

A life course approach to diet, nutrition and the prevention of chronic diseases

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Abstract

Objective: To briefly review the current understanding of the aetiology and prevention of chronic diseases using a life course approach, demonstrating the life-long influences on the development of disease.

Design: A computer search of the relevant literature was done using Medline-‘life cycle’ and ‘nutrition’ and reviewing the articles for relevance in addressing the above objective. Articles from references dated before 1990 were followed up separately. A subsequent search using Clio updated the search and extended it by using ‘life cycle’, ‘nutrition’ and ‘noncommunicable disease’ (NCD), and ‘life course’. Several published and unpublished WHO reports were key in developing the background and arguments.

Setting: International and national public health and nutrition policy development in light of the global epidemic in chronic diseases, and the continuing nutrition, demographic and epidemiological transitions happening in an increasingly globalized world.

Results of review: There is a global epidemic of increasing obesity, diabetes and other chronic NCDs, especially in developing and transitional economies, and in the less affluent within these, and in the developed countries. At the same time, there has been an increase in communities and households that have coincident under- and over-nutrition.

Conclusions: The epidemic will continue to increase and is due to a lifetime of exposures and influences. Genetic predisposition plays an unspecified role, and with programming during fetal life for adult disease contributing to an unknown degree. A global rise in obesity levels is contributing to a particular epidemic of type 2 diabetes as well as other NCDs. Prevention will be the most cost-effective and feasible approach for many countries and should involve three mutually reinforcing strategies throughout life, starting in the antenatal period.

Keywords
Nutrition
Life course
Fetal origins of adult disease
Chronic disease
Noncommunicable disease
Nutrition transition
Life-cycle
Public health nutrition

The burden of chronic diseases is rapidly increasing worldwide. It has been calculated that, in 2001, chronic diseases contributed approximately 46% of the global burden of disease¹. About half of these deaths are attributable to cardiovascular diseases; obesity and diabetes are also showing worrying trends, not only because they already affect a large proportion of the population, but also because they have started to appear earlier in life. Based on current estimates, the proportion of the burden of chronic diseases is expected to increase to 57% by the year 2020, at enormous healthcare and other costs for societies and governments^{2,3}. Already, 79% of deaths attributable to chronic, or noncommunicable, diseases are occurring in developing countries, predominantly in middle-aged men⁴. Cardiovascular diseases are now commoner in India, and also in

China, than in all economically developed countries in the world added together⁴.

Much of the early research into cardiovascular diseases, and hence the subsequent preventive activities, was carried out on middle-aged and older western men. However, there has been considerable work in recent years which led to a recognition of gender and age issues in chronic disease prevention and control^{5–7}. More recently, there has been a growing awareness of the exploding noncommunicable diseases (NCDs) epidemic in the developing countries and countries in transition. It is now clear that the development, treatment and particularly prevention of the NCDs are applicable to all populations, although regional and national differences such as age of onset, continue to vary. This may be due to the rapid rate of the societal changes in countries

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undergoing the epidemic now, as opposed to the more gradual evolution of the NCDs in the last century in European and North American countries⁸.

Chronic diseases or NCDs are, themselves, a series of overlapping and complicated disease entities, some of which markedly amplify the likelihood of developing a further disease, and in that sense become risk factors themselves, e.g. obesity and diabetes. The so-called metabolic syndrome is a clustering of risk factors including hyperglycemia, hypertension, dyslipemia, mediated by insulin resistance and resulting in a range of end-point diseases beginning with type 2 diabetes. Increasingly common in the developing countries, nearly a quarter of US adults have been identified as having the syndrome⁹. Other combinations occur, meaning that the person at risk of one chronic disease is likely to have an underlying disorder predisposing to other diseases. These risk factors are indicative of disease processes progressing throughout the life course. There is increasing evidence that these risks begin in fetal life and continue into old age. Adult chronic disease, therefore, reflects cumulative differential lifetime exposures to damaging physical and social environments. To quote Kuh and Ben-Shlomo¹⁰, such an approach ‘does not draw false dichotomies between adult lifestyle and early life influences, or between biological and social risk factors’.

This paper reviews the development of chronic disease and its prevention and control over the life course with some emphasis on the developing countries and countries in transition. The number of people in the developing world with diabetes will increase by more than 2.5 times (from 84 to 228 million) in 2025⁷. Many of the communities are already bearing a double burden of disease—both undernutrition in infants, children and women, often in the same household, and overnutrition in the adults, especially in older women^{11,12}. Both forms of malnutrition†, and the resulting chronic disease patterns of stunting obesity, cardiovascular diseases, hypertension and cancer, and other NCDs, occur predominantly in the more disadvantaged and poorer sectors of the society. Economic disparities are virtually increasing in virtually all countries, as well as internationally, and can be expected to worsen the incidence and outcomes of NCDs, especially for the more disadvantaged¹³. Many studies show a relationship between health and the relativity of income between the rich and poor in a given society, so this increased ‘social disadvantage’ may disproportionately affect the incidence of chronic (and other) diseases, as well as affect the access to treatment. The disadvantage will also be reflected in the uptake, or more usually lack of uptake, of health promoting behaviours amongst the poorest sections of the society.

†The term malnutrition is used to express both under- and over-nutrition in this paper.

Taking a life course perspective has great potential and several challenges. It is now generally accepted that the risk of many NCDs is not just determined by risk factors in mid-adult life, but begins in childhood or adolescence, and likely even earlier, i.e. during fetal development¹⁴. A WHO Report⁷ identifies three reasons for the current interest in this approach: (i) the increasing evidence of ‘tracking’ of conventional risk factors from childhood to adulthood; (ii) the evidence for ‘programming’ as a potential model of disease aetiology with, in particular, ‘the fetal origins of adult disease’ hypothesis; and, (iii) emerging evidence to indicate that some early risk factors may act across generations. It is also necessary to consider both ‘critical’ and ‘sensitive’ periods throughout the life course where exposures are deterministic or especially powerful in predisposing to, or lessening, the risk of disease. To add to this complexity, it is necessary to recognize and include the relative role of, and interaction between, earlier and later influences on risk factors, as well as the environments in which populations live and which help to shape the total life experience of health.

The same WHO report identifies four theoretical and overlapping models from Ben-Shlomo and Kuh¹⁵ that explains ways in which such factors may act to cause chronic diseases over the life course:

1. Critical period model—where an insult during a specific period of growth or development has a lasting, lifelong effect on physical functioning or structure that results in disease later on;
2. Critical period influences with later modifiers of their effects, i.e. the later factors modify an earlier-incurred risk;
3. Accumulation of risk with correlated results—where risk factors cluster in socially or biologically patterned ways, and hence raise the risk of disease through social and/or biological chains or pathways of risk where one adverse (or protective) experience will tend to lead to another adverse (or protective) experience in a cumulative way; and,
4. Accumulation of risk with independent and uncorrelated results—where separate and independent risk factors at each stage of life combine to raise disease risk.

One further issue becomes apparent, that much of the evidence available is from research and experience in developed/industrialized countries. There is more limited research available in some countries in transition such as Brazil¹⁶, and quite limited data from developing countries. Some important work has been published from China and India which is particularly helpful.¹⁷

The life course

This paper will review the processes and environmental and societal influences that cause or modify the risk of chronic diseases developing and progressing throughout

the life course (Fig. 1), with an emphasis on prevention. For convenience, the paper discusses five stages of the life course, such as fetal development and the maternal environment, infancy and childhood, adolescence, adulthood, and ageing and older people. Although distinct in themselves, they merge imperceptibly into one another with different influences becoming more or less important over the course of one's life. The term 'life course' is used by the WHO to emphasize the elderly and that it is not solely a reproductive 'life cycle'.

Other factors essential for the discussion are the social and economic changes that are operating on a scale and at a speed unprecedented in history, resulting in rapid changes in dietary and physical activity patterns worldwide. These rapid global changes are the major causes of the increasing global NCD epidemic.

The process of modernization and economic transition has seen most of the countries of the world move towards industrialization with national economies based on trade within a global market. This has brought about a number of improvements to the standard of living and services available to people throughout the world. However, it has also had a number of negative consequences that have directly and indirectly led to deleterious dietary and physical activity patterns that contribute to the development of a number of NCDs. Indeed, some changes in the industrialization of food production have contributed to the consumption of a diet higher in fat (particularly saturated fat) and protein content and lower in complex carbohydrates.

The decline in the demands for physical activity seen with modernization, and other societal changes, usually lead to a more sedentary lifestyle. Motorized transport, mechanized equipment, and labor-saving devices both in the home and at work have replaced physically arduous tasks. In addition, changing societal structures have also led to an increasing proportion of the population working in service, clerical and other professional occupations that demand considerably less energy expenditure than the physically demanding manual work of more traditional societies.

At the same time there are many other social, economic and demographic challenges to countries, including environmental degradation and pollution, emerging and re-emerging diseases such as HIV/AIDS, malaria, TB and BSE, as well as the continuing scourge of wars and their victims, including refugees, and displaced children and adults. In developing policies to confront these changes, countries are powerfully influenced by international and global forces. Among them the factors that need to be addressed in a progressive and coherent manner are: global trade and the effects of world trade agreements; business practices of multinational food and drug companies; the role of mass media on lifestyles; ethical issues; and, issues of human rights^{4,18}.

Fetal development and the maternal environment

The four relevant factors in fetal life are: (i) intra-uterine growth retardation (IUGR); (ii) premature delivery of a

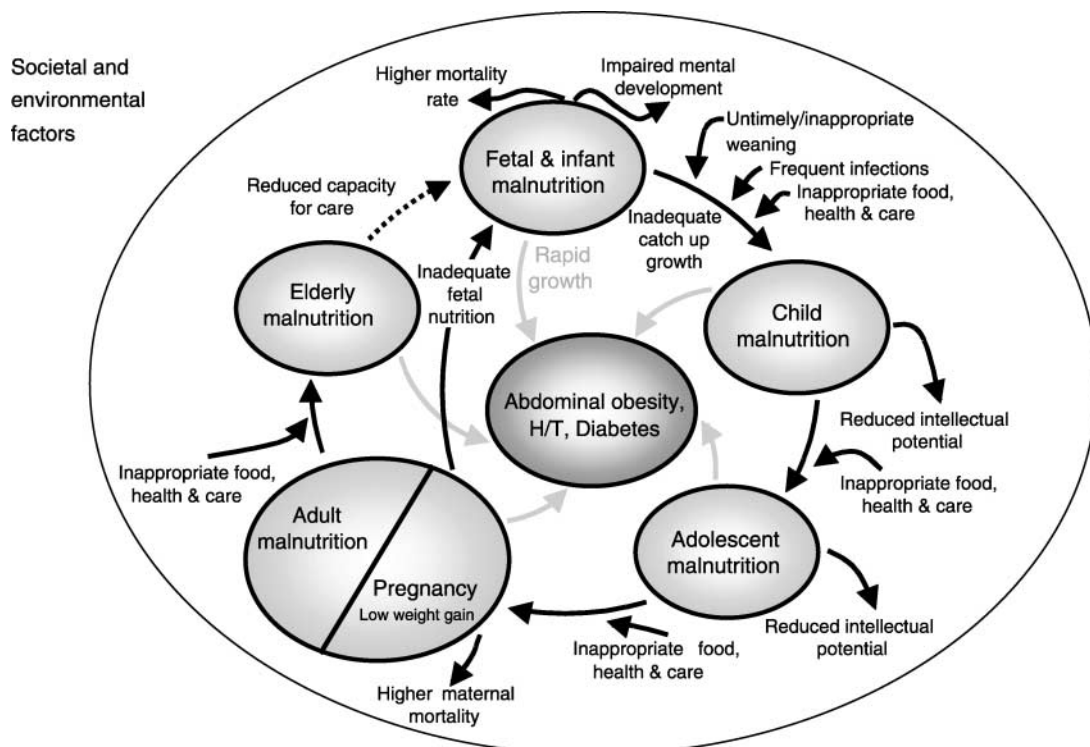


Fig. 1 Life course: the proposed causal links. Source: adapted from ACC/SCN, 2000

normal growth-for-gestational-age fetus; (iii) overnutrition *in utero*; and, (iv) intergenerational factors. Intergenerational factors will be addressed later. There are recognized limitations in using low birth weight to capture the range of potentially important exposures *in utero*¹⁹. For example, a finding in the study of the Dutch famine was that of an association between high blood pressure and exposure to famine in early gestation even though this was not seen to be linked with low birth weight⁷. It is useful to keep in mind that the following epidemiological findings of metabolic and structural programming have been found experimentally in animals such as rodents and some studies of primates in a way consistent with the disease susceptibility observed in human studies²⁰.

Intra-uterine growth retardation

There is considerable evidence, mostly from developed countries, that IUGR is associated with an increased risk of coronary heart disease (CHD), stroke, and diabetes^{7,14}. Evidence from historical cohorts or retrospective studies has shown clear associations between retarded fetal growth (as evidenced by small size at birth) and risk of CHD^{21–23}, diabetes^{24–28}, stroke^{21,29,30}.

While low birth weight is the indicator commonly used, due to its relative convenience and availability, research using more specific indices of fetal growth have shown important differences in the strength of associations between disease and different kinds of fetal or IUGR³¹. Further evidence for an association between IUGR and later chronic disease has been looked for in the ‘famine studies’ from populations, such as those of the Dutch famine (from 1944 to 1945³²) and of the Russian famine in the Leningrad siege (from 1941 to 1944³³) during World War II. The Dutch study showed that exposure to famine in early gestation is associated with an increased risk of heart disease, but the Russian study showed no such effect. In the developing world, only a limited number of studies, e.g. India, have examined this relationship³⁴. An association between low birth weight and CHD was found in one³⁵ but in the other, subsequent diabetes was found to be associated with obesity (higher ponderal index) rather than low birth weight³⁶.

Blood pressure in childhood has also been found to be associated with low birth weight in cohort studies from both the developed and developing world, including Chile, China, DR Congo, Guatemala, India, Jamaica, South Africa, UK, and Zimbabwe⁷. Fewer studies, including the two ‘famine studies’, have not found this relationship and in Hong Kong greater length at birth was associated with higher blood pressure³⁷. As noted before, the association of low birth weight with childhood BP may depend on the type of growth retardation or impairment experienced *in utero*.

While there appears to be good, although not conclusive, associative evidence for reduced fetal growth

and increased risk of metabolic syndrome in middle life³⁸, the association of fetal growth to impaired glucose tolerance (IGT) or dyslipidemias is not clear⁷, and studies have found conflicting results. The Dutch famine study showed a significant association between the exposure to famine in early pregnancy (not related to lower size at birth) and a more diverse lipid profile (higher LDL:HDL ratio)³⁹. In neither the Dutch nor the Russian studies was there a significant association between exposure to famine *in utero* and adverse HDL or TG levels³³. Evidence from the developing countries has been more supportive of an association, e.g. China⁴⁰. In India, a link was found between low birth weight and adverse total serum cholesterol and LDL-cholesterol levels in 8-year-old children, highest in those with high fat mass⁴¹, and in Jamaica, between total cholesterol levels and low birth weight in 6–16-year-olds⁴².

An association between IUGR and IGT appears stronger with a consistent association between small size at birth and IGT in adulthood in historical cohort studies and in China, India and South Africa⁷. Law *et al.*⁴³ found that low birth weight was associated with blood pressure at the early age of 3. As will also be suggested later, it may not be the low birth weight *per se* but rather a pattern of growth, e.g. restricted fetal growth followed by very rapid postnatal catch-up growth, that is important in these underlying disease pathways⁴⁴.

There is consistent evidence that high systolic blood pressure in adulthood is associated with retarded fetal growth (as measured by low birth weight)^{45–47}. It is not known, however, if this association mediates the link between IUGR and CVD⁷. A recent meta-analysis has questioned this apparent relationship, citing possible methodological problems⁴⁸ and concluding that birth weight is of little importance to blood pressure levels in later life. Nevertheless, there is supportive evidence that comes from both developed and developing countries, e.g. China⁴⁰ and South Africa⁴⁹.

Furthermore, there appears to be an interacting effect between obesity or gained weight enhancing the risk of CHD or diabetes associated with impaired fetal growth, and there may be a similar effect for blood pressure. In the Swedish study, the effect of low birth weight on high blood pressure, increased with rising adult body mass index (BMI), and the association of current BMI to blood pressure was enhanced in those with low birth weight⁵⁰.

Premature delivery with normal growth-for-gestational age

There are important nutritional and developmental outcomes of prematurity, particularly depending on the degree of early delivery. However, there has not been animal or human work to suggest a linkage with later development of chronic disease, although presumably a proportion of the low birth weight infants in many of the

studies showing such a relationship, were outcomes of prematurity rather than fetal retardation. Nevertheless, apart from this context, this category of low birth weight will not be considered further.

Overnutrition in utero

Large size at birth (macrosomia) is also associated with an increased risk of diabetes and CVD^{21,51}. In India, and in contrast to the above, among adults (and in contrast to the relationship found among children) an association was found between IGT and high ponderal index (i.e. fatness) at birth³⁶. In Pima Indians, a U-shaped relationship to birth weight was found, whereas no such relationship was found among Mexican Americans^{51,52}. Higher birth weight has also been related to an increased risk of breast and other cancers¹⁰.

Infancy and childhood

Ideally, one would like to consider neonates, infancy, young childhood and the 'school-aged' child as separate stages, as early available evidence suggests that there may be subtly different influences during each of these phases, at least for some risk factor development⁷. However, there does not appear to be enough evidence to do so at present, and so infancy and childhood will be considered together, and differentiation noted when relevant. Breast-feeding is also considered in this section. Retarded growth in infancy and childhood can be reflected in (i) failure to gain weight, and (ii) failure to gain height, while (iii) excessive gain in both weight or height ('crossing the centiles') also appears to be a factor in later chronic disease incidence, and then (iv) other factors, such as growing up in a disadvantaged socioeconomic environment will also be noted.

Breastfeeding

There is increasing evidence that among term and pre-term infants, breastfeeding is associated with significantly lower blood pressure levels in childhood^{53,54}. Singhal *et al.*⁵⁴ have shown that consumption of formula instead of breast-milk in infancy also increases diastolic and mean arterial blood pressure in later life. Nevertheless, studies with older cohorts³⁶ and the Dutch famine study⁵⁵ have not identified such associations. Evidence on the effect of breastfeeding on dyslipidemias is conflicting. There is also evidence suggesting a lower risk of developing obesity^{56–59} and which may be directly related to length of exclusive breastfeeding and may not become evident until later in their childhood⁶⁰. Some of the discrepancy may be explained by socioeconomic and maternal education factors confounding the findings.

Data from most, but not all, observational studies of term infants have generally suggested adverse effects of formula consumption on the other CVD risk factors (as

well as blood pressure), but little information is available from controlled clinical trials⁶¹. Nevertheless, the weight of current evidence indicates adverse effects of formula milk on CVD risk factors, which is consistent with observations among older adults who were fed formula as infants^{61,62}. The risk for several chronic diseases of childhood and adolescence (type 1 diabetes, celiac disease, some childhood cancers, and inflammatory bowel disease) have also been associated with artificial infant feeding and short term breastfeeding⁶³. There are, of course, other more immediate and long term developmental reasons to promote breastfeeding, both for the child's and the mother's sake⁶⁴.

Postnatal growth in weight

An association between low growth in early infancy (low weight at 1 year) and an increased risk of CHD, has also been described, irrespective of size at birth^{65,66}. This would support a role, only from developed country research at this point, for the importance of immediate postnatal factors in shaping disease risk. Infant growth rates in Bangladeshi infants, most of whom had chronic intrauterine undernourishment and were breast-fed, showed similar growth rates to breast-fed western infants, but catch-up growth was limited and weight at 12 months was largely a function of weight at birth⁶⁷.

In a study of 11–12-year-old Jamaican children, blood pressure levels were found to be highest in those with retarded fetal growth and greater weight gain between the ages 7 and 11⁶⁸, and similarly in India⁴¹. Low birth weight Indian babies have been described as having a characteristic poor muscle but high fat preservation, the so-called 'thin-fat' babies. This phenotype persists through post-natal period and is associated with increased central adiposity in childhood, that is linked to the highest risk of raised blood pressure and disease risk^{34,69,70}. In most studies, the association between the low birth weight and high blood pressure has been found to be particularly strong if adjusted to current size (BMI) suggesting the importance of weight gain after birth⁷¹, although it has been questioned whether this is an appropriate adjustment to make⁴⁸.

Relative weight in adulthood and weight gain have also been found to be associated with increased risk of cancer of the breast, colon, rectum, prostate, and other sites⁷². Whether there is an independent effect of childhood weight is difficult to determine, as childhood overweight is usually continued in to adulthood. Relative weight in adolescence was significantly associated with colon cancer in one retrospective cohort study⁷³. In a study following up an earlier survey of Boyd-Orr in the late 1930s, after accounting for confounding effects of social class, it was found that for both sexes, there was a significant positive relationship between childhood energy intake and adult cancer mortality⁷⁴. The recent

review by the International Agency for Research into Cancer in Lyon, France concluded there was clear evidence of a relationship between early, and later, onset of obesity and cancer risk⁷⁵.

Childhood growth in height

Short stature (including measures of childhood leg length), a reflection of socioeconomic deprivation in childhood⁷⁶, is associated with an increased risk of CHD and stroke, and to some extent, diabetes^{28,77–82}. Given that short stature, and specifically short leg-length are particularly sensitive indicators of early socioeconomic deprivation, their association to later disease very likely reflects an association between early undernutrition and infectious disease load^{83,84}.

Height serves partly as an indicator of socioeconomic and nutritional status in childhood. As has been seen, poor fetal development and poor growth during childhood have been associated with increased cardiovascular disease risk in adulthood, as have indicators of unfavorable social circumstances in childhood. Conversely, a high calorie intake in childhood may be related to an increased risk of cancer in later life⁷⁴. Height is inversely associated with all cause, CHD, stroke, and respiratory disease mortality among men and women⁸⁵.

On the other hand, height has been used as a proxy of usual childhood energy intake, which is particularly related to body mass and the child's activity. However, it is clearly an imperfect proxy because when protein intake is adequate (energy appears to be important in this regard only in the first 3 months of life), genetics will define adult height⁷². Protein, particularly animal protein, has been shown to have a selective effect in promoting height growth, and it has been suggested that childhood obesity is related to excess protein intake. Overweight or obese children tend to be in the upper percentiles for height. Height has been shown to be related to cancer mortality at several sites, including breast, uterus, and colon⁷². The risk of stroke is increased by accelerated growth in height during childhood⁴⁵. As accelerated growth has been linked to development of hypertension in adult life, this may be the mechanism (plus an association with low socioeconomic status).

Other factors in childhood

There is a higher prevalence of raised blood pressure with low socioeconomic status^{86–92}, in adults but also in children coming from low socioeconomic backgrounds, although the latter is not always associated with higher blood pressure later in life⁷. Blood pressure has been found to track from childhood to predict hypertension in adulthood, but with stronger tracking seen in older ages of childhood and in adolescence⁹³.

The higher blood pressure in childhood (in combination with other risk factors) causes target organ and anatomical changes associated with cardiovascular risk,

including reduction in artery elasticity, increased ventricular size and mass, hemodynamic increase in cardiac output and peripheral resistance^{7,94,95}. High blood pressure in children is strongly associated with obesity, in particular central obesity and clusters and tracks with an adverse serum lipid profile (especially LDL-cholesterol) and glucose intolerance^{94,96,97}. There may be some ethnic differences although these often seem to be explained by differences in BMI. A retrospective mortality follow-up of a UK survey of family diet and health (1937–1939) identified significant associations between childhood energy intake and mortality from cancer⁷⁴.

The presence and tracking of blood pressure in children and adolescents occurs against a background of unhealthy lifestyles, including excessive intakes of total and saturated fats, cholesterol and salt, inadequate intakes of potassium, and reduced physical activity, often accompanied by high levels of television viewing⁷. In adolescents, habitual alcohol and tobacco use contributes to raised blood pressure^{98,99}.

Adolescence

There are three critical issues in adolescence impacting on chronic diseases: (i) development of risk factors during this period; (ii) the tracking of risk factors throughout life; and, in terms of prevention, (iii) the development of healthy, or conversely, unhealthy habits that tend to stay throughout life.

Development of risk factors

It was recognized during the Vietnam war that US recruits killed in warfare, although apparently fit young men, already had clear evidence of atherosclerotic damage to their blood vessels. There has been a trend towards overweight and obesity in adolescence (with high levels of unhealthy eating and physical inactivity patterns) throughout the world. This is true in all industrialized countries, especially in low socioeconomic groups, and increasingly true of transitional economies¹⁰⁰. Television viewing has been specifically implicated^{101,102}.

Raised blood pressure is usually measured in mid or later life and is a main risk factor for cardiovascular diseases, especially stroke and CHD¹⁰³. Some long term cohort studies (Harvard Alumni, Chicago Heart Association Detection Project, Glasgow University Students Study) have shown that high blood pressure in adolescence or young adulthood is strongly related to later risk of stroke or CHD, independently of blood pressure in mid-life^{104–108}. In other words, risk of CVD, through high blood pressure, already starts well before middle age⁷, and this clearly has repercussions for prevention and treatment.

While mean blood pressure levels have decreased over the past decades in industrialized countries^{109–111}, in developing countries they appear to be rising—usually

along with GNP¹¹². One study documenting such adverse trends shows them particularly in the younger population¹¹³. High blood pressure tracking from childhood to adulthood is related to the onset of early atherosclerosis as shown in the Bogalusa Heart Study^{95,98}. Early high blood pressure is particularly found to be a problem in Sub-Saharan Africa, consonant with the higher rates of stroke and susceptibility to hypertension observed among African and African-American populations^{114,115}.

Tracking of risk factors

Clustering of risk factor variables already occurs in childhood and adolescence and is associated with atherosclerosis in young adulthood, and thus risk of later cardiovascular disease^{98,116,117}. As noted earlier, this clustering has been described as the metabolic or 'syndrome X'—the clustering of physiological disturbances associated with insulin resistance including hyperinsulinemia, IGT, hypertension, elevated plasma triglyceride and low HDL-cholesterol^{118,119}. Raised serum cholesterol both in middle age and in early life are known to be associated with an increased risk of disease later on. The Johns Hopkins precursor study showed serum cholesterol levels in adolescents and young white males were strongly related to subsequent risk of CVD mortality and morbidity¹²⁰.

Although the risk of obesity does not apparently increase in adults who were overweight at 1 and 3 years of age, the risk rises steadily thereafter, regardless of parental weight¹²¹. Tracking has also been reported in the transitional country of China, where overweight children were 2.8 times as likely to become overweight adolescents (and conversely underweight children were 3.6 times as likely to remain underweight as adolescents). The authors found that parental obesity, and underweight, the children's initial BMIs, dietary fat intake, and family income helped predict tracking and changes¹²². However, in a British prospective cohort study, little tracking from childhood overweight to adulthood obesity was found when using a measure of fatness (percentage body fat for age) that was independent of build. The authors also found only children obese at 13 years to have an increased risk of obesity as adults, and that no excess adult health risk from childhood or adolescent over weight was found¹²³. Interestingly, they found the thinnest children tended to have the highest adult risk at every level of adult obesity.

The real concern about these early manifestations of chronic disease, besides that they are occurring earlier and earlier, is that once developed they tend to track in that individual throughout life. On the more positive side, there is also evidence that they can be corrected, but overweight and obesity are notoriously difficult to correct after becoming established, and there is the established risk of overweight during childhood persisting into adolescence and adulthood¹⁰¹. A recent meta-analysis by Parsons *et al.*^{124,125} showed that the later the weight gain in childhood and adolescence, the greater the persistence.

More than 60% of overweight children have at least one additional risk factor for cardiovascular disease, such as raised blood pressure, hyperlipidemia, or hyperinsulinemia, and more than 20% have two or more risk factors¹⁰¹.

Developing habits leading to NCD development during adolescence

It seems increasingly likely that there are widespread effects of early diet on later body composition, physiology and cognition⁶¹. Such observations 'provide strong support for the recent shift from defining nutritional needs for prevention of acute deficiency symptoms to long term prevention of morbidity and mortality'⁶¹. It is recognized that increased birth weight increases the risk of obesity later, but children with low birth weights tend to remain small into adulthood^{101,126}. However, in industrialized countries there have been only modest increases in birth weights, so the increased levels of obesity described earlier must reflect environmental changes¹⁰¹.

The 'obesogenic' environment appears to be largely directed at the adolescence market, making healthy choice that much more difficult. At the same time, exercise patterns have changed and considerable parts of the day are spent sitting at school, in a factory, or in front of a TV screen or a computer. Raised blood pressure, IGT and dyslipidemia are also associated in children and adolescents with unhealthy lifestyles, such diets containing excessive intakes of fats (especially saturated fats), refined carbohydrates, cholesterol and salt, inadequate intake of fiber and potassium, along with a lack of exercise⁷. Physical inactivity and smoking have been found to independently predict CHD and stroke in later life⁷.

It is increasingly recognized that unhealthy lifestyles do not just appear in adulthood but drive the early development of obesity, dyslipidemia, high blood pressure, IGT and associated disease risk. In many countries, perhaps most typified by the USA, in the last 30 years changes in family eating patterns and the consumption of fast foods, pre-prepared meals and carbonated drinks, have taken place¹⁰¹. Likewise, the amount of physical activity has been greatly reduced both at home and at schools, and in transport.

Adulthood

The three critical issues in adulthood are: (i) to what extent do risk factors continue to be important in the development of the chronic diseases; (ii) to what extent will modifying them make a difference to the emergence of disease; and, (iii) the role in risk factor reduction and modification in secondary prevention and treatment in those with disease. A recent WHO/FAO Expert Consultation on diet, nutrition and the prevention of chronic diseases, devoted to reviewing the evidence¹²⁷ in a life course approach demonstrated the importance of the adult phase as a key phase in life—both in terms of

expression of most chronic disease but also as a critical time in the preventive reduction of risk factors, and as well as increasingly effective treatment¹²⁸. Modifying risk factors and the impact of doing this is discussed under the discussion of interventions. As this paper is addressing primary prevention, secondary prevention and treatment is not further discussed here, but have been identified as major factors in the decline of chronic disease mortality in more affluent countries¹²⁸.

Adult risk factors

The most firmly established associations between CVD or diabetes and factors in the life span are those between diseases and the major known 'adult' risk factors—tobacco use, obesity, physical inactivity, cholesterol, high blood pressure, and alcohol^{127,129}. The factors confirmed to lead to increased risk of CHD, stroke and diabetes are: high blood pressure for CHD or stroke^{130,131}; high cholesterol (diet) for CHD^{132,133}, and tobacco use for CHD¹³⁴. Other associations are robust and consistent though have not necessarily been shown to be reversible⁷: obesity, physical inactivity for CHD, diabetes and stroke^{135–137}; and, heavy and/or binge drinking for CHD and stroke^{134,138}. Most of the studies are from developed countries, but supporting evidence from developing countries is beginning to emerge, as for example in India¹³⁹.

There is also evidence of adult tracking. There is a strong association between the serum cholesterol level, e.g. measured in early adult life in men and cardiovascular disease in mid-life, as well as total mortality¹²⁰. Similarly, the Chicago Heart Association Detection Project in Industry found that in young men, blood pressure above normal was significantly related to increased long term mortality due to CHD, CVD, and all causes¹⁰⁷. Their conclusion was that population-wide primary prevention, early detection, and control of higher blood pressure are indicated in the young adult and on. The majority of cases of adult onset type II diabetes are characterized by the early development of insulin resistance with compensatory true hyperinsulinemia¹⁴⁰.

In developed countries, low socioeconomic status is associated with higher risk of cardiovascular disease and diabetes¹⁴¹. As in the affluent Western countries, there appears to be an initial preponderance of CVD among the higher socioeconomic groups, e.g. China¹⁴², which then is presumed will progressively shift to the more disadvantaged sectors of society⁷, with some evidence this is already happening, especially in low income women, e.g. Brazil¹⁴⁶ and South Africa¹⁴³ and is in transition in countries such as Morocco¹⁴⁴.

The evidence is strong in adults, more so in men, as to the risk factors in the development of chronic disease, but also their role in secondary prevention and treatment. However, the known risk factors have been calculated to account for only about half of the known risk, and so presumably other factors such as genetics and

programming make up much of the rest. However, a recent article by Magnus and Beaglehole¹⁴⁵ have been able to account for most of the NCD epidemic, using the known risk factors. Likewise, apparent anomalies are deceptive: most men at apparently low visible risk (e.g. slim, never smoked, etc.) who die prematurely, have poorer risk profiles on other less visible risk factors, and vice versa for men of high visible risk who survive¹⁴⁶.

Other factors are being continually recognized or proposed. These include the role of high levels of homocysteine, the related factor of low folate, the role of iron¹⁴⁷ and others. From a social sciences perspective, Losier¹⁴⁸ has suggested that socioeconomic level is less important than a certain stability in the physical and social environment, and an individual's sense of understanding of his/her environment and of control over the course and setting of his/her own life that is induced by this stability, that appear to be most important as determinants of health. Marmot¹⁴⁹ and others have demonstrated the impact of the wider environment and societal and individual stress on contributing to the development of chronic disease.

Ageing and older people

There are three critical issues in the chronic diseases in the later part of the life cycle: (i) most chronic diseases will be manifested in this later stage of life; (ii) there is an absolute benefit for ageing individuals and populations in changing risk factors and adopting health-promoting behaviours such as healthy diets and exercise; and, (iii) the need to maximize health and quality of life by avoiding or delaying preventable disability. Along with the societal and disease transitions has been a major demographic shift. Consequently what is defined as elderly, is very different from the middle of last century, when 60 years of age and above often exceeded the average life expectancy, especially in industrialized countries.

Despite fears of increasing longevity leading to longer periods of disability, there is increasing evidence that the main burden of disability, is most often seen in those over 85 years and increasingly confined to the last year of life^{150,151}. In the US, statistically significant declines in chronic disability prevalence rates were observed in those over 65 years between 1982 and 1989¹⁵².

Chronic diseases in later life

Most chronic diseases present at this time of life would be the result of interactions of multiple disease processes as well as more general losses in physiological functions^{152,153}. Cardiovascular disease peaks at this period, as does type 2 diabetes and cancer. While still a problem, obesity becomes, on a population basis, less of a problem, and in populations where weight is not increased throughout adult life, hypertension may actually decrease. Some cancers, e.g. breast, may occur earlier in life. Nevertheless, the main burden of chronic diseases is at this

stage of life and needs to be addressed. It is particularly of concern to governments observing demographic trends, especially in countries with rapidly declining birth rates, and who foresee a greatly increased financial burden of prolonged life but increased prevalence, especially as health care for chronic diseases can be frighteningly expensive. In other countries, less affluent, there is also a concern about the double burden of disease (both under- and over-nutrition) and the cost of treating chronic diseases, often with low health budgets^{154,155}.

These are concerns that need to be addressed, and factual information provided to societies and policy makers. However, recent analyses in some developed countries such as Australia, suggest the concern is overplayed, and that it is unlikely to be the health crisis often portrayed, and that, with a calculated increase in expenditure of only 0.54% due to ageing, 'is not likely to create significant problems in the future'¹⁵⁶. As has been pointed out in a recent editorial, there has been virtually no attention to this issue in the developing countries¹⁵⁷. Whereas the burden of chronic diseases are definitely greater in the elderly, the other advantages of seniority, in terms of experience, knowledge and guidance are generally uncosted variables that all countries, and especially those with limited educated work force, can ill afford not to use maximally¹⁵¹.

On the other hand, those suffering from these NCDs will often be those who are most influential (at least in the first phase of the disease transition) and will slant health care investment towards the establishment of expensive treatment and diagnostic facilities. There is considerable evidence that primary prevention (and probably secondary prevention) is cost-efficient and of proven effectiveness¹⁵⁸. Now that the epidemic has moved into the less affluent populations, the emphasis on treatment facilities, disadvantages those who cannot afford them, not least in the most affluent countries such as the USA. Thus, the most important aspect to promote is: that intervening to effect lifestyle change and reduce prevalence of risk factors in later life, is extremely cost-effective. As the elderly population vastly increases throughout the world, interventions, of proven effectiveness, will have an impact on a greater and greater number of people. Not only that, the improved health will result in enhanced further productivity, as well as less dependency, and less spent on health and institutional costs. This great cost benefit is also very immediate and will be addressed again later.

Changing behaviours in older people

In the 1970s, it was thought that, in epidemiological terms, risks were not significantly increased after certain late ages and, therefore, that there was no benefit in changing habits, e.g. dietary habits after 80 years of age¹⁵⁹ as there was no epidemiological evidence that changing habits would affect mortality, or even health conditions, among older people. There was also a feeling that people 'earned'

some unhealthy behaviours simply because of reaching 'old age'. Then, there was a more active intervention phase when older people were actively encouraged to make changes in their diet that probably were overly rigorous for the expected benefit. More recently, older people are being encouraged to eat a healthy diet, as large and as varied as possible while maintaining weight, and particularly to continue exercise^{153,158}. Liu *et al.*¹⁶⁰ have reported an observed risk of incident atherosclerotic disease among older women that was approximately 30% less in women who ate 5–10 servings of fruits and vegetables per day (cf. 2–5 servings/day). It is our contention that, on a population basis, because elderly patients have a higher cardiovascular risk they are more likely to gain from risk factor modification¹⁶¹.

Although this age group have received relatively little attention for primary prevention, the acceleration in decline caused by external factors is generally reversible at any age¹⁵¹. Interventions aimed at supporting the individual and promoting healthier environments will often also lead to increased independence in older age.

Maximizing quality of life in old age

The dramatic changes in fertility and mortality rates during the 20th century has led to a rapidly ageing world in the 21st century. One of the big questions then becomes: are we living healthier as well as longer lives, or are our added years accompanied by disabilities and generally poor health? The wider public perception appears to be that healthcare personnel are there to make old peoples' lives miserable by getting them to give up everything they might enjoy, urging them to be more active and so on. However, there is increasing evidence of the positive effects of exercise, at virtually all levels, for both mental and physical health. Stress and depression are reduced and lack of appetite stimulated, by appropriate exercise¹⁶³. Likewise, being mobile to undertake daily activities of living, subjective feelings of well-being, and economic security are all seen as among the most important contributors to quality of life in older people (at least in western and Asian populations)¹⁵⁰. As has been seen, rates of disability are actually continuing to decrease in US elderly populations (despite increasing overweight) and there are data indicating this is likely happening in other industrialized countries¹⁵².

Interactions between early and later factors throughout the life course

In addition to the evidence on independent associations of IUGR, infancy and adulthood factors with later disease, there are very suggestive indications that the interaction between some of these early and later factors may lead to a particularly high risk of chronic disease.

Low birth weight, followed by subsequent adult obesity, has been shown to impart a particularly high risk of

CHD^{164,165}, as well as diabetes²⁵. Risk of IGT has been found to be highest in those who had low birth weight but who subsequently became obese as adults²⁵. A similar effect has been seen in India where the raised risk of insulin resistance and dyslipidemia was linked to the central obesity driven by the distinct thin–fat phenotype of IUGR Indian babies^{34,69,70,164}.

In addition to the effect already mentioned of later obesity, there is evidence to suggest an interaction between small size at birth and accelerated growth in height in raising risk of disease, e.g. in Finnish⁴⁶ and Swedish studies⁵⁰, in adolescents as well as in younger children. Several studies have demonstrated an interaction between rapid catch-up growth in weight and IUGR in increased risk of disease, e.g. in Finland where the highest risk of CHD or metabolic syndrome, for both men and women, was found to be associated with this sequence^{22,27,66}. The precise period in which increased growth may increase risk of later disease is currently unclear, although has major public health ramifications.

While there is limited evidence to demonstrate an impact with height, Forsen *et al.*²³ in Finland found that short length at birth followed by enhanced growth in height that resulted on average in tall height, was found to be associated with an increased risk of CHD in women (as opposed to tallness in girls with a longer birth weight who showed a lower risk). Likewise, and also from Finland, increased stroke risk for men and women was shown to be associated with small birth size at birth, followed by accelerated growth in height to reach average levels later in childhood^{45,46}. In the Indian subcontinent children studied, there was some suggestion of a mediating effect of height gained postnatally; the highest insulin levels were found in children who had low birth weight but had subsequently grown tall at 8 years, and highest yet in those who had short parents⁴¹. This again may signal more the importance of the postnatally gained weight or height, as opposed to simply the low birth weight.

Conversely there is consistent evidence of higher risk of CHD, stroke, and probably adult onset diabetes with shorter stature. This could be working through a variety of mechanisms, e.g. short stature as a marker for early childhood deprivation, nutritional deprivation with infectious disease load, psychosocial deprivation, socioeconomic deprivation, low fetal growth, and genetic influences (suggesting an intergenerational link).

Obesity, in particular abdominal obesity in adults, is one of the main risk factors for CHD, stroke and diabetes¹⁶⁵. The adverse effects in adults of obesity are influenced by degree of overweight, location of body fat, central obesity, magnitude of weight gain and sedentary life style¹⁶⁶. Obesity in childhood and adolescence is already related to risk of later CHD or diabetes^{165,167}. Furthermore, if obesity in childhood persists into the adult years, the morbidity and mortality is greater than if the obesity developed in the adult¹⁶⁸. The question might be which is more

important—obesity gained in adulthood, or in childhood and adolescence? It may be that the earlier onset also means longer periods of insulin resistance, where it appears to enhance risk associated with adult obesity¹⁶⁹. Willet and others have demonstrated evidence of added importance of weight gain in the decade before the disease was manifested¹⁷⁰.

It has been suggested that the apparent role of weight gained in mediating the link between IUGR and disease risk is indicated by the fact that most studies find a significant link or strong link only after adjustment for current weight or BMI⁷. This has led some to suggest that these linkages are about postnatal growth, more than low birth weight, and that it is the importance of the magnitude of centile crossing on later health that is important, and that treating current BMI status as a confounder is missing the point⁷¹.

There are four (not mutually exclusive) interpretations of the above interactions—which have also been seen to be linked with raised blood pressure, dyslipidemia and IGT⁷:

1. Accelerated growth in weight or height could in itself have negative consequences in terms of later diseases developing;
2. The difference in size between birth and the later growth and size with respect to established norms may be most important—with greater difference related to greater risk⁷¹;
3. An underlying susceptibility induced by impaired early growth is revealed or activated by subsequent obesity, i.e. obesity is particularly harmful in those with early growth retardation; and,
4. The impaired fetal growth itself, (perhaps due to placental insufficiency), may be a factor rather than the effect of postnatal growth, that underlies the increased risk of disease⁵⁰.

While the particular interpretation may depend on the specific disease or risk factor concerned, each indicates the importance of an adequate postnatal nutritional environment in bringing to the fore a risk associated with fetal growth retardation⁷. To some extent, the actual explanation will not alter the public health attention to reducing and modifying risk factors, and advice to the individual. It may, however, give greater emphasis to addressing poverty, the environment and women's health and nutrition. While increased attention to postnatal growth is equally self-evident, it is perhaps, even more challenging¹⁷¹.

Clustering of risk factors throughout the life course

IGT and an adverse lipid profile are seen already in childhood and adolescence, where they typically appear clustered together with higher blood pressure and relate strongly to obesity, and in particular central obesity.

This has been observed in the Bogalusa Heart Study, the Young Finns study and in Japan^{94,97,172,173}. There may be ethnic differences with more adverse levels of triglycerides and HDL-cholesterol in children of European extraction and a weaker relationship of obesity to dyslipidemia in girls of African origin⁹⁴. Ethnic differences in risk factors have also been identified in some Asian populations, e.g. between Caucasian populations and Chinese, Indian, and Japanese^{174,175}. Raised blood pressure, IGT and dyslipidemia also tend to be clustered in children and adolescents with unhealthy lifestyles and diets. Lack of exercise, and increased television viewing, and in older children and adolescents, habitual alcohol and tobacco use also contribute to raised blood pressure and the development of other risk factors in early life⁷. Much the same, factors continue to act throughout the life course.

As has been seen, obesity and overweight throughout the life course appears to mediate or enhance the risk of disease or risk factor prevalence associated with retarded fetal growth. The important question is whether IUGR enhances the risk of obesity itself. The evidence is conflicting and difficult to interpret⁷. Although studies have found a relationship between small size at birth and central adiposity¹⁶⁴, this is usually only found after adjustment of current size^{41,176}, and it is questioned as to whether it is appropriate to do this⁷¹. In Guatemalan adults it has been demonstrated very clearly that there is a relationship between waist:hip ratio and per cent fat according to degree of stunting in childhood, adjusted for adult age, socioeconomic status and so on, including BMI; and quite clearly those adults most severely malnourished stunted in childhood have higher waist:hip ratios¹⁷⁷. However, it is important to keep in mind that most studies find a consistent, often linear, positive relationship of BMI with birth weight¹⁷⁶.

From the perspective of older populations, a life course perspective allows one to see health differences among populations, social classes etc. as resulting from an accumulation of material disadvantages that reflect widely differing economic and social life circumstances¹⁷⁸. The clustering of risk factors, and disease outcomes in later life, represents the result of interactions of multiple disease processes throughout life, as well as more general losses in physiological functions such as some decline in immune function¹⁵².

Intergenerational effects

Young girls who grow poorly become stunted women and are more likely to give birth to low-birth weight babies who are then likely to continue the cycle by being stunted in adulthood and so on¹⁷⁹. Maternal birth size has been demonstrated in Guatemala to be a significant predictor of a child's birth size even after controlling for gestational age, sex of child, socioeconomic status, and maternal age, height, and pre-pregnant weight¹⁸⁰. During the Dutch

Famine, women who had been *in utero* in the last third of pregnancy gave birth to children with lower birth weights than normal, thus projecting the effect of the famine into the next generation¹⁷¹.

The review by Aboderin *et al.*⁷ describes the evidence of intergenerational transmission of CVD risk associated with fetal growth in humans. Low birth weight in offspring has also conversely been found to relate to parental cardiovascular mortality^{181,182}. While the mechanisms remain unclear, animal models provide evidence of such intergenerational transmission⁷. However, such relationships appear to be very complex as, e.g. in one Norwegian study that showed an impact of maternal age on risk of type 2 diabetes among children, which increased with rising birth order, but not in first-born children, but actually decreased with mothers under 30 years¹⁸³.

There are clear indications of intergenerational factors in obesity such as parental obesity, maternal gestational diabetes, and maternal birth weight. Maternal birth weight and risk of blood pressure show low maternal birth weight to be associated with higher blood pressure levels in the offspring, independent of the relation between the offspring's own birth weight and blood pressure¹⁸⁴. Several strands of evidence link IGT and fetal growth as being transmitted intergenerationally⁷. Maternal gestational diabetes leads to large birth weight leading to gestational diabetes in the offspring, and greater risk of subsequent diabetes¹⁸⁵. This risk of maternal gestational diabetes is a clear intergenerational effect with increased risk of hyperglycemia *in utero* resulting in increased risk of IGT in the offspring, and this effect has been demonstrated to be transmissible from one generation to the next²⁶. In the Pima Indians, exposure to maternal gestational diabetes is associated with a higher risk of IGT in the offspring, as well as higher risk of their developing gestational diabetes, independently of the offspring's weight¹⁸⁵. Evidence from other populations indicates that the risk of developing gestational diabetes mellitus is enhanced by maternal obesity¹⁷⁶, and short stature^{186,187}.

Using a 1958 British longitudinal cohort study, Parsons *et al.*¹²⁴ concluded that maternal weight or body mass largely explained the association between birth weight and adult BMI and may be a more important risk factor for obesity in the child than birth weight. They further suggest that intergenerational associations between the mother's and her offspring's BMI seem to underlie the 'well documented association between birth weight and BMI'¹²⁴.

Unhealthy lifestyles, in particular smoking, have a direct effect also on the health of the next generation, e.g. smoking during pregnancy and low birth weight, and the increased risk of children's diseases such as respiratory disease. A recent study from the UK demonstrated that maternal smoking during pregnancy is also a risk factor for early adult onset diabetes in their off-spring¹⁸⁸. Smoking during pregnancy may represent another important determinant of metabolic dysregulation in offspring.

It was also noted that cigarette smoking as a young adult was also independently associated with an increased risk of subsequent diabetes. A strong inverse relation between infants' birth weights and mothers' mortality from cardiovascular disease has been described, possibly representing intergenerational influences on birth weight and cardiovascular risk¹⁸¹.

The adoption of unhealthy behaviours by children and adolescents has been shown to be heavily influenced by massive marketing and media pressures, which are reinforced through peer pressure, as well as through parents' own health behaviours such as physical inactivity and their diet^{7,189}. Socio-economic status plays a major role, probably throughout the life course but certainly in adulthood, although different relationships are found in different populations and the nature and extent of the association varies depending on cohort, gender, race, life trajectories and stage in the epidemiological transition process of those involved⁷. The social gradient of unhealthy lifestyles in developing countries, just as that of the biological risk factors, is generally assumed to be opposite to that in developed countries, i.e. unhealthy diets, physical inactivity and smoking are assumed to be higher in more affluent, urban 'westernized' urban populations. While this is generally true,¹⁹⁰ the rate of shift to less well-off sections of all societies is now increasingly rapid—far swifter than the rate that occurred in the industrialized countries⁸.

Interventions throughout the life course

The evidence presented demonstrates that risk factors must be addressed throughout life course. However, the important corollary to that, is whether it is actually possible to reduce or modify these same risk factors and behaviours using a life course approach?

The evidence is clear for adults, especially in affluent males in developed countries where there has been extensive experience. There is, however, no evidence that

changing maternal nutrition, and thus impacting on birth weight, has been shown, as an intervention, to have a subsequent impact on later chronic disease outcomes of the offspring. Likewise, while there is some evidence of the possibility of changing risk factors and behaviours in children and adolescents, the impact has been shown on risk factors rather than chronic disease outcomes. With older people, there is a limited experience and documentation, although with some encouraging evidence of falling disability levels in US populations. Clearly, there are tremendous logistical and epidemiological challenges to getting the evidence basis needed. However, the existing evidence suggests that it may not be unreasonable to extrapolate to older children and adolescents from the adult experience, and the data suggest that there is a definite place to intervene in older populations, at least up to 80 years.

However, the whole point of a life course approach is to look at people more holistically (Fig. 2). Clearly, there are many other reasons to improve the quality of life of the very old, such as the increasing independence that good diet and appropriate exercise are likely to bring. Likewise, one does not need to invoke the likelihood of reduced or delayed chronic disease in their offspring to promote the best diet and health possible to pregnant women. Attention to postnatal growth increasingly appears to be critical but more complex. If an infant has been born with some degree of IUGR, should we not then recommend catch-up growth for fear of encouraging chronic diseases later? Several studies have described associations between higher birth weight (or other early growth indices) and later ovarian, prostate and breast cancer¹⁹¹. However, there are other reasons, such as those to do with resistance to infectious disease, and later intellectual development and improved productivity, to suggest that maximizing growth potential, without shifting into overweight, remains an intervention objective.

It is important to emphasize the point that it is primary prevention and moving population profiles that are being

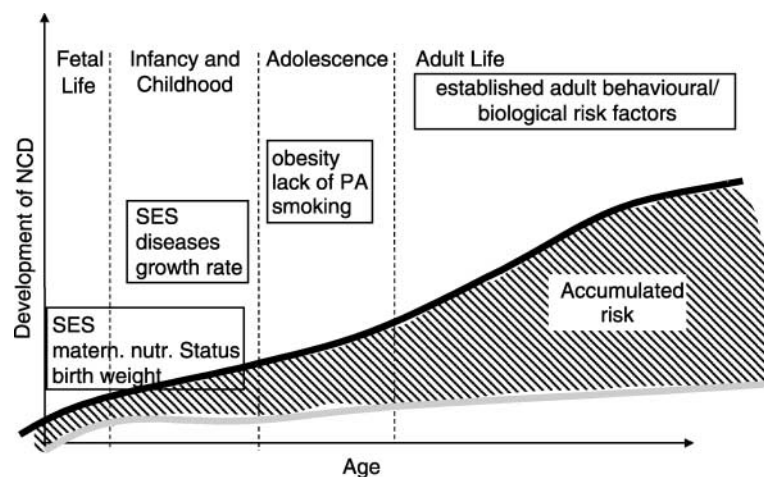


Fig. 2 Scope for NCD prevention—a life course approach. Source: adapted from Aboderin *et al.*⁷

suggested. Individual change, especially related to obesity is notoriously difficult, especially in terms of sustainability. It has been said that the ever increasing levels of overweight and obesity in the industrialized countries, and now globally, shows a singular failure of focusing on personal behaviour¹⁸⁹. Nevertheless, The Nurses' Health Study showed that the effect of a combination of lifestyle practices among women adhering to lifestyle guidelines involving diet, exercise, and not smoking, was associated with a very low risk of CHD¹⁹². Calculating from women defined as low-risk, 82% of the coronary events in the cohort might have been prevented if all women had been of the same low-risk profile¹⁹². This work was not, however, evidence of change, but of what would happen if all women adhered to certain very healthy lifestyle choices.

However, there are studies where actual change has taken place, e.g. in physical activity¹⁶², and also persuasive evidence from diabetes reduction¹⁹³. Other evidence and experience shows that it is possible to influence communities and nations^{194–198} although the suitability of this approach in developing countries has been questioned^{199,200}. Mann has suggested that the declining rates of CHD in many affluent societies and the steady global increase in type 2 diabetes mellitus, suggest differing risk and/or protective factors worldwide for the two diseases, but with the epidemic of obesity clearly a factor in the dramatic rise in type 2 diabetes prevalence¹²⁸.

The importance of a low saturated fat diet in lowering cholesterol levels in children has been demonstrated in a randomized, controlled trial amongst Finnish children²⁰¹. Primary care-based interventions when targeted properly can help prevent obesity in children from a very young age²⁰², and because children generally spend so much time in school, school based interventions are important²⁰². Singapore has successfully controlled, and even, reduced, childhood obesity rates²⁰³. Almost three decades ago the Finns successfully implemented the community-based North Karelia project¹⁹⁷. More recently, Tuomilehto *et al.*¹⁹³ demonstrated that lifestyles can reduce the risk of progression to diabetes by a striking 58% over 4 years. In this case, each person received individual counseling aimed at reducing weight, improving diet and increasing physical activity, which may limit its transferability to less affluent settings, and perhaps sustainability²⁰⁴. However, it graphically demonstrates the potential of intervening and prevention. Two earlier studies from China²⁰⁵ and from Sweden²⁰⁶ had shown similar results but with less randomized methods²⁰⁷. The recent study by the US National Institutes of Health has added further convincing evidence²⁰⁸.

Other trials and population studies have shown up to 80% of cases of CHD and up to 90% of type II diabetes could potentially be avoided through changing lifestyle factors, and about one third of cancers could be avoided by eating healthily, maintaining normal weight, and

exercising throughout the life span^{127,192,209,210}. The contribution of diet to risk of cancer in Developing Countries is lower, perhaps around 20%²¹⁰. Likewise, long term reduction in serum cholesterol concentration by 10%, which can be achieved by moderate dietary change, lowered the risk of IHD by 50% at age 40, falling to 20% at age 70²¹¹.

However, there is much general agreement that for interventions to have a lasting effect on the risk factor prevalence and health of societies, more than health education and health promotion are needed. Changing or modifying the environment in which these diseases develop is essential, and there is some evidence, e.g. Mauritius and Poland where changes in tariffs and taxes have had positive, if not always intended, effects¹²⁷. Conversely, changes in dietary patterns, the influence of advertising and the globalization of diets, and widespread reduction in physical activity have generally had negative impacts in terms of risk factors, and presumably subsequent disease. Reversing current trends will, according to Nestle and Jacobson¹⁸⁹, amongst many others, 'require a multifaceted public health policy approach as well as considerable funding'. For the latter, they suggest revenues from small taxes on selected products that supply 'empty' calories such as soft drinks, or that reduce activity such as cars¹⁸⁹.

It is clear from all the above that risk of disease is influenced by factors at all stages of the life course; that life course influences are disease specific, but that there is considerable overlap of risk factors, outcomes and influences; and that life course impacts on disease are population specific—reflecting social, economic, cultural, nutritional and probably ethnic differences. It is also clear that primary prevention at the individual, community and national level can be effective in modifying risk factor prevalence in adults. There are examples of successful primary prevention programmes in many countries in reducing mortality and morbidity due to CHD through risk factor modification, so that deaths from cardiovascular diseases have declined quite dramatically in the industrialized countries over the last three decades or so^{2,110,212}. Some recent trials examining changes in risk factors have cast doubts on the effectiveness of these multiple risk factor interventions in their present form for all populations²¹³. The workload on primary care providers such as general practitioners should also not be underestimated²¹⁴.

Government policy has an essential role in producing/-facilitating a conducive economic and legal environment for health change to happen effectively. But, as is also clear, there are obvious other good reasons, such as cost savings and personal well-being, to intervene, and more broadly to promote, and facilitate healthy diets and physical activity, and to ensure that governments and others, help provide environments in which such healthy choices are made easy. Shaw *et al.*¹⁷⁸ call for changes in

the tax structure, strengthening of health and other services, improved equity in service delivery and increasing payments through pensions, disability and social assistance, as necessary to lessen the differences in outcomes of chronic diseases over the life course. The high importance of such approaches is that they will impact on all stages of the life course and society in general. Societal shifts towards healthy behaviours tend to act on portions of the population less influenced and able to make personal change—the socially disadvantaged, adolescents and the elderly. Such shifts impact on all the population, including those hard to reach, such as adolescent mothers, and is thus an essential component of interventions addressing chronic disease in societies.

Conclusions

From all the above, it is clear that, although there is a vast volume of scientific evidence addressing a life course approach to chronic disease prevention and control, the final picture is still not complete, and even sometimes contradictory. However, from the available evidence, it is possible to state the following:

- unhealthy diets, physical inactivity and smoking are confirmed risk behaviours;
- the biological risk factors of hypertension, obesity and dyslipidemia are firmly established as risk factors for CHD, stroke and diabetes;
- globally, risk factor trends are rising, especially obesity, and in the developing countries particularly, smoking;
- the major biological risk factors emerge and act in early life, and continue to have a negative impact throughout the life course;
- they can continue to effect the health of the next generation;
- an adequate and appropriate postnatal nutritional environment is important; and,
- interventions are effective but must extend beyond individual risk factors and continue throughout the life course.

The most significant risk factors in terms of the life course are diet, physical activity and smoking. However, the effects of global transition and changing environments are critical and also need to be addressed. Very often the environmental and societal factors are modifiable, but require concerted community action and governmental support and commitment, as well as global action and partnerships. Without such societal and broader political change, it will be difficult to create an enabling environment for many lifestyle changes at the individual level—and it will increasingly be the most disadvantaged in all societies who bear the brunt of this epidemic of chronic diseases, and whose risk factors multiply and worsen one another. It is likely this article has underemphasized the enormous impact of socioeconomic status²¹⁵ because it is

generally, but probably wrongly, not seen as modifiable and of concern to public health practitioners²¹⁶.

Furthermore, the prevailing macro-structural context is clearly critical throughout the life course in the manifestation of chronic disease, and increasingly so within the developing world. As many^{18,217,218} have pointed out, it is the macro-economic and political context that determines the resources available to different groups, the resources necessary for opting for healthy or unhealthy lifestyles, the exposure to risk factors, the nature and extent of advertising, the social meaning that risk factors have for different populations, and the political will, and societal support for reducing the prevalence of risk factors.

A commentary by Kramer²¹⁹ suggested that the rising CHD prevalence in developing countries is largely explicable by adult-level risk factors with little room available for independent contributions from restricted fetal growth. He clarifies that this is not to imply there is no true (causal) effect of fetal growth on subsequent CHD, but to suggest it is dwarfed by adult lifestyle factors, such as diet, physical activity and smoking²¹⁹. Others such as Harding²⁰ conclude that altered fetal nutrition influences both fetal growth and later disease risk. However, Marmot¹⁴⁹ has emphasized the influences of both, and sees an unnecessary dichotomy in the argument. Growth factors associated with growth *in utero* or the first year of life, and contemporaneous influences, are certainly both important, and conditions throughout life determine social inequalities in adult disease. In the recent review document on programming of chronic disease by impaired fetal nutrition¹⁴, Delisle concluded that 'prevention of impaired fetal growth through improved nutrition of girls and women not only contributes to lower maternal mortality, and better child survival and development, it may also help to prevent chronic disease, and in particular, the obesity, diabetes and cardiovascular disease epidemic in developing countries'.

The prevention and control of chronic diseases should be intimately integrated into normal daily life to be sustainable. How this is to be done will vary according to culture, life stage and socioeconomic context. It is clear that disease promoting and inhibiting factors are operating throughout the life course, not least during the antenatal period. Therefore, strategies to address the major risk factors of unhealthy diet, physical inactivity and smoking must also take into account the underlying economic, gender, political, behavioural and environmental factors that foster these disease risks (Fig. 3). Furthermore, strategies must take into account the varied ways in which urbanization and globalization can predispose to risk behaviours and factors in different socioeconomic contexts and populations. Particular attention should also be paid to primary prevention strategies, including those well 'up-stream', to counter the emergence of risk factors and behaviours in childhood and adolescence, especially in developing countries.

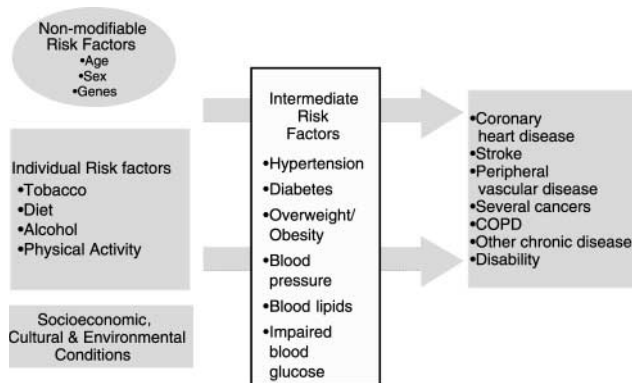


Fig. 3 CVD, cancer and chronic respiratory diseases risk factors

As the causes, stresses and changing lifestyles and environments leading to the current global epidemic act on people throughout the life course—from fetus to oldest age—so must prevention and control. Three mutually reinforcing strategies, that will have different magnitudes of impact over differing time frames, are therefore suggested as necessary and mutually reinforcing.

Firstly, and with greatest and most immediate impact is to address risk factors in adulthood, and increasingly, the elderly. Risk factor behaviours can be modified in these groups and changes seen within 3–5 years. With all populations ageing, the sheer numbers and potential cost savings are enormous and realizable. Much more effort needs to be made to make the positive experiences seen in Australia, Europe, and North America accessible to those less enabled to take advantage of the experience.

Secondly, the limited success with societal change needs to be greatly expanded as an integral part of any intervention. Ways that reduce the intake of soft drinks, cigarette smoking and high-energy diets, and increase physical activity will have an impact throughout society. Properly addressed, such social, cultural and political change will produce an environment in which those more disadvantaged and less empowered to make behavioural change will live in societies in which such change is made easier, and where healthier options are the norm. Such change, already happening in many cities and towns, needs the active, and sometimes coerced and encouraged, participation of communities, politicians, health systems, town planners and municipalities and the food and leisure industries.

Thirdly, is a more targeted, and potentially more costly approach, but with likely cost-effective returns. This approach is even longer term than that above, and again aims to change the health environment in which those most at risk, grow up. This specifically acknowledges that the greatest burden of disease will be in the developing world and in the transitional and in the industrialized world, amongst the most disadvantaged socioeconomically. This approach needs to actively target those most vulnerable, such that along with the changes outlined above, adolescent girls do not get pregnant, and if they do,

their nutritional status is such that the infant does not come from an intra-uterine environment that leads to a low birth weight and emerges into a disadvantaged environment hostile to its development and health.

The three approaches address the most numerous and the most vulnerable, but also those who have some influence on society. It might appear optimistic, but we have seen that there is enough information, and enough successful programmes around, to suggest it is possible. If not, the looming greatest burden of disease in both the industrialized and developing worlds will become the longest running and most destructive epidemic since that of the on-going undernutrition of the world's poorest children. Given both epidemics affect those most vulnerable, the two are intimately linked, both in causing disease, and how they must be addressed.

Acknowledgements

An earlier version of this paper was prepared as a background paper for the Joint WHO/FAO Expert Consultation on diet, nutrition and the prevention of chronic diseases (Geneva, 28 January–1 February, 2002) and is based on a number of WHO reports and documents, as well as a review of recent literature and expert critical reviews. The authors particularly acknowledge the contribution of the report of the WHO expert meeting on Life Course and Health (Annecy, France, 2–4 May 2001). An earlier version of this paper received helpful input from Dr Pekka Puska, Director, Department of Noncommunicable Disease Prevention and Health Promotion (NPH), WHO, Geneva, Switzerland (currently Director-General, National Public Health Institute, Helsinki, Finland), Dr Alex Kalache, Coordinator, Ageing and Life Course, NPH, WHO, Geneva, Switzerland, Professor John Powles from the Institute of Public Health, University of Cambridge, Cambridge, UK, and Dr Isabella Aboderin and Ms Ingrid Keller from NPH, WHO, Geneva, Switzerland. Nevertheless any errors or inadequacies are those of the authors. Great assistance was also provided by Mr Yasunori Miyasaka, Tohoku University School of Medicine, Sendai, Japan in undertaking part of the literature review.

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