Dramatic increases in life expectancy, combined with profound changes in lifestyles, are leading to global epidemics of cancer and other chronic diseases. For instance, the number of cases of cancer is expected to at least double in developing countries during the next 25 years, and there is likely to be a similar rise in cases of diabetes. The result will be a huge increase in human suffering and disability. In addition to the many millions dying prematurely from these diseases each year, hundreds of millions of people will face many years of chronic disability and suffering, with profound socioeconomic consequences. Already, chronic diseases kill more than 24 million people a year—equal to almost half of all deaths worldwide.

**Life expectancy, health expectancy**

The dramatic increases in life expectancy achieved during the 20th century are certain to have profound consequences for humanity far into the new millennium. Half a century ago, the great majority of the global population died before the age of 50. Today, the great majority survive well beyond that age. Average life expectancy in developing countries is now 64 years, and is projected to reach 71 years by the year 2020. It is already higher in many industrialized countries. A child born in Japan today, for example, can expect to live to be 80 years old.

These are outstanding landmarks on the pathway of human evolution, and could not have occurred without the tremendous advances in medicine and public health, in science and technology, that have occurred since the beginning of this century. Such advances are continuing at a remarkable pace, and offer real hope for a better and healthier future for mankind.

But while extending our life span is desirable in itself, it is much more so if it can be accompanied by freedom from additional years of suffering poverty, pain or disability. Unfortunately, for many millions of people, there is as yet no such freedom. The quality of human life is at least as important as its quantity. Individuals are entitled to be concerned not so much about their life expectancy as about their health expectancy—and are rightly demanding to be better informed about it.

Health expectancy can be defined as life expectancy in good health, and amounts to the average number of years that an individual can expect to live in such a favourable state. For all of us who look forward to a longer life than that of our predecessors, it is vital to realize that increased longevity does not come free. While the ideal vision for everyone may be to lead a physically and mentally healthy life well into old age, every year many millions die prematurely or are disabled by diseases and conditions that are to a large extent preventable. Longer life can be a penalty as well as a prize. A large part of the price to be paid is in the currency of chronic disease, the main subject of this report.

*The World Health Report 1996 – Fighting disease, fostering development* showed the enormous burden that infectious diseases impose on humanity, particularly in the developing world, killing about 17 million people a year and affecting hundreds of millions of others. This toll continues despite vaccines, medicines and other preventive and curative treatments which save millions of lives every year.
The health transition

In the industrialized world, infectious diseases are well under control, thanks to progress in areas such as clean water and sanitation, immunization, and firmly-established health services. It is noninfectious diseases – particularly cancer, circulatory diseases, mental disorders including dementia, chronic respiratory conditions and musculoskeletal diseases – that now pose the greatest threat to health in terms of life lost and disability in developed countries. These are essentially the chronic diseases that strike later in life, and which, as life expectancy increases, will become more prevalent.

Globally, chronic diseases are responsible for almost half of the 52 million or so deaths that occur every year. Among adults, the leading causes are circulatory diseases, including heart disease and stroke, which kill more than 15 million people. Cancer kills more than 6 million; chronic obstructive pulmonary disease almost 3 million. All impose heavy burdens of disability, social cost and economic loss.

But the same threat is also growing in developing countries, for as life expectancy there also increases, so too does the certainty that people will become more and more prone to diseases that are more common among older age groups. Already, the outlook for most individuals in the developing world is that if they do manage to survive the infections of infancy, childhood and maturity, they will become exposed in later life to noninfectious diseases that threaten to shorten or disable their remaining years.

Health researchers often refer to this situation as the “epidemiological transition” – the changing pattern of health in which poor countries inherit the problems of the rich, including not merely illness but also the harmful effects of tobacco, alcohol and drug use, and of injuries, suicide and violence.

The phenomenon is also sometimes known as the “double burden”. The description is all too accurate: hundreds of millions of people now live under two shadows – the long-familiar one of infectious diseases, such as malaria or tuberculosis, and in addition the new and growing shadow of noninfectious, chronic diseases, for which they lack adequate treatment, and of the social ill health that all too frequently accompany socioeconomic development.

Increasingly, health is influenced by social and economic circumstances over which the individual has little control, and over which the conventional health sector also has little sway. As a result, many countries are now experiencing not merely an epidemiological transition, but an “epidemiological polarization” – a widening gap in health terms between rich and poor. This was the theme of The World Health Report 1995 – Bridging the gaps.

For richer, for poorer?

That report showed that infectious diseases are more prevalent among poorer and rural people, while middle- and upper-income urban dwellers – whose life expectancy is higher – are more exposed to noninfectious diseases and conditions. In other words, the poorer an individual is, the more probable it is that he or she will become ill and die of an infectious disease; the richer the person, the greater are the odds of suffering and dying from a noninfectious disease. Furthermore, as the gaps in life expectancy clearly demonstrate, the poor die young, while the rich die old.

These facts raise a fundamental issue: global health priorities which emphasize infectious diseases will benefit the poor much more than the rich. Shifting priorities significantly away from infectious diseases towards chronic diseases would benefit the rich at the expense of the poor, and further widen the gaps that currently exist between them. This would be in direct conflict with the goals of equity in health. The aim is to achieve adequate health for all, rather than simply to achieve still better health for those whose health is already adequate.

Any further improvements in health thus demand integrated, comprehensive action addressing all the determinants
of ill-health. Countries, particularly in the developing world, can no longer afford to deal with the two challenges of infectious diseases and chronic diseases sequentially, as in the past: they must address them simultaneously, and the international community must help them to do so. While these will certainly be challenges reaching far into the future, they already exist today, and must be confronted today.

Indeed, separating infectious and noninfectious diseases creates something of a false division. It is becoming more and more difficult to establish a firm borderline between them. For example, several forms of cancer are known to be linked to infectious agents, and infections also play a role in some cardiovascular diseases – rheumatic heart disease, for instance.

Perhaps more important is the recognition that physical and mental health are interrelated. Physical illness frequently has serious psychological consequences. It is little wonder, given how much long-term pain and distress chronic diseases impose on individuals, that depression and other affective disorders are themselves emerging as major disease burdens. At the same time, there is mounting evidence that some mental disorders, such as dementia, have a biological basis.

Curing and caring

One crucial and controversial difference between infectious and chronic diseases needs to be recognized. The history of medicine and public health shows that infectious diseases can be cured – eliminate or destroy the infectious agent, and the disease is defeated. The eradication of smallpox is the supreme example, but many other infectious diseases are steadily being defeated, among them poliomyelitis and leprosy. This could not be achieved without strong community participation – immunization campaigns, for example, cannot succeed without active community support.

Chronic diseases, however, are another matter. With a few exceptions, they have not so far lent themselves so easily to cure. They are less open to direct community action. They do not spread from person to person. Every case of chronic disease represents a burden borne by one individual who, depending on circumstances, may or may not have access to treatment or support (Box 1).

**Box 1. Essential drugs for chronic diseases**

Many chronic diseases can be treated effectively with drugs, and every year more of these drugs enter the market, especially in industrialized countries. Some of the new drugs, but not all, represent real therapeutic advances; most are very expensive. They are often taken for long periods, if not for life, which leads to high treatment costs and increased chances of unwanted side-effects. Chronic diseases are increasingly prevalent in developing countries and the need for drugs to treat them is therefore also rising, although they often remain untreated, because people either have no access to regular medical care or cannot afford it.

The best way to ensure the availability of and equitable access to essential drugs, including those for chronic diseases, is to develop standard treatment protocols and lists of essential drugs for different levels of health care, and to use these as the basis for the supply of drugs, for the training and supervision of health workers, and for reimbursement schemes. Essential drugs should be selected on the basis of evidence and in accordance with the criteria used for compiling the WHO Model list of essential drugs, which is updated every two years.

The need for drug selection is not restricted to developing countries. Health care costs in general, and drug costs in particular, are rising everywhere. Most of the increased drug cost is due to the use of new medicines, and many of these are for chronic diseases. In order to ensure an optimal use of limited resources, a careful evaluation is needed of their cost-effectiveness in relation to existing treatment alternatives. Some industrialized countries have developed very detailed procedures for this difficult process. One example is the pharmaceutical benefit scheme in Australia, which requires proof that a drug is more cost-effective than existing treatments, before it is being approved for reimbursement. It is interesting to note that the list used in the Australian scheme contains approximately the same number of active ingredients as the national list of essential drugs in Zimbabwe.

Another example is the Scottish intercollegiate guidelines network, which is developing national treatment protocols entirely on the basis of evidence. For every treatment recommendation, the strength of the supporting scientific evidence is indicated according to four levels – the strength of the evidence defines the strength of the recommendation. The main objective of the Scottish guidelines is to attain the highest standards in health care, rather than cost-containment. Some of the recommendations lead to increased health care cost, for example in the treatment of diseases which are generally known to be underdiagnosed and undertreated (e.g. diabetic retinopathy).

These two examples show that essential drugs are not for poor countries only or for rural areas only. The concept of essential drugs is just as valid in developed countries, in teaching hospitals, and in health insurance schemes. It is as valid for the treatment of cancer, cardiovascular diseases and metabolic disorders as it is for malaria, acute diarrhoea and pneumonia.
Despite enormous investments in cancer research, and great progress in that field in recent years, the most common cancers stubbornly resist medical control. Intertwined as they are with heredity and natural ageing, occurring gradually and stealthily as they often do over decades, they and other chronic diseases pose far greater problems for medical science than do many infectious diseases.

This stark fact demands a realistic response: if the majority of chronic diseases cannot as yet be cured, the emphasis must be on preventing their premature onset, delaying their development in later life, reducing the suffering that they cause, and providing the supportive social environment to care for those disabled by them.

This must be particularly true of dementia sufferers. Today there are an estimated 29 million people worldwide with dementia, and the number will rise dramatically in the coming years with an ageing population. Already robbed of their memories and rendered helpless by the disease, the last thing they have to lose is their dignity. They will need from health professionals, families and society an extra degree of care with compassion.

Today there are an estimated 380 million people aged 65 years or more, including around 220 million in developing countries. By 2020, the figures are projected to reach more than 690 million and 460 million respectively. It is also forecast that by the same year chronic diseases may be responsible for a large proportion of deaths in the developing world. Cancer and circulatory disease, which have long been dominant in the industrialized world, are already the major causes of death in South-East Asia.

**Hazards of living**

The development of these diseases is seldom, if ever, due to one single cause. Vulnerability to them may be inherited – an area which geneticists have only begun to explore, but undoubtedly of great importance. In addition, many lifestyle and environmental factors are known to increase the risks – factors such as smoking, heavy alcohol consumption, inappropriate diet, and inadequate physical activity. These are at least to some extent within the control of the well-informed individual. But there are others, such as the effects of poverty; poor reproductive and maternal health; undernutrition in infancy and childhood; genetic predisposition; environmental pollution; and unhealthy living and dangerous or stressful working conditions, over which the individual alone has little control.

The ascendancy of chronic diseases is not simply a question of age, although natural ageing plays a fundamental role, or of genetic predisposition. Today, premature mortality and disability from chronic diseases are more common than in previous times. The trend is also a reflection of the way our lives are changing in response to a changing world. For instance, the rapid emergence of middle classes in many developing countries has brought with it unhealthy dietary and behavioural changes.

In many parts of the world, lifestyles are undergoing radical changes – from physical, outdoor labour to sitting at a desk or working in a factory, from rural life to urban existence, from traditional diet to convenience foods, from strict codes of sexual behaviour to more permissive standards, from negligible consumption of alcohol and tobacco to daily or heavy consumption of one or both.

Tobacco-related deaths – primarily from lung cancer and heart disease – already account for 3 million a year, or 6% of total deaths. Other cancers are also linked to smoking. Researchers estimate that during the 1990s, 30 million people will have been killed by smoking, more than half of them while in middle age. While in the past most of these deaths have been in industrialized countries, there are ominous trends in the developing world, where there are estimated to be about 800 million people who smoke, and that number is increasing.

Major work-related illnesses include cardiovascular diseases, respiratory dis-
eases, cancer, musculoskeletal disorders, and reproductive and psychological disorders. Occupational injuries alone affect more than 120 million persons and cause at least 200,000 deaths a year. Up to 350 different substances have been identified as occupational carcinogens. In western Europe alone, some 16 million people are exposed to carcinogenic agents at work.

The interplay of these and other factors is complex and is only gradually being investigated and understood. So too are the interaction between one chronic disease and another, and the genetic components that either predispose some individuals to certain diseases or offer protection against them.

For example, inherited predisposition is important in some common diseases of later life, including coronary heart disease and diabetes mellitus. The number of people suffering from diabetes worldwide is projected to more than double from 135 million now to almost 300 million by 2025.

Millions of people are born every year with hereditary diseases, such as haemophilia or cystic fibrosis, which may require lifelong treatment. Of some 140 million infants born each year, about 4 million enter the world already disabled by major congenital anomalies. Reproductive health, including the health of the mother before, during and after pregnancy, is fundamental to the well-being of her infant, and influences that child’s development into adulthood.

Largely at the other end of the age spectrum, hundreds of millions of adults suffer from mental illnesses ranging from chronic depression and schizophrenia to Alzheimer disease, and huge numbers are disabled for many years by musculoskeletal disorders such as rheumatoid arthritis, back pain and osteoporosis.

**Making a difference**

Although many chronic diseases most commonly appear only after middle age, some strike much earlier. This report examines them, or the factors influencing them, across the entire human life span. Many of the seeds of adult disease are sown in infancy, childhood and adolescence. Children are vulnerable to a wide range of chronic diseases, including rheumatic heart disease, asthma, and some forms of cancer.

At every stage, opportunities exist for prevention or treatment, for promoting healthy behaviour, for cure or for care. Major efforts have also been made, and continue to be made, in these fields, in attacking risk factors, in promoting health as a component of social policies, and in protecting the environment through pollution control.

As this report shows, there is much that remains to be done, and must be done now – in preventing chronic diseases, treating them, curing them; in renewing attacks on the many risk factors, including those outlined above, that contribute to them; in alleviating suffering and reducing disability; in improving standards of care, and access to that care.

Throughout, the report attempts to keep the health of the individual as the centre of interest. Indeed, a key approach to the preparation of the report has been the recognition that the impact of disease on the individual is fundamental to improving health for the community at large.

One person’s suffering can often be overshadowed by the social ramifications of disease in general. In such circumstances, the individual may feel neglected, or forgotten. Involving that person to a greater degree in the protection of his or her health is increasingly necessary.

In terms of setting priorities, the report considers chronic diseases that are major causes of death or avoidable ill-health and disability. These are areas where actions or interventions that have a direct and tangible effect on individual health – that make a difference, and make it sooner, rather than later – are possible.

In recent years action may often have been less direct, requiring legislation or regulation, with slower repercussions for individual health. At the same time, the report outlines what individuals can do to take care of their own
health, and how the family and society can support them.

Future action must go beyond the mere repetition of familiar health education messages. It is no longer enough to say simply: don’t smoke, don’t drink excessively, take exercise and consume a better diet. These messages are indispensable. If followed, they will help substantially in reducing the risks of some chronic diseases; but in terms of prevention they will not in themselves be enough. Enabling people to adopt healthy lifestyles, and creating supportive environments for health are two core elements of health promotion action. But such action requires time to produce results.

Latterly, the emphasis has been on protecting and promoting health rather than on prevention, treatment, cure and rehabilitation. The global trends in chronic disease indicate that short-term approaches, such as the development of new drugs, treatments and vaccines, are urgently needed. Research into the biological origins of disease is essential to prevention, and the importance of treatment and rehabilitation for those who have already contracted disease cannot be overlooked.

Following a general section giving an overall assessment of the global health situation in 1996, this report deals with the chronic diseases that are leading causes of death and disability. It gives a brief description of each disease, and estimates the global numbers affected by it; identifies risk factors that contribute to it; and explains the methods of prevention, detection, diagnosis and treatment. Together, these methods form a basis for reducing and conquering suffering, reducing its social and economic costs to families and society, and thereby enriching humanity.

The global situation — 1996 update

The global political situation

The global trends towards democratization continued unabated during 1996. Many countries carried out popular elections, considered to be reasonably free and fair, to choose their governments. These elections laid the foundations for increased participation of people in building their nations, deciding on development priorities, shaping the style of governance and determining its degree of transparency and accountability.

Although the transition towards democracy has in some instances frustrated popular hopes and aspirations, people have in general not given up pursuing this goal. But the pace of progress was being cautiously set. In an ageing world, the proportion of the elderly among electorates is increasing. Their empowerment through education and information should ensure, in a democratic environment, that their interests and priorities are reflected in health and welfare policies and programmes.

Liberal democracy has given billions of people the right to express their opinions freely and openly. Thanks to modern communication media, there has been rapid and wide diffusion of information on many of the issues that are fundamental to human development.

Unfortunately many nations and states where sharp differences among ethnic and religious groups were set aside in the pursuit of economic development, now experience bitter feuds that lead to new social divisions. Political maps are being redrawn as numerous ethnic and political groups emerge, make claims and parcel out new territories. The increase in the number of Member States of WHO from 170 in 1991 to 190 in 1996 partly reflects this phenomenon.

A number of local conflicts and threats to peace became internationally known owing to almost immediate glo-
The flow of arms to many of these areas afflicted by civil violence has been increasing, and major victims have been civilians, primarily women and children (Box 2).

In many cases, massive new population movements within and across international borders have also taken place. It is estimated that in December 1995, more than 26 million people belonged to "populations of concern to UNHCR", which include in addition to more than 13 million refugees, persons granted temporary protection and those allowed to stay in another country on humanitarian grounds. More than 40% of refugees (5.7 million) were in Africa and about 35% (4.5 million) in Asia.

As emergency relief and humanitarian assistance are provided to these people, another battle must be fought to overcome the difficulties they face in having access to preventive and curative care, to food and water and to rehabilitation in a context of general anarchy when basic infrastructure is disrupted or destroyed and human and material resources are diverted elsewhere. A major concern is the outbreak of epidemics of diseases such as cholera, dysentery, meningitis, malaria, typhus and measles, as well as the spread of antibiotic resistance among the displaced populations.

WHO, in collaboration with UNHCR and UNICEF and other national and international nongovernmental organizations, undertakes activities to contain and control epidemics during complex emergencies and mass population movements, through early detection and timely response using surveillance systems adapted to the population groups concerned and local situations, bearing in mind the need to strengthen local capability (Box 3). The International Committee of the Red Cross has been focusing on developing capability in "war surgery" through training seminars and transmitting its experience to wider medical and health circles through publications and videos. Many of the refugees suffer mental distress as a result of problems and difficulties encountered before, during or after the flight from their home regions. At each stage of these journeys, specific steps – such as organizing programmes dealing with the trauma of political violence – have been taken to lessen their risk of ill-health.

The world economy

The growth of the world economy accelerated slowly during 1996. Global economic and financial conditions were considered to be encouraging on the whole, despite a disappointing performance in Europe generally. The strength of economic activity was particularly impressive in the emerging market economies of the developing world with an increasing number of them reaping the benefits of structural reforms and a favourable macroeconomic situation. In most of the economies in transition, the
Box 3. WHO in Rwanda

In November and December 1996, the massive and sudden return of nearly 1.2 million Rwandan refugees from eastern Zaire and the United Republic of Tanzania to Rwanda surpassed the capacity of the government of Rwanda and the international community to take care of them, resulting in significant threats to health. WHO responded immediately at the field level by coordinating health activities and monitoring their health status.

Potential for epidemics. Cases of cholera and dysentery, and deaths due to severe diarrhoea were frequently reported. One of the main concerns was the spread of drug resistance which could significantly affect the treatment of these diseases. Sporadic outbreaks of meningitis had occurred in the past in Rwanda, but were contained thanks to an efficient early detection system.

Threat of other infectious diseases. Malaria and acute respiratory diseases were the two most common causes of morbidity in the country. HIV prevalence was high among the general population, with sexually transmitted diseases one of the 10 most common causes of morbidity. Cases were poorly managed, and condoms rarely provided at the peripheral level. The treatment and control of tuberculosis cases was hampered by a shortage of drugs.

Weakness of health care services. Only 43% of the health facilities had the minimum necessary equipment. Some hospitals reported an increase of 60% in the occupation of beds after the repatriation movement. Facilities at health centres for delivery and postdelivery care were rudimentary and often unsatisfactory. The significant number of women among the returnee population increased the need for enteral, natal and postnatal care services. The massive return of the refugees exacerbated the shortage of drugs in most of the health centres as well as of beds, mattresses, gloves, needles and other pieces of equipment.

Lack of health care personnel. Most health facilities were reported to be understaffed. The Ministry of Health estimated that 80 additional medical doctors and 80 nurses needed to be recruited. The health management structures were not functional in some areas, mainly those bordering eastern Zaire, due to the insecurity which prevailed before the massive repatriation.

WHO provided prompt assistance to Rwanda and the subregion by:

- sending experts in the areas of epidemiology, public health, water and sanitation to provide technical support in response to the urgent situation;
- recruiting United Nations volunteer medical officers to provide medical care in the district health facilities in the communes that received the greatest number of refugees;
- conducting, at the request of the Ministry of Health, a rapid assessment of the health situation in Rwanda after the massive influx of returnees;
- coordinating the activities of nationals and nongovernmental organizations in districts and communes;
- assisting the Ministry of Health in elaborating the health component of the Government Emergency Programme for Repatriation and Resettlement of Returnees;
- providing essential drugs and other medical supplies for the control of cholera and malaria;
- supporting laboratory diagnosis of cholera in Rwanda, including drug sensitivity testing.

move towards capitalism was becoming increasingly successful, with the private sector responding to macroeconomic stability, market forces, and to countries' integration into the world economy. Overall the global economic expansion is expected to continue at a satisfactory pace during the rest of this decade, stimulated by the growing interaction of countries in world trade, foreign direct investment and capital markets – the globalization process.

The global economic decline of the early 1990s seemed to have ended, with the world's gross output of goods and services growing at about 2.5% in 1996, that is, for the third consecutive year. At least 109 countries with a combined population of 5.3 billion (all but about 300-400 million of the world's people) saw their per capita output rise in real terms during 1996.

Developing countries continued to experience a rise in per capita GDP in 1996. There were 75 countries with a combined population of at least 4.3 billion in this group in 1996 compared to 50 countries in 1993. The least developed countries in particular have made significant progress in this regard. At least 21 out of the 48 least developed countries (with about 80% of the total population of these countries) registered growth in per capita GDP in both 1995 and 1996. This compares impressively with the experience of the early 1990s, when only about a dozen least developed countries, with about half the population, were in this category. The gain in countries with rising per capita GDP has been most pronounced in Africa, where the percentage of the population living in countries with growing per capita GDP increased from 67% in 1995 to over 87% in 1996. The total output of the economies in transition was one-third less in 1995 than in 1990. Whereas these economies in central and eastern Europe and the Baltic States began to grow from 1994, the output of the newly independent States continued to decline, and the prospects for positive growth in the near future are uncertain. Developed countries experienced a growth rate of about 2% in 1996 with
an uneven growth and labour market performance. Inflation was successfully contained, but unemployment remained stubbornly high, notwithstanding respectable economic growth, and became a major concern in many of these countries. Overall, the short-term outlook for the global economy is a continued but modest increase, with growth rates in real terms for 1997 projected at more than 6% for the developing countries, 3% for the economies in transition and 2.5% for the developed countries.

The global economic environment for developing countries has also been relatively favourable over the past five years. Growth in world trade averaged more than 6% annually during 1991-1995, which is more than the growth of world output during this period. Private capital inflows to developing countries quadrupled, yet marked disparities in growth in capital inflows persisted among and within developing regions. The extent to which countries benefited from the increased integration of the world’s goods and capital markets was also highly uneven (Table 1). Available data reveal, however, that the fastest growing regions over the past five years also showed the greatest advances in integration with the world economy. A boost to international trade was given both by the establishment of the World Trade Organization (WTO) at the beginning of 1995 and by the creation of several new regional economic groups. As a result of trade liberalization, a growing number of developing countries are expected to experience gains in real income as a result of their increasing integration in the global economy.

Among the many individual trade agreements that WTO administers, several have implications for the health sector, particularly those regarding standards. Aimed at ensuring that national health and safety regulations are not used as a disguised form of protectionism, the agreements on technical barriers to trade and on sanitary and phytosanitary measures encourage countries to use internationally agreed quality and safety standards. They cover such health-related items as pharmaceuticals and biologicals, together with food products—a major export of developing countries—and their application should lead to the production of safer, higher-quality goods. Pharmaceuticals are further affected by the agreement on intellectual property rights, by virtue of which their patenting has become compulsory. The eventual impact of that measure on the continuing availability of low-cost drugs in developing countries remains to be seen.

To guard against the risk of financial interests taking precedence over public health and to enable national authorities to handle the impact of an

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* Ranked by real GDP growth per capita.
Source: World Bank, Global economic prospects and the developing countries 1996.

expansion of international trade in services, UNCTAD and WHO in 1996 jointly launched a project on international trade in health services. Following a global analysis and case studies, the plan is to examine the problems and opportunities that developing countries face in the sector of trade in health services, as well as associated social advantages and disadvantages, as a basis for strengthening the capacity of developing countries to maximize net benefits.

Many developing countries have succeeded in establishing markets for their goods in both developed economies and developing countries. Current international economic conditions are providing an opportunity for growth from which many countries have been
able to benefit. The challenge now is to translate this growth into reductions in unemployment and poverty.

Though some progress has been made in reducing poverty in the developing world since 1987, overall gains have been small and uneven. Recent studies by the World Bank indicate that while overall poverty (its threshold level being an income of less than $1 per capita per day), fell slightly from 30% of the world population in 1987 to 29% in 1993, the number of people living on less than $1 a day rose by about 85 million to 1.3 billion in 1993. Significant progress has been made in reducing the number and share of households with low incomes in South and East Asia and in the Eastern Mediterranean and northern Africa in the last decade; they are more or less static in Latin America and in sub-Saharan Africa, but are rising in eastern Europe and central Asia.

There is hope that poverty in the world can be considerably reduced during the next decade. This will depend on political commitment and sustained action, at national and international levels, for implementing the World Bank’s The heavily indebted poor countries (HIPC) debt initiative – a program of action and country-focused activities for achieving at least the global target of the Organization of Economic Cooperation and Development for shaping the 21st century.

Success in these efforts would ironically pose great challenges for the control of “diseases of affluence” such as chronic and debilitating diseases. For, with even small improvements in living standards, people become exposed to a lifestyle and behaviour such as consumption of high-fat foods, alcohol and tobacco, a more sedentary life and inadequate physical activity. Several studies have shown that not only poverty but also affluence can lead to a wide variety of causes of death, disease and disability.

Population and its growth

One encouraging statistic from the United Nations Population Division’s 1996 assessment of world population prospects was that the average annual increase of the global population fell from 87 million persons during the period 1985-1990 to 81 million during 1990-1995.

The population increased globally by more than 80 million during the year, reaching a total of 5.8 billion in mid-1996. It increased by 17 million children and adolescents aged 0–19, 55 million adults aged 20–64, and 9 million elderly aged 65 and above (of which 3 million aged 75 and above). The age group 0–19 years grew by about 0.7% during the year, while the elderly population grew by about 2.4%; the adult population increased by 1.8%. The increase in the elderly population aged 65 and above consisted of more women (4.7 million) than men (4.2 million) during the year.

Fertility

The world population in 1995 was about 29.5 million fewer (34 million less in developing countries and about 4.5 million more in developed countries) than assessed in 1994. This was because in 1990-1995 fertility declined to 3 children per woman instead of 3.1 as predicted. If this trend continues, the population of 9.4 billion in 2050 may well be nearly half-a-billion less than the 1994 projection. The population of developing countries is now estimated to have grown by about 1.8% per annum between 1990 and 1995 instead of 2.1% in 1980-1985 – due to a decline in fertility in a number of countries of south-central Asia and sub-Saharan Africa. For example fertility declined in Bangladesh, Côte d’Ivoire, India, Kenya, Syria and Turkey. Added to this fertility decline was the higher mortality in countries affected by wars, such as Burundi, Iraq, Liberia and Rwanda, and by the spread of AIDS.
Population Ageing

The number of people aged 65 years and above increased to 380 million, accounting for 7% of the total global population of 5.8 billion in 1996; those aged above 80 years formed more than 16% of the over-65s. While the proportion of females among those aged 65 and above was about 55%, among those aged 80 and above it was 65%.

Between 1990 and 1995, the population aged 65 and above increased by 14% globally; by 17% in developing countries and 11% in the least developed countries; but by only about 10% in developed countries. Compared with 1996, by the year 2020 the over-65 population is projected to increase by 82% globally; by about 100% in the least developed and developing countries; and by about 40% in the developed countries. In 1996, less than 5% of the population were aged 65 and above in 124 countries. By 2020, this will be the case in only 68 countries. Among those over 80 years, there will be a more rapid increase in the number of older women than men. A major challenge will be to develop innovative ways of tackling the special health and welfare problems of elderly women.

Education

The context for educational development in the 1990s has been profoundly affected by recent changes in the world political and economic order. These changes include the emergence of new democratic governments, the continuing globalization of the world economy, expansion of the service sector and the rapidity of new information and communication technologies – all of which call for new knowledge, skills and attitudes. About 103 million children aged 6-11 need a place in primary school in the developing regions during the 1990s. The World Declaration on Education for All adopted in March 1990 broadened the scope of basic education to include early childhood development, primary education, nonformal learning (including literacy and life skills) for youth and adults, and learning conveyed through the media and social action. A global assessment for the period 1990-1995 indicated that there has been definite progress in basic education. Programmes for early childhood development which integrate education, health and nutrition components are a fast-growing area of basic education reaching more than 56 million children in the developing regions, i.e., about one out of five in the 3-6-year age group.

The single most positive and significant feature of the mid-decade balance sheet was, however, in primary education in most developing countries. Enrolments increased from 496 million pupils in 1990 to 545 million pupils in 1995 – with the pace of enrolment growth being twice as fast during 1990-1995 as in the 1980s; sub-Saharan Africa and South Asia enrolled the most additional pupils – some 33 million since 1990. In spite of economic hardship, many countries affected by serious declines in enrolment during the 1980s appeared to have reversed the downward trend. Compared with an estimated 128 million school-age children with no access to schooling in 1990, the number of out-of-school children in the 6-11 age group in all developing countries in 1995 was some 110 million. Sub-Saharan Africa was the only region where the number of out-of-school children continued to grow.

Most developing countries still lack the capacity to monitor learning achievement in primary schools. Grade repetition and drop-out continue to be serious obstacles to universal primary education. Against this background, developing countries in 1995 had an estimated 870 million illiterate youth and adults aged 15 years and over – some 4 million more than in 1990. The overall adult literacy rate increased from 75% in 1990 to 77% in 1995; however, nearly two-thirds of all illiterate adults were women, a proportion that has not changed since 1990. In developing countries, there was an increase in female enrolment from about 225 million in 1990 to about 250 million in 1995. Literacy rates among women have in-
creased slightly to 71% in 1995 but lag behind men’s literacy rates in nearly all developing countries. The nine high-population countries—Bangladesh, Brazil, China, Egypt, India, Indonesia, Mexico, Nigeria and Pakistan—which account for more than 70% of the world’s illiterate adults, have identified the provision of basic education through mass media as one of the main areas whose potential has yet to be fully exploited. Education plays a key role in tackling ill-health, particularly when it includes “life skills” related to central issues of daily life, such as health, hygiene, nutrition, the environment and civil rights. Positive developments such as those outlined above and progress towards “education for all”, though not spectacular, augur well for the control of diseases and reduction of suffering in the future.

Environment, housing and homelessness

Housing-poverty contributes significantly to ill-health. The term describes households that lack safe shelter, piped water and adequate sanitation and drainage. An estimated 1 billion rural households lack water supplies. Several hundred million people rely on simple latrines. At least 600 million urban dwellers in Africa, Asia and Latin America live in life- and health-threatening homes and neighbourhoods. The estimated number of homeless people worldwide varies between 100 million and 1 billion, depending on how homelessness is defined. The estimate of 100 million includes those who sleep outside or in public buildings or in overnight shelters. The 1 billion estimate includes those in refugee camps or in insecure or temporary accommodation.

Homelessness rose in the developed world during the 1980s. In the United States, the number of shelter beds available for the homeless in cities of over 100,000 inhabitants nearly tripled during that period—from 41,000 to 117,000. In the United Kingdom, the number of households recognized as homeless by public authorities rose from around 20,000 in 1970 to 117,900 in 1986 and to 167,300 in 1992. In the early 1990s, 1.8 million people in the 12 countries of the European Union depended on the course of a year on public or voluntary services for temporary shelter, or slept outside. At least another 15 million people lived with more than two persons per room, in substandard housing.

The dwelling-place is a critical component of the interaction between people and their environment. Studies in developed countries show that people spend more than 90% of their time indoors; there are few similar studies in developing countries.

The construction of water and sanitation facilities represents only a fraction, often relatively small, of the total effort necessary to achieve the desired health benefits, particularly reducing risks of infection. Many water resource development projects have failed to establish any health objectives or even to consider the likely indirect health outcomes of the projects. Concern about the possible carcinogenic risks arising from exposure to chemical contaminants in drinking-water focuses mainly on certain pesticides, halogenated organic compounds and inorganic compounds. The causal association between high arsenic concentrations in drinking-water and skin cancer is now well established. Furthermore, elevated mortality from several cancers, including bladder cancer, has been observed in populations exposed to high concentrations of arsenic in drinking-water. Procedures for the collection, disposal and treatment of wastes can be sources of carcinogenic hazard. For example, chemical agents may be present in the wastes and particulates emitted during waste incineration, or in leachates from landfill sites that find their way into surface water and groundwater.

There are tens of thousands of man-made chemicals in common use throughout the world, and each year up to 2000 new chemicals are introduced onto the market. An estimated 50 million people work on plantations in de-
veloping countries and are in direct contact with pesticides. Over 500 million more are exposed through traditional agriculture and as seasonal workers. Even the theoretically non-exposed population may suffer toxic effects through food or water contamination with pesticides. Examples of the most dramatic pesticide-related incidents include methyl contamination of seeds in Iraq (over 6000 people affected and over 400 deaths) or the contamination of flour with parathion in Colombia (600 affected and 88 deaths). The consequences of chronic poisoning with heavy metals include heart failure, kidney disorders and hypertension arising from exposure to cadmium, and cardiovascular disease associated with exposure to arsenic. Exposure to high levels of lead has a direct toxic effect on the heart. The risk could grow in urban areas in developing countries with the rising number of vehicles using leaded petrol, despite restrictions.

Four years after the accident at Chernobyl nuclear power station, increased incidence of thyroid cancer was observed in children in Belarus and Ukraine. This was much sooner than would have been predicted from the radiation studies of Japanese survivors of the atomic bomb. Thyroid cancer is normally rare in children, but more than 420 cases were observed in children aged under 15 in Belarus between 1986 and 1995, compared to only 3 cases during 1981-1985. The main sources of nonionizing radiation are ultraviolet radiation from the sun and artificial light sources, and natural and human-made electromagnetic fields. Over 100,000 malignant melanomas of the skin are estimated to occur globally each year. The main risk at present, however, arises from excessive exposure to ultraviolet light, particularly as a result of sunbathing.

About 3 million deaths are estimated to be attributable to air pollution globally each year. Evidence, mostly from industrialized countries, links outdoor air pollution with cardiovascular diseases and asthma. Heart failure has been linked to airborne particles, carbon monoxide, and sulphur dioxide levels. Some lung diseases, such as pneumoconiosis, are caused by inhalation of industrial dusts.

**Food security and nutrition**

Hunger persists at a time when global food production could meet the needs of every person on the planet. Freedom from hunger and malnutrition, essential to the enjoyment of the highest attainable standard of health, is among the fundamental rights of human beings. Current food availability for the world as a whole was estimated by the Food and Agricultural Organization (FAO) at 2720 calories per person per day in 1990-1992, up from 2300 calories in 1961-1963. Food availability has increased in all regions, except sub-Saharan Africa. It is projected that by 2010, even developing countries as a group will have achieved the per capita food availability of 2730 calories.

Progress towards increasing food security has been uneven within and among countries, leaving an unacceptably large number of undernourished or food-insecure individuals. Increased production and distribution supplemented by food aid can help promote food security. Nutritional status, however, reflects not only the quantity of food available and consumed but also its quality, including safety, and the extent to which the body transforms food into nutrients, which will protect and promote health and enable people to function to their potential capacity. Malnutrition must therefore be considered from two points of view: undernutrition and obesity.

While over 800 million people are estimated to lack access to food to meet their daily basic needs for energy and protein, more than 3 billion people are deficient in essential micronutrients such as iodine, vitamin A and iron. These deficiencies lead to poor physical and cognitive development as well as to lowered resistance to illness, brain damage, blindness and even death. More than half of the deaths occurring annu-
ally among children aged under 5 in developing countries are associated with malnutrition.

Simultaneously, these countries are also currently experiencing a different type of nutrition crisis: diet-related chronic diseases and disorders. Too often, one type of malnutrition is being exchanged for, or - worse still - being superimposed upon another in many of these countries. It is increasingly recognized that cultural aspects of food production, distribution and preparation play a crucial role in the promotion of good nutrition, apart from the types of food themselves.

Obesity, or overweight, is a lifestyle risk factor associated with increased morbidity and mortality from chronic diseases such as circulatory diseases, cancer, diabetes and chronic musculoskeletal and respiratory diseases. In many cases these diseases are preventable. An increase in glucose intolerance among school-age children is linked to consumption of sugary soft drinks and is an example of unhealthy dietary habits. More often than not, obesity is the result of unhealthy eating habits coupled with a sedentary way of life. When intake of energy with food exceeds energy expenditure, the excess is stored in the form of body fat. Energy storage is part of the body’s natural protection against famine and is fundamental for survival when food is scarce. However, when energy storage becomes the rule rather than the exception, it leads to obesity, which can be described as the point beyond which increasing body fat storage is associated with elevated health risks.

Interventions focus on weight-loss therapy. Weight loss is difficult to sustain, but is likely to benefit health in the long term if it is sustained. Many overweight individuals who lose an appreciable amount of body weight regain it later. Repeated attempts to lose weight may thus lead to “weight cycling”, which itself may be associated with adverse health consequences.

A recent FAO study predicts that the trends towards increasing per capita food supplies will continue in most developing countries, and that the incidence of undernutrition may fall by the year 2010 to a fairly low level of 12% of the total population. It is therefore likely that increasing incidence of obesity may evolve as a major concern with far-reaching implications for health, in view of the massive burden of disability and death that would result from diet-related heart disease, cancer and other chronic diseases. The Rome Declaration on World Food Security and the World Food Summit Plan of Action adopted in November 1996 have also set the objective of ensuring that food supplies are safe, appropriate and adequate to meet the energy and nutrient needs of the population. Adequate nutrition, achieved through regular consumption of an adequate and balanced diet, is indispensable for good health and essential to avoid many of the diet-related chronic diseases.

Life expectancy at birth for both sexes continued to improve globally, reaching a global value of 65 years by 1996.

Life expectancy and mortality

Life expectancy at birth for both sexes continued to improve globally, reaching a global value of 65 years by 1996 (63 for men and 67 for women). In 30 countries, it was under 60 years for both sexes. In 53 countries, the value was less than 60 for men and in 48, it was less than 60 for women.

Estimates of life expectancy at birth between 1980 and 1995 are available for 171 WHO Member States. Between 1980 and 1995, life expectancy at birth increased by about 4.6 years globally for both sexes, with an increase of about 4.4 for men and 4.9 for women. There were increases of at least 5 years for men in 74 countries, and for women in 80. In three Member States, the increase represented 10 years or more; in 74, the increase was between 5 and 10 years; in 94 it was less than 5. In 10 countries, however, there was a decrease, 7 of which are economies in transition and 3 developing countries.

A significant trend in global mortality can be observed if the patterns of death in 1960 and 1996 are compared. Of 50 million deaths in 1960, 19 million were in children under 5, whereas the number had declined to 11 million for the same age group in 1996. On the
<table>
<thead>
<tr>
<th>Diseases/conditions (based on ICD-10)</th>
<th>Deaths</th>
<th>New (incidence)</th>
<th>All (prevalence)</th>
<th>Disabled persons (permanent and long-term)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALL CAUSES</strong></td>
<td>52,037</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Certain infectious and parasitic diseases (selected), of which:</strong></td>
<td>17,312</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute lower respiratory infection (ALRI)</td>
<td>3,905</td>
<td>394,000&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>3,000&lt;sup&gt;b&lt;/sup&gt;</td>
<td>7400&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhoea (including dysentery)</td>
<td>2,473</td>
<td>4,022,000&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malaria</td>
<td>1,500-2,700</td>
<td>300,000-500,000</td>
<td></td>
<td>22,600&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>1,500</td>
<td>3,100</td>
<td>22,600&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1,156</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Measles</td>
<td>1,010</td>
<td>42,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Whooping cough (pertussis)</td>
<td>355</td>
<td>40,000</td>
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<td></td>
</tr>
<tr>
<td>Neonatal tetanus</td>
<td>310</td>
<td>385</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trypanosomiasis, African (sleeping sickness)</td>
<td>150</td>
<td>200</td>
<td>300</td>
<td>100</td>
</tr>
<tr>
<td>Dengue fever/dengue haemorrhagic fever</td>
<td>138</td>
<td>3100</td>
<td></td>
<td></td>
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<tr>
<td>Leishmaniasis (total), of which:</td>
<td>80</td>
<td>2000</td>
<td>3820</td>
<td></td>
</tr>
<tr>
<td>Leishmaniasis, visceral (kala-azar)</td>
<td>80</td>
<td>500</td>
<td>1270</td>
<td></td>
</tr>
<tr>
<td>Leishmaniasis, cutaneous and mucocutaneous</td>
<td>1,500</td>
<td>2,500</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoebiasis (Entamoeba histolytica)</td>
<td>70</td>
<td>48,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hookworm diseases (ascariasis and necatoriasis)</td>
<td>65</td>
<td>151,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rabies (dog-mediated)</td>
<td>60</td>
<td>60&lt;sup&gt;c&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ascarasis (roundworm)</td>
<td>60</td>
<td></td>
<td>250,000</td>
<td></td>
</tr>
<tr>
<td>Onchocerciasis (river blindness)</td>
<td>47</td>
<td></td>
<td>17,655</td>
<td></td>
</tr>
<tr>
<td>Trypanosomiasis, American (Chagas disease)</td>
<td>45</td>
<td>300</td>
<td>18,000</td>
<td></td>
</tr>
<tr>
<td>Meningococcal meningitis (see also bacterial meningitis)</td>
<td>40</td>
<td></td>
<td>400</td>
<td>50</td>
</tr>
<tr>
<td>Schistosomiasis</td>
<td>20</td>
<td></td>
<td>200,000</td>
<td></td>
</tr>
<tr>
<td>Japanese encephalitis</td>
<td>10</td>
<td>40</td>
<td></td>
<td>8</td>
</tr>
<tr>
<td>Trachoma infections (foodborne)</td>
<td>10</td>
<td></td>
<td>40,000</td>
<td></td>
</tr>
<tr>
<td>Trichuriasis (whipworm)</td>
<td>10</td>
<td></td>
<td>45,500</td>
<td></td>
</tr>
<tr>
<td>Poliomyelitis, acute</td>
<td>7</td>
<td>20</td>
<td></td>
<td>10,600</td>
</tr>
<tr>
<td>Cholera (1996 notifications)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>6</td>
<td>120</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leprosy</td>
<td>2</td>
<td>530</td>
<td>1,260</td>
<td>3,000</td>
</tr>
<tr>
<td>Yellow fever (1995 notifications)</td>
<td>0.2</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plague (1995 notifications)</td>
<td>0.1</td>
<td>1.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Giardiasis</td>
<td>5</td>
<td></td>
<td>500</td>
<td></td>
</tr>
<tr>
<td>Endemic treponematoses</td>
<td>...</td>
<td>460</td>
<td>2,600</td>
<td>260</td>
</tr>
<tr>
<td>Dracunculiasis (guinea-worm infection)</td>
<td>...</td>
<td>1300</td>
<td></td>
<td>140</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>...</td>
<td></td>
<td>170,000&lt;sup&gt;e&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Trachoma</td>
<td>...</td>
<td></td>
<td>152,420</td>
<td>5,600</td>
</tr>
<tr>
<td>Lymphatic filariasis</td>
<td>...</td>
<td></td>
<td>119,100</td>
<td>119,100</td>
</tr>
<tr>
<td>Sexually transmitted diseases (selected), of which:</td>
<td>...</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Syphilis</td>
<td>...</td>
<td>12,000</td>
<td>28,000</td>
<td></td>
</tr>
<tr>
<td>Gonococcal infection (gonorrhea)</td>
<td>...</td>
<td>62,000</td>
<td>23,000</td>
<td></td>
</tr>
<tr>
<td>Chlamydial infections, including lymphogranuloma (venereum)</td>
<td>...</td>
<td>89,000</td>
<td>85,000</td>
<td></td>
</tr>
<tr>
<td>Chancroid</td>
<td>...</td>
<td>2,000</td>
<td>2,000</td>
<td></td>
</tr>
<tr>
<td>Trichomoniasis</td>
<td>...</td>
<td>170,000</td>
<td>113,000</td>
<td></td>
</tr>
<tr>
<td>Anogential herpes</td>
<td>...</td>
<td>20,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anogential warts</td>
<td>...</td>
<td>30,000</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Others (including emerging diseases e.g. influenza, Ebola, Lassa)</td>
<td>683</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Figure refers to episodes.
<sup>b</sup> Subject to revisions following completion of country-specific estimates.
<sup>c</sup> In addition, 10 million people receive treatment every year.
<sup>d</sup> As at 31 January 1997.
<sup>e</sup> Based on studies reviewed, the prevalence is 3% of the world population.
### Diseases/conditions (based on ICD-10)

<table>
<thead>
<tr>
<th>Diseases/conditions (cancers) – all sites</th>
<th>Deaths</th>
<th>New (incidence)</th>
<th>All (prevalence)</th>
<th>Disabled persons (permanent and long-term)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Malignant neoplasms (cancers) – all sites</td>
<td>6,346</td>
<td>10,320</td>
<td>17,930</td>
<td>...</td>
</tr>
<tr>
<td>Trachea, bronchus and lung</td>
<td>989</td>
<td>1,320</td>
<td>1,205</td>
<td>...</td>
</tr>
<tr>
<td>Stomach</td>
<td>776</td>
<td>1,015</td>
<td>970</td>
<td>...</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>495</td>
<td>875</td>
<td>1,850</td>
<td>...</td>
</tr>
<tr>
<td>Liver</td>
<td>386</td>
<td>540</td>
<td>265</td>
<td>...</td>
</tr>
<tr>
<td>Breast (female)</td>
<td>376</td>
<td>910</td>
<td>2,810</td>
<td>...</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>358</td>
<td>480</td>
<td>270</td>
<td>...</td>
</tr>
<tr>
<td>Mouth and pharynx</td>
<td>324</td>
<td>575</td>
<td>1,075</td>
<td>...</td>
</tr>
<tr>
<td>Cervix</td>
<td>247</td>
<td>525</td>
<td>1,560</td>
<td>...</td>
</tr>
<tr>
<td>Lymphomas</td>
<td>232</td>
<td>395</td>
<td>735</td>
<td>...</td>
</tr>
<tr>
<td>Pancreas</td>
<td>227</td>
<td>200</td>
<td>125</td>
<td>...</td>
</tr>
<tr>
<td>Leukaemia</td>
<td>217</td>
<td>280</td>
<td>370</td>
<td>...</td>
</tr>
<tr>
<td>Prostate</td>
<td>194</td>
<td>400</td>
<td>1,015</td>
<td>...</td>
</tr>
<tr>
<td>Bladder</td>
<td>143</td>
<td>310</td>
<td>780</td>
<td>...</td>
</tr>
<tr>
<td>Ovary</td>
<td>129</td>
<td>190</td>
<td>455</td>
<td>...</td>
</tr>
<tr>
<td>Kidney</td>
<td>92</td>
<td>165</td>
<td>360</td>
<td>...</td>
</tr>
<tr>
<td>Larynx</td>
<td>91</td>
<td>190</td>
<td>505</td>
<td>...</td>
</tr>
<tr>
<td>Body of the uterus</td>
<td>67</td>
<td>170</td>
<td>600</td>
<td>...</td>
</tr>
<tr>
<td>Melanoma of skin</td>
<td>39</td>
<td>115</td>
<td>315</td>
<td>...</td>
</tr>
<tr>
<td>Other malignant neoplasms</td>
<td>965</td>
<td>1,665</td>
<td>2,665</td>
<td>...</td>
</tr>
</tbody>
</table>

### Diseases of the blood and bloodforming organs and certain disorders involving the immune mechanism (selected), of which:

| Thalassaemias and sickle cell disorder   | 240    | 290             | 2,320            | ...                                       |
| Haemophilia                              | ...    | 10              | 420              | ...                                       |
| Anaemia, of which:                      | ...    | ...             | 1,987,300        | ...                                       |
| Iron deficiency anaemia                  | ...    | ...             | 1,788,600        | ...                                       |

### Endocrine, nutritional and metabolic diseases (selected), of which:

| Diabetes mellitus                        | 571    | 10,540          | 135,000          | ...                                       |
| Malnutrition including protein-energy malnutrition (PEM) | 372   | ...             | 200,000          | ...                                       |
| Iodine deficiencies (disorders of thyroid gland), of which: | ... | ...             | 760,000          | 76,000                                    |
| Goitre                                   | ...    | ...             | 120,800          | ...                                       |
| Cretinoids                               | ...    | ...             | 33,600           | ...                                       |
| Cretinism                                | ...    | ...             | 11,200           | ...                                       |

### Mental and behavioural disorders (selected), of which:

| Dementia                                 | 200    | 2,610           | 29,000           | 15,950                                    |
| Alcohol dependence syndrome             | 103    | 75,000          | 120,000          | ...                                       |
| Substance abuse (drug dependence syndrome) | 20    | ...             | 28,000           | ...                                       |
| Schizophrenic disorders                  | ...    | 4,500           | 45,000           | 27,000                                    |
| Mood (affective) disorders               | ...    | 122,865         | 340,000          | 146,000                                   |
| Anxiety disorders                        | ...    | ...             | 400,000          | ...                                       |
| Mental retardation (all types)           | ...    | ...             | 60,000           | 36,000                                    |

### Diseases of the nervous system (selected), of which:

| Bacterial meningitis (excluding neonatal meningitis) | 120 | ... | 1,100 | 145 |
| Parkinson disease                              | 58  | 305 | 3,765 | 2,635 |
| Multiple sclerosis                             | 25  | 105 | 2,505 | 750  |
| Epilepsy                                      | ... | 2,000 | 40,000 | 10,000 |

### Diseases of the circulatory system (selected), of which:

<p>| Ischaemic (coronary) heart disease           | 7,200 | ... | ...   | ... |
| Cerebrovascular disease                     | 4,600 | ... | 9,000 | ... |
| Other heart diseases (e.g. peri-, endo-, and myocarditis and cardiomyopathy) | 3,000 | ... | ... | ... |
| Rheumatic fever and rheumatic heart disease | 500   | ... | 12,000 | ... |
| Hypertensive disease                         | ...   | ... | 690,600 | ... |</p>
<table>
<thead>
<tr>
<th>Diseases/conditions (based on ICD-10)</th>
<th>Deaths</th>
<th>New (incidence)</th>
<th>All (prevalence)</th>
<th>Disabled persons (permanent and long-term)</th>
</tr>
</thead>
</table>
| **Diseases of the respiratory system (selected), of which:** | 2 888 | 600 000 | 155 000 | ...
| Chronic obstructive pulmonary disease (COPD) | 2 888 | ... | ... | ...
| Asthma | ... | ... | ... | ...
| **Diseases of the musculoskeletal system and connective tissue (selected), of which:** | | | | |
| Neck and back disorders | ... | ... | ... | ...
| Arthritis and arthrosis, of which: | | | | |
| Osteoarthritis | ... | 1039 200 | ... | ...
| Rheumatoid arthritis | ... | ... | ... | ...
| **Pregnancy, childbirth and the puerperium (selected), of which:** | 585 | 76 500 | | |
| Haemorrhage | 145 | 14 000 | ... | ...
| Indirect obstetric causes | 115 | 13 200 | ... | ...
| Sepsis | 99 | 11 800 | ... | ...
| Abortion | 76 | 19 900 | ... | ...
| Hypertensive disorders in pregnancy | 73 | 6 900 | ... | ...
| Obstructed labour | 45 | 7 200 | ... | ...
| Other direct obstetric causes | 42 | 3 500 | ... | ...
| **Certain conditions originating in the perinatal period (selected), of which:** | 3 745 | | | |
| Prematurity | 1 150 | ... | ... | ...
| Birth asphyxia | 940 | ... | ... | ...
| Congenital anomalies | 520 | 3 600 | ... | ...
| Neonatal sepsis and meningitis | 460 | ... | ... | ...
| Birth trauma | 440 | ... | ... | ...
| Other causes | 235 | ... | ... | ...
| **External causes (selected), of which:** | 1 058 | | | |
| Suicide | 833 | ... | ... | ...
| Occupational injuries due to accidents at work | 225 | 125 000 | ... | 12 500
| Occupational diseases | ... | 160 000 | ... | ...
| **Other and unknown causes** | 3 094 | | | |
| **Visual disability, of which:** | 179 200 | | | |
| Blindness (total): | | | | |
| Onchocerciasis-related | ... | ... | 44 800 | 44 800
| Cataract-related | ... | 45 | 290 | 290
| Glaucoma-related | ... | ... | 19 340 | 19 340
| Trachoma-related | ... | ... | 6 400 | 6 400
| Vitamin A deficiency-xerophthalmia | ... | ... | 5 600 | 5 600
| Other | ... | ... | 2 850 | 2 850
| **Hearing loss (41 or more decibels)** | 121 000 | | | |

---

1 Figures refer to 5-year prevalent cases (patients who are still alive between 0 and 5 years after diagnosis).
2 To this figure should be added:
   (i) 13 200 deaths in the neonatal period diagnosed as due to low birth weight and attributable to intrauterine growth retardation;
   (ii) 590 000 under-5 deaths listed as terminal infections (usually diarrhoea, respiratory infections or measles), but basically due to severe malnutrition.
3 Figure refers to children under 5.
4 30% of global population aged 20 and above.
5 50% of elderly show radiographic changes. The percentage of those with symptomatic and potentially symptomatic osteoarthritis is even greater.
6 Total number of deaths is about 5 million, which includes 755 000 deaths from neonatal pneumonia (under ALRI), 310 000 deaths from neonatal tetanus and 60 000 deaths from diarrhoea.
other hand, from 12 million deaths in those aged 65 and above in 1960, the figure had increased to 22 million in 1996. While in 1960 most deaths occurred in those aged under 50, they now occur in those aged 50 and above.

The ratio of deaths among those aged 65 and above to deaths among those aged 15 or less has increased from 0.9 in 1980 to 1.6 in 1996. Whereas 16 years ago, there were equal numbers of deaths in both age groups, now there are three deaths among the elderly for two among children and adolescents. If the trend continues, it is expected that by the year 2025, more than 60% of all deaths will be among those aged 65 and above, more than 40% being among those aged 75 and above, while 10% of the population will be aged 65 and above, and more than 3% aged 75 and above. The population distributions by age for 1965, 1995 and 2025 given in Fig. 1 show the ageing of the population.

An approximate distribution by cause of the estimated 52 million deaths worldwide in 1996 is given in Table 2. Of these deaths, over 17 million were ascribable to infectious and parasitic diseases; over 15 million to circulatory diseases; over 6 million to malignant neoplasms; and about 3 million to respiratory diseases. Fig. 2 gives an approximate distribution of deaths worldwide in 1996.

Deaths due to three major killers – circulatory diseases, malignant neoplasms (cancers) and noninfectious respiratory diseases – globally account for more than 24 million or about 40% more than those due to infectious and parasitic diseases. Heart disease and stroke are the leading causes of death among circulatory diseases. Lung cancer is the leading cause among the malignant neoplasms, and chronic obstructive pulmonary diseases among respiratory diseases. Table 3 shows the leading causes of death, based on the best available estimates. Though quite a few deaths can be ascribed to infection, most of the leading causes of death just mentioned are related to long-term exposure to risk factors and to population ageing.
<table>
<thead>
<tr>
<th>Diseases/conditions$^a$ (based on ICD-10)</th>
<th>Deaths</th>
<th>Cases</th>
<th>Disabled persons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rank</td>
<td>Number</td>
<td>Rank</td>
<td>New</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>1</td>
<td>7 200</td>
<td>39 000</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>2</td>
<td>4 600</td>
<td>9 000</td>
</tr>
<tr>
<td>Acute lower respiratory infection</td>
<td>3</td>
<td>3 900</td>
<td>7 600</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>4</td>
<td>3 000</td>
<td>600 000</td>
</tr>
<tr>
<td>COPD</td>
<td>5</td>
<td>2 888</td>
<td>600 000</td>
</tr>
<tr>
<td>Diarrhoea (including dysentery)</td>
<td>6</td>
<td>2 473</td>
<td>4 902 000</td>
</tr>
<tr>
<td>Malaria</td>
<td>7</td>
<td>2 700</td>
<td>300 000-500 000</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>8</td>
<td>1 500</td>
<td>22 900</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>9</td>
<td>1 150</td>
<td>10</td>
</tr>
<tr>
<td>Prematurity</td>
<td>10</td>
<td>1 150</td>
<td>11</td>
</tr>
<tr>
<td>Measles</td>
<td>11</td>
<td>1 150</td>
<td>12</td>
</tr>
<tr>
<td>Cancer of trachea, bronchus and lung</td>
<td>12</td>
<td>1 150</td>
<td>13</td>
</tr>
<tr>
<td>Trichomoniasis</td>
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<td>2 125</td>
<td>1 125</td>
</tr>
<tr>
<td>Occupational diseases</td>
<td>15</td>
<td>1 125</td>
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<td>Occupational injuries</td>
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<td>1 125</td>
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<td>Mood (affective) disorders</td>
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<td>1 125</td>
<td>1 125</td>
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<tr>
<td>Chlamydial infections</td>
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<td>1 125</td>
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<tr>
<td>Amoebiasis</td>
<td>23</td>
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<tr>
<td>Alcohol dependence syndrome</td>
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<tr>
<td>Gonococcal infection</td>
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<td>Iron deficiency anaemia</td>
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<tr>
<td>Neurontic and parkinsonian disorders</td>
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<tr>
<td>Alcohol dependence syndrome</td>
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<td>1 125</td>
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<td>Schizophrenia and other psychoses</td>
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<td>1 125</td>
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<tr>
<td>Schizophrenia and other psychoses</td>
<td>61</td>
<td>1 125</td>
<td>1 125</td>
</tr>
</tbody>
</table>

Leading selected causes of mortality

<table>
<thead>
<tr>
<th>Deaths</th>
<th>Number (000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischaemic heart disease</td>
<td>7 200</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>4 600</td>
</tr>
<tr>
<td>Acute lower respiratory infection</td>
<td>3 900</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>2 888</td>
</tr>
<tr>
<td>COPD</td>
<td>4 000</td>
</tr>
<tr>
<td>Diarrhoea (including dysentery)</td>
<td>2 700</td>
</tr>
<tr>
<td>Malaria</td>
<td>1 500</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>1 150</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1 150</td>
</tr>
<tr>
<td>Prematurity</td>
<td>1 150</td>
</tr>
<tr>
<td>Measles</td>
<td>1 150</td>
</tr>
<tr>
<td>Cancer of trachea, bronchus and lung</td>
<td>989</td>
</tr>
</tbody>
</table>

Leading selected causes of morbidity

<table>
<thead>
<tr>
<th>New cases annually (incidence)</th>
<th>Total cases (prevalence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischaemic heart disease</td>
<td>4 000 000</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>3 900 000</td>
</tr>
<tr>
<td>Acute lower respiratory infection</td>
<td>3 900 000</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>2 888 000</td>
</tr>
<tr>
<td>COPD</td>
<td>4 000 000</td>
</tr>
<tr>
<td>Diarrhoea (including dysentery)</td>
<td>2 700 000</td>
</tr>
<tr>
<td>Malaria</td>
<td>1 500 000</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>1 150 000</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1 150 000</td>
</tr>
<tr>
<td>Prematurity</td>
<td>1 150 000</td>
</tr>
<tr>
<td>Measles</td>
<td>1 150 000</td>
</tr>
<tr>
<td>Cancer of trachea, bronchus and lung</td>
<td>989</td>
</tr>
</tbody>
</table>

Leading selected causes of disability

<table>
<thead>
<tr>
<th>Disabled persons (permanent and long-term)</th>
<th>Number (000)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischaemic heart disease</td>
<td>7 200</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>4 600</td>
</tr>
<tr>
<td>Acute lower respiratory infection</td>
<td>3 900</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>2 888</td>
</tr>
<tr>
<td>COPD</td>
<td>4 000</td>
</tr>
<tr>
<td>Diarrhoea (including dysentery)</td>
<td>2 700</td>
</tr>
<tr>
<td>Malaria</td>
<td>1 500</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>1 150</td>
</tr>
<tr>
<td>Hepatitis B</td>
<td>1 150</td>
</tr>
<tr>
<td>Prematurity</td>
<td>1 150</td>
</tr>
<tr>
<td>Measles</td>
<td>1 150</td>
</tr>
<tr>
<td>Cancer of trachea, bronchus and lung</td>
<td>989</td>
</tr>
</tbody>
</table>

$^a$ Source: Table 2.
$^b$ Chronic diseases given in italics.
Of the 40 million deaths in the developing world in 1996, more than 17 million were due to infectious and parasitic diseases, with about 10 million due to circulatory diseases, 4 million to cancers and 2 million to respiratory diseases (Fig. 4). Even though about 65% of deaths due to circulatory diseases, 60% of deaths due to cancers and more than 65% of deaths due to respiratory diseases occur in developing countries, the most important killer conditions in these countries as a group remain infectious and parasitic diseases. Recent studies indicate that these diseases continue to predominate among the disadvantaged, and distinguish the health situation in poor countries from that of the rich (Box 4). However, chronic diseases such as those mentioned above are emerging as major causes of premature death and disability in the developing world, accounting for almost 40% of all deaths.

As shown in Table 3, leading causes of ill-health due to noncommunicable chronic conditions (given in italics) are broadly: circulatory diseases, respiratory diseases, mental and behavioural disorders, iron deficiency disorders, occupational diseases and injuries, and visual disability and hearing loss. Of over 15 million deaths due to circulatory diseases, more than 7 million were due to ischaemic (or coronary) heart disease; for cancers, nearly 2 million deaths (of more than 6 million) were due to cancer at only three sites, all related to the digestive tract, namely stomach, colon-rectum and liver.

**Health expectancy**

The continuing decline in the human mortality rate has important consequences. Not only is it increasing life expectancy and the proportion of the population reaching advanced ages in many (especially developed) countries, but it is also modifying the average state of health of populations. In particular, the growing prevalence of chronic diseases and disabilities — which best reflects this change in the relation between mortality and morbidity — has focused attention on the increasing tension be-
As traditional health indicators were not adequate to cover this new epidemiological transition, several indicators with various assumptions are being investigated to reflect the state of health: years of (potential) productive life lost (YPLL); disability-free life expectancy (DFLE); quality-adjusted life years (QALY); disability-adjusted life years (DALY) (Box 5). One interesting new indicator is "health expectancy". This indicator integrates information on mortality and morbidity, especially the consequences of diseases. The international network of researchers on health expectancy (REVES), which is working on this new indicator, has adopted the WHO International Classification of Impairments, Disabilities and Handicaps (ICIDH) as a framework.

Over the last decade calculations of health expectancies have been carried out in 37 countries. Analysis of all these studies by REVES allows important conclusions to be drawn concerning inequalities between the sexes, between regions and according to social status. Generally the inequalities found emphasize the differences which already exist in life expectancies. Women have greater life expectancies than men, but the proportion of life that they spend free of disability or handicap is slightly lower; health expectancy in more developed (urban) regions is longer than in less developed (rural) areas; and the poorest and least educated not only experience shorter lives but also a larger proportion of ill-health. The available chronological series show some general trends over a 30-year period: in most developed countries, concurrent with the increase in life expectancy, an equivalent increase in life expectancy free of severe disability is found. When all severity levels are combined, however, disability-free life expectancy seems to be stabilizing. Thus, contrary to widely held beliefs, on the basis of available evidence and this first analysis, years with severe handicap and/or disability are not increasing. While the results for all severity levels combined seem to favour the "expansion of morbidity" hypothesis, the evolution of severe disability and handicap appears to follow the equilibrium theory. Level of severity and reversibility will be important issues in future health expectancy studies.

Fig. 3. Main causes of death among children under age 5, developing world, 1995

Total deaths: 11.2 million

- Diarrhoea, excluding neonatal diarrhea: 19% (2.1)
- ALRI, excluding neonatal pneumonia: 13% (1.5)
- Other neonatal and perinatal causes: 10% (1.1)
- Prematurity: 10% (1.1)
- Birth asphyxia: 8% (0.9)
- Congenital anomalies: 4% (0.5)
- Other: 10% (1.1)

Vaccine preventable: 18% (2)

Fig. 4. Causes of death, developed and developing world, 1996

Developed world (including economies in transition)

- Infectious and parasitic diseases: 43.6 (% 522)
- Diseases of the circulatory system: 21.0 (% 2544)
- Cancers: 8.1 (% 979)
- Diseases of the respiratory system: 1.0 (% 119)
- Perinatal and neonatal causes: 0 (% 3)

Developing world (including least developed countries)

- Infectious and parasitic diseases: 43.0 (17 161)
- Diseases of the circulatory system: 24.5 (9 778)
- Cancers: 9.5 (3 802)
- Diseases of the respiratory system: 4.8 (1 919)
- Perinatal and neonatal causes: 9.1 (3 626)
- Maternal causes: 1.5 (582)
- Other and unknown causes: 7.7 (3 063)

Figures in brackets refer to the number of deaths in thousands.
Box 4. Reducing rich-poor health disparities

How can the health gaps between rich and poor be bridged effectively? One answer is to focus prime attention on the causes of death and disability that most affect the world’s disadvantaged — in other words, infectious and related diseases.

Globally, infectious diseases, maternal and perinatal conditions are killing seven times as many people among the world’s poorest billion than the richest billion. Chronic diseases are responsible for 40% fewer deaths among the poorest billion than the richest. On the other hand, cancers kill twice as many among the richest billion, and cardiovascular diseases two-thirds more.

However, chronic diseases and accidents are quickly emerging as leading causes of death and disability worldwide. At present, they cause almost as much death and disability globally as infectious diseases — 41% compared to 44%. In the developing world alone, chronic diseases account for some 36% of total death and disability, and that proportion is expected to rise to more than 55% by the year 2020. Diseases are not distributed equally among social classes; for example, in the emerging middle and upper classes of the developing world, infectious diseases among infants and children are now increasingly coming under control.

Nevertheless, the fact remains that the poorer an individual is, the more likely it is that he or she will die of an infectious disease; while the richer an individual is, the more likely it is that he or she will suffer and die from a chronic condition. Furthermore, life expectancy comparisons show that the poor die sooner than the rich. The comparison holds good within countries as well as between them. Thus, the poor tend to benefit much more than the rich from a continued emphasis on infectious diseases.

If all continues to go well in the fight against these diseases, the time will come when chronic diseases will require higher priority in actions oriented towards the poor as well as the rich. In the meantime, it is important to carry on with recently-initiated efforts to develop less expensive, more effective ways of preventing and controlling those chronic conditions which are of greatest importance to the poor. But improving the health of the poor demands in addition a renewed determination to combat infectious diseases, especially among the young.

Achievement of adequate health for all remains the goal, rather than simply still better health for those whose health is already adequate.


Confronting chronic conditions

Cancer

The growing burden

More than 10 million people developed cancer in 1996, and at least 6 million others who already had the disease died from it. Globally, a clear trend is emerging: cancer is becoming a leading cause of death in old age. The explanation is simple: the gradual elimination of other fatal diseases, combined with rising life expectancy, means that the risks of developing cancer are steadily growing. Most cancers arise in adults and at an advanced age, and the risk increases exponentially with age. The burden of cancer is, therefore, much more important in populations with a long life expectancy, relative to other groups of diseases.

Probably more than any other single disease, cancer provokes fearful images of pain, disfigurement and inevitable death. Yet cancer is not one single disease; it exists in more than 100 forms and has many causes, from genetic factors to infections. Many types of cancer are both preventable and curable, all are treatable (even those which are not curable), and advances in pain relief have greatly reduced suffering.

The growing cancer burden calls for greater investment in health facilities specific to cancer treatment and for preventive strategies. However, rational planning of the use of resources depends on knowledge of the frequency and distribution of the disease in the population concerned. Unfortunately, good-quality data are still largely missing. In many developing countries, setting up reliable monitoring systems — at least to understand the magnitude of the problem — should be given high priority.

The eight leading cancer killers worldwide are also the eight most common in terms of incidence. Together, they account for about 60% of all cancer cases and deaths. An analysis of the risk factors involved in the development of these cancers shows that a few major factors dominate: diet, tobacco, alcohol,
infections and hormones—all of which lend themselves to preventive actions.

Among men, the leading eight cancer killers are lung, stomach, liver, colon-rectum, oesophagus, mouth-pharynx, prostate and lymphoma. Among women, they are cancers of the breast, stomach, colon-rectum, cervix, lung, ovary, oesophagus and liver.

Cancers now account for about 20% of all deaths in developed regions and about 10% of all deaths in developing regions. In 1996 there were an estimated 17.9 million persons with cancer surviving up to five years after diagnosis. Of these, 10.5 million were women, 5.3 million of whom had cancer either of the breast, cervix or colon-rectum. Among men, prostate, colorectal and lung cancer were the most prevalent (Fig. 5).

Of more than 10 million cancer cases newly diagnosed in 1996 worldwide, 57% occurred in developing countries. For both developed and developing countries the most common cancer site in men was the lung. In developed regions it is followed by prostate cancer (289,000 new cases), colorectal cancer (273,000); and stomach cancer (226,000). In developing regions stomach cancer is second with 408,000 new cases per year, followed by cancer of the liver (309,000) and cancers of the mouth and pharynx (288,000) (Fig. 6).

In women, breast cancer is the most common in affluent populations with 494,000 cases followed by colon and rectum (282,000) and then by cancer of the lung (168,000) and of the stomach (147,000). In developing areas, cancer of the cervix is the most common (421,000 cases), but breast cancer is almost as common (416,000). Third is cancer of the stomach (231,000) and fourth is cancer of the lung (164,000).

The most remarkable changes in the ranking compared to 10 years ago are the steep upward trend of prostate cancer (partly due to the introduction of programmes for early detection), the increase in breast cancer (a site more common in high-income populations), and the increase in lung cancer in women worldwide.

**Box 5. Measuring health**

Because of the complexity of health and disease, there are severe practical difficulties in collecting, analysing and interpreting the data needed to express the full facts. Concepts such as “burden of disease” have been introduced for use as a guide to health status and as a basis for planning policies and actions for health improvement. In order to assess the scale of the burden of disease, and the need for intervention, indicators are needed that capture—and do not obscure—the important components contributing to it. The real determinants of health need to be identified so as to plan where interventions should be directed. In order to decide how to intervene, it is necessary to understand the effectiveness and consequences of various types of intervention. Formulating these issues illustrates the dimensions of the “health measurement” problem and underlines the need for fresh consideration.

As a measure of burden of disease, the disability adjusted life year (DALY) indicator has been proposed. This purports to represent, on a common footing, the years of healthy life lost either through premature death or as a result of life lived with a disability. Adding these two numbers produces a single measure: the DALY. The total number of DALYs in a population in any given year is supposed to indicate that population’s disease burden for that year.

However, WHO’s Advisory Committee on Health Research (ACHR) has serious reservations on the application of the DALY approach for decision-making and policy formulation. Pooling mortality and morbidity data hides facts that are known to be important to the economics of a given intervention, whether at family or community level; it obscures the socioeconomic circumstances and sociocultural environment of the sick within different communities, which both have an impact on the allocation of scarce resources. In addition, using a DALY-type approach does not take into consideration the multifactorial origins of diseases, their multiple manifestations nor, above all, the problem of inequity.

Determinants of health are not necessarily wholly biological: economic, sociocultural and behavioural elements are involved. However, methodologies to identify the fundamental determinants of health, in the health sector or elsewhere, are not yet available. Cauter insights into the determinants of health are required as a basis both for informed allocation of resources and for effectively targeted interventions. Methodological advances are needed, not only for identifying determinants but also for decision-making about interventions.

Recognizing these needs, in the face of a rapidly changing global demographic and epidemiological situation, and continuing pressure on resources for health improvement, the ACHR has established a subcommittee on measurement of health. It aims to identify new approaches to health measurement, new indicators, and methodologies usable for linking health to its underlying determinants, for establishing research priorities and for supporting decision-making about interventions.

**Trends in cancer cases**

In the United States, mortality from all cancers increased by 7% from 1973 to 1990 (both sexes combined) but all such increase occurs after the age of 65, while a decline of 4.5% has been recorded in younger age groups. In some European countries, e.g. Sweden and Finland, can-
The burden of cancer, 1996
Mortality, worldwide

5-year prevalence, worldwide

Incidence, developed world

Incidence, developing world

Cancer mortality is also declining in the population below age 75.

Much of the upward trend in the last few decades in rich countries is due to tobacco smoking, which became widespread during the first half of the century. Smoking is now declining in men in most of these countries and the effect of this – a reduction in deaths from lung cancer and heart disease – is already apparent in some populations. Conversely, the tobacco epidemic is now affecting women, particularly in southern Europe, and the effects of these changing habits will become apparent in some 10-20 years.

The risk of cancer unrelated to tobacco is not increasing dramatically in high-income countries in spite of the increasing number of cases observed. The diminished risk of dying from other causes such as cardiovascular disease leaves a greater proportion of the population, and for a longer period, exposed to the risk of developing cancer. Thus, effective interventions to prevent and treat other diseases contribute to the upward trend of the proportion of deaths.
attributed to cancer. Continuous efforts are therefore required to improve the understanding of the causes and mechanisms of cancer and to develop effective preventive and therapeutic protocols.

The weight of cancer relative to other diseases is increasing in countries currently undergoing rapid economic development. Developing countries succeeding in improving life expectancy often perceive the outbreak of a "cancer epidemic". Indeed any increase in the size of the population induces an increase in the number of cases and deaths observed, even if the risk, or rate, does not change. The risk of developing those cancers typical of higher socioeconomic groups (e.g. breast, colon and rectum) is expected to increase with economic development.

In the world's less developed regions, the cancer problem still largely relates to those sites linked to infectious agents and tobacco smoking. In sub-Saharan Africa at least 38% of all cases can be attributed to some type of infection.

Many of these cancers, namely those of the liver related to chronic infection with hepatitis B, are readily preventable by immunization in childhood. Vaccines to prevent infection with the papilloma viruses which cause cervical cancer are being developed and tested (Box 6).

**Understanding cancer**

In their healthy state, human cells reproduce and proliferate in an orderly, controlled way.

Cells normally contain a group of genes controlling cell growth called "oncogenes". Damage or mutations in these genes may interfere with the ability of oncogenes to regulate normal cell growth (Box 7). This is how abnormal cancer cells develop. These cells multiply in an uncontrolled way, and eventually invade surrounding tissues and distant organs. This invasion (metastasis) is characteristic of cancers, and is responsible for most of the treatment failures in this disease.
Box 6. Vaccines against cancer

In recent years, the link between some cancers and infectious agents—viruses, bacteria and parasites—has been firmly established, opening the way to producing vaccines against them. Leading researchers are hopeful that vaccines against several deadly cancers caused by infections can be developed in the near future. A more distant but still exciting prospect is that advances in molecular biology will lead to vaccines against other forms of cancer that are not connected to infections. They would work by inducing human T cells or other components of the immune system to seek out and attack malignant tissue.

There already is one extremely efficient vaccine in use—the hepatitis B vaccine, which protects against chronic hepatitis that leads to liver cancer. WHO estimates that globally there are about 540,000 new cases a year of liver cancer, of which 89%, or 448,000 cases, are attributable to infection with the hepatitis B virus.

The hepatitis vaccine became available in 1982 and has since been used to immunize almost 400 million people. Safe and effective, it can be given to people of any age, but is most effective when used as part of routine infant immunizations. This is now the case in about 75 countries. Dramatic cuts in the cost of the vaccine in developing countries are allowing it to be more widely available. WHO is recommending that general hepatitis B vaccination of newborns, children and adolescents be implemented in 1997. Such use could reduce the number of liver cancers by up to 70% in areas such as sub-Saharan Africa and eastern Asia, including China (see Box 9).

There is also optimism that the number of cases of cancer of the cervix can ultimately be reduced by the introduction of a human papilloma virus vaccine. It is well known that sexually transmitted infection of the cervix with human papilloma viruses types 16 and 18 involves a very high risk of developing cervical cancer. The viruses are responsible for an estimated 436,000 cases of the disease a year—83% of the annual total. Of all cases, 65% in industrialized countries and 87% in developing countries are due to these viruses. The viruses also cause 51,000 cases a year of vaginal cancer—80% of the annual total. Vaccine research has been progressing for more than five years and several candidate vaccines have undergone trials. However, as and when a safe and effective vaccine does reach the market, its cost will be a crucial factor in determining the extent to which it will be available in developing countries.

A third potential vaccine under investigation is against Helicobacter pylori. About 550,000 cases a year of stomach cancer—55% of the total—are attributed to infection with this bacterium. First identified in 1982, it has been shown to cause duodenal ulcers and gastritis. Although other factors must also be involved in the development of stomach cancer, the role of the bacterium is significant enough to justify research into a vaccine against it.

• Lymphomas, myeloma and leukaemias arising from the cells of bone marrow and immune systems.

The term “primary tumour” is used to denote cancer in the organ of origin, while “secondary tumour” denotes cancer that has spread to regional lymph nodes and distant organs. When cancer cells multiply and reach a critical size, the cancer is clinically evident as a lump or ulcer localized to the organ of origin in early stages. As the disease advances, symptoms and signs of invasion and distant metastases become clinically evident.

Cancer treatment

Surgery and radiotherapy are the main ways of treating cancer. Surgery usually involves the removal of the primary tumour with some surrounding tissue to prevent further spread. For many early cancers surgery alone is often enough to remove the tumour completely and cure the patient. Where the tumour has spread to nearby lymph nodes, these too must be removed surgically. Chemotherapy and hormone therapy are used to treat cancers which are too advanced locally for surgery or radiotherapy. A combined approach involving all of these methods provides the best results for many patients with moderately advanced disease but without distant spread, and is increasingly used to treat many forms of cancer.

At the outset, individual cancer patients are usually assessed to decide whether there is a possibility of cure or whether treatment should be palliative or symptomatic. This decision is based on the stage of tumour and the patient’s age and general health. If the clinical evidence indicates a reasonable chance of cure, radical single or combined curative treatment is provided. However, if there is no chance of cure, palliative treatment is given, aimed at relieving symptoms and improving quality of life without inducing treatment-related toxicity or complications. Symptomatic measures such as pain relief with opioid and non-opioid analgesics are almost always used in advanced cancers. Due to considerable progress in this area in
Box 7. From laboratory to medical practice: the results and prospects of cancer research

Advances in molecular and cellular biology add substance to the fundamental ideas on the nature of cancer, which date back to the early years of this century, and even before. At their core is the notion that cancer is essentially a genetic disease at the cellular level, and that its initiation and progression is a form of somatic evolution. But now we are at the threshold of new opportunities for the application of the rapidly accumulating fundamental knowledge to new approaches for preventing, treating and curing cancer.

The most dramatic and worthwhile changes in the last two decades have been in the science, the new discoveries, the technology that comes with them and above all the exciting pointers to future developments which will have a major impact on cancer. Oncogenes and tumour suppressor genes with known functions have now been identified and there is a whole range of new knowledge concerning the mechanisms within cells which control growth, cell division and programmed cell death. Understanding of the immune system has been revolutionized so that cancer immunotherapy and even vaccination have become plausible targets.

Cells will only divide when they receive the appropriate stimuli from one or more external growth factors. Certain substances (neuropeptides and bombesin) could act as growth factors. This provides a rationale for the mechanism of oncogene mutations as facilitating the division of cancer cells, through their effects on growth factor production and other functions.

DNA repair mechanisms are essential for maintaining the integrity of genetic material. Their absence leads to a high incidence of mutations and therefore of cancers. Damage to the DNA induces relevant repair activity. Mutations in these repair genes explain a major subset of colorectal cancer families and also occur in sporadic colorectal tumours.

The complement of cell division is cell death, now realized to be an important and programmed part of the maintenance, differentiation and development of all living organisms. The process of tumour growth is a balance between division and differentiation or death. Cancer has often been described as a form of de-differentiation. Fundamental studies of differentiation and development should thus help in the understanding of the cancerous process.

Over the last 15 years, the combination of modern molecular and cellular biology and animal experimentation has made a fundamental contribution to our understanding of the immune system. Any change protein, whether expressed inside or outside the cell, is a potential target for immunotherapy, or even vaccination. This new understanding opens up opportunities for developing immune therapies for cancer. Another important application of immunology is the use of monoclonal antibodies for in vitro and in vivo diagnosis and eventually the therapy of cancer. The first promising clinical results are in the treatment of colorectal and ovarian cancer. Most genes work through the proteins they specify. The study of protein structure is therefore a key part of understanding genetic functions and therefore of the functions of the changes that occur in cancer cells.

Now that the range of biological processes which underlie the initiation and progression of a cancer is better understood, we can envisage a basic framework for the carcinogenic process. In the case of tumours derived from epithelial cells (the carcinomas), which are still the most common cancers and the most difficult to treat or prevent, initiating a cancer most probably involves the facilitation of independent growth by loosening or disorganizing the attachment of cells to each other and to their extracellular matrix substrates. The long lag periods, sometimes 20 years from initiation to final cancer, can be explained by a series of steps, each determined by a new mutation and each leading to a new plateau in growth until the next mutation occurs.

Many parts of the puzzle are still missing. The function of each step remains to be elucidated and reconstructed in the laboratory. The discoveries of the last two decades have, however, provided a striking new range of targets for the development of novel and more specific drugs for the treatment of cancer.

Computing is only one, though a major, example of the importance of techniques and equipment in modern cancer research. Genome analysis has stimulated the automation of laboratory procedures so that robots are now almost as common in laboratories as big computers were 15 years ago. Enzymes and complicated procedures that used to be painstakingly put together in laboratories can now be elaborated using commercially available kits. New and more powerful techniques in the laboratory can be incorporated almost overnight into a developing experimental programme.

We have witnessed a golden age of discoveries about cancer. The future prospect is a golden age of new approaches to the prevention and treatment of cancers based on these fundamental discoveries. The challenge for the future is to develop more and better ways of translating the laboratory research into practice, whether in the clinic, the general practitioner's office or the population at large through the adoption of preventive strategies.

Even the full implementation of current best practice in the clinic could increase overall cancer survival by as much as 10%. Current trends in smoking cessation and the projected effects of breast cancer screening, adjuvant therapy and tamoxifen prevention, could reduce the overall mortality due to breast cancer by 50% of what it otherwise might be in 25 years' time. A similar effect could be seen for colorectal cancer if sigmoidoscopy screening turns out to be effective.

Many new drugs will be discovered by the new molecular and cell biology approaches. Forms of gene-based or DNA-based therapy will target a cancer in such a way that it becomes susceptible to a particular drug whereas normal tissue is not. However, all successful drug developments, and most applications of diagnostic procedures, depend on the involvement of the pharmaceutical industry.

The challenge is not only to maintain excellence in cancer research, but also to ensure a balance between basic and applied research. We have already seen the tremendous advances in the laboratory over the past two decades beginning to be translated into effective ways of improving the prevention, early diagnosis and treatment of cancer. In future years it may be possible to realize the promise of better understanding, and the reality of conquering cancer.

Personal communication from Sir Walter Boden, formerly Director of Research, Imperial Cancer Research Fund.
recent years, a painful death from cancer can most often be avoided.

**Advances in cancer therapies**

Increasing understanding of the natural history of cancers and advances in radiotherapeutic techniques and equipment, as well as in chemotherapy, have allowed less and less radical surgery to be performed for certain cancers (e.g., cancers of the breast, ovary, testis). This helps avoid complications arising from tissue loss, cosmetic problems and some loss of function.

**Radiation** can selectively destroy malignant cells while sparing normal cells. Radiotherapy involves radiation delivered from external radiotherapy machines or from sealed radioactive isotope sources placed in the tissues or body cavities. The total radiation dose required depends on the radiosensitivity of the tumour.

**Cytotoxic chemotherapy** involves the use of drugs that interfere with the ability of the cells to divide, and with synthesis of essential proteins. These drugs have their maximum effect on dividing cells. Spectacular improvement in survival and cure rates from childhood cancers and testicular cancers, and significant improvements in other cancers, are mainly due to advances in chemotherapy.

**Hormone therapy** is part of the management of tumours that occur in tissues under hormonal regulation, such as cancers of the breast, endometrium and prostate. Therapy is carried out either by removing or destroying the organs that produce hormones which promote tumour growth (e.g., removal of the ovaries in premenopausal patients with breast cancer) or by supplementing hormones that interfere with tumour growth.

**Adjuvant therapy** with chemotherapy or hormone therapy is used in situations where a cancer has been treated with surgery and/or radiotherapy but the risk of local or general recurrence is judged to be high. Examples include breast cancer with local lymph node involvement, some childhood cancers and ovarian cancer.

**Supportive care**, to alleviate both the psychological and physical impact of cancer, has a distinct role that is likely to enhance the patient's ability to withstand the side-effects of treatment and to improve quality of survival. Palliative care aiming at relief of distressing symptoms is important in managing advanced incurable disease. Relief of cancer pain by radiotherapy, surgery, chemotherapy and/or opioid and non-opioid analgesics is an integral part of cancer care.

**The main targets**

The eight most common cancers, with a combined total of over 6 million new cases a year, should be the main targets for prevention and cure. These account for more than 50% of these cases—lung cancer (1.3 million), stomach cancer (1 million) and breast cancer (0.9 million). All of them have one or more major risk factors which can be considered under five headings: tobacco-related; alcohol-related; infection-related; hormone-related. Some of these factors are common to several cancers. Each of these cancers is briefly described below in terms of its risk factors, clinical features, treatment, survival and prospects for prevention.

**Lung cancer**

**Risk factor: tobacco**

Lung cancer (including cancer of the trachea and bronchus) is the most common cancer in the world, with 51% of cases occurring in developed countries, and 75% occurring in men. Globally, 85% of cases in men and 46% in women are due to smoking. In developed countries the proportions are 91% for men and 62% for women, and in developing countries 76% for men and 24% for women. These patterns reflect the earlier adoption of smoking by men. Rates in men are increasing in most countries, although where the smoking epidemic began first, and has now passed its peak, the rates are beginning to fall (e.g., Finland, United Kingdom, United States). The highest national rates are currently found in eastern Europe.
In developing countries and regions the highest rates are seen where the smoking habit has been longest established - e.g. South Africa and Zimbabwe in Africa, China in the Western Pacific, and in the Eastern Mediterranean. Incidence rates in women are rising briskly in countries where female smoking is long established, and lung cancer is now the most common cause of death from cancer in women in the United States. In most developing countries, women rarely smoke, so rates there remain low.

Tobacco smoking is by far the most important risk factor. A lifetime smoker has a risk some 20-30 times that of a non-smoker. The risk increases with the amount smoked. Passive exposure to tobacco smoke is generally accepted as increasing risk by 30-50%. Genetic mechanisms define susceptibility to tobacco smoke.

Chinese women, although few of them smoke, have a modestly raised incidence of lung cancer, possibly because of exposure to environmental smoke, particularly cooking fumes, but they may be at genuinely higher risk too. Other factors known to increase risk of lung cancer are occupational exposures to asbestos, some metals (e.g. nickel, arsenic and cadmium), radon and ionizing radiation.

The disease usually presents with cough or breathlessness; the first signs may result from the spread of the disease to other parts of the body, as this occurs early in lung cancer. It is readily diagnosed by chest X-ray and bronchoscopy, or by examining cells taken from sputum.

About 20% of lung cancers (small-cell carcinoma) are treated with chemotherapy, while for non-small-cell carcinoma surgery and/or radiotherapy are used.

Overall, survival is poor (7-12% alive after five years). Although 50% of persons with small, localized tumours survive five years, such cases are rare.

Individuals can be convinced to give up smoking or persuaded not to start. But this is very difficult in the absence of reinforcing social pressures that make smoking unattractive, and a legislative framework that makes smoking expensive and difficult. The opposing pressures (from agricultural and finance ministries, tobacco companies) are enormous.

Tobacco consumption has been rising in most countries (at least in men), so that it is easy to predict a continuing evolution of the epidemic over the next 10-20 years.

**Stomach cancer**

*Risk factors: diet, infection*

Stomach cancer is the world's second most common cancer, with over 1 million new cases per year. Nearly two-thirds occur in developing countries. High-risk areas include Central and South America and eastern Asia, and also Japan. Incidence in men is nearly twice that in women. Cases have declined steadily in most affluent countries over the last 30 years. Similar trends are apparent in some less developed regions of the world. Most gastric cancers are adenocarcinomas. In contrast to the overall decreasing trend, there has recently been a rapid increase of cancers localized to the cardia (the upper part of the stomach). The reasons for this increase are not known.

The constant decline of stomach cancer in industrialized countries is linked to improved food preservation practices; better nutrition more rich in vitamins from fresh vegetables and fruits; and less consumption of preserved, cured and salted foods. Infection with the bacterium *Helicobacter pylori* contributes to the risk, probably by interacting with the other factors.

Symptoms are nonspecific, which explains why most of the cases are diagnosed when the disease is at an advanced-stage. Patients may complain of weight loss, fatigue or gastric discomfort. Diagnosis is performed by barium X-rays and with biopsy.

This cancer is treated by surgical removal of the tumour, with or without adjuvant chemotherapy.

Stomach cancer cases have a generally poor survival prognosis, averaging no more than 20% survival after five years. If the tumour is localized to the stomach, 60% of patients survive five
years or more. However, only 18% of all cases are diagnosed at this early stage.

Consumption of fresh vegetables and fruit and reduced intake of salty and cured foods decrease the risk. Screening by photofluoroscopy has been widespread in Japan since the late 1960s and mortality rates are declining. It is unclear whether this trend can be attributed to mass screening alone.

Despite declining rates in developed countries in the last 30 years, stomach cancer is still the second most common cancer worldwide, and is a highly lethal disease.

**Breast cancer**

**Risk factors: hormones**

The most common cancer in women, breast cancer causes 376,000 deaths a year worldwide; about 900,000 women a year are diagnosed with the disease. More than half of these cases are in industrialized countries – about 220,000 in Europe and about 180,000 in North America, for example. The disease is not yet as common among women in developing countries but is increasing. The highest reported rates are for white or Hawaiian women in the United States. High rates are also found for North America in general and some parts of Europe. In contrast, low rates are found in Africa and Asia. Studies indicate that when women migrate from low-risk to high-risk regions, after two or three generations their descendants slowly acquire the rates of the host country, which illustrates the importance of lifestyle in addition to genetics. Breast cancer incidence is still increasing in most parts of the world, particularly in regions which previously had low rates.

The strongest risk factor is age, with more than half of the cases occurring after menopause. The risk is also linked to reproductive and hormonal factors. It is increased by early menarche, late age at first birth, never having given birth, and late menopause. All of these reflect a hormonal pattern. Other risk factors include obesity after menopause, exposure to ionizing radiation (especially at the time of breast development) and exogenous hormones such as oral contraceptives at an early age and estrogen replacement therapy at menopause.

Recently, genetic predisposition has been much better understood with the identification of at least two genes which carry a high risk of breast cancer, but in only 2-5% of cases.

The most common clinical sign is a lump in the breast. Diagnosis is confirmed by biopsy or fine-needle aspiration.

Depending on the stage of the tumour, treatment may include surgical removal of the tumour and surrounding tissue from the breast (lumpectomy); surgical removal of the whole breast (mastectomy); radiotherapy; chemotherapy. Combinations of surgery followed by chemotherapy, hormonal therapy and radiotherapy improve the chances of long-term survival.

At least half of all cases will survive for five years if treated adequately. Trends in survival show clear improvement over time. The main determinant of survival is the stage of the tumour, localized disease being associated with an excellent prognosis. In contrast, distant spread carries a high risk of death in the five years following diagnosis.

Currently, the only effective prevention strategy is mammography with routine breast examination, which can reduce by one-third the risk of death from breast cancer among women over 55. In the developing world, detection by breast examination may lead to a reduction of the disease.

Improved facilities for radiography and clinical diagnosis should be made available worldwide. General health promotion, including avoidance of obesity from childhood onwards, could also help. Chemoprevention (Box 8) is currently only a research exercise. No optimal strategy has yet been defined for women who are at a very high risk. Advances in the control of cancer pain, in palliative care and in psychological counselling for cancer sufferers are also needed.
Colorectal cancer

Risk factor: diet

This is one of the most common cancers worldwide, with about 870,000 new cases per year. It is more frequent in North America, Europe and Australia than in Africa, Asia and Central or South America, but the incidence is increasing in several populations previously at low risk. Cancer of the colon occurs with similar frequency in men and women, but cancer of the rectum is 20-50% more frequent in men than in women in most populations. Migrant studies indicate that when populations move from a low-risk area (e.g. Japan) to a high-risk area (e.g. the United States) the incidence of colorectal cancer increases rapidly within the first generation of migrants.

Studies in both developed and developing countries consistently show a higher risk of colorectal cancer in people consuming a diet low in vegetables and in unrefined plant foods (i.e. whole cereals, legumes, etc.). Studies in developed countries have also found that frequent consumption of red meat (beef, lamb, etc.) increases the risk, while consumption of fish and poultry has been found to be either unrelated to risk or even associated with a slight reduction in risk. The mechanisms by which a diet rich in vegetables and whole plant foods and moderate in meat may protect against colorectal cancer are still unclear.

The disease usually presents with intestinal symptoms including pain, rectal bleeding, and/or alternating diarrhea and constipation. Diagnosis can be made by means of endoscopy and/or X-ray.

For small tumors of limited extent, a segment of the colon is removed by surgery. For larger tumors more extensive removal of the large bowel may be necessary. Radiation therapy and chemotherapy are used together with surgery, or if the tumor recurs.

Overall, five-year survival is about 50-60%. For localized cancers it is almost 90%, but when diagnosed at advanced stages with distant localization, it is only 3-8%.

Box 8. Cancer chemoprevention: trials and troubles

Chemoprevention is an attempt to use natural and synthetic compounds to intervene in the early stages of cancer development, before invasive disease actually begins. Such substances taken as pills or tablets, for example, could protect individuals at high risk of cancer.

Food is the source of some of the most promising chemopreventive compounds. Many vegetables, fruits and grains are known to offer protection against various cancers. However, such compounds must be non-toxic and relatively free of side-effects, because they are meant to be administered to healthy people for long periods of time. Isolating the effects of individual food constituents has proved difficult. For instance, while fruits and vegetables rich in betacarotene have reduced the risk for certain types of cancer—especially lung cancer—large-scale chemopreventive trials with betacarotene in pills have produced unexpected and even disappointing results.

Beginning in 1985, betacarotene was included in two such long-term trials, one conducted in Finland and the other in the United States. For several years, daily doses of betacarotene and either vitamin E or vitamin A were administered to tens of thousands of people at high risk of developing lung cancer, particularly cigarette smokers. Expectations were based largely on the results of dietary studies in which the daily intake of betacarotene was associated with a lower risk of lung cancer.

The hypothesis was that administering the nutrients would protect against the disease. Surprisingly, however, the rate of lung cancer in cigarette smokers taking betacarotene increased slightly in both trials, for reasons that are still to be explained. Possibly other substances found in fruits and vegetables are responsible for the protective effects. These disappointing results show some of the difficulties faced by chemoprevention researchers, and help explain why progress in cancer research is often painstakingly slow.

The "gold standard" of chemoprevention trials is still the large prospective study, which monitors future development of disease in either high-risk individuals or the general population. In these trials, the experimental agent may need to be administered for many years, after which another number of years will be needed to assess the effects fully.

To help speed up the results of such trials, researchers are now investigating the use of biomarkers as surrogate measures of a compound's success. Biomarkers are physiological manifestations of changes that may occur in the pathway to cancer. If an intervention reduces the incidence of these signs in a population, the chances are better that the agent will lower the incidence of the cancer itself.

As an example, current trials of chemoprevention agents for colon cancer will determine the efficacy of nonsteroidal anti-inflammatory drugs on the incidence of intestinal polyps, a benign precursor to colon cancer, rather than the incidence of the cancer itself. These drugs seem to protect the body against cancer, especially cancer of the colon, in a number of ways; but their prolonged use may cause gastrointestinal side-effects, such as bleeding or ulcers.

Difficulties and disappointments inevitably occur in cancer research. But with increasing knowledge of how cancer develops, chemoprevention will undoubtedly play a significant role in future cancer control.
Box 9. Chronic liver diseases and liver cancer — the Gambia Hepatitis Intervention Study

A population-based vaccination campaign against hepatitis B virus (HBV) was initiated in the Gambia in 1986 with the objective of evaluating the effectiveness of hepatitis B vaccination in the prevention of hepatitis B infection, chronic liver diseases and primary liver cancer in a population at high risk. The study comprises three overlapping phases:

Phase I Vaccination of approximately 60,000 children during the first five years, concluded in 1990;

Phase II Longitudinal and cross-sectional surveys of selected groups of vaccinated (Group 1) and unvaccinated (Group 2) children, up to 10 years of age, now in progress;

Phase III Long-term follow-up for 40 years.

Hepatitis B vaccine, which was approved by the World Health Organization, was integrated into the Gambian Expanded Programme on Immunization (EPI) in a phased manner over a four-year period. During this period, two groups of children were recruited, one comprising some 60,000 children who received all vaccines in the EPI schedule plus the hepatitis B vaccine, the other comprising a similar number of children who received the EPI vaccines but not the hepatitis B vaccine. These two cohorts are being followed up over a 30-40-year period in order to evaluate the effectiveness of hepatitis B vaccination in preventing liver cancer and chronic liver diseases. A population-based national cancer registry was also established in 1986 with the aim of improving the reporting of cancers in both public and private health sectors, so that the net effect of vaccination in preventing liver cancer can ultimately be assessed.

The study clearly shows that HBV vaccination can be effectively integrated in the EPI vaccination programme in developing countries. Phase II of the study is now approaching 10 years and serological markers of hepatitis B infection in two cohorts (10,000 children each) of vaccinated and unvaccinated children show that vaccine efficacy in preventing primary infection and carrier state is 84% and 94%.

Other important outcomes from the study relevant to the implementation of HBV vaccination in other developing countries are: the evidence that dose interval is unimportant in immunogenicity; the evidence that infection in the family does not affect the response of the child; the relatively low contribution of hepatitis C to liver cancer in this population; and the high cost-effectiveness of the vaccination in prevention of the carrier state.

The Gambia Hepatitis Intervention Study is a project run by the International Agency for Research on Cancer, in collaboration with the Government of the Republic of The Gambia and the United Kingdom Medical Research Council Laboratories in The Gambia. It is supported by the Direzione Generale per la Cooperazione allo Sviluppo of the Ministry of Foreign Affairs of Italy, the Regione Autonoma Valle d’Aosta, Italy, and the Medical Research Council of Sweden.

Oral cancer

Risk factors: tobacco, alcohol, diet

Oral and pharyngeal cancers are common in regions where tobacco use and alcohol consumption are popular. Each year, about 575,000 new cases and 320,000 deaths occur worldwide. Increases in cases and deaths have been reported in recent years in western, central and eastern Europe, Japan and Australasia, and among nonwhites in the United States.

Patients generally present with red lesions in the mouth. Those with pharyngeal cancers may complain of difficulty in swallowing or hoarseness, particularly at advanced stages. Cancers of the oral cavity are often preceded by restricted mouth opening and tongue mobility.

Treatment is by surgery and radiotherapy, alone or in combination. Advanced disease is generally treated with both, with or without chemotherapy.

Five-year survival approaches 70–80% in early stages and ranges from 5% to 20% in advanced disease.

Tobacco and alcohol control and a healthy diet can effectively prevent some cancers. Whether long-term chemopreventive therapy can prevent oral cancers is not known. Screening by visual inspection of the mouth has been shown to be feasible, although its effectiveness is not yet clear.

Liver cancer

Risk factors: infection, alcohol, diet

Liver cancer is a major problem of developing countries, where 82% of the world total (540,000 new cases per year) occur, with 55% of all cases in China. The risk in men is twice that in women.

83% of the cases worldwide are attributable to infection with the hepatitis B virus. The attributable fraction is 91% in developing countries and 52% in the more affluent areas of the world, where the majority of the remaining cases are explained by excessive consumption of alcohol. Exposure to aflatoxins, naturally occurring contaminants of grains, enhances the effect of chronic hepatitis B infection.

Epidemiological studies strongly suggest that a diet rich in vegetables and minimally refined plant food and moderate in meat can reduce the risk of colorectal cancer. Early detection of colorectal polyps and of localized cancers is possible by means of a laboratory test or endoscopic examination of the large bowel.
Common symptoms are abdominal pain, weight loss, fatigue, abdominal swelling, loss of appetite and jaundice. The majority of the cases can be diagnosed by ultrasonography.

There is no effective treatment. Only 6% of the cases survive at least five years in the United States and similar figures or worse are likely to apply in developing countries.

In developed areas, 30% and in developing areas 70% of cases could be prevented by the introduction of vaccination against hepatitis B virus into the primary immunization schedule for infants (Box 9). Screening programmes have not proved effective in reducing mortality.

Primary liver cancer is a highly lethal disease the burden of which could be substantially reduced by preventing hepatitis B and C infection (Map 1).

**Cervical cancer**

**Risk factor: infection**

This is the second most common cancer among women worldwide, with an estimated 524,000 new cases in 1995. Developing countries, where it is often the most common cancer among women, account for 80% of cases. Wide variations in incidence and mortality from the disease exist between countries; North America, western Europe and some countries in the Eastern Mediterranean have the lowest rates, and Latin America, sub-Saharan Africa and South-East Asia have the highest. Cases and deaths have declined markedly in the last 40 years in most industrialized countries, partly owing to a reduction in risk factors, but mainly as a result of extensive screening programmes. More limited improvements have been observed in developing countries, where persistently high rates tend to be the rule.
Early age at initiation of sexual activity, increasing number of sexual partners of females or their sexual partners, and other indicators of sexual behaviour have long implicated a sexually transmitted agent. Additional factors include number of pregnancies, and possibly exposure to oral contraceptives.

Recently, certain types of human papilloma virus (HPV) have been established as the sexually transmitted agents responsible for initiating the disease in the vast majority of cases. The virus is found in more than 95% of the cancers. Current evidence suggests that the virus is a necessary but not sufficient cause of the disease and researchers are now trying to define other cofactors.

The initial infection with HPV is very common after initiation of sexual activity, and is usually latent and only detectable with laboratory methods. Infections usually regress spontaneously after variable periods of time, probably by immunological mechanisms. In a small minority of affected women, the condition progresses to invasive cancer, which usually appears more than a decade after the initial infection. The diagnosis can be made years before the initiation of cancer. When invasive disease is established, symptoms include vaginal bleeding or discharge, pelvic pain, and eventually rectal and urinary complications.

Treatment is by surgery or radiotherapy for early stages, and radiotherapy for more advanced disease. Results depend on the stage of the disease at the time when it is diagnosed.

Survival depends on the stage of the disease, with 90% of localized cases surviving five years, but less than 10% of cases with distant spread. Important differences in survival are related to age and ethnic or socioeconomic characteristics, probably because of variations in access to medical care.

Mass screening programmes covering large proportions of the female population and providing high-quality screening and treatment are the most effective secondary prevention method. These have proved effective in developed countries, but their potential impact is limited in developing areas, because of the extensive resources and organization required. Simpler, cheaper and more reproducible screening methods are needed. Increased use of condoms and the development of vaccines may help to reduce the incidence of disease in the future now that HPV has been recognized as the central cause of the disease.

**Oesophageal cancer**

**Risk factors: tobacco, alcohol, diet**

About 480,000 cases of cancer of the oesophagus occur worldwide each year, of which about 85% are in developing countries. The highest risk areas of the world are in the Asian “oesophageal cancer belt” (stretching from northern Islamic Republic of Iran through the central Asian republics to north-central China). High rates are also present in parts of East and South-East Africa, eastern South America and certain parts of western Europe.

Smoking accounts for 45% of cases in men, but only 11% of cases in women. Nutritional deficiency (especially of micronutrients) has long been suspected to be the major factor in Asian high-risk areas. Drinking home-brewed alcohol in Africa, and herb tea (mate) in South America, is also implicated. The combination of tobacco and alcohol is a significant risk.

Almost all patients complain of difficulty in swallowing, first liquids and later all foods, with accompanying weight loss. Diagnosis is by oesophagoscopy or barium swallow X-ray examination.

Treatment is by surgery, for instance, bypass operations pulling up the stomach or colon, to provide temporary relief from obstructed swallowing. Radiotherapy can palliate advanced cases.

About 75% of patients die within a year of diagnosis, and survival after five years is only 5-10%.
Prostate cancer

Risk factors: diet, hormones

Prostate cancer is much more frequent in Europe, North America and Australia than in other regions of the world. About 400,000 new cases are diagnosed yearly around the world. Black populations of African origin living in Central America, the Caribbean, and the United States have a particularly high risk. The incidence increases particularly after 60-70 years of age.

High consumption of meat and animal fat is a risk factor, and hormonal patterns may also be involved.

Depending on the stage of the condition, clinical characteristics and the age of the patient, different combinations of hormonal treatment, radiotherapy and surgery are used.

Five-year survival is generally quite high, of the order of 70-90%. Survival is lower for patients presenting with distant metastases (20-30% after five years).

Prevention is through dietary advice (moderate intake of meat and animal fat, avoidance of obesity), and early detection. The disadvantage of generalized early detection is that such screening detects cancers in elderly men who would otherwise have suffered no symptoms during their lifetime.

Bladder cancer

Risk factors: tobacco, infection (diet)

An estimated 236,000 new cases of bladder cancer occur each year in men and 74,000 in women. Just over half the cases occur in industrialized countries. Incidence is particularly high in North America, Europe, northern Africa and in Chinese populations.

Cigarette smoking is the single most important risk factor and is responsible for 37% of cases in men and 14% in women. Carcinogens that affect the bladder occur in certain populations; for instance, there is an increased risk among rubber workers. Chronic infection with Schistosoma haematobium is an important risk factor, where infection with this parasite is still endemic. A diet rich in fruits and vegetables is associated with lower risk.

Treatment is by surgical removal of the tumour; surgical removal of the whole bladder (cystectomy); chemotherapy and radiotherapy.

For localized tumours, five-year survival is over 90%, but is 50% or less for more advanced stages.

This cancer can be prevented by control of tobacco smoking, occupational carcinogens and S. haematobium infection. Occupational screening has been ineffective but the control of occupational carcinogens has taken place in many countries. Screening procedures are being developed.

Ovarian cancer

Risk factors: hormones, diet

About 190,000 cases occur each year, with slightly more in developing than in developed countries. Recent trends are decreases in countries which previously had high rates, and increases in countries previously at low risk.

Cancer of the ovary is influenced by hormones and reproductive factors. Risk is slightly increased in women who have never given birth and those with a personal history of breast cancer or a family history of breast or ovarian cancer. A clearly decreased risk is found in those who have used oral contraceptives, and the degree of protective effect is proportional to the length of treatment. In contrast, treatment for infertility entails a clearly increased risk, whereas treatment of the menopause is only associated with a small risk. Diet plays a role, with increased risk linked to obesity and height, as well as some nutritional factors. Recently, genetic factors have been shown to play an important role, particularly in young women.

Small tumours are generally clinically silent and symptoms appear late. The use of endovaginal echography can lead to a diagnosis, which has to be confirmed by biopsy.

Surgery is used in early disease; radiotherapy and chemotherapy for more advanced stages.

Chronic infection with Schistosoma haematobium is an important risk factor for bladder cancer, where infection with this parasite is still endemic.
The five-year survival rate is less than 30% in most countries, and is highly dependent on the stage of disease. No screening has been shown to be effective in reducing incidence or mortality. The only factor linked to a reduced risk of ovarian cancer is use of oral contraceptives. Effective forms of therapy have still to be found for advanced forms of the disease. Better understanding of the genetics of ovarian cancer will help to define better strategies for research and treatment.

Cancer of the body of the uterus

Risk factors: hormones, diet
About 170,000 cases of cancer of the uterus occur worldwide each year, with slightly more than 100,000 in developed countries. Africa and Asia have low rates; the highest are in the United States and Canada, where a clear decline in cases and deaths has occurred, particularly among young women. Most cancers appear after the age of menopause.

Cancer of the endometrium, the internal lining of the uterus, is linked to reproductive life, with increased risk among women who have never given birth and women undergoing late menopause. It is clearly associated with obesity, diabetes and hypertension. Unopposed estrogen therapy for menopause, without the use of progestins, increases the risk whereas combined oral contraceptives lower it.

Surgery is the main treatment, although chemotherapy and hormone therapy may be used.

Survival is usually good, in particular for localized disease. Poor prognosis is associated with distant spread, and some types may be more aggressive.

So far screening has not shown any real benefit. The only recommendation may be general good health including the avoidance of obesity and of treatment with unopposed estrogens.

In order to evaluate changes in incidence, there is a need to have detailed population statistics on hysterectomy rates. In the United States, up to 40% of women undergo hysterectomy after the age of menopause, which means that most analyses of trends in the incidence of uterine cancer can only be tentative.

Testicular cancer

Risk factors: hormones
The highest incidence of testicular cancer is recorded in Denmark and Germany and in general in white populations of high-income countries. The maximum risk is during the third and fourth decades of life and declines after age 50. A rapid increase in incidence has been observed in most countries, for reasons that are not well understood. Deaths have markedly declined since the introduction of effective chemotherapy in the mid-1970s.

Hormonal and genetic factors are likely to be important but their role is currently unclear. In general, testicular cancer is more common in higher social classes.

Treatment is by surgery combined with chemotherapy.

Above 95% survive after five years except for the small fraction of patients in whom the condition is at an advanced stage. Survival in developing countries is only 40-60%, indicating limited access to appropriate therapy.

No effective preventive strategies exist. Therapeutic improvement has reduced deaths, but the causes of this cancer remain largely unknown, so that there is little scope for preventive action.

Laryngeal cancer

Risk factors: tobacco, alcohol, diet
About 190,000 new cases of cancer of the larynx occurred worldwide in 1995, of which more than 60% were in developing countries. High-risk countries are found in Latin Europe (France, Italy, Spain) and Latin America (Brazil, Uruguay), India is an intermediate risk country. The disease is much more frequent in males than in females.

Tobacco smoking and alcohol consumption, which have a synergistic effect, are the main risk factors. Studies show a protective effect of a diet rich in fruit. This cancer may be induced by exposure to asbestos.
The early symptoms are hoarseness, difficulty in swallowing or pain in the throat, depending on the exact site of the tumour. Diagnosis is carried out by laryngoscopy and biopsy.

Cryotherapy or laser treatment is used for the less advanced lesions; for more advanced lesions, surgery and radiotherapy are the more frequent treatment. Overall, 50-60% of patients survive five years.

**Leukaemias**

**Risk factor: radiation**

Incidence rates for all types of leukaemia together vary from 2 to 12 per 100,000 population. These cancers constitute 3% of all new cancers worldwide. Occurrence in North America, western Europe, Australia, Israel, Japan, and New Zealand is high. Most leukaemias in children are acute lymphoblastic leukaemia (ALL), with a distinct peak of occurrence at 1-4 years of age. Death rates, particularly in childhood, have fallen substantially, thanks to therapeutic advances which improve survival. At other ages, broad categories of leukaemia are: acute non-lymphoblastic or myeloid (AML - young adulthood); chronic myeloid (CML - usually age 30-50); and chronic lymphocytic (CLL - rare before the age of 50).

Risk factors include ionizing radiations, certain drugs and chemicals (e.g. benzene) and industrial exposure to hydrocarbons. A high risk is observed among long-term survivors of cancer treated with chemotherapy and radiotherapy. However, all these factors are unlikely to account for a large proportion of leukaemias. Genetic conditions, such as Down syndrome and chromosomal anomalies, are also associated with increased risk. Viral infections are suspected of playing a role.

Patients with acute leukaemias (ALL and AML) present with anaemia, pallor, features of infection, and bleeding which are of rapid onset; enlargement of liver and spleen are common. Patients with ALL in addition present with bone and joint pain and multiple lymph node enlargements (lymphadenopathy). Patients with CML present with slow onset of symptoms of anaemia and weight loss, and massive enlargement of spleen. CLL develops gradually and presents with multiple lymph node enlargement, with or without splenic enlargement. As the disease progresses anaemia sets in slowly.

Combinations of chemotherapy and steroids, with intensive supportive care, are used for treatment. Prophylactic treatment is mandatory in the management of ALL against a possible involvement or relapse in the central nervous system. Bone marrow transplantation is one form of therapy for inducing remission in young patients with AML when other treatment fails. Relapse is still a major problem in acute leukaemias; treatment is essentially palliative in chronic leukaemias.

60-70% of complete responders in ALL, and 20-30% of complete responders in AML survive in excess of five years. 30-50% of the patients diagnosed with chronic leukaemias survive five years.

**Lymphomas**

**Risk factor: infection**

There are two major groups: Hodgkin and non-Hodgkin lymphomas. An estimated 229,000 new cases of lymphoma occur each year in men, and 164,000 in women. In both sexes, 65% of all lymphomas are non-Hodgkin lymphoma with about 60% of all lymphomas occurring in developing countries. Incidence rates are highest in Europe and North America. Specific types of lymphoma have distinct geographical patterns, such as Burkitt lymphoma, which is endemic in certain areas of Africa and Oceania and affects children.

Infection with Epstein-Barr virus, a common herpes virus, has been linked with Burkitt lymphoma and Hodgkin lymphoma. Infection with HIV is another risk factor. However, these explain only a small percentage of all the cases. Exposure to herbicides and dioxins is suspected. Lymphomas tend to occur in families.

Leukaemia death rates, particularly in childhood, have fallen substantially, thanks to therapeutic advances which improve survival.
Superficial lymph node enlargement is the most common clinical feature of lymphomas. General symptoms, such as fever and weight loss, are more common in patients with Hodgkin lymphoma. Involvement of tissues other than lymph nodes is common in non-Hodgkin lymphomas, resulting in a variety of clinical pictures. Diagnosis is based on biopsy complemented by laparotomy and radiological examinations to determine the extent of the disease.

Control of known risk factors, such as HIV infection, is likely to prevent only a small fraction of lymphomas. Effective screening methods are not available.

Treatment is by combinations of chemotherapy and radiotherapy, and in advanced disease, options include bone marrow transplantation.

Survival of Hodgkin lymphoma patients after five years is between 70% and 80% in North America and Europe, but only 30-55% in developing countries. Survival for non-Hodgkin lymphoma patients in developed countries is 50%.

Malignant lymphomas are an important group of cancers showing an increase in incidence. Their etiology is mostly unknown, making it difficult to develop effective preventive strategies.

**Myeloma**

**Risk factor: radiation**

Multiple myeloma, a malignant tumour of the plasma cells in the bone marrow, is very rare in persons under 40 years of age. A slow increase in cases and deaths is being seen in most regions of the world.

Ionizing radiation is the only well-established risk factor. An increased risk is observed among survivors of atomic bomb explosions in Japan, women irradiated for cervical cancer, and in radiologists and nuclear industry workers. Chemicals, such as benzene and carbon monoxide, and occupational exposures in farming and in the wood, rubber and petroleum industries are associated with an increased risk.

Patients with multiple myeloma present with bone pain, anaemia, and symptoms and signs of infections. As the disease progresses bone and soft tissue tumours, fractures, features of kidney failure and neurological dysfunctions including partial paralysis become clinically evident. The proliferation of plasma cells within the bone marrow leads to skeletal destruction of the skull, spine, ribs, pelvis and long bones.

Treatment is by chemotherapy with or without steroids, to which 50-60% of the patients respond. Radiotherapy effectively relieves bone pain and other symptoms. Opioids are effective in controlling generalized bone pain and neuropathy in advanced disease. The five-year survival rate is 15-25%. Control of ionizing radiation exposures in related occupations and applications is the only preventive measure available.

**Malignant melanoma**

**Risk factor: ultraviolet radiation**

Of 115,000 cases worldwide each year, 70% are in Australasia, Europe, and North America. Rapid increases in incidence and mortality are observed in both sexes in many countries, even where rates were formerly low, such as Japan. In the Nordic countries, for example, this increase has averaged some 30% every five years.

Malignant melanoma of the skin is a tumour of the white-skinned races (Caucasians), when they are exposed to strong ultraviolet irradiation at low latitudes. Early signs — benign naevi, believed to be precursors of melanoma — are induced by ultraviolet irradiation, particularly in childhood. The tumour eventually presents as a pigmented mole that increases in size and colour, developing into a nodule that often bleeds.

While ultraviolet radiation is the main risk factor, the risk is determined by susceptibility, related to skin type. Fair-skinned individuals who sunburn readily are at highest risk. Intermittent exposure to strong sunlight — e.g. recreational (sunbathing) — is more dangerous than chronic exposure (e.g. in outdoor occupations).

Melanomas are divided into three histological types; most melanomas in white populations are superficial spread-
ing and nodular melanomas. These are proportionately most common on the back and face in men, and on the legs in women. Lentigo malignant melanoma occurs later in life and on sun-exposed sites. Acral lentiginous melanoma is proportionately more common in populations in eastern Asia.

Treatment is by surgery, with excision of the regional lymph nodes only when these are obviously involved. Malignant melanoma is generally resistant to radiotherapy. Chemotherapy for metastatic melanoma has not been successful.

Survival depends on the stage of disease. In localised melanoma, some 90-95% cases survive five years. Females have better survival rates than males.

White-skinned populations should take precautions to limit the exposure of their skin to ultraviolet radiation (avoid direct sunlight, use of hats, appropriate clothing, sun screens). Awareness of melanoma risk in susceptible populations can lead to earlier presentation.

Increased ultraviolet exposure (due to thinning of the ozone layer) may lead to an increase in the risk of melanoma. However, the potential for prevention is good; recent data suggest that mortality rates in young persons (recent generations) are no longer rising in several high-risk countries, and in some (e.g. Canada, Denmark, United States) are actually decreasing.

**Cancer in childhood**

Cancer is rather rare in children; about 2 children in every 1000 develop a cancer before their 15th birthday. However, the importance of cancer in children depends on two other factors. The first is the age structure of the population – in some developing countries, children comprise 40-50% of the population, so that some 3% of cancers occur in this age group, compared with 0.9% in developed countries. Secondly, other competing illnesses are important. Thus, although cancer accounts for some 4-5% of childhood deaths in developed countries, only some 0.7% of deaths are due to cancer in developing countries, where infectious diseases play a much more important role.

Acute leukaemia, especially in early childhood, is the most common cancer in children in most countries, although in tropical Africa, lymphomas are more common. Brain tumours generally account for one-fifth to one-quarter of childhood cancers. Many of the other solid tumours are the so-called "embryonal cell" cancers (arising in primitive cells found in the human embryo); they occur in the first years of life in the kidney, eye, adrenal gland and liver. The sarcomas of bones and soft tissue are also much more common in children, accounting for over 10% of cancers, compared with 1-2% in adults.

Little is known about the causes of childhood cancer. As might be expected in cancers occurring so early in life, exposure to environmental factors, either in utero or after birth, seem to play a very small part. A few cases are the result of genetic defects passed on to children by their parents – for example, a sizeable proportion of retinoblastomas (eye tumours) are inherited.

### Circulatory diseases

Circulatory diseases such as heart attacks and stroke kill more people than any other disease, accounting for at least 15 million deaths every year.
action, could prevent about half of the annual deaths from circulatory diseases.

In the past, circulatory diseases were thought of as affecting exclusively industrialized nations since they were regarded largely as lifestyle diseases because the risk of developing them was increased by smoking, obesity, unhealthy diet and heavy alcohol consumption. Now, as developing countries modernize, they are gradually controlling infectious diseases, and the life expectancy of their populations is increasing. Unfortunately, the risks of circulatory diseases are also increasing, partly because of the adoption of lifestyles similar to those common in industrialized countries, and these diseases now account for about 25% of all deaths in developing countries – 10 out of 40 million. In developed countries almost half of all deaths – more than 5 out of 12 million – are attributable to these same diseases.

The most important circulatory diseases are high blood pressure (hypertension), coronary heart disease, cerebrovascular disease, and cardiomyopathies (diseases affecting the heart muscle). Worldwide, there are more deaths from coronary heart disease (7.2 million) than stroke (4.6 million), although their relative importance varies considerably from country to country. For example, more than twice as many deaths from stroke occur in developing countries as in developed countries.

Developing countries, however, also still suffer from other heart conditions such as rheumatic heart disease, which is linked to poverty, and from cardiac damage related to Chagas disease, a parasitic illness afflicting about 17 million people in Latin America. About 30% of those who develop chronic Chagas disease become incapacitated because of heart damage that may also lead to sudden death. Rheumatic fever is the commonest cause of heart disease in young people worldwide, accounting for about one-third of all deaths from cardiovascular diseases.

Circulatory diseases, like other noncommunicable conditions, are emerging rapidly as a major public health concern in most developing countries, which are already heavily burdened with infectious diseases. In all countries, the costs of caring for patients with circulatory diseases are rapidly rising. In developed countries, they already account for about 10% of direct health care costs, equal to between 0.5% and 1% of a country’s gross national product.

Because of their prevalence and importance, circulatory diseases have been the subject of intensive research in recent decades. It has become clear that their incidence and impact can be reduced substantially through a range of well-established measures.

**Cardiovascular diseases**

The two main cardiovascular diseases examined in this section are coronary heart disease and rheumatic heart disease. Whereas in coronary heart disease, lifestyle and socioeconomic factors play a major role, the main underlying cause of rheumatic heart disease is bacterial infection, against a background of poverty, leading to rheumatic fever.

**Coronary heart disease** (CHD), accounted for more than 7 million deaths worldwide in 1996. Although these deaths are only 14% of the global total, they are responsible for about one-third of all deaths in industrialized countries.

Most cases of CHD result from narrowing of the arteries due to fatty deposits called plaques (atherosclerosis). When a coronary artery is completely blocked, usually by the formation of a blood clot on top of a plaque, the result is a heart attack (myocardial infarction) or disturbed heart rate (cardiac arrhythmia), either of which may cause sudden death.

Atherosclerosis, together with its complications, underlies most cases of coronary heart disease, including clinical manifestations such as angina pectoris, congestive heart failure, and other major disturbances of cardiac function. The atherosclerotic process in major arteries, including the coronary arteries, has its origin early in life. Its initial stages often occur in children and young
people and it tends to progress silently and without symptoms from the beginning of the second decade of life onwards until illness strikes.

In a large proportion of cases, the first manifestation is sudden death. A substantial majority of CHD deaths occur outside hospitals because the time between onset of the event and death is too short to permit effective emergency care and hospitalization. These problems persist, despite significant recent advances in many countries in emergency services and acute and long-term care. Possibilities for rehabilitation of survivors are limited.

The CHD epidemic began in North America, Europe and Australia in the early decades of this century. In many industrialized countries death rates peaked in the 1960s and early 1970s and have since declined dramatically. In Australia, New Zealand and the United States, for example, CHD deaths have fallen by over 50% since the mid-1960s. But CHD is now increasing in developing countries as their populations age and adopt unhealthy habits and behaviours. The mortality rates in eastern and central Europe are now the world’s highest, and they are still rising in countries such as Bulgaria and Hungary, in both men and women.

Decades of research have shown conclusively that a number of determinants – most of them associated with lifestyle – operating from early childhood onwards, are responsible for coronary heart disease. The term “risk factor” was first used for CHD. Some risk factors facilitate the development of atherosclerosis, while others sustain or accelerate the formation of plaques, producing the clinical manifestations. CHD and all cardiovascular diseases are multifactorial in origin.

The major risk factors for CHD are high blood pressure, cigarette smoking, dietary habits (particularly excessive intake of saturated fat), elevated blood cholesterol levels, lack of physical activity, obesity and diabetes. The role of dietary fat and blood cholesterol in the production of atherosclerosis is complex; it is necessary to consider the whole diet, rather than any single nutrient, since some dietary components have a protective effect and others cause damage.

High blood pressure (hypertension) is a significant risk factor for CHD. The primary prevention of hypertension is critically important in the prevention of premature death from CHD.

Cigarette smoking is the most readily preventable risk factor for coronary heart disease and all other cardiovascular diseases. It causes around 15% of all CHD deaths, mostly in people over 65, and accounts for one-quarter of all CHD morbidity in people under 45. Restrictions on smoking in public places, economic incentives and disincentives and health education are effective in helping to decrease smoking.

High blood cholesterol levels are a major risk factor, contributing to CHD deaths more commonly among women than men (Box 10). The causes can be genetic, but are more commonly related to a diet rich in animal fats. Cholesterol levels can be reduced by dietary change or by medicines.

Lack of physical activity is also increasingly recognized as a major risk factor for CHD; it is the most prevalent modifiable risk factor in many industrialized countries.

Obesity which itself is related to inappropriate nutrition and inactivity, and diabetes mellitus, are two other important risk factors. In diabetes, the relative risk is higher in women than in men. Diabetics are at increased risk because the increased levels of glucose in their blood damages blood vessels. Premenopausal women are normally less liable to heart disease than older women or than men, but they lose this protection if they suffer from diabetes.

Genetic factors interact with environmental factors to produce variations in individual risk factor levels. Differences between populations in genetic make-up have been shown to play only a minor role at most in large inter-population differences in morbidity and mortality from CHD, for which other factors are mainly responsible.

Coronary heart disease is now increasing in developing countries as their populations age and adopt unhealthy habits and behaviours.
Box 10. Women – neglected victims of heart disease?

Coronary heart disease (CHD) is often regarded, both by doctors and the general public, as primarily a man’s disease. This is partly because it kills fewer younger women than their male contemporaries. Also, heart attacks are usually seen as striking men who have a combination of stressful occupations and unhealthy lifestyles — the workaholic executive who smokes and drinks too much, has a heavy-fat diet and takes too little exercise has become a stereotype for the heart attack candidate.

This is a dangerously misleading picture — dangerous, most of all, for women. It has bred a certain complacency among doctors and health professionals, and among women themselves, who in many countries have become a neglected group as far as both the prevention and treatment of heart disease are concerned. Much of the research on causes, prevention and treatment has focused on men. Symptoms of heart disease in women are often not recognized, or even suspected, as early as they are in men. As a consequence, many women with the condition are diagnosed too late, and some studies have shown that they are treated less promptly and less efficiently than men.

The fact is that in many parts of the world, CHD is the single most common cause of death among women, even among those under 65 years of age. While women on average live longer than men, their extra years are often years of disability, in which the impact of heart disease plays a large part. With an increasingly ageing population worldwide, together with evidence that women are going to be at increased risk of heart disease, and given that much heart disease is eminently preventable, there are major implications for health and social services.

The major risk factors for CHD are the same for women as for men — smoking, high blood pressure and high blood cholesterol levels. But there are good reasons why women should receive special attention. For example:

- Teenage girls are now more likely to smoke than boys, and fewer women smokers stop than men — fear of weight gain being one reason. The epidemic of smoking-related heart disease in women will become more evident in the years ahead.
- Women taking oral contraceptives who also smoke have an increased risk of heart disease.
- Blood cholesterol levels among women increase with age. After the menopause, women’s cholesterol levels are on average higher than those of men about the same age.
- After the age of 45, women’s blood pressure is also on average higher than men’s.
- Obesity is linked to heart disease in women, and the number of overweight, obese women is increasing in many countries.
- Middle-aged women have particularly low levels of exercise, which again increases their risk.
- Although hormone replacement therapy for post-menopausal women reduces their risk of suffering from heart disease, there are now concerns about the increased risk of cancer of the endometrium as a result of the therapy.

These facts underline the need for more attention to be focused on women and heart disease. Women need to be better informed of their risks of CHD in order to respond better to preventive health advice and to recognize symptoms in themselves. At the same time, health professionals need to improve diagnosis, referral and treatment of women with CHD symptoms.

The widespread adoption of cigarette smoking and a reduction in regular physical activity may also have played a part in the emergence of the epidemic, together with the ageing of the population due to the decline in deaths from infectious diseases.

It appears that primary preventive efforts — such as encouragement to give up smoking or to change the diet — have made a major contribution to the recent decline in mortality, although medical and surgical treatment have also contributed. It is likely that the relative contribution of prevention and treatment has varied between countries and also over time.

Premature CHD is preventable and the disease can be treated at all ages. Furthermore, it appears that the epidemic of CHD is being substantially prevented in at least some industrialized countries. The most likely major contributor to the dramatic decline in death rates in North America, Australasia and some European countries is the control of major risk factors as a result of the preventive strategies mentioned above.

It therefore seems likely that at least half and perhaps as much as two-thirds of the burden of CHD is preventable. Prevention and treatment among elderly people, which have hitherto generally been given a low priority, require greater attention. Age in itself should not be a barrier to promoting health and preventing or postponing disease and disability, but there has been little enthusiasm in many countries for preventive approaches to heart disease in the elderly.

The treatment of established CHD involves both medical and surgical interventions. Low-cost, effective medical interventions have been identified such as the prescription of aspirin and “clot buster” drugs such as streptokinase which are simple to administer.

Surgery for CHD is widely practised in industrialized countries and is gradually becoming established in developing countries, although it is obviously relatively expensive for them. The cost-effectiveness of surgical interventions depends on the risk status of the patient.
Both the physical and mental health of people recovering from a heart attack, other heart conditions or cardiac surgery can be greatly improved by a combination of exercise, health education and counselling. The main components of cardiac rehabilitative care can be applied even in societies with minimal medical personnel and equipment resources. The goals of rehabilitation are to improve functional capacity, alleviate or lessen activity-related symptoms, reduce unwarranted invalidism, and enable the cardiac patient to return to a useful and personally satisfying role in society.

Rheumatic fever/rheumatic heart disease (RF/RHD) is the most common cardiovascular disease in children and young adults. Now very rare in developed countries, it remains a major public health issue in developing countries. At least 12 million people are estimated to be currently affected by RF/RHD. More than 2 million require repeated hospital admission, and 1 million will need heart surgery in the next 5-20 years.

There are 500,000 deaths annually, and hundreds of thousands of people disabled, mainly children and young adults, who have no access to the expensive medical and surgical care that their condition demands. Thus, RF/RHD is both a biological and a social problem. It is very costly because of repeated hospitalizations, and causes much suffering to patients and their relatives.

A devastating childhood disease in developed countries in the 19th century, RF began to decline in incidence in these countries slowly but steadily after 1900, and much more emphatically after the 1940s. A really dramatic decline occurred in the late 1960s, due to steady improvement in standards of living, and the benefits of improved medical care, especially the introduction of antibiotics.

The condition now rarely occurs in developed countries, although small outbreaks of RF which occurred in the mid-1980s in the United States and other countries show that the risk still remains. In contrast, since the 1940s RF/RHD has become a significant health problem in tropical and subtropical countries—often with very severe effects similar to those observed in Europe a century ago. In some developing countries, the RHD mortality rate varies from almost 1 to 8 per 100,000 population. The prevalence in schoolchildren ranges from 1 to 10 per 1000 and incidence ranges from 10 to 100 per 100,000, with a high rate of recurrence.

Rheumatic fever results from bacterial (streptococcal) infections of the upper respiratory tract, and has a marked tendency to recur. It affects mainly the large joints and the heart, and less frequently the brain, skin and underlying tissues. The effect on the heart (rheumatic heart disease) is the only one that may cause death or disability.

RF/RHD often results in significant, chronic morbidity for children and young adults, with two important features. Firstly, frequent outpatient and inpatient care is a drain on already limited family resources, and involves work absenteeism for the family members who accompany the patient to hospital or visit the patient in hospital. Secondly, educational opportunities are lost (as many as 60% of children debilitated by RHD drop out of school in some areas).

Medical treatment for RF/RHD is not curative and usually has to be continued indefinitely. The costs progressively increase, further adversely affecting the cost-benefit balance in favour of prevention. Surgical treatment is even more expensive and often unaffordable or unattainable.

Climate and socioeconomic factors linked to low income, poverty, overcrowding, poor housing conditions and inadequate health services appear to influence the occurrence of RF/RHD. Those aged 5-19 years are at greatest risk.

Although there is, as yet, no available safe and effective antirheumatic streptococcal vaccine or genetic marker to identify people at high risk of developing RF, there are proven, cost-effective methods for the secondary and primary prevention of RF/RHD. Effective methods also exist for the diagno-
sis and treatment of acute attacks of RF, as do clinical and surgical methods for the palliative care of RHD and for its rehabilitation.

Although RF/RHD has been declining in some developing countries recently, the decline is slowing, because few of these countries are implementing prevention and control strategies that would help raise living standards and access to effective medical care. In contrast, prevention programmes which have been implemented in several countries achieved reductions in the mortality, prevalence, incidence, hospital admissions and severity of RF/RHD.

RF/RHD is a chronic disease for which an eminently feasible and cost-effective prevention strategy exists.

Primary prevention consists in early detection and correct treatment of streptococcal sore throat or pharyngitis whenever feasible (to prevent the first attack of acute RF). The initial acute attack can be avoided if such conditions are correctly treated.

Secondary prevention consists in early detection, diagnosis and long-term secondary prophylaxis with oral penicillin for all patients with RF/RHD (to prevent a recurrence of acute RF attack and more severe RHD). When secondary prophylaxis is applied, more than 75% of RF/RHD patients recover completely.

### Cerebrovascular diseases

Among circulatory diseases, stroke and other cerebrovascular diseases are the second most common cause of death, accounting for more than 4.6 million deaths worldwide, one-third in industrialized countries, and the rest in developing countries. As is the case with CHD, there is considerable geographical variation, and morbidity and mortality occur mainly in the over-65 age group.

Cerebrovascular diseases are diseases of the central nervous system of vascular origin. They include transient cerebral ischaemia, stroke and vascular dementia, all involving disturbance of blood circulation in the brain. In a large proportion of cases, the first manifestation of cerebrovascular disease is stroke. As with CHD, atherosclerosis is the underlying determinant in most cases.

**Stroke** is a sudden neurological impairment, due to a cerebrovascular disorder. It can take the form of bleeding from a blood vessel in the brain (haemorrhagic stroke) or of an obstruction of a brain blood vessel (ischaemic or thrombotic stroke). About one-third of stroke patients die within six months of the event; most of these deaths occur in the first month. Survivors may be severely disabled, with partial paralysis or other physical disability, loss of speech, loss of memory and damage to other intellectual functions.

High blood pressure is the most important risk factor for both ischaemic and haemorrhagic stroke. Even modest blood pressure reduction in hypertensive people could reduce half of the stroke events worldwide.

Other major risk factors mentioned above in the context of CHD are equally important for cerebrovascular disease, in particular smoking. Alcohol consumption also increases the risk.

In developed countries, there has been a consistent decline in stroke mortality over the last 40 years, with an acceleration of this decline in the mid-1970s. The fall in stroke deaths has been greater than that in CHD deaths. For example, in Canada, Japan, Switzerland and the United States stroke mortality has declined by more than 50% in men and women aged 65-74 years since the 1970s. Although the reasons for this decline are not fully understood, the limited evidence available suggests that a decline in case-fatality may be related to decreased severity of the disease, with the acute event becoming more mild, probably as a result of prevention efforts. Improved management in the acute phase may also have contributed.

Control of hypertension and smoking cessation are of the utmost importance for stroke prevention. Other approaches, as described for CHD, should also be considered since many
Strokes occur in people who do not have high blood pressure. As regards other modifiable risk factors, antithrombotic therapy for chronic atrial fibrillation has been found to be useful for primary prevention. Control of hypertension may also be a key factor in reducing vascular dementia.

A WHO study published in 1996 on the risk of haemorrhagic stroke associated with the use of oral contraceptive pills showed that the pill does not increase the risk in women below 35 years, who form the great majority of pill users worldwide. In current users over 35, however, the study found a small increase in risk. This was also found in relation to ischaemic stroke in current pill users, but was lower in women under 35, in non-smokers and in those who did not have high blood pressure. For both types of stroke, the study found no increased risk in women who had used the pill in the past. Women’s risk of stroke can be reduced by avoiding using the pill if they have high blood pressure, and for users of the pill, by avoiding smoking.

**Hypertension**

Hypertension, or high blood pressure, is the most common cardiovascular disorder, affecting about 20% of the adult population, both in the developed and developing world, and is an important public health problem of global dimensions. It affects an estimated 50 million people in the United States alone, costing 29 million working days and $2 billion per year in lost earnings.

Although it is virtually symptomless, except in its severe form, high blood pressure is considered both as a disease category and as one of the major risk factors for heart disease, stroke and kidney disease.

In most populations, average blood pressure increases with age and elevated blood pressure is particularly common in elderly men and women. The risk of cardiovascular events is substantially increased by the presence and levels of other risk factors such as smoking, elevated serum cholesterol and diabetes.

Equal blood pressure levels therefore carry different risks when associated with different combinations of risk factors.

A number of determinants — many of them associated with lifestyle — are directly linked with the development of hypertension. While some risk factors and predictors of high blood pressure such as heredity, age and genetic factors are not modifiable, others can be modified in a variety of ways.

The major risk factors for hypertension are overweight, poor dietary habits — in particular, excessive intake of salt (sodium chloride) and alcohol — and inadequate physical activity. Studies suggest that taking less salt every day could result in smaller rises in blood pressure so that by the age of 55 there could be a 16% reduction in mortality for CHD, 23% for stroke and 13% for deaths from all causes. In contrast, potassium, found in some fruits and other foods, is considered to be a protective factor.

Both acute and chronic effects of alcohol on blood pressure have been noted. Regular aerobic physical activity, adequate to achieve at least a moderate level of physical fitness, has been shown to be beneficial for both prevention and control of hypertension.

A family history of elevated blood pressure is one of the strongest predictors for future development of hypertension. Several genetic factors have been identified as determinants of high blood pressure.

A number of aggravating factors contribute to variations of blood pressure within countries. In developed countries, higher prevalence of hypertension has been noted in groups with lower socioeconomic status (education, income, occupation). However, in developing countries, higher levels of blood pressure are found in upper socioeconomic groups. Generally, this corresponds to emerging middle-class populations; and it probably represents the initial stage of the epidemic of cardiovascular disease. Major geographical and ethnic variations also occur within countries.

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In developing countries, higher levels of blood pressure are found in the emerging middle-class populations, and probably represent the initial stage of the epidemic of cardiovascular disease.
**Chronic nonspecific lung diseases**

Chronic nonspecific lung diseases include asthma, chronic bronchitis and emphysema. Together they kill almost 3 million people every year, representing around 6% of deaths globally. Chronic bronchitis and emphysema are usually grouped as chronic obstructive pulmonary disease (COPD), which is especially prevalent in older age groups. Deaths from COPD worldwide are expected to increase significantly with the rise in smoking prevalence and environmental pollution.

Asthma and COPD have common characteristics such as obstruction of the airways (respiratory passages). However, the airway obstruction in asthma is variable and reversible whilst in COPD it is poorly reversible and usually progressive. There is a large overlap between asthma and COPD, and asthma can evolve into COPD.

**The asthma epidemic**

Asthma is a chronic inflammatory disorder of the airways which causes recurrent episodes of wheezing, breathlessness, chest tightness and cough, particularly at night and/or in the early morning. These symptoms are usually associated with widespread but variable airflow limitation that is at least partly reversible either spontaneously or with treatment. The disease is also characterized by recurrent exacerbations often provoked by factors such as allergens, irritants, exercise and virus infections.

Asthma occurs in all races, and its highest prevalence is found in Australia. While genetic factors are of major importance as predisposing factors in the development of atopy (increased allergic response) and probably asthma, present evidence (especially regarding the increasing prevalence of asthma in developing countries all over the world) suggests that environmental rather than racial factors are important in the onset and persistence of asthma. Studies clearly suggest a true increase in asthma prevalence in the past two to three decades in both children and young adults.

In children, there is evidence of increased prevalence worldwide. In adults the data are more controversial.

Asthma is more prevalent in children, causes a high morbidity and can be fatal even in young people. The reasons are poorly understood. It may be due to changes in the indoor or outdoor environment and may involve allergens in the air, especially domestic mites and occupational allergens. Climate is of importance because it directly affects the amount of allergen present in the environment, for example, a damp and warm climate favours the growth of mites and moulds. Possibly the increased prevalence of allergy and asthma is due to the synergistic action of air pollution or tobacco smoking with allergic sensitization. Passive smoking has also been involved in the allergic sensitization of children, boys especially, to common allergens in the air. Links with urbanization in some parts of the world have been suggested, as have housing environments, and dietary factors. Socioeconomic status within countries may also be involved because of related problems in obtaining appropriate medical care.

**COPD and smoking**

The two main symptoms of COPD are breathlessness and cough, sometimes accompanied by wheezing or sputum production. Breathlessness develops gradually over many years and eventually limits daily activities. The chronic cough is very frequently associated with sputum production. The coughing and expectoration of sputum is usually worst in the morning. In contrast with asthma, most patients with COPD do not have nocturnal symptoms. The symptoms and signs of COPD, more frequent in winter, may be worsened by viral or bacterial infection, increased air pollution, cigarette smoking and changes in weather conditions. In COPD, lung function is characterized by progressive airflow limitation.

The prevalence of COPD largely depends on the prevalence of its most important risk factor - cigarette smoking. The disease is highly prevalent in
affluent and partly affluent populations worldwide. At least 15% of middle-aged smokers have abnormal lung function, and a chronic cough with phlegm. Evidence suggests only about 25% of cases of COPD are diagnosed. The disease is more common in men than in women, even for the same degree of smoking, but the trend towards increased smoking in women will undoubtedly increase the prevalence of COPD among them.

Respiratory diseases rank among the three principal causes of lost workdays and COPD is responsible for the majority of these. It leads to substantial disability, loss of productivity and reduced quality of life. The disease is almost always progressive, with frequent exacerbations and respiratory failure, resulting in frequent hospitalizations and sometimes death.

Most deaths due to COPD occur in individuals over the age of 65, and rates vary from country to country; in Europe, for example, from 2.41 deaths per 100,000 males per year. Smoking cessation is not associated with any decrease in mortality until at least 10 years after stopping.

**Economic and social costs**

Chronic nonspecific lung diseases have a high economic and social cost due to their high prevalence, substantial morbidity and mortality and chronicity. It is estimated that asthma is responsible for about 2% of the health care costs in affluent populations. About half of the costs are direct costs including those for long-term treatment of the disease and for hospital care of patients with exacerbations of asthma. The remaining half are indirect costs to society such as loss of productivity in the case of the asthma patient and of relatives who have to care for the patient. The increasing prevalence of the disease and the increasing cost of asthma medications will necessitate the development of national strategies aimed at reducing morbidity and mortality due to asthma in a cost-effective way.

The social and economic burdens of COPD are greater than those of asthma due to its high prevalence and significant morbidity, disability and mortality. The direct cost of managing COPD, which frequently results in hospitalization, is high. The treatment of complications such as respiratory failure (chronic oxygen therapy) is expensive. COPD occurs typically in middle-age and results in loss of productivity either intermittently during exacerbations or permanently because of disability.

Early detection of COPD may increase the success of secondary prevention, including the possibility of pharmacological prevention.

**Metabolic disorders**

**Diabetes mellitus**

Diabetes mellitus is one of the most daunting challenges posed today by chronic diseases. Recent data show that approximately 135 million people suffer from diabetes mellitus worldwide, and that this number will rise to almost 300 million by the year 2025. This more than twofold rise is projected to occur because of population ageing, unhealthy diets, obesity and a sedentary lifestyle. While the rise will be of the order of 45% in developed countries, it will be almost 200% in developing countries (Fig. 7).

**Fig. 7. Diabetes mellitus, regional estimates, 1995–2025**
Box 11. The cost of diabetes

Because of its chronic nature, the severity of its complications and the means required to control them, diabetes is a particularly costly disease for the health care services, the affected individual and society. However, costs vary enormously, depending on social, economic and health service factors. A meeting convened by the International Diabetes Federation in December 1996 and cosponsored by WHO reviewed these variations and some of the factors responsible for them. The main purpose of the meeting was to prepare a detailed report on the current situation for the benefit of health planners, programme managers, decision makers and teachers.

Recent estimates suggest that the annual per capita health care cost for persons with diabetes was $13 in Bangladesh (1988), $103 in the United Republic of Tanzania (1990), $104 in Mexico (1992), and as much as $8500 in the United States (1992). These are “cost of illness” estimates, but in order to understand the potential for improvement, and the efficiency of interventions, the cost-effectiveness of alternative prevention and control strategies in different health systems and physical environments should be estimated.

Evidence has accumulated in recent years that improved blood glucose control substantially reduces both the development and progression of some of the more important diabetic complications such as retinopathy, neuropathy, and nephropathy. These are major contributors to the morbidity and premature mortality of people with diabetes. Measures which improve blood glucose control are therefore likely to have far-reaching economic benefits in both the short and long term. The cost-effectiveness of such improvements is likely to be greatest in countries which have the least developed health care systems.

Attention has also focused on the involvement of people with diabetes in the management of their own disease and thus on the benefits of patient education, in addition to adequate treatment. National diabetes programmes dealing with these issues (a number of which already exist in all WHO regions) have a central role to play. Such programmes may also form the basis for developing an integrated approach to the control of other chronic diseases.

Because of the relationship between diabetes and increased risk of other diseases, its prevention and treatment are priority issues. Diabetes is closely linked with heart disease, kidney failure and blindness; it adversely affects the outcome of pregnancy and can lead to male impotence. Peripheral vascular disease and neuropathy can give rise to foot lesions which may progress to gangrene and limb amputations, entailing high costs to individuals and to health services (Box 11).

Diabetes mellitus is a chronic disease caused by inherited and/or acquired deficiency in the production of insulin by the pancreas, or by ineffectiveness of the insulin produced. Such a deficiency results in increased concentrations of glucose in the blood, and this in turn results in damage to many parts of the body’s systems, especially the blood vessels and nerves.

Diabetes mellitus is a hereditary disease. Certain genetic markers are known to increase the risk of developing insulin-dependent diabetes. Such markers have not been described for non-insulin-dependent diabetes, though this form is strongly familial.

There are basically two major forms of diabetes: the insulin-dependent (IDDM) and non-insulin-dependent (NIDDM) forms (these terms are currently under review). In IDDM, the pancreas fails to produce the insulin which is essential for survival. This form develops most frequently in children and adolescents, but is becoming increasingly recognized later in life.

NIDDM is much more common and accounts for up to 90% of all diabetes cases worldwide. It occurs principally in adults and results from the body’s inability to respond properly to the action of insulin produced by the pancreas.

Malnutrition-related diabetes has also been described in some developing countries. It is found in undernourished individuals in some tropical countries. The cause and distribution of this form are still not clearly understood.

The symptoms of diabetes may be pronounced or subdued. In IDDM the classic symptoms are excessive secretion of urine (polyuria), thirst (polydipsia), weight loss and a feeling of fatigue. These symptoms may be less marked in NIDDM; it can also happen that no early symptoms appear in this form and the disease is only diagnosed several years after its onset, when complications are already present.

Insulin was discovered in 1921 and revolutionized the treatment of diabetes and prevention of its complications. It transformed IDDM from a fatal into a treatable disease. Diet, physical exercise and oral hypoglycaemic agents are other important components of treatment.

People with IDDM are totally dependent on daily insulin injections, which for them is a life-saving medica-
tion. Although most people suffering from diabetes have the non-insulin-depen-
dent form, up to 30% of them may use insulin injections, some or all of the
time to control their condition.

The price of insulin (without syringes and necessary equipment for
monitoring blood glucose levels) varies widely internationally, ranging from
only a few dollars per vial in some coun-
tries to the equivalent of a month’s sal-
ary in many African countries.

Recent research provides clear evi-
dence of the potential for adequate
treatment to delay or even prevent the
long-term complications of diabetes,
including blindness, kidney failure,
heart attacks, and amputation of the limbs.

Diabetic retinopathy, which is
caused by damage to the small blood
vessels in the retina, is the leading cause
of blindness and visual disability in
adults in economically developed soci-
eties. After 15 years of diabetes, approxi-
ately 2% of people become blind and
about 10% develop severe visual handi-
cap. Loss of vision due to certain types
of glaucoma and cataract may also be
more common in people with diabetes
than in those without the disease.

Loss of vision and blindness in per-
sons with diabetes can be prevented by
early detection and treatment of vision-
threatening retinopathy: regular eye
examinations and timely intervention
with laser treatment, or surgery in cases
of advanced retinopathy. A recent study
has demonstrated that good metabolic
control can also delay the onset and pro-
gression of diabetic retinopathy. There
is evidence that, even in developed
countries, many of those in need are not
receiving such care due to lack of pub-
lic and professional awareness. In de-
veloping countries, in most of which
diabetes is now epidemic, the majority
of the population does not have access
to such care.

Diabetes is a leading cause of renal
failure, the frequency of which varies in
different populations and is related to
the severity and duration of the disease.
Measures to slow down the progress of
renal damage include control of hyper-
glycaemia and of hypertension. Screen-
ing and early detection of diabetic kid-
ney disease are an important means of
prevention.

Heart disease accounts for 75% of
all deaths among people of European
origin with diabetes. Risk factors for

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**Box 12. Diabetes in New Zealand**

Studies suggest that diabetes affects 2.5% of all New Zealanders, 5-10% of Maori and 4-8%
of Pacific Islands people. The higher prevalence of diabetes in Maori has been known for
several decades. A recent survey in South Auckland found the diabetes rate in Maori to be
2.5 times higher than in European New Zealanders. For Pacific Islands people the figure was
1.6. Other studies have yielded similar results. Non-insulin-dependent diabetes mellitus is
relatively more common in Maori and Pacific Islands people than in New Zealanders of
European origin, while Pacific Islands people appear to have a generally low rate of insulin-
dependent diabetes mellitus.

Maori are thus disproportionately affected by diabetes, which is one of many factors
contributing to their low health status. A strategy for reducing the impact of diabetes on
Maori must be set within the context of making general improvements in their health. Maori
health services recognize the importance of family support for the diabetic person. Con-
versely, the direct threat of diabetes can lead to behaviour changes for the family as well as
the individual concerned (healthy food, smoking cessation, exercise and freedom from drugs).
Thus, diabetic patients can also be effective educators.

The national organization of Maori diabetes workers is developing a family approach to
diabetes care, as well as ensuring that diabetes services are appropriate and safe for Maori.
The good relationship between diabetes educators and the community has been one of the
most significant factors in achieving long-term changes in the Maori diet.

In New Zealand, diabetes is among the leading causes of hospitalization and death
among Pacific Islands people, especially in the age group 44-64. Those affected have high
rates of obesity, poor blood glucose control, inadequate knowledge of their condition, inad-
quate blood glucose monitoring, and poor blood lipid control. They are the least physically
active ethnic group and an estimated 75% are overweight. Genetic predisposition and diet
are major risk factors. Diabetes is more prevalent in Polynesians than Melanesians, and in
those living a modern rather than traditional lifestyle. Dietary changes and physical inactivity
have contributed to the rise in diabetes prevalence amongst Pacific Islands people over the
last 30 years, both in New Zealand and in the Pacific. In some communities the degree of fat
or richness in certain foods is associated with status and prestige, as is large body size.
Preventing some modifiable risk factors is thus more difficult.

Maori and Pacific Islands people suffer more diabetic complications than Europeans,
including end-stage renal failure, proteinuria, blindness, severe retinopathy, cataracts and
foot amputations. Intervention programmes for the prevention of diabetes and its complica-
tions must address specific needs of ethnic groups within the population. Similar initiatives
with migrant populations overseas have been shown to be effective. Some progress is al-
ready being made through local diabetes intervention programmes. Expertise gained from
these initiatives, such as the South Auckland Diabetes Project, should be made available to
other regions.
heart disease in people with diabetes include cigarette smoking, hypertension, raised blood cholesterol and obesity. Recognition and management of these factors may delay or prevent heart disease in people with diabetes. Premenopausal women with diabetes are more prone to heart disease than those without diabetes.

Diabetic neuropathy, leading to sensory loss and damage to the limbs, is probably the most common complication of diabetes. Studies suggest that at least 50% of people with diabetes are affected to some degree. It is also a major cause of impotence in diabetic men. Major risk factors are the level and duration of hyperglycaemia. Foot care is an important means of reducing the impact of diabetic neuropathy; foot ulceration and amputation is one of the most costly complications of diabetes, resulting from both vascular and neurological disease processes. Diabetes is the most common cause of nontraumatic amputation of the lower limb, which may be prevented by regular inspection and good care of the feet.

Overall, a parallel approach is recommended in strategies for diabetes prevention. Short-term gains may be made by improving health services and the availability of essential medications, blood glucose monitoring and patient education (Box 12). An integrated approach to the primary prevention of diabetes and other common, communicable diseases by lifestyle modification and risk factor reduction should be developed as a long-term strategy for containment.

Developing countries will bear the brunt of the diabetes epidemics in the 21st century. National plans and policies for prevention and control will be needed, together with improved availability of essential drugs and materials. Many countries have already begun to move in this direction.

**Nutrition-related disorders**

Adequate food and nutrition are essential for proper growth and physical development from conception to adulthood, to ensure optimal work capacity and normal reproductive performance, and also to ensure the adequacy of immune mechanisms and resistance to infections.

An inadequate diet produces two main types of metabolic nutritional disorders: protein-energy malnutrition (PEM), and micronutrient disorders (mainly deficiencies).

Nutritional disorders, besides being disease entities, are underlying factors in chronic diseases. Thus, an appropriate diet is also essential to avoid a number of diet-related noncommunicable diseases such as cardiovascular disease, diabetes mellitus, certain forms of cancer and liver disease, and dental caries.

**Chronic undernutrition** occurs when long-term food consumption is insufficient to cover the requirements for daily energy expenditure. It is usually assessed in terms of body measurements: in adults, thinness; in children, stunting. Acute malnutrition (wasting) occurs when food consumption is suddenly severely reduced.

The causes of chronic undernutrition are multiple and include chronically insufficient food availability or access to food, recurrent infection, and inadequate care, especially of children and mothers. All these factors are common in poorer countries, and in some poor communities in industrialized countries. Poverty and low levels of education are often but not always present. Acute malnutrition occurs particularly, but not exclusively, in emergency conditions, such as warfare or prolonged drought.

The consequences include diminution of body size and work capacity and performance, and enhanced severity of and mortality from infections. Malnutrition has been found to underlie more than half of deaths among children in developing countries.

Global data show no change in overall PEM prevalence in children aged under 5 from 1990 to 1995; but in South Asia and sub-Saharan Africa, there were large increases in the numbers of malnourished children.
Various types of micronutrient malnutrition are important causes of disability in themselves and often underlie other types of morbidity as outlined below. Their prevalence is even more widespread than that of protein-energy malnutrition.

Anaemia is clinically defined on the basis of the haemoglobin level in the blood. Iron deficiency is present when body iron stores are depleted; this is usually assessed on the basis of serum ferritin levels. Anaemia is a late sign of iron deficiency; about twice as many persons are affected by iron deficiency as are anaemic.

In addition to nutritional anaemias, there are haemolytic, genetically-determined and other types of anaemia. While iron is the nutrient that is usually deficient, deficiencies of folic acid, ascorbic acid, riboflavin and various minerals can contribute to anaemia. Iron deficiency is usually due to inadequate iron intake or absorption. Concurrent factors which may often play a role, particularly in developing countries, include: blood loss (menstruation, childbirth, hookworm disease, schistosomiasis), and haemolysis due to malaria.

Mainly women of reproductive age and children aged under 5 years are affected by iron deficiency, with prevalences of 40-50% in developing countries (over 50% in pregnant women). In industrialized countries about 10% of women, and 17% of pregnant women, are anaemic, and twice as many are iron-deficient. The prevalences are highest in South Asia (80% in some countries). Globally nearly 2 billion people are estimated to be anaemic and 3.6 billion iron-deficient.

In infants and young children even mild anaemia can impair intellectual as well as physical development.
Map 2. Iodine deficiency disorders, 1996

Vitamin A deficiency (VAD) occurs when body stores are depleted to the extent that the physiological functions are impaired.

Depletion occurs when the diet contains, over a long time, too little vitamin A to replace the amount used by tissues or for breast-feeding. Intakes are low when the intake of foods of animal origin is low, and particularly when the consumption of dark green leafy vegetables and orange-coloured vegetables and fruits (the main vegetable sources) is low.

The consequences include night blindness and eventual blinding conditions. VAD is the most common cause of blindness in young children, and can raise young-child mortality rates by 20-30%. It is known that 76 countries have a VAD problem. An estimated 2.8 million children aged under 5 years are clinically affected, and 258 million are subclinically affected. The highest prevalence and numbers are in South-East Asia.

As with iron deficiency, usually a variety of strategies may be needed, including: dietary improvement; fortification of fats or sugar; and supplementation with large doses of vitamin A.

The elimination of this deficiency by the year 2000 was adopted as a goal of the World Declaration on Nutrition.

Vitamin D deficiency and inadequate exposure to sunlight result in rickets in young children, and osteomalacia in adults, which are still widespread in parts of northern Africa and Asia.

Scurvy, beriberi and pellagra occur mainly in emergency conditions, due to deficiencies of ascorbic acid, thiamine and niacin respectively.
**Human genetics, hereditary diseases and birth defects**

Recent progress in medical research, particularly in molecular genetics, has shown that inherited predisposition plays an important role not merely in well-recognized congenital defects or in hereditary diseases such as haemophilia, but also in common diseases of later life, such as coronary heart disease, high blood pressure, diabetes, some cancers and some musculoskeletal and mental disorders. (Box 13). This section deals with some major genetic disorders and congenital abnormalities.

The term "birth defect" is defined as any structural, functional or biochemical abnormality present at birth, whether detected at that time or not, and includes the overlapping categories of genetic disorders and congenital abnormalities. Accurate prevalence data are difficult to collect because of the great diversity of the conditions, and because many that cause early death remain undiagnosed in the absence of specialist services. In typical developed societies, congenital and genetic disorders are the second most common cause of infant death after perinatal factors and of death in children aged 1-4, after accidents.

Although the causes of all birth defects are not known, some can be prevented by making use of past knowledge and recent research breakthroughs. Women can increase their chances of having a healthy baby by taking steps that include the following: adequate nutrition throughout the childbearing years (e.g. rich in vitamins and iodine); avoiding sexually transmitted diseases; being vaccinated against rubella and hepatitis; seeking advice early from qualified health workers; getting early and adequate prenatal care; and during pregnancy, avoiding alcohol and tobacco, and certain medicines (e.g. thalidomide).

Some of these disorders are hereditary diseases. They include haemoglobin disorders also known as hereditary anaemias, such as thalassaemias and sickle cell disorder. Each year about 300,000 infants are born with major haemoglobin disorders. Almost 70% of cases of sickle cell disorder occur in sub-Saharan Africa. Increasing global migration has introduced the disorder into many areas where it was not originally

**Box 13. Chronic diseases: discovering the genetic links**

Although the limits of intelligence, physical ability and longevity are genetically determined, external and environmental influences such as infections, malnutrition and war have long been the main determinants of health and survival. Now, with increased control of the environment, genetic make-up is becoming an ever more important determinant of individual health. Genetic predisposition may lead to the premature onset of common diseases of adult life such as cancer, coronary heart disease, diabetes, hypertension and mental disorders.

The Human Genome Project is an international research venture that aims to draw up a complete map of the sequence of DNA. This research will eventually lead to the identification of every gene linked to susceptibility or resistance to disease.

**Cancer.** It is not yet certain whether most cancers are hereditary. But a genetic predisposition may be involved in as many as 10-25% of cases of cancer of the breast or colon. Numerous genes are being identified that may affect susceptibility to tumour development. This may lead to a general improvement in the diagnosis and treatment of cancer. For example, a DNA screening test for breast cancer could soon be available. Advice could be offered on the chemoprevention of cancers, tailored for families with different types of cancer risk.

**Coronary heart disease.** Until recently, it was generally believed that environmental factors alone cause coronary heart disease. But investigating family histories often uncovers genetic risk. Mapping the human genome will make the genetic predisposition to CHD much easier. High blood pressure and high blood cholesterol levels, major risk factors in CHD, are also genetically influenced. A combination of risk detection and lifestyle counselling, with drug treatment, might cut the incidence of heart attacks to the low levels of two or three generations ago.

**Diabetes.** Evidence for a genetic element in insulin-dependent diabetes mellitus has emerged from studies showing a higher concordance in identical twins (25-30%) than in non-identical twins (5-10%). About 85% of cases of diabetes in developed countries are of the non-insulin-dependent form of the disease, which has a particularly strong familial tendency. Diabetes of all types is an important candidate for future treatments such as gene therapy or pancreatic tissue transplantation.

**Mental disorders:** Evidence from family and twin studies demonstrates the existence of genetic predisposition to some common mental diseases. Alzheimer disease, the most common form of senile dementia, has a strong familial tendency and is known to be caused by at least four different genes. Research may lead to the development of drugs useful in preventing or delaying the onset of the disease.

Enough is already known about the genetics of common diseases to introduce a family-oriented approach into basic as well as specialist medical practice. A major effort will be made in the foreseeable future to study the genetic factors involved, develop appropriate therapies, and determine how these approaches can best be applied in practice.

Among more than 140 million births each year, about 3 million fetuses and infants are born with major congenital malformations.

There are different forms of haemophilia. While the disorder affects males, it is carried by females, who are only occasionally affected, usually mildly. The disorder concerns the absence, decrease or deficient function in sufferers of blood coagulating factors, leading to excessive, prolonged or delayed bleeding. In severe cases it most commonly occurs in the large joints of the limbs.

Unless such bleeding is controlled promptly by infusion of the deficient factor, there is progressive joint disease and muscle atrophy, leading to serious physical, psychological and social handicaps. Until recently, the foremost cause of death was haemorrhage, especially in the skull.

In countries with highly developed haemophilia care programmes, therapy with plasma derivatives has reduced mortality. In the past decade, the main causes of death have stemmed from infections as the side-effects of treatment, including AIDS and liver disease secondary to hepatitis. Survival in patients without these infections is almost the same as that of the general population.

Improvement in haemophilia care worldwide depends on persistence in and support for proven methods of care, on continued research into possible means of cure, such as gene therapy, and on expansion of care to areas of the world where it is inadequate. Whenever possible, the mechanism for providing haemophilia care should be linked with that for sickle cell disease or thalassaemia. This will not only strengthen the control and prevention of these disorders, but will also improve health services generally, including public health, blood transfusion and laboratory services.

Among more than 140 million births each year, about 3 million fetuses and infants are born with major congenital malformations. In recent years, these have become a relatively more important cause of death and morbidity in children as well as the reasons for hospitalization and causes of disability. Despite their significance, however, little progress has been made in determining their cause: the causes of about 70% are still unknown.

Endemic. In the United States, for example, 10% of the population is at risk.

Haemoglobin disorders can be prevented by testing and counselling. Comprehensive control programmes that combine optimal treatment with a community-based approach to intervention exist in many countries and are successful. In the case of thalassaemia, practically no new births of thalassaemic children now occur in Cyprus or Sardinia, where it used to be a problem. In Greece and mainland Italy, the rate of such births is falling.

Cystic fibrosis is a genetic disease occurring worldwide which affects the respiratory and gastrointestinal tracts and the sweat glands. Incidence ranges from 2.5 to 5 per 10,000 live births in most European populations. The condition is less common in blacks and rare in orientals.

Until a few years ago, life expectancy of children with the disease was below 5 years of age. Now that it is recognized and treated earlier and more effectively, life expectancy in developed countries is about 30 years, and projections for young children alive with cystic fibrosis now suggest that they may live for 40 years or more, even without the development of new treatments. However, up to 95% of cases in Latin America are never diagnosed, and the life expectancy of those that are is only about 10 years.

The gene defect in cystic fibrosis was identified in 1989, since when there has been unprecedented progress in understanding the disease, leading to new approaches to drug treatment and hopes for gene therapy. Such treatments are expected to be available within the lifetime of most current patients, with a corresponding anticipated improvement in outlook.

Haemophilia is a hereditary bleeding disorder affecting 15–20 of every 100,000 males born, with equal incidence in all ethnic groups and geographical areas that have been surveyed. Prevalence, which depends on survival, varies according to available medical care. There are an estimated 420,000 people with haemophilia worldwide.
Supplements of folic acid before and during pregnancy have been shown to reduce neural tube defects, including spina bifida. Women with chronic diseases which also increase the risk of congenital malformations, such as diabetes, multiple sclerosis and epilepsy, should be under the care of a physician or other adequately trained health care provider.

**Outlook**

Current trends in the management of genetic diseases are strongly linked with the progress of international human genome research. Genetic technology may soon be used to identify people with genetic risk factors for common diseases. More needs to be known about the biochemical and social implications of genetic testing and the potential for gene therapy.

**Musculoskeletal diseases**

Musculoskeletal diseases, also often referred to as chronic rheumatic diseases, include about 200 conditions affecting joints, bones, soft tissues and muscles. Together they amount to a huge burden in pain and often crippling disability, and consequently, huge costs in terms of both health care and lost productivity.

Most chronic rheumatic diseases involve all organs and tissues of the body and require expert diagnosis. Well-established, standardized epidemiological criteria for use in the study of their global prevalence are lacking. Only a few of these diseases have been thoroughly investigated.

The most prevalent of these conditions are inflammatory joint diseases – rheumatoid arthritis and ankylosing spondylitis; gout; osteoarthritis; connective tissue disease; non-articular disorders, such as back pain and soft tissue rheumatism; and bone disease, particularly osteoporosis. This section concentrates on osteoarthritis, rheumatoid arthritis, osteoporosis and low back pain.

The prevalence of major rheumatic diseases in adults ranges from 24% in China and Indonesia to 45% in Chile. Although prevalence is best documented in industrialized countries, it is likely to be the same or even higher in developing countries. For example, these diseases are the most common cause of disability in the United Kingdom, accounting for 44% of all such disability in the elderly, and are estimated to cost $60 billion a year in the United States, where about a third of all adults are affected.

**Osteoarthritis**, also known as osteoarthritis or degenerative joint disease, is the oldest disease known to have affected humans, and has emerged as the most common and important form of joint disease in almost all populations studied. It is strongly age-related. With ageing populations, severe osteoarthritis of the hip and knee joints has become an increasingly important burden on health services. It is rare in the knee before age 35 years, but 20-40% of people over the age of 70 years are affected; the hip is less commonly affected than the knee.

Osteoarthritis of the knee is predominantly a disease of women and is strongly related to age and associated with previous trauma. The other major risk factor is obesity. Osteoarthritis of the hip predominantly affects men. Some congenital/developmental bone and joint disorders lead to osteoarthritis of the hip in later life. Prior inflammatory joint disease could also be a risk factor; others may include joint usage, diabetes mellitus, and hysterectomy.

Medical management aims to reduce pain and maintain optimum function. Surgery is used to treat joints that are grossly damaged and causing severe pain. Hip replacement is well established as the best treatment for a badly damaged hip joint. Knee surgery includes osteotomy, which can promote healing, as well as joint replacement. Almost 80% of osteoarthritis patients have some form of limitation of movement, and a quarter cannot perform the activities of daily living.

**Rheumatoid arthritis** usually starts in early adulthood or middle age, but can also develop in children, and affects two to three times more women than men.
It is an autoimmune disorder, that is, body tissues are attacked by their own immune system, which has been disturbed in some way. The condition causes painful inflammation or even destruction of joints. So-called rheumatoid juvenile arthritis is a major cause of disability in children and is more common in girls than boys; seven forms of this disease have been classified.

Treatment for rheumatoid arthritis includes nonsteroidal anti-inflammatory drugs, immunosuppressant drugs, physical therapy and surgery.

Osteoporosis and associated fractures are a major cause of death, illness and disability, and a cause of huge medical expense worldwide. Bone fractures are the main complication of osteoporosis. The lifetime risks for osteoporotic fractures in women are at least 30% and probably closer to 40%. In men the risk is 13%. The incidence is higher in women than men and higher in Caucasian populations than others. Even among white populations, however, rates vary by geographical region — hip fracture rates are higher in the Nordic countries, for example, than in North America or Oceania, and lower in the countries of southern Europe.

The reason for these regional differences is unclear. The race and sex differences are partly explained by the heritability of skeletal size. Bone mass is greatest in those of African heritage, who have the lowest fracture rate, and is least in Caucasian women of northern European extraction, who have the highest fracture rate. Differences in bone mass might also relate to regional patterns of diet and exercise.

Given that osteoporotic fractures are most common in the elderly, the influence of increasing life expectancy on the number and regional distribution of hip fractures will be dramatic. Worldwide, it is estimated that the number of hip fractures could rise from 1.7 million in 1990 to 6.3 million by 2050.

Lifestyle factors are also associated with the development of osteoporosis (diet, physical activity, smoking), opening a perspective for primary prevention.

The primary aim is to prevent fractures; this may be achieved by increasing bone mass at maturity, by preventing subsequent bone loss or by restoring the bone mineral. Lifestyle modifications could be of great importance. To prevent osteoporosis, hormone therapy is used generally, especially in women at the menopause.

Low back pain blights the lives of many millions, and afflicts almost everyone at least once. It accounts for much absenteeism from work and impaired quality of life. It is self-limiting regardless of therapeutic approach, and no specific therapy has been satisfactorily validated.

Mental and neurological disorders

In recent decades, scientific research has considerably extended knowledge of the functions of the human brain, and of mental and neurological illnesses. Many disorders whose origins were mysterious can now be investigated, using painless, noninvasive methods. Some of these conditions can now be treated either with well-tested and effective drugs (e.g., drugs for anxiety, depression, schizophrenia or epilepsy) or with a wide range of other psychiatric and psychological tools.

Nevertheless, mental and neurological illnesses continue to account for a significant proportion of disability due to disease — larger, for instance, than hypertension, arthritis and diabetes combined. They impose a heavy burden of human suffering on individuals and their families, and have enormous direct and indirect financial costs.

Their impact on society is likely to become more and more profound in future years. Already, many hundreds of millions of people worldwide are affected by some form of mental disorder, from the relatively minor to the incurable and life-threatening; many individuals suffer from several simultaneously.

There are an estimated 400 million cases of anxiety disorders and 340 million of mood disorders. Estimates of peo-
People with mental retardation range as high as 60 million; there may be as many as 29 million people with dementia, and 45 million with schizophrenia. One of the most common neurological disorders is epilepsy (40 million). In addition, stroke, which should be regarded as a neurological as well as a circulatory condition, kills more than 4.6 million people a year and disables many millions more.

Different types of substance abuse have a major impact on both mental health and public health in general. About 120 million people are dependent on alcohol. Most of the world’s 1.1 billion smokers are probably dependent on nicotine. There are an estimated 28 million drug users.

The serious challenges ahead include improving mental health care at the primary level, including neuropsychiatric care, essential drugs and essential psychosocial interventions.

Community participation and support need to be promoted in providing non-institutional care, especially for the elderly. The psychological causes of violence and suicide need to be better understood and dealt with. The healthy growth and development of children, particularly as regards brain functions, should be encouraged. A set of global activities should be developed for the prevention of mental disorders, and the improvement of mental health care, focusing on reducing both individual suffering and the overall prevalence of mental disorders. The best and most widespread use must be made of the knowledge and technology currently available for dealing with schizophrenia, depression, sleep disorders, epilepsy, dementia, mental retardation and substance abuse. Good practice and ethical standards should be promoted in this area which fully take into account the rights of people with mental disorders.

**Schizophrenia**

It is estimated that approximately 45 million people are affected by schizophrenia worldwide. An increase in its prevalence is expected, largely as a result of demographic changes, with an increase in the proportion of the population moving into the age range at risk. Relatively greater numbers of the population will be in their twenties and beyond.

Schizophrenia is a disorder affecting mostly young people around the age of 20. It is characterized by distorted thinking, perception and judgement. In approximately a quarter to a third of cases, the outcome is complete recovery from an episode which may last just a few months. In the majority of cases however, the disease becomes chronic, lasting for the rest of the person’s life, either being continuous or with episodes between which the person may be less affected or even normal. The sexes are almost equally affected but the onset tends to be a little later in women. The condition is very disabling and it is difficult for those affected to lead a normal life.

Given the chronic nature of schizophrenia, in addition to its frequently disturbing symptoms, the disease represents a burden not only for the sufferers, but also for their families. Social rejection and discrimination often reinforce a spontaneous tendency to withdraw, which is observed in most people affected by schizophrenia.

The causes of schizophrenia are not known, probably because this label covers a group of related disorders, each having a different, specific cause. Vulnerability to schizophrenia may partly be inherited. Scientific advances in recent decades have led to a much better understanding of the way that the brain is affected in schizophrenia, and it is now known that some kind of disturbance associated with one of the natural chemical transmitters in the brain (dopamine) is linked to the disorder.

The introduction of neuroleptics (e.g. chlorpromazine) in the early 1950s was a major breakthrough in the treatment of schizophrenia. These medicines, if taken every day, greatly reduce the symptoms, often allowing the patient to function well in the community, with many fewer episodes of disorder. In view of the great family involvement and disruption that schizophrenia
Many people with schizophrenia unnecessarily remain in or return to mental hospitals, with a great deal of personal suffering and at huge costs to health budgets. This situation could be reversed, in the short term, with appropriate supplies of essential drugs for the treatment of schizophrenia and with the widespread introduction of psychoeducational programmes for families affected by schizophrenia. There is good evidence that this approach is feasible within the primary health care strategy.

**Dementia**

The ageing of the global population will inevitably result in huge increases in the number of cases of dementia, of which the incurable Alzheimer disease is the most common form. The other major type of dementia is cerebrovascular dementia, which is related to stroke. Less commonly, dementia occurs in other brain diseases such as Parkinson disease, Creutzfeldt-Jakob disease and AIDS. Already, around 29 million people worldwide are estimated to suffer from dementia, and the risk of developing the condition rises steeply with age in people over 60 years, to as much as 25% in people aged 90 or over. Alzheimer disease is likely to become one of the leading causes of disability in the elderly worldwide. Africa, Asia and Latin America between them could have more than 80 million people with senile dementia in the year 2025.

For some diseases causing dementia (Alzheimer disease, for instance) a genetic factor has been identified as contributing to its cause, whereas for others (such as vascular dementia) characteristics of lifestyle (such as excessive alcohol use or a diet which contributes to hypertension) are major predisposing factors.

Alzheimer disease is a brain disorder characterized by a progressive dementia that occurs later in life, but occasionally occurs earlier. It involves the decline of memory and other cognitive functions such as comprehension, learning capacity, language and judgement, as well as the ability to think and calculate. Forgetfulness, a symptom in the early stages, and often a part of normal ageing, is overtaken gradually by severe memory loss, especially of recent events, confusion about time and place, and mood and personality changes.

The possibilities for prevention of Alzheimer disease are extremely limited because the major determinants—age and family history—cannot be modified. Vascular dementias are, however, amenable to prevention through the modification of factors associated with vascular disease in general, for example, control of hypertension.

Electroencephalograms reveal slowing of the electrical impulses in the brain, and other types of hospital scanning show evidence of reduced brain size.

Most cases are diagnosed from an examination of the patient’s mental state. The disease can be definitely diagnosed by biopsy—removal of a sample of brain tissue for microscopic analysis—or by postmortem examination.

Some important advances have occurred in recent decades in understanding the brain changes that take place in dementia. However, an effective treatment for Alzheimer disease has yet to be found. Vascular dementia, on the other hand, can be prevented or slowed down by treatments that reduce the risk.
of stroke. Research is continuing into drug treatment to restore brain chemicals, particularly acetylcholine, which are depleted in Alzheimer disease, and important advances are being made, but such treatments only temporarily improve symptoms and do not stop the progress of the disease.

The management of dementia is based on long-term care, preferably at home, with support from a community-based health care team, which also provides continuity of care. Admission to hospital or a special home should be envisaged only when the disease is so advanced that specialized care is necessary on a more or less continuous basis, or when family care cannot be provided.

The objectives of treatment for people with dementia include general attention to their health, improving quality of life, minimizing disability and preserving autonomy. Too often, an elderly person’s mental deterioration is considered to be part of an inevitable decline. In many cases, however, it is due to, or at least aggravated by, a treatable physical or mental disease or the inappropriate use of drugs, especially sedatives and tranquilizers. Proper treatment sometimes leads to a dramatic restoration of function in people who were considered “lost”.

Living with and caring for a person with dementia can be very burdensome and caregivers are at a high risk of becoming exhausted (i.e. of suffering from “burn-out”). The needs of these carers should be kept in mind when planning services for people with dementia.

Depending on their general health, their age at the onset of the disease and the quality of the care that they receive, Alzheimer sufferers may survive for 10 years or more.

The biological complexity of the disease and restricted understanding of its causes limits hopes that drugs specifically designed to treat it will be forthcoming in the near future, and the best prospect may be treatments that delay its onset.

More women than men suffer from Alzheimer disease, given that in general they outlive men. Women account for more than 70% of the chronically mentally ill in nursing homes, where those exist, and these women are likely to be widowed. Compared with some other groups, elderly women in general have a greater need for health care, social welfare and economic support; this is especially true of those with Alzheimer disease.

Mood disorders

Mood disorders are estimated to affect some 340 million people in the world at any given time. At least 10% of people using primary health care services suffer from depression at the time of the visit. However, the main complaint may not immediately be perceived as related to depression or indeed may not be related to depression. In 1990, depression was estimated to rank fourth in terms of the burden caused by diseases in developing countries. It is likely to be first by the year 2020. In the United States alone, the yearly cost of depression is estimated at $44 billion, equal to the total cost of all cardiovascular diseases.

The fundamental disturbance in mood disorders is usually towards depression (with or without anxiety) and/or occasionally towards elation. This mood change is normally accompanied by a change in the person’s level of activity, and in depression there is often a loss of interest and enjoyment, reduced energy, ideas of guilt and unworthiness, a bleak and pessimistic view of the future, and disturbed sleep and appetite. Suicide is an ever-present risk. Most of these disorders tend to be recurrent and the onset of individual episodes is often related to stressful events or situations. They affect all age groups, including children and adolescents. About twice as many women as men are affected by depression.

Effective drugs to treat depression have been developed over the last 40 years, as have useful psychotherapeutic approaches over the last 20 years. These treatments can be implemented within primary health care settings, but unfortunately are not always available to people in need, particularly in developing countries. This is mainly due to the
absence of a regular supply of essential drugs and to a lack of appropriate training for health personnel.

With appropriate training of health personnel (particularly general physicians and other general health care staff) and the availability of essential drugs, individual suffering and social and economic losses due to depression can be dramatically reduced.

**Anxiety disorders**

As many as 400 million people at any one time are affected by one form or another of anxiety disorders, a group of mental disorders which can produce a considerable degree of disability. Among them are generalized anxiety disorder, obsessive-compulsive disorder, phobic disorders, panic disorder, acute stress reaction, dissociative disorders and somatoform disorders. Although they differ in their symptoms, their common trait is an abnormally high level of anxiety. Unless appropriately treated, they have a tendency to run a chronic course and in some instances can be disabling and can last a lifetime. Not uncommonly, these disorders occur in association with depressive disorders.

Although the potential for prevention of anxiety disorders is low, there are a few very effective treatment approaches for them, including psychotherapy, pharmacological treatments and psychosocial interventions. These approaches can considerably shorten the duration of these otherwise long-lasting disorders.

**Epilepsy**

More than 40 million people worldwide suffer from different types of epilepsy.

It is a recurrent condition characterized by fits (seizures) during which there are usually loss of consciousness and convulsions, or brief movements or sensations that start suddenly and stop abruptly with or without loss of consciousness. Some of these movements may look like bizarre behaviour. Although each fit lasts for only a few minutes, fits occur repeatedly, sometimes more than once a day, but sometimes as infrequently as once a month or less.

Epilepsy may be caused by genetic factors, infectious diseases in the prenatal period, by birth asphyxia and brain injury during labour, and in the postnatal period by infections (e.g. meningitis, encephalitis), parasitic diseases (e.g. malaria, schistosomiasis) or brain damage induced by alcohol, trauma or toxic substances (e.g. lead, pesticides).

People affected by epilepsy are frequently highly stigmatized, often because the condition is wrongly perceived as a contagious disease or as a result of sins and the misdeeds of the affected person or of his or her ancestors. Not infrequently, the affected people and their relatives are shunned to the point of isolation. Children with the disease are often kept away from school for absolutely no medical reason.

Some epilepsy can be prevented using simple methods such as proper prenatal care, safe delivery, control of fever in children, reduction of brain injury and control of infectious and parasitic diseases (e.g. through sanitation, immunization and appropriate treatment).

More than 80% of newly diagnosed cases of epilepsy can now be successfully treated and controlled with antiepileptic drugs. These need to be taken every day, sometimes for life. Where the medication is effective the person can lead a normal life. In many cases, medication which can be provided even at the primary health care level is very effective for as many as 50% of sufferers and need cost only $6 per patient per year. Unfortunately, in many countries, a large proportion of those affected are improperly treated or not treated at all, mainly because of the unavailability of essential drugs, inadequate training of health personnel and misinformation of the general public.

While an occasional fit need not be markedly disabling, the stigma and consequent handicap of being known to be "an epileptic" imposes an enormous burden. Showing that fits are reduced (or even disappear altogether) with medication, coupled with public information
to destigmatize the condition, can lead to a marked improvement in the lives of those affected.

**Post-traumatic stress disorder**

Post-traumatic stress disorder occurs after a catastrophic or other severely disturbing experience and persists long after that event, and can interfere with day-to-day functioning. Typical symptoms include flashbacks and disturbing dreams of the traumatic event, and efforts to avoid activities and situations that can reawaken painful memories.

The disorder is common among victims of man-made and natural disasters, military activities affecting both service personnel and civilians, violence, ethnic cleansing, rape, genocide, torture and repression.

Until fairly recently, most health sector attention was focused on the physical injuries and illnesses resulting from such traumatic incidents. There is now increasing recognition of the psychological harm that is also suffered, and psychological counselling for sufferers of post-traumatic stress disorders has been established in a number of countries.

**Tobacco, alcohol and psychoactive drug dependence**

The use of alcohol, illicit drugs and other psychoactive substances causes at least 123,000 deaths annually. Each year tobacco causes about 3 million deaths, mainly from lung cancer and circulatory diseases.

Alcohol-dependence syndrome is estimated to affect 120 million people. Alcohol is also implicated in a range of social problems including crime, violence (particularly against women and children), marital breakdown and major losses in industrial productivity.

The global trend among those dependent on drugs is towards the use of multiple psychoactive substances, with people moving from one substance to another, and using drugs in various combinations. Amphetamines or other psychostimulant drugs are increasingly used in every region of the world (Box 14). In many countries the use of amphetamines is more widespread than that of cocaine and heroin combined. It is likely that public health consequences, particularly intoxication, poisoning and overdoses will increase as these new combinations of substances are used.

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**Box 14. Substance abuse: the example of amphetamines**

Amphetamines and other similar psychostimulants are used in every region of the world, and pose serious health and social problems. In many countries, amphetamine abuse, particularly among young people, is already more widespread than cocaine and heroin abuse combined. To make matters worse, the rate of spread is outpacing scientific knowledge of the health risks and of other associated problems. These may include psychiatric and neurological disorders (inability, anxiety and apprehension), cardiac arrhythmias (rapid or irregular heartbeat), high blood pressure, liver damage and fatal overdose. When these drugs are injected, there is a risk of transmitting HIV and other viruses, such as the viruses of hepatitis B and C. Gaps in knowledge are a major obstacle to prevention, treatment and policy responses.

These drugs often have longer-lasting effects than, for example, cocaine. Because they increase endurance and delay sleep, and give a sense of added energy or euphoria, the consumption of some of them, such as MDMA ("ecstasy"), has become an established part of the all-night parties of youth culture in many countries. They and other drugs are also consumed by some groups of workers, such as long-distance truck drivers and others who work through the night or seek greater alertness.

Globally, the production and trafficking of illicit psychostimulants have increased dramatically over the last 20 years. Their production is relatively simple, and the chemicals used in their manufacture are cheap and freely available in most countries. The "illicit" market for amphetamine-type stimulants is also significant, although it accounts for less than 1% of the world pharmaceutical market. In the United States alone, such a market is worth over $100 million a year. The legitimate medical use of amphetamines has declined in recent years, but overprescribing of them continues in many countries.

Some psychostimulants are of particular concern in certain countries. Methamphetamine, sometimes known as "ice", poses a significant public health threat in Japan, the Philippines, the Republic of Korea, Thailand and the United States. In some cities of the United States its use is believed to result in more deaths than the use of heroin or cocaine. Previously rare in Europe, its manufacture and use are now increasing in some central and eastern European countries, such as the Czech Republic.

To tackle the problem and help governments formulate policy responses, WHO convened in November 1996 the first-ever global scientific meeting on the health and social implications of amphetamine abuse. This meeting, attended by experts from 14 countries and observers from 11 international organizations, produced a state-of-the-art review of the nature, extent, context and public health consequences of psychostimulant use.

This is being followed by specific studies that will help identify and test policy approaches based on promising prevention and treatment initiatives in different cultural settings.
In many countries drug injection is becoming increasingly common, and associated with this is the sharing of injecting equipment, which carries the risk of spreading of HIV/AIDS, hepatitis B and C, and other bloodborne infections. At least 28 million people worldwide incur a significant risk to their health as a result of using psychoactive substances other than alcohol, tobacco and volatile solvents. It is estimated that about one-third of them inject drugs.

In both developed and developing countries, the intentional inhalation of volatile solvents is an increasing problem, especially in marginalized groups such as street children and indigenous young people. These substances may cause neurological and psychological dysfunction, liver and kidney damage and sudden death.

Public health responses to psychoactive substance abuse need to reflect the fact that these substances present different grades of health risk. Levels of harm can be minimized through primary prevention including educational approaches. Persons whose problems related to drug use have been diagnosed at an early stage may be susceptible to brief interventions for reducing their individual risk and the potential risk to others.

The seriousness of health problems caused by tobacco warrants serious attention if the current epidemic of tobacco-related mortality and morbidity is to be reduced. While the health implications of tobacco use are largely individual and physical, the ramifications of premature mortality and morbidity are felt by families, communities and society at large.

Benefits to the individual patient with alcohol-related problems will also serve the health and welfare of family, friends, workmates and innocent bystanders who suffer third-party injury as a consequence of alcohol misuse. The cost of alcohol-related harm is estimated to account for 2-3% of GNP in many European countries.

Genetic traits may lead some individuals to experience alcohol in a different way, or render them more susceptible to dependence. The identification of genetic markers could have a major impact on prevention and treatment, and may also predict an individual’s likelihood of suffering various physical consequences such as hepatic cirrhosis. The relationship between alcohol dependence and other psychiatric conditions such as depression, anxiety and eating disorders is currently being studied. New techniques of neuroscience investigation are improving understanding of the effect of alcohol on neurotransmitter and receptor systems in the brain, and research into drugs which will influence this process is under way. Although in many parts of the world, women either abstain from alcohol or drink very little, this situation is changing rapidly, and the consequences of increasing consumption by women need to be investigated.

Detection of hazardous drinking in primary care and early intervention have proved both effective and low-cost, in both developing and developed countries, and this is one of the most promising areas for secondary prevention of alcohol-related problems, although such simple interventions are insufficient for those patients who are more damaged, or have an established dependence. A recent study has shown the importance of the attitude and skill of the individual therapist, and has revealed that most patients with alcohol problems can be helped on an outpatient basis, with residential care needed for only a minority of the most affected individuals. Self-help groups are very effective in facilitating recovery from alcohol problems, but they need to be introduced in a way that is culturally appropriate. Most individuals who are physically dependent can be detoxified at home provided suitable supervision is available, with family involvement enhancing outcome.

Educational interventions directed towards children and the general population have been of unproven benefit, and the search for more effective methods continues, for example by focusing on particular at-risk groups such as pregnant women. Other approaches include local community action aimed at creating environments which reduce the
demand for alcohol and promoting alternatives to alcohol as a locus for leisure pursuits, particularly for young people. Reducing the drink-driving limit and the introduction of random breath testing can be beneficial, with the likelihood of detection being a key factor in determining efficacy. Introducing successful alcohol control policies is a major challenge in developing countries and eastern Europe, where the commercialization of alcohol production and expanding international trade are important influences.

**Living with risk and associated ill-health**

Even in the absence of disease, human life is frequently put at risk, whether by accident or design. Wars, conflicts and violence between individuals date as far back in history as the oldest recorded diseases, and are at least as difficult to eradicate, if not more so. Technological advances, particularly in industry and transport, bring with them new dangers to human health, both in the workplace and in transport systems.

This section covers violence, including homicide and suicide. It also examines occupational health hazards, in terms of both injury and disease.

**Violence**

Violence in all its forms has increased dramatically worldwide in recent decades. Apart from civil conflict and war, violence can be interpersonal, self-directed, physical, sexual and mental, and its burden is disproportionately borne by young people and women. During 1993, at least 4 million deaths (8% of the total) resulted from unintentional or intentional injury, including 300 000 murders. Of the violent deaths, some 3 million were in the developing world.

Like other diseases, violence has its own risk factors. These include serious family problems, shortcomings in education, academic failure, idleness, alcohol and drug abuse, which predispose people to violence. Poverty, insecure living conditions, weakness and physical or mental handicap are among the factors which mark out the victims.

Target groups of violence can be grouped in the following ways:

- **By sex.** Almost everywhere, women are the victims of violence ranging from sexual abuse to social and economic disadvantage.
- **By age.** Children (and girls more than boys); adolescents, who are often the agents and the victims of their own risk-taking; and old people, especially elderly women living alone.
- **By social position.** The homeless, the unemployed, the underclass, whether they be street children, adults of no fixed abode, groups regarded as deviant (e.g. homosexuals), migrants, refugees or members of ethnic minorities.
- **By state of health.** The chronically ill, the physically and mentally disabled.
- **For economic and/or political reasons.** Victims of war, the wounded and displaced; the poor and the indigent.

**Homicide**

In many developing and developed countries, 20-40% of deaths in males aged 15-34 are from homicide or suicide. In some countries, the figure can be over 70%, and the homicide rates in the 15-34 age group have more than doubled in the last five years.

In Latin America and the Caribbean, violence has become endemic. In 1993, 456 000 violent deaths were recorded, averaging 1 250 a day. In half the countries of the region, homicide is the second leading cause of death in people aged 15-24.

In the United States, an average of 65 people are killed each day and over 6000 wounded in acts of interpersonal violence. During the 1980s in that country, more than 200 000 people died as a result of violence, and 20 million more suffered nonfatal injuries. The lifetime chance of becoming a homicide victim in the United States is approximately 1 in 240 for whites and 1 in 45 for blacks and other ethnic minorities. Homicide is the leading cause of death among
African American males aged 15-34. The death rate due to murder for all ages increased in the United States by 44% between 1968 and 1985.

**Suicide**

Suicide is an act, deliberately initiated and performed by an individual in the knowledge or expectation that it will result in a fatal outcome. It should be differentiated from a suicide attempt or parasuicide, which is an act of deliberate self-harm, not necessarily intended to result in death.

In addition to the more than 800,000 deaths from suicide recorded every year around the world, an unknown number are not recorded for religious, cultural or other reasons. Experts believe that many deaths attributed to accidents are, in reality, disguised suicides. Nevertheless, it is likely that certain cultural pressures strongly influence the rate of suicide, with the highest rates being some 10 times the lowest.

Suicide is more frequent among men and increases in direct relationship with age. Thus the group at highest risk is men above the age of 65 years who live alone. Recently, however, an increase in suicide rates of young people (both men and women) has been observed. Suicide is closely associated with some mental disorders, particularly depression, personality disorders, substance abuse and schizophrenia.

Suicide rates can be considerably reduced by appropriate preventive measures. A few interventions have demonstrated their efficacy, among which are treatment of psychiatric patients at risk, gun-possession control, detoxification of domestic gas and of car emissions, control of toxic substances and the turning down of reports on suicide in the press. Concerted action involving many sectors, in addition to the health sector, is needed.

**Violence against women**

Gender violence is a universal plague, grossly underreported. In some countries, domestic violence is the leading cause of injury among women of child-bearing age; up to 35% of women’s visits to emergency treatment centres are for that reason. Studies in selected countries indicate that violence against women is an important cause of morbidity and mortality throughout their life span.

Such violence takes numerous forms, only a few of which are sexual abuse, rape, physical assault and genital mutilation. Women are exposed to violence in the home, where the assailant is either related or known to them; in outside settings where they may be victims of random violence by people unknown to them; they are vulnerable to large-scale systematic violence in situations of conflict and mass movements of people. Studies show that the prevalence of violence against pregnant women ranges from 7% to 20%, and that such violence is more common than many other conditions routinely screened for during pregnancy.

**Occupational risks**

The figures seem like the casualties of a major war: over 200,000 killed, over 120 million injured. However, these losses occur not on a battlefield but in the workplace. They represent the annual number of occupational deaths and in-
Injuries worldwide. Even so, they are only part of the much wider impact of health hazards at work. To a large extent these are involuntarily imposed risks which the worker simply has to face in order to make a living.

Occupational risks become evident in two main ways. First, there may be an association of a particular occupation with a disease which appears among its workers to an extent greater than would normally be expected. When allowance has been made for age and other non-work factors. Second, a worker is exposed to some risk of injury from the unexpected release of energy (mechanical, chemical, electrical, radioactive and so on), which accounts for “accidents”.

For an occupational injury to occur, a hazard has to exist in association with a particular pattern of worker behaviour. A worker whose performance is impaired by fatigue, alcohol or inexperience is more likely to be injured. Overall, injury rates are highest among males in their late teens and lowest in the middle years. They tend to rise again among older workers. Female employees generally have lower rates of death and injury than their male counterparts, although the differences are small in some industries.

Estimates suggest that there are up to 160 million cases a year of occupational diseases, of which 30-40% may lead to chronic disease, and about 10% to permanent work disability. These are largely “silent” epidemics, as most occupational diseases and injuries go undiagnosed and unreported.

The many hazards of the work environment include exposure to chemical and biological agents, and adverse factors which can be ergonomic, psychological or psychosocial. Workers in the chemical industry are exposed to a rather special set of risks, and injurious events often manifest themselves in the form of an illness a long time after exposure.

About 100,000 different chemicals are in use in modern work environments, and the number is growing constantly. They often affect the immune system, leading to dermal and respiratory allergies, and may increase susceptibility to cancers and to infections such as those of the gastrointestinal, urinary and female genital tracts, and of the respiratory system. Other known consequences include metal (e.g., lead) and pesticide poisoning, solvent damage to the central nervous system and liver, and reproductive disorders. Around 850 chemicals used in industry, agriculture and forestry are neurotoxic.

Some 200 biological agents present in the workplace include viruses, bacteria, parasites, fungi, moulds and organic dusts. They are estimated to be a risk for 15% of workers in industrialized countries. Hepatitis B and C and tuberculosis infections (particularly among health care workers), asthma (among persons exposed to organic dusts) and chronic parasitic diseases (particularly among agricultural and forestry workers) are the most common occupational diseases resulting from such exposures.

There are about 3000 allergenic factors in our environment, most of them occurring as workplace exposures. Allergic dermatoses are among the most prevalent occupational diseases, with the respiratory tract, followed by the skin surface, being the most important route for hazardous agents to enter the body.

Physical factors such as noise, vibration, ionizing and non-ionizing radiation and microclimatic conditions affect up to 40% of the workforce in industrialized countries and up to 80% in developing and newly industrialized ones. Noise-induced hearing loss has been found to be one of the most prevalent occupational diseases in both developing and industrialized countries. Computers and other video display terminals are now an integral part of many workers’ lives. Research into their potentially harmful effects remains inconclusive.

In many industrialized countries musculoskeletal disorders are the main causes of both short-term and permanent work disability. It is estimated that 10-30% of the workforce in industrialized countries, and 50-70% in developing countries, may be exposed to a heavy physical workload and unergonomic working conditions.
physical workload, and \textit{unergonomic working conditions} such as lifting, moving heavy objects or repetitive manual tasks. The main consequences of these hazards are damage to the cardiorespiratory or musculoskeletal systems and traumatic injuries.

Recent surveys show increasing exposure to \textit{psychological stress} and overload at work, particularly in industrialized countries. Apart from the loss of health and working capacity which may result, these human factors have been associated with sleep disturbances, burn-out syndrome, depression, and increased risk of cardiovascular disorders, particularly coronary heart disease and hypertension.

\textbf{Women at special risk}

Growing attention is being paid to reproductive health risks at work. Some 200-300 chemicals known to be mutagenic or carcinogenic tend to have adverse effects on reproduction (including infertility in both sexes, spontaneous abortions, fetal deaths, fetal cancer, or retarded development of the fetus or the newborn). Numerous organic solvents and toxic metals are associated with adverse effects on reproductive health. Many biological agents and heavy physical work are also associated with an increased risk of reproductive disorders. The reproductive health hazards caused by ionizing radiations have been well established, while hazards from non-ionizing radiations are still under intensive study. Both male and female workers may be affected by occupational hazards but women of fertile age and during pregnancy in particular need to be protected. In addition to the conventional preventive activities of occupational health and hygiene services, special arrangements have been made in some countries to remove pregnant women from exposure that may be hazardous to the health of the mother or fetus. Exposure at work should not be allowed for women who have recently given birth or are breast-feeding.

The special occupational health problems of working women are recognized in both developing and industrialized countries. In the former, heavy physical work, the double work burden of job and family, less developed working methods and traditional social roles increase the burden of female workers. In industrialized countries, where women also have the double work burden, lower-paid manual jobs are often left to female workers. In addition, machinery and work tools are often designed to be physically suitable only for men, although female workers use such equipment. In many service occupations the female workers may be exposed to the threat of violence from clients or to sexual harassment from fellow workers.

\textbf{Prevention of occupational diseases}

As explained above, a wide variety of occupational risks can lead to chronic diseases ranging from cancer to mental disorders, yet because of lack of properly trained human resources in occupational health, the majority of occupational diseases are not recognized, particularly in developing countries. Only 5-10\% of workers in developing countries, and 20-50\% in industrialized countries, have access to adequate occupational health services.

Estimates suggest that the total cost to society of work-related illnesses and accidents varies from about 3\% of GNP, when the total sickness absence costs are considered, up to 20\% where direct and indirect losses are taken into account. The majority of these illnesses, if not all, are easily preventable, for two reasons: first, their causal agents can be identified, measured and controlled; second, the populations at risk are usually easily accessible and can be regularly supervised and treated. Furthermore, the initial changes are often reversible if treated promptly. The early detection of occupational diseases is consequently of prime importance.

Medical intervention in the form of preplacement and periodic health examinations is essential for the early detection and management of occupational diseases, taking account of individual risk factors such as age, sex and individual susceptibility.
Workers should be informed about the principles and practice of occupational health and the nature of potential health hazards in the workplace, and should be encouraged to adopt practices that reduce health risks.

Other risks

Risks at home

Falls kill more people from unintentional injury than anything except traffic accidents, and most falls occur at home. Most deaths from burning happen at home. In addition, the air inside the home may be far more polluted than the air outside. Most injuries at home are sustained by children under 5 and elderly women, particularly those aged 75 and over. Others at high risk are those affected by alcohol or by ill-health. After falls, the most common cause of death from accidents in the home is fire (Box 15), with the elderly again over-represented. Poisoning comes next, followed by suffocation, usually from inhaling food. Stairs are the most common source of injury, followed by glass doors, windows and fences, and baths.

With improved insulation and sealing of windows and doors, the air exchange rate in many houses may be as slow as once in every 10 hours. The effect of this is that an enormous range of pollutants can gather in the household air, many of which have been linked to respiratory disorders, allergies and cancer.

Risks in transport

The measurable outcomes of road crashes include the number of deaths, the number of injuries and the number of crashes. Deaths are counted reliably and quite accurately. Serious injuries are counted fairly accurately, but a large number of minor injuries are not counted at all, and definitions of the various categories of injury tend to be inconsistent. A very high proportion of all crashes that do not result in injury go unreported. Those at highest risk are motorcycle riders, with the major cause

Box 15. Burn injuries

There is no international system for reporting and recording burn injuries or even deaths from burns. However, data collected in several countries, both developed and developing, indicate that annually around 300 individuals per million population sustain burns which require care in hospital because of extent, associated injury or other conditions related to the burns.

The rate of fire and burn deaths in the United States and Japan ranges from 0.2 to 3.8 per 100,000 population. Factors influencing the occurrence of burn injury include poverty, season of the year, tobacco smoking, type of building construction and occupation. The majority of fire deaths occur in residential fires (40% in Japan and 73% in the United States). Fire, typically that caused by ignition of flammable liquids, is the most common cause of burn injury in adults, and hot liquid scalding is the most common cause of burns in children. Recent studies suggest that the incidence of burn injury has decreased in developed countries. This has been attributed to improved construction, better quality of appliances, increased use of smoke and fire detectors, the use of flame retardant sleepwear for children, and effective prevention programmes.

The mortality and morbidity caused by burn injury have been significantly reduced by improvements in the management of burn patients. The prompt administration of adequate volumes of resuscitation fluid has essentially eliminated acute renal failure as an early post-burn complication. The use of fiberoptic bronchoscopy to diagnose smoke inhalation injury (the most important related condition in burn patients) has significantly reduced the occurrence of bronchopneumonia. Effective topical antimicrobial chemotherapy and surgical excision of the burned tissue in the early post-burn period have led to a substantial decrease in the incidence of invasive burn wound infection and facilitated early closure of the wound in all but those patients with very extensive burn injury. Recently, culture-derived tissue has been utilized with variable success to achieve permanent wound closure in patients with massive burns.

Effective regimens of dietary support have been used to minimize erosion of lean body mass, and hormonal interventions have been identified to improve the effectiveness of nutritional support regimens, hasten wound closure and accelerate convalescence. Lastly, new techniques of tissue expansion and tissue transfer have led to improved reconstruction capability, and current rehabilitation programmes facilitate the re-entry of extensively burned patients into society.

Prevention programmes should focus on the common causes of burn injury as the most effective means of reducing its consequences. Research should place emphasis on identifying pharmacological agents to reduce and reverse oedema formation, on developing improved means of mechanical ventilation to reduce barotrauma, and on elaborating techniques to quantify the severity of inhalation injury. Other important research areas include improved topical chemotherapeutic agents, non-antigenic culture-derived composite tissue, nutritional support regimens tailored to meet the specific metabolic needs of patients with sepsis and infection, and growth factor therapy to enhance wound healing.

Personal communication from the President, International Society of Burn Injuries.
An estimated 180 million people worldwide are visually disabled, of whom nearly 45 million are blind.

especially in developed countries. Team sports involving violent body contact result in the highest risk of nonfatal injury, while mountaineering, motor racing, sport parachuting and hang gliding have lower injury rates overall, but much higher death rates. Boxing is particularly dangerous, as repeated blows to the head cause progressive and irreversible brain damage.

The state of physical conditioning is an influential risk factor for most sports, as well as the degree of natural talent and extent of experience and learned skill, and the equipment used. Typical injuries include drowning (which affects children most, and has been found in adults to be linked to alcohol use); impact injuries suffered from striking hard surfaces while diving (with alcohol again implicated as a risk factor); fractures and head injuries from skiing and riding; and heat stroke from long-distance running. Considering the whole spectrum of risks to participants in sporting and recreational activities, remarkably little systematic information is currently gathered on injury-producing events and on the risk that injury will be suffered. The epidemiology of this group of injuries is one of the major unstudied fields in risk assessment and injury control.

Other issues

Blindness

An estimated 180 million people worldwide are visually disabled, of whom nearly 45 million are blind, four out of five of them living in developing countries. About 80% of blindness is avoidable (treatable or potentially preventable). However, a large proportion of those affected remain blind for want of access to affordable eye care. Blindness leads not only to reduced economic and social status but may also result in premature death. The major causes of blindness and their estimated prevalence are cataract (19 million); glaucoma (6.4 million); trachoma (3.6 million);
million); childhood blindness (more than 1.5 million); onchocerciasis (0.29 million); other causes (10 million).

Prevalence varies dramatically between countries, from 0.2% or less in developed countries to more than 1% in some sub-Saharan countries. About 32% of the world’s blind are aged 45-59 but the large majority, 58%, are over 60 years old.

Cataract is the loss of transparency of the lens of the eye, leading to progressive loss of clarity and detail of images. It is generally age-related, but congenital cataract may result from maternal infection in pregnancy or from genetic conditions. Direct injury to the eye could also result in cataract. The condition is painless and causes only visual symptoms.

Intensive cataract surgical programmes, which have reached millions of persons blind from cataract in many countries worldwide, restore sight to the afflicted who usually do not have ready access to cataract surgical services. These programmes need to be expanded and sustained in the next 20 years if the backlog of cataract-related blindness is to be reduced and new cases are to be effectively managed. The development of affordable intraocular lens implantation procedures has improved the quality of life for those patients following surgery.

Trachoma is a major preventable cause of blindness. Apart from the 5.6 million presently blind, another 147 million, most of them in Africa and Asia, have an active form of the disease. The cause is an infectious microorganism, *Chlamydia trachomatis*, which spreads through contact with eye discharge from the infected person, for example via fingers, handkerchiefs or towels, and is also spread by eye-seeking flies. After years of repeated infections, the inside of the eyelids becomes severely scarred with the eyelashes rubbing on the eyeball.

Trachoma mainly affects women and children in the poorest communities in the developing world. A worldwide programme to target the elimination of trachoma as a blinding disease began in 1996. It is a coordinated effort to provide surgery, antibiotic treatment and improved environmental conditions to populations at risk, largely in Africa.

Glaucoma is a condition generally caused by excessive pressure of fluid in the eye leading to damage of the optic nerve and gradual, irreversible loss of vision. The fluid pressure rises because of a gradually increasing blockage of the outflow channels in the eye. The condition is uncommon below the age of 40 and commonly occurs over the age of 60. However congenital glaucoma may also occur. Chronic glaucoma often has no symptoms until late in the disease, because of its gradual onset and slow progression. However an acute form may present with dull severe pain in and above the eye. Diagnosis is by routine and specialized eye examination. Drugs administered as eye drops or laser treatment to lower the eye pressure could control the condition, but in advanced cases surgery is required to open new outflow channels.

Childhood blindness is largely caused by vitamin A deficiency, corneal blindness and cataract. The goal of the World Summit for Children in 1990 was to eliminate vitamin A deficiency as a cause of blindness by the year 2000; in many countries this is being achieved.

Onchocerciasis is a blinding parasitic disease found mainly in Africa, transmitted by blackflies. The disease has been targeted for control with distribution of the drug ivermectin, following the successful Onchocerciasis Control Programme which used vector control methods to eliminate the disease from a large area of West Africa. A new programme is targeting the remaining countries where the disease occurs.

**Hearing impairment**

Some 121 million people are estimated to have a disabling hearing impairment.

Some 121 million people are estimated to have a disabling hearing impairment. There is an urgent need for more, accurate population-based data on the prevalence and causes of hearing impairment, so that countries may set priorities and determine needs. As more countries
Map 3. Oral health status, 1996

A. At age 12

B. At ages 35–44
conduct surveys, WHO collates the information so that an accurate global picture is progressively revealed.

The inappropriate use of ototoxic drugs, at all ages, is a considerable cause of hearing impairment in developing countries. Better professional, public and health education is needed to counter this problem, as well as enforcement of drug regulatory measures in some instances to limit access to such drugs. Industrial and other excessive noise is an increasing cause of hearing loss in many settings. Again, public education and hearing conservation programmes and, in some cases, legislation are needed measures.

**Chronic otitis media** is a major preventable cause of hearing impairment in children; it is a serious problem because it retards language development and educational progress. Chronic otitis media can be managed through primary health care, but it requires proper detection and follow-up of affected children.

**Presbycusis** is the most common cause of hearing impairment with increasing ageing. It is therefore becoming a major global concern because of the growth of the proportion of elderly persons. The most effective measure in these cases is the fitting of hearing aids, although globally there is still a lack of affordable, good-quality hearing aids in developing countries.

## Oral health

Dental diseases are chronic conditions that adversely affect quality of life, especially in the elderly where they may have serious adverse effects on nutrition. Although great progress has been made over the last 20 years in combating them, dental caries and periodontal disease remain the most prevalent dental conditions. Caries, or tooth decay, is the more prevalent of the two.

### Dental caries

Dental caries affects almost everyone at some stage of life, and may involve complications such as pain, abscesses, severe infections and teeth extractions. In industrialized countries about 50% of children have dental caries; 15-20% are in the high-risk group of having more than four teeth affected (Map 3).

In all industrialized countries up to 40% of people aged over 65 have no teeth at all. The underprivileged - poor, disabled, ethnic minorities, refugees, migrants - all suffer more oral disease than the rest of the population. In countries whose economies are in transition, because of the breakdown in state health care systems and privatization of oral care services, large percentages of the populations cannot get access to or afford preventive, restorative or rehabilitative treatment.

In developing countries, most people get five or six decayed teeth and keep most of their teeth into old age. However, oral diseases are increasing, related to changes in dietary and other habits, and often linked with moves to large cities.

Although bacteria on the teeth are the direct cause of dental caries, many environmental and host factors interact to determine whether the individual will be affected, when, and to what extent. The contribution of sugars to the metabolic activities of the responsible bacteria is well established.

Altered lifestyles and understanding of risk behaviours play a major role in the prevention of a wide range of oral diseases, including dental caries. Current knowledge is sufficient to control caries, if not eliminate it.

In all developing countries the possibility of getting care for oral problems is limited, with perhaps only 5% of decayed teeth treated. For too many people, oral problems are seen as inevitable, painful and costly, and thus are tolerated rather than treated. Appropriate re-
habitivative care — replacement of lost teeth — is often not carried out, which causes further problems such as infections and loss of teeth.

The consumption of fluorides during tooth formation and the application of fluorides to the teeth at any age enhance resistance of the teeth to decay. Fluoridation of community water supplies can reduce tooth decay by at least 50% and the benefits are long-lasting. In the absence of community water supplies, fluoridation of school water can prove effective. The use at home of toothpastes containing fluoride, or their supervised use by children in schools and similar settings are highly desirable as well as avoiding sugar-containing snacks and sticky sweets between meals.

**Outlook**

Traditional dentistry uses expensive equipment dependent on reliable electricity and clean pressurized water, services that are unavailable in most communities in developing countries. A new approach, atraumatic restorative treatment (ART), using basic sets of instruments and simple, easily assembled dental care beds or benches, is both effective and low cost. Essential instruments and materials can be carried in a hand bag, allowing the dental worker to reach isolated communities to provide essential care. This technology is minimally invasive and has successfully been taught to non-dentally-trained personnel, and helps prevent oral diseases in the community.

Research to establish even cheaper and simpler ways of treating early dental caries is needed, as many communities cannot afford even basic instrument sets.

**Periodontal disease**

There are two main types of periodontal disease: inflammation of the gums (gingivitis) and inflammation of the periodontium (periodontitis). Gingivitis consists of swelling of the gum tissue and destruction of the connective tissue fibres that hold the gum tissue in position. Gingivitis, which occurs most frequently in young adults, may progress to periodontitis if untreated, in which case there is bone damage and loosening and eventual loss of teeth.

Accumulation of the bacterial plaque associated with periodontal diseases is promoted by various conditions including poor oral hygiene, cigarette smoking and diabetes.