The Importance of a Life Course Approach to Health: Chronic Disease Risk from Preconception through Adolescence and Adulthood

Chandni Maria Jacob [1], Janis Baird [2,3], Mary Barker [2,3], Cyrus Cooper [2,3] and Mark Hanson [1,3]

[1] Institute of Developmental Sciences, University of Southampton, Southampton S016 5YA, United Kingdom
[2] MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton SO16 6YD, United Kingdom
[3] National Institute for Health Research Southampton Biomedical Research Centre, University Hospital Southampton, NHS Foundation Trust, Southampton SO16 6YD, United Kingdom

Table of Contents

Synopsis

Non-communicable diseases (NCDs) including obesity, diabetes and cardiovascular disease, musculoskeletal, mental and neurological disorders have been identified as the 'world's largest killers', and multiple major international organizations have stressed the importance of adopting a life course approach to address them. The life course concept recognizes the opportunity to prevent and control diseases at key stages of life from preconception through pregnancy, infancy, childhood and adolescence, through to adulthood. This does not follow the model of health where an individual is healthy until disease occurs. The trajectory is determined earlier in life, and evidence suggests that age related mortality and morbidity can be predicted in early life with factors such as maternal diet and body composition (before and during pregnancy), low childhood intelligence, adverse childhood experiences acting as antecedents of late-life disease. A life course perspective enables the identification of a high-risk phenotype and markers of risk early, supporting current efforts for primary prevention of NCDs by providing timely interventions in early life. Part 1 of this paper summarizes existing models that explore the influences of the life cycle on chronic disease. Part 2 is a scoping review of risk factors of NCDs through the life course, highlighting issues in key life stages, with a special focus on the adolescent age group. Studies based on Developmental Origins of Health and Disease (DOHaD) have shown the transgenerational nature of NCD risk, and called for the need to attain optimum health in the preconception period. Multiple life-long health behaviours are established during adolescence making it an important stage for intervention.

1. Introduction

Over the past century, changes in patterns of mortality globally have included a reduction in infectious disease mortality and an increase in chronic non-communicable diseases (NCDs).[1] Though this shift started in high-income countries, there is now a double burden of NCDs and communicable diseases on the low- and middle-income countries. Mortality due to NCDs – mainly cardiovascular diseases and diabetes – is projected to rise along with the economic and social development in these countries.[2] The risks for NCDs are also changing due to demographic shifts, changing patterns of diet, physical activity, alcohol and tobacco consumption.[3] High blood pressure, high plasma glucose, obesity and overweight are some of the leading risk factors for non-communicable diseases, and thus improving nutrition is essential to improve health globally.[4]

Attention has recently shifted from adult lifestyle and risk factors as a cause for NCDs to early life experiences that influence adult health and mortality risk.[5] The 2030 Sustainable Development Goals (SDGs) promote commitment to health through the goal "Ensure healthy lives and promote well-being for all at all ages". In addition, the significance of the growing problem of NCDs is brought out in SDG 3 as it aims to "reduce by one third premature mortality from noncommunicable diseases through prevention and treatment and promote mental health and well-being", by 2030.[6] The need to control NCDs using a life course approach by preventing risk factor exposure, beginning in early life and continuing with interventions for adults and the elderly, is supported by multiple recent strategies and

recommendations. These include: the World Health Organization's Global status report on non communicable diseases [7], the World Report on ageing and Health [8], the Every Woman Every Child Global Strategy for Women's, Children's and Adolescents' Health (2016–2030)[9] and from the UK Department of Health.[10]

2. The life course approach to health

Key stages in people's lives have particular relevance for their health; the life course approach acknowledges the importance of these stages. The growing interest in the relationship between adverse circumstances across the life course leading to an increased risk of chronic disease and early mortality led to research that explains disease etiology within a life course framework.[11]

This review outlines the models and methods of the life course approach and concepts in life course epidemiology. The key life stages and issues in them are discussed, followed by a detailed discussion on the life stage of adolescence. The latter represents a central focus for intervention to promote health in future adults and also in the next generation, thus having the potential to affect two lives.

2.1 What is a life course approach?

Life course epidemiology investigates the long-term effects of physical and social exposures during gestation, childhood, adolescence, young adulthood and later adult life on health and disease risk in later life.[12] It also encompasses pathways (biological, behavioural and psychosocial) influencing the development of chronic diseases and operating across an individual's life course or across generations. It highlights a temporal and social perspective, looking back across an individual's or a cohort's life experiences, or across generations to understand current patterns of health and disease, while recognizing that both past and present experiences are shaped by the wider social, economic and cultural context.

Conventionally, the life course approach has been chosen to study chronic disease epidemiology, but it is also applicable within the context of infectious diseases, reproductive health and general health and well-being.[11] Collaboration between the social and medical sciences is emphasized in life course epidemiology as important to understanding social patterning and etiological processes of diseases. [13]

2.2 Origins of life course epidemiology

The idea that exposures early in the life course may have long-term effects on the development of chronic diseases became strengthened towards the end of the twentieth century. The causative models of NCDs that mainly focused on adult lifestyle factors such as smoking, poor diet and lack of exercise was challenged by the increasing amount of research supporting the importance of health in early life , leading to the emergence of life course epidemiology.[12] According to one study, strands of medical and social research – biological programming, risk accumulation and health inequalities – converged in life course epidemiology in the 1990s.[13] The idea of biological "programming" is that the development of organs and metabolism in utero and during early infancy determines the maximum functional

capacity that an individual can attain and sets the limits for the entire life course. The fetal programming hypothesis (also called the Barker hypothesis) proposed that fetal undernutrition, resulting from poor maternal diet and/or problems with the mobilization and transfer of nutrients from mother to fetus,[14] would induce phenotypic changes in the fetus, enabling survival in the short-term but having longer-term health consequences. Animal studies have added much weight to the idea by showing that alterations in the diet of pregnant animals can produce lasting changes to offspring physiology and metabolism.[15] Such studies also show that maternal overnutrition, achieved in animals by feeding mothers high-energy diets or making the mother obese/diabetic, also causes insulin resistance and diabetes in the offspring.[16,17] Recently there has been accumulating evidence that paternal diet, body composition and health can also affect the health of the offspring.[18] Together, these studies provided the basis for the rapidly growing field of science known as the developmental origins of health and disease (DOHaD). DOHaD concepts postulate that an altered long-term risk of disease is initially brought about through adaptive responses that the fetus or infant makes to cues from environment in utero or in early life.[17] These responses may not be just for fetal survival, because they can be induced even within the normal range of developmental environmental influences. They appear to be fundamental aspects of biology, seen across a variety of species, in which cues about the developmental environment are detected by the developing organism and used to induce phenotypic changes, which may have important adaptive value later. These so-called predictive adaptive responses are suggested to have evolved to optimize Darwinian fitness.[19]

Birth cohort studies and prospective longitudinal studies have been the best available methods to study life course phenomena in humans.[13] Studies in Hertfordshire, UK, were the first of a series of cohort studies that used historical records, combined with later follow-up, to explore the association of early life with chronic disease in adulthood.[20] In Hertfordshire, 16 000 men and women born between 1911 and 1930 were traced from birth to the present day. Death rates from coronary heart disease fell two-fold between those at the lower and upper ends of the birth weight distribution. Findings of the Swedish cohort study that followed up 14 611 babies also support the inverse association between cardiovascular disease and birth weight.[21] Further studies have shown that the relationship is U-shaped, as risk of later chronic disease also increases at the high birth weight end of the spectrum – a particular concern with rising prevalence of obesity and diabetes in women of reproductive age.[22]

2.3 Conceptual models in life course epidemiology

An understanding of the natural history and physiological trajectories of normal biological systems, along with biological and social pathways is needed when using the life course approach. These models suggest pathways linking exposures across the life course to later life health and include the temporal ordering of exposure variables, their inter-relationships (directly or through intermediary variables) and the outcome measures. The conceptual model can later be tested using exposure data across the life course, although this approach has not been extensively utilized.

The most commonly used approaches to studying life course processes are defined in terms of four, relatively overlapping models from Ben- Shlomo and Kuh.[11] These explain ways in which different factors may act to cause chronic diseases across the life course: they focus on a critical period (with or without effect modifiers), an accumulation of risk model and a chain of risk model. Hertzman and Power propose a similar three-fold model of life course influences on health – using the terms latency, cumulative effect and pathway.[23]

2.3.1 The critical period model

The critical period model (Model (a) in Figure 1) is when an exposure acting during a specific (sensitive) period has lasting or lifelong effect on the structure or physical functioning of organs, tissues and body systems, which are not modified in any way by later experience, and which results in disease later.[11] Also referred to as "biological programming" or a "latency model", this model forms the basis of early versions of the fetal origins of adult disease hypothesis. A critical period involves the concept of biological programming, in which an environmental influence causes irreversible metabolic consequences that alter susceptibility to later adverse outcomes.[24] Theoretically the critical period model advocates that an exposure during this period results in permanent and irreversible damage. However, in the context of chronic diseases the effects of exposure on structure from those on function should be differentiated.[11] For instance, poor growth in utero leads to a variety of chronic disorders such as cardiovascular diseases, but other exposures in later life may still influence disease risk. The latency model [23] (including the concepts of critical and sensitive periods) involves relationships between an exposure at one point in the life course and the probability of health outcomes years or decades later, irrespective of intermediate events in life. For example, studies of the Dutch Hunger Winter showed that maternal nutritional deficiency in pregnancy is associated with an increased risk of antisocial personality disorder and schizophrenia among offspring in their adult life (the effects seemed to be dependent on prenatal insult).

The critical period model also includes key social transitions, thus combining biological and social elements that interact to cause changes in health. Such periods do not necessarily only occur during early development and include: the transition from primary to secondary school; school examinations; the transition from school to work; leaving the parental home; establishing one's own residence; and the transition to parenthood.[25]

A critical period needs to be differentiated from a sensitive period.[11] The latter is a time period when an exposure has a stronger effect on development, though the same exposure outside this time period would still produce an effect that may be weaker, and there may be scope to reverse these changes outside this time period. A critical period, however, is a limited time window when an exposure can have adverse or protective effects; outside this period there is no excess risk.

2.3.2 The critical period model with later effect modifiers

This is an extension of the critical period model, including the possibility that later life factors (physiological or psychological stressors) may modify the effect of an exposure during a critical period of development on later disease risk.[12] The influence of exposures acting later

in life may enhance the effect on disease development (synergism) or diminish them (antagonism), as seen in model (b) in figure 1. Risk exposures may be independent as in model (a) or clustered as seen in model (b). A common reason for clustering of risk factors is when all the exposures relate to a single factor such as an individual's or family's socioeconomic status. For example, low childhood socioeconomic status is associated with other risk factors for poor health in later life such as low educational attainment, family stress, inadequate diet, passive smoking etc. This is suggested to be the case for the associations of birth weight with some chronic diseases in which associations are stronger among those who become obese during adolescence or adulthood.[26]

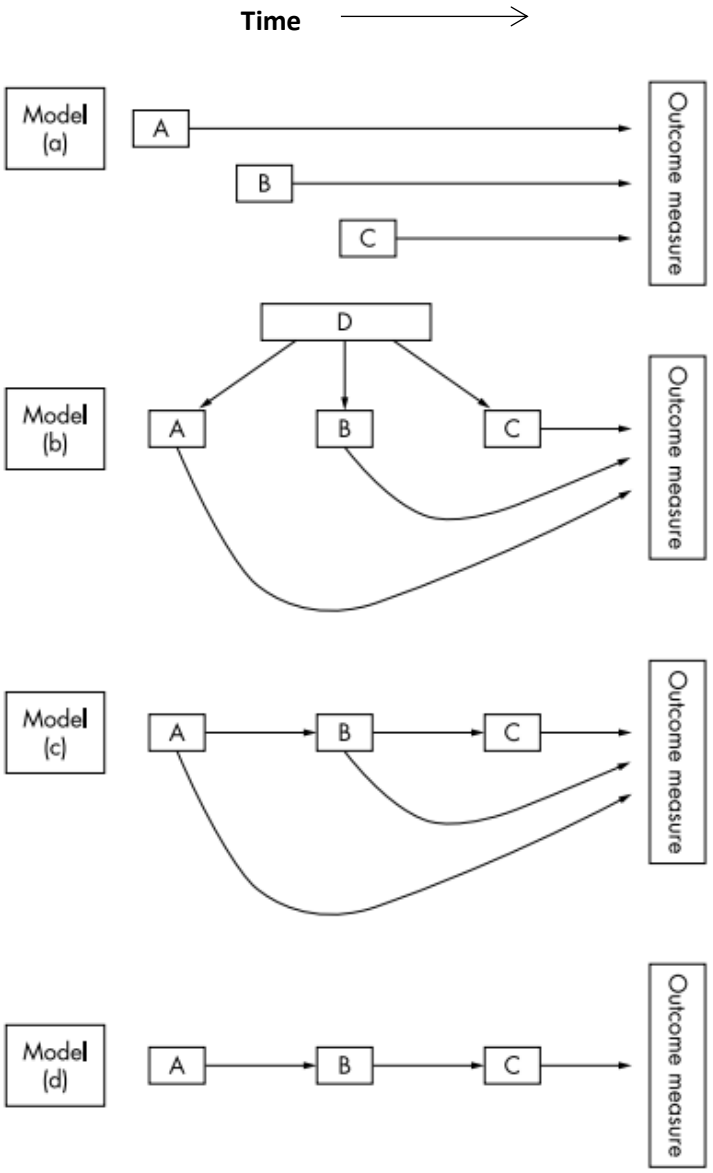

Figure 1. Life course causal models
From Kuh D, Ben-Shlomo Y, Lynch J, et al. Life course epidemiology. *Journal of epidemiology and community health* 2003 [27]

2.3.3 Accumulation of risk model/Cumulative model

This model focuses on the total amount and/or sequence of exposure, suggesting that multiple effects accumulate over the life course. However, it also allows for developmental periods during which susceptibility may be greater, so the sequence or trajectory of accumulation may also be important.[12] As the number, duration and severity of exposures increase, there is cumulative damage to biological systems (Model (c) in Figure 1). Accumulation of risk can also be due to clustering of exposures. For example, children from poorer socioeconomic backgrounds are also more likely to be of low birth weight, to have poorer diets, to be more exposed to passive smoking and some infectious agents, and to have fewer opportunities for physical activity.

The accumulation model has been considered to be more advantageous in life course epidemiology as it has better predictive power, can provide etiological insights and addresses social inequalities in health.[13] For instance, the model suggests that an individual's health is related to the proportion of their life spent exposed to disadvantages; thus a person's position in the social structure regulates the risk for mortality. The cause of morbidity and mortality is determined by the specifics of the person's life trajectory in terms of nature of exposures accumulated.

2.3.4 Pathway model/Chain of risk model/Trigger model

The fourth model refers to a sequence of linked exposures where one leads on to the next.[12,25,26] It suggests that various intermediate factors between early life and adult health – such as lifestyle, educational attainment, social class and health behaviours – may all play roles. This pathway model proposes integration of biological and psychosocial pathways, along with recognition of the fact that the timing of exposures may affect disease risk in many different ways. It shares similarities with the accumulation model, but differs on the timing of etiological exposure, with early advantage or disadvantage setting a person on a pathway to a later exposure that is the etiologically important event (Model (d) in Figure 1). For instance, a child from a disadvantaged background might encounter fewer educational opportunities. This in turn restricts socioeconomic wealth and resources, and later influences health behaviours and results in poorer health in later life.[25] The pathways model also supports the notion that early events influence the life course trajectory, leading to particular social destinations and ultimately influencing health outcomes.[23]

2.3.5 Other conceptual models in life course epidemiology

Research has suggested other models, which have similarities to the above models, to explore the influence of the life cycle on chronic diseases.

Merlo proposes a conceptual framework to explore the geographical, socioeconomic and cultural disparities in health.[28] This framework involves identifying the relevant contexts that

influence individual health by measuring general contextual effects and characteristics, identifying the specific effects of these characteristics on individual health, and investigating general and specific contextual effects from a life-course perspective across generations.

The Meikirch model of health suggests that an individual's health is the result of the interactions between their personally acquired potential (the sum of all physiological, mental and social resources a person acquires during life) and biological potential (the biologically given finite potential a person has from birth, influenced by genetics and the quality of pregnancy).[29] Health is dependent on the interaction between all three determinants – environmental, social and individual. Figure 2 [29] illustrates three possible time courses of the two potentials during a person's life. Biological potential has a finite value that is different for each person and decreases with age until death, while personally acquired potential increases rapidly after birth, and possibly throughout life based on life's demands.

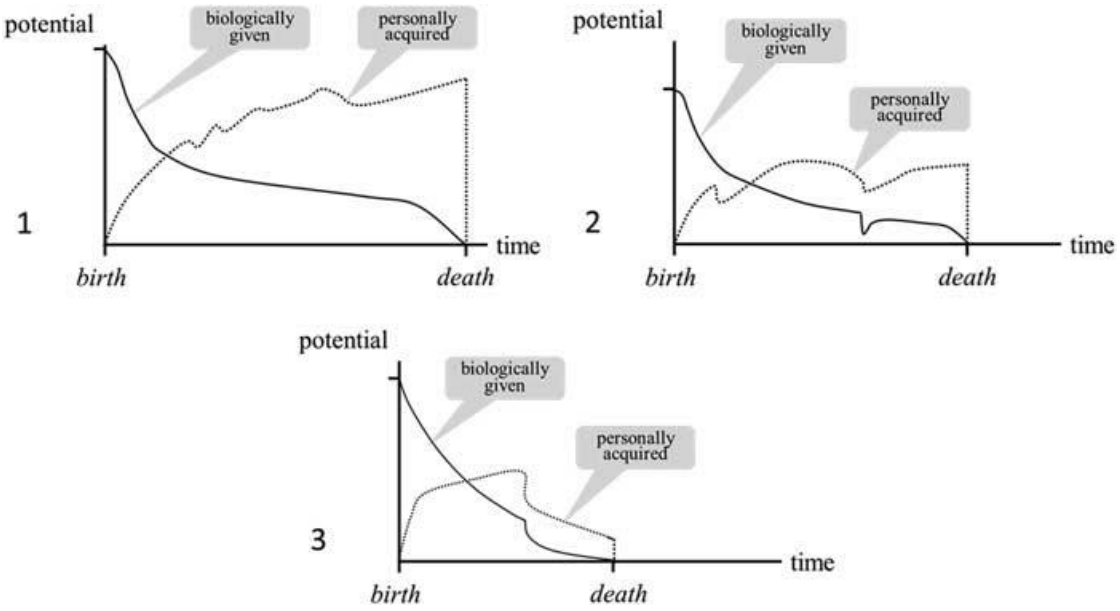

Figure 2. Examples of different time course of an individual's biologically given and personally acquired potential
From Bircher J, Kuruvilla S. Defining health by addressing individual, social, and environmental determinants: New opportunities for health care and public health. *Journal of Public Health Policy* 2014 [29]

These general conceptual models are, however, representations of life course processes that are likely to be more complex, and even such simple models may be difficult to distinguish empirically. Recent research and developments in epigenetics have allowed us to build on these models.

2.3.6 A new model based on the pathways model

The model in Figure 3 suggests that the rate of decline of an organ system depends on the level of peak function attained earlier in life, which also depends on developmental processes and early environmental influences.

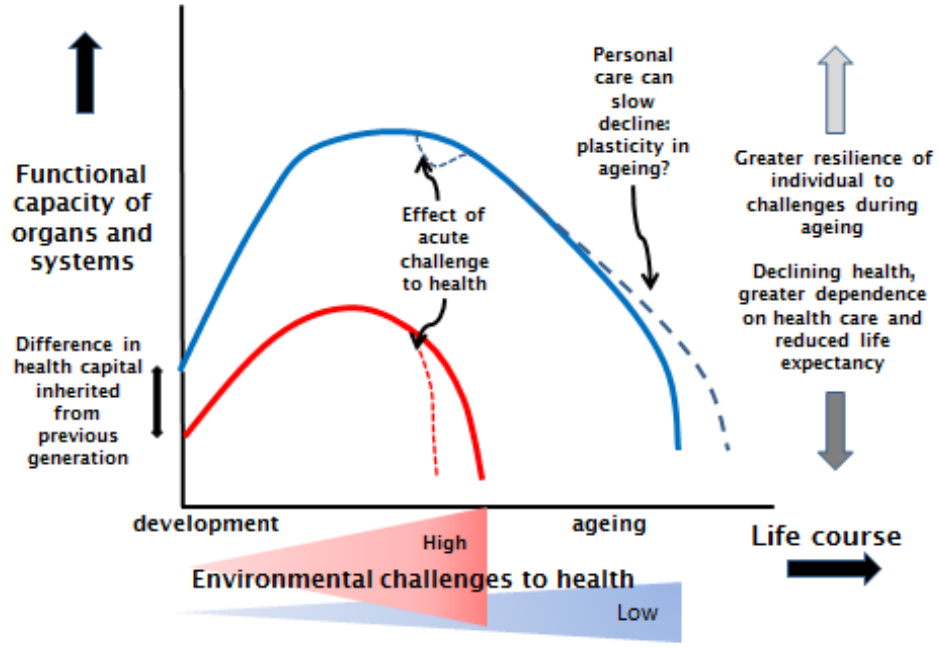

Figure 3. The lifecourse model showing average hypothetical trajectories of functional capacity for organs and systems in individuals from low- (red) and high- (blue) income settings. Low-income settings are associated with a poorer start to life in terms of inherited health capital. Functional capacity develops more slowly in a low-income setting, but reaches a lower peak capacity earlier in the life course. Throughout life the environmental challenges to function are likely to be greater in the low-income setting, leading to faster and earlier decline. In addition, an acute challenge such as an accident or infection in mid-life may produce a dip in function followed by recovery in a high-income setting, but a drastic loss of function in a low-income setting (broken red line). Provision of personal care, most often in high-income settings, can slow the rate of decline, sustaining resilience in a manner similar to plasticity (broken blue line).From Hanson M, Cooper C, Sayer AA, et al. Developmental Aspects of a Life Course Approach to Healthy Ageing. *The Journal of physiology* 2015 [30]

This model can be further refined by stressing that what matters for an individual or population group at any point in the life course is not so much the level of risk – the vertical height on the ordinate in Figure 4 – as the response to an acute challenge in the form of a more rapid increase in risk. This is shown in Figure 3 as the departure from the curve, which may lead to only a temporary reduction in function, but in those susceptible may lead to a more serious decline. At any point on the life course trajectory, the responsiveness can be viewed as the tangent to the line (Figure 4). It can be measured by a challenge such as a transient weight loss or exercise regime, or standard physiological tests such as a glucose tolerance test, heart rate response to exercise or immune response to a routine vaccination. The importance of such a model is that it reveals more about functional capability than does risk assessment alone. In addition, responses to such challenges can be incorporated into intervention strategies, to monitor their effectiveness and to maintain subject motivation.

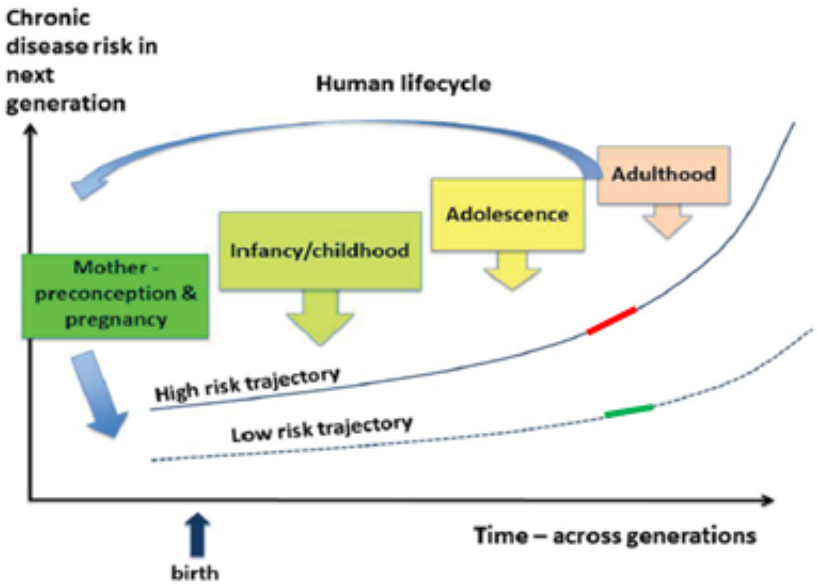

Figure 4. Life course model for chronic disease risk, illustrating the importance of the adolescent and young adult periods for interventions to reduce risk in the current and future generations. Tangents to trajectory are measured in terms of response to a brief challenge and show high risk (or poor response, red) and low risk (or good response, green). From Hanson et al. Chief Medical Officer's Report for England (11 Dec 2015)

2.4 Healthy ageing

The *World Report on Ageing and Health* [8] defines intrinsic capacity as 'the composite of all the physical and mental capacities of an individual'. Functional ability on the other hand comprises of the intrinsic capacity of the individual, relevant environmental characteristics and the interactions between the individual and these characteristics. It comprises the health-related attributes that enable people to be and to do what they have reason to value. The report also introduces the definition of *Healthy Ageing* as the process of developing and maintaining the functional ability that enables well-being in older age. Thus, Healthy aging is not merely the absence of disease, but is also based on influences throughout the life course. The report highlights the need to go beyond a systemic approach to measuring disease risk, and the shortage of evidence to determine the trajectories that may have preceded significant loss of function. A comprehensive understanding of the interactions between an individual's intrinsic capacity and these broader environmental influences, that leads to differences in ageing trajectories, is currently needed to develop instruments that evaluate intrinsic capacity efficiently, across all critical life stages.

2.5 Common concepts in life course epidemiology:

- Plasticity: the potential for change in intrinsic characteristics as a response to environmental stimuli is called plasticity and is measured by within-person variability. Developmental plasticity also uses cues from the environment to optimize the life course strategy for attaining maximum fitness and preparing for a future environment, and can lead to a variation in human phenotype.[31] The epigenetic mechanisms such as DNA methylation, changes in histone structure and small non-coding RNA activity provide the basis to the process of developmental plasticity. The emergence of epigenetics is giving insights into the molecular mechanisms that underlie such developmental changes.
- Resilience (or robustness): the ability of a phenotype to resist change without changing its initial stable configuration.
- Trajectory: the path established after an initial impetus, by analogy with a ballistic model. It may nonetheless be altered by subsequent influences, in which case a different trajectory is followed, so there is little flexibility.
- Path dependency: a life course where the response to a challenge, or the next step on the trajectory, depends on the previous one(s). Thus, future responses to a challenge or a particular level of risk will differ in individuals depending on the path they followed to the present point.

Thus, a life course approach is key to prevention and control of NCDs. An individual's lifespan includes the broader socioeconomic, environmental and genetic effects that cumulatively influence health and health behaviours. Connecting the biological, psychological and social models of the life course approach has potential to help elucidate new mechanisms of disease causation and develop measures for the maintenance and improvement of health.

3. Risk factors for NCDs across the life course

Supporting efforts to prevent NCDs through the human development have often been advocated [32] as they are leading causes of mortality and morbidity that also affect the societal, economic and environmental aspects of life, hindering future development. The interaction of social, economic and environmental factors – which can be conceptualized as intertwined strands in a triple helix – makes human development sustainable. The effects of NCDs, such as the need for chronic care, and stigma and secrecy associated with cancers, further contribute to inequities in a population and have a disproportionate effect on the poorer sections of society.[32] There are several such contextual, as well as constitutional factors, that shape health in different stages of the life course.

3.1 Constitutional and biological factors: genetics and epigenetics

There has been considerable interest in the identification of genes that are responsible for NCDs. A study carried out by the Wellcome Trust Case Control Consortium provided links between people's genes and common NCDs.[33] The study found several new genetic loci and genes that influence an individual's susceptibility to bipolar disorder, coronary heart

disease, type 1 and type 2 diabetes, rheumatoid arthritis, Crohn's disease and hypertension. Identifying the variants, genes and pathways involved in particular diseases opens prospective pathways to new therapies, diagnostic methods and better disease prevention. However, purely fixed genetic effects have not to date been shown to account for a substantial proportion of the NCD risk at the population level.

Of late, there has been increasing interest in epigenetic mechanisms as determinants of NCDs. Epigenetic modification does not result from changes to DNA itself but rather from changes to gene expression caused by DNA methylation or chromatin modification as an adaptive response to the environment in which they find themselves.[17,31] There is increasing evidence that maternally mediated environmental modulation of gene expression in offspring and gene-environment interactions are important determinants of later disease risk. Blum et al. (2015) suggest that progenetic and epigenetic correlates of adolescent predisposition to, and risk for, addictive behaviours could be a function of prefrontal cortex dysregulation.[34] An important cause of addictive behaviour in adolescents may be early childhood attachment (social) experiences, which are mediated by interactions with the environment (epigenetic), and by neurogenetic factors that affect a child's psychological trait/state, requiring both parental and peer co-regulation.

Influences of developmental and biologically based determinants on satiety and food preferences suggest that once set points are established in early life (with both prenatal and early postnatal components), it may be difficult or even impossible to reverse them, thus explaining why lifestyle interventions are difficult to sustain.[19]

3.2 Contextual factors affecting health and well-being throughout the life course

3.2.1 Behavioural factors

Risk factors such as smoking, alcohol consumption, excess weight and dietary factors are responsible for a large share of the global disease burden.[3] This can be directly or through conditions such as high blood pressure and elevated blood glucose and cholesterol levels, ultimately responsible for raising the risk of chronic diseases such as heart disease, diabetes and cancers. The transition in Health risks occurring in different populations due to decrease in incidence of infectious disease, changing patterns of physical activity and diet and an ageing population has led to issues such as a double burden of increasing chronic, non-communicable conditions, as well as the communicable diseases in LMICs.[35]

Alcohol

According to the recent global status report on alcohol and health,[36] in 2012, about 5.9% of all global deaths were attributable to alcohol consumption. Excessive alcohol consumption is associated with increased risk of a range of health problems, including chronic liver disease, cardiovascular disease, unintentional injuries, neuropsychiatric conditions, certain cancers and social issues such as alcohol-related violence and domestic abuse. Alcoholism's effects on the brain and behaviour are diverse and are mediated by many factors such as age, gender, health and family history.[37] Significant sex differences exist in the proportion of

global deaths attributable to alcohol, with mortality and morbidity due to alcohol consumption being higher in males. Economic development, cultural practices, availability of alcohol and the level and effectiveness of alcohol policies in a country are relevant factors in explaining differences and historical trends in alcohol consumption and related harm caused by it. The volume of alcohol consumed, the pattern of drinking also influence alcohol-related harm, and in certain cases the quality of alcohol consumed. Children, adolescents and elderly people are typically more vulnerable to alcohol-related harm from a given volume of alcohol than other age groups.[36] Young people also engage in more reckless behaviour while under the influence of alcohol. Early initiation of alcohol use (before 14 years of age) is a predictor associated with increased risk for alcohol dependence and abuse at later ages. Genetic risk factors also account for a substantial proportion of the variation in alcohol dependence as multiple genes influence alcohol use initiation, metabolism and reinforcing properties in different ways. [38] This leads to the increased susceptibility to toxic, psychoactive and dependence-producing properties of alcohol-vulnerable groups.

In some regions with a high prevalence of binge and harmful drinking, such as eastern Europe, a large death toll from cardiovascular diseases and alcohol consumption is the leading single cause of the disease burden.[35] Social change and policy interventions have shown effectiveness in modifying alcohol-drinking behaviours in some countries, such as a decrease in per capita alcohol consumption in traditional wine-producing and wine-drinking countries such as Italy and France. Mortality attributable to alcohol declined temporarily in the 1980s in Russia.[35,39]

Smoking

Nearly 80% of the more than 1 billion smokers worldwide live in low- and middle-income countries, where the burden of tobacco-related illness and death is heaviest.[40] The highest overall prevalence for smoking is estimated at nearly 29% in the European Region.[41] Mortality due to lung and other cancers, heart disease, stroke, chronic respiratory disease and other conditions is significantly increased due to smoking. Environmental tobacco smoke and smoking during pregnancy also causes harm to others. Smoking is increasing in many low- and middle-income countries, while steadily but slowly decreasing in many high-income countries.[3] It is more prevalent among people of lower socioeconomic status in high-income countries, and longitudinal studies have shown that smoking tracks strongly in adolescence and up until the late twenties.

Smoking during pregnancy still remains an issue in several countries. In England, despite decrease in prevalence compared to previous years, 12% of mothers were recorded as smokers at the time of delivery for 2013/2014. Smoking during pregnancy can cause a range of serious health problems such as lower birth weight, pre-term birth, placental complications and perinatal mortality. Some prospective studies have also shown that the offspring of mothers who smoked a pack or more of cigarettes a day during pregnancy are at elevated risk of developing nicotine dependence as adults.[42]

Control measures in most countries usually consist of: measures to protect people from the harms of second-hand tobacco smoke; the provision of help to quit tobacco use; effective health warnings through tobacco package labelling and mass media campaigns; regulations

on marketing; taxation policies designed to decrease tobacco use; and funding tobacco control and other health programmes.[40]

Physical activity

Insufficient physical activity is the fourth leading risk factor for mortality.[41] Globally, 31% of adults aged 15 years or older were insufficiently active (men 28% and women 34%) in 2008. Physical activity reduces the risk of cardiovascular disease, some cancers and type 2 diabetes and is beneficial for musculoskeletal health, maintaining optimum body weight and reduces symptoms of depression. In high-income countries, most activity occurs during leisure time, while in low-income countries most activity occurs during work, chores or transport. Physical inactivity has severe implications and is estimated to cause around 21–25% of breast and colon cancer burden, 27% of diabetes and about 30% of ischemic heart disease burden.[3] Women and girls are often seen to have lower rates of physical activity. A social shift away from energy-intensive occupations, such as agriculture, towards service-sector occupations – and concurrent reductions in the level of physical activity in each occupation – has led to the trend of decreased physical activity.

Most countries provide age-appropriate guidelines for physical activity, and in some cases for limiting sedentary time,[43] mainly as a measure to prevent childhood obesity. Limiting screen time (television, video games) in children, encouraging active play and transport and promoting physical activity in schools are seen to be effective measures to prevent childhood obesity. To improve the rates of physical activity in all age groups multisectoral approaches are often recommended. This includes environmental and policy approaches such as: creation and improvement of access to places for physical activity; informational outreach activities; community-scale and street-scale urban design and land use; active transport policy and practices; and community-wide policies and planning.[44]

Diet and nutrition

For an individual to become obese, their energy intake must exceed their energy expenditure over a prolonged period of time.[43] Diet-related risk factors lead to a range of diseases (which further act as risk factors) such as hypertension, high cholesterol, overweight and obesity and high blood glucose. The energy density of the diet (energy per unit of weight) is of importance; experimental studies have consistently shown that increases in the energy density of the diet lead to increases in spontaneous energy intake. Different types of fat in the diet have different metabolic effects, leading to differences in the risk of weight gain. Fruit and vegetables tend to have low energy density and are high in fiber, which may enhance satiety. Insufficient intake of fruit and vegetables is estimated to cause around 14% of gastrointestinal cancer deaths, about 11% of ischemic heart disease deaths and about 9% of stroke deaths worldwide. Most of the benefit of consuming fruits and vegetables comes from reduction in cardiovascular disease.[3]

There has been interest in the consumption of sugar-rich beverages as a specific risk factor for obesity, since experimental studies suggest relatively poor compensation for energy consumed as drinks as opposed to solid food. Some studies have found that energy consumed in liquid form appears to supplement habitual food intake, leading to increases in body weight. It is estimated that decreasing dietary salt intake from the current global levels

of 9–12 grams per day to the recommended level of 5 grams per day would have a major impact on reducing blood pressure and cardiovascular disease.[7]

3.2.2 Environmental factors

Environmental determinants of health include all the physical, chemical, and biological factors external to a person, and all the related factors impacting behaviours.[29] A growing amount of evidence shows the close relation between risk factors for NCDs and greenhouse-gas emissions in sectors such as household energy, electricity generation, transport (especially in urban environments) and food and agriculture.[32] Fine particulate air pollution results from burning coal or from vehicle emissions, which are also responsible for large amounts of greenhouse-gas emissions. The increasing use of cars has significantly contributed to an increased sedentary lifestyle, which is a risk factor for several NCDs. Increased active travel can help prevent these NCDs and also reduce costs for associated health services. Several communities in rural and deprived areas are dependent on inefficient combustion of solid fuels (coal and biomass), causing high levels of indoor air pollution, which is a major risk factor for chronic obstructive pulmonary disease and contributes to climate change through emission of black carbon and other pollutants.[32]

Microenvironmental and macroenvironmental determinants of dietary patterns exist that lead to obesity in different age group.[43] The microenvironmental factors include parents' body mass index (BMI) and dietary pattern, and a family environment in which parents strongly control children's food intake, which reduces the children's ability to self-regulate their eating behaviour. A higher occurrence of family meals and a better meal environment are considered to be essential to developing healthy dietary habits. School meals and availability of soft drinks are also microenvironmental determinants of childhood obesity, while dietary habits at the workplace and food outlets in surrounding areas are contributors to obesity in adults. The macroenvironmental factors are: the country's policies that affect food pricing and availability; industrialization of agriculture; food supply and the associated decline in prices; rising income and affordability; and mass media, education and information conveyed through product labelling that influence consumer's food choices.[43] The WHO Commission on Ending Childhood Obesity recommends that interventions should be focused on sensitive periods during the life course to address specific risk factors, while also addressing the environmental influences to enable behaviour change.[45]

3.2.3 Psychosocial factors

The first principle of a life course perspective on social status and health is that social status can affect health at any point from birth (or even before) until death.[46] Results of a review of observational studies in biomedical literature by Pollitt et al. (2005) suggest evidence to support the role of low socioeconomic status during early life in elevated levels of cardiovascular disease risk factors, morbidity and mortality.[47] They also suggest that the accumulation of negative socioeconomic status experiences/conditions across the life course could have a detrimental impact on cardiovascular disease risk. Different studies have suggested that deprivation in early life followed by later affluence combine to produce elevated coronary heart disease mortality risk, partly via elevation of adult cholesterol levels.

Education creates most of the relationship between achieved social statuses and health, and it is mainly through the increased sense of personal control that results from higher levels of schooling that greater health outcomes are achieved. Education is also highly dependent on parental socioeconomic status. Family socioeconomic status and pre-adult intellectual resources have significant effects on health outcomes in mid-life. There is growing evidence that childhood adversity linked to social inequalities in childhood has important consequences for health later in life.[46]

There are marked associations between positive psychological states and health outcomes, including reduced cardiovascular disease risk and increased resistance to infection.[48] A positive affect is also associated with protective psychosocial factors such as greater social connectedness, perceived social support, optimism and preference for adaptive coping responses. There is growing evidence that positive psychological well-being is associated with reduced risk of physical illness and prolonged survival, while serious illness frequently leads to a decreased sense of vitality and mood disorders. Studies have shown that systolic blood pressure is inversely associated with positive effect after controlling for age, gender, socioeconomic status, smoking and BMI. Being part of a social network has been shown to contribute to higher levels of positive well-being across many domains of life.

4. Key stages of the life course affecting health and well-being

4.1 Before birth

4.1.1 Fetal development

The way that a fetus obtains and allocates nutritional resources has profound consequences for its lifelong health. Research based on the developmental origins of health and disease (DOHaD) has shown that multiple developmental factors operate from preconception through early life to affect the risk for later NCDs. The possibilities of preventing NCDs by achieving optimal fetal development are now increasing, as early life programming is now thought to be important in the etiology of obesity, type 2 diabetes and cardiovascular diseases.[5] Influences on obesity and other NCDs in early life fall into biological, behavioural and contextual domains.[49] The biological factors affecting fetal development include maternal nutrition (under and overnutrition) and hyperglycemia, and recent studies have shown that prenatal exposure to gestational diabetes mellitus could lead to epigenetic alterations that increase the risk for type 2 diabetes later in life. Intrauterine growth retardation (including low birth weight), premature delivery, over nutrition in utero and intergenerational transmission of risk are all known risk factors for chronic diseases such as ischemic heart disease, stroke and diabetes [50]. Evidence from low- and middle-income countries (LMICs) has also supported these findings. In India a link was found between low birth weight and insulin resistance in children along with adverse total serum cholesterol and low-density lipoprotein cholesterol levels.[51] Findings of the Pune maternal nutrition study suggest that micronutrient deficiencies (such as vitamin B12) can also lead to low birth weight and a later risk of diabetes in the offspring.[52] Animal studies have also shown that

supplementation with folic acid during pregnancy can potentially prevent some of the epigenetic changes.[53]

Studies have shown that resource allocation to different organs in utero based on maternal environment can have severe consequences on health in later life.[54] When exposed to adverse conditions during fetal development, development of low priority organs and systems is traded-off to protect more important ones. In utero, male fetuses grow more rapidly and invest less in placental growth, which puts them at greater risk of becoming undernourished. Ethnic differences also exist in developmental strategies for the conservation of resources, and hence differences in body composition through life, and this could underlie ethnic health disparities.

Optimum fetal and child nutrition provides several benefits such as: cognitive, motor and socioemotional development; healthier adult stature; better work capacity and productivity; and a decreased risk of obesity and NCDs throughout the life course.[55] This is, however, acquired when supported by various other factors such as an enabling environment that includes nutrition-sensitive programmes (agricultural and food security, maternal health, sanitation) and nutrition-specific programmes for adolescents and during the preconceptional period. The impact of early life on long-term outcomes through its effects on physiological processes is accepted in the life course perspective, highlighting the potential for early intervention to reduce disease risk or severity.

4.1.2 Preconception

There is an increasing amount of evidence supporting the need to target the preconception period to prevent future NCD risk in offspring.[56] Recent recommendations by the International Federation of Gynecology and Obstetrics (FIGO) state that maternal nutrition should be part of a life course approach including perinatal health within the context of women's overall health. This can provide potential benefits to the health of the next generation – achieved by adopting healthy habits prior to conception.[57] Recent research also shows that nutritional factors can affect both male and female germ cells preconceptionally to modify fetal development. Hence, the impact of paternal genes on the offspring's health also needs to be addressed. Evidence shows that many women (especially young women) do not plan or prepare for pregnancy. For instance, unplanned pregnancies are still common in the UK.[58]

Exposure to toxic substances such as alcohol during pregnancy, deficiencies of essential nutrients (preconceptionally and during pregnancy), and other conditions such as diabetes and increased maternal age are all known risk factors for causing congenital anomalies, which accounted for 0·276 million neonatal deaths (4·4%) in 2013.[59] Common abnormalities were heart defects and neural tube defects (NTDs). Folic acid during pregnancy and the preconceptional period (for high-risk cases) is recommended in high-income and LMICs to prevent NTD-related mortality and morbidity.[57] Congenital anomalies associated with gestational diabetes and pregestational diabetes such as renal agenesis and neural tube defects (anencephaly and encephalocoele) have been widely studied.[60,61] Studies have shown that maternal obesity is also associated with a range of structural anomalies in the baby such as cardiovascular anomalies, spina bifida and septal anomalies.[62] The preconceptional period thus offers great potential to provide interventions to prevent such conditions in the fetus.

A woman's social circumstances can be a barrier to healthy choices, leading to poorer pregnancy outcomes and less optimal child development. Studies have shown that only a small proportion of women planning a pregnancy follow the recommendations for nutrition and lifestyle, such as increased fruit and vegetable consumption, intake of folic acid and cessation of smoking and alcohol consumption.[63] Greater publicity for such recommendations is needed. However, as many pregnancies are unplanned, improved nutrition and lifestyles of women of childbearing age generally is also required. Smoking in pregnancy is still prevalent and the preconceptional period provides an opportunity to address the issue along with other important issues such as folic acid and micronutrient intake. Asthma and other lung diseases, mental illness, cognitive decline and some forms of cancer have also been linked with unhealthy early life environmental exposures. This novel transgenerational mode of disease "inheritance" from parents to children is likely to account for a greater proportion of risk in the population than fixed genetic effects.[58]

4.2 Pregnancy

Healthy weight management, diet, physical activity, contraception, healthy sexual relationships, folic acid intake and smoking avoidance are essential preconceptional issues that are often not discussed with women before pregnancy. The pregnancy period presents another opportunity for intervention, and there is some evidence that women improve health behaviours, such as decreasing smoking, alcohol and caffeine consumption at this time.[64]

Both smoking and alcohol consumption during pregnancy are associated with poor pregnancy outcomes, including miscarriage, preterm delivery, low birth weight and impaired fetal development. [65] Children born of diabetic pregnancies are more likely to develop diabetes and have higher BMI than their siblings who were born in a normoglycemic pregnancy [66]. Improving glycemic control during pregnancy offers a key opportunity for effective intervention by potentially reducing crossgeneration 'transmission' of both diabetes and adiposity. Teenage pregnancy is also seen to repeats across generations. Different Cochrane reviews have shown that women receiving interventions for diet, exercise or both were less likely to gain weight during pregnancy and that antenatal aerobic exercise helped in maintaining physical fitness.[67,68]

Evidence also suggests that hypertension and chronic kidney disease can occur due to developmental programming in the kidney, leading to reduced nephron number.[69] This links intrauterine growth retardation, LBW and preterm birth with low nephron number, and hypertension in later life. Maternal stunting (height <145 cm) put infants at risk of term and preterm SGA (small for gestational age).[55] To reduce the risk of SGA births in populations in which a substantial proportion of births occur in adolescents, reproductive and family planning interventions should be strengthened to optimize age at first pregnancy.[70] Iron and calcium deficiencies contribute substantially to maternal deaths, and maternal anaemia is associated with low birth weight. Maternal and child undernutrition, and an unstimulating household environment, are known to contribute to deficits in children's development and health and productivity in adulthood.[55] Mental illnesses such as depression and anxiety are common during pregnancy and in the perinatal period,[71] with almost 20% of women experiencing symptoms of mental illness at some point during this period. Stigma

surrounding mental illness worsens the condition by preventing women from being open about their worries and seeking support.

Since most paediatric HIV cases are acquired from the mother, the effective means of preventing them is primary prevention by preventing mother-to-child-transmission, and also protecting vulnerable young women by providing female-controlled contraceptive barrier methods etc.[72] Strategies to prevent diseases in women in later life have been successfully implemented, such as such as human papillomavirus (HPV) vaccination for girls aged 11–12 to prevent cervical cancer and Chlamydia trachomatis screening for those less than 25 years to prevent ectopic pregnancy or tubal infertility. Almost half of the breast cancer incidence has been attributed to risk factors from adolescence and adulthood, especially reproductive factors such as late age of first birth, nulliparity, early menarche and late menopause.[65,73]

4.3 Newborn and early childhood

Infancy (birth to one year) along with early childhood involves children attaining a number of important developmental milestones relating to their physical development, along with social and emotional development. This includes establishing healthy patterns of eating and activity, developing a capacity for self-regulation, language and cognitive development and wider learning skills.

Lower birth weight – including shorter gestation and being small for gestational age – and a low socioeconomic status are associated with higher infant mortality and poorer long term health and educational outcomes in childhood. Higher levels of deprivation were also associated with increased risk of death independent of other factors know to influence infant mortality. Factors included births outside marriage, non-white ethnicity of the infant, maternal age under 20 and male gender of the infant [74] in a study conducted in England and Wales**.**

Breastfeeding: Low maternal age and educational attainment, and a low socioeconomic status, negatively impact on infant feeding. To improve initiation of breastfeeding and provide adequate care for the newborn, implementation of the Baby Friendly Hospital initiative at the country level is recommended by the World Health Organization and several Cochrane and other reviews.[75-77] It is recommended that support should be provided to mothers for initiation of breastfeeding, and that exclusive breastfeeding for the first six months does not cause weight loss but does protect from issues such as gastrointestinal infections. Studies have shown that suboptimum breastfeeding results in an increased risk of mortality in the first two years of life. [55] More recently, WHO infant and young child feeding indicators were studied in 14 Demographic Health Survey datasets from low-income countries: consumption of a minimum acceptable diet with dietary diversity reduced the risk of both stunting and underweight, whereas minimum meal frequency was associated with lower risk of underweight only. There are several possible reasons for the link between feeding method and later adiposity. Bottle-feeding may discourage appetite self-regulation, especially if the mother expects the standard bottle portion to be fully consumed at a feeding session.[43] In addition, weaning practices from milk on to solid food may differ between mothers who breastfeed and those who bottle-feed, with earlier weaning and more energy-dense weaning food being introduced for the bottle-fed infant. Further, the nature of the weaning food may differ as there is some evidence that infants given formula may be less

likely to consume vegetables and fruit and more likely to consume commercial infant drinks compared with infants who were breastfed.

During early childhood, nutritional status is an important determinant of physical health, and both under and overnutrition during this period can pose health problems in later life. Vitamin A and zinc deficiencies, severe childhood undernutrition, unsafe water and sanitation are still prevalent risk factors causing significant morbidity and mortality in LMICs [4]. On the other hand rates of childhood obesity is also on the rise due to introduction of energy-dense foods during the preschool years and infancy introduced in infancy.[78] In the UK over 20% of children entering school at age 4 to 5 years are overweight or obese and around 12.5% of toddlers are obese.[78] Similarly a recent report from seven eastern Caribbean countries shows that rates of overweight and obesity in children aged 0 to 4 years doubled from 7.4% in 2000 to 14.8%.[79] Weight gain at such an early age puts children at increased risk of on-going overweight and obesity and of developing physical health problems such as diabetes, coronary heart disease and early osteoarthritis in later life.

The early years also present a critical period for promoting physical activity and preventing sedentary behaviours. The Canadian Society for Exercise Physiology recommends that toddlers (aged 1–2 years) and pre-schoolers (aged 3–4 years) should accumulate at least 180 minutes of physical activity at any intensity spread throughout the day. For those under 2 years, screen time (e.g., TV, computer, electronic games) is not recommended and should be limited to less than an hour per day. Results of a systematic review [80] to evaluate health benefits of physical activity in the early years suggest a positive relationship between increased or higher physical activity and favourable measures of adiposity, bone and skeletal health, motor skill development, psychosocial health (social competence and externalizing behaviour), cognitive development and aspects of cardio metabolic health – though the evidence was mainly of low quality.

4.4 Childhood

Relative poverty has a wide range of effects on health, and there has been a persistent inverse association between socioeconomic status and childhood mortality in high-income countries.[81] The socioeconomic environment through childhood also affects adult health and disease through different pathways linking educational statues attained, health behaviours adopted during childhood and adolescence and parental socioeconomic position.[82] For example, Kuh and Ben-Shlomo (2004) describe a social pathway whereby adverse childhood socioeconomic position increases the risk of adverse childhood exposures as well as adult socioeconomic position and smoking behaviour.[12] Adverse childhood socioeconomic position is also associated with poor postnatal lung function and subsequently with poor adult lung function through its effects on immune function and the likelihood of exposure to infectious agents.

The influence of parents and peers on social and emotional development during childhood cannot be overlooked and it is suggested that the parent-child relationship may be a life-course health determinant.[83] Young children whose parents show resentment or hostility have an increased risk of poor health in later childhood and negative parenting qualities have been used as a predictor of ill health and higher use of health services, independent of socioeconomic status.

Evidence strongly supports a positive association between the intake of calorically sweetened beverages along with behaviours such as skipping breakfast, inadequate sleep and snacking with adiposity in children.[84] Factors such as total dietary intake and fat intake have shown weaker associations with childhood obesity, and having family meals together has been associated with improved dietary quality. Physical activity, which is an important contributor to optimal weight, is also associated with physical and mental health gains in the short and long term. Child overweight is a rising issue in high-income as well as LMICs. It has been associated with growing up in an obesogenic environment, in which population changes in physical activity and diet are the main drivers. Modifiable risk factors for childhood obesity are maternal gestational diabetes, high levels of television viewing, low levels of physical activity, parents' inactivity, and high consumption of dietary fat, carbohydrate and sweetened drinks.[55] Parental feeding practices and control over eating affect children's early eating patterns and risk of childhood obesity. Parental levels of physical activity and sedentary behaviour have also been shown to predict levels of activity in their children. More detailed discussion of these risk factors, and of possible interventions and actions by organizations at many levels, is given in the final report of the WHO Commission on Ending Childhood Obesity (released January 2016).[45]

4.5 Adolescence

Rapid brain development and the attainment of new cognitive abilities, such as complex abstract thinking, leads to several significant changes in terms of identity and relationships with families, peers and schools in a young adult's life. Impulsivity and an increase in risky behaviours are often observed in this period leading to adverse outcomes such as teenage pregnancy, substance abuse and mental health disorders**.** Adolescence is a crucial time for establishing health behaviours that affect health and wellbeing in later life. Half of lifetime mental illness (excluding dementia) is said to start by the age of 14, more than 8 out of 10 adults who have ever smoked regularly started smoking before 19. Studies have shown that 8 in 10 obese teenagers went on to be obese as adults [10].

Key transitions occurring during adolescence as identified by the World Bank are: from dependent child to independent adult; from primary to secondary and higher education; from education into the workforce; and into responsible and productive citizenship.[85] This also includes an important shift to becoming an adult responsible for their own health care. Successful negotiation of these transitions is necessary for young people to become economically productive members of society and to have the best chances for good health and well-being across the life course. Adolescents and young adults also have a high prevalence of anaemia. In India, for example, 55·8% of adolescents aged 15–19 years and 56·7% of women aged 20–24 years were anaemic.[55]

We discuss the life stage of adolescence in depth in section 5 with respect to causes for concerns in the health and well-being of adolescents and the lack of current effective interventions in place.

4.6 Adulthood

Individuals entering adulthood bring with them risks for their later health that have been acquired during fetal life, childhood and adolescence. Socioeconomic disadvantages have an important influence on health behaviours, as individuals from more disadvantaged backgrounds are more likely to smoke, have an unhealthy diet and be less physically active by not participating in regular sports activities than those from more affluent backgrounds .[10]

Almost half of all deaths caused by NCDs in LMICs occur in people younger than 70 years, and nearly 30% occur in people younger than 60 years. Employment and occupational health is an important aspect of adulthood and NCDs in this age group and can affect national economies because people with such diseases are likely to be less productive at work, lose their jobs and retire prematurely, decreasing household earnings and increasing the risks of poverty.[32] Unemployment is also associated with a number of elevated health risks such as increased rates of limiting long-term illness, mental illness and cardiovascular disease and an increase in overall mortality, and in particular with suicide.[10] Smoking, alcoholism and substance abuse are other risk factors in this age group that are of concern. Results of a systematic review suggested that working long hours (≥55 hours per week) compared with standard hours was associated with a significant increase in risk of incident coronary heart disease (relative risk [RR] 1·13, 95% CI 1·02–1·26; p=0·02) and incident stroke (1·33, 1·11–1·61; p=0·002). Other occupational risk factors include exposure to carcinogens, airborne particulate matter, ergonomic stressors and noise pollution, leading to conditions such as cancers (leukaemia, lung cancer, mesothelioma), chronic obstructive pulmonary disease, asthma, asbestosis, musculoskeletal pain and injuries and hearing loss. [86]

Multiple risk factors for cancers are considered to develop over an individual's lifetime or operate at different developmental periods. While a "western" lifestyle has been linked to prostate cancer, studies attempting to link early life and perinatal factors such as birth order, paternal age and birth weight to prostate cancer have produced inconsistent results.[73] Evidence has also suggested that testicular cancer could be associated with perinatal factors such as the hormonal environment. About 15% of cancers worldwide are related to long-term consequences of infections.[87] Stomach cancer is associated with chronic infection with Helicobacter pylori, and cervical cancer – which causes significant mortality and morbidity among women from LMICs – has been linked to persistent infection with certain types of HPV. Chronic infection with the hepatitis B virus is an important aetiological factor in liver cancer, and transmission often occurs at birth and early childhood and in adult life.[87]

4.7 Ageing

Increasing life expectancy and falling fertility rates has led to a dramatic increase in the proportion and numbers of older people.[8] Ageing is associated with several changes in intrinsic capacity and functional ability such as declines in strength, musculoskeletal function and immune function (particularly T-cell activity), and a decrease in cognitive functions is not uncommon. Different models exist to explore the process of ageing, and research on healthy ageing lacks, and has not adequately taken into account, the growing evidence that social and biological factors from early life onwards affect later health.[88] A life course model to understand the ageing process has often been used [30,88,89] to consider ageing as a lifelong process that needs to be studied in younger age groups as well. It suggests that genetic and environmental determinants of the need for maintenance and repair, as well as the capacity

to carry it out are likely to be responsible for the effects of ageing and possibly contribute to the wide variation in rates of ageing between individuals. The life course model suggests that the rate of decline in function depends on the peak function attained, as well as later life conditions, and a better understanding of the developmental components of ageing is required to identify markers of disease risk earlier in life.[29]

Findings in relation to nutrition in early life and ageing suggest that diet restriction in early life potentially causes accelerated ageing unlike that in adulthood. Environmental influences in adult life and genetic factors have been associated identified for causing musculoskeletal ageing in the form of thinning of bone (osteoporosis), reduced muscle mass strength (sarcopenia) and changes in cartilage (osteoarthritis).[89] Links between birth weight, weight in infancy and adult bone mass have been suggested by studies [90] and findings from the Hertfordshire study supported these links by showing similar results. The decline in certain cardiovascular and musculoskeletal functions is also associated with a decrease in physical activity along with changes in body composition due to ageing. Interventions to support healthy ageing and prevent a shift in trajectory are recommended when a person is healthy.[91]

Multi morbidity has significant impacts in older age and intrinsic capacity decreases with an increase in the number of chronic conditions, and the risk for multiple diseases in old age is higher for women and individuals from lower social classes.[92]

It is seen that brain plasticity, rapid maturation of organ systems during puberty and the behavioural and social changes that occur during adolescence make it a critical period. Interventions at this stage could have a high impact in a short period of time, preparing young adults for healthier later life and also for passing health to the next generation. We thus propose from the review that adolescence is a key life stage that needs to be addressed to influence the health of future generations.

5. Application of the life course approach to the adolescent age group

Recently the need for making adolescent health more prominent in future global public health programmes and policies has been emphasized.[9,57,93] WHO identifies the adolescent age group (young people between the ages of 10 and 19 years) as distinct from children and adults and requiring specific attention. With a population of around 1.8 billion, 10–24 year olds comprise a quarter of the world's population, with almost 90% of them living in LMICs.[93] Though a growth in the young adult population indicates an improvement in issues such as infant and early childhood mortality, it also leads to a surge in health issues related to sexual and reproductive health, substance misuse, obesity, injury and mental health (WHO global health risks 2009).[94] Yet, adolescence as a discrete stage in the life course has not been widely discussed within epidemiology. Research and efforts to prevent chronic diseases during adulthood have focused on very early life and the effects of parenting and education in early childhood [12,95]. Adoption of health-compromising behaviours during early adolescence can adversely affect overall adolescent development, set the course throughout the adult years and have significant repercussions on the health of the future generation.[57,96]

5.1 Factors influencing health and well-being in adolescents

5.1.1 Biological development

Puberty

Puberty is initiated in late childhood through a cascade of endocrine changes leading to rapid somatic growth, brain development, sexual maturation and attainment of reproductive capacity. Substantial brain development and psychosocial changes accompany this transition – features that are unique to humans.[97] Improvements in childhood nutrition, health and hygiene in developed countries is suggested to have caused a decrease in the age of onset of puberty; the mean age at menarche now is around 13 years for white girls and 12.5 years for black girls.[94,98] Young adults now take on characteristically adult roles at an older age in several developed nations and this has led to an increase in the length of the adolescent period.[94] The changes during puberty also affect the incidence and clinical manifestations of a number of diseases such as polycystic ovarian syndrome, eating disorders and depression.[97]

Brain development

Recent research has shown that the brain continues to develop through adolescence well into early adulthood, and that the adolescent brain has significant neural plasticity. This provides opportunities in adolescence to amend the impact of negative experiences earlier in life and to promote positive developments that will enhance intellectual ability and emotional functioning. However, research also suggests that executive functioning (a theorized network that regulates behaviour and influences behaviours such as smoking, drinking, overeating and being physically inactive) is linked to the social, physical and economic environments during early years of life.[99]

These physical changes occur alongside psychological and social changes, making adolescence a sensitive period during which normative and maladaptive patterns shape future trajectories.

5.1.2 Onset of risky behaviours

Neurodevelopment has implications for the exploration and experimentation that takes place during adolescence, because biological maturity precedes psychosocial maturity. Research suggests that pubertal hormones might affect the structure and function of the developing human brain.[100] The limbic system governing appetite, pleasure-seeking behaviours and reward processing, develops earlier in adolescence than the prefrontal cortex that controls executive functioning. Hence impulsivity and poor decision making demonstrated by drug use, unintentional injuries (car accidents) and unprotected sexual activity in adolescents could be due to the delayed development of the prefrontal cortex.[94,101] Cognitive development in adolescence also includes the capacity for abstract thinking and an increased capacity for setting goals. This dynamic interaction between body changes, changing identity and changing social groups during adolescence gives rise to both great potential and significant risk in young people's lives and changing relationships with families, peers and schools.[94,102]

Many of the risk factors and lifestyle patterns that lead to NCDs in adulthood arise from behaviours that begin in adolescence, such as tobacco use, alcohol consumption, unhealthy diets and physical inactivity.[102] Impulsiveness and risky behaviours during adolescence are not only due to the limitations in brain development, but also to a lack of experience with novel adult behaviours.[101] Research has also shown that developmental risks can be reduced and trajectories changed to favour constructive development. Forming positive relationships with adults and developing good intellectual functioning has been shown to predict resilience in young adults during adversity. Lessened antisocial behaviour, increased restraint in sexual behaviour, and decreased patterns of risk behaviour related to alcohol, tobacco and drugs were seen in modelling studies related to positive peer influences.[103]

5.1.3 Psychosocial determinants

Factors such as deprivation, poor parental support, family conflict and poor mental health are known to be responsible for several adverse outcomes, such as substance abuse and teen pregnancy.[102] Addressing such common risk factors in interventions provides opportunities to prevent multiple issues in adolescence. Young adults are also influenced by the socioeconomic circumstances of their community, along with gender norms and practices. These factors lead to differential exposures and susceptibility to health risks such as depressive disorders, sexually transmitted infections (STIs) and eating disorders.[104] Viner et al. (2012) state that the strongest determinants of health are structural factors such as national wealth, income inequality and access to education.[105] Safe, supportive families and schools and peers are important determinants of health in teenagers as they transition from childhood into adult life,[102,105] and can be useful resources to improve adolescent health, which later predicts educational outcomes as well as employment. There are strong associations of deprivation with unhealthy lifestyles in adults, leading to similar patterns in young people from such families, and there is evidence supporting the adoption of unhealthy behaviours among adolescents from low socioeconomic backgrounds. Low socioeconomic status is also associated with unhealthy diets, reduced physical activity and increased cigarette smoking in adolescents.[34]

Studies have shown that adolescents and young adults with addiction experience affect dysregulation, resulting in an inability to reach out to others for emotional soothing and comfort. Clinically, certain environmental interventions that provide a support network (maternal care, a positive family environment, the support of a close friend) have been shown to reduce the impact of childhood abuse.[34]

5.1.4 Genetic and epigenetic influences

As discussed earlier, there is now increasing evidence that epigenetic processes are central to the mechanism by which the early nutritional environment can increase susceptibility to obesity and other NCDs in later life.[17,91,106] Altered epigenetic regulation has been shown to be induced by maternal malnutrition in genes that control lipid and carbohydrate metabolism, and those involved in the central appetite–energy balance neural networks. This suggests that not only is development in adolescence affected by the individual's prenatal and

childhood environments, but also that risk for chronic diseases can be passed on to the next generation if issues such as malnutrition (both over and undernutrition) are not tackled early, considering that young girls often become pregnant during this period. A recent study on the prospective associations between adversities in early childhood and the epigenetic conformation of adolescents' genomic DNA [107] showed differential methylation among adolescents whose parents reported high levels of stress during their children's early lives. It also showed that maternal stressors in infancy and paternal stressors in the pre-school years were strong predictors. This suggests that early experiences can cause changes in the epigenome affecting metabolic and physiological pathways, possibly changing trajectories of individual phenotypic development and critically affecting health.

5.1.5 Environmental factors

Exposure to marketing and advertisements of energy-dense foods has been an issue that has contributed to the burden of obesity in children and young adults.[10] Advanced marketing techniques using social networks, mobile phones and mobile phone applications – and other novel methods such as e-voucher messaging, behaviour profile capture and interactive advert creation – have the potential to expose children to marketing.
WHO suggests an ecological framework for the determinants of health in the adolescent period [93] that includes several factors that protect or undermine adolescents' health. These are at the familial and community levels and also consider the influences of mass media and digital interactive media. Higher level policies and political decisions about the distribution of resources and power also eventually affect the health of young adults by creating enabling environments to improve health.

Most of these factors are interrelated. For example, the development of obesity in adolescents is influenced by a range of factors, including physiological (decreased insulin sensitivity, change in location of body fat), psychosocial (body dissatisfaction and increased risk of depression) and behavioural (decreased quality of diet and participation in sports).[108]

5.2 Concerns in the adolescent period

Most adolescents believe that they are healthy, and they discount future steps to improve or maintain health until later in the life course. While this may be true from the point of view of current risk, it is clearly not correct in terms of the underlying trajectory of risk, which is set in early life and can be modified in adolescence. Moreover many adolescents, especially those of low socioeconomic status or educational attainment, are not on the radar of public health in their community. Contrary to popular belief, there is a significant burden of disease during the adolescent years, and most causes of such disease and mortality are preventable. Mortality is higher in boys than in girls and in older adolescents (15–19 years) than in the younger group (10–14 years). The leading causes of death among adolescents in 2012 were road injury, HIV, suicide, lower respiratory infections and interpersonal violence.[9,93,109] While most of these causes are common to boys and girls, violence is a particular problem in boys, and complications related to pregnancy and childbirth are among the leading causes of death in girls of this age group. The burden is also higher in LMICs that also have additional

problems such as HIV and malaria causing significant mortality and morbidity in adolescents.[110,111] Significant regional variations exist for mortality and morbidity in adolescents, and hence efforts for prevention should be tailored to the needs of the population. However, some of the common priority areas for improving adolescent health, identified in most countries, are discussed further below.

5.2.1 Reproductive and sexual health

Early marriage and teenage pregnancy

Nearly one in every four adolescent girls aged 15–19 in the developing world (excluding China) is currently married or in union, and in South Asia nearly one in every three adolescent girls aged 15–19 is married or in union.[112] Pregnancy at a young age and early marriage not only affect the health and self-efficacy of girls but also disrupts their education and development of skills and social networks – all of which undermines their future health and well-being, along with the health of their children. Adolescents often lack knowledge of the need to prepare for pregnancy. Many pregnancies at a younger age are unplanned, so risk factors that can influence early development of the fetus may not be addressed, such as folic acid intake, alcohol use and other dietary and lifestyle issues such as achieving a healthy BMI.[57]

Adolescent pregnancy is associated with higher risk of maternal mortality and morbidity than seen in women in their 20s, along with stillbirths, neonatal deaths, preterm births, low birth weight and postnatal depression.[30,113] Calcium supplementation is often required.[114]

Other issues in sexual health

High risk sexual behaviour in adolescence also places an individual at a higher risk of STIs such as chlamydia, gonorrhoea and HPV, potentially leading to long-term issues such as infertility.[115] There are currently more than 2 million adolescents between the ages of 10 and 19 years living with HIV. Many do not receive adequate care and support to maintain health or prevent transmission.[116] In addition, millions more adolescents are at risk of infection.

5.2.2 Obesity

The adolescent period is marked by critical changes in body composition, insulin sensitivity, physical activity, sedentary and diet behaviours, and psychological issues that place adolescents at an increased risk of becoming overweight and maintaining obesity in adulthood. It has been suggested that almost 80% of obese adolescents become obese adults (Daniels et al., 2005). Physical activity and participation in sport and physical education decrease during adolescence, especially in girls.[108] The transition from childhood to adolescence is associated with significant increases in sedentary activity, more exposure to screen time (i.e. TV, internet, video games), an unhealthy diet and shorter sleep duration – all of which have been associated with obesity. The influence of media advertisements promoting unhealthy food and beverage choices has been addressed by the World Health Organization in its Set of Recommendations on the Marketing of Foods and Non-alcoholic Beverages to Children' (2010),[117] and in its Report of the Commission on Ending Childhood Obesity [45] to reduce the impact on children of marketing of foods high in saturated fats, trans-fatty acids, free sugars, or salt. Adolescents in particular may have more freedom

when it comes to food and beverage choices made outside the home, and so may be more vulnerable to the impact of such marketing.

The adverse effects of obesity in the adolescent period on later life are well known. Findings from the National Child Development study in 1958 suggested that pubertal timing is associated with changes in BMI from childhood to adulthood [118] and that it influences BMI and blood pressure in adulthood in males.[119] Results from the Harvard Growth study of 1922 to 1935 show that overweight in adolescence was associated with an increased all-cause mortality risk among men, along with an increased risk of morbidity due to coronary heart disease, arthritis, and atherosclerosis.[120] Also, adults who were obese adolescents are more likely to have lower incomes and experience higher degrees of social exclusion.[43]

5.2.3 Substance abuse

Often the first experiences with tobacco, alcohol and illicit drugs occur during adolescence. In several countries about one in four adolescents aged 13–15 reported having had an alcoholic drink sometime within the past month. Alcohol provides an example of behaviour where there is clear evidence that adolescent initiation is important for adult alcohol burden.[95] However, the nature of the pathways between adolescent and adult drinking is not well understood and not often addressed in research.[121] Similarly, almost 90% of lifetime smoking is initiated between the ages of 10 and 20 years in the UK.[102]

5.2.4 Mental health and suicide

Most mental disorders begin during childhood or adolescence (12–24 years of age), although they are often first detected later in life [122] so diagnosis and treatment may be delayed for years (World mental health survey). Mental health problems such as depression and anxiety, when left undiagnosed and untreated, have subsequent effects on adult mental health, social functioning and parenting.[93] The prevalence of reported suicide attempts in the last 12 months is also high, ranging widely among adolescents aged 12–18. Many high-income countries report rates of 5–10%. Rates are slightly higher – around 15% – in several LMICs. In a few countries more than one in every three adolescents reports attempting suicide in the preceding year. [93]

5.3 Scope for action

Of the several frameworks existing for adolescent health behaviours, Blum et al. (2014) propose four central goals to be achieved by early adolescence: engagement with learning; emotional and physical safety; positive sense of self/self-efficacy; and acquisition of life/decision-making skill. They recommend that interventions targeted towards early adolescence should aim to promote these key skills.

Zimmerman and Fergus (2005) [123] recommend the concept of resilience for prevention of unhealthy behaviours in adolescents when designing interventions. Resilience involves overcoming the negative effects of risk exposure and coping successfully with traumatic

experiences, while avoiding the negative trajectories associated with risks. The central idea is that interventions may need to focus on developing assets such as self-efficacy for health-promoting behaviours, academic skills and participation in extracurricular and community activities.

5.3.1 Prevention of teenage pregnancy and services for sexual and reproductive health

Ideally, adolescent clinical services should include prevention of teenage pregnancy, and care during pregnancy and childbirth. Prevention, diagnosis and treatment of STIs and HIV, and prevention of cervical cancer, are also required. [124] The results of a Cochrane review suggest that multiple interventions (combination of educational and contraceptive interventions) lowered the rate of unintended pregnancy among adolescents.[125] Commonly used approaches also include a combination of health worker training, adolescent-friendly facility improvements, and broad information dissemination via the community, schools and mass media. However, strategies based outside of health facilities are often lacking.[126] Low health-care-seeking behaviour and fear of being chastised or punished are some of the barriers to youth-friendly care faced by adolescents.[124]

Approaching preconception during adolescence to improve health

Young girls who are not physically mature might enter pregnancy with depleted nutrition reserves and anaemia, especially in LMICs. Adolescent pregnancy is associated with a 50% increased risk of stillbirths and neonatal deaths, and increased risk of preterm birth, low birth weight and asphyxia. Such pregnancies are especially prone to complications of labour and delivery, such as obstructed and prolonged labour, vesico-vaginal fistulae and infectious morbidity. In societies in which most births are within a marital relationship, interventions to increase women's age at marriage and first pregnancy are important.[70]

Effective interventions are needed to improve access to and use of contraception to prevent unintended pregnancies and STI transmission. They include: enacting and implementing laws and policies requiring the provision of comprehensive sex education and contraceptive services for adolescents within and outside school settings; making health services adolescent-friendly; and integrating contraceptive services with other health services. There is evidence that mobile phones and social media provide promising means of increasing contraceptive use among adolescents.[127] Sex education programmes should provide accurate information and build skills for negotiating sexual behaviours, for both girls and boys [124]. Interventions to promote adolescent health and prevent teenage pregnancies should encourage contraceptive use and appropriate birth spacing, optimize weight and micronutrient status, and screen for and manage chronic conditions.[128] Young women who receive preconception care are more likely to adopt healthy behaviours, and therefore have better pregnancy outcomes.

Projects in Nepal and India provide evidence for the efficacy of interventions to increase uptake of reproductive services (antenatal and postnatal) and contraceptive use among young women and couples. The Reproductive Health for Married Adolescent Couples Project (RHMACP) in Nepal delivers a package of family planning, safe abortion and maternal health interventions during the antenatal period, childbirth, and the postnatal

period. The Promoting Change in Reproductive Behaviour in Bihar (PRACHAR) project in India delivers a package of promotional, preventive and curative interventions in the pre-pregnancy period.[129]

The UK's Teenage Pregnancy Strategy: Beyond 2010 predominantly focuses on prevention of pregnancy through improving contraceptive and sex-education services. However, the recent report by the Chief Medical Officer for England [58] draws attention to the need to focus on adolescent health and nutrition, along with achieving optimum nutrition preconceptionally, to improve pregnancy-related outcomes for the mother and baby. Early interventions preconceptionally are promising, as epigenetic processes have been shown to be reversible in animal models during a crucial window of developmental plasticity that declines over the life course.[130]

5.3.2 Preventing obesity and achieving optimum nutrition and physical activity during adolescence

The importance of healthy behaviours in adolescents, young women and men before conception and in early pregnancy is reiterated in the report of the World Health Organization on Ending Childhood Obesity.

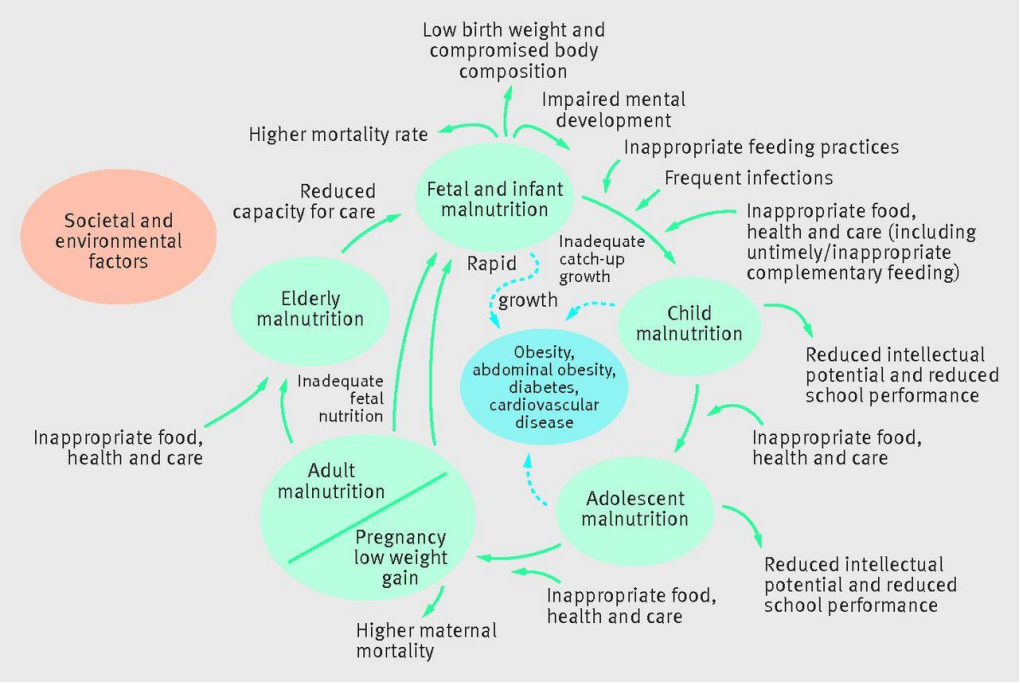

Figure 5. Nutrition through the life course – proposed causal links: Adapted from WHO childhood overweight policy brief, based on figure from Darnton-Hill I, Nishida C, James WPT. A life course approach to diet, nutrition and the prevention of chronic diseases. *Public Health Nutr* 2004;7:101-21.

Figure 5 illustrates current understandings related to the importance of different life stages and the effect of malnutrition across generations.[131] The importance of adolescence in achieving optimal nutrition is reinforced as it has potential effects on future pregnancies, fetal and infant malnutrition and malnutrition in adulthood.

Results of a systematic review show that interventions including the use of computer/smart phone technology that combined one or more features such as parental involvement, education, goal setting and self-monitoring, were effective in improving dietary behaviours in adolescents. [132]

The recent FIGO recommendations for nutrition emphasize the importance of the adolescent and young adult periods for long-term health.[57] Gaining optimum nutrition prior to conception has benefits for the next generation along with resolving micronutrient deficiencies through interventions focusing on dietary diversity and fortification of foods. Deficiencies of iron, iodine, folate, calcium, vitamin B12 and vitamin D are commonly seen in the adolescent age group and supplementation as necessary should be provided. Results from the Victorian Cohort study, Australia, [133-135] have suggested that, in adolescents, controlling weight by exercise rather than diet restriction seems to carry less risk of the development of eating disorders. School-based physical activity programmes are more effective for promoting physical activity and fitness in children and adolescents aged 6 to 18.[136]

Research on utilizing social media to promote the health of adolescents is increasing and studies evaluating the effectiveness of interventions using information and communication technology suggest positive effects.[137] The LifeLab intervention is an educational intervention in the UK targeting teenage boys and girls. It aims to improve their health literacy and understanding of the long-term influences of their health behaviours on their subsequent health and that of their future children.[138] The intervention uses an empowerment approach by improving the self-efficacy of teenagers in order that they can improve their own health behaviours with respect to diet and lifestyle. Improving the health and nutrition of teenage girls and boys has great potential to improve the health and well-being of the future generation. Similar approaches are being used in low-income settings. In South Africa, for example, rates of obesity are high among adolescent girls, leading to both high rates of gestational diabetes and low birth weight. An intervention being planned in South Africa to reduce obesity among adolescent girls to improve glycaemic control will use community health workers trained in behaviour change techniques.[139]

5.3.3 Other interventions for common risky behaviours in adolescence

Interventions to improve behaviours related to smoking, diet and physical activity have been recommended for the prevention of NCDs as following evidence that changes in lifestyle are associated with changes in biological risk factors in adolescents.[140] Structured universal interventions for improving mental health in children living in low-income settings have shown significant positive effects on students' emotional and behavioural well-being, including improved self-esteem and coping skills. Benefits accrued from utilizing the school and community settings.[141] Raised prices, taxation, restricting settings of use, and raising legal purchase age have been tested and seen to be effective in reducing use of alcohol and tobacco and related harms. In addition, developmental prevention interventions aiming to reduce pathways to drug-related harm by improving conditions for healthy development in the earliest years through to adolescence are recommended to prevent substance abuse in adolescence.[142] These preconceptional interventions aim to reduce drug use motivated by escape from distress, by reducing risk factors such as use of tobacco, alcohol or other drugs in pregnancy and exposure of children to environmental tobacco smoke.

Conclusion

The high disease burden in young people suggests that they are particularly affected by the persistent low global investment in NCDs and injury relative to the global disease burden. The changing patterns of mortality suggest that future global health targets should have an increased emphasis on the health of adolescents and young adults. Adolescence is a critical developmental stage after fetal and infant life, with rapid growth and development and widespread change across body systems. These major transitions and developmental changes make this a time of immense potential for preventive interventions. Providing opportunities for development during this period may consolidate early gains, or offer a second chance to young people who missed out during childhood.[9,93] Initiatives such as the *Global Accelerated Action for the Health of Adolescents (AA-HA!)*[143] by the World Health Organisation encourages engagement and participation among adolescents in interventions and puts adolescent health in the forefront of health care policy making at all levels.

Adopting a life course approach to child development, with greater attention given to the care, empowerment and protection of adolescents, girls in particular, is the soundest way to break the intergenerational transmission of poverty.[112] Evidence has repeatedly shown that educated girls are less likely to marry early and get pregnant as teenagers, more likely to have correct and comprehensive knowledge of HIV and AIDS, and more likely to have healthy children when they eventually become mothers. There is a need to identify specific risk and protective factors in LMICs that can help further to develop interventions tailored for adolescents. Reducing the emergence of problems during adolescence should have a substantial effect on reducing the burden of health problems that follow into adulthood.

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