 100 000	DALYs	% total	per 100 000	DALYs	% total	per 100 000
SOUTH-EAST ASIA (HIGH CHILD, HIGH ADULT MORTALITY)									
	2005			2015			2030		
Population	1 352 957 715			1 525 318 552			1 718 832 463		
TOTAL DALYs	350 334 880			334 051 808			334 625 216		
Epilepsy	1 846 603	0.53	136.49	1 755 114	0.53	115.07	1 596 885	0.48	92.91
Alzheimer and other dementias	1 313 584	0.37	97.09	1 629 104	0.49	106.80	2 271 094	0.68	132.13
Parkinson's disease	222 096	0.06	16.42	256 981	0.08	16.85	324 249	0.10	18.86
Multiple sclerosis	290 158	0.08	21.45	329 272	0.10	21.59	360 861	0.11	20.99
Migraine	1 756 274	0.50	129.81	1 793 948	0.54	117.61	1 783 945	0.53	103.79
Cerebrovascular disease	9 309 524	2.66	688.09	10 744 744	3.22	704.43	13 685 517	4.09	796.21
Poliomyelitis	42 889	0.01	3.17	17 555	0.01	1.15	4 456	0.00	0.26
Tetanus	2 023 976	0.58	149.60	1 119 986	0.34	73.43	480 138	0.14	27.93
Meningitis	1 591 141	0.45	117.60	932 822	0.28	61.16	494 587	0.15	28.77
Japanese encephalitis	235 243	0.07	17.39	142 203	0.04	9.32	78 097	0.02	4.54
Total	18 631 487	5.32	1 377.09	18 721 728	5.60	1 227.40	21 079 828	6.30	1 226.40
EUROPE (VERY LOW CHILD, VERY LOW ADULT MORTALITY)									
	2005			2015			2030		
Population	417 799 202			417 841 350			411 754 930		
TOTAL DALYs	51 143 804			49 025 240			44 716 336		
Epilepsy	239 993	0.47	57.44	220 376	0.45	52.74	193 205	0.43	46.92
Alzheimer and other dementias	2 090 437	4.09	500.34	2 422 371	4.94	579.73	2 875 209	6.43	698.28
Parkinson's disease	291 838	0.57	69.85	300 765	0.61	71.98	302 935	0.68	73.57
Multiple sclerosis	154 835	0.30	37.06	144 594	0.29	34.61	125 997	0.28	30.60
Migraine	721 342	1.41	172.65	670 731	1.37	160.52	600 497	1.34	145.84
Cerebrovascular disease	2 559 576	5.00	612.63	2 389 485	4.87	571.86	2 178 577	4.87	529.10
Poliomyelitis	1 130	0.00	0.27	854	0.00	0.20	588	0.00	0.14
Tetanus	429	0.00	0.10	301	0.00	0.07	209	0.00	0.05
Meningitis	55 054	0.11	13.18	30 142	0.06	7.21	14 196	0.03	3.45
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	6 114 632	11.96	1 463.53	6 179 619	12.60	1 478.94	6 291 414	14.07	1 527.95
EUROPE (LOW CHILD, LOW ADULT MORTALITY)									
	2005			2015			2030		
Population	227 350 229			236 868 370			243 016 939		
TOTAL DALYs	37 466 008			36 742 964			35 907 916		
Epilepsy	187 986	0.50	82.69	181 046	0.49	76.43	163 317	0.45	67.20
Alzheimer and other dementias	416 799	1.11	183.33	480 419	1.31	202.82	601 148	1.67	247.37
Parkinson's disease	69 244	0.18	30.46	71 106	0.19	30.02	75 668	0.21	31.14
Multiple sclerosis	63 435	0.17	27.90	62 695	0.17	26.47	58 444	0.16	24.05
Migraine	250 906	0.67	110.36	233 551	0.64	98.60	207 238	0.58	85.28
Cerebrovascular disease	2 549 285	6.80	1 121.30	2 510 333	6.83	1 059.80	2 577 873	7.18	1 060.78
Poliomyelitis	1 135	0.00	0.50	435	0.00	0.18	95	0.00	0.04
Tetanus	1 744	0.00	0.77	722	0.00	0.31	254	0.00	0.10
Meningitis	245 592	0.66	108.02	113 510	0.31	47.92	40 438	0.11	16.64
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	3 786 125	10.11	1 665.33	3 653 819	9.94	1 542.55	3 724 475	10.37	1 532.60
EUROPE (LOW CHILD, HIGH ADULT MORTALITY)									
	2005			2015			2030		
Population	235 511 792			206 753 120			175 407 940		
TOTAL DALYs	60 788 080			50 205 500			38 508 288		
Epilepsy	173 504	0.29	73.67	132 677	0.26	64.17	94 739	0.25	54.01
Alzheimer and other dementias	547 330	0.90	232.40	558 594	1.11	270.17	571 909	1.49	326.04
Parkinson's disease	89 160	0.15	37.86	74 137	0.15	35.86	60 079	0.16	34.25
Multiple sclerosis	83 868	0.14	35.61	68 588	0.14	33.17	51 033	0.13	29.09
Migraine	225 793	0.37	95.87	175 429	0.35	84.85	127 749	0.33	72.83
Cerebrovascular disease	5 697 447	9.37	2 419.18	4 817 814	9.60	2 330.23	3 716 728	9.65	2 118.91
Poliomyelitis	166	0.00	0.07	76	0.00	0.04	29	0.00	0.02
Tetanus	390	0.00	0.17	232	0.00	0.11	142	0.00	0.08
Meningitis	59 808	0.10	25.40	27 120	0.05	13.12	10 201	0.03	5.82
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	6 877 466	11.31	2 920.22	5 854 665	11.66	2 831.72	4 632 609	12.03	2 641.05

	DALYs	% total	per 100 000	DALYs	% total	per 100 000	DALYs	% total	per 100 000
EASTERN MEDITERRANEAN (LOW CHILD, LOW ADULT MORTALITY)									
	2005			2015			2030		
Population	150 452 139			176 204 370			207 555 239		
TOTAL DALYs	24 617 306			26 572 560			29 720 006		
Epilepsy	123 278	0.50	81.94	128 471	0.48	72.91	131 638	0.44	63.42
Alzheimer and other dementias	109 755	0.45	72.95	143 648	0.54	81.52	233 023	0.78	112.27
Parkinson's disease	41 032	0.17	27.27	45 034	0.17	25.56	53 874	0.18	25.96
Multiple sclerosis	37 457	0.15	24.90	41 969	0.16	23.82	46 541	0.16	22.42
Migraine	131 573	0.53	87.45	137 927	0.52	78.28	135 035	0.45	65.06
Cerebrovascular disease	609 782	2.48	405.30	719 923	2.71	408.57	966 963	3.25	465.88
Poliomyelitis	3 073	0.01	2.04	1 205	0.00	0.68	275	0.00	0.13
Tetanus	3 689	0.01	2.45	1 810	0.01	1.03	534	0.00	0.26
Meningitis	69 506	0.28	46.20	35 406	0.13	20.09	13 153	0.04	6.34
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	1 129 145	4.59	750.50	1 255 392	4.72	712.46	1 581 036	5.32	761.74
EASTERN MEDITERRANEAN (HIGH CHILD, HIGH ADULT MORTALITY)									
	2005			2015			2030		
Population	388 102 585			488 304 210			638 188 559		
TOTAL DALYs	115 736 624			120 818 488			129 212 256		
Epilepsy	518 728	0.45	133.66	582 379	0.48	119.27	641 906	0.50	100.58
Alzheimer and other dementias	261 563	0.23	67.40	342 501	0.28	70.14	509 229	0.39	79.79
Parkinson's disease	62 573	0.05	16.12	72 760	0.06	14.90	92 341	0.07	14.47
Multiple sclerosis	80 277	0.07	20.68	101 462	0.08	20.78	135 640	0.10	21.25
Migraine	440 044	0.38	113.38	538 081	0.45	110.19	640 098	0.50	100.30
Cerebrovascular disease	2 100 098	1.81	541.12	2 535 459	2.10	519.24	3 377 608	2.61	529.25
Poliomyelitis	9 809	0.01	2.53	4 378	0.00	0.90	1 233	0.00	0.19
Tetanus	1 126 181	0.97	290.18	877 700	0.73	179.74	524 966	0.41	82.26
Meningitis	1 070 558	0.92	275.84	823 949	0.68	168.74	482 625	0.37	75.62
Japanese encephalitis	75 600	0.07	19.48	56 599	0.05	11.59	32 109	0.02	5.03
Total	5 745 431	4.96	1 480.39	5 935 268	4.91	1 215.49	6 437 755	4.98	1 008.75
WESTERN PACIFIC (VERY LOW CHILD, VERY LOW ADULT MORTALITY)									
	2005			2015			2030		
Population	156 684 271			154 795 439			145 921 920		
TOTAL DALYs	16 471 606			16 072 011			14 289 616		
Epilepsy	63 026	0.38	40.22	57 128	0.36	36.91	48 395	0.34	33.16
Alzheimer and other dementias	838 385	5.09	535.08	1 053 026	6.55	680.27	1 230 880	8.61	843.52
Parkinson's disease	118 451	0.72	75.60	119 030	0.74	76.89	106 668	0.75	73.10
Multiple sclerosis	28 761	0.17	18.36	26 463	0.16	17.10	22 753	0.16	15.59
Migraine	143 723	0.87	91.73	127 925	0.80	82.64	112 524	0.79	77.11
Cerebrovascular disease	1 215 436	7.38	775.72	1 142 950	7.11	738.36	953 952	6.68	653.74
Poliomyelitis	342	0.00	0.22	232	0.00	0.15	149	0.00	0.10
Tetanus	50	0.00	0.03	43	0.00	0.03	30	0.00	0.02
Meningitis	9 649	0.06	6.16	5 796	0.04	3.74	2 881	0.02	1.97
Japanese encephalitis	248	0.00	0.16	116	0.00	0.07	59	0.00	0.04
Total	2 418 071	14.68	1 543.28	2 532 708	15.76	1 636.16	2 478 290	17.34	1 698.37
WESTERN PACIFIC (LOW CHILD, LOW ADULT MORTALITY)									
	2005			2015			2030		
Population	1 601 382 302			1 688 392 664			1 753 380 614		
TOTAL DALYs	242 183 984			241 587 312			245 479 984		
Epilepsy	1 072 726	0.44	66.99	969 657	0.40	57.43	851 044	0.35	48.54
Alzheimer and other dementias	2 563 998	1.06	160.11	3 271 378	1.35	193.76	4 852 313	1.98	276.74
Parkinson's disease	280 059	0.12	17.49	317 676	0.13	18.82	389 041	0.16	22.19
Multiple sclerosis	352 664	0.15	22.02	344 518	0.14	20.41	324 207	0.13	18.49
Migraine	1 749 402	0.72	109.24	1 677 157	0.69	99.33	1 485 053	0.60	84.70
Cerebrovascular disease	16 400 456	6.77	1 024.14	17 158 812	7.10	1 016.28	18 914 550	7.71	1 078.75
Poliomyelitis	31 706	0.01	1.98	10 943	0.00	0.65	2 173	0.00	0.12
Tetanus	268 357	0.11	16.76	114 934	0.05	6.81	41 286	0.02	2.35
Meningitis	607 530	0.25	37.94	310 381	0.13	18.38	136 147	0.06	7.76
Japanese encephalitis	226 304	0.09	14.13	93 314	0.04	5.53	35 030	0.01	2.00
Total	23 553 201	9.73	1 470.80	24 268 771	10.05	1 437.39	27 030 841	11.01	1 541.64

Table A.4.2 Burden of neurological disorders, in DALYs, by cause and country income category, projections for 2005, 2015 and 2030

	DALYs	% total	per 100 000	DALYs	% total	per 100 000	DALYs	% total	per 100 000
LOW INCOME									
	2005			2015			2030		
Population	2 698 990 297			3 157 941 695			3 786 445 271		
TOTAL DALYs	863 355 456			878 944 512			928 855 040		
Epilepsy	4 272 843	0.49	158.31	4 520 584	0.51	143.15	4 769 515	0.51	125.96
Alzheimer and other dementias	2 447 944	0.28	90.70	3 015 554	0.34	95.49	4 178 842	0.45	110.36
Parkinson's disease	407 152	0.05	15.09	468 466	0.05	14.83	592 196	0.06	15.64
Multiple sclerosis	542 866	0.06	20.11	633 335	0.07	20.06	742 842	0.08	19.62
Migraine	3 075 717	0.36	113.96	3 292 940	0.37	104.27	3 484 761	0.38	92.03
Cerebrovascular disease	17 881 426	2.07	662.52	20 698 738	2.35	655.45	26 672 044	2.87	704.41
Poliomyelitis	68 690	0.01	2.55	28 491	0.00	0.90	7 468	0.00	0.20
Tetanus	6 169 162	0.71	228.57	4 772 255	0.54	151.12	3 144 548	0.34	83.05
Meningitis	3 865 716	0.45	143.23	2 745 058	0.31	86.93	1 696 933	0.18	44.82
Japanese encephalitis	350 279	0.04	12.98	222 037	0.03	7.03	121 899	0.01	3.22
Total	39 081 794	4.53	1 448.02	40 397 457	4.60	1 279.23	45 411 047	4.89	1 199.31
LOWER MIDDLE INCOME									
	2005			2015			2030		
Population	2 267 665 265			2 394 506 774			2 504 674 883		
TOTAL DALYs	396 248 352			390 254 624			388 888 288		
Epilepsy	1 813 961	0.46	79.99	1 698 068	0.44	70.92	1 542 638	0.40	61.59
Alzheimer and other dementias	3 417 084	0.86	150.69	4 263 380	1.09	178.05	6 133 343	1.58	244.88
Parkinson's disease	446 605	0.11	19.69	482 673	0.12	20.16	560 720	0.14	22.39
Multiple sclerosis	527 563	0.13	23.26	518 073	0.13	21.64	493 924	0.13	19.72
Migraine	2 421 814	0.61	106.80	2 324 256	0.60	97.07	2 085 111	0.54	83.25
Cerebrovascular disease	24 063 276	6.07	1 061.15	24 385 588	6.25	1 018.40	25 586 734	6.58	1 021.56
Poliomyelitis	36 435	0.01	1.61	12 774	0.00	0.53	2 574	0.00	0.10
Tetanus	245 781	0.06	10.84	93 989	0.02	3.93	26 771	0.01	1.07
Meningitis	1 159 835	0.29	51.15	618 082	0.16	25.81	270 382	0.07	10.80
Japanese encephalitis	203 368	0.05	8.97	78 458	0.02	3.28	26 320	0.01	1.05
Total	34 335 721	8.67	1 514.14	34 475 340	8.83	1 439.77	36 728 516	9.44	1 466.40
UPPER MIDDLE INCOME									
	2005			2015			2030		
Population	528 081 304			574 892 329			622 970 241		
TOTAL DALYs	91 247 080			93 943 736			96 092 552		
Epilepsy	734 826	0.81	139.15	739 788	0.79	128.68	704 562	0.73	113.10
Alzheimer and other dementias	881 181	0.97	166.86	1 110 803	1.18	193.22	1 586 853	1.65	254.72
Parkinson's disease	92 265	0.10	17.47	101 366	0.11	17.63	114 497	0.12	18.38
Multiple sclerosis	131 579	0.14	24.92	136 702	0.15	23.78	135 916	0.14	21.82
Migraine	776 542	0.85	147.05	783 032	0.83	136.20	744 397	0.77	119.49
Cerebrovascular disease	3 232 834	3.54	612.18	3 361 867	3.58	584.78	3 570 041	3.72	573.07
Poliomyelitis	4 860	0.01	0.92	1 957	0.00	0.34	499	0.00	0.08
Tetanus	6 993	0.01	1.32	4 032	0.00	0.70	1 959	0.00	0.31
Meningitis	209 522	0.23	39.68	104 866	0.11	18.24	41 624	0.04	6.68
Japanese encephalitis	1 824	0.00	0.35	945	0.00	0.16	405	0.00	0.07
Total	6 072 426	6.65	1 149.90	6 345 357	6.75	1 103.75	6 900 753	7.18	1 107.72
HIGH INCOME									
	2005			2015			2030		
Population	947 138 427			975 884 050			1 002 892 462		
TOTAL DALYs	118 750 184			118 245 712			112 894 104		
Epilepsy	486 287	0.41	51.34	460 841	0.39	47.22	424 689	0.38	42.35
Alzheimer and other dementias	4 331 265	3.65	457.30	5 149 842	4.36	527.71	6 495 107	5.75	647.64
Parkinson's disease	670 491	0.56	70.79	709 829	0.60	72.74	747 640	0.66	74.55
Multiple sclerosis	307 679	0.26	32.49	297 810	0.25	30.52	275 597	0.24	27.48
Migraine	1 385 579	1.17	146.29	1 335 981	1.13	136.90	1 281 723	1.14	127.80
Cerebrovascular disease	5 606 824	4.72	591.98	5 368 321	4.54	550.10	5 034 698	4.46	502.02
Poliomyelitis	5 180	0.00	0.55	3 723	0.00	0.38	2 719	0.00	0.27
Tetanus	673	0.00	0.07	489	0.00	0.05	353	0.00	0.04
Meningitis	101 685	0.09	10.74	59 427	0.05	6.09	29 921	0.03	2.98
Japanese encephalitis	5 563	0.00	0.59	2 680	0.00	0.27	1 303	0.00	0.13
Total	12 901 225	10.86	1 362.13	13 388 941	11.32	1 371.98	14 293 750	12.66	1 425.25

Table A.4.3 Deaths attributable to neurological disorders, by cause, WHO region and mortality stratum, projections for 2005, 2015 and 2030

	Deaths	% total	per 100 000	Deaths	% total	per 100 000	Deaths	% total	per 100 000
WORLD									
	2005			**2015**			**2030**		
Population	**6 441 919 466**			**7 103 297 899**			**7 917 115 397**		
TOTAL DALYs	58 028 152			63 458 962			73 247 767		
Epilepsy	126 096	0.22	1.96	130 569	0.21	1.84	139 276	0.19	1.76
Alzheimer and other dementias	425 331	0.73	6.60	513 230	0.81	7.23	671 372	0.92	8.48
Parkinson's disease	105 012	0.18	1.63	127 293	0.20	1.79	165 418	0.23	2.09
Multiple sclerosis	16 275	0.03	0.25	16 669	0.03	0.23	17 012	0.02	0.21
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	5 745 748	9.90	89.19	6 466 232	10.19	91.03	7 787 656	10.63	98.36
Poliomyelitis	774	0.00	0.01	654	0.00	0.01	577	0.00	0.01
Tetanus	191 592	0.33	2.97	145 640	0.23	2.05	95 587	0.13	1.21
Meningitis	152 004	0.26	2.36	106 372	0.17	1.50	69 946	0.10	0.88
Japanese encephalitis	11 625	0.02	0.18	7 282	0.01	0.10	4 318	0.01	0.05
Total	6 774 457	11.67	105.16	7 513 942	11.84	105.78	8 951 162	12.22	113.06
AFRICA (HIGH CHILD, HIGH ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**335 459 111**			**419 571 880**			**550 082 900**		
TOTAL DALYs	4 784 001			5 361 866			6 219 324		
Epilepsy	19 203	0.40	5.72	23 662	0.44	5.64	30 834	0.50	5.61
Alzheimer and other dementias	3 462	0.07	1.03	4 403	0.08	1.05	5 877	0.09	1.07
Parkinson's disease	2 610	0.05	0.78	3 344	0.06	0.80	4 501	0.07	0.82
Multiple sclerosis	144	0.00	0.04	180	0.00	0.04	251	0.00	0.05
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	186 783	3.90	55.68	240 909	4.49	57.42	340 954	5.48	61.98
Poliomyelitis	22	0.00	0.01	20	0.00	0.00	15	0.00	0.00
Tetanus	47 653	1.00	14.21	45 915	0.86	10.94	35 731	0.57	6.50
Meningitis	8 225	0.17	2.45	8 212	0.15	1.96	7 203	0.12	1.31
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	268 102	5,60	79.92	326 645	6,09	77.85	425 366	6,84	77.33
AFRICA (HIGH CHILD, VERY HIGH ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**382 647 820**			**478 419 411**			**628 734 321**		
TOTAL DALYs	6 097 012			6 767 650			7 914 237		
Epilepsy	21 099	0.35	5.51	24 959	0.37	5.22	31 346	0.40	4.99
Alzheimer and other dementias	3 975	0.07	1.04	5 051	0.07	1.06	6 401	0.08	1.02
Parkinson's disease	2 956	0.05	0.77	3 801	0.06	0.79	4 860	0.06	0.77
Multiple sclerosis	183	0.00	0.05	214	0.00	0.04	274	0.00	0.04
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	203 945	3.35	53.30	255 352	3.77	53.37	340 351	4.30	54.13
Poliomyelitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Tetanus	34 832	0.57	9.10	33 288	0.49	6.96	26 878	0.34	4.27
Meningitis	11 250	0.18	2.94	10 233	0.15	2.14	8 462	0.11	1.35
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	278 240	4,56	72.71	332 899	4,92	69.58	418 572	5,29	66.57
THE AMERICAS (VERY LOW CHILD, VERY LOW ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**343 363 701**			**372 395 661**			**413 323 652**		
TOTAL DALYs	2 805 833			2 999 574			3 450 260		
Epilepsy	1 863	0.07	0.54	1 870	0.06	0.50	1 904	0.06	0.46
Alzheimer and other dementias	111 596	3.98	32.50	123 880	4.13	33.27	170 499	4.94	41.25
Parkinson's disease	20 348	0.73	5.93	23 466	0.78	6.30	32 175	0.93	7.78
Multiple sclerosis	3 735	0.13	1.09	3 896	0.13	1.05	3 910	0.11	0.95
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	192 402	6.86	56.03	200 803	6.69	53.92	243 062	7.04	58.81
Poliomyelitis	369	0.01	0.11	355	0.01	0.10	369	0.01	0.09
Tetanus	5	0.00	0.00	6	0.00	0.00	6	0.00	0.00
Meningitis	1 186	0.04	0.35	941	0.03	0.25	747	0.02	0.18
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	331 503	11.81	96.55	355 216	11.84	95.39	452 671	13.12	109.52

	Deaths	% total	per 100 000	Deaths	% total	per 100 000	Deaths	% total	per 100 000
THE AMERICAS (LOW CHILD, LOW ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**463 707 779**			**511 277 519**			**560 127 320**		
TOTAL DALYs	2 869 172			3 406 656			4 251 795		
Epilepsy	6 045	0.21	1.30	6 268	0.18	1.23	6 334	0.15	1.13
Alzheimer and other dementias	12 463	0.43	2.69	15 929	0.47	3.12	22 295	0.52	3.98
Parkinson's disease	4 281	0.15	0.92	5 479	0.16	1.07	7 933	0.19	1.42
Multiple sclerosis	903	0.03	0.19	1 058	0.03	0.21	1 291	0.03	0.23
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	248 042	8.65	53.49	285 390	8.38	55.82	371 920	8.75	66.40
Poliomyelitis	14	0.00	0.00	10	0.00	0.00	5	0.00	0.00
Tetanus	226	0.01	0.05	146	0.00	0.03	96	0.00	0.02
Meningitis	6 986	0.24	1.51	4 086	0.12	0.80	2 130	0.05	0.38
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	278 960	9.72	60.16	318 365	9.35	62.27	412 003	9.69	73.56
THE AMERICAS (HIGH CHILD, HIGH ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**77 739 657**			**90 194 020**			**106 740 220**		
TOTAL DALYs	543 838			591 295			724 097		
Epilepsy	1 568	0.29	2.02	1 749	0.30	1.94	1 931	0.27	1.81
Alzheimer and other dementias	600	0.11	0.77	713	0.12	0.79	1 011	0.14	0.95
Parkinson's disease	699	0.13	0.90	864	0.15	0.96	1 286	0.18	1.20
Multiple sclerosis	37	0.01	0.05	44	0.01	0.05	55	0.01	0.05
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	28 472	5.24	36.62	34 757	5.88	38.54	48 277	6.67	45.23
Poliomyelitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Tetanus	221	0.04	0.28	150	0.03	0.17	79	0.01	0.07
Meningitis	7 676	1.41	9.87	5 381	0.91	5.97	3 064	0.42	2.87
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	39 271	7.22	50.52	43 659	7.38	48.41	55 704	7.69	52.19
SOUTH-EAST ASIA (LOW CHILD, LOW ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**308 761 163**			**336 961 332**			**364 048 380**		
TOTAL DALYs	2 220 363			2 492 408			3 083 806		
Epilepsy	5 031	0.23	1.63	4 641	0.19	1.38	4 155	0.13	1.14
Alzheimer and other dementias	9 836	0.44	3.19	13 829	0.55	4.10	19 577	0.63	5.38
Parkinson's disease	1 551	0.07	0.50	2 168	0.09	0.64	3 110	0.10	0.85
Multiple sclerosis	148	0.01	0.05	183	0.01	0.05	224	0.01	0.06
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	172 702	7.78	55.93	216 099	8.67	64.13	274 913	8.91	75.52
Poliomyelitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Tetanus	5 735	0.26	1.86	2 086	0.08	0.62	481	0.02	0.13
Meningitis	8 049	0.36	2.61	5 398	0.22	1.60	3 521	0.11	0.97
Japanese encephalitis	195	0.01	0.06	129	0.01	0.04	80	0.00	0.02
Total	203 248	9.15	65.83	244 534	9.81	72.57	306 062	9.92	84.07
SOUTH-EAST ASIA (HIGH CHILD, HIGH ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**1 352 957 715**			**1 525 318 552**			**1 718 832 463**		
TOTAL DALYs	12 368 446			12 943 856			14 999 705		
Epilepsy	27 634	0.22	2.04	25 583	0.20	1.68	23 277	0.16	1.35
Alzheimer and other dementias	86 338	0.70	6.38	108 673	0.84	7.12	148 917	0.99	8.66
Parkinson's disease	9 598	0.08	0.71	12 086	0.09	0.79	16 467	0.11	0.96
Multiple sclerosis	1 230	0.01	0.09	1 417	0.01	0.09	1 725	0.01	0.10
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	963 383	7.79	71.21	1 166 198	9.01	76.46	1 568 600	10.46	91.26
Poliomyelitis	143	0.00	0.01	79	0.00	0.01	34	0.00	0.00
Tetanus	60 687	0.49	4.49	33 875	0.26	2.22	14 848	0.10	0.86
Meningitis	56 178	0.45	4.15	38 059	0.29	2.50	25 629	0.17	1.49
Japanese encephalitis	7 233	0.06	0.53	4 735	0.04	0.31	2 954	0.02	0.17
Total	1 212 424	9.80	89.61	1 390 705	10.74	91.17	1 802 452	12.02	104.86

	Deaths	% total	per 100 000	Deaths	% total	per 100 000	Deaths	% total	per 100 000
EUROPE (VERY LOW CHILD, VERY LOW ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**417 799 202**			**417 841 350**			**411 754 930**		
TOTAL DALYs	4 019 118			4 364 652			4 356 278		
Epilepsy	6 061	0.15	1.45	6 033	0.14	1.44	5 647	0.13	1.37
Alzheimer and other dementias	102 492	2.55	24.53	122 786	2.81	29.39	138 128	3.17	33.55
Parkinson's disease	23 516	0.59	5.63	28 938	0.66	6.93	32 551	0.75	7.91
Multiple sclerosis	4 071	0.10	0.97	3 974	0.09	0.95	3 554	0.08	0.86
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	410 165	10.21	98.17	427 915	9.80	102.41	420 472	9.65	102.12
Poliomyelitis	161	0.00	0.04	139	0.00	0.03	116	0.00	0.03
Tetanus	74	0.00	0.02	61	0.00	0.01	49	0.00	0.01
Meningitis	2 011	0.05	0.48	1 440	0.03	0.34	978	0.02	0.24
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	548 551	13.65	131.30	591 287	13.55	141.51	601 496	13.81	146.08
EUROPE (LOW CHILD, LOW ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**227 350 229**			**236 868 370**			**243 016 939**		
TOTAL DALYs	1 937 483			2 125 833			2 282 373		
Epilepsy	4 147	0.21	1.82	4 104	0.19	1.73	3 909	0.17	1.61
Alzheimer and other dementias	3 577	0.18	1.57	3 906	0.18	1.65	4 286	0.19	1.76
Parkinson's disease	1 837	0.09	0.81	1 951	0.09	0.82	2 138	0.09	0.88
Multiple sclerosis	1 362	0.07	0.60	1 383	0.07	0.58	1 448	0.06	0.60
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	298 450	15.40	131.27	328 305	15.44	138.60	350 321	15.35	144.15
Poliomyelitis	2	0.00	0.00	1	0.00	0.00	1	0.00	0.00
Tetanus	82	0.00	0.04	49	0.00	0.02	30	0.00	0.01
Meningitis	7 760	0.40	3.41	3 902	0.18	1.65	1 726	0.08	0.71
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	317 216	16.37	139.53	343 601	16.16	145.06	363 860	15.94	149.73
EUROPE (LOW CHILD, HIGH ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**235 511 792**			**206 753 120**			**175 407 940**		
TOTAL DALYs	3 819 475			3 566 264			2 904 723		
Epilepsy	4 319	0.11	1.83	3 223	0.09	1.56	2 238	0.08	1.28
Alzheimer and other dementias	6 406	0.17	2.72	6 120	0.17	2.96	5 439	0.19	3.10
Parkinson's disease	1 504	0.04	0.64	1 438	0.04	0.70	1 274	0.04	0.73
Multiple sclerosis	2 293	0.06	0.97	1 844	0.05	0.89	1 359	0.05	0.77
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	766 147	20.06	325.31	752 231	21.09	363.83	633 833	21.82	361.35
Poliomyelitis	7	0.00	0.00	3	0.00	0.00	1	0.00	0.00
Tetanus	44	0.00	0.02	30	0.00	0.01	22	0.00	0.01
Meningitis	2 649	0.07	1.12	1 351	0.04	0.65	641	0.02	0.37
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	783 370	20.51	332.62	766 239	21.49	370.61	644 807	22.20	367.60
EASTERN MEDITERRANEAN (LOW CHILD, LOW ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**150 452 139**			**176 204 370**			**207 555 239**		
TOTAL DALYs	740 590			876 987			1 191 727		
Epilepsy	1 853	0.25	1.23	1 953	0.22	1.11	2 158	0.18	1.04
Alzheimer and other dementias	2 186	0.30	1.45	2 977	0.34	1.69	4 690	0.39	2.26
Parkinson's disease	1 803	0.24	1.20	2 203	0.25	1.25	3 164	0.27	1.52
Multiple sclerosis	272	0.04	0.18	326	0.04	0.19	433	0.04	0.21
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	58 439	7.89	38.84	72 354	8.25	41.06	107 995	9.06	52.03
Poliomyelitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Tetanus	112	0.02	0.07	56	0.01	0.03	18	0.00	0.01
Meningitis	1 831	0.25	1.22	1 014	0.12	0.58	480	0.04	0.23
Japanese encephalitis	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	66 497	8.98	44.20	80 882	9.22	45.90	118 939	9.98	57.30

	Deaths	% total	per 100 000	Deaths	% total	per 100 000	Deaths	% total	per 100 000
EASTERN MEDITERRANEAN (HIGH CHILD, HIGH ADULT MORTALITY)									
	2005			2015			2030		
Population	388 102 585			488 304 210			638 188 559		
TOTAL DALYs	3 522 774			3 867 656			4 577 913		
Epilepsy	8 704	0.25	2.24	9 518	0.25	1.95	10 283	0.22	1.61
Alzheimer and other dementias	10 072	0.29	2.60	13 189	0.34	2.70	20 151	0.44	3.16
Parkinson's disease	1 682	0.05	0.43	2 120	0.05	0.43	3 044	0.07	0.48
Multiple sclerosis	493	0.01	0.13	621	0.02	0.13	861	0.02	0.13
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	186 281	5.29	48.00	238 972	6.18	48.94	344 667	7.53	54.01
Poliomyelitis	11	0.00	0.00	8	0.00	0.00	4	0.00	0.00
Tetanus	33 662	0.96	8.67	26 309	0.68	5.39	15 885	0.35	2.49
Meningitis	21 861	0.62	5.63	16 787	0.43	3.44	9 925	0.22	1.56
Japanese encephalitis	2 169	0.06	0.56	1 650	0.04	0.34	986	0.02	0.15
Total	264 936	7.52	68.26	309 174	7.99	63.32	405 805	8.86	63.59
WESTERN PACIFIC (VERY LOW CHILD, VERY LOW ADULT MORTALITY)									
	2005			2015			2030		
Population	156 684 271			154 795 439			145 921 920		
TOTAL DALYs	1 224 679			1 435 189			1 443 363		
Epilepsy	878	0.07	0.56	862	0.06	0.56	787	0.05	0.54
Alzheimer and other dementias	11 140	0.91	7.11	14 497	1.01	9.37	18 527	1.28	12.70
Parkinson's disease	4 745	0.39	3.03	6 049	0.42	3.91	6 913	0.48	4.74
Multiple sclerosis	225	0.02	0.14	235	0.02	0.15	239	0.02	0.16
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	154 475	12.61	98.59	176 628	12.31	114.10	175 495	12.16	120.27
Poliomyelitis	34	0.00	0.02	30	0.00	0.02	27	0.00	0.02
Tetanus	12	0.00	0.01	12	0.00	0.01	11	0.00	0.01
Meningitis	401	0.03	0.26	344	0.02	0.22	260	0.02	0.18
Japanese encephalitis	1	0.00	0.00	1	0.00	0.00	1	0.00	0.00
Total	171 910	14.04	109.72	198 660	13.84	128.34	202 259	14.01	138.61
WESTERN PACIFIC (LOW CHILD, LOW ADULT MORTALITY)									
	2005			2015			2030		
Population	1 601 382 302			1 688 392 664			1 753 380 614		
TOTAL DALYs	11 075 368			12 659 077			15 848 165		
Epilepsy	17 690	0.16	1.10	16 143	0.13	0.96	14 471	0.13	0.83
Alzheimer and other dementias	61 187	0.55	3.82	77 277	0.61	4.58	105 573	0.61	6.02
Parkinson's disease	27 882	0.25	1.74	33 387	0.26	1.98	46 002	0.26	2.62
Multiple sclerosis	1 179	0.01	0.07	1 294	0.01	0.08	1 389	0.01	0.08
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	1 876 062	16.94	117.15	2 070 319	16.35	122.62	2 566 796	16.35	146.39
Poliomyelitis	12	0.00	0.00	8	0.00	0.00	5	0.00	0.00
Tetanus	8 247	0.07	0.51	3 657	0.03	0.22	1 453	0.03	0.08
Meningitis	15 941	0.14	1.00	9 224	0.07	0.55	5 180	0.07	0.30
Japanese encephalitis	2 027	0.02	0.13	766	0.01	0.05	297	0.01	0.02
Total	2 010 227	18.15	125.53	2 212 076	17.47	131.02	2 741 165	17.47	156.34

Table A.4.4 Deaths attributable to neurological disorders, by cause and country income category, projections for 2005, 2015 and 2030

	Deaths	% total	per 100 000	Deaths	% total	per 100 000	Deaths	% total	per 100 000
LOW INCOME									
	2005			**2015**			**2030**		
Population	**2 698 990 297**			**3 157 941 695**			**3 786 445 271**		
TOTAL DALYs	28 672 778			30 854 969			35 900 272		
Epilepsy	79 248	0.28	2.94	85 525	0.28	2.71	96 579	0.27	2.55
Alzheimer and other dementias	117 006	0.41	4.34	147 611	0.48	4.67	203 293	0.57	5.37
Parkinson's disease	18 481	0.06	0.68	23 210	0.08	0.73	31 322	0.09	0.83
Multiple sclerosis	2 557	0.01	0.09	2 848	0.01	0.09	3 377	0.01	0.09
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	1 839 308	6.41	68.15	2 212 111	7.17	70.05	2 926 235	8.15	77.28
Poliomyelitis	177	0.00	0.01	108	0.00	0.00	53	0.00	0.00
Tetanus	183 622	0.64	6.80	142 332	0.46	4.51	94 390	0.26	2.49
Meningitis	110 589	0.39	4.10	81 490	0.26	2.58	55 933	0.16	1.48
Japanese encephalitis	10 003	0.03	0.37	6 800	0.02	0.22	4 209	0.01	0.11
Total	2 360 989	8.23	87.48	2 702 035	8.76	85.56	3 415 391	9.51	90.20
LOWER MIDDLE INCOME									
	2005			**2015**			**2030**		
Population	**2 267 665 265**			**2 394 506 774**			**2 504 674 883**		
TOTAL DALYs	17 652 714			19 527 556			22 973 178		
Epilepsy	30 565	0.17	1.35	28 746	0.15	1.20	26 985	0.12	1.08
Alzheimer and other dementias	60 684	0.34	2.68	74 768	0.38	3.12	100 342	0.44	4.01
Parkinson's disease	31 952	0.18	1.41	38 119	0.20	1.59	51 958	0.23	2.07
Multiple sclerosis	4 124	0.02	0.18	4 088	0.02	0.17	4 154	0.02	0.17
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	2 791 658	15.81	123.11	3 045 869	15.60	127.20	3 537 725	15.40	141.24
Poliomyelitis	12	0.00	0.00	8	0.00	0.00	5	0.00	0.00
Tetanus	7 584	0.04	0.33	3 027	0.02	0.13	994	0.00	0.04
Meningitis	32 066	0.18	1.41	18 680	0.10	0.78	10 009	0.04	0.40
Japanese encephalitis	1 620	0.01	0.07	481	0.00	0.02	109	0.00	0.00
Total	2 960 266	16.77	130.54	3 213 785	16.46	134.21	3 732 280	16.25	149.01
UPPER MIDDLE INCOME									
	2005			**2015**			**2030**		
Population	**528 081 304**			**574 892 329**			**622 970 241**		
TOTAL DALYs	3 566 059			4 137 547			4 903 171		
Epilepsy	7 115	0.20	1.35	7 168	0.17	1.25	6 984	0.14	1.12
Alzheimer and other dementias	16 506	0.46	3.13	20 434	0.49	3.55	27 069	0.55	4.35
Parkinson's disease	5 439	0.15	1.03	6 807	0.16	1.18	9 432	0.19	1.51
Multiple sclerosis	1 736	0.05	0.33	1 796	0.04	0.31	1 909	0.04	0.31
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	343 741	9.64	65.09	389 884	9.42	67.82	464 680	9.48	74.59
Poliomyelitis	16	0.00	0.00	12	0.00	0.00	7	0.00	0.00
Tetanus	284	0.01	0.05	190	0.00	0.03	124	0.00	0.02
Meningitis	5 750	0.16	1.09	3 481	0.08	0.61	2 013	0.04	0.32
Japanese encephalitis	1	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Total	380 587	10.67	72.07	429 773	10.39	74.76	512 219	10.45	82.22
HIGH INCOME									
	2005			**2015**			**2030**		
Population	**947 138 427**			**975 884 050**			**1 002 892 462**		
TOTAL DALYs	8 136 260			8 938 508			9 470 662		
Epilepsy	9 168	0.11	0.97	9 129	0.10	0.94	8 725	0.09	0.87
Alzheimer and other dementias	231 134	2.84	24.40	270 416	3.03	27.71	340 667	3.60	33.97
Parkinson's disease	49 139	0.60	5.19	59 155	0.66	6.06	72 704	0.77	7.25
Multiple sclerosis	7 857	0.10	0.83	7 938	0.09	0.81	7 572	0.08	0.76
Migraine	0	0.00	0.00	0	0.00	0.00	0	0.00	0.00
Cerebrovascular disease	771 010	9.48	81.40	818 338	9.16	83.86	858 977	9.07	85.65
Poliomyelitis	570	0.01	0.06	527	0.01	0.05	512	0.01	0.05
Tetanus	103	0.00	0.01	90	0.00	0.01	78	0.00	0.01
Meningitis	3 595	0.04	0.38	2 718	0.03	0.28	1 988	0.02	0.20
Japanese encephalitis	1	0.00	0.00	1	0.00	0.00	1	0.00	0.00
Total	1 072 577	13.18	113.24	1 168 312	13.07	119.72	1 291 225	13.63	128.75

Table A.4.5 Burden of neurological disorders, in YLDs, by cause, WHO region and mortality stratum, projections for 2005, 2015 and 2030

	YLDs	% total	per 100 000	YLDs	% total	per 100 000	YLDs	% total	per 100 000
WORLD									
	2005			**2015**			**2030**		
Population	**6 441 919 466**			**7 103 297 899**			**7 917 115 397**		
TOTAL DALYs	570 766 387			592 406 432			620 989 911		
Epilepsy	4 167 285	0.73	64.69	4 323 495	0.73	60.87	4 402 862	0.71	55.61
Alzheimer and other dementias	9 494 517	1.66	147.39	11 750 573	1.98	165.42	16 144 423	2.60	203.92
Parkinson's disease	1 137 991	0.20	17.67	1 228 128	0.21	17.29	1 353 366	0.22	17.09
Multiple sclerosis	1 286 458	0.23	19.97	1 371 367	0.23	19.31	1 453 083	0.23	18.35
Migraine	7 659 687	1.34	118.90	7 736 261	1.31	108.91	7 596 089	1.22	95.95
Cerebrovascular disease	11 389 442	2.00	176.80	12 423 121	2.10	174.89	14 073 668	2.27	177.76
Neuroinfections	6 337 373	1.11	98.38	5 099 627	0.86	71.79	3 613 205	0.58	45.64
Nutritional and neuropathies	12 557 068	2.20	194.93	12 381 343	2.09	174.30	10 603 690	1.71	133.93
Neurological injuries	27 402 985	4.80	425.39	27 952 326	4.72	393.51	28 566 683	4.60	360.82
Total	81 432 806	14.27	1 264.11	84 266 242	14.22	1 186.30	87 807 069	14.14	1 109.08
AFRICA (HIGH CHILD, HIGH ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**335 459 111**			**419 571 880**			**550 082 900**		
TOTAL DALYs	39 757 166			46 874 383			55 477 689		
Epilepsy	283 212	0.71	84.43	340 342	0.73	81.12	391 907	0.71	71.25
Alzheimer and other dementias	150 597	0.38	44.89	187 472	0.40	44.68	259 332	0.47	47.14
Parkinson's disease	25 093	0.06	7.48	30 415	0.06	7.25	43 450	0.08	7.90
Multiple sclerosis	58 067	0.15	17.31	75 385	0.16	17.97	101 149	0.18	18.39
Migraine	206 278	0.52	61.49	255 460	0.54	60.89	315 904	0.57	57.43
Cerebrovascular disease	201 642	0.51	60.11	258 428	0.55	61.59	386 282	0.70	70.22
Neuroinfections	1 883 305	4.74	561.41	1 787 505	3.81	426.03	1 388 398	2.50	252.40
Nutritional and neuropathies	1 234 252	3.10	367.93	1 288 195	2.75	307.03	1 198 182	2.16	217.82
Neurological injuries	1 993 030	5.01	594.12	2 506 683	5.35	597.44	3 281 196	5.91	596.49
Total	6 035 477	15.18	1 799.17	6 729 886	14.36	1 603.99	7 365 799	13.28	1 339.03
AFRICA (HIGH CHILD, VERY HIGH ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**382 647 820**			**478 419 411**			**628 734 321**		
TOTAL DALYs	45 155 172			52 429 855			62 319 016		
Epilepsy	409 059	0.91	106.90	480 175	0.92	100.37	567 435	0.91	90.25
Alzheimer and other dementias	156 813	0.35	40.98	195 498	0.37	40.86	253 632	0.41	40.34
Parkinson's disease	27 746	0.06	7.25	31 434	0.06	6.57	43 185	0.07	6.87
Multiple sclerosis	44 545	0.10	11.64	58 521	0.11	12.23	82 066	0.13	13.05
Migraine	267 571	0.59	69.93	321 413	0.61	67.18	391 515	0.63	62.27
Cerebrovascular disease	197 776	0.44	51.69	238 846	0.46	49.92	335 577	0.54	53.37
Neuroinfections	1 896 016	4.20	495.50	1 787 682	3.41	373.66	1 412 743	2.27	224.70
Nutritional and neuropathies	1 792 207	3.97	468.37	1 775 869	3.39	371.20	1 552 311	2.49	246.89
Neurological injuries	1 608 254	3.56	420.30	2 020 694	3.85	422.37	2 729 220	4.38	434.08
Total	6 399 986	14.17	1 672.55	6 910 130	13.18	1 444.37	7 367 685	11.82	1 171.83
THE AMERICAS (VERY LOW CHILD, VERY LOW ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**343 363 701**			**372 395 661**			**413 323 652**		
TOTAL DALYs	27 424 860			29 218 777			30 362 527		
Epilepsy	142 844	0.52	41.60	145 672	0.50	39.12	148 862	0.49	36.02
Alzheimer and other dementias	1 098 397	4.01	319.89	1 321 126	4.52	354.76	1 881 645	6.20	455.25
Parkinson's disease	193 420	0.71	56.33	213 375	0.73	57.30	233 076	0.77	56.39
Multiple sclerosis	74 882	0.27	21.81	78 170	0.27	20.99	83 615	0.28	20.23
Migraine	511 142	1.86	148.86	526 028	1.80	141.26	559 602	1.84	135.39
Cerebrovascular disease	800 860	2.92	233.24	844 620	2.89	226.81	852 316	2.81	206.21
Neuroinfections	53 322	0.19	15.53	28 613	0.10	7.68	11 942	0.04	2.89
Nutritional and neuropathies	439 068	1.60	127.87	764 411	2.62	205.27	723 902	2.38	175.14
Neurological injuries	629 861	2.30	183.44	578 786	1.98	155.42	507 043	1.67	122.67
Total	3 943 797	14.38	1 148.58	4 500 801	15.40	1 208.61	5 002 001	16.47	1 210.19

	YLDs	% total	per 100 000	YLDs	% total	per 100 000	YLDs	% total	per 100 000
THE AMERICAS (LOW CHILD, LOW ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**463 707 779**			**511 277 519**			**560 127 320**		
TOTAL DALYs	45 054 114			46 814 643			48 413 568		
Epilepsy	612 176	1.36	132.02	630 457	1.35	123.31	616 295	1.27	110.03
Alzheimer and other dementias	652 387	1.45	140.69	853 641	1.82	166.96	1 315 578	2.72	234.87
Parkinson's disease	36 931	0.08	7.96	43 162	0.09	8.44	50 015	0.10	8.93
Multiple sclerosis	95 617	0.21	20.62	101 743	0.22	19.90	103 463	0.21	18.47
Migraine	760 969	1.69	164.11	783 250	1.67	153.19	759 916	1.57	135.67
Cerebrovascular disease	691 265	1.53	149.07	797 905	1.70	156.06	935 815	1.93	167.07
Neuroinfections	231 993	0.51	50.03	123 838	0.26	24.22	58 135	0.12	10.38
Nutritional and neuropathies	461 022	1.02	99.42	630 089	1.35	123.24	619 622	1.28	110.62
Neurological injuries	3 112 433	6.91	671.21	3 306 741	7.06	646.76	3 424 932	7.07	611.46
Total	6 654 794	14.77	1 435.13	7 270 826	15.53	1 422.09	7 883 770	16.28	1 407.50
THE AMERICAS (HIGH CHILD, HIGH ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**77 739 657**			**90 194 020**			**106 740 220**		
TOTAL DALYs	7 526 243			8 100 445			8 797 225		
Epilepsy	107 611	1.43	138.42	118 806	1.47	131.72	125 913	1.43	117.96
Alzheimer and other dementias	78 281	1.04	100.70	98 776	1.22	109.51	149 912	1.70	140.45
Parkinson's disease	4 058	0.05	5.22	4 791	0.06	5.31	6 185	0.07	5.79
Multiple sclerosis	15 849	0.21	20.39	18 521	0.23	20.53	21 164	0.24	19.83
Migraine	155 043	2.06	199.44	165 994	2.05	184.04	171 234	1.95	160.42
Cerebrovascular disease	59 933	0.80	77.09	75 746	0.94	83.98	104 519	1.19	97.92
Neuroinfections	53 657	0.71	69.02	35 231	0.43	39.06	17 348	0.20	16.25
Nutritional and neuropathies	94 844	1.26	122.00	121 415	1.50	134.61	121 256	1.38	113.60
Neurological injuries	379 972	5.05	488.77	423 553	5.23	469.60	455 172	5.17	426.43
Total	949 248	12.61	1 221.06	1 062 833	13.12	1 178.38	1 172 703	13.33	1 098.65
SOUTH-EAST ASIA (LOW CHILD, LOW ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**308 761 163**			**336 961 332**			**364 048 380**		
TOTAL DALYs	29 192 942			29 559 126			30 625 968		
Epilepsy	230 664	0.79	74.71	228 970	0.77	67.95	219 000	0.72	60.16
Alzheimer and other dementias	342 972	1.17	111.08	461 668	1.56	137.01	702 335	2.29	192.92
Parkinson's disease	29 751	0.10	9.64	33 833	0.11	10.04	35 286	0.12	9.69
Multiple sclerosis	62 728	0.21	20.32	65 397	0.22	19.41	64 881	0.21	17.82
Migraine	339 628	1.16	110.00	329 367	1.11	97.75	305 781	1.00	83.99
Cerebrovascular disease	358 648	1.23	116.16	417 908	1.41	124.02	506 734	1.65	139.19
Neuroinfections	148 955	0.51	48.24	65 463	0.22	19.43	23 302	0.08	6.40
Nutritional and neuropathies	705 161	2.42	228.38	650 504	2.20	193.05	534 179	1.74	146.73
Neurological injuries	1 159 558	3.97	375.55	1 141 632	3.86	338.80	1 055 000	3.44	289.80
Total	3 378 064	11.57	1 094.07	3 394 742	11.48	1 007.46	3 446 499	11.25	946.71
SOUTH-EAST ASIA (HIGH CHILD, HIGH ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**1 352 957 715**			**1 525 318 552**			**1 718 832 463**		
TOTAL DALYs	131 383 680			134 080 889			138 967 789		
Epilepsy	1 035 382	0.79	76.53	1 048 587	0.78	68.75	1 024 835	0.74	59.62
Alzheimer and other dementias	947 241	0.72	70.01	1 195 702	0.89	78.39	1 680 655	1.21	97.78
Parkinson's disease	180 689	0.14	13.36	207 974	0.16	13.63	257 984	0.19	15.01
Multiple sclerosis	270 885	0.21	20.02	308 778	0.23	20.24	338 732	0.24	19.71
Migraine	1 756 274	1.34	129.81	1 793 948	1.34	117.61	1 783 945	1.28	103.79
Cerebrovascular disease	1 693 829	1.29	125.19	2 016 085	1.50	132.17	2 646 134	1.90	153.95
Neuroinfections	670 551	0.51	49.56	390 475	0.29	25.60	192 850	0.14	11.22
Nutritional and neuropathies	2 996 430	2.28	221.47	2 565 498	1.91	168.19	2 075 062	1.49	120.73
Neurological injuries	7 357 484	5.60	543.81	7 407 802	5.52	485.66	7 250 907	5.22	421.85
Total	16 908 766	12.87	1 249.76	16 934 850	12.63	1 110.25	17 251 104	12.41	1 003.65

	YLDs	% total	per 100 000	YLDs	% total	per 100 000	YLDs	% total	per 100 000
EUROPE (VERY LOW CHILD, VERY LOW ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**417 799 202**			**417 841 350**			**411 754 930**		
TOTAL DALYs	27 610 816			26 642 716			24 777 376		
Epilepsy	155 845	0.56	37.30	146 958	0.55	35.17	134 248	0.54	32.60
Alzheimer and other dementias	1 803 137	6.53	431.58	2 106 469	7.91	504.13	2 529 668	10.21	614.36
Parkinson's disease	214 964	0.78	51.45	215 201	0.81	51.50	209 109	0.84	50.78
Multiple sclerosis	106 037	0.38	25.38	99 719	0.37	23.87	90 370	0.36	21.95
Migraine	721 342	2.61	172.65	670 731	2.52	160.52	600 497	2.42	145.84
Cerebrovascular disease	964 090	3.49	230.75	922 228	3.46	220.71	865 531	3.49	210.21
Neuroinfections	75 613	0.27	18.10	57 040	0.21	13.65	46 731	0.19	11.35
Nutritional and neuropathies	281 902	1.02	67.47	305 417	1.15	73.09	269 085	1.09	65.35
Neurological injuries	626 253	2.27	149.89	517 606	1.94	123.88	384 566	1.55	93.40
Total	4 949 182	17.92	1 184.58	5 041 370	18.92	1 206.53	5 129 805	20.70	1 245.84
EUROPE (LOW CHILD, LOW ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**227 350 229**			**236 868 370**			**243 016 939**		
TOTAL DALYs	17 678 271			17 368 886			16 773 659		
Epilepsy	87 172	0.49	38.34	84 516	0.49	35.68	78 059	0.47	32.12
Alzheimer and other dementias	379 974	2.15	167.13	443 628	2.55	187.29	564 896	3.37	232.45
Parkinson's disease	51 897	0.29	22.83	53 876	0.31	22.75	58 399	0.35	24.03
Multiple sclerosis	45 790	0.26	20.14	46 291	0.27	19.54	43 580	0.26	17.93
Migraine	250 906	1.42	110.36	233 551	1.34	98.60	207 238	1.24	85.28
Cerebrovascular disease	534 109	3.02	234.93	551 693	3.18	232.91	599 220	3.57	246.58
Neuroinfections	52 903	0.30	23.27	31 345	0.18	13.23	17 841	0.11	7.34
Nutritional and neuropathies	362 898	2.05	159.62	276 475	1.59	116.72	205 173	1.22	84.43
Neurological injuries	702 802	3.98	309.13	623 501	3.59	263.23	506 991	3.02	208.62
Total	2 468 450	13.96	1 085.75	2 344 876	13.50	989.95	2 281 396	13.60	938.78
EUROPE (LOW CHILD, HIGH ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**235 511 792**			**206 753 120**			**175 407 940**		
TOTAL DALYs	22 197 055			17 666 220			13 902 539		
Epilepsy	78 380	0.35	33.28	62 765	0.36	30.36	47 892	0.34	27.30
Alzheimer and other dementias	487 307	2.20	206.91	509 996	2.89	246.67	534 153	3.84	304.52
Parkinson's disease	77 078	0.35	32.73	64 187	0.36	31.05	52 110	0.37	29.71
Multiple sclerosis	44 105	0.20	18.73	37 404	0.21	18.09	29 180	0.21	16.64
Migraine	225 793	1.02	95.87	175 429	0.99	84.85	127 749	0.92	72.83
Cerebrovascular disease	1 023 157	4.61	434.44	881 652	4.99	426.43	715 286	5.15	407.78
Neuroinfections	28 055	0.13	11.91	22 393	0.13	10.83	19 462	0.14	11.10
Nutritional and neuropathies	466 319	2.10	198.00	314 373	1.78	152.05	174 053	1.25	99.23
Neurological injuries	1 401 926	6.32	595.27	1 101 024	6.23	532.53	832 680	5.99	474.71
Total	3 832 120	17.26	1 627.15	3 169 224	17.94	1 532.85	2 532 566	18.22	1 443.81
EASTERN MEDITERRANEAN (LOW CHILD, LOW ADULT MORTALITY)									
	2005			**2015**			**2030**		
Population	**150 452 139**			**176 204 370**			**207 555 239**		
TOTAL DALYs	13 501 935			14 650 861			16 286 148		
Epilepsy	76 282	0.56	50.70	83 269	0.57	47.26	89 420	0.55	43.08
Alzheimer and other dementias	97 087	0.72	64.53	128 325	0.88	72.83	210 609	1.29	101.47
Parkinson's disease	15 562	0.12	10.34	19 169	0.13	10.88	25 826	0.16	12.44
Multiple sclerosis	32 689	0.24	21.73	36 823	0.25	20.90	40 810	0.25	19.66
Migraine	131 573	0.97	87.45	137 927	0.94	78.28	135 035	0.83	65.06
Cerebrovascular disease	150 006	1.11	99.70	190 911	1.30	108.35	267 892	1.64	129.07
Neuroinfections	44 447	0.33	29.54	21 587	0.15	12.25	7 131	0.04	3.44
Nutritional and neuropathies	297 321	2.20	197.62	316 784	2.16	179.78	303 130	1.86	146.05
Neurological injuries	1 029 319	7.62	684.15	1 048 314	7.16	594.94	1 034 270	6.35	498.31
Total	1 874 287	13.88	1 245.77	1 983 110	13.54	1 125.46	2 114 125	12.98	1 018.58

	YLDs	% total	per 100 000	YLDs	% total	per 100 000	YLDs	% total	per 100 000
EASTERN MEDITERRANEAN (HIGH CHILD, HIGH ADULT MORTALITY)									
	2005			2015			2030		
Population	388 102 585			488 304 210			638 188 559		
TOTAL DALYs	39 623 952			44 895 159			53 022 485		
Epilepsy	265 587	0.67	68.43	314 334	0.70	64.37	373 064	0.70	58.46
Alzheimer and other dementias	215 420	0.54	55.51	284 474	0.63	58.26	423 140	0.80	66.30
Parkinson's disease	45 050	0.11	11.61	52 644	0.12	10.78	67 919	0.13	10.64
Multiple sclerosis	74 124	0.19	19.10	94 108	0.21	19.27	126 171	0.24	19.77
Migraine	440 044	1.11	113.38	538 081	1.20	110.19	640 098	1.21	100.30
Cerebrovascular disease	303 348	0.77	78.16	384 625	0.86	78.77	553 881	1.04	86.79
Neuroinfections	612 629	1.55	157.85	480 754	1.07	98.45	298 203	0.56	46.73
Nutritional and neuropathies	1 437 613	3.63	370.42	1 408 013	3.14	288.35	1 239 083	2.34	194.16
Neurological injuries	2 238 881	5.65	576.88	2 677 914	5.96	548.41	3 285 653	6.20	514.84
Total	5 632 695	14.22	1 451.34	6 234 948	13.89	1 276.86	7 007 211	13.22	1 097.98
WESTERN PACIFIC (VERY LOW CHILD, VERY LOW ADULT MORTALITY)									
	2005			2015			2030		
Population	156 684 271			154 795 439			145 921 920		
TOTAL DALYs	9 224 931			8 950 894			8 121 455		
Epilepsy	47 370	0.51	30.23	43 636	0.49	28.19	37 984	0.47	26.03
Alzheimer and other dementias	805 387	8.73	514.02	1 014 704	11.34	655.51	1 186 645	14.61	813.21
Parkinson's disease	100 793	1.09	64.33	99 312	1.11	64.16	86 543	1.07	59.31
Multiple sclerosis	26 219	0.28	16.73	24 018	0.27	15.52	20 623	0.25	14.13
Migraine	143 723	1.56	91.73	127 925	1.43	82.64	112 524	1.39	77.11
Cerebrovascular disease	555 167	6.02	354.32	524 231	5.86	338.66	441 683	5.44	302.68
Neuroinfections	36 368	0.39	23.21	33 492	0.37	21.64	31 667	0.39	21.70
Nutritional and neuropathies	138 728	1.50	88.54	137 362	1.53	88.74	114 520	1.41	78.48
Neurological injuries	208 128	2.26	132.83	171 403	1.91	110.73	122 436	1.51	83.91
Total	2 061 882	22.35	1 315.95	2 176 082	24.31	1 405.78	2 154 625	26.53	1 476.56
WESTERN PACIFIC (LOW CHILD, LOW ADULT MORTALITY)									
	2005			2015			2030		
Population	1 601 382 302			1 688 392 664			1 753 380 614		
TOTAL DALYs	115 435 250			115 153 579			113 142 467		
Epilepsy	635 699	0.55	39.70	595 008	0.52	35.24	547 946	0.48	31.25
Alzheimer and other dementias	2 279 518	1.97	142.35	2 949 094	2.56	174.67	4 452 224	3.94	253.92
Parkinson's disease	134 959	0.12	8.43	158 755	0.14	9.40	184 281	0.16	10.51
Multiple sclerosis	334 921	0.29	20.91	326 490	0.28	19.34	307 278	0.27	17.52
Migraine	1 749 402	1.52	109.24	1 677 157	1.46	99.33	1 485 052	1.31	84.70
Cerebrovascular disease	3 855 611	3.34	240.77	4 318 244	3.75	255.76	4 862 796	4.30	277.34
Neuroinfections	549 560	0.48	34.32	234 210	0.20	13.87	87 453	0.08	4.99
Nutritional and neuropathies	1 849 303	1.60	115.48	1 826 936	1.59	108.21	1 474 133	1.30	84.07
Neurological injuries	4 955 084	4.29	309.43	4 426 671	3.84	262.18	3 696 617	3.27	210.83
Total	16 344 057	14.16	1 020.62	16 512 565	14.34	978.01	17 097 780	15.11	975.13

Table A.4.6 Burden of neurological disorders, in YLDs, by cause and country income category, projections for 2005, 2015 and 2030

	YLDs	% total	per 100 000	YLDs	% total	per 100 000	YLDs	% total	per 100 000
LOW INCOME									
	2005			**2015**			**2030**		
Population	**2 698 990 297**			**3 157 941 695**			**3 786 445 271**		
TOTAL DALYs	274 869 775			296 212 785			327 825 374		
Epilepsy	2 162 379	0.79	80.12	2 345 818	0.79	74.28	2 508 911	0.77	66.26
Alzheimer and other dementias	1 887 847	0.69	69.95	2 358 215	0.80	74.68	3 298 981	1.01	87.13
Parkinson's disease	308 756	0.11	11.44	353 265	0.12	11.19	441 287	0.13	11.65
Multiple sclerosis	501 366	0.18	18.58	590 060	0.20	18.68	696 371	0.21	18.39
Migraine	3 075 717	1.12	113.96	3 292 940	1.11	104.27	3 484 761	1.06	92.03
Cerebrovascular disease	2 961 840	1.08	109.74	3 497 473	1.18	110.75	4 623 403	1.41	122.10
Neuroinfections	5 178 007	1.88	191.85	4 484 971	1.51	142.02	3 295 399	1.01	87.03
Nutritional and neuropathies	7 806 618	2.84	289.24	7 321 821	2.47	231.85	6 284 158	1.92	165.96
Neurological Injuries	13 836 513	5.03	512.66	15 166 127	5.12	480.25	16 970 828	5.18	448.20
Total	37 719 043	13.72	1 397.52	39 410 691	13.30	1 247.99	41 604 099	12.69	1 098.76
LOWER MIDDLE INCOME									
	2005			**2015**			**2030**		
Population	**2 267 665 265**			**2 394 506 774**			**2 504 674 883**		
TOTAL DALYs	180 841 215			179 114 557			176 548 919		
Epilepsy	1 083 085	0.60	47.76	1 051 524	0.59	43.91	996 999	0.56	39.81
Alzheimer and other dementias	3 092 955	1.71	136.39	3 912 760	2.18	163.41	5 720 544	3.24	228.39
Parkinson's disease	255 194	0.14	11.25	277 039	0.15	11.57	307 805	0.17	12.29
Multiple sclerosis	464 515	0.26	20.48	460 503	0.26	19.23	443 061	0.25	17.69
Migraine	2 421 813	1.34	106.80	2 324 256	1.30	97.07	2 085 110	1.18	83.25
Cerebrovascular disease	5 256 334	2.91	231.79	5 698 033	3.18	237.96	6 238 042	3.53	249.06
Neuroinfections	773 549	0.43	34.11	370 936	0.21	15.49	159 203	0.09	6.36
Nutritional and neuropathies	3 277 499	1.81	144.53	3 045 262	1.70	127.18	2 424 744	1.37	96.81
Neurological Injuries	9 200 404	5.09	405.72	8 521 185	4.76	355.86	7 594 651	4.30	303.22
Total	25 825 349	14.28	1 138.85	25 661 498	14.33	1 071.68	25 970 159	14.71	1 036.87
UPPER MIDDLE INCOME									
	2005			**2015**			**2030**		
Population	**528 081 304**			**574 892 329**			**622 970 241**		
TOTAL DALYs	48 512 303			50 027 602			51 204 031		
Epilepsy	574 453	1.18	108.78	588 084	1.18	102.29	573 146	1.12	92.00
Alzheimer and other dementias	804 632	1.66	152.37	1 025 454	2.05	178.37	1 483 308	2.90	238.10
Parkinson's disease	66 408	0.14	12.58	71 217	0.14	12.39	75 045	0.15	12.05
Multiple sclerosis	108 140	0.22	20.48	113 803	0.23	19.80	114 563	0.22	18.39
Migraine	776 542	1.60	147.05	783 032	1.57	136.20	744 397	1.45	119.49
Cerebrovascular disease	841 607	1.73	159.37	925 989	1.85	161.07	1 030 004	2.01	165.34
Neuroinfections	207 991	0.43	39.39	115 195	0.23	20.04	60 222	0.12	9.67
Nutritional and neuropathies	540 532	1.11	102.36	707 179	1.41	123.01	698 714	1.36	112.16
Neurological Injuries	2 831 533	5.84	536.19	2 954 590	5.91	513.94	2 963 659	5.79	475.73
Total	6 751 839	13.92	1 278.56	7 284 542	14.56	1 267.11	7 743 058	15.12	1 242.93
HIGH INCOME									
	2005			**2015**			**2030**		
Population	**947 138 427**			**975 884 050**			**1 002 892 462**		
TOTAL DALYs	66 539 151			67 046 328			65 404 060		
Epilepsy	347 335	0.52	36.67	338 021	0.50	34.64	323 722	0.49	32.28
Alzheimer and other dementias	3 709 039	5.57	391.60	4 454 081	6.64	456.41	5 641 486	8.63	562.52
Parkinson's disease	507 626	0.76	53.60	526 601	0.79	53.96	529 223	0.81	52.77
Multiple sclerosis	212 428	0.32	22.43	206 989	0.31	21.21	199 064	0.30	19.85
Migraine	1 385 579	2.08	146.29	1 335 981	1.99	136.90	1 281 723	1.96	127.80
Cerebrovascular disease	2 329 596	3.50	245.96	2 301 556	3.43	235.84	2 182 130	3.34	217.58
Neuroinfections	177 788	0.27	18.77	128 477	0.19	13.17	98 343	0.15	9.81
Nutritional and neuropathies	932 307	1.40	98.43	1 306 923	1.95	133.92	1 195 901	1.83	119.25
Neurological Injuries	1 534 400	2.31	162.00	1 310 269	1.95	134.26	1 037 296	1.59	103.43
Total	11 136 099	16.74	1 175.76	11 908 897	17.76	1 220.32	12 488 887	19.09	1 245.29

Table A.4.7 Prevalence (per 1000) of neurological disorders, by cause, WHO region and mortality stratum, projections for 2005, 2015 and 2030

	Number	per 1 000	Number	per 1 000	Number	per 1 000
WORLD						
	2005		2015		2030	
Population	6 441 919 466		7 103 297 899		7 917 115 397	
Epilepsy	39 891 898	6.19	44 568 780	6.27	50 503 933	6.38
Alzheimer and other dementias	24 446 651	3.79	31 318 923	4.41	44 016 718	5.56
Parkinson's disease	5 223 897	0.81	5 967 673	0.84	7 236 712	0.91
Multiple sclerosis	2 492 385	0.39	2 823 092	0.40	3 279 199	0.41
Migraine	326 196 121	50.64	364 432 879	51.30	412 894 420	52.15
Cerebrovascular disease	61 537 499	9.55	67 212 050	9.46	76 826 249	9.70
Neuroinfections	18 169 479	2.82	15 714 399	2.21	13 290 180	1.68
Nutritional and neuropathies	352 494 535	54.72	321 738 424	45.29	285 369 403	36.04
Neurological injuries	170 382 211	26.45	197 627 526	27.82	242 728 912	30.66
AFRICA (HIGH CHILD, HIGH ADULT MORTALITY)						
	2005		2015		2030	
Population	335 459 111		419 571 880		550 082 900	
Epilepsy	3 887 787	11.59	4 887 589	11.65	6 425 567	11.68
Alzheimer and other dementias	301 529	0.90	390 872	0.93	558 471	1.02
Parkinson's disease	77 310	0.23	96 484	0.23	139 094	0.25
Multiple sclerosis	90 125	0.27	118 905	0.28	171 479	0.31
Migraine	5 301 369	15.80	6 958 945	16.59	10 049 321	18.27
Cerebrovascular disease	922 165	2.75	1 177 212	2.81	1 752 287	3.19
Neuroinfections	3 429 358	10.22	3 455 514	8.24	3 063 637	5.57
Nutritional and neuropathies	34 447 298	102.69	37 749 963	89.97	37 452 942	68.09
Neurological injuries	13 046 081	38.89	16 885 887	40.25	24 827 838	45.13
AFRICA (HIGH CHILD, VERY HIGH ADULT MORTALITY)						
	2005		2015		2030	
Population	382 647 820		478 419 411		628 734 321	
Epilepsy	3 572 218	9.34	4 476 346	9.36	5 826 652	9.27
Alzheimer and other dementias	320 683	0.84	416 691	0.87	560 199	0.89
Parkinson's disease	83 143	0.22	98 722	0.21	132 208	0.21
Multiple sclerosis	85 170	0.22	109 363	0.23	161 820	0.26
Migraine	6 889 476	18.00	8 829 595	18.46	12 309 881	19.58
Cerebrovascular disease	875 178	2.29	1 058 100	2.21	1 468 215	2.34
Neuroinfections	3 547 669	9.27	3 400 301	7.11	3 021 709	4.81
Nutritional and neuropathies	39 641 466	103.60	40 133 334	83.89	39 426 363	62.71
Neurological injuries	11 528 595	30.13	14 935 805	31.22	21 909 861	34.85
THE AMERICAS (VERY LOW CHILD, VERY LOW ADULT MORTALITY)						
	2005		2015		2030	
Population	343 363 701		372 395 661		413 323 652	
Epilepsy	1 830 517	5.33	1 960 485	5.26	2 157 642	5.22
Alzheimer and other dementias	3 236 120	9.42	3 809 436	10.23	5 630 271	13.62
Parkinson's disease	1 042 640	3.04	1 180 495	3.17	1 543 063	3.73
Multiple sclerosis	181 870	0.53	199 324	0.54	220 144	0.53
Migraine	29 434 637	85.72	32 303 593	86.75	35 115 150	84.96
Cerebrovascular disease	5 181 015	15.09	5 514 921	14.81	5 762 804	13.94
Neuroinfections	331 319	0.96	297 476	0.80	273 074	0.66
Nutritional and neuropathies	8 470 890	24.67	14 078 189	37.80	15 706 201	38.00
Neurological injuries	3 761 512	10.95	3 838 293	10.31	3 950 758	9.56

Prevalence (per 1000) of neurological disorders, by cause, by WHO region and mortality stratum, projections for 2005, 2015 and 2030

	Number	per 1 000	Number	per 1 000	Number	per 1 000
THE AMERICAS (LOW CHILD, LOW ADULT MORTALITY)						
	2005		2015		2030	
Population	463 707 779		511 277 519		560 127 320	
Epilepsy	5 995 062	12.93	6 483 590	12.68	6 950 211	12.41
Alzheimer and other dementias	1 563 720	3.37	2 111 608	4.13	3 382 089	6.04
Parkinson's disease	131 149	0.28	162 062	0.32	219 316	0.39
Multiple sclerosis	169 790	0.37	199 298	0.39	235 538	0.42
Migraine	26 424 577	56.99	31 327 545	61.27	37 412 092	66.79
Cerebrovascular disease	3 579 817	7.72	4 173 211	8.16	5 039 977	9.00
Neuroinfections	1 130 487	2.44	803 085	1.57	589 365	1.05
Nutritional and neuropathies	10 977 028	23.67	12 455 700	24.36	12 609 273	22.51
Neurological injuries	18 428 772	39.74	22 348 470	43.71	27 329 074	48.79
THE AMERICAS (HIGH CHILD, HIGH ADULT MORTALITY)						
	2005		2015		2030	
Population	77 739 657		90 194 020		106 740 220	
Epilepsy	836 072	10.75	966 534	10.72	1 130 346	10.59
Alzheimer and other dementias	177 298	2.28	228 977	2.54	364 489	3.41
Parkinson's disease	14 415	0.19	17 608	0.20	25 160	0.24
Multiple sclerosis	25 390	0.33	31 655	0.35	41 305	0.39
Migraine	4 664 146	60.00	5 713 736	63.35	7 277 075	68.18
Cerebrovascular disease	295 893	3.81	373 202	4.14	521 080	4.88
Neuroinfections	222 767	2.87	178 873	1.98	133 484	1.25
Nutritional and neuropathies	1 747 300	22.48	2 006 469	22.25	2 049 464	19.20
Neurological injuries	2 451 434	31.53	3 055 072	33.87	4 002 293	37.50
SOUTH-EAST ASIA (LOW CHILD, LOW ADULT MORTALITY)						
	2005		2015		2030	
Population	308 761 163		336 961 332		364 048 380	
Epilepsy	1 716 803	5.56	1 869 945	5.55	2 030 893	5.58
Alzheimer and other dementias	750 947	2.43	1 109 965	3.29	1 758 876	4.83
Parkinson's disease	83 755	0.27	101 189	0.30	127 726	0.35
Multiple sclerosis	115 420	0.37	133 396	0.40	155 365	0.43
Migraine	12 452 696	40.33	14 276 937	42.37	16 357 388	44.93
Cerebrovascular disease	1 753 574	5.68	2 069 695	6.14	2 577 753	7.08
Neuroinfections	603 533	1.95	489 621	1.45	414 406	1.14
Nutritional and neuropathies	23 486 575	76.07	19 023 347	56.46	15 013 037	41.24
Neurological injuries	6 360 357	20.60	7 562 330	22.44	9 000 303	24.72
SOUTH-EAST ASIA (HIGH CHILD, HIGH ADULT MORTALITY)						
	2005		2015		2030	
Population	1 352 957 715		1 525 318 552		1 718 832 463	
Epilepsy	7 949 495	5.88	8 852 768	5.80	9 751 328	5.67
Alzheimer and other dementias	2 109 176	1.56	2 830 478	1.86	4 151 049	2.42
Parkinson's disease	601 514	0.44	748 737	0.49	1 043 266	0.61
Multiple sclerosis	467 985	0.35	559 474	0.37	685 168	0.40
Migraine	58 123 761	42.96	68 872 969	45.15	83 386 832	48.51
Cerebrovascular disease	8 080 667	5.97	9 654 382	6.33	12 810 896	7.45
Neuroinfections	2 700 495	2.00	2 106 911	1.38	1 712 605	1.00
Nutritional and neuropathies	102 584 258	75.82	82 871 325	54.33	65 739 960	38.25
Neurological injuries	48 694 670	35.99	56 565 467	37.08	68 317 201	39.75

	Number	per 1 000	Number	per 1 000	Number	per 1 000
EUROPE (VERY LOW CHILD, VERY LOW ADULT MORTALITY)						
	2005		2015		2030	
Population	417 799 202		417 841 350		411 754 930	
Epilepsy	2 145 979	5.14	2 161 029	5.17	2 158 279	5.24
Alzheimer and other dementias	5 362 157	12.83	6 611 650	15.82	8 053 138	19.56
Parkinson's disease	1 365 849	3.27	1 512 916	3.62	1 614 797	3.92
Multiple sclerosis	259 275	0.62	262 457	0.63	254 097	0.62
Migraine	53 492 555	128.03	54 275 528	129.90	53 586 117	130.14
Cerebrovascular disease	6 278 185	15.03	6 116 704	14.64	5 887 278	14.30
Neuroinfections	530 651	1.27	472 683	1.13	438 486	1.06
Nutritional and neuropathies	6 659 295	15.94	7 554 085	18.08	7 564 726	18.37
Neurological injuries	3 856 936	9.23	3 670 108	8.78	3 290 918	7.99
EUROPE (LOW CHILD, LOW ADULT MORTALITY)						
	2005		2015		2030	
Population	227 350 229		236 868 370		243 016 939	
Epilepsy	955 206	4.20	995 872	4.20	1 023 780	4.21
Alzheimer and other dementias	987 308	4.34	1 233 107	5.21	1 558 168	6.41
Parkinson's disease	250 849	1.10	275 108	1.16	319 164	1.31
Multiple sclerosis	91 104	0.40	98 909	0.42	107 864	0.44
Migraine	11 127 627	48.94	12 009 067	50.70	12 923 428	53.18
Cerebrovascular disease	2 909 121	12.80	3 011 979	12.72	3 314 164	13.64
Neuroinfections	288 785	1.27	258 413	1.09	239 714	0.99
Nutritional and neuropathies	5 806 482	25.54	5 018 573	21.19	4 397 770	18.10
Neurological injuries	4 654 920	20.47	4 931 436	20.82	5 161 201	21.24
EUROPE (LOW CHILD, HIGH ADULT MORTALITY)						
	2005		2015		2030	
Population	235 511 792		206 753 120		175 407 940	
Epilepsy	986 267	4.19	874 450	4.23	749 294	4.27
Alzheimer and other dementias	1 385 473	5.88	1 558 787	7.54	1 650 510	9.41
Parkinson's disease	338 403	1.44	305 100	1.48	270 942	1.54
Multiple sclerosis	110 444	0.47	98 774	0.48	86 042	0.49
Migraine	12 519 404	53.16	11 380 891	55.05	9 993 768	56.97
Cerebrovascular disease	5 578 425	23.69	4 899 001	23.69	4 094 427	23.34
Neuroinfections	214 736	0.91	189 090	0.91	176 088	1.00
Nutritional and neuropathies	7 706 356	32.72	5 309 161	25.68	3 544 585	20.21
Neurological injuries	8 121 815	34.49	7 053 326	34.11	5 848 082	33.34
EASTERN MEDITERRANEAN (LOW CHILD, LOW ADULT MORTALITY)						
	2005		2015		2030	
Population	150 452 139		176 204 370		207 555 239	
Epilepsy	612 616	4.07	713 756	4.05	833 149	4.01
Alzheimer and other dementias	207 025	1.38	284 456	1.61	488 949	2.36
Parkinson's disease	52 892	0.35	66 868	0.38	105 629	0.51
Multiple sclerosis	50 491	0.34	63 382	0.36	83 451	0.40
Migraine	4 486 529	29.82	5 414 528	30.73	6 760 297	32.57
Cerebrovascular disease	758 271	5.04	963 285	5.47	1 381 731	6.66
Neuroinfections	187 741	1.25	140 870	0.80	111 484	0.54
Nutritional and neuropathies	4 325 183	28.75	4 648 624	26.38	5 094 358	24.54
Neurological injuries	5 661 387	37.63	6 874 140	39.01	8 985 853	43.29

	Number	per 1 000	Number	per 1 000	Number	per 1 000
EASTERN MEDITERRANEAN (HIGH CHILD, HIGH ADULT MORTALITY)						
	2005		2015		2030	
Population	388 102 585		488 304 210		638 188 559	
Epilepsy	2 307 484	5.95	2 905 715	5.95	3 780 009	5.92
Alzheimer and other dementias	433 980	1.12	599 142	1.23	949 710	1.49
Parkinson's disease	153 850	0.40	187 726	0.38	260 147	0.41
Multiple sclerosis	118 755	0.31	154 093	0.32	220 508	0.35
Migraine	12 122 159	31.23	15 724 788	32.20	22 272 136	34.90
Cerebrovascular disease	1 449 886	3.74	1 843 680	3.78	2 674 703	4.19
Neuroinfections	2 040 970	5.26	1 738 470	3.56	1 324 728	2.08
Nutritional and neuropathies	29 803 040	76.79	28 239 576	57.83	25 847 645	40.50
Neurological injuries	14 044 340	36.19	18 063 186	36.99	25 714 352	40.29
WESTERN PACIFIC (VERY LOW CHILD, VERY LOW ADULT MORTALITY)						
	2005		2015		2030	
Population	156 684 271		154 795 439		145 921 920	
Epilepsy	868 123	5.54	865 621	5.59	826 117	5.66
Alzheimer and other dementias	2 184 654	13.94	2 996 308	19.36	3 794 924	26.01
Parkinson's disease	511 384	3.26	603 106	3.90	626 385	4.29
Multiple sclerosis	72 700	0.46	72 033	0.47	67 012	0.46
Migraine	11 547 332	73.70	11 488 613	74.22	10 715 929	73.44
Cerebrovascular disease	3 792 785	24.21	3 667 047	23.69	3 178 620	21.78
Neuroinfections	257 304	1.64	245 428	1.59	237 127	1.63
Nutritional and neuropathies	3 347 308	21.36	3 552 062	22.95	3 333 547	22.84
Neurological injuries	1 491 604	9.52	1 495 519	9.66	1 342 770	9.20
WESTERN PACIFIC (LOW CHILD, LOW ADULT MORTALITY)						
	2005		2015		2030	
Population	1 601 382 302		1 688 392 664		1 753 380 614	
Epilepsy	6 228 270	3.89	6 555 079	3.88	6 860 667	3.91
Alzheimer and other dementias	5 426 580	3.39	7 137 446	4.23	11 115 873	6.34
Parkinson's disease	516 744	0.32	611 552	0.36	809 814	0.46
Multiple sclerosis	653 867	0.41	722 028	0.43	789 406	0.45
Migraine	77 609 852	48.46	85 856 144	50.85	94 735 006	54.03
Cerebrovascular disease	20 082 517	12.54	22 689 633	13.44	26 362 316	15.04
Neuroinfections	2 683 663	1.68	1 937 664	1.15	1 554 271	0.89
Nutritional and neuropathies	73 492 056	45.89	59 098 014	35.00	47 589 533	27.14
Neurological injuries	28 279 787	17.66	30 348 487	17.97	33 048 410	18.85

Table A.4.8 Prevalence (per 1000) of neurological disorders, by cause and country income category, projections for 2005, 2015 and 2030

	Number	per 1 000	Number	per 1 000	Number	per 1 000
LOW INCOME						
	2005		**2015**		**2030**	
Population	**2 698 990 297**		**3 157 941 695**		**3 786 445 271**	
Epilepsy	18 767 673	6.95	22 219 076	7.04	26 963 317	7.12
Alzheimer and other dementias	4 187 247	1.55	5 519 844	1.75	7 941 472	2.10
Parkinson's disease	1 026 261	0.38	1 236 644	0.39	1 679 946	0.44
Multiple sclerosis	861 399	0.32	1 050 073	0.33	1 356 892	0.36
Migraine	97 386 421	36.08	117 150 189	37.10	147 040 876	38.83
Cerebrovascular disease	14 233 869	5.27	16 804 274	5.32	22 324 143	5.90
Neuroinfections	12 219 114	4.53	11 095 507	3.51	9 461 215	2.50
Nutritional and neuropathies	229 490 905	85.03	206 778 850	65.48	181 940 616	48.05
Neurological Injuries	90 262 196	33.44	109 630 501	34.72	143 849 509	37.99
LOWER MIDDLE INCOME						
	2005		**2015**		**2030**	
Population	**2 267 665 265**		**2 394 506 774**		**2 504 674 883**	
Epilepsy	10 651 319	4.70	11 308 222	4.72	11 942 124	4.77
Alzheimer and other dementias	7 498 331	3.31	9 730 403	4.06	14 587 111	5.82
Parkinson's disease	1 016 623	0.45	1 134 671	0.47	1 399 970	0.56
Multiple sclerosis	905 993	0.40	997 151	0.42	1 101 687	0.44
Migraine	104 870 967	46.25	115 096 758	48.07	126 818 106	50.63
Cerebrovascular disease	27 616 112	12.18	30 176 588	12.60	33 975 321	13.56
Neuroinfections	3 822 412	1.69	2 835 263	1.18	2 262 956	0.90
Nutritional and neuropathies	89 556 278	39.49	73 313 524	30.62	60 403 913	24.12
Neurological Injuries	54 090 897	23.85	59 112 199	24.69	66 769 005	26.66
UPPER MIDDLE						
	2005		**2015**		**2030**	
Population	**528 081 304**		**574 892 329**		**622 970 241**	
Epilepsy	5 636 336	10.67	6 057 319	10.54	6 449 477	10.35
Alzheimer and other dementias	2 002 209	3.79	2 656 367	4.62	3 952 642	6.34
Parkinson's disease	282 273	0.53	320 603	0.56	381 415	0.61
Multiple sclerosis	201 706	0.38	230 675	0.40	266 357	0.43
Migraine	29 450 329	55.77	33 885 778	58.94	39 155 596	62.85
Cerebrovascular disease	4 482 667	8.49	4 965 600	8.64	5 651 784	9.07
Neuroinfections	956 305	1.81	724 346	1.26	578 551	0.93
Nutritional and neuropathies	13 267 582	25.12	14 561 442	25.33	14 555 473	23.36
Neurological Injuries	16 551 721	31.34	19 589 370	34.07	23 272 762	37.36
HIGH INCOME						
	2005		**2015**		**2030**	
Population	**947 138 427**		**975 884 050**		**1 002 892 462**	
Epilepsy	4 836 322	5.11	4 983 733	5.11	5 148 237	5.13
Alzheimer and other dementias	10 758 768	11.36	13 412 189	13.74	17 535 293	17.48
Parkinson's disease	2 898 718	3.06	3 275 732	3.36	3 775 357	3.76
Multiple sclerosis	523 272	0.55	545 176	0.56	554 231	0.55
Migraine	94 487 271	99.76	98 298 715	100.73	99 877 490	99.59
Cerebrovascular disease	15 204 544	16.05	15 265 253	15.64	14 874 570	14.83
Neuroinfections	1 171 502	1.24	1 059 129	1.09	987 315	0.98
Nutritional and neuropathies	20 177 668	21.30	27 082 158	27.75	28 466 544	28.38
Neurological Injuries	9 476 767	10.01	9 294 786	9.52	8 836 820	8.81

Annex 5 *International nongovernmental organizations working in neurological disorders*

Organization	Contact details	Mission statement, scope of activity or purpose
GENERAL		
International Child Neurology Association (ICNA)	Pediatric Neurology University of Rome Tor Vergata P. le Umanesimo 10 144 Rome Italy tel: +39 335 834 89 21 fax:+39 06 941 14 63 e-mail: curatolo@uniroma2.it web site: http://www.child-neuro.net	The general purpose of ICNA is: ■ to create a non-profit association of child neurologists and members of allied professions from all parts of the world dedicated to promoting clinical and scientific research in the field of child neurology and encouraging the recognition of child neurologists' competence and scope of practice; ■ to provide, at an international level, an outlet for interchange of scientific and professional opinions for the benefit and advancement of the neurological sciences in infancy and childhood; ■ to establish international scientific meetings, international cooperative studies, publications, translations, audio-visual material and to encourage international exchange of teachers and students in the field of child neurology.
World Federation of Neurology (WFN)	12 Chandos Street London W1G 9DR England tel: +44 20 7323 4011 fax:+44 20 7323 4012 e-mail: WFNLondon@aol.com web site: http://www.wfneurology.org	It is the purpose of WFN to improve human health worldwide by promoting prevention and the care of persons with disorders of the entire nervous system by: ■ fostering the best standards of neurological practice; ■ educating, in collaboration with neuroscience and other international public and private organizations; ■ facilitating research through its Research Groups and other means.
European Federation of Neurological Societies (EFNS)	EFNS Head Office Breite Gasse 4–8 1070 Vienna Austria tel: +43 1 889 05 03 fax: +43 1 889 05 03 13 e-mail: headoffice@efns.org web site: http://www.efns.org	EFNS is an organization that unites and supports neurologists across the whole of Europe. It aims: to broaden the base of clinical neurology in Europe; raise public awareness about the importance of the brain and its disorders; to strengthen the standard, availability and uniformity of neurological services in Europe; to create and maintain continuing medical education guidelines and accreditation; support and encourage European clinical neuroscience research programmes; to strengthen the standard, quantity and equality of pre-graduate and postgraduate teaching and training; to strengthen WFN, EU and WHO relations; to strengthen collaboration with related professional and lay organizations; organize European Neurology Congresses and Neurological Teaching Courses; to publish the *European Journal of Neurology*.
European Neurology Societies (ENS)	ENS Administrative Secretariat c/o AKM Congress Service P.O. Box 4005 Basel Switzerland tel: +41 61 686 77 77 fax: +41 61 686 77 88 e-mail: info@akm.ch web site: http://www.ensinfo.com	The aims of ENS are to provide continuing education in all fields of neurology, to create a scientific forum for the presentation of original research work for all the neurologists, to guarantee a high level of scientific standard, and to support the younger generation by continuing promotions such as travel grants, fellowships stipends or the new neurologist in training offer.

Organization	Contact details	Mission statement, scope of activity or purpose
DEMENTIA		
Alzheimer's Disease International (ADI)	64 Great Suffolk Street London SE1 0BL England tel: +44 20 7981 0880 fax: +44 20 7928 2357 e-mail: info@alz.co.uk web site: http://www.alz.co.uk/	ADI is the umbrella organization of Alzheimer associations around the world. It aims to help establish and strengthen Alzheimer associations throughout the world and to raise global awareness about Alzheimer's disease and all other causes of dementia.
EPILEPSY		
International Bureau for Epilepsy (IBE)	International Bureau for Epilepsy Unit 4 Hillview House Bracken Road Sandyford Dublin 18 Ireland tel: +353 1 293 4961 fax: +353 1 293 4963 e-mail: ibedublin@eircom.net web site: http://www.ibe-epilepsy.org	IBE is an organization of lay persons and professionals interested in the medical and non-medical aspects of epilepsy. It addresses such social problems as education, employment, insurance, driving-licence restrictions and public awareness. It provides assistance by offering international support, by creating means for worldwide exchange of information and, where possible, by setting standards that provide an international policy focus and identity for all persons with epilepsy. IBE works in close liaison with the International League against Epilepsy.
International League Against Epilepsy (ILAE)	204 avenue Marcel Thiry 1200 Brussels Belgium tel: + 32 (0) 2 774 9547 fax: + 32 (0) 2 774 9690 e-mail: dsartiux@ilae.org web site: http://www.ilae-epilepsy.org	ILAE is the world's pre-eminent association of physicians and other health professionals working towards a world where no persons' life is limited by epilepsy. Its mission is to provide the highest quality of care and wellbeing for those afflicted with the condition and other related seizure disorders. The League aims to advance and disseminate knowledge about epilepsy, to promote research, education and training and to improve services and care for patients, especially by prevention, diagnosis and treatment.
HEADACHE DISORDERS		
International Headache Society (IHS)	c/o Griffin Stone, Moscrop and Co. 41 Welbeck Street London W1G 8EA England e-mail: info@i-h-s.org web site: http:// www.i-h-s.org	A worldwide professional society, the mission of IHS is to work with others to reduce the world burden of headache. The web site includes all published guidelines and recommendations of the IHS, and professional educational pages are planned.
World Headache Alliance (WHA)	c/o Griffin Stone, Moscrop and Co 41 Welbeck Street London W1G 8EA England e-mail: info@w-h-a.org web site: http://www.w-h-a.org	A worldwide lay alliance, WHA exists to relieve the suffering of people affected by headache throughout the world, in particular by sharing information among headache organizations and by increasing the awareness and understanding of headache as a public health concern with profound social and economic impact. The web site includes a regularly updated source of detailed and quality-controlled information on headache for the general public, with many useful links.
European Headache Federation (EHF)	c/o Kenes International 17 rue du Cendrier PO Box 1726 1211 Geneva 1 Switzerland. tel: +41 22 906 9154 fax: +41 22 732 2852 e-mail: info@ehf-org.org web site: http://www.ehf-org.org	A European professional federation, EHF dedicates its efforts to improving awareness among governments, health-care providers and consumers across Europe of headache disorders and their personal and socioeconomic impact. Ultimately EHF seeks to create the optimal environment for headache sufferers and their carers across all Europe, so that they have access to appropriate treatment and therefore enjoy a better quality of life.

Organization	Contact details	Mission statement, scope of activity or purpose
MULTIPLE SCLEROSIS		
Multiple Sclerosis International Federation (MSIF)	200 Union Street London SE1 0LX England tel: +44 20 7620 1911 fax: +44 20 7620 1922 e-mail: info@msif.org web site: http://www.msif.org	MSIF was established in 1967 as an international body linking the activities of national multiple sclerosis societies around the world. MSIF seeks to work in worldwide partnership with member societies and the international scientific community to eliminate multiple sclerosis and its consequences, and to speak out globally on behalf of those affected by multiple sclerosis. MSIF works to achieve this through the following key priorities: international research; development of new and existing societies; exchange of information; advocacy.
European Multiple Sclerosis Platform (EMSP)	144/8 rue Auguste Lambiotte 1030 Brussels Belgium tel: +32 2 305 80 12 fax: +32 2 305 80 11 e-mail: ms-in-europe@pandora.be web site: http://www.ms-in-europe.com	The mission of EMSP is to exchange and disseminate information relating to multiple sclerosis, considering all issues relevant to people affected by it: to encourage research of all kinds that is appropriate to multiple sclerosis through recognized medical and other organizations; to promote the development of joint action programmes with the participation of national multiple sclerosis societies in Europe, aimed at improving the quality of their activities and services; to act as focal point for liaison with the institutions of the European Union, the Council of Europe and other European organizations, in order to study and propose measures to improve the autonomy of handicapped persons and promote their full participation in society.
PAIN ASSOCIATED WITH NEUROLOGICAL DISORDERS		
The International Association for the Study of Pain (IASP)	Queen Anne Avenue N, Suite 501 Seattle, WA 98109 – 4955 United States of America tel: +1 206 283 0311 fax: +1 206 283 9403 e-mail: iaspdesk@iasp-pain.org web site: http://www.iasp-pain.org	To foster and encourage research of pain mechanisms and pain syndromes and to help improve the management of patients with acute and chronic pain by bringing together basic scientists, physicians and other health professionals of various disciplines and backgrounds who have an interest in pain research and management.
The European Federation of IASP-Chapters (EFIC)	Mrs Sarah Wheeler Executive Officer Foukithidou 2 16343 Iliopoulis, Athens Greece tel: +30 210 992 6335 mobile: + 30 694 447 8978 fax: + 30 210 992 6382 e-mail: efic@internet.gr web site: http://www.efic.org	To promote research, education, and the clinical management of pain, to create a forum for European collaboration on pain issues and to encourage communication at a European level between IASP Chapters, and also with other bodies interested or involved in the fields of pain research and therapy.
PARKINSON'S DISEASE		
Asian and Pacific Parkinson's Association (APPA)	PO Box 12042 50766 Kuala Lumpur Malaysia tel: +603 2454648 fax: +603 2454649 e-mail.: appda@po.jaring.my	The objectives of APPA are: to establish and operate projects rendering service to persons suffering from Parkinson's disease; to encourage and promote research and other activities relating to the prevention, diagnosis, causes and treatment of Parkinson's disease; to cooperate with all relevant public and private agencies in services for persons suffering from Parkinson's disease; to collect, compile and disseminate information on causes, prevention, research programmes and available aids to combat Parkinson's disease, and to carry on a vigorous general public education programme within this field; generally to do what may be required to give effect and carry forward the purposes of APPA without discriminating against any person or organization because of race or religion.
European Parkinson's Disease Association (EPDA)	4 Golding Road Sevenoaks Kent TN13 3NJ England tel/fax: +44 17 3245 7683 e-mail: lizzie@epda.eu.com web site: http://www.epda.eu.com	Formed in 1992, EPDA now has a membership of 36 European organizations and eight associates. It is non-political, non-religious and non-profit making, concerned with the health and welfare of people with Parkinson's disease and their families. Collaboration with European patient and neurological organizations, the European Commission, WHO, WFN and the pharmaceutical industry has resulted in the development of quality of life research projects, education materials and multidisciplinary conferences.

Organization	Contact details	Mission statement, scope of activity or purpose
STROKE		
International Stroke Society (ISS)	Dr Takenori Yamaguchi, Acting President National Cardiovascular Centre 5-7-1 Fujishirodai, Suita City Osaka 565-8565 Japan tel: +81 6 6833 5012 fax: +81 6 4863 7052 e-mail: tyamaguc@hsp.ncvc.go.jp web site: http://www.internationalstroke.org Dr Bo Norrving, Secretary Department of Neurology University Hospital 221 85 Lund Sweden tel: +46 4617 1466 fax: +46 4615 89 19 e-mail: bo.norrving@neurol.lu.se	The mission of ISS is to provide access to stroke care and to promote research and teaching in this area that will improve the care of stroke victims by: promoting prevention and care of persons with stroke and/or dementia; fostering the best standards of practice; educating, in collaboration with other international, public and private organizations; facilitating clinical research.
TRAUMATIC BRAIN INJURIES		
World Federation of Neurosurgical Societies	5 rue du Marché 1260 Nyon Switzerland tel: +41 22 362 4303 tax: +41 22 362 4352 e-mail: janjoseph@wfns.ch web site: http://www.wfns.org	To advance neurological surgery in all its aspects by facilitating the personal association of neurosurgeons throughout the world; to aid in the exchange and dissemination of knowledge and ideas in the field of neurosurgery; to encourage research and investigation in neurosurgery and allied sciences.

Index

As all countries in the WHO Member States are included in Annex 1 (p. 183–4), specific country references to the Annexes are not included in the index. A list of abbreviations used in the text can be found in page xi of the preface.