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The influence of childhood circumstances on adult health

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[About the Victoria Institute of Strategic Economic Studies](#)

VISES is led by former Director of the Centre for Strategic Economic Studies, Professor Bruce Rasmussen, and incorporates the Centre of Policy Studies, which operates in a semi-autonomous manner under the leadership of Professor James Giesecke.

The VISES vision is to focus on the study of the fundamental economic, social and technological changes that are recasting the global economy, and to develop effective policy responses to them. One of its research programs is 'health and innovation', which seeks to understand the pivotal role of health in modern economic development, and in particular, the analysis of the economic case for innovation in health – the so-called 'returns to health innovation'.

[About the Mitchell Institute for Health and Education Policy](#)

The Mitchell Institute is an independent research and policy institute that works to improve the connection between evidence-based research and public policy reform. The Institute was founded on the principle that health and education are critical components of the development and progress of an economically and socially prosperous society. This is reflected in its focus on disadvantaged communities and the transformational change effective education and good health can deliver. The Mitchell Institute was established in 2013 through the generous financial support of the Harold Mitchell Foundation and Victoria University, Melbourne.

Foreword

Early childhood provides the foundation for many outcomes in later life. In the case of education and learning, there is a substantial and growing body of evidence that is influencing understanding of the importance of early childhood in providing the foundation for good learning outcomes at school and beyond. In health, however, our understanding of how physical and mental development in early childhood affects health outcomes in adolescence and adulthood, particularly in terms of the onset of chronic diseases, is not so well informed.

The following statistics highlight the need for a focus on early childhood in order to improve both health and educational outcomes for all Australians.

Currently, in Australia:

- 22 per cent of first year primary school students are vulnerable on one or more Australian Early Development Census (AEDC) domains (physical health and wellbeing, social competence, emotional maturity, language and cognitive development and communication skills and general knowledge);
- 10.8 per cent of Australian children are vulnerable on two or more AEDC domains;
- 25 per cent of Year 9 students cannot read well enough for further learning;
- 25 per cent of 17 – 25 year olds are not in education, training or work;
- 25 per cent of young people have mental health issues;
- Roughly 25 per cent of young people are overweight or obese;
- Unemployment for young people is climbing, reaching 21 per cent in some areas of Australia.

The Mitchell Institute for Health and Education Policy is an independent think tank focused on the importance of health and education outcomes, particularly for socioeconomically and culturally diverse population groups in Australia. The early years of life are well recognised as representing the most critical development period and important foundation years in enabling individuals to contribute and participate in their communities. It is also the best time for educational impact and a critical period for chronic disease risk prevention.

In light of the significant risks and failures for young people demonstrated in the statistics, the Mitchell Institute commissioned the Victoria Institute of Strategic Economic Studies to conduct a review of the literature to provide an overview of our current understanding of how childhood disadvantage affects health and wellbeing in later life.

The work that is reviewed here clearly shows a link between early childhood circumstances and subsequent health outcomes. This implies that policies and programs that prevent the most serious detrimental impacts – many of which are rooted in socioeconomic disadvantage – are critical to improved outcomes. Perhaps more importantly for our work, it also highlights the extent to which the effect of many of these events can be remedied or mitigated after they have occurred.

The Mitchell Institute seeks to use evidence to help improve how policy is developed, and by examining which factors have most influence on health and education outcomes, we hope to lay the foundation for further research work on how to shape early childhood programs and systems.

Through partnerships with our academic and community partners, we plan to support and demonstrate early intervention programs that will effectively target the most relevant indicators of risk to health and education outcomes.

Rosemary Calder
Director, Health Policy
Mitchell Institute

Summary

A growing body of literature, both internationally and in Australia, is showing that there are very strong economic cases to be made for a greater level of investment in addressing established risks and vulnerabilities in early childhood.

Detailed demographic, health and economic modelling research by Stenberg et al. (2013), has demonstrated that a suite of interventions in developing countries to reduce maternal and child mortality and morbidity could generate benefit: cost ratios over 10 using conservative assumptions in the modelling. Drawing on this research, the Lancet Commission on Investing in Health (Jamison et al., 2013) concluded that there were enormous payoffs from investing in health, particularly in childhood.

In the Australian context, Access Economics (2010), on behalf of the Australian Government, calculated the cost and benefits associated with three early childhood intervention programs and found that they generated very large returns on investment with benefit: cost ratios ranging from 1.8 to 13.8.

There is considerable evidence that a person's health status in adulthood is strongly affected by the degree of disadvantage that they suffer, whether this is due to their socioeconomic position measured by factors such as education, income, and occupation, their location, or other aspects of their life such as disability status.

In Australia, a number of studies have shown the relationship between disadvantage and health. For instance, Begg et al. (2007), in their study of the burden of disease in Australia, found clear socioeconomic and location gradients for mortality as measured by life expectancy at birth and for morbidity associated with a range of diseases.

The most dramatic difference in health status is between Indigenous and non-Indigenous Australians - life expectancy is around 10-11 years less, age standardised death rates are about twice as high, and the risk of diabetes is about 3.4 times higher than for non-Indigenous Australians.

While it is well established that current socioeconomic status (SES) is related to health, there is a growing body of literature that links adult health to a person's status at critical stages of the life course and, in particular, to conditions at conception, gestation and early childhood.

As an example, the comprehensive review by Galobardes, Lynch and Davey Smith (2004), which looked at 29 studies of childhood SES and adult mortality, found that:

People experiencing poorer socioeconomic circumstances during childhood carry a higher risk of overall mortality, independently of adult socioeconomic position...

The evidence from individual-level studies suggests that childhood socioeconomic circumstances contribute to a variety of different causes of death. In particular, childhood conditions appear strongly related to mortality from stomach cancer and haemorrhagic stroke. Childhood circumstances, together with the person's socioeconomic position in adulthood, contribute to mortality from coronary heart disease, lung cancer, and respiratory-related diseases.

One of the mechanisms linking childhood disadvantage to health status in later life that has been generating a lot of interest is epigenetics, which is the study of how a person's genome is modifiable by circumstances, particularly in early life.

Lillycrop and Burdge (2012) reviewed a number of studies that looked at the role of epigenetic mechanisms in the impact of early nutrition on long-term health and concluded that:

There is now a considerable body of evidence to suggest that our genotype is not the sole determinant of disease risk but that variations in the quality of the early life environment affects future disease risk through the altered epigenetic regulation of genes. The demonstration of a role for altered epigenetic regulation of genes in the developmental induction of non-communicable diseases together with the identification of potential epigenetic biomarkers of future disease risk suggest the possibility that individuals at increased risk could be identified at an early stage of the life course and their long term risk of noncommunicable disease (NCD) modified either through nutritional or lifestyle interventions.

A number of studies in Australia have confirmed that adverse circumstances in early life can have long-term impacts in adulthood if they are not addressed. For instance, in their analysis of data from the Mater-University of Queensland Study of Pregnancy (MUSP), Najman et al. (2004) found that:

Children from socioeconomically disadvantaged families (previous generations' socioeconomic status as well as current socioeconomic status) begin their lives with a poorer platform of health and a reduced capacity to benefit from the economic and social advances experienced by the rest of society.

Similarly, Jansen et al. (2013), using data from the Longitudinal Study of Australian Children (LSAC), found that:

Socioeconomic differences in mean BMI scores already present at age 4–5 more than doubled by age 10–11 years, reflecting decreasing mean BMI among advantaged rather than increasing means among disadvantaged children.

Risks of persistent and late-onset childhood overweight were highest among low SES families, and only partly explained by birth weight and parental overweight.

A report by the Centre for Community Child Health for the Benevolent Society reviewed the evidence on the efficacy of a number of major early childhood intervention programs shown to reduce the factors associated with disadvantage (e.g. poor academic achievement, unstable housing) in the long-term (i.e. into adolescence and adulthood). Based on this, they recommended that programs in Australia:

1. Provide free or low-cost preschool provision to three-year-old children experiencing significant disadvantage to ameliorate some of the negative impacts of disadvantage, ensuring a more level 'playing field' upon school entry.
2. Provide support to families experiencing disadvantage during the prenatal period to promote the optimal development of children.
3. Deliver programs of sufficient duration and intensity to families experiencing significant disadvantage as it appears that programs of less than 12 months are generally ineffective at shifting outcomes for disadvantaged children and families.

4. Provide direct services to children and families that promote the quality of the environments in which young children spend their time to ensure that parents and other caregivers relate to children in ways that protect, nourish and promote their development and wellbeing.

In conclusion, there is strong evidence for a distinctive socioeconomic gradient in adult health in Australia and that disadvantage has its origins in the circumstances of childhood. There are multiple pathways linking poor nutrition and other adverse impacts in gestation with both high and low birth weight. Combined with poor external environments in early childhood, this leads to physical and mental health problems in adolescence and in adulthood.

However, there is a growing body of literature that shows properly designed and managed childhood intervention programs can generate very large returns on investment, by avoiding or ameliorating the conditions that cause costly problems in later life.

Sustained programs that provide free or low-cost preschooling to children experiencing significant disadvantage, support to families, and developing parenting skills have all been shown to be highly effective.

1. Introduction

This report for the Mitchell Institute is concerned with understanding how childhood circumstances determine the health of people in adult life and at other stages of the life course. It reviews the growing body of evidence detailing the pathways through which these effects occur, as the basis for a discussion of programs that seek to modify childhood circumstances in order to avoid premature mortality and morbidity in later life.

A growing body of literature, both internationally and in Australia, is showing that there are very strong economic cases to be made for a greater level of investment in addressing established risks and vulnerabilities in early childhood.

Detailed demographic, health and economic modelling research by Stenberg et al. (2013) has demonstrated that a suite of interventions in developing countries to reduce maternal and child mortality and morbidity could generate benefit: cost ratios over 10, using conservative assumptions in the modelling. Drawing on this research, the Lancet Commission on Investing in Health (Jamison et al., 2013) concluded that there were enormous payoffs from investing in health, particularly in childhood.

In the Australian context, Access Economics (2010), on behalf of the Australian Government, calculated the cost and benefits associated with three early childhood intervention programs and found that they generated very large returns on investment with benefit: cost ratios ranging from 1.8 to 13.8.

These studies highlight the need for carefully designed and managed programs aimed at overcoming adverse circumstances in gestation, after birth and in the early years of life. Such programs could realise great benefits.

2. Social determinants of health and socioeconomic gradient

There is considerable evidence that a person's health status in adulthood is strongly affected by the degree of disadvantage that they suffer, whether this is due to their socioeconomic position measured by factors such as education, income, and occupation, their location, or other aspects of their life such as disability status.

Many studies have shown that there is a socioeconomic gradient which demonstrates that health status is higher the further up the socioeconomic ladder a person is placed. This relationship has been demonstrated in many countries, at different levels of development and income, and has led to calls for international action (Marmot et al., 2008) to address the inequalities arising from these social determinants of health (Wilkinson & Marmot, 2003).

In their comprehensive review of the relationship between SES and health, Cutler, Lleras-Muney and Vogl (2008) considered four aspects of SES, namely - education, financial resources, rank, and race and ethnicity. They found that socioeconomic status and health are strongly related in most countries regardless of the overall level of income of the country or the kind of health system. Their conclusions were that:

The mechanisms linking the various dimensions of SES to health are diverse. Some dimensions of SES cause health, some are caused by health, and some are mutually determined with health; some fall into all three categories at once. These differential patterns of causality make a single theory of socioeconomic gradients in health difficult to imagine.

Nonetheless, the authors concluded that the best way to analyse these relationships is to model them over the course of a person's lifecycle and to concentrate in particular on how childhood circumstances influence adult health.

In Australia, a number of studies have demonstrated the relationship between disadvantage and mortality.

Kelsall et al. (2009) studied colorectal cancer (CRC) survival, using data from the Melbourne Collaborative Cohort Study (MCCS) of some 41,528 people. They found that participants with CRC who resided in the least disadvantaged areas or who had tertiary-level education had higher overall CRC-specific survival compared with participants from the most disadvantaged areas or who had lower educational attainment.

Begg et al. (2007), in their study of the burden of disease in Australia, calculated various measures of that burden in 2003 by state, socioeconomic group and location. They found clear socioeconomic and location gradients, as demonstrated for one of these measures - life expectancy at birth (Table 1), which provides an estimate of the average years of life a person can expect to live to, given current risks of mortality.

Similar findings on the relationship between SES and mortality risk were made by Turrell et al. (2007) and Korda et al. (2007).

There is also considerable evidence of the relationship between disadvantage and higher morbidity or poor health (e.g. Begg et al., 2007; Glover, Hetzel and Tennant, 2004; Korda et al., 2009; Kavanagh et al., 2007; Turrell et al., 2006).

Table 1 Life expectancy at birth by area and sex, Australia, 2003

	Males	Females	Persons
Socioeconomic quintile			
Low	76.9	82.3	79.6
Moderately low	77.4	82.8	80.0
Average	77.7	82.7	80.2
Moderately high	79.0	83.5	81.2
High	80.9	84.5	82.7
Remoteness			
Major cities	78.8	83.5	81.2
Regional	77.5	82.7	80.0
Remote	75.4	81.5	78.1
Australia	78.3	83.2	80.7

Burden of disease studies seek to quantify the amount of disease in a society by combining data about the amount of life lost due to premature mortality with information about the prevalence of non-fatal conditions adjusted for their degree of severity. The resulting estimate of disability adjusted life years (DALYs) lost to disease was calculated by Begg et al. (2007) in Australia for the year 2003.

They found that the burden of disease was greater for those in the lower socioeconomic quintiles than in the higher quintiles (Table 2) and for those in remote and regional locations compared to those in the major cities.

Table 2 Differentials in burden (DALY rates) by socioeconomic quintile for the 10 leading broad cause groups, standardised rate ratios, Australia, 2003

Broad cause group	Socioeconomic quintile					
	DALYs per 1000	Low	Mod. low	Average	Mod. high	High
Cancer	25.1	1.05	1.05	1.05	0.97	0.88
Cardiovascular	23.8	1.10	1.08	1.05	0.95	0.84
Mental	17.6	1.22	1.05	1.02	0.92	0.80
Neurological	15.7	1.02	1.02	1.03	1.00	0.93
Chronic respiratory	9.4	1.15	1.07	1.01	0.95	0.83
Diabetes	7.2	1.30	1.05	1.09	0.91	0.70
Unintentional injuries	6.3	1.14	1.12	1.12	0.93	0.72
Musculoskeletal	5.3	1.08	1.02	1.05	0.97	0.89
Genitourinary	3.3	1.07	1.02	1.04	0.97	0.92
Intentional injuries	3.0	1.28	1.11	1.00	0.91	0.73
All causes	132.4	1.12	1.05	1.04	0.96	0.85

Drawing on the results of the Australian Diabetes, Obesity and Lifestyle (AusDiab) study from 2000 to 2005, Beauchamp et al. (2011) found that:

Lower educational attainment was associated with an increased risk of developing overweight/obesity and diabetes over a 5-year period in women. Men with lower education were also more likely to develop incident diabetes than those with higher education.

The most dramatic and well-known difference in health status is between Indigenous and non-Indigenous Australians as shown in the comprehensive statistics compiled by McRae et al. (2013). Life expectancy is around 10-11 years less, age standardised death rates are about twice as high, and the risk of diabetes is about 3.4 times higher than for non-Indigenous Australians.

Zhao et al. (2013) analysed data for the Northern Territory on deaths, public hospital admissions between 2005 and 2007, and Socio-Economic Indexes for Areas (SEIFA) from the 2006 Census. They found:

Strong inverse association between socioeconomic status (SES) and both mortality and morbidity rates. Mortality and morbidity rates in the low SES group were approximately twice those in the medium SES group, which were, in turn, 50% higher than those in the high SES group. The gradient was present for most disease categories for both deaths and hospital admissions. Residents in remote and very remote areas experienced higher mortality and hospital morbidity than non-remote areas. Approximately 25-30% of the NT Indigenous health disparity may be explained by socioeconomic disadvantage.

However, in their review of 16 studies on social gradients in the health of Indigenous Australians, Shepherd, Li and Zubrick (2012) concluded that:

In contrast to the ubiquitous, strong associations between SES and health in the general population, there is a less universal and less consistent SES patterning in Indigenous Australian health ... we believe the unique historical circumstances, social and cultural characteristics, and profound and persistent marginalization of Indigenous populations in Australia are plausible explanations for a much less consistent social gradient in Indigenous health.

3. Childhood status and adult health

While it is well established that current SES is related to health, there is a growing body of literature that links adult health to a person's status at critical stages of the life course and, in particular, to conditions at conception, gestation and early childhood.

In their recent overview of life course epidemiology, Ben-Shlomo, Mishra and Kuh (2014) point out that in the early part of the twentieth century a concern for public health centred on the role maternal and infant health played in the development of child health and subsequent adult health. This concern highlighted the need for maternal and infant welfare services to improve public health. However, this emphasis on early childhood tended to be superseded in the middle of the century as more information emerged about the impact of adult risk factors such as hypertension, diet, smoking and alcohol consumption on adult mortality and morbidity, specifically on cardiovascular disease.

Over the past 30 years or so, there has been a revival of the earlier emphasis on maternal and infant health determinants through a more formalised life course approach. This is supported by information from an increasingly broad set of longitudinal and other studies.

According to Ben-Shlomo, Mishra and Kuh (2014), life course epidemiology can be defined as 'the study of long-term biological, behavioural, and psychosocial processes that link adult health and disease risk to physical or social exposures acting during gestation, childhood, adolescence, and earlier or adult life or across generations'. This latter aspect extends the influences to the conditions of the mother and father prior to conception.

The development of this life course approach began with a number of studies on the link between early childhood and cardiovascular disease in adulthood. One of the earliest studies was the examination by Forsdahl (1977) of county-level data in Norway on the incidence of heart disease and infant mortality. He found:

A significant positive correlation between the county age-adjusted mortality from arteriosclerotic heart disease in people aged between 40 and 69 years and county infant mortality relating to the early years in the same cohorts. The findings suggest that great poverty in childhood and adolescence followed by prosperity is a risk factor for arteriosclerotic heart disease.

Barker (1989) found similar results when examining the outcomes for 5,654 men born during the period 1911 to 1930 in six districts of Hertfordshire, England whose birth weights were known. He found that:

Men with the lowest weights at birth and at one year had the highest death rates from ischaemic heart disease. The standardised mortality ratios fell from 111 in men who weighed 18 pounds (8.2 kg) or less at one year to 42 in those who weighed 27 pounds (12.3 kg) or more.

Similar studies by Barker and others, which contributed to the development of the 'foetal origins' or 'developmental origins' hypothesis, are reviewed in Barker (1998, 2007). The hypothesis asserts that chronic diseases in later life are 'established by "programming" of processes during embryological development and this in turn was influenced by nutritional influences acting either in pregnancy or pre-pregnancy through the development of the mother during her childhood or adolescence' (Ben-Shlomo, Mishra & Kuh, 2014). Gluckman and Hanson (2004) proposed a more general approach that included the influences of conditions after birth and into childhood, as well as those during pregnancy.

Life course models

As this literature has developed, a number of models have been proposed to explain the influence of socioeconomic status at various stages of life on health outcomes. Ben-Shlomo, Mishra and Kuh describe 7 such models and these are reproduced in the appendix to this paper. Other reviewers, such as Pavalko and Caputo (2013), Montez and Haywood (2013) and Pollitt, Rose and Kaufman (2005), have been content with fewer broader classifications. Cohen et al. (2010), in their review of childhood SES and adult health propose 3 basic models namely,

1. The timing model

According to the timing model, SES-related factors have the greatest influence on adult health if experienced during specific developmental periods defined as age ranges (e.g. birth to three years) or more broadly as periods of development (e.g. childhood, adolescence). The fit of this model to the actual processes linking early life SES with adult health depends upon the identification of sensitive periods when individuals are most vulnerable to SES exposures.

2. The accumulation model

The accumulation model suggests that the detrimental effects of low SES accrue throughout the life course such that risk for poor adult health increases with increasing intensity of socioeconomic disadvantage and with increasing duration of exposure to such disadvantage. In contrast to the timing model, the accumulation model is indifferent to when during childhood and adolescence the SES-related exposures occur.

3. The change model

The change model suggests that the direction of SES mobility across childhood and adolescence has important implications for adult health outcomes. Predictions of this model include the belief that upward mobility - a change from lower to higher levels of SES - would result in better adult health. Put differently, it predicts that negative effects of low SES during early childhood would be partly or wholly remediated by higher SES later in childhood or adolescence.

Pollitt, Rose and Kaufman (2005), in their influential review of the evidence for life course socioeconomic influences on cardiovascular outcomes, further differentiate the timing model. This disaggregation consists of those models that emphasise the importance of early sensitive periods and their direct impact on later health, as opposed to those that focus on pathway effects that place individuals on life trajectories that establish adult risk factors, which determine health in later life.

Cohen et al. (2010) discuss the evidence supporting the link between childhood and adolescent SES and adult health, and explore different environmental, behavioural, and physiological pathways that could explain how early SES would influence adult health. In doing so, they differentiate between physical and psychosocial exposures that are related to SES.

Within the home, children with lower SES are more likely to experience higher *physical* environmental risk because of greater crowding, exposure to smoking, and poorer housing stock. At school, they may have a higher exposure to inadequate facilities, while their neighbourhood may have fewer amenities, such as open areas, and suffer from a greater level of noise, air and water pollution.

Adverse *psychosocial* exposures that may be experienced by children with lower SES include higher levels of conflict among family members, less supportive family relationships, parental absence and poorer parenting practices. Neighbourhoods with a greater proportion of lower SES are likely to have lower

social capital, and higher crime and violence rates. Schools in such neighbourhoods are more likely to have problems with educational quality, student attendance, classroom behaviour and physical violence.

These exposures singly and in combination during childhood can predispose individuals to anxiety, depression, as well as difficulties in forming relationships, poor emotional regulation and other psychological problems. They can also predispose to risk factors for disease such as reduced physical activity, poor dietary habits, smoking and excessive alcohol consumption. Psychosocial exposures such as chronic stress can create an allostatic load of wear and tear. This can contribute to the development of a range of chronic diseases through their impact on the body's nervous, endocrine and immune systems.

Cohen et al. (2010) note that adult and childhood SES are correlated so they highlight those studies that control for adult SES in examining the link between childhood SES and adult health. They cite the comprehensive review by Galobardes, Lynch and Smith (2004), which looked at 29 studies of childhood SES and adult mortality, most of which were longitudinal prospective of cohort designs. Galobardes et al. (2004) found that:

People experiencing poorer socioeconomic circumstances during childhood carry a higher risk of overall mortality, independently of adult socioeconomic position ... The risk associated with lower childhood socioeconomic position was, not surprisingly, partly mediated by adult socioeconomic position and adult risk factors.

The evidence from individual-level studies suggests that childhood socioeconomic circumstances contribute to a variety of different causes of death. In particular, childhood conditions appear strongly related to mortality from stomach cancer and haemorrhagic stroke. Childhood circumstances, together with adulthood socioeconomic position, contribute to mortality from coronary heart disease, lung cancer, and respiratory-related diseases. Poorer childhood conditions are not generally associated with mortality from non-smoking related cancers and prostate cancer, but they may contribute to external and alcohol-related causes of death...

The findings relating childhood social circumstances to cause-specific mortality are congruent with data from studies relating height and mortality. Adult height is determined early in life, so shorter stature is partly a marker for an unfavourable profile of socially patterned exposures acting during the growing period (from the intrauterine period until final height is achieved). Height is negatively associated with risk of haemorrhagic stroke, stomach cancer, coronary heart disease, and chronic obstructive pulmonary disease, and it is either not associated or positively related to mortality from site-specific cancers, such as breast cancer.

The association between childhood social circumstances and mortality probably comes about through a variety of processes... Infection with *Helicobacter pylori* during infancy and childhood offers a plausible mechanism to explain the association between poor childhood circumstances and stomach cancer and possibly illustrates a critical period model during early life when individuals are most susceptible to acquiring this infection. Moreover, the similarity of associations of stomach cancer and hemorrhagic stroke with poor childhood circumstances, together with similarities in their association with height, and the cross-national relation between hemorrhagic stroke and stomach cancer risk raise, speculatively, the possibility that an early life infection—or a factor related to early life infection such as dehydration due to childhood diarrhoea—is associated with haemorrhagic stroke risk. On the other hand, coronary heart disease, ischemic stroke, lung cancer, and chronic obstructive pulmonary disease appear to be influenced by factors acting across the entire life course and therefore may conform more to a cumulative risk model. For example, poor

childhood and adult social circumstances could independently influence lung cancer risk via increased probability of initiation, earlier age of initiation, lower probability of quitting, and higher age of quitting smoking. Similarly, an accumulation of adverse exposures over the life course may result in higher risk of coronary heart disease.

This review was updated by Galobardes et al. (2008), with a further 11 studies and 5 updates of previous studies. This review confirmed most of their original findings, as outlined in the following paragraph:

In summary, the newer evidence available from this update allows us to more strongly affirm that poor socioeconomic circumstances during childhood are associated with higher mortality among men and women and that this association persists among younger cohorts. The new evidence highlighted the difficulty in establishing a particular life course model to explain this association, but several studies established the importance of education as mediator between early life SES and adult mortality.

An interesting study cited here is that of Osler et al. (2006), which examined data from 12,608 children born in Denmark from 1924 to 1947 who had been placed with adoptive parents early in life. They found that:

Adoptees with biological fathers from higher social classes had a lower rate of mortality after their fifth decade of life, mainly due to a lower risk of cardiovascular, infectious, and respiratory diseases. Adoptive father's social class showed no clear relation with adoptee's mortality risk. The risk estimates for paternal social class were slightly attenuated after adjustment for adoptee's adult social class, which as expected was inversely related to mortality from both natural and external causes.

Genetic and/or prenatal environmental factors contribute to the development of the relation of paternal social class to mortality from natural causes later in adult life independently of the effect of own social class, whereas there is no evidence for such long-term effect of the rearing environment.

Pollitt, Rose and Kaufman (2005) came to conclusions similar to those of Galobardes, Lynch and Davey Smith (2004) with respect to cardiovascular disease:

Study results suggest that low SES throughout the life course modestly impacts CVD [cardiovascular disease] risk factors and CVD risk. Specifically, studies reviewed provided moderate support for the role of low early-life SES and elevated levels of CVD risk factors and CVD morbidity and mortality, little support for a unique influence of social mobility on CVD, and consistent support for the detrimental impact of the accumulation of negative SES experiences/conditions across the life course on CVD risk.

They also drew attention to the limitations of existing studies and the difficulties of clearly delineating models:

The wide range of populations, analysis designs, exposures, and outcomes used in the life course studies reviewed precludes a simple, quantitative analysis of the impact of life course SES on CVD risk. Nevertheless, the results thus far modestly support the existence of life course SES effects on risk of adult CVD. The cumulative life course model is more consistently supported by extant studies than other models.

Cohen et al. (2010) were also cautious in their conclusions:

The models we examined present alternative and sometimes complementary hypotheses about the ages at which childhood and adolescent SES matter most for adult health, and how long SES exposures of specific types need to last to influence health. To date, there are few empirical data testing the models against one another in the prediction of physical health. There are practical, conceptual, and analytical explanations for this lack of data ...

[In addition] more than one model could apply at the same time. For example, it is possible that there are cumulative effects of early SES exposure across childhood and adolescence (accumulation model), but that exposures at specific developmental periods are more impactful than those at others (timing model) ...

Another conceptual issue concerns the possibility that both the mechanisms linking early SES with adult health outcomes and the models describing when during childhood and adolescence these mechanisms are most influential, vary across diseases or disease stages. For example, disease processes that are progressive, such as atherosclerosis, may fit the accumulation model, whereas those that involve exposure to a critical triggering event, such as early viral or antigen exposures associated with increased risk for adult respiratory disease, may fit the timing model.

4. Epigenetic mechanisms linking early life to adult health

There is growing evidence linking variants in a number of genes to both birth weight and adult height and metabolism. The Early Growth Genetic Consortium has recently published the results of an expanded genome-wide association study of birth weight in some 69,308 people and specific genes (Horikoshi, 2013). They identified or confirmed that 7 loci in the genome are associated with birth weight and explain a similar proportion of variance to that explained by maternal smoking in pregnancy. Furthermore:

The associations between five of the loci and adult traits (i) highlight biological pathways of relevance to the foetal origins of type 2 diabetes; (ii) reveal complexity, in that type 2 diabetes risk alleles can be associated with either higher or lower birth weight; (iii) illuminate a new genetic link between foetal growth and adult blood pressure and (iv) show substantial overlap between the genetics of prenatal growth and adult height.

A person's genetic material is contained in 23 chromosomes each of which consists of a long strand of DNA built from 4 nucleobases. The genes consist of sections of DNA, which serve as the basis for production of proteins. These are the building blocks of the body. Genetic material inherited from parents is largely unchanged throughout a person's life.

Each cell in the body contains all a person's genes, which are replicated in each cell division. However, the particular function of a cell is controlled by the differential silencing of genes through processes such as DNA methylation and histone modification. These are known as epigenetic processes and also include chromatin remodelling and microRNA. In the early stages of the embryo, the genome is 'wiped clean' of most epigenetic modifications, which are progressively re-established during embryonic development (Gluckman et al. 2009). The epigenome changes as the organism develops and reflects environmental and other influences on its development.

The fact that the epigenome can change while the underlying genetic material is unchanged enables the organism to have some plasticity during its development so that it can respond to changing circumstances. However, a mismatch may arise between the circumstances in which the epigenome developed and the circumstances faced by the organism at later stages. This mismatch in the development of humans in pregnancy and early childhood has been investigated as the source of increased risk of chronic non-communicable disease in adulthood.

Most of the scientific research on epigenetic processes has been carried out in animal models, such as rats and mice, although there is a growing evidence-base from research in humans.

Lillycrop and Burdge (2012) reviewed a number of studies that looked at the role of epigenetic mechanisms in the impact of early nutrition on long-term health. They asserted that:

Traditionally it has been widely accepted that our genes together with adult lifestyle factors determine our risk of developing noncommunicable diseases such as type 2 diabetes mellitus, cardiovascular disease and obesity in later life. However, there is now substantial evidence that the pre and early postnatal environment plays a key role in determining our susceptibility to such diseases in later life. Moreover the mechanism by which the environment can alter long term disease risk may involve epigenetic processes. Epigenetic processes play a central role in regulating

tissue specific gene expression and hence alterations in these processes can induce long-term changes in gene expression and metabolism which persist throughout the life course.

Lillycrop and Burdge (2012) also found that:

There is now a considerable body of evidence to suggest that our genotype is not the sole determinant of disease risk but that variations in the quality of the early life environment affects future disease risk through the altered epigenetic regulation of genes. The demonstration of a role for altered epigenetic regulation of genes in the developmental induction of NCD together with the identification of potential epigenetic biomarkers of future disease risk suggest the possibility that individuals at increased risk could be identified at an early stage of the life course and their long term risk of NCD modified either through nutritional or lifestyle interventions. However further understanding of the mechanism by which nutrition can modify the epigenome, the periods of epigenetic susceptibility, the nutritional factors that induce epigenetic changes and the stability of the induced changes are all critical for both the robust identification of individuals at risk and for the development of novel intervention strategies, to reverse this current epidemic of NCD.

Although the research is in its early stages, there is some limited evidence linking epigenetic modifications to early life socioeconomic circumstance. Using data from a cohort study of New York women born between 1959 and 1963, Tehranifar et al. (2013) found that low family income and a single parent family at birth was associated with higher white blood cell methylation in adulthood.

5. The impact of birth weight and other factors on health in later life

Many of the earlier studies linking childhood status to adult health have examined the relationship between birth weight and health outcomes. Initially this concentrated on the negative effects of low birth weight and under-nutrition but more recent studies now also consider high birth weight and over-nutrition.

Important early studies were those of Forsdahl and Barker, as discussed earlier. Other significant works involved the study of people exposed to famine in pregnancy, such as those in the Dutch Winter Famine of 1944 to 1945 and the famine in China from 1959 to 1961 associated with the Great Leap Forward (Chen, Nembhard and Stockwell 2014).

An analysis by Painter, Roseboom and Bleker (2005) of the Dutch Winter Famine showed that individuals whose mothers were exposed to the famine around the time of conception and in the first trimester of pregnancy did not have reduced birth weights compared to unexposed individuals. However, as adults they exhibited an increased risk of obesity and CVD. Individuals whose mothers were exposed in the later stages of gestation had reduced birth weights and showed increased incidence of insulin resistance and hypertension.

Further analysis by Roseboom, de Rooij and Painter (2006) found that women exposed to famine in early gestation had an increased risk of breast cancer and people exposed to famine in mid gestation had increased risk of obstructive airways disease.

A recent systematic review and meta-analysis by Risnes et al. (2011) considered the results from 10 studies that assessed the association between birth weight and adult mortality from all causes, CVD or cancer. They found:

an inverse but moderate association of birth weight with adult mortality from all-causes and a stronger inverse association with cardiovascular mortality. For men, higher birth weight was strongly associated with increased risk of cancer deaths.

Rainkokonen et al. (2012) reviewed the evidence on the early determinants of mental health. They noted the findings from studies of the Dutch Winter Famine and the Chinese Famine, which found that those exposed to these events had twice the rate of schizophrenia of people in these countries not exposed in this way. In addition, there was evidence of higher rates of antisocial personality disorders, affective psychoses, depression and addictive disorders among the Dutch Winter Famine cohort. From the results of these and other studies of low birth weight children, the authors concluded that:

Environmental adversities in early pre- and postnatal life seem to have widespread consequences on mental health outcomes later in life.

They further assert that, although the evidence is still limited:

Epigenomic mechanisms influencing gene expression at the level of the placenta and the offspring may play key roles.

In their review of studies concerned with the early determinants of type 2 diabetes (T2D), Berends and Ozanne (2012) cite the results of numerous animal and human studies, including those of the Dutch

Winter Famine, which showed that low birth weight was associated with impaired glucose tolerance and type 2 diabetes in later life. More recent studies however, have demonstrated a U-shaped relationship in which risk of diabetes increases with both low birth weight and high birth weight. In addition:

Over more recent years it has become apparent that a variety of expositions, including maternal obesity and/or maternal diabetes, can have a significant effect on offspring health outcomes. Further complicating matters, paternal and trans-generational transmission of T2D can occur thus mediating a perpetuating cycle of disease risk between generations.

In their review of the epigenetic and other mechanisms involved in the early determinants of **cardiovascular and kidney disease**, Santos and Joles (2012) discuss the role of development plasticity or programming in the adaptation of the organism during pregnancy and early childhood to environmental insults. Drawing upon studies using animal models, they assert that these mechanisms can be reprogrammed:

Potentially a genetic predisposition or known deleterious environmental factors acting in the early life can be counterbalanced during gestation and lactation through provision of nutritional supplements or pharmaceuticals, such as citrulline, to pregnant women with hypertension, preeclampsia, diabetes, etc. where the foetus is at risk to develop CV disease later in life. Thus, we may be able to reprogram CV health and prevent or delay the onset of a CV disease. Epigenetics offers exciting opportunities, such as perinatal and personalized administration of supplements such as folate, acting on DNA methylation, compounds such as butyrate, with HDAC inhibitory activity, or the soy isoflavone genistein, to alter miRNAs, to repress or derepress gene expression according to the genetic or programmed predisposition to develop CV disease.

These findings have led to the concept of an 'epigenetic diet' as a way of preventing or reversing adverse epigenetic modifications during pregnancy and postnatally.

In their paper on nutritional influences on epigenetics and age-related disease, such as cancer, CVD and neurodegenerative disorders, Park, Friso and Choi (2012) identified a number of agents that can modify the epigenome beneficially:

Nutrients involved in onecarbon metabolism, namely folate, vitamin B12, vitamin B6, riboflavin, methionine, choline and betaine, are involved in DNA methylation by regulating levels of the universal methyl donor S-adenosylmethionine and methyltransferase inhibitor S-adenosylhomocysteine. Other nutrients and bioactive food components such as retinoic acid, resveratrol, curcumin, sulforaphane and tea polyphenols can modulate epigenetic patterns by altering the levels of S-adenosylmethionine and S-adenosylhomocysteine or directing the enzymes that catalyse DNA methylation and histone modifications.

Similarly, Hardy and Tollefsbol (2011), in discussing the role of epigenetic diet and cancer, find that:

A growing body of evidence suggests that dietary agents as well as non-nutrient components of fruits and vegetables can affect epigenetic processes and are involved in processes, including the reactivation of tumour suppressor genes, the initiation of apoptosis, the repression of cancer-

related genes and the activation of cell survival proteins in different cancers. Dietary phytochemicals such as tea polyphenols, genistein, sulforaphane (SFN), resveratrol, curcumin and others have been demonstrated to be effective agents against cancer and to act through epigenetic mechanisms that affect the epigenome.

Australian studies

A number of studies in Australia have also provided evidence on the link between childhood circumstances and later health, in addition to those already discussed.

In Australia, the Mater-University of Queensland Study of Pregnancy (MUSP) is a large, prospective, pre-birth cohort study that enrolled 8,556 pregnant women at their first clinic visit over the period 1981 to 1983. These mothers (and their children) were followed up at intervals until 14 years after the birth. A number of publications have looked at the relationship between SES of mothers and a variety of outcomes for mothers and children. As examples, Morrison et al. (1989) examined the relationship to pregnancy outcomes, while Najman et al. (2004) assessed the impact on child cognitive development (CD) and emotional health (EH). This latter study found that:

Family income was related to all measures of child CD and EH and smoking, independently of all other indicators of the socioeconomic status of the child. In addition, the grandfathers' occupational status was independently related to child CD (at 5 and 14 years of age). Children from socioeconomically disadvantaged families (previous generations' socioeconomic status as well as current socioeconomic status) begin their lives with a poorer platform of health and a reduced capacity to benefit from the economic and social advances experienced by the rest of society.

Similarly, Raposa et al. (2013), using the same data set found that:

Early adverse conditions have lasting implications for physical health, and that continued exposure to increased levels of both social and nonsocial stress in adolescence, as well as the presence of depression, might be important mechanisms by which early adversity impacts later physical health.

Looking specifically at maternal depression, Raposa et al. (2014) found that:

Prenatal maternal depressive symptoms predicted worse physical health during early childhood for offspring, and this effect was partially explained by ongoing maternal depression in early childhood. Offspring poor physical health during childhood predicted increased health-related stress and poor social functioning at age 20. Finally, increased health-related stress and poor social functioning predicted increased levels of depressive symptoms later in young adulthood. Maternal depression had a significant total indirect effect on youth depression via early childhood health and its psychosocial consequences.

Hoy and Nichols (2010) reported on a longitudinal cohort study of 995 people with recorded birth weights who were born between 1956 and 1985 to an Aboriginal mother in a remote Australian Aboriginal community. Participant development was followed through to the end of 2006. The authors found that low birth weight was associated with a 2-3 times higher risk of death among adults from all causes and for cardiovascular and renal disease in particular.

The Longitudinal Study of Australian Children (LSAC) is a major study following the development of 10,000 children and families from all parts of Australia. It is managed by the Department of Social Services. The study commenced in 2004 with two cohorts - families with 4-5 year old children and families with 0-1 year old infants. It is investigating the contribution of children's social, economic and cultural environments to their adjustment and wellbeing. A major aim is to identify policy opportunities for

improving support for children and their families and for early intervention and prevention strategies. The study survey promises to be a good source of insights into the relationship between childhood circumstance and wellbeing in later life. A number of publications using data from the survey are listed on the *Growing Up in Australia* website.

As an example, Jansen et al. (2013) investigated the timing and strength of the association between SES and children's body mass index (BMI) in the pre- and primary school years, and examined socioeconomic differences in overweight trajectories across childhood. They found that:

Socioeconomic differences in mean BMI scores already present at age 4–5 more than doubled by age 10–11 years, reflecting decreasing mean BMI among advantaged rather than increasing means among disadvantaged children.

Risks of persistent and late-onset childhood overweight were highest among low SES families, and only partly explained by birth weight and parental overweight.

6. Childhood health and future socioeconomic status

Currie (2009) examined the link between a parent's SES and the child's level of income and wealth in later life. She made the obvious connection that income is strongly determined by level of education but extended her analysis by exploring the link between parental SES and both educational and labour market outcomes. In doing so, she was concerned to determine whether this occurs because of the effect of parental SES on child health.

Partly because she drew on the studies that have been reviewed earlier, Currie found a strong relationship between parental SES and child health, and between child health and future outcomes. One important study cited by Currie is that of Smith (2007), who used data from the United States (US) Panel Study of Income Dynamics to show that better health in childhood is related to higher incomes, greater wealth, more weeks worked, and a higher growth rate in income. The estimates imply that within families, a sibling who enjoyed excellent or very good health in childhood earns 24 per cent more than a sibling who was not in good health.

Case and Paxson (2010) examined the literature on the relationship between child health and economic and health outcomes in adulthood, using height as the measure of child health.

They concluded that taller individuals attain higher levels of education and that height is positively associated with better economic, health, and cognitive outcomes.

Drawing upon a United Kingdom (UK) longitudinal study of 12,686 young men and women who were 14-22 years old when they were first surveyed in 1979, Case and Paxson showed that:

Even among children with the same mother, taller siblings score better on cognitive tests and progress through school more quickly. Part of the differences found between siblings arises from differences in their birth weights and lengths attributable to mother's behaviours while pregnant. Taken together, these results support the hypothesis that childhood health influences health and economic status throughout adulthood.

7. Policy and research implications

Policies and programs

A recent study by the Center on the Developing Child at Harvard University (2010), reviewing policies and programs for strengthening lifelong health, argued that health promotion and disease prevention policies focused on adults would be more effective if evidence-based investments were also made to strengthen the foundations of health and mitigate the adverse impacts of toxic stress in the prenatal and early childhood periods.

The study identified three critical areas in which programs should be developed:

- a. Creating a stable and responsive environment of relationships
- b. Safe and supportive chemical, physical and built environments
- c. Sound and appropriate nutrition

a. Creating a stable and responsive environment of relationships

The first of these categories encompasses a range of different programs to strengthen the ability of parents and other caregivers to provide a stable responsive and nurturing environment for children to develop. This might be achieved, for example, through enabling more secure attachments between children and caregivers, and through the development of consistent and predictable sleeping patterns and other aspects of daily routine.

Examples of policy responses include parenting education, home visiting programs and expanded professional development for early care and education providers.

b. Safe and supportive chemical, physical and built environments

The second category of programs are those aimed at reducing exposures to harmful chemicals and improving the physical and built environment at home, at school and in neighbourhoods.

c. Sound and appropriate nutrition

The third category consists of programs to provide sound and appropriate nutrition over the life course, beginning with the mother's pre-conception nutritional status, extending through pregnancy to early infant feeding and weaning, and continuing with diet and activity throughout childhood and into adult life. The importance of adequate intake of folate, iron, and vitamins A and D during pregnancy is acknowledged but nutrition is critically important for the developing foetus and in early childhood.

Examples of responses within this category include policies and programs that support breastfeeding at home and at work, and supplemental nutrition programs for mothers and infants.

In their report to the WHO on the policy and research implications of the life course perspectives on coronary heart disease, stroke and diabetes, Aboderin et al. (2002) recommended that, because scientific understanding of the pathways of life course impacts on disease is still evolving, policies should concentrate on prevention addressing risk factors such as tobacco use and obesity. In addition, there is a need for school-based and other public health programs aimed at promoting healthy diets and exercise.

In Australia and other countries, programs have been developed to address various aspects of childhood disadvantage and its effects on development over the life course. There have also been a number of reviews on the effectiveness of these interventions.

Bowes and Grace (2014) have examined the prevention and early intervention research literature focused on improving outcomes for Australian Indigenous children in the early childhood years. They identified:

- 13 programs covering mainstream parenting programs for disadvantaged families, Indigenous-specific parenting programs, and home visiting programs
- 10 pre-school early childhood education programs
- Over 20 programs aimed at addressing the health inequities in early childhood for Indigenous children

In their review, they also identified a number of specific programs that were working, including:

- Parenting programs that involved active skills training for Indigenous parents, for example, the Indigenous Triple P program and Let's Start
- Early childhood education programs that had positive learning outcomes for Indigenous children such as HIPPY and Let's Start
- Health programs targeting particular disorders and diagnoses (including new treatment methods and ways of encouraging treatment compliance) and community-embedded maternal and infant health programs such as the Mums and Babies program

They concluded that:

- Program characteristics that seem to be associated with successful implementation in Indigenous communities have a strengths-based, family-centred approach; flexibility and sustainability; adaptations to suit the local needs and context; and models of service integration and collaboration.

The literature on the evaluation of childhood intervention programs is mainly concerned with programs that have been undertaken in the United States or Europe. The Benevolent Society commissioned the Centre for Community Child Health to review the literature on early childhood intervention programs (Moore & McDonald, 2013). They concentrated on five early intervention programs that have been shown to reduce factors associated with disadvantage (e.g. poor academic achievement, unstable housing) in the long-term (i.e. into adolescence and adulthood) using data collected through experimental or quasi-experimental research methods. These are:

- Nurse-Family Partnership: a home visiting program delivered from the antenatal period until the child reaches two years of age.
- High/Scope Perry Preschool project: a program for children and parents from low SES backgrounds that involved (a) daily classes every weekday for young children; and (b) weekly teacher conducted home visits with mother and child.
- Carolina Abecedarian Project: a program for low income families with high risk factors that involved: (a) fulltime child care facility and preschool program; (b) home visits (school-aged program) by a specialist teacher with supplemental educational activities; and (c) summertime supports (school aged program).
- Better Beginnings, Better Futures: available to all children within eight disadvantaged communities; the mix of programs in each site varies, however, all eight sites provided home visits to parents and worked with teachers to improve children's experiences.
- Chicago child-parent centre program: centre-based interventions that offer comprehensive services to children, encourage parent involvement and have a child-centred 'basic skills' focus.

Moore and McDonald's report identifies a number of recommendations for early childhood programs, including:

1. Provide free or low-cost preschool provision to three year old children experiencing significant disadvantage to ameliorate some of the negative impacts of disadvantage, ensuring a more level 'playing field' upon school entry.
2. Provide support to families experiencing disadvantage during the prenatal period to promote the optimal development of children.
3. Deliver programs of sufficient duration and intensity to families experiencing significant disadvantage as it appears that programs of less than 12 months are generally ineffective at shifting outcomes for disadvantaged children and families.
4. Provide direct services to children and families that promote the quality of the environments in which young children spend their time to ensure that parents and other caregivers relate to children in ways that protect, nourish and promote their development and wellbeing.

A number of economic analyses have argued that early intervention programs aimed at overcoming social problems yield a much greater return on investment than those aimed at interventions in later life. Heckman (2006), for instance, quoted a benefit: cost ratio of 8.74 for the Perry Preschool Program described above.

In Australia, Access Economics (2009), on behalf of the Australian Research Alliance for Children and Youth (ARACY), estimated the potential benefits of conducting a wide-ranging, long-term national prevention strategy aimed at improving the wellbeing of children and young people. They calculated net present value (NPV) of a 50% reduction for a set of preventable problems over the period 2008 to 2050 and found that:

The greatest economic gains result from interventions that are effective in enhancing human capital, reducing obesity, addressing mental illness in youth and preventing child abuse and neglect. In the base case, over the 42-year period (as well as in the first 5-years), while not being additive:

- investment in human capital could save around \$87 billion (\$1.7 billion);
- successful childhood obesity prevention programs could save around \$21 billion (\$370 million);
- mental health initiatives could save around \$12 billion (\$240 million);
- prevention of child abuse could save around \$5 billion (\$100 million);
- other initiatives to reduce alcohol harms, prevent teen pregnancies, address crime and delinquency and reduce bullying could save around \$2 billion (\$46 million)

The Department of Families, Housing, Community Services and Indigenous Affairs (FaHCSIA) commissioned Access Economics (2010) to calculate the cost and benefits associated with three intervention programs and found that they generated very large returns on investment:

- The Communities for Children program, targeting pre-school and primary school aged children improves outcomes in various areas including hostile parenting, parenting self-efficacy, parent mental health, quality of the home learning environment, parental relationship conflict, child total emotional and behavioural problems, childhood overweight, receptive vocabulary

achievement and verbal ability. The benefit: cost ratio for this program was estimated at 4.8:1, a 377% return on investment.

- The Positive Parenting Program improves outcomes in parental sense of competency, the dyadic adjustment scale, the Strengths and Difficulties Questionnaire (SDQ) emotional and conduct scales, the Eyberg Child Behaviour Intensity score, parental depression, parental laxness, parental over-reactivity, and parental verbosity. The benefit: cost ratio for this program was estimated at 13.8:1, a substantial 1,283% return on investment.
- The Reconnect program targets an older cohort of children and was found to improve outcomes in school bonding and conflictual relationships, with proxied effect sizes estimated for attachment to parents and harsh parenting. The benefit: cost ratio for this program was estimated at 1.8:1, an 81% return on investment. (pp 71-72)

Research

Almost all authors cited in this report have cautioned that more evidence and research is needed to strengthen and confirm their findings and to further elucidate pathways between childhood circumstances and adult health, particularly for different disease states.

Echoing this, Aboderin et al. (2002) have called for more well-designed prospective maternal and birth (or child) cohort studies, and the development and greater use of historical cohort and multi-generational studies.

Some of the research questions to which they give priority are:

- a. The nature of the effects of foetal and post-natal growth on later disease risk.
- b. The influence of maternal factors on foetal growth and offspring's risk of disease.
- c. The biological mechanisms underlying the association of foetal growth to later disease risk.
- d. The association of infectious disease to chronic disease risk.
- e. The social, psychological, economic and biological processes leading to unhealthy lifestyles and risk factors in different populations.
- f. The relative importance of early vs. later life exposures on risk of disease at individual and population level.

8. Conclusions

There is strong evidence for a distinctive socioeconomic gradient in adult health in Australia and that this has its origins in the circumstances of childhood. There are multiple pathways linking poor nutrition and other adverse impacts in gestation with both high and low birth weight. Combined with poor external environments in early childhood, this leads to physical and mental health problems in adolescence and in adulthood. However, a growing body of literature shows that properly designed and managed intervention programs can generate very large returns on investment, by avoiding or ameliorating the conditions that cause costly problems in later life.

Sustained programs that provide free or low-cost preschooling to children experiencing significant disadvantage, support to families, and developing parenting skills, have all been shown to be highly effective.

The evidence on epigenetic mechanisms in the transfer of early disadvantage to adulthood can provide guidance for the development of maternal and child nutrition programs and for other types of intervention.

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Appendix: Life Course Epidemiology Models

The life course approach has evolved a number of different models to explain the influence of status at various stages of life on health outcomes. According to Ben-Shlomo, Mishra and Kuh (2014), there are 7 models, as follows:

1. Critical Period Model.

In this model, it is assumed that an exposure (e.g. a specific viral infection) acting within a predefined time window (e.g. first trimester of pregnancy), may result in a specific disorder (e.g. schizophrenia). This model does not preclude other causes of schizophrenia that are unrelated to viral infection (e.g. genetic factors), or that other exposures (e.g. expressed familial hostility) cannot also increase risk of schizophrenia. It does assume that maternal exposure after the first trimester or if a subject is exposed postnatally, is not associated with any increased risk compared to an unexposed subject.

2. Sensitive Period Model.

An obvious variant of the above scenario is that exposure in the second trimester is associated with a milder form of the disease and that exposure in the third trimester is associated with a schizophreniform type of personality but not overt clinical disease. This is what is meant by a sensitive rather than a critical period model, namely, that exposure within specific time windows has a greater or lesser risk of disease.

3. Critical/Sensitive Period Model with Later Effect Modification.

Even though the timing of an exposure may be essential to have any effect or a stronger effect on a disease outcome, this does not mean that it is inevitable that disease will always emerge. Unrelated exposures in later life that are not themselves secondary to the initial insult could still modify disease risk either through independent or interactive effects. For example, if maternal under-nutrition in pregnancy, as seen in the Dutch Hunger Winter (Stein et al., 1975), was associated with a permanent reduction in the number of muscle cells at birth, this could be compensated by increased physical activity in later life resulting in muscle hypertrophy.

4. Accumulation of Risk with Uncorrelated Exposures.

We live in an associational world whereby many non-genetic exposures are correlated to varying degrees due to social patterning of exposures. It is therefore rare to have environmental associations that are truly randomly distributed. In such a scenario, the risk of being exposed to A is unrelated to B and C so that unexposed individuals are equally as likely to be exposed to B and C. For example, the risk of depression may be associated with a genetic variant (A), death of a father due to military conflict, and (C) unemployment in adult life due to the subject's employer going bankrupt. In this example, there is no reason to believe any of these exposures are correlated with each other. If each exposure increases risk (although this may be to varying degrees), then individuals exposed to more than one factor will have a greater risk than those exposed to fewer factors. In this case, we are assuming that these exposures do not interact with each other and the effects are additive.

5. Accumulation of Risk with Correlated Exposures.

Exposures are more commonly correlated because of risk clustering. For example, living in a poor neighbourhood may be associated with being exposed to a less healthy diet, reduced opportunities to exercise, and greater peer influences on smoking. Each of these factors may additively increase risk of

coronary heart disease but, in this case, one exposure will be associated with the others due to the common factor of neighbourhood poverty, which is an upstream determinant of the other mediating factors.

6. Chain of Risk Additive Model.

In this scenario, each exposure increases risk, but A is itself a determinant of B which in turn increases the risk of C. Hence, a chain effect may be established whereby an exposure may only have a modest effect directly on outcome, but its overall effect, including the indirect pathways, may be much larger. For example, smoking may directly result in subclinical atherosclerosis through an inflammatory effect on the arterial wall, but it also reduces exercise behaviour due to respiratory symptoms. This in turn results in reduced aerobic capacity but also increases obesity. This in turn results in insulin resistance syndrome and is a risk factor for coronary heart disease. In this case, intervening on obesity alone would have health benefits, but obese individuals who have followed this pathway would still be at increased risk due to their life course history compared to non-obese individuals.

7. Chain of Risk Trigger Model.

In contrast to the previous model, the trigger model is only associated with risk due to the last exposure in the chain. For example, a poor childhood socioeconomic environment results in overcrowding which in turn increases exposure to *Helicobacter pylori*, and this is associated with peptic ulcers. In this scenario, eradication of *Helicobacter pylori* will eliminate the risk, and there will no longer be any residual risk associated with the socioeconomic environment. Such pathways are interesting as they may explain why some epidemiological studies show marked heterogeneity of effects (assuming this is not due to random variation). In these pathways, variations in temporal or cultural differences can abolish associations. So, for example, the association of socioeconomic conditions with any smoking-mediated disease can legitimately vary by time and place due to cultural or temporal changes in smoking behaviour.



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