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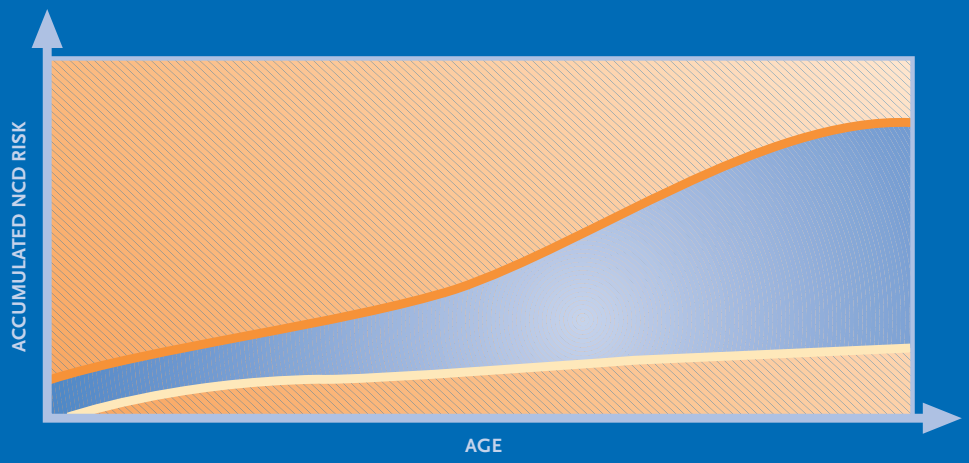
Life course perspectives on coronary heart disease, stroke and diabetes

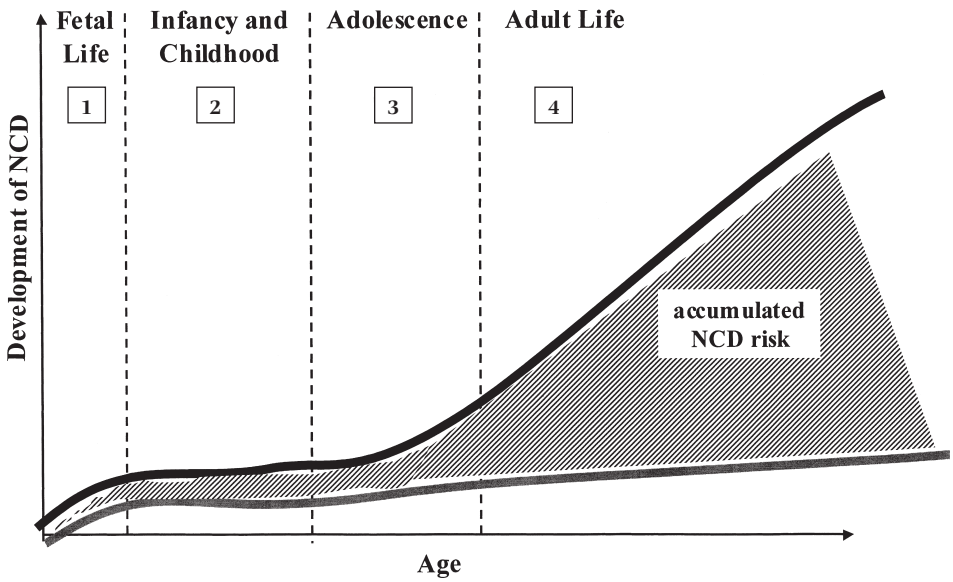


Key issues and implications for policy and research

**SUMMARY REPORT
OF A MEETING OF EXPERTS
2–4 MAY 2001**

Ageing and Life Course
Department of Noncommunicable Diseases Prevention and Health Promotion
Noncommunicable Diseases and Mental Health Cluster
WORLD HEALTH ORGANIZATION

A Life Course Approach to NCD Prevention



The risk of noncommunicable diseases accumulates with age and is influenced by factors acting at all stages of the life span. The main factors at different stages of life include the following:

1 Fetal Life

fetal growth, maternal nutritional status, socioeconomic position at birth

2 Infancy and Childhood

growth rate, breastfeeding infectious diseases, unhealthy diet, lack of physical activity, obesity socioeconomic position

3 Adolescence

unhealthy diet, lack of physical activity, obesity tobacco and alcohol use

4 Adult life

know adult behavioural and biological risk factors

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Geneva

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Copies can be obtained from:

Ageing and Life Course
Dept. of Noncommunicable Diseases Prevention and Health Promotion
Noncommunicable Diseases and Mental Health Cluster
NMH/NPH/ALC
20 Avenue Appia
1121 Geneva 27
Switzerland
Fax: +41 (22) 7914839
e-mail: leey@who.ch

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Contents

Executive Summary 1

Introduction: Setting the scene 2

Part I The life course perspective and NCD prevention: potential and challenge 5

1.1 Introduction 7
1.2 Global trends in CVD and diabetes 7
1.3 The life course perspective—potential and challenge 8

Part II Key themes and gaps in evidence on life course links to disease 11

2.1 Introduction 13
2.2 Key themes and gaps in evidence on life course links to disease 14

Part III Emerging policy implications and research priorities 23

3.1 Emerging implications and recommendations for policy 25
3.2 Key priority areas for future research 28
3.3 Conclusion: Taking policy and research agendas forward 30

Bibliography 31

Appendix A. List of participants 34

Appendix B. Programme of Meeting 35

Executive Summary

The Life Course and Health Perspective considers chronic disease in terms of the social and physical hazards, and the consequent biological, behavioural and psychosocial processes, that operate across all stages of the life span to cause or modify risk of disease.

This perspective carries a substantial potential for identifying the most appropriate and effective policies for NCD prevention and health promotion—a potential that is yet to be fully realized in public health policy.

Through the preparation for, and the conduct of a meeting of experts on life course and health (2–4 May, 2001), the WHO Department of Noncommunicable Diseases Prevention and Health Promotion (NPH) made a first step towards harnessing the potential of the life course approach for policy.

The meeting has established the state of the art knowledge regarding life course impacts on risk of coronary heart disease, stroke and diabetes and, on the basis of this, has identified emerging agendas for policy and research. The limited initial focus on three diseases was deemed necessary for the task to remain manageable. However, it provides a starting point upon which future assessments of life course and other NCDs can build.

The emerging policy recommendations follow a hierarchy according to the firmness of available evidence. The strongest recommendation, currently, is to continue the focus on the major known risk factors. In doing so, particular attention should be paid to primordial/primary prevention strategies to counter the emergence of risk factors and behaviours in childhood or adolescence, particularly in developing countries. Most importantly, such strategies must take into account the varied processes by which urbanisation and 'westernisation' can lead to risk behaviours and factors in different socioeconomic contexts and populations. It is important to recognize the cultural, economic and social circumstances within which such behaviours and risks emerge, and that these may be specific to different countries in different stages of economic development. Thus, research to inform the development of such preventive strategies in individual countries is urgently needed.

Despite the high profile of evidence linking early life factors such as reduced fetal growth to later disease, evidence is still insufficient for firm policy recommendations to be made. Further research is urgently needed to establish the relative role and importance of early life exposures, and the mechanisms by which they affect future risk of disease. Key priority areas for research have been identified.

NPH is taking forward the policy and research agendas emerging in light of current evidence on life course, through collaborative work and consultation across departments within WHO, and with outside institutions.

Introduction

Setting the scene: Purpose of the meeting

In May 2001, a first meeting of experts on Life Course and Health was convened by the WHO Ageing and Life Course Programme (ALC) in the Department of Noncommunicable Disease Prevention and Health Promotion (NPH). The main aim of the meeting was to establish the state of the art in knowledge regarding life course influences on risk of chronic disease (specifically coronary heart disease, stroke and diabetes) and, on the basis of that, to pinpoint key implications for policy and research.

An important aspect of the meeting was to specifically consider this scientific knowledge and its implications within both developed and developing world contexts.

The specific aims of the meeting were:

i. To establish what evidence currently exists regarding the role of life course influences on risk of coronary heart disease, stroke and diabetes

ii. To identify emerging indications for policy and to examine the feasibility for action/intervention/policy development

iii. To pinpoint gaps in knowledge, which need to be addressed by immediate research

iv. To stimulate policy makers to take into account the life course perspective

v. To establish a WHO expert advisory group on life course and health

In order to achieve these objectives, twenty-one experts/researchers representing both developed and developing countries (see Appendix A), were brought together in three days of structured discussions. The basic framework for the discussions were the central concepts and perspectives of a life course approach to chronic disease, as set out in a background paper prepared, in consultation with ALC, by the two main scientific advisers to the meeting: Dr. Ben-Shlomo, University of Bristol; and Dr. Kuh, University College London (see Appendix B).

The structure of the discussions was devised, in close consultation with Drs. Kuh and Ben-Shlomo, on the basis of the main themes and issues identified by the expert invitees in answer to a set of questions regarding life course research and its implications prior to the meeting. A synthesis of the experts' comments, circulated to all experts in advance, provided a main background for the discussions.

A second background paper provided a broad overview of life course research and emerging evidence in the developing world. The paper was prepared in view of the fact that, to date, no comprehensive reviews on life course research in developing countries exist. This contrasts with the growing prominence that life course research has been attaining in the developed world, reflected in the number of recent reviews (e.g Kuh and Ben-Shlomo, 1997; Kuh and Hardy, forth-

coming; Terry and Susser, 2001), as well as critical commentaries and discussions (e.g Kramer, 2000; Lucas *et al.* 1999; the Lancet, 2001)

The meeting itself consisted of five main sessions. The first four, each, focused on one of the following key biological or lifestyle related domains:

- Obesity and height in relation to CVD and diabetes
- Blood pressure in relation to CVD
- Dyslipidaemias and glucose intolerance in relation to CVD and diabetes
- Life course roots of unhealthy lifestyles (tobacco use, physical inactivity, unhealthy diet)

While there is considerable overlap between these domains, the division was deemed necessary for rendering discussions in the sessions manageable. The discussions of each domain focused on the following aspects:

- Secular trends for developed and developing countries
- Patterns with respect to gender, ethnicity, adult socio-economic status
- Life course determinants in adulthood, childhood, *in utero*, and intergenerationally
- Interactions with earlier life risk factors
- Needs for further research

A fifth session discussed the potential underlying mechanisms linking life course exposures to CVD and diabetes. Specific points considered included:

- Genetics
- Intergenerational factors (genetics; imprinting; maternal vitality; shared socio-economic status)
- Intrauterine factors; nutrition in pregnancy, fetal nutrition
- Post-natal factors; infectious disease, childhood diet, psychosocial influences, timing and duration of puberty
- Endocrine programming and modulation

The five main sessions were followed by several small-group and plenary discussions which were dedicated to teasing out emerging implications for policy and research and then developing these into firm policy and research agendas. In particular experts were asked to consider:

- Evidence for reversibility and effective interventions
- Need to modify current health policies (population and/or high risk)
- Evidence for simple policy interventions that influence pathways

This abridged report of the meeting provides an overview of the identified key themes and gaps in current understanding of the life course influences on CHD, stroke and diabetes; the emerging implications for public health policy, and the priority areas for future research.

The detailed review of the state of the art evidence on life course is presented in the full version of the meeting's report.

Structure of the report

This report is divided into two parts:

Part I provides the background to, rationale for, and nature of WHOs initiative on the life course. It begins by showing how the life-course perspective fits into, and is a vital underpinning of WHO's work on

NCD prevention and health promotion, and by briefly outlining the alarming global NCD trends, especially in CVD and diabetes, that make this work imperative. This is followed by a description of the content, focus and basis of the life course perspective, emphasizing its potential for effective policy development. Finally, the key challenges that need to be met in order to translate this potential into practice are described.

Part II provides an overview of the main conclusions emerging from the meeting's discussions. It describes the key themes, issues, and the main gaps in current knowledge regarding the influence of life course factors on disease risk.

Part III pinpoints the emerging recommendations for public health policy and, finally, highlights the priority areas for future research.

A comprehensive review of the current evidence on life course and CHD, stroke and diabetes is available in the full report: *Life Course Perspectives on Coronary Heart Disease, Stroke and Diabetes: The Evidence and Implications for Policy and Research*.

PART I

Life course as a central part of WHO's work on NCD prevention and health promotion

1.1 Introduction

The WHO initiative on life course and health is situated within, and is a central aspect of the work of the Department of Noncommunicable Disease (NCD) Prevention and Health Promotion (NPH). The department's overall goal is to prevent noncommunicable diseases and thus to reduce premature morbidity, mortality and disability caused by them. Particular focus is given to most common NCDs such as cardiovascular diseases (CVD) and diabetes, as they cause much human suffering, pose substantial threats to the economies of individual countries, and are important in the increasing health inequalities between countries and within populations worldwide.

1.2 Global trends in CVD and diabetes

Although already high, the burden of CVD and diabetes is expected to rise further in the coming decades—above all in developing countries, i.e. those countries with the least resources to effectively deal with them (see e.g. Murray and Lopez, 1996):

- In developed countries, cardiovascular diseases are and will remain the first cause of death and disability, despite the gradual decline in disease rates experienced in most of them in the last few decades. In 2000, 48.6% of deaths were caused by CVD. By 2020, still 46.4% of all deaths are expected to be attributable to CVD. Meanwhile, the number of those suffering from diabetes will have risen from 51 million in 1995 to 72 million in 2025.
- In the developing world, CVD will soon become the main cause of death and disability: by 2020, a third (33.8%) of all deaths are expected to be due to CVD. The number of those with diabetes will increase more than 2.5 times, from 84 million in 1995 to 228 million in 2025.
- It is projected that by 2020 71% of ischaemic heart disease (IHD) deaths, 75% of stroke deaths and 70% of diabetes deaths will occur in developing countries
- The current 'epidemic' in adult and childhood obesity, not just in developed but also in many developing countries may indicate even sharper rises in the burden of CVD and diabetes.

Although already high, the burden of CVD and diabetes is expected to rise further in the coming decades—above all in developing countries, i.e. those countries with the least resources to effectively deal with them.

The spectre of rising CVD and diabetes underscores the imperative need to develop effective and appropriate prevention policies, especially in poor and marginalized populations. Such policies, as has long been recognized, need to address the major risk factors predisposing to disease (the current focus is on the behavioural risk factors smoking, physical inactivity and unhealthy diet), and take into consideration underlying economic, social, gender, political, behavioural and environmental factors that foster disease risk.

However, what the most valuable concrete strategies are in different contexts and populations, whom they should be

targeted at, when and how, remains to be firmly established and will depend in large part on the cultural, social and economic conditions.

This represents the core charge of NPH's work and is the reason why NPH has adopted the life course as the underpinning perspective of its work. In doing so, WHO recognizes the potential of the life course perspective to enable policy-makers to identify the most effective and appropriate prevention strategies and to gain maximum leverage for interventions where prevention resources may be scarce.

WHO recognises the potential of the life course perspective to enable policy-makers to identify the most effective and appropriate prevention strategies and to gain maximum leverage for interventions where prevention resources may be scarce.

1.3 The life course perspective —potential and challenge

The current epidemiological focus on a life course approach to chronic disease emerged in the 1980s. However, the notion that experiences in early life shape adult health is not new. It was, in fact, a prominent perspective in public health in the first half of the century, but was superseded by the "life style" model of chronic disease which focused almost exclusively on adulthood risk factors. This was, largely, a result of the success of cohort studies in confirming, for example, smoking or high cholesterol levels as major risk factors for several chronic diseases.

The current revived emphasis on a life course perspective has arisen against a background of increasing evidence, especially from revitalised historical cohorts, maturing birth or child-cohort studies, that the risk of many NCDs such as CVD or diabetes is not just determined by risk factors in mid-adult life, but already begins in childhood or adolescence—and potentially even earlier during fetal development.

Specifically, it has been boosted by prominence given to (a) the increasing evidence on the 'tracking' of conventional risk factors from childhood to adulthood from large and extended cohort studies such as the Bogalusa Heart Study (e.g. Bao *et al.* 1994); (b) the rise of 'programming' as a model of disease aetiology, in particular the fetal origins of adult disease hypothesis (Barker, 2000); and (c) emerging evidence to indicate that some early risk factors may act across generations thus increasing cardiovascular risk in offspring (Sterne *et al.* 2001; Davey Smith *et al.*2000a).

Whilst consideration of early life factors or exposures is a main focus of the life course perspective, it is much broader than that. Its aim is to transcend the dichotomy between traditional 'adult lifestyle' and 'early origins' models of adult disease, both of which, on their own, are unable to fully explain individual risk as well as geographical, social and temporal variations in disease patterns (Kuh and Ben-Shlomo, 1998).

Thus, the life course perspective considers the social and physical hazards, and the resulting behavioural, biological and psychosocial processes, that act across ***all*** stages of the life span—gestation, infancy, childhood, adolescence, young adulthood and midlife—to affect risk of disease later on. It considers, in particular, the existence of both "critical" and "sensitive" periods throughout life where exposures are deterministic or especially powerful

in predisposing to, or lessening risk of disease later on. The term "critical period" implies exposures that must occur in some specified window(s) of time and often involve exposures that alter normal biological development. "Sensitive period" exposures refer to a broader class of influences that may have greater impact on later outcomes if they occur in certain periods than in others. In empirical terms, both critical and sensitive period exposures imply time by exposure interactions. Better understanding of critical and sensitive period exposures thus offers the potential for identifying the most appropriate and effective interventions or strategies for disease prevention or health promotion. In addition, a life course perspective on NCDs invokes concepts of "accumulation" of both correlated or uncorrelated exposures that over time additively increase the risk of adverse outcomes.

The life course perspective considers the social and physical hazards; and the resulting behavioural, biological and psychosocial processes, that act across all stages of the life span—gestation, infancy, childhood, adolescence, young adulthood and midlife—to affect risk of disease later on.

The major challenge in harnessing the potential of the life course perspective for public health policy is to fully elucidate the pathways and mechanisms by which, in different populations and at different historical periods, factors or exposures in earlier and later life act to determine subsequent risk of disease. Of particular importance is to identify the relative role of, and interaction between, earlier and later factors, and the critical periods and exposures that may shape chronic disease risk later on.

So far, and on the basis of available evidence, several theoretical models have been advanced to explain the possible ways in which factors over the life course may act to cause chronic disease (Ben-Shlomo and Kuh, 1999).

1. A critical period model—where an insult during a specific period of growth or development has a lasting, life long effect on physical functioning or structure thus resulting in disease later on.

2. A critical period with later effect modifiers—where later factors may modify such a risk earlier incurred.

3. Accumulation of risk with independent and uncorrelated results—where separate and independent risk factors at each stage of life combine to raise disease risk.

4. Accumulation of risk with correlated results—where risk factors cluster in socially or biologically patterned ways, and may raise the risk of disease through social and/or biological chains (or pathways) of risk. That is, where one adverse (or protective) experience will tend to lead to another adverse (or protective) experience in a cumulative way.

Disentangling the ways in which factors at each stage of life act or interact to shape disease risk is, obviously, complex and difficult. This is added to by the fact that explanations are not only disease specific, but may also vary from one cohort, population, or context to another. It is crucial to understand that the effects of early life exposures on later disease risk are likely to be highly contextualized in both time and space. For example, being born into poverty in Bangladesh in 2000 is likely to be associated with very different early life

exposures than being born into poverty in the USA in the 1950s. The social meaning of poverty and its life course links to particular types of exposures, as well as the prevailing disease environment will all influence the potential for early life factors to be expressed in different adverse outcomes later in life.

Despite the complexity and difficulty of the challenge, and despite the fact that work is only in its early stages, a critical mass or body of evidence, in particular from developed countries, has accumulated over the last decade.

The time is thus now ripe for taking a first step towards capturing some of the potential of the life course perspective for policy—by taking stock of what knowledge has accumulated, by considering what policy implications are already emerging, and by pinpointing the key gaps in knowledge that need to be addressed by future research.

PART II

Key themes and gaps in current evidence on life course links to disease

2.1 Introduction

Most of the relevant evidence comes either from historical or retrospective cohort studies, or from ongoing or recently established prospective birth or child cohort studies. A selection of some of the former studies, which are mostly from developed countries, include:

UK—the 1946 and 1950 birth cohorts; the Hertfordshire, Sheffield, and Caerphilly cohorts (see Leon and Ben-Shlomo, 1997); the Glasgow University Students cohort (McCarron *et al.* 1999); and the Boyd Orr cohort (Gunnell *et al.* 1998a)

US—the Harvard Alumni Studies (Paffenbarger and Williams, 1967) or Johns Hopkins Precursor Study (e.g. Klag *et al.* 1993)

Finland—the Helsinki Central Hospital Cohort (Eriksson *et al.* 1999)

Netherlands—the Dutch Famine Cohort (e.g. Ravelli *et al.* 2000)

Russia—the Leningrad Siege Cohort (Stanner *et al.* 1997).

Sweden—the Uppsala cohort (e.g. Leon *et al.* 1996, 1998)

A few such cohorts have, however, also been studied in developing countries, for example in Mysore, India (Stein *et al.* 1996; Fall *et al.* 1998) or Beijing, China (Mi *et al.* 2000).

Prospective child or adolescent cohort studies, too, are predominantly from developed countries, e.g.

US—the Bogalusa Heart Study (Berenson *et al.* 1991)

UK—the ALSPAC Study (ALSPAC, 2001)

Finland—the Young Finns Study (Åkerblom *et al.* 1999).

However, several developing country child cohort studies do exist including:

India—the Pune Birth Cohort (Bavdekar *et al.* 1999) and the Pune Maternal Nutrition Studies (Fall *et al.* 1999)

South Africa—the Birth to Ten Study in South Africa (Yach *et al.* 1991).

A few retrospective child cohort studies, such as for example in Jamaica (Forrester *et al.* 1996), the Gambia (Margetts *et al.* 1991), Zimbabwe (Woelk *et al.* 1998), or the Democratic Republic of Congo (Longo-Mbenza *et al.* 1999), have provided further evidence on early life course risk factors in developing populations.

Additional developing world insights come, moreover, from child health and nutrition surveys such as the CEBU Longitudinal Health and Nutrition Survey in the Philippines (CLHNS) (Cebu Study Team, 1991) or the INCAP Nutrition Supplementation Trial in Guatemala (Martorell, 1995). Whilst these studies did not specifically set out to investigate life course impacts on chronic disease risk, some of their findings are, nevertheless, relevant.

The experts' assessment of the currently available evidence—in their written comments prior to, and their discussions at the meeting—has clearly shown the complexity of trying to disentangle the various life course influences that act to shape the risk of CHD, stroke and diabetes. They have highlighted, in particular, the limitations imposed by the serious lack of evidence from developing countries.

Despite the complexity and limitations, however, the assessment has also shown that much knowledge has already accumulated and that it is possible to identify key themes in evidence, key

emerging implications for policy, and priority areas for future research. These are presented in the subsequent sections.

2.2 Key themes and gaps in evidence on life course links to disease

The following key themes and factors are identified as characterizing the influence of life course factors on risk of CHD, stroke and diabetes in different populations. At the same time, the main gaps in knowledge are highlighted.

2.2.1 *Key general points*

Three general, but extremely important issues regarding the use of the life course perspective for policy, warrant re- emphasis at the outset:

a. Risk of disease is influenced by factors at all stages of the life course

The risk of developing CHD, stroke or diabetes is influenced by biological or social factors acting at ***all*** stages of the life course—in fetal life, childhood, adolescence, and adulthood.

Life time risk, however, cannot simply be understood as an additive model: Earlier and later factors are likely to interact, and the consequences of some influences may depend on events at earlier (or later) critical stages of development. For example, negative consequences of fetal growth retardation appear especially in conjunction with high post-natal weight gains. The relative importance of early and later factors in causing later disease, however, is not yet fully understood.

The risk behaviours of unhealthy diet, lack of exercise, and tobacco use, and the associated biological risk factors of high blood pressure, obesity and dyslipidaemia, remain the most firmly established risk factors for CHD, stroke and diabetes.

b. Life course influences are disease specific

CHD, stroke and diabetes are likely not the results of the same processes and exposures acting over the life course. The life course influences on risk are specific for each disease, or even subtype of disease—as, for example, for haemorrhagic and ischaemic stroke—thus posing important challenges for research and for integrated policy development.

c. Life course impacts on disease are population (and cohort) specific

Life course impacts on disease cannot simply be generalized from one population to the next, or from one cohort to the next. Important differences appear to exist, reflecting either genetic differences and/or differing social, economic, cultural and nutritional contexts, and differences in the manner of gene expression across a variety of environmental conditions. What determines population or cohort differences, particularly what the relative role is of different social contexts, is not well understood, but is a key area for future research.

2.2.2 *Disease and 'established' risk factors over the life course*

a. 'Known' risk factors remain the most firmly established link to disease

The risk behaviours of unhealthy diet, lack of exercise, and tobacco use, and the

associated biological risk factors of high blood pressure, obesity and dyslipidaemia, remain the most firmly established risk factors for CHD, stroke and diabetes.

Efforts to disentangle the life course impacts on- and effects of these risk factors, especially in developing countries, are seriously hampered by the dearth of, and methodological limitations in the existing studies on their prevalence, social patterning, and trends. The latter include the inability of body mass index (BMI), as the most commonly used index of obesity, to adequately distinguish between lean and fat tissue; the methodological difficulties of accurately identifying hypertension; and the lack of appropriate population norms for both blood pressure and adiposity.

Nevertheless, several key issues can be identified.

Contrary to what was long assumed, high blood pressure, dyslipidaemia, impaired glucose tolerance (IGT) and obesity already emerge in childhood and adolescence, and often clustered together.

b. Rising risk factor trends: obesity and tobacco use

The little evidence that exists shows that in the developing world, the prevalence of the major risk factors obesity and tobacco use is rising.

In developed and developing populations the prevalence of obesity among both adults and children has shown sharp increases, somewhat offsetting the progress made with some of the other biological risk factors in many countries. The rise in obesity particularly, is a reflection of the increased marketing and availability of a westernised diet rich in refined foods, saturated fats, sugar and salt (the 'nutrition transition'), as well as changes in lifestyles towards decreased physical activity.

Tobacco use, though declining in some, mainly developed country populations, is showing alarming rates or increases in others. A particularly worrying trend is the marked rise in smoking amongst women and teenagers in many developing and developed countries.

c. Major biological risk factors emerge and act in early life

Contrary to what was long assumed, high blood pressure, dyslipidaemia, impaired glucose tolerance (IGT), and obesity already emerge in childhood and adolescence, and are often clustered together. Obesity, especially abdominal adiposity, seems to play a central role in the development of the other factors, although some race and gender differences in the clustering of risk factors do appear to exist.

Three critical periods or exposures in early life appear to increase the risk of developing obesity that persists into adulthood: 1) exposure to gestational maternal diabetes and high birth weight; 2) an early adiposity rebound (the age at which BMI increases after its nadir in early childhood), and 3) development of obesity in adolescence. The mechanisms underpinning these apparent associations are not yet understood.

The presence of risk factors ***early*** in life already influences risk of later disease, either through the social and biological tracking of these behaviours over time, and /or through their direct biological effects. Obesity, high blood pressure and dyslipidaemia track from childhood through to adolescence and young adult-

hood, where they lead to atherosclerosis and, in many cases, diabetes. The presence of risk factors in adolescence or young adulthood (e.g. high blood pressure) has additionally been shown to independently predict an increased risk of CVD later on.

The relative predictive power of risk factors present in childhood, compared to risk factors in mid-life will depend on the disease concerned. In many cases, however, it is indicated to be equal, if not stronger, than that of risk factor presence in mid-adulthood.

What is not yet understood, for example in the case of blood pressure, is the relative importance of long-term exposures to raised levels as opposed to acute high transient levels. In the case of obesity and insulin resistance syndrome it appears that long-term exposure to obesity has an aggravating effect. Risk factors in early life, particularly tobacco use and obesity, moreover, not only affect one's own later health but also the health of the ***next generation***.

The prevalence of behavioural or biological risk factors is clearly influenced by socio-economic position over the life course.

Obesity, especially in mothers, for example, clearly increases the risk of obesity and, consequently, disease risk in their offspring.

Similarly, tobacco use during pregnancy is strongly linked to low birth weight and associated disease or mortality risk in the offspring. Parental smoking, moreover, exposes children to environmental tobacco smoke (ETS), and thus an increased risk of asthma, certain infections and reduced lung functioning.

2.2.3 *Disease and unhealthy lifestyles over the life course*

a. Unhealthy lifestyles drive the emergence of disease risk in early life

Unhealthy lifestyles—tobacco use, physical inactivity and unhealthy diet (a diet high in sugar, saturated fat, salt and calorie content)—are already taken up by children, leading to the early development of obesity, high blood pressure, dyslipidaemia, IGT and the associated disease risk. In addition, unhealthy lifestyles in early life, for example physical inactivity, are shown to independently predict later CVD—regardless of their presence in mid or late adulthood.

Unhealthy lifestyles are taken up by children or adolescents largely as a result of massive marketing and media pressures, as well as parents' own health behaviours. Parents' lifestyles, for example, have an important impact on children's dietary habits, level of physical activity, and uptake of tobacco use.

b. Socioeconomic position over the life course influences risk factor development

The prevalence of behavioural or biological risk factors is clearly influenced by socio-economic position (SEP) ***over the life course***. In adults, for example, the prevalence of risk factors is not just determined by adult SEP, but also by their socioeconomic position in childhood and the different social trajectories that individuals traverse as they become educated, enter the labour market, generate income, change jobs, and gather assets.

In developed countries, prevalence of

risk behaviours and factors among adults, just as prevalence of disease, is generally higher among those from lower socio-economic strata. Similarly, it is typically poorer childhood SEP that is associated with more risk behaviour, suggesting that early socio-economic disadvantage may increase later disease risk through developmental processes whereby children adopt particular detrimental behaviours and attitudes.

Poor early SEP can also have inter-generational effects on disease risk. Among young females in Japan, for example, raising SEP through education has been shown to not only decrease their own risk of disease, but also that of their offspring in the next generation. (Hasegawa, personal communication)

The processes by which 'urbanisation' and 'development' lead to increased risk cannot simply be assumed to be the same across different societies.

The general developed country pattern of low SEP = high risk, however, clearly does not hold in all cases. The effect, detrimental or protective, of SEP on risk behaviours can differ considerably between populations, ethnic groups, cohorts and genders. For example, among older women cohorts, low early SEP was shown to protect against smoking, whereas among younger cohorts at present it is associated with an increased risk.

In developing countries the social gradient of disease risk is commonly assumed, and often found to be opposite to that in developed countries. Risk factors are often highest in those population groups that are the most westernised or modern—i.e. the affluent, urban population. However, the patterns of risk are at times more complex and do not follow this uniform pattern. Obesity, for example, is emerging as a serious problem among the poor in Latin America. In India, smoking rates are found to be higher in rural than in urban areas.

c. Importance of the macro-structural context

The specific socio-economic and rural-urban risk factor patterns that prevail in different populations are shaped, to a large degree, by the underlying macro-structural context—the prevailing social, economic, political and cultural forces. These forces determine the exposure to risk inducing environments, the resources necessary and available to opt for healthy lifestyles, and the social meaning that risk behaviours have for different population groups.

For the developing world in particular, this means that the processes by which 'urbanisation' and 'development' lead to increased risk cannot simply be assumed to be the same across different societies.

d. Additional influence of poor childhood SEP

The relationship of poor early SEP to risk factors or behaviours only partly explains its association to later disease. The clear link of lower early SEP to CHD and stroke, which is reflected in the consistent association shown between short stature (i.e. impaired linear growth) and these diseases is possibly mediated by two other factors.

Infectious factors

A first factor thought to possibly underpin the association of poor childhood SEP to CVD is early exposure to infectious agents. The specific bacterial pathogens

that appear linked to poor conditions and have so far been implicated include *Helicobacter pylori* and *Chlamidia pneumoniae*, though evidence is far from conclusive.

A further, possibly infectious but yet unidentified factor is assumed to underpin the particularly consistent association that is seen between poor childhood SEP and haemorrhagic stroke.

The possible role of other infectious agents in the development of chronic disease risk, especially in developing countries where infectious disease is still pervasive, has not yet been explored.

Nutritional factors

A further indirect way in which childhood deprivation, especially nutritional deprivation, may be associated to a raised disease risk, is through the apparent association between stunting (especially severe stunting) and an increased risk of (abdominal) adiposity. This association is possibly due to impaired fat oxidation in stunted children and a consequent increased susceptibility (in terms of weight gain) to high fat 'urban' diets.

A link between stunting and risk of central adiposity would be of particular importance in those developing countries who have recently or are currently undergoing the 'nutrition transition.

In addition to factors in childhood and adolescence, factors relating to fetal growth are clearly involved in shaping risk of disease.

2.2.4 *Disease risk and protective factors in childhood*

a. Breastfeeding

In contrast to the detrimental effects of unhealthy diet and lack of exercise in childhood, breast-feeding is indicated to have a protective effect on the development of disease risk.

Apart from its well-established short term benefits for child health and development, breast-feeding is increasingly indicated to confer a lower risk of high blood pressure, as well as of dyslipidaemia and obesity. However, this protective effect is not yet unequivocally established, as some weak evidence of a long-term negative impact of breastfeeding on CVD risk exists.

2.2.5 *Disease, risk factors and fetal growth*

In addition to factors in childhood and adolescence, factors relating to fetal growth are clearly involved in shaping risk of disease.

a. Fetal growth and later disease

In many populations intrauterine growth retardation (IUGR) (as indexed by small size at birth or exposure to famine in gestation) is shown to be associated with a higher risk of CHD, stroke and diabetes. This association forms the basis of the 'Barker' or the 'Fetal Origins of Adult Disease' (FOAD) hypothesis. Some evidence suggests moreover that this risk may be transmitted intergenerationally.

At the same time, however, large size at birth, too, is found to be linked to an increased risk of diabetes or CVD. Thus, the relationship of fetal growth to later disease is, in fact, U-shaped. This effect of fetal overnutrition is important to bear in mind, particularly in view of the current prominence of the FOAD hypothesis

b. Fetal growth, blood pressure, dyslipidaemias and impaired glucose tolerance (IGT)

In addition to its link to adult disease, IUGR is clearly found, in both adults and children, to be associated to a higher risk of high blood pressure and impaired glucose tolerance. Its association to the most important dyslipidaemias (i.e. high triglyceride and low HDL-c levels) is less clear cut.

At least in a statistical sense, the association of IUGR to these biological risk factors does not appear to mediate its link to CVD, though this may reflect the limitations of available data. In the case of diabetes, a mediating effect of the association to IGT seems more indicated.

c. Population and cohort differences: importance of the post-natal context

Though associations between IUGR and disease risk are found in most populations studied, some evidence shows conflicting results, indicating the existence of important population and cohort differences in the relationship of fetal growth to later disease. Examples include the apparent lack of an association between small size at birth and diabetes in Indians; the absence of a relationship between IUGR and blood pressure in some black populations; and the divergent relationship between IUGR and impaired glucose tolerance in children and adults in India.

These population and cohort differences may reflect underlying genetic differences, expression of genes, and/or the impact of divergent post-natal contexts and environments. The latter may reflect differences in a particular populations' stage of the epidemiological or nutritional transition or, between cohorts of the same population, the result of rapid social and economic change.

d. Interaction between IUGR and later weight or height gained: importance of post-natal nutrition

Increasing evidence indicates the association between IUGR and later disease risk is somehow mediated or enhanced by the rate of growth in weight or height in childhood or adolescence.

The apparent role of growth in weight or height is indicated by three factors:

- in most cases significant associations between low size at birth and later disease risk factor are only found *after* adjustment for current weight
- in many cases the association between low birth weight and disease risk is strongest in those with highest BMI or fatness
- in some studies the association between IUGR and disease risk is shown to be highest in individuals who have had accelerated growth in height to become tall.

It is not yet clear how this apparent effect of post-natally gained weight or height is to be interpreted, but four (not mutually exclusive) interpretations are possible:

i. It represents a negative effect of enhanced growth in childhood or adolescence *per se*. In other words, accelerated growth in weight (or height) itself could have negative consequences.

ii. It is the *difference* in size between birth and the later stage that better defines detrimental impaired early growth: the higher the difference, the higher the risk (see e.g. Lucas *et al*. 1999).

iii. Obesity reveals/activates an underlying susceptibility induced by impaired early growth and, vice versa, low birth

weight enhances the risk associated to obesity, i.e. obesity is particularly harmful in those with early growth retardation.

iv. The effect of enhanced growth in height in IUGR babies may reflect a failure of the fetus to realise its genetic growth potential *in utero*, possibly due to placental failure. It may be this insult on fetal growth that underlies the increased risk of disease (e.g. Leon *et al*. 1996).

Whilst the particular interpretation may depend on the specific disease or risk factor concerned, they all indicate the importance of an adequate post-natal nutritional environment in bringing to the fore a risk associated with fetal growth retardation.

Further evidence for this comes from the discrepant findings of the two existing famine studies. Whereas an associations between exposure to famine and later disease risk were found in the Dutch famine, which was followed by a period of adequate nutritional supply, no association was found in the Russian famine, which was followed by a long period of inadequate nutritional supply. Another indication of the importance of the post-natal nutritional context are the marked rural-urban differences in CVD and diabetes risk, for example in India. While low birth weight is more common in rural areas, disease risk is much higher in the nutritionally more adequate urban areas (e.g. Yajnik, 2000).

e. IUGR and increased risk of obesity—a paradox?

The crucial question of whether IUGR also enhances the risk of obesity in a nutritionally rich post-natal environment (i.e. the thrifty phenotype hypothesis) is still unresolved.

The available evidence is inconclusive and presents a paradox by consistently showing a positive, often linear, relationship between birth weight and obesity (BMI) which is difficult to reconcile with the association between low birth weight and higher risk of disease.

A possible explanation of this paradox may lie in the inadequacy of BMI to adequately measure fatness, thus disguising a possibly important relationship between low birth weight and greater risk especially of central body fat.

f. Mechanisms underpinning the association of fetal growth to disease risk

The mechanisms and processes underpinning the association between retarded fetal growth and later disease risk remain poorly understood.

The mechanisms and processes underpinning the association between retarded fetal growth and later disease risk remain poorly understood.

The generation of a greater understanding has, amongst others, been hampered by the somewhat haphazard use of multiple measures of birth size, and by the limitations of low birth weight (the currently most commonly used index of fetal growth retardation) as an adequate marker to capture the range of possibly important exposures or birth outcomes.

The main unresolved issues include the following:

- the relative role of environmental versus genetic exposures
- the nature and role of intergenerational transmission of risk,

including the role of maternal gestational diabetes, and parental body size and nutritional history

- the nature of the exposures that may lead to detrimental fetal growth retardation in particular the role of maternal nutrition in this
- the potential importance of the timing of insults *in utero*
- the potential endocrine, metabolic and haemodynamic adaptations that may occur in the fetus in response to insults, in particular the population relevance of the apparently important adaptations in the cortisol stress response system.
- the nature and significance of the apparent mediating effect of rapid post-natal weight and height gain, including the questions as to why catch-up growth is detrimental? and whether it has to occur in a specific period to be detrimental?

In many populations, fetal undernutrition may increase susceptibility to the adverse effects of life style or environmental change. In addition, it may have a potentiating effect on the risk of disease associated with obesity.

2.2.6 *Importance of fetal vs. post-natal factors for population trends in disease*

a. A greater importance of post-natal factors

The clear association of both fetal and of post-natal factors (incl. the classical established risk factors) to risk of CHD, stroke and diabetes raises the crucial question as to the relative importance of fetal vs. later factors in determining population patterns and trends in disease.

The evidence so far points to a limited role of fetal factors. Serious doubts exist concerning the causality of their association to disease, and indications are that their population attributable risk is small. The rapid increases as well as the social patterns of risk factors, CVD, and diabetes in developing countries, are clearly not explained by changes in fetal growth. Impaired fetal growth (low birth weight) has been pervasive for a long time whereas the epidemic in CVD and diabetes are a recent occurrence. In most countries, moreover, disease rates are much higher in urban areas although birth weights are much lower in rural areas.

The temporal trends and patterns of risk factors and disease in populations thus seem largely related to changes in post-natal lifestyle and environment. The period in which the trends, for example of CVD in developing countries, have evolved is too short for any changes in the gene pool to account for them.

b. Interaction (potentiating effect) between fetal and post-natal effects

Despite questions over the limited direct role of fetal factors in determining trends and patterns of disease, they may nevertheless have a potentially important influence if their effects depend in part on interactions with exposures in later life. The association of IUGR to risk factor development as well as its apparent interaction with obesity to enhance risk of disease suggests that, in many populations, fetal undernutrition may ***increase susceptibility*** to the adverse effects of life style or environmental change. In addi-

tion, it may have a ***potentiating*** effect on the risk of disease associated with obesity. These effects, given the apparent intergenera-tional transmission of risk associated to fetal growth, may last not just for one, but for several generations.

A potentiating effect of fetal growth retardation (which in statistical analyses would manifest in steeper slopes in the link between obesity and disease found in developing compared to developed countries) would have grave implications for the expected future rates of disease in the developing world.

PART III

Emerging policy implications and research priorities

3.1 Emerging implications and recommendations for policy

In light of their assessment of the state of the art evidence regarding life course links to the risk of CHD, stroke, and diabetes, several implications for policy have been identified by the experts, and a set of firm recommendations have been made.

3.1.1 *The challenge for integrated policy*

Whilst carrying a great potential for disease prevention, the move from research to policy based on the life course impacts on disease presents a great challenge. The disease specific nature of life course impacts on disease risk means that integration of policies may be difficult. There are no simple models such as, for example, in the case of tobacco.

Policies specifically geared to reducing the risk of one disease, may have no, or even adverse effects on the risk of another. Policies may, moreover, have different effects in different settings and cohorts, and could have possible unintended detrimental outcomes in the short term.

Much more, therefore, needs to be known about the life course influences on various diseases, in particular what aspects may be common to them, what trade-offs exist between short and possible long-term outcomes, and what effects prevail in different environmental contexts and in different cohorts. This notwithstanding, some clear implications and recommendations for policy already emerge.

The major known risk behaviours—unhealthy diet, physical inactivity and tobacco use—and the associated biological risk factors of obesity, high blood pressure, dyslipidaemias should remain the focus of prevention policy.

Given that the scientific knowledge on life course and disease is still evolving, these recommendations are placed in a hierarchy according to the firmness of currently available evidence.

1. Firm positive recommendations for policy

Continue focus on major known risk factors

The major known risk behaviours—unhealthy diet, physical inactivity and tobacco use—and the associated biological risk factors of obesity, high blood pressure, dyslipidaemias, remain the most firmly established causal factors for CHD, stroke and diabetes. These factors should therefore remain the focus of prevention policy.

Fetal factors, given their potential importance in shaping risk of disease, also need to be considered. Above all, efforts are needed to develop a fuller understanding of the nature and basis of their effect.

Prevention policies should specifically ***focus on tobacco use*** and ***obesity***.

Prevention of tobacco use and, perhaps more importantly, reductions in total exposure to smoking over the life course by encouraging young adults to stop, must be a priority given its clear and reversible link to CVD and certain cancers; its alarming and rising prevalence among women and youth in many countries; and its detrimental effect not only on the health of those who use tobacco but also of the next generation.

A focus on obesity prevention is needed in view of the alarming global rises in its prevalence; its central role in

the development of other risk factors; its potential interaction with retarded early growth to enhance disease risk; and finally its adverse effect also on the health of the subsequent generation.

In developing countries, obesity prevention policies must go hand in hand with strategies to prevent undernutrition.

Need for strategies of primary and primordial prevention

Given that risk behaviours and factors are more commonly established in childhood and adolescence and 'track' through to adulthood, and given the difficulty of reversing especially obesity in adulthood, strategies of primary and primordial prevention are of utmost importance—though high risk lifestyle intervention strategies can clearly also be effective.

Primary prevention strategies should be aimed particularly at children, and preferably involve school-based health education and promotion programmes, focusing on behavioural and psychosocial components and aimed at promoting healthy diets, exercise and reduced tobacco use. Such strategies must be appropriate and responsive to the particular setting and to the prevailing cultural perceptions, for example regarding body weight.

Strategies of primary and primordial prevention are of utmost importance.

Targeting primary prevention policies at the following groups may be beneficial:

- Young girls or women. Preventing tobacco use will not just reduce their own risk of disease but also the risk of low birth weight and later disease risk in their offspring. In the same vein, preventing obesity in girls or young women will not just benefit their own health, but also the risk of obesity and associated disease in their children. Given the critical effect of obesity development in adolescence, policies may perhaps focus particularly on pre-puberty girls
- Those socially or biologically disadvantaged from early life, for example, those with low birth weight, stunting, or exposed to gestational maternal diabetes, or with parents who are obese
- Youth at those ages where particular 'lifestyles' are adopted, i.e. where 'programming of lifestyle' occurs
- Adolescents and young adults who already smoke should be specifically targeted by efforts to help them quit smoking—the earlier one quits the greater the benefit

Primary prevention strategies must be underpinned and complemented by **policies of primordial prevention**. Such policies must address the various macro-structural social, economic, and cultural forces that influence and determine (or protect from) the uptake of risk behaviours among different populations in different settings, in particular in the developing world. Specifically, such policies should aim at:

- Reduction of advertising or positive cultural representations of known risk factors—e.g. tobacco or unhealthy foods
- Wide use of smoke-free environments
- Fiscal policies to reduce smoking
- Promotion of public healthy food policies
- Reduction of the influence of big

food corporations, especially on the young

- Encouragement of public and private partnerships. This is the most realistic and promising way to move forward on creating healthy developmental environments, in particular with regard to adoption of risk behaviours such as tobacco use, poor diet and lack of physical activity.

Reduction of poverty

Reducing poverty and increasing education will improve children's health trajectories both in relation to infectious and non-communicable diseases. Among girls, such strategies will not just improve their own health trajectories, but also that of their offspring in the next generation.

Policies, specifically to prevent severe undernutrition and stunting—as have already been successfully pursued in some populations—are likely to increase work capacity, intellectual functioning and educational achievement, and reduce risk of developing central adiposity. By additionally lowering the risk of low birth weight in offspring, such interventions may also reduce disease risk in the next generation. Concrete interventions, thus, could thus take the form of public support for nutrition programmes from infancy through school.

2. Unspecified recommendations

No clear direction regarding fetal growth

Despite the high profile of evidence linking early life factors such as impaired fetal or childhood growth to risk of later disease, no firm policy recommendations can yet be made.

First, there are potentially important short and long-term negative effects and trade-offs of strategies to increase fetal growth. For increased fetal growth these include, in the short term, a raised risk for obstetric complications through growing larger babies in many developing populations. In the long term they may cause a possibly increased risk of other chronic diseases: higher birth weight and stature, for example, are associated with a higher risk of some neoplasms.

Second, the U-shaped relationship between size at birth and risk of later diabetes or CVD, as well as the existence of apparent population and cohort differences in the association between fetal growth and later disease, indicate that no clear direction can yet be given in terms of what is the 'optimum' birth size to target for.

Third, current evidence casts serious doubt on the feasibility and effectiveness of currently available interventions to modify fetal growth, in particular through maternal nutrition. Some strategies such as protein supplementation of maternal diet have, moreover, been shown to have negative effects including increased fetal mortality and reduced birth weight.

No direction on initiation, duration and exclusivity of breastfeeding

Though breastfeeding seems promising as a protective factors against CVD and diabetes risk, the existence of evidence suggesting also potentially adverse long term consequences means that no specific recommendations can yet be made regarding initiation, duration and exclusivity. However, given its indisputable benefits to overall childhood mortality, unqualified support is given to breastfeeding *per se*.

Reducing stress

There is some, though weak, evidence to suggest that general strategies to reduce stress in the adult environment (e.g. in

the workplace) may be beneficial in reducing CVD risk—perhaps especially in poor populations, exposed to undernutrition *in utero*.

3. Firm negative recommendations for policy

Do not discourage post-natal growth

Despite the existence of evidence showing that under certain conditions, enhanced growth (in weight or height) in childhood may be linked to a higher risk of insulin resistance or cardiovascular disease, this long term effect is outweighed by a far greater and more certain and scientifically established benefit in the short term for child health, through its links for instance with greater resilience to infectious diseases. Moreover, it is not yet clear in what particular period in childhood rapid growth has a detrimental effect. Strategies to reduce such growth are therefore, at this point, clearly not recommended.

3.2 Key priority areas for future research

The many gaps remaining in our knowledge of how early and later factors impact on risk of CHD, stroke and diabetes, highlight the vital need for more research. Only further research will be able to provide the information base necessary for effective and appropriate policy development in different populations.

The following four key areas have been identified by the experts as priority topics for future research:

1. **Research on causes and interactions**
2. **Trends analysis and surveillance**
3. **Intervention research**
4. **Refinement of methodology**

1. Research on causes and interactions

The core focus of, and challenge for future research must be efforts to investigate the early and later causes and interactions of life course links to later disease. Such research must address the following questions:

a. *The nature of the effects of fetal and post-natal growth on later disease risk*. This includes the interaction between intrauterine growth retardation and rapid post-natal catch-up growth, and obesity

b. *The influence of maternal factors on fetal growth and offspring's risk of disease*. This includes maternal nutrition, GDM, maternal cardiovascular function and maternal psychosocial factors

c. *The biological mechanisms underlying the association of fetal growth to later disease risk*. This includes the role of stress and hormonal response systems, and intergenerational processes of risk transmission

d. *The association of infectious disease to chronic disease risk*. This includes the possibly infectious factor underpinning the particularly strong link of poor child SEP to haemorrhagic stroke

e. *The social, psychological, economic and biological processes leading to unhealthy lifestyles and risk factors in different populations*

f. *The relative importance of early vs. later life exposures on risk of disease* at individual and population level

g. *The major risk factors for CVD and diabetes in developing country populations*

Ideally, such research would involve:

- Well designed **prospective maternal and birth (or child) cohort stud-**

ies, to generate integrated life time measures of growth, risk factors, socio-economic, and psychosocial parameters. One opportunity in this respect would be extension of the WHO road to health studies of child health and growth studies, beyond the age of five.

- **Historical cohort studies** with available data sets on early growth parameters. Possible examples include the Bambui or Pelotas longitudinal study cohorts in Brazil, or possibly a cohort from the 1956 famine in India. Potentially valuable cohorts may also be identified from past monitoring studies on maternal and/or child growth and development, especially in developing countries. Efforts are necessary, in this respect, to preserve and make such existing data sets accessible.
- **Multi-generational studies**, especially of migrants (and those remaining in the country of origin). The by now three generations of Asian migrants in the U.K., as well as Japanese migrants in Brazil may provide important opportunities for this.

2. Trends analysis and surveillance

Investigations of causes and interactions of life course links to later disease must be complemented by research to establish and analyse trends in risk factors and disease This would specifically involve:

a. *Surveillance of trends and socio-economic patterns in major risk factors*

b. Surveillance of trends and patterns in *maternal and child health, nutrition and growth*

3. Intervention research

Investigations of causes and interactions, and surveillance and analysis of trends must be complemented by research to asess the potential effectiveness and impact of interventions. This specifically includes:

a. *Comprehensive policy reviews on actions targeting under- and over-nutrition in developing countries*

b. *Investigation of the efficacy, long and short term effects (on both mother and child) of interventions to increase birth weight*

c. *Investigation of the short and long-term outcomes of enhanced early growth for infants born small*

d. *Establishment of the long term effects of breastfeeding with regard to non communicable diseases*

e. *Research to identify ways of applying current knowledge to prevention programmes*

4. Methodological issues

Finally, for life course research to be as effective as possible, efforts are necessary to improve on existing, or foster certain methodologies. This involves:

a. *Improvement of measures of intra-uterine growth retardation (alternatives to low birth weight)*. These must reflect new born body composition and fetal exposures that may not necessarily be expressed in birth size.

b. *Improvement of measures of early socio-economic disadvantage and psychosocial experiences*

c. *Improvement of measures for adiposity, and establishment of appropriate population norms across the life course*

d. *Improvement of reliability and accuracy of measures for blood pressure and establishment of appropriate population norms*

e. *Development of specific measures for underlying pathophysiological factors, e.g. endothelial dysfunction*

f. *Conduct of comparative research between populations at different stages of the epidemiological/nutritional transition, as well as between cohorts*. Comparative analyses can powerfully illuminate the role of the postnatal environment in shaping disease risk in interaction with early growth experiences.

3.3 Conclusion: Taking policy and research agendas forward

The experts' recommendations on policy and research in light of current evidence on the life course links to CHD, stroke and diabetes present a vital starting point for harnessing the potential of the life course perspective to identify the most appropriate and effective prevention policies in different populations.

WHO, together with the group of experts who are committed to guiding and supporting its efforts, is taking steps to foster this life course initiative, through collaborative work and consultation across departments within WHO and with partner institutions.

A specific focus of this work will be the development, in consultation with the experts, of a protocol for a multi-centre comparative study to address some of the key gaps in knowledge on life course and NCD risk in different populations—especially in developing countries.

Bibliography

Åkerblom, H.K., Viikari, J., Raitakari, O.T., Uhari, M. (1999) "Cardiovascular Risk in Young Finns Study: General Outline and Recent Developments" *Ann Med* 31 Suppl.1: 45–54

ALSPAC (2001) "ALSPAC: The Avon Longitudinal Study of Parents and Children: Aims and Study Design" [Internet—WWW, URL] http://www.ich.bris.ac.uk/ALSPACext/MainProtocol/Default.htm (28th February, 2001)

Bao, W., Srinivasan, S.R., Wattigney, W.A., Berenson, G.S. (1994) "Persistence of Multiple Cardiovascular Risk Clustering Related to Syndrome X from Childhood to Young Adulthood: the Bogalusa Heart Study" *Arch Intern Med* 154: 1842–1847

Barker, D.J.P. (ed.) (1992) *Fetal and Infant Origins of Adult Disease*. London: BMJ Books

Barker, D.J.P. (ed.) (2000) *Fetal and Infant Origins of Adult Disease*. London: BMJ Books

Barros, F.C., Victora, C.G., Vaughan, J.P., Tomasi, E., Horta, B.L., Cesar, J.A., Menezes, M.B., Halpern, R., Post, C.L., del Mar Garcia, M. (2001) "The Epidemiological Transition in Maternal and Child Health in a Brazilian City, 1982–93: a Comparison of Two Population-Based Cohorts" *Paediatr Perinat Epidemiol* 15: 4–11

Bavdekar, A., Yajnik, C.S., Fall, C.H.D., Bapat, S., Pandit, A.N., Deshpande, V., Bhave, S., Kellingray, S.D., Joglekar, C.V. (1999) "Insulin Resistance in 8 year old Indian Children" *Diabetes* 48: 2422–2429

Ben-Shlomo, Y., Kuh, D. (1999) "A Life Course Approach to Chronic Disease Epidemiology" *Paper Presented at International Workshop 'Synthetic Biographies: State of the Art and Developments*, 6–9 June, San Miniato (Pisa), Italy

Berenson, G.S., Srinivasan, S.R., Webber, L.S., Nicklas, T.A., MacD.Hunter, S., Harsha, D.W., Johnson, C.C., Arbeit, M.L., Dalferes, E.R., Wattigney, W.A., Lawrence, M.D. (1991) *Cardiovascular Risk in Early Life: The Bogalusa Heart Study*. Current Concepts Series. Kalamazoo, Michigan: Upjohn

Cebu study team (1991) "Underlying and Proximate Determinants of Child Health: The Cebu Longitudinal Health and Nutrition Study" *Am J Epidemiol* 133: 185–201

Eriksson, J.G., Forsén, T., Tuomilehto, J., Winter, P.D., Osmond, C. (1999) "Catch – up Growth in Childhood and Death from Coronary Heart Disease: A Longitudinal Study" *BMJ* 318: 427–431

Fall, C.H.D, Yajnik, C.S., Rao, S., Coyaji, K.J. (1999) "The Effects of Maternal Body Composition Before Pregnancy on Fetal Growth: The Pune Maternal Nutrition Study" In P.M.S. O'Brien, T.Wheeler, D.J.P. Barker (eds) *Fetal Programming Influences on Development and Disease in Later Life*. London: RCOG Press: pp231–245

Forrester, T.E., Wilks, R.J., Bennett, F.I., Simeon, D., Osmond, C., Allen, M., Chung, A.M., Scott, P. (1996) "Fetal Growth and Cardiovascular Risk Factors in Jamaican Schoolchildren" *BMJ* 312: 156–160

Gunnell, D.J., Davey Smith, G., Frankel, S., Nanchahal, K., Braddon, F.E.M., Pemberton, J., Peters, T.J. (1998) "Childhood Leg Length and Adult Mortality: Follow Up of the Carnegie (Boyd Orr) Survey of Diet and Health in Pre-war Britain" *J. Epidemiol Community Health* 52: 142–152

Klag, M.J., Ford, D.E., Mead, L.A., He, J., Whelton, P.K., Liang, K.Y., Levine, D.M. (1993) "Serum Cholesterol in Young Men and Subsequent Cardiovascular Disease" *NEJM* 328: 313–318

Kramer, M.S. (2000) "Association Between Restricted Fetal Growth and Adult Chronic Disease: Is it Causal? Is it Important? " *Am.J.Epidemiol*. 152: 605–608

Kuh, D., Ben-Shlomo, Y. (eds) (1997) *A Life Course Approach to Chronic Disease Epidemiology* , Oxford: Oxford University Press

Kuh, D., Ben-Shlomo, Y. (1998) "A Life Course Approach to Chronic Disease Epidemiology—What's New?" *Paper presented at American Epidemiological Society*, March 26, Boston, Massachussetts

Kuh, D., Hardy, R. (2001) *A Life Course Approach to Women's Health*. Oxford University Press

Lancet, Editorial,(2001) *Lancet* 357 (9254) 405

Leon, D.A., Koupilova, I., Lithell, H.O., Berglund, L., Mohsen, R., Vagero, D., Lithell U-B., McKeigue, P.M. (1996) "Failure to Realise Growth Potential in Utero and Adult Obesity in Relation to Blood Pressure in 50 year Old Swedish Men" *BMJ* 312: 401–406

Leon, D.A., Ben-Shlomo, Y. (1997) "Preadult Influences on Cardiovascular Disease and cancer" in D.Kuh and Y. Ben-Shlomo (eds) *A Life Course Approach to Chronic Disease Epidemiology*. Oxford: Oxford University Press, pp.45–77

Leon, D.A., Lithell, H.O., Vagero, D., Koupilova, I., Mohsen, R., Berglund, L., Lithell, U.B., McKeigue, P.M. (1998) "Reduced Fetal Growth Rate and Increased Risk of Death from Ischaemic Heart Disease: Cohort Study of 15000 Swedish Men and Women born 1915–29" *BMJ* 317: 241–245

Longo-Mbenza, B., Ngiyulu, R., Bayekula, M., Vita, E.K., Nkiabungu, F.B., Seghers, K.V., Luila, E.L., Mandundu, F.M., Manzanza, M. (1999) "Low Birth Weight and Risk of Hypertension in African School Children" *J Cardiovasc Risk* 6: 311–314

Lucas, A., Fewtrell, M.S., Cole, T.J. (1999) "Fetal Origins of Adult Disease—The Hypothesis Revisited" *BMJ* 319: 245–249

Margetts, B.M., Rowland, M.G.M., Foord, F.A., Cruddas, A.M., Cole, T.J., Barker, D.J.P. (1991) "The Relation of Maternal Weight to the Blood Pressure of Gambian Children" *Int J Epidemiol* 20: 938–943

Martorell, R. (1995) "Results and Implications of the INCAP follow-up Study" *J Nutr* 125 (suppl.4) 1127S–1138S

Martorell, R., Stein, A.D., Schroeder, D.G. (2001) "Early Nutrition and Later Adiposity" *J Nutr* 131: 874S–880S

McCarron, P., Davey Smith, G., Okasha, M., McEwen, J. (1999) "Life Course Exposure and Later Disease: A Follow-up Study Based on Medical Examinations Carried Out in Glasgow University (1948–1968) *Public Health* 113: 265–271

Mi, J., Law, C.M., Zhang, K-L., Osmond, C., Stein, C.E., Barer, D.J.P. (2000) "Effects of Infant Birthweight and Maternal Body Mass Index in Pregnancy on Components of the Insulin Resistance Syndrome in China" *Ann Intern Med* 132: 253–260

Murray, C.J.L., Lopez, A.D. (eds) (1996) *The Global Burden of Disease. A Comprehensive Assessment of Mortality and Disability from Disease, Injury and Risk Factors in 1990 and Projected to 2020*. World Health Organization, Geneva

Paffenbarger, R.S., Williams, J.L. (1967) "Chronic Disease in Former College Students V. Early Precursors of Fatal Stroke" *Am J Public Health* 57: 1290–1299

Ravelli, A.C., van der Meulen, J.H., Osmond, C., Barker, D.J.P., Bleker, O.P. (2000) "Infant Feeding and Adult Glucose Tolerance, Lipid Profile, Blood Pressure, and Obesity" *Arch Dis Child* 82: 248–252

Stanner, S.A., Bulmer, K., Andrés, C., Lantsena, O.E., Borodina, V., Poteen, V.V., Yudkin, J.S. (1997) "Malnutrition in Utero as a Determinant of Diabetes and Coronary Heart Disease in Adult Life: The Leningrad Siege Study" *BMJ* 315: 173–177

Stein, C.E., Fall, C.H.D., Kunaran, K., Osmond, C., Cox, V., Barker, D.J.P. (1996) "Fetal Growth and Coronary Heart Disease in South India" *Lancet* 348: 1269–1273

Sterne, J.A.C., Davey Smith, G., Leon, D.A., Tynelius, P., Rasmussen, F. (2001) "Fetal Growth is Associated with Parents' Cardiovascular Mortality: Record Linkage Study" *Pediatric Research* (in press) Supplement, Abstract FC9/4.

Terry, M.B., Susser, E. (2001) "Commentary: The Impact of Fetal and Infant Exposures along the Life Course" *Int J Epidemiol* 30: 15–23

Woelk, G.B., Emanuel, I., Weiss, N.S., Psaty, B.M. (1998) "Birthweight and Blood Pressure Among Children in Harare, Zimbabwe" *Arch Dis Child Fetal Neonatal Ed* 79: F119–F122

Yach, D., Cameron, N., Padayachee, N., Wagstaff, L., Richter, L., Fonn, S. (1991) "Birth to Ten: Child Health in South Africa in the 1990s. Rationale and Methods of a Birth Cohort Study" *Pediatr Perinatal Epid* 5: 211–233

Yajnik, C.S. (2000) "Interactions of Perturbations of Intrauterine Growth and Growth During Childhood on the Risk of Adult-Onset Disease" *Proc Nutr Soc* 59: 257–265

APPENDIX A

Expert Meeting on Life Course and Health, 2–4 May 2001

List of participants

Invited experts

Dr. Fernando Barros, Latin American Centre for Perinatology (CLAP), URUGUAY

Dr. Yoav Ben-Shlomo, Dept. of Social Medicine, University of Bristol, UK

Dr. Gerald Berenson, School of Public Health & Tropical Medicine, Tulane University, New Orleans, USA

Prof. George Davey Smith, Dept. of Social Medicine, University of Bristol, UK

Dr. Johan Eriksson, Dept. of Epdemiology and Health Promotion, National Public Health Institute, FINLAND

Prof. Hua Fu, School of Public Health, Fudan University, Shanghai, CHINA

Dr. Toshihiko Hasegawa, National Institute of Health Services Management, Tokyo, JAPAN

Dr. Henry Kitange, National Sentinel Surveillance, Ministry of Health, TANZANIA

Dr. Mike Kramer, Dept. of Epidemiology and Biostatistics, McGill University, Quebec, CANADA

Dr. Diana Kuh, MRC Survey of Helath and Development, Dept. of Epiodemiology and Public Health, University College London, UK

Dr. Claudia Langenberg, MRC Survey of Helath and Development, Dept. of Epiodemiology and Public Health, University College London, UK

Prof. David Leon, Dept. of Epidemiology and Public Health, LSHTM, London, UK

Dr. Maria Fernanda de Lima e Costa, Dept. of Social and Preventative Medicine, Federal University of Minas Gerais, BRAZIL

Dr. John Lynch, School of Public Health, University of Michigan, USA

Dr. Reynaldo Martorell, Dept. of International Health, School of Public Health, Emory University, Atlanta, USA

Dr. Francis Ofei, Dept of Medicine, University of Ghana Medical School, Accra, GHANA

Dr. David Phillips, Environmental Epidemiology Unit, MRC, Southhampton, UK

Dr. Bela Shah, Non-Communicable Diseases Programme, MRC, INDIA

Dr. Krisela Steyn, Chronic Diseases of Lifestyle Programme, MRCouncil, SOUTH AFRICA

Dr. Jacob Sweiry, Wellcome Trust, London, UK

Dr. Elisabeth Uchoa, Dept. of Social and Preventative Medicine, Federal University of Minas Gerais, BRAZIL

Dr. Chittaranjan Yajnik, King Edward Memorial Hospital, Pune, INDIA

WHO Staff

Dr. Isabella Aboderin, NPH/ALC

Dr. Myron Belfer, MSD/MBD

Ms. Irene Hoskins, NPH/ALC

Dr. Alexandre Kalache, NPH/ALC

Ms. Ingrid Keller, NPH/ALC

Dr. Pekka Puska, Director NPH

APPENDIX B

WHO Life Course and Health Meeting 2–4 May 2001

Programme Outline

2nd May

12.00–13.30	**LUNCH**
13.30–15.00	Welcome Introduction to objectives of meeting Short introductions from each participant
15.00–15.30	**COFFEE**
15.30–17.30	Global trends in CVD and diabetes Brief life course overview: key issues and terminology Discussion of the structure of meeting
19.30	**DINNER**

3rd May Biological domains

8.30–10.00	Session I:	Life course perspectives on obesity and height in relation to CVD and diabetes
10.00–10.30	**COFFEE**	
10.30–12.00	Session II:	Life course perspectives on blood pressure in relation to CVD
12.00–13.00	**LUNCH**	
13.00–14.30	Session III:	Life course perspectives of dyslipidaemias and impaired glucose tolerance in relation to CVD and diabetes
14.30–15.00	**COFFEE**	
15.00–16.30	Session IV:	Potential underlying mechanisms linking life course exposures to CVD and diabetes
16.30–18.00	Small Group Discussions: Emerging implications for policy	
19.30	**BOAT LEAVES FOR DINNER AT 'VILLA DES FLEURS', TALLOIRES**	

4th May Lifestyle domains

8.30–10.00	Session V:	Life course roots of unhealthy lifestyles (smoking, physical inactivity, unhealthy diet)
10.00–10.30	**COFFEE**	
10.30–12.00	Small Group Discussions: Emerging implications for policy	
12.00–13.00	**LUNCH**	

Synthesis

13.00–14.30	Session VI:	Reports back from small group discussions Consensus recommendations for policy
14.30	**COFFEE AVAILABLE**	
14.30–16.00	Session VII:	Consensus recommendations for action by WHO and participating institutions: focus on the research agenda that is needed and how to carry it forward.

Close of meeting

Ageing and Life Course
Department of Noncommunicable Diseases Prevention and Health Promotion
World Health Organization
Avenue Appia 20
1211-Geneva-27
Switzerland

e-mail: kalachea@who.ch
Telephone: +41-22 791 3405
Fax: +41-22 791 4839