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Non-communicable diseases in low- and middle-income countries: context, determinants and health policy

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Summary

The rise of non-communicable diseases and their impact in low- and middle-income countries has gained increased attention in recent years. However, the explanation for this rise is mostly an extrapolation from the history of high-income countries whose experience differed from the development processes affecting today's low- and middle-income countries. This review appraises these differences in context to gain a better understanding of the epidemic of non-communicable diseases in low- and middle-income countries. Theories of developmental and degenerative determinants of non-communicable diseases are discussed to provide strong evidence for a causally informed approach to prevention. Health policies for non-communicable diseases are considered in terms of interventions to reduce population risk and individual susceptibility and the research needs for low- and middle-income countries are discussed. Finally, the need for health system reform to strengthen primary care is highlighted as a major policy to reduce the toll of this rising epidemic.

Keywords

chronic diseases; developing countries; epidemiology; health transition; non-communicable diseases; population; public health; risk factors; urbanisation; world health

The impact of non-communicable diseases in low- and middle-income countries

Non-communicable diseases in low- and middle-income countries can no longer be ignored or seen as a distraction from the business of prevention and control of infectious diseases (Ebrahim & Smeeth 2005; Horton 2007). The case has been highlighted in recent reports describing the global burden in terms of mortality- and disability-adjusted life years (Leeder *et al.* 2004; Strong *et al.* 2005; World Health Organization 2005; Adeyi *et al.* 2007) and also their economic impact (Suhrcke *et al.* 2006). Until recently, communicable diseases remained virtually the sole priority for global health policy. However, they do not constitute the major contributor to the burden of disease in terms of disability-adjusted life years or mortality in any region of the world apart from sub-Saharan Africa (Ollila 2005; Gaziano *et al.* 2006). Non-communicable diseases cause more than half of deaths in adults aged 15-59 in all regions except South Asia and sub-Saharan Africa, where infectious disease

conditions, including HIV/AIDS, result in one-third and two-thirds of deaths, respectively (Lopez *et al.* 2006). However, non-communicable diseases are also becoming a significant burden in sub-Saharan Africa (Baingana & Bos 2006). The Global Burden of Disease Study, conducted in 2001, showed that 20% of deaths in sub-Saharan Africa were caused by non-communicable diseases (Lopez 2006). Figure 1 shows the top 10 conditions in terms of disability and mortality in low- and low-middle-income countries. Cardiovascular disease, cancer and injuries rank consistently as the top three conditions in these countries (World Health Organization 2005; Anderson & Chu 2007).

Chronic conditions kill people at economically and socially productive ages: 80% of chronic disease deaths occur in low- and middle-income countries, reflecting both the size of these populations and the epidemiologic transition from infectious to chronic diseases (World Health Organization 2005). Cardiovascular disorders are the second most common causes of adult deaths in sub-Saharan Africa, in addition to a major cause of chronic illness and disability. Half of cardiovascular disease deaths occur among people 30-69 years of age, which is 10 or more years younger than in more developed regions (Baingana & Bos 2006). Recent global and regional burden of disease analyses suggest that almost half the disease burden in low- and middle-income countries is now from non-communicable diseases, a rise of 10% in its relative share since 1990. Disease burden per head in sub-Saharan Africa and the low- and middle-income countries of Europe and Central Asia increased between 1990 and 2001 (Lopez *et al.* 2006). Verbal autopsy studies suggest that estimates for cause of death within broad categories (e.g. cardiovascular diseases) are accurate when compared with clinical records (Gajalakshmi & Peto 2006; Yang *et al.* 2006).

According to the World Health Organization (2005), from a total of 58 million deaths from all causes in 2005 globally, chronic diseases accounted for an estimated 35 million or 60% of all deaths, which is double the number of deaths from all infectious diseases (including HIV/AIDS, tuberculosis and malaria), maternal and perinatal conditions and nutritional deficiencies combined. In low- and middle-income countries, 53.8% of all deaths are attributed to non-communicable diseases and 36.4% to communicable diseases (Lopez *et al.* 2006).

This epidemiological transition - the change from a burden of disease dominated by mortality from infectious causes to degenerative or chronic causes (Omran 1971) - currently being experienced in low- and middle-income countries is compressed into a shorter time frame than that experienced historically in high-income countries. Furthermore, developing countries not only have to deal with their current burden of infectious diseases and ill-functioning health systems, but also with the growing burden of chronic diseases (Yusuf *et al.* 2001; Reddy 2004; Perel *et al.* 2006), a situation that has been described as 'a race against time' (Leeder *et al.* 2004).

Decades of research in the developed world have shown that much of the burden of chronic diseases is attributable to environmental and lifestyle factors, including tobacco consumption and decreased physical activity. Variation in the risk of non-communicable diseases between high-income countries and trends over time within countries also indicate that the factors determining incidence must be modifiable, and therefore, that many non-communicable diseases are preventable (World Health Organization 2002b). Despite this wealth of information available in the developed world, it is also clear that there is an important research gap between developing and developed countries (Mendis *et al.* 2003). Research findings from developed settings are not necessarily appropriate to other contexts; thus, local knowledge is imperative (Ebrahim & Davey Smith 2001). Much of the robust evidence for prevention and control of chronic diseases comes from randomised clinical trials. Such trials tend to study highly selected groups of people, which means that the

results may not be applicable to the broader population, resulting in a conflict between the proof of concept and generalisability (Mark *et al.* 2007). Trials often fail to take into account whether the intervention, if found to be effective, would be affordable, nor do they provide information on prospects of scaling up to achieve broad population coverage. For example, in South Africa, application of a coronary risk factor reduction community programme unexpectedly failed to demonstrate the effects of personalised intervention in high-risk participants, and was not tested in black or Asian South Africans (Rossouw *et al.* 1993). This lack of transferability might be considered worthy of research but more would probably be gained by evaluating complex interventions of this nature in the context within which they will be used.

The term non-communicable diseases is used interchangeably with chronic diseases and refers to cardiovascular diseases, diabetes, chronic respiratory diseases, cancers, mental illnesses and injuries. As cardiovascular diseases - that is coronary heart disease and stroke - are the leading cause of death globally, accounting for 30% of all deaths in 2005 (Strong *et al.* 2005), this review focusses largely on them from a low- and middle-income country's perspective.

Understanding the epidemic of non-communicable diseases: does context matter?

Figure 2 depicts changes in rates owing to ischemic heart disease death rates that occurred between 1988 and 1998 in some selected countries. These divergent trends in countries of the former USSR and other high-income countries indicate that different environmental factors are driving ischaemic heart disease rates up or down over the same decade. To understand non-communicable diseases in today's low- and middle-income countries and their growing burden, a contextualisation appropriate to their greatly different circumstances is needed.

When evaluating the nutritional transition in low- and middle-income countries, relevant questions for the understanding and contextualisation of the burden of non-communicable diseases have been posed. Popkin (2002) asked: 'Is the experience related to the rapid onset of obesity and nutrition related non-communicable diseases in low and middle-income countries ... different from what occurred in Western European countries, the United States and Japan at a similar stage in their economic development?' The answer leans towards a unique scenario where current phenomena being experienced in today's low- and middle-income countries differ from those experienced in the past by today's developed nations. Of note are the much more rapid rates of population ageing in low- and middle-income countries than those experienced by high-income countries, which are attributed to dramatic declines in fertility and mortality resulting in large increases in the population at risk from non-communicable diseases (Murray & Lopez 1997; Lutz *et al.* 2008). Furthermore, the process of rural out-migration and associated urbanisation and modernisation in today's low- and middle-income countries, in addition to their divergent degrees of economic development, differed from the developed nations when they started their rise of non-communicable diseases in the late 19th century. Greater understanding of the roles of these major factors would be helpful in addressing potential context-specific strategies to prevent and control the growing problem of non-communicable diseases in low- and middle-income countries.

Some arguments to understand the unique contextual differences between countries affected by non-communicable diseases at different times have been put forward (Popkin 2002). First, the speed of change appears unique owing to the timing of the economic, technological and social transformations. Second, as the problem of under- and over-nutrition arises (Subramanian & Davey Smith 2006; Subramanian *et al.* 2007), finding both under- and over-nutrition in the same household is indicative of the complexity of different

sets of stresses and societal changes. Third, the political environments differ, as does the capacity of low- and middle-income countries to address the rapid increase in the prevalence of non-communicable diseases (Popkin 2002).

Such analysis must be superimposed on the common realities of today's low- and middle-income countries, a world marked by increased urbanisation with high levels of urban poverty (Fay 2005; Mercado *et al.* 2007; United Nations Population Fund 2007), and the rural poor increasingly marginalised. Of critical importance to future social inequalities in chronic disease risk will be the speed with which social patterning of risk factors spread from the more affluent to affect poorer people (Zaman & Brunner 2008). In west Africa, marketing of imported wheat and rice has supplanted the consumption of local less-refined cereals (millet and sorghum) and even the pastoral Masai in Tanzania have experienced rapid changes in eating habits associated with rises in blood cholesterol (Steyn & Damasceno 2006).

An additional factor is that beyond biological risk factors of lipid and blood pressure profiles, health behaviours strongly related to non-communicable diseases show different patterns. For example, smoking patterns are markedly different between countries, and therefore, their population-attributable risk towards non-communicable diseases and mortality is not the same throughout the low- and middle-income countries (Ezzati & Lopez 2004). The strong social patterning of many non-communicable diseases forces us to consider approaches to their prevention well beyond the simple risk factor profile of an individual. For example, from a merely economic perspective, belonging to a lower socioeconomic status confers protection from obesity up to a level of USD\$2500 per capita per year when inequities in obesity start to appear. If obesity is approached as a social networking issue, an interesting pattern also appears that shows clustering of individuals with obesity - and increased risks for the development of such condition in individuals closer to obese ones (Christakis & Fowler 2007).

Non-communicable diseases have developmental and degenerative causes

Risk factors for non-communicable diseases include socioeconomic factors, modifiable behaviours and genetic factors, which in the case of atherosclerosis and diabetes act through different intermediate pathophysiological pathways, such as glucose/insulin homeostasis, lipid metabolism and insulin-like growth factor systems, to affect disease risk. The inter-relationships of these different distal and proximal risk factors in relation to the specific disease outcome are complex and include chains of risk, clustering of risk factors, and effect modification (interaction) of one risk factor (genetic or non-genetic) by another risk factor (genetic or non-genetic). In general, these processes act across the lifecourse to affect disease risk (Ben-Shlomo & Kuh 2002). The traditional 'degenerative' hypothesis of chronic diseases has been relatively successful in identifying the proximal causes of disease operating in adult life (e.g. smoking and lung cancer), but much less attention has been paid to the 'developmental' hypotheses, particularly in developing countries. Effective mass prevention of non-communicable diseases will require an understanding of how to unravel complex causal nets of risk factors that reflect the history of countries, communities, families and individuals.

Models of non-communicable disease aetiology have tended to focus on processes that can be broadly characterised as 'degenerative' (Olshansky & Ault 1986). Chronic obstructive pulmonary disease (COPD) is a paradigmatic case, with a large number of environmental (e.g. cigarette smoking and occupational exposures) and genetic (e.g. alpha-1 antitrypsin mutations) factors leading to more rapid decrease in adult lung function and increased risk of COPD (Strachan & Sheikh 2004) (Fig. 3). Similarly, coronary heart disease can be

viewed as reflecting a breakdown in arterial wall resilience, owing to atherosclerosis, with acute disruptive events, such as plaque rupture, leading to the catastrophic end-stage event of myocardial infarction.

The degenerative model pays little attention to processes that lead up to the peak or optimal phenotypic state, usually a feature of early adulthood, such as the greatest lung volume or peak bone mass. More recently, however, the degenerative model has been supplemented by approaches that view the development of anatomic and physiologic systems as key to later disease susceptibility. This approach to understanding disease processes recognises the importance of peak phenotypic states (in addition to how rapidly one degenerates from this peak) as having important relevance to the likelihood of developing chronic diseases and is embodied in WHO's lifecourse approach to ageing (Stein & Moritz 1999). These development models of non-communicable disease's causation echo, but with increased biological motivation, earlier discussions of determinants of health (Kuh & Davey Smith 2004).

Evidence for developmental origins of cardiovascular disease

It is increasingly recognised that atherosclerosis develops in childhood, but its underlying risk factors are not fully understood (Strong *et al.* 1999; Labarthe *et al.* 2006). The importance of poor living conditions was highlighted by Forsdahl (1978), but it was David Barker *et al.* who improved this idea with the formulation of the 'foetal origins of adult disease' hypothesis, subsequently modified to 'developmental origins of adult disease' (Barker 1998; Godfrey & Barker 2000). From their observations in epidemiological studies linking small size at birth to later risk of cardiovascular disease, they concluded that cardiovascular disease and other related diseases are 'programmed' in uterus through the persistence of endocrine, physiological and metabolic adaptations that the foetus makes when it is undernourished. The idea that inadequate diet in early life may result in some form of heightened sensitivity to the lifestyle-related risk factors is of some importance to the unfolding cardiovascular disease epidemic in low- and middle-income countries, where under-nutrition and urbanisation now frequently co-exist.

Animal experiments of dietary restriction provide strong evidence of programming of several cardiovascular disease risk factors (Armitage *et al.* 2004), although the extreme nature of some of these interventions and developmental differences between animals and humans limits the inferences that can be drawn. Indirect evidence also comes from observational studies in humans that have demonstrated associations between various anthropometric measures relevant to early life, as proxies for inadequate nutrition and cardiovascular disease risk (Barker 1998; Godfrey & Barker 2000). Inverse associations have been consistently demonstrated between birth weight and coronary heart disease and stroke, in addition to their risk factors, i.e. blood pressure, insulin resistance and type 2 diabetes (Barker 1998; Godfrey & Barker 2000; Huxley *et al.* 2002; Newsome *et al.* 2003). Evidence from Soweto, South Africa and Kinshasa, Democratic Republic of Congo also indicates that low birth weight is associated with higher blood pressure in childhood and adolescence (Levitt *et al.* 1999; Longo-Mbenza *et al.* 1999). Small size - height, weight or body mass index - in infancy has also been associated with later disease outcomes (Bhargava *et al.* 2004). The relationship of growth with cardiovascular disease appears to be more complex, as both slower and faster growths in infancy have been associated with increased cardiovascular disease risk (Bhargava *et al.* 2004; Singhal & Lucas 2004). Poor infancy growth appears to be more disadvantageous in populations affected by general under-nutrition which may explain the inconsistent associations. However, more data are needed to clarify this issue.

Despite strong circumstantial evidence from animal experiments and anthropometric studies, there is limited direct evidence from nutrition data to support this hypothesis. The effects of balanced protein-calorie deficiency in pregnancy have been examined in two natural experiments of starvation and a randomised controlled trial. The Dutch famine birth cohort study is based on a follow up of children born in a single hospital in Amsterdam during 1943-47 (Painter *et al.* 2005). All children born during 1945 were considered to be potentially exposed to famine, while a random sample of children born before and after the famine period (i.e. before: 1943-44; after: 1946-47) was regarded as unexposed. An increased prevalence of coronary heart disease was associated with famine exposure in early gestation, increased adiposity in women, increased low density lipoprotein:high-density lipoprotein cholesterol ratio, and abnormal glucose homeostasis associated with famine exposure in late gestation. The other study was based on the starvation experience of Leningrad's (now St. Petersburg) residents born during the German blockade of the city in 1941-44 (Stanner & Yudkin 2001). Those born during 1941-42, when the starvation conditions were at their worst, were considered to be exposed, while controls were recruited from a local hospital and workplaces. In contrast to the Dutch famine, no association of famine exposure with blood pressure, adiposity, dyslipidaemia or abnormal glucose homeostasis was found. A trial was conducted near Guatemala City, during 1969-77, in which four villages were randomised within pairs to receive either of the two supplement types: Atole (containing 900 kcal/l, 6.4 g protein/100 ml, and micronutrients) or Fresco (containing 330 kcal/l, proteins niland micronutrients) (Conlisk *et al.* 2004; Webb *et al.* 2005). Supplement was offered to pregnant and lactating women and offspring up to age 7 years. No association of supplement type with blood pressure or adiposity was found. In women alone, atole supplementation was associated with lower fasting glucose. Overall, these studies have failed to provide convincing evidence to support an effect of balanced protein-calorie reduction in pregnancy on offspring blood pressure. In all the three studies, birth weights never fell below 3.0 kg, suggesting that malnutrition may not have been severe or prolonged enough for effects of undernutrition to be manifested (Hawkesworth *et al.* 2008).

Apart from balanced-calorie restriction, studies have also examined the effects of protein and calcium deficiency in pregnancy on offspring blood pressure, but the results have been inconsistent (Campbell *et al.* 1996; Belizan *et al.* 1997; Shiell *et al.* 2001; Leary *et al.* 2005). There is randomised evidence to suggest that sodium intake in infancy may be positively associated with blood pressure in the short term (Hofman *et al.* 1983). Evidence on longer-term effects of sodium intake in infancy is lacking.

Further work on birth cohorts set up in low- and middle-income countries is likely to provide further insights into developmental causes of non-communicable diseases. However, it is important to note that for most non-communicable diseases, early life factors operate in concert with exposures that are acquired and accumulate over the life course (Victora *et al.* 2008). The past and current investment in improving maternal and child health may well turn out to be both a driver of the epidemic of non-communicable diseases in low and middle-income countries through increasing population ageing and also protective of atheroma through more optimal early life nutrition.

Evidence-based health policy for non-communicable diseases in low- and middle-income countries

Improving health through spreading know-how and health technology

The strong cross-sectional associations between markers of national wealth and mortality consistently observed over the last 70 years show a steep upward relationship followed by a

steady plateauing off. Successive more recent associations show the same strength of association but an upward shift - the 'Preston curves' (Preston 1975) - implying that economic growth is an insufficient explanation for improvements in health status of a population (Kunitz 2007; Leon 2007; Mackenbach 2007; Preston 2007). Preston's own explanation was that external factors - in particular, knowledge diffusion and medical technology - were at least as important as economic growth. These ideas are of particular relevance in the context of low- and middle-income countries where there is marked variation in survival prospects with some regions and countries, such as Kerala in India and Cuba, currently having life expectancies as good as the UK (Marmot 2001). The strategic implication of this evidence is that improving life expectancy may be achieved through spreading know-how and application of health and social technology, with particular emphasis on avoiding increases in health inequalities (by place, race/ethnicity, occupation, gender, religion, education, socio-economic position and social capital) associated with implementation of health services (Whitehead *et al.* 2001).

Interventions for cardiovascular disease prevention and control

Reducing population levels of risk

Focussing on the population determinants of chronic diseases is necessary to shift risk levels downwards (Rose 1981, 1985). Such strategies currently endorsed by a recent international 'call to action' on chronic diseases promoted by the Lancet (Beaglehole *et al.* 2007) include implementation of World Health Organization's tobacco control convention and reduction of 'hidden' dietary salt intake through voluntary agreements with food industries (Asaria *et al.* 2007). While there is some scepticism that governments will have the political will to implement such measures, there is growing evidence that change can be made. For example, ultra-radical tobacco control measures - total bans on importing, selling and using tobacco - have been successfully implemented in Bhutan (Koh *et al.* 2007) and substitution of soya bean oil for palm oil in Mauritius resulted in population-wide reductions in blood cholesterol (Uusitalo *et al.* 1996).

Reducing individual susceptibility to non-communicable diseases

Reducing individual susceptibility to cardiovascular disease through reducing blood pressure, blood cholesterol and smoking has extremely strong supporting evidence from many randomized trials (Gaziano *et al.* 2007; Lim *et al.* 2007). However, in low- and middle-income countries, this evidence is difficult to apply. Currently, health services for chronic diseases are fragmented, organisationally weak and are not rising to the challenge of preventing or managing chronic diseases. World Health Organization's proposals for chronic disease have emphasized advocacy to improve recognition of the burden of disease, both in terms of suffering and premature death (World Health Organization 2005), and in terms of economic impacts (Abegunde *et al.* 2007), and to apply the knowledge we already have from the developed world. However, evidence of how best to implement clearly cost-effective interventions in developing countries remains limited. For example, detection and treatment of high blood pressure reduces stroke and heart attacks; evaluating how to achieve coverage and compliance with protocols among health professionals is where research studies can be usefully conducted in low- and middle-income countries (Jafar 2006). On the other hand, interventions such as lifestyle modification of diet, exercise and smoking targeted at individuals are now a common inclusion in national chronic disease policies in South Asian countries. Evidence from their use in developed countries is disappointing with failure to show any impact on mortality or morbidity (Ebrahim & Davey Smith 1997). Trials to demonstrate whether or not such interventions are cost-effective in low and middle-income countries would be helpful.

Managing non-communicable diseases in the community

Managing and preventing chronic diseases - the secondary and tertiary prevention agendas of reducing recurrence, slowing progression, avoiding complications and maximising function and quality of life - will be a major challenges for health services (United Nations Programme on Ageing 2002; World Health Organization 2002a; Epping-Jordan *et al.* 2004). Clear evidence of cost-effectiveness of interventions that are feasible to implement at individual and societal levels is likely to be culture specific and require nationally relevant evidence to be credible to policy makers. Methods to aid surveillance and evaluation of changes in national and local policies are also needed.

The costs of implementing prevention and control programmes for non-communicable diseases have been estimated (Asaria *et al.* 2007; Beaglehole *et al.* 2007; Gaziano *et al.* 2007; Lim *et al.* 2007) and certainly the population interventions of tobacco control and dietary salt reduction appear to be affordable for virtually all low- and middle-income countries. However, for interventions for individuals (e.g. drug treatments for high blood pressure), out-of-pocket expenditure on health care remains a cause of concern, even in countries that have established health systems providing universal care free at the point of use (Barros & Bertoldi 2008).

There is a massive agenda of research focussed on evaluations of public health interventions (e.g. monitoring impact of tobacco control measures, voluntary restrictions in salt and saturated fat in processed foods) and household and individual interventions (e.g. detection and treatment of high blood pressure; smoking cessation, diet and exercise advice; substitution of saturated with polyunsaturated cooking fats) in low- and middle-income countries. Most currently available interventions are appropriate for only a relatively small minority (i.e. the urban high-income populations of low- and middle-income countries) and scant attention has been paid to non-communicable disease prevention and control in the urban poor and rural populations which still comprise the majority of the population of many low- and middle-income countries.

Conclusion

The organised efforts of societies have resulted in the most remarkable improvements in child and maternal survival, control and eradication of major infectious diseases and fertility control that have resulted in population ageing - an underlying cause of the increase in non-communicable diseases - over the last 50 years. We now need to seek ways of building on these successes by strengthening existing health-care systems in their ability to provide comprehensive, accessible, community-based, family health care - preventive, curative and rehabilitative - for both communicable and non-communicable diseases. This will involve re-integration of current vertical programmes (e.g. for malaria, polio, tuberculosis, HIV) into novel forms of family-orientated primary care (Janssens *et al.* 2007; Harries *et al.* 2008). Setting up new vertical chronic disease programmes for non-communicable diseases would simply perpetuate an approach that has undermined the ability of the health system to operate effectively in many countries. The primary care agenda embodied in Alma Ata in 1978 and now revitalized by World Health Organization's new framework for strengthening of health systems (World Health Organization 2007) is the main priority for making a start in tackling non-communicable diseases in low- and middle-income countries.

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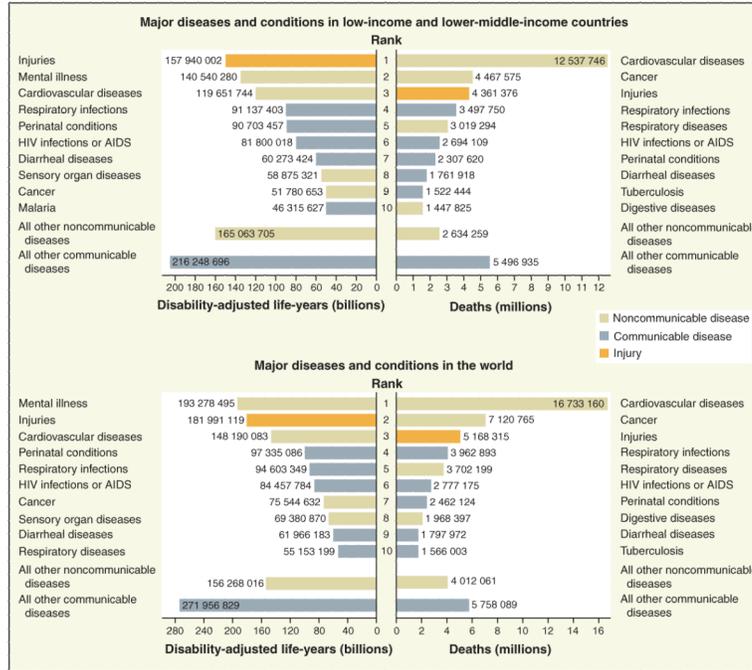


Figure 1. Years of healthy life lost (disability-adjusted life years) and deaths according to disease or condition. Perinatal conditions include low birth-weight, prematurity, birth asphyxia and birth trauma. Data are from the WORLD HEALTH ORGANIZATION (2005). *Source:* Anderson and Chu (2007). Available at: <http://content.nejm.org/cgi/content/full/356/3/209/F1>.

Percent change in death rates for coronary heart disease, selected countries, 1988–1998

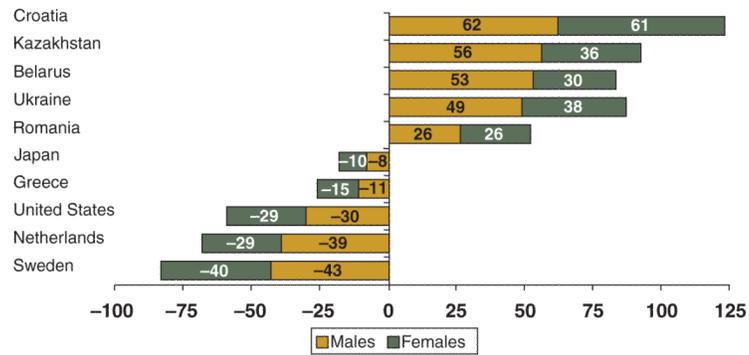


Figure 2. Percentage change in ischemic heart disease death rates in people aged 35 to 74 years during 1988-98 (selected countries).
Source: Mackay & Mensah (2004). Available at: http://www.who.int/cardiovascular_diseases/en/cvd_atlas_14_deathHD.pdf.

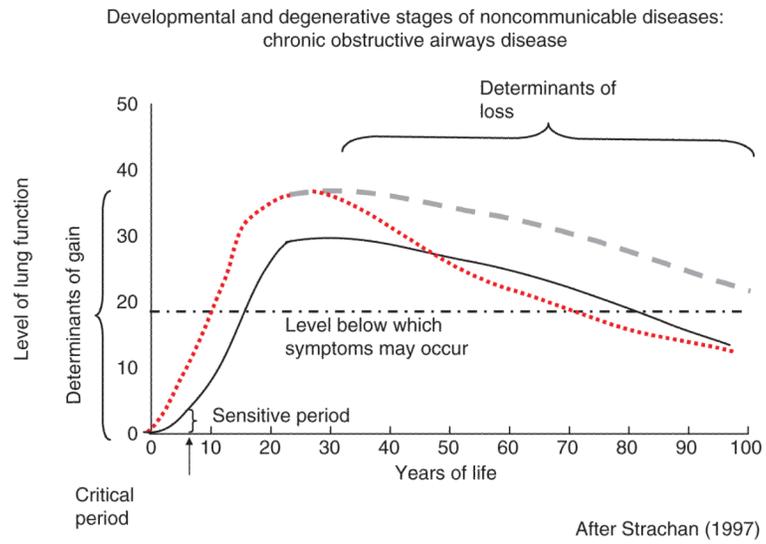


Figure 3.
A life course model of non-communicable disease causation.