

Social and biological pathways in childhood and consequent adult mortality risk:

A review of evidence and some research implications

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SAMMENDRAG

Artikkelen diskuterer den prinsipielle betydningen av sosiale og biologiske faktorer i barndommen for dødelighetsrisikoen i voksen alder. Ulike modeller av livsløpet blir presentert; kritisk og sensitiv periode, akkumulering av risiko og til sist en forløpsmodell. Disse modellene blir diskutert i lys av empiriske studier hvor sosiale og biologiske faktorer i barndommen er vist å ha en assosiasjon med dødelighet i voksen alder. En slik livsløpsmodell har potensial til å forklare ulikhet i helse på en biologisk og sosialt plausibel måte. Men den stiller også spørsmål ved om årsaksfaktorer fra tidligere i livet kan hevdes å være uavhengige før vi kjenner hvordan de biologiske og sosiale kjedene av risiko henger sammen og har utviklet seg over tid. Det blir derfor hevdet av en del forskere at for å forstå kroniske sykdommers etiologi fullt ut må både sosiale og biologiske årsakskjeder inngå i modellen.

INTRODUCTION

A strong graded association between adult socioeconomic position and mortality and morbidity has been repeatedly observed in several populations at different points in time (1-3). Adult mortality and morbidity has also been linked to social conditions in childhood in numerous reports (4-6). Even after taking adult socioeconomic position into account, childhood socioeconomic conditions seem to have a strong and independent effect on mortality risk in adulthood. It is a matter of ongoing research to identify what particular aspects in childhood may be of importance for these associations.

In recent years a life course approach to adult chronic diseases has been adopted in several studies. Researchers within this approach have explicitly stated that dichotomies between social and biological factors prevent us from understanding the full natural history of many chronic diseases in adult age (7). As it is argued, extending the focus from adult risk factors to biological and social chains of risk through the full life course offers the opportunity to explain social inequality in health more fully within a framework that is both socially and biologically plausible.

THE LIFE COURSE APPROACH TO CHRONIC DISEASE EPIDEMIOLOGY

Life course epidemiology examines various potential processes through which exposures located at different stages of life may exert alone or in combinations, influence on disease risk. Several models have been

adopted. A critical period model suggests that an exposure acting at a specific time has long-lasting effects on bodily functions and structures (8). Outside this developmental window there is no excess disease risk associated with exposure. The fetal origin hypothesis took this approach (9). There are several examples other than in utero programming that depends upon the time window during which an exposure may have long lasting effects, such as postnatal infection with hepatitis B and later risk of liver cancer. A related concept is sensitive period. In comparison with critical periods, a sensitive period is a time period when an exposure has a stronger effect on development and subsequent disease risk than it would in other times (10). This is comparable to learning a foreign language as it is well known that children may do that far quicker than adults. The influence of exposures acting during critical periods of susceptibility may be modified by later life exposures. Low birth weight may increase the risk of coronary heart disease, high blood pressure, and insulin resistance, when or only when individuals become obese later on in their life.

Another model of the life course suggests that effects accumulate over the life course (8). Duration and/or number of detrimental exposures may increase risk of later health damage. This has been shown in relation to exposure to poor socioeconomic conditions, where additive effects of experiencing disadvantage across different stages of the life course influence mortality risk of several causes (11,12). This accumulation of risk may be due to clustering of exposures. A child from a disadvantaged background may be more

likely to have low birth weight, poor diet during infancy, to be more exposed to passive smoking and infectious diseases and have fewer educational opportunities (8). But there may also be chains of risk where one risk may lead to another (13). A person with low educational attainment will strongly influence later occupation which again is determining risk of occupational hazards and income.

EVIDENCE RELATING SOCIAL CONDITIONS IN CHILDHOOD AND ADULT MORTALITY

According to a recent review, 29 studies of childhood socioeconomic position and all-cause or cause-specific mortality have been conducted (14). The majority of these studies found an influence of childhood social conditions on all cause mortality risk. Coronary heart disease was related to childhood conditions in most studies. Four of six studies reported an association for stroke. There was no such association for non-smoking related cancers. A strong effect on stomach cancer was seen in two British studies where this was investigated. Four of the studies found an effect on lung cancer which was largely mediated by adult socioeconomic conditions. Poorer childhood conditions were not related to non-smoking related cancers but were found to contribute to external- and alcohol related causes of death. Only a few of the studies were able to look into the cause specific pattern in more detail. Overall, it appears as if social conditions in childhood may have played out differently for various causes in these populations. For causes known to be related to adult lifestyle, such as lung cancer, the effect of childhood may be explained by later life social conditions and the uptake of smoking. Other causes, such as coronary heart disease, appears to be related to both childhood and adulthood. And for stomach cancer and stroke, childhood seems to have a strong effect alone.

The majority of these studies used father's social class as indicator of childhood social conditions. They also comprise cohorts of varying age-spans and born at different points in time through the early decades of the twentieth century. This represents a problem because it is difficult to assess to what extent occupational class is measuring childhood conditions similarly. Stages of urbanization and industrialization may not have been the same for the different populations at that time.

Other more indirect sources have provided evidence of early life socioeconomic effects. Leon and Davey Smith found strong correlation between cause-specific mortality in 1991-93 with infant mortality 1921-23 across 27 countries (15). A higher correlation was found for stroke than for coronary heart disease. Stomach cancer was strongly associated with infant mortality. Migrant studies have suggested susceptibility periods in childhood for some diseases, such as stomach cancer, and to a lesser degree cardiovascular causes (16,17). Studies of long-term disease trends

have provided evidence for childhood determinants of later adult mortality. In these trend studies, diseases that are plausibly related to childhood conditions can be differentiated from those where this is not as likely. Massive improvement in hygiene may not have played out similarly for all diseases. Cohort effects of stomach cancer have been studied which could follow a falling prevalence of *Helicobacter pylori* infection due to improved hygienic conditions (18). Similar trends have been found for haemorrhagic stroke throughout the 20th century (16,19-20).

BIOLOGICAL INFLUENCES OCCURRING DURING INFANCY

An association between social conditions in childhood and adult mortality are probably explained by a variety of processes. Several biological factors in childhood have been suggested. Childhood exposure to poor hygiene and the secular improvement of sanitation during the 19th and 20th centuries was probably an important explanation for the fall in mortality from diseases related to childhood conditions, such as from the valvular complications of rheumatic heart disease, tuberculosis and stomach cancer (14). Some studies have related infection with *Chlamydia pneumoniae* and *Helicobacter pylori* to the process of atherosclerosis (21,22). The evidence is inconsistent. An association between chronic inflammation and coronary heart disease may be unrelated to infections (23). Nutritional disruption in childhood of an enteric infection, such as *Helicobacter pylori*, or any other childhood infection affecting appetite, may programme future disease if it happens during critical periods of organ, hormonal, or metabolic development or be an indicator of poor childhood socioeconomic conditions. Chronic obstructive pulmonary disease as a consequence of reduced ventilatory function has been related to childhood chest illness such as asthmatic tendencies and or chest infections (24).

Temporal trend patterns and international comparisons of mortality rates have suggested that haemorrhagic stroke and coronary heart disease follow different patterns where stroke has had more similarities with tuberculosis and stomach cancer (25). Stroke mortality has also been related to number of siblings in childhood, a proxy for childhood infections (26).

The cause-specific pattern of the relative importance of childhood and adulthood social conditions follows data relating height and mortality (14). Adult height is determined predominantly by inheritance but also partly by influences early in life, and shorter stature is to some extent a marker for social conditions in childhood. Height has been found to be negatively associated with risk of hemorrhagic stroke, stomach cancer, coronary heart disease and chronic obstructive pulmonary disease (27-30). But even if height may seem to be a useful proxy for postnatal exposures, it could also simply be a reflection of the established

birthweight-cardiovascular association. Factors affecting childhood growth, such as infant feeding, childhood infections, childhood diet, and parental smoking could influence cardiovascular disease risk and explain this association. Separating the effect of in utero and postnatal influences on later disease has been challenging (31). Researchers have compared the effect of leg length with trunk length on mortality because the effect of leg length as opposed to trunk may be confounded by birth weight. Gunnell et al. found similar effects of leg length and trunk length suggesting the effects of leg length found in numerous studies reflect childhood conditions (32).

SOCIAL PATHWAYS BETWEEN CHILDHOOD AND ADULTHOOD

There is plenty of evidence showing that those from more advantaged family backgrounds have a much better chance of achieving a high socioeconomic position in adult life (33). The extent of intergenerational social mobility may be related to various factors some of which may depend on the local social and economic context such as level of industrialization and urbanization. And these processes may not be the same at different points in time (34).

Some of this continuity between childhood and adulthood socioeconomic position may be mediated by education. Studies from Norway have shown that family background has a strong effect on achieved length of education and future income and occupation (35,36). The strength of these relationships varies by place and over time. Apart from the mediating role of education for the future socioeconomic position, it also reflects the process of developing social and personal skills, such as motivation and self-direction, in the offspring (37). Disentangling the specific components of the education and mortality association remains to be studied.

In theory, there are some principal pathways via which aspects of the childhood socioeconomic environment may affect later mortality risk. First, parental socioeconomic position may influence adult socioeconomic position through access to social and economic resources, partly through education (34). Adult socioeconomic circumstances may in turn affect disease risk by determining exposure to causal factors in adult life. Second, the social environment children experience may put them at risk of exposures to known and unknown factors during gestation, infancy, childhood and adolescence that are thought to have causal effects on later disease risk. Third, childhood socioeconomic environment may influence health related behavior that may have long-lasting effects on health.

RESEARCH IMPLICATIONS

A great challenge for a life course epidemiology that aims at explaining socioeconomic inequalities in adult

mortality is to generate testable hypothesis. Hallqvist et al. demonstrated that the theoretical models presented as critical period, accumulation and so forth are not possible to disentangle (38). It is not theoretically or empirically possible to provide exposure contrasts free of confounding which could separate the effect of critical period and accumulation. This problem corresponds to the "non-identifiability problem" which hinders separation of age, period and cohort effects (39).

Extending the causal model to the full life-course poses additional challenges in terms of specifying the causal factors. As Ben-Shlomo and Kuh discuss, even though separate biological and social pathways may be identified in the etiology of adult chronic disease, estimating their independent effects are not straightforward (8). The social and biological pathways may be interrelated. And furthermore, if some factors along the pathway are mediating the effect of another located earlier in time, simply adjusting one with the other as is commonplace in regression models, will bias the effect of the exposure. A specific exposure located somewhere along the biological and social pathways may exert partly a direct effect and partly an indirect effect mediated via later factors. Identifying this direct effect net of the indirect is according to Robins & Greenland not possible in standard regression models (40).

The relative contribution of childhood and adulthood social conditions appears to depend on the specific outcome studied (41). This suggests that there are distinct social and biological processes for each disease which may explain inequality in adulthood. There appears to be no general social process able to explain the overall tendency for a social gradient pointing in the same direction in most, though not all, causes of death. Adding social and biological pathways in childhood into the causal model of adult chronic diseases poses new challenges for researchers. Until we know better how these social and biological factors are interwoven and operate along the life course, it will be misleading to claim they have an independent effect (42,43).

Linked to this, the way these pathways are related may depend on any given patterning of risk which may be of different importance in various populations and time periods. Differential associations with different indices of childhood and later life circumstances will not necessarily be replicable across time and space (44). Life course processes cannot ultimately be separated from the wider historical and political factors that shape the relation between disadvantage and health although most studies to this point have been constrained to study these processes at the individual level (45). Explanations for findings rely on how exposures in both childhood and adulthood are socially patterned. And these may not be the same in different contexts. Studies of earlier life factors in different populations and time periods will provide additional clues to the degree various factors are stable in various contexts.

The prospect of new analytical techniques in life course research is still uncertain. Structural equation modelling is designed to investigate the extent to which a factor in early life, such as birth weight, has a direct effect on mortality or is mediated through education later on as Susser and Levin suggest (32). This technique can test these direct and indirect effects but ultimately rests on the assumption that the proposed causal model is theoretically plausible and unconfounded by other factors. More generally, as exposures along the life course often will have a dependent structure, multilevel models are more flexible than single level regression models to take this into account. Socially mediated exposures, such as hypertension and body mass index, may track from childhood into adulthood and give rise to increased mortality risk. These dependencies may also be extra individual as group level attributes may have strong influence (46).

CONCLUSIONS

Life course epidemiology has in recent years developed a research programme which aims at mediating

the apparent incongruence between in utero programming and adult risk factors. Both biological and social pathways of causation are seen as necessary in order to fully understand the natural history of chronic diseases and to avoid biased estimates of effect. But extending the causal model to the full life course challenges researchers because it becomes more complex to tease out independent effects of environmental exposures. When etiological research in epidemiology adopts a life course approach, this will imply moving from a biologically deterministic model to a probabilistic one where one has to acknowledge that some of the socially patterned factors may not be as stable over time. Inequalities in health have moved up on the policy agenda in many European countries. Norwegian authorities have more recently taken an initiative to adopt such policies here as well (47). The evidence-base on the effect of particular policies is still rather weak if one compares with the standards in randomized controlled trials. But the evidence of strong long-term effects of childhood factors are increasing and it is widely acknowledged that interventions targeting children most likely will have knock-on effects later on in life.

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