1.1 Environmental influences on development

This report sets out our current understanding of the links between early life and later health, and examines the role played by variations in early diet and nutrition in the aetiology of adult disease. Every individual has a ‘blueprint’ for growth and development determined by their genome, but realisation of this growth potential is only possible if nutrient supplies in intrauterine life and in childhood are adequate (Jackson 1996). While it is widely recognised that low birthweight is common among babies born to chronically malnourished women, and that stunting in children is prevalent in communities where food supplies are insufficient, the importance of more moderate variations in diet and nutritional status and their influence on early growth and development are currently less well understood.

1.1.1 Nutrition and the early environment

The supply of nutrients to the growing fetus is influenced by the nature of the maternal diet and nutrient stores. Animal studies show clearly that the fetus is sensitive to variations in its nutrient supply (Harding 2001), and experimental manipulations of this supply can have a profound impact on growth and development (Luther et al. 2005; McArdle et al. 2006). Compared with many other species, human gestation is long and the fetus is small in relation to maternal size (Widdowson 1976); thus synthetic demands and additional nutrient needs in pregnancy are relatively low. As most babies born to women in the Western world are above recognised cut-offs for low weight at birth, the human fetus has been regarded as being well protected from wide variations in maternal diet and nutritional status (Harding 2001; Jackson and Robinson 2001). However, although the intrauterine environment may be protective, there are well-known examples of adverse effects of variations in maternal nutrition – either from excessive exposure or due to insufficiency.

Damage effects of alcohol have been recognised for many years, but a consistent pattern of malformations in children whose mothers consumed excessive alcohol in pregnancy was described around 40 years ago (Hoyme et al. 2005). The effects include a range of structural anomalies and behavioural and neurocognitive disabilities, and are now termed fetal alcohol spectrum disorders (FASD) (Hoyme et al. 2005). The specific effects on the fetus of variations in the level and frequency of maternal alcohol consumption, as well as its timing in pregnancy, are not fully understood and require further research. We currently do not have reliable estimates of the incidence of FASD in the UK (Morleo et al. 2011). Although FASD may not be common, as many women stop drinking alcohol in pregnancy (Crozier et al. 2009), it is considered to be an important cause
of intellectual disability in the Western world (Abel and Sokol 1986). Another nutrient with recognised teratogenic effects when in excess in the diet is vitamin A (retinol). High intakes of retinol are associated with a specific pattern of craniofacial and other abnormalities in the fetus (Miller et al. 1998). The safe upper limit of intake is uncertain, but intakes from supplements above 10,000 IU have been associated with adverse outcomes (Rothman et al. 1995). Current UK guidance for pregnant women is that they should avoid eating liver, as it has a very high retinol content, and avoid dietary supplements that contain retinol (Department of Health 2009a).

In terms of effects of nutrient insufficiency, the clearest evidence we have is for the link between inadequate maternal folate status and the occurrence of neural tube defects (NTDs) in the fetus (De-Regil et al. 2010). A randomised controlled trial conducted in the 1980s provided conclusive evidence of the protective effects of folic acid supplementation (Medical Research Council 1991). It has since been shown that the inverse association between folate status and the risk of NTDs shows a dose–response relationship (Daly et al. 1995). A second nutrient for which there is good evidence of adverse developmental effects linked to insufficiency is iodine (Hetzel 2000). In areas of severe iodine deficiency, maternal and fetal hypothyroxinaemia can cause cretinism and have adverse effects on cognitive development in children (Zimmermann 2009). Whether mild or moderate maternal iodine deficiency causes more subtle changes in cognitive function in offspring is unclear as there are no controlled intervention studies in which long-term clinical outcomes have been assessed (Zimmermann 2009). For women living in iodine-deficient areas, maternal supplementation significantly reduces the incidence of these disorders. Ensuring adequate iodine status among women of reproductive age should thus be a high priority.

Developmental consequences of variation in nutrient intake are not restricted to fetal life. Growth faltering in infancy is widespread in many parts of the world and results in permanent height deficits. Stunting is linked to many indices of functional impairment, including intellectual development (Jackson 1996). The primary driver of infant growth is thought to be nutritional (Karlberg et al. 1994), and young children are vulnerable to the effects of chronic energy and nutrient restriction (SACN 2011a). The secular changes in height observed in most European populations since the nineteen century are attributed to increased height gain in late infancy (Cole 2000), arising at least in part from improvements in diet and nutrition.

In each of these examples, there are adverse effects of inappropriate nutrition – with nutrients either acting as damaging teratogens, or being supplied in insufficient amounts to meet needs during intrauterine and early postnatal life. The key issue is that in all cases the effects are permanent – and they will have lifelong consequences. Exactly how they affect the individual will depend on the nature of the nutritional insult, its severity and timing. These examples describe the effects of extremes in nutrient intake that have measurable effects, allowing examination of the role of nutrition in their aetiology. What we need to understand more about are the developmental consequences of more modest variations in nutrition arising from existing differences in dietary habits and food choice.

1.1.2 Variations in growth and development

The measure that is widely used to judge the success of pregnancy is the weight of the baby at birth. This varies over a wide range: weights between 2.5 kg and 4 kg are considered normal for babies born at term. While babies of low birthweight (< 2.5 kg) are recognised as being at increased risk of mortality in infancy (McCormick 1985), until recently, variations above 2.5 kg were seen as unremarkable and regarded as a result of differences in fetal growth due to genetic variation. A growing body of epidemiological data now shows that this may not be the case as these ‘normal’ variations in fetal growth and size at birth are predictive of differences in the incidence of specific disease conditions in adult life – and this is evident even in developed communities such as the UK (Barker 1998). If constraint of fetal growth is linked to changes in physiology that have long-term health consequences, we clearly need to reconsider whether we know enough about the current determinants of normal variations in fetal growth.

Variation in postnatal growth may also be important for long-term health. Growth monitoring is widely used to assess the nutritional status of infants and children and as an indicator of health and well-being. There are growth reference curves to enable judgement of adequacy of growth between birth and adulthood (see Chapter 2, Section 2.8). But what
constitutes optimal growth in infancy and childhood is not clear. In the same way as for fetal growth, we need to reconsider what is an optimal pattern of infant growth. For example, although poor infant growth is clearly of concern as it may be an indicator of failure to thrive, systematic reviews of infant growth studies show that rapid infant growth (or ‘catch-up’ growth) is predictive of obesity in older children and adults (Baird et al. 2005; Ong and Loos 2006).

As we begin to take account of the long-term consequences of variations in early growth and development, we expose a lack of understanding of the importance of current variations in diet and nutrition, particularly in the developed world. As adequate nutrition is key to successful fetal and infant growth, to address differences in adult health and risk of disease, we need to define what is optimal in terms of maternal and infant diet and nutrition.

### 1.2 Links between early life and adult disease

#### 1.2.1 Animal studies

The classic studies of McCance and Widdowson carried out five decades ago provided evidence that permanent changes can occur in response to manipulation of early nutrition. For example, in their studies of rats, they showed that by altering litter size at birth the pups were overfed or underfed during the period of lactation. The overfeeding of rats raised in small litters promoted early growth and, compared with rats raised in large litters, the achieved adult size was greater (Fig. 1.1) (McCance 1962). Altering the plane of nutrition between 9 and 12 weeks did not have this effect, suggesting that there is a critical period within which variations in postnatal nutrition determine growth and body composition. More recently, rats raised in small litters have been shown to develop hyperphagia and greater adiposity in adult life (Plagemann 2005). Other important early studies include the work of Stewart and colleagues who showed that, in rats maintained on a low-protein diet for 10–12 generations, refeeding for several generations was required in order to correct the physical and behavioural deficits in the offspring (Stewart et al. 1980). Thus the physiological changes resulting from dietary restriction were evident beyond the immediate offspring.

These studies clearly demonstrated the principle that permanent changes in physiology occur in early life as a result of variations in maternal and/or postnatal nutrition. Although at the time of these early studies the physiological mechanisms involved were not understood, recent experimental studies have made enormous progress in explaining these links (see Chapter 4).

#### 1.2.2 Evidence from human populations

One of the earliest studies to propose a role for early experience in the aetiology of adult disease was carried out by Forsdahl (1977). In a comparison of the past infant mortality rates of Norwegian counties with their current mortality rates from arteriosclerotic heart disease, he showed that they were highly correlated (Fig. 1.2). Forsdahl proposed that the increased risk for adults living in some counties was a result of their experience of poverty earlier in life – and that poor living conditions in childhood and adolescence led to a lifelong vulnerability that remained, even if the environment improved in adult life.
In the UK, Barker and colleagues showed that mortality rates for cardiovascular disease were also high in geographical areas that in the past had been areas with high infant mortality (Barker and Osmond 1986; Barker, Osmond et al. 1989). In these studies the authors were able to subdivide deaths occurring in the first year of life into those occurring in the first month (neonatal) and those occurring in the rest of the year (postneonatal). Stroke mortality was linked to neonatal mortality but not to postneonatal mortality (Table 1.1), while mortality from coronary heart disease (CHD) related to both neonatal and postneonatal mortality rates. In contrast, death rates from chronic bronchitis showed an association only with postneonatal mortality rates. These data suggested that the origins of cardiovascular disease might be even earlier in the life course than childhood and adolescence – and that events in fetal life were important in the aetiology of adult cardiovascular disease (see Chapter 10).

Table 1.1 Death rates (standardised mortality ratios) from stroke, coronary heart disease and chronic bronchitis (1968–78, men and women aged 35–74 years) in the 212 areas of England and Wales, grouped by neonatal and postneonatal mortality (1911–25)

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<thead>
<tr>
<th>Postneonatal mortality</th>
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<td>1 (low)</td>
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<td>5 (high)</td>
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<td>Coronary heart disease</td>
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<td>5 (high)</td>
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<td>114</td>
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<tr>
<td>Chronic bronchitis</td>
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<td>Neonatal mortality</td>
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<td>1 (low)</td>
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<td>–</td>
<td>108</td>
<td>123</td>
<td>144</td>
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</table>

Barker and colleagues went on to identify a number of cohorts of adult men and women whose early growth had been recorded, and whose records had survived to the present day. By tracing these men and women they were able to link measures of early growth to disease-specific mortality rates, as well as to risk factors for those conditions. Figure 1.3 shows the risk of dying prematurely from cardiovascular disease among 15 726 men and women who were followed up in this way (Osmond et al. 1993).

In both men and women there was a graded inverse association between weight at birth and risk of death from cardiovascular disease. Studies of other cohorts have shown that the associations are not explained by variations in gestational age at birth, or by differences in adult lifestyle. These associations have been replicated in a number of studies in a wide range of populations in Europe (Frankel et al. 1996; Leon et al. 1998; Lawlor, Ronalds et al. 2005), North America (Rich-Edwards et al. 1997) and India (Stein et al. 1996). We now know that there are similar associations between weight at birth and risk of hypertension and type 2 diabetes in adult life – two disorders closely linked to cardiovascular disease (Hales et al. 1991; Curhan et al. 1996; Bergvall et al. 2005; Gamborg et al. 2007) (see Chapter 10).

It seems that people who were smaller at birth remain biologically different from people who were larger, consistent with Forsdahl’s proposition that an adverse environment in early life results in a lifelong vulnerability to cardiovascular disease. The work of Barker and colleagues (Barker 1998) indicated that, for cardiovascular disease, the early environment included experience in fetal life as well as in later childhood.

### 1.2.3 The interaction of fetal and postnatal experience and adult disease

Many of the historical cohorts studied do not provide information about postnatal growth, and it is not possible to gain any insight into how postnatal experience impacts on the link between fetal growth and adult disease. Important information about the interaction of prenatal and postnatal experience on adult disease has therefore come from the study of men and women born in Helsinki, Finland, where birth records can be linked both to records of childhood
growth and to hospital admission and mortality data (Eriksson et al. 1999). In a cohort of 8760 men and women who were born between 1934 and 1944, there were 357 men and 87 women who had developed or died from CHD (Barker et al. 2005). As in the Hertfordshire study (Osmond et al. 1993), the body size of children, who as adults had coronary events, was below average at birth. Between birth and 2 years their growth relative to other men and women in the cohort who did not develop the disease was poorer, and weight, height and body mass index (BMI) was low (Fig. 1.4). Beyond 2 years the men and women who went on to have CHD gained weight rapidly, such that they reached average or above average weight and BMI by the age of 11 years.

It has been shown that hypertension and type 2 diabetes are associated with the same general pattern of growth as CHD (Eriksson et al. 2000; Forsen et al. 2000). Similarly to CHD, the risk of disease is not determined only by the absolute value of BMI in childhood, but by the combination of body size at birth and during childhood (Eriksson et al. 2000; Forsen et al. 2000). The influence of different pathways of growth on later health has also been described in a study of young Indian adults (Bhargava et al. 2004). Thinness at the age of 2 years, but followed by rapid growth and a relatively high BMI at the age of 12 years, was associated with the highest rates of impaired glucose tolerance or diabetes (see Chapter 9).

Singhal and Lucas (2004) have proposed that it is the effect of rapid postnatal growth that is particularly damaging in relation to cardiovascular disease. For example, in an intervention study they showed that feeding a high-nutrient diet to pre-term infants promoted weight gain, but that this was associated with later insulin resistance (Singhal, Fewtrell et al. 2003). Additionally, there is an increased risk of obesity in individuals who exhibited rapid infant growth (Baird et al. 2005; Ong and Loos 2006). These contrasting findings highlight our current lack of understanding about what is optimal in terms of pathways of postnatal growth.

1.2.4 Vulnerability to stressors acting in adult life

The American Nurses’ Health Study found that in the men and women born in Helsinki, the significance of a single measure of their BMI at any age, in relation to cardiovascular risk and impaired glucose tolerance, differed according to earlier pathways of growth. The study also provided evidence that the effects of BMI are conditioned by early growth. Interactive effects were found, such that higher BMI
in adulthood was an especially strong risk factor for CHD among women who were small at birth (Richard-Edwards et al. 2005). Such heterogeneity in response, originating in early life, could also apply to other influences. For example, variations in adult diet may have different metabolic effects among adults who differ in their early experience. There is some evidence that this is the case, as total and saturated fat intakes have been shown to differ in their associations with serum high-density lipoprotein (HDL) cholesterol concentrations, and with the ratio of HDL-cholesterol to low-density lipoprotein (LDL) cholesterol, in men of different birthweights (Robinson et al. 2006). In men in the Hertfordshire cohort, comparable interactive effects of early growth and adult lifestyle have also been described in relation to bone status (see Chapter 12), as smoking was associated with a lower bone mineral density, but only among men of lower birthweight (Moinuddin et al. 2008).

In addition there is evidence that adult responses to psychosocial stressors differ according to early experience. Among men studied in the Helsinki cohort, born between 1934 and 1944, low income was associated with increased rates of CHD (Barker et al. 2001). This effect has been described many times and is a major component of the social inequalities in health in Western countries (Marmot and McDowall 1986; Macintyre et al. 2001). In the Helsinki study, however, the effect of low income was shown to be limited to men who were thin at birth, defined by a ponderal index less than 26 kg/m$^3$ (Fig. 1.5). Men who were not thin at birth appeared to be resilient to the effects of low income on CHD.

One explanation of these findings is that perceptions of low social status and lack of success lead to changes in neuroendocrine pathways and hence to disease (Marmot and Wilkinson 2001), and that this may differ according to early experience. This possibility is consistent with the finding that there are persisting alterations in responses to stress, including raised serum cortisol concentrations in adults who were small at birth (Phillips et al. 2000).

The finding that there are interactive effects of early life and adult experience in determining disease risk is consistent with the ideas of Dubos (1987), who wrote: ‘The effects of the physical and social environment cannot be understood without knowledge of individual history.’

### 1.3 Biological mechanisms

#### 1.3.1 Fetal programming

The link between early experience and later disease was described by Lucas (1991) as ‘programming’. This was defined as a process whereby a stimulus or insult, acting at a critical phase of development,
results in long-term changes in the structure or function of the organism.

Central to the programming hypothesis was the proposition that variations in fetal nutrition were responsible for permanent changes in physiology and function, which had lifelong consequences for the individual including their risk of cardiovascular disease and type 2 diabetes in adult life (Barker 1998). While the growth of the fetus is influenced by its genes, determining its potential for growth, the intrauterine environment appears to have a greater effect on the growth achieved. The classic studies of Penrose (1954) concluded that 62% of the variation in birthweight was the result of the intrauterine environment, 20% the result of maternal genes and 18% the result of fetal genes. Support for the importance of the fetal environment has come from the study of babies born following ovum donation, since weight at birth was found to be strongly related to the weight of the recipient mother, but not to the weight of the donor mother (Brooks et al. 1995). However, it has also been proposed that there may be genetic factors that are linked both to low birthweight and to adult disease, which could also contribute to the association, and there is some evidence to support this (Dunger et al. 1998; Hattersley et al. 1998).

1.3.2 Developmental plasticity

In 2005, Bateson challenged the use of the term ‘programming’ to explain the observations that the environment, during development, has long-term effects on the offspring, and proposed that environmental induction of ‘developmental plasticity’ was more appropriate (Bateson 2007). Developmental plasticity describes the ability of a single genotype to produce more than one alternative form of structure, physiological state or behaviour in response to environmental conditions. Thus a range of phenotypes can arise from a single genotype in response to variations in the environment. This has evolutionary benefits, as it enables better matching of individuals to their postnatal environment than would be possible if one genotype produced the same phenotype in all environments. However, in a changing environment, the resulting phenotype may be poorly suited to its postnatal conditions because its environmental forecast was incorrect (Fig. 1.6) (Bateson et al. 2004; Bateson 2007). This has obvious implications for populations undergoing rapid changes in diet and lifestyle.

The environmental cues that lead to different phenotypes are largely undiscovered, but considerable progress in understanding mechanisms has been made using animal models. In terms of the early proposition that variations in fetal nutrition were central to the associations between fetal growth and later disease (Barker, Osmond et al. 1989), there is now a significant body of experimental evidence that shows long-term effects of manipulations of maternal diet that are consistent with these epidemiological associations (Luther et al. 2005; McArdle et al. 2006) (see Chapters 8–14).

1.4 Nutrition of mothers and children

Despite decades of interest in maternal nutrition we know little about the long-term effects on the offspring of variations in women’s diets and their
Introduction to Early Life and Later Disease

There are far fewer observational studies in which variations in maternal nutrition can be linked to the adult health of the offspring. Some insights have come from studies of women who were subjected to acute starvation over a short period, and in which birth outcomes can be compared for individuals born during and after a period of famine. Much of this information has come from the study of men and women who were conceived and born during the Dutch Hunger Winter. In 1944–5, food supplies to the population of western Holland were restricted such that official rations fell below 4184 kJ/day (1000 kcal/day) for a period of about 5 months (see Chapter 4, Section 4.4.2 for more details) (Lumey et al. 2007). The population was previously well nourished and food supplies were restored quickly after May 1945. Birthweight fell by around 300 g in babies exposed to the famine in the last trimester of pregnancy (Stein et al. 2004). Follow-up of the men and women who were exposed to famine in intrauterine life has shown that its effects differed according to timing in gestation. Marked effects were seen in the men and women conceived during the famine, and include a more atherogenic lipid profile, and a tripling of coronary artery disease prevalence at the age of 50 years (Painter et al. 2006a). Exposure to the famine in early gestation was also associated with differences in food choice at age 50 years, as these men and women were twice as likely to consume a high-fat diet (Lussana et al. 2008).

1.4.1 Observational studies of maternal diet

Most of the information we have on the relationship between maternal nutrition and pregnancy outcomes has come from observational studies, which does not allow us to make inferences about causality in the links between early nutrition, growth and later health. Diet in pregnancy has been assessed in a number of studies and related, most commonly, to variations in size at birth and other short-term outcomes. Although individual studies have provided evidence of links between variations in maternal nutrient intake and some of these outcomes, there is little consistency in the findings across studies, and there are few nutrients for which definitive intake guidelines can be established (Jackson and Robinson 2001).

There are many methodological reasons why direct comparison of these observational studies may be difficult – not least due to differences in dietary assessment methods, timing in gestation and differences in the populations studied. The studies often rely on birthweight as the outcome, which is an incomplete statement of the success of pregnancy, and they also fail to take account of heterogeneity among women in their responses to pregnancy (Jackson and Robinson 2001). But perhaps the greatest issue is that many of the studies have looked for simple relationships between maternal intake and fetal growth – whereas the supply line that links maternal diet to fetal nutrient supply is complex (Fig. 1.7) (Harding 2001).

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1.4.2 Supplementation studies

Dietary interventions to increase nutrient intake in pregnancy have largely had disappointing results, as the effects on birthweight have been small, even in marginally nourished populations (de Onis et al.
1.4.3 Maternal body composition

Although poorer perinatal outcomes have been associated with mothers who are both underweight and overweight, the long-term consequences of variations in maternal body composition on the offspring have been little studied. Higher maternal BMI is associated with greater adiposity in the child (Gale et al. 2007), but the extent to which this is due to the shared postnatal environment is not known, nor whether there are persisting influences of variations in the intrauterine environment on the child’s body composition. A role of prenatal experience is likely to be important. For example, women who have poor glycaemic control in pregnancy are at increased risk of having a baby large for gestational age, with greater adiposity (Catalano and Ehrenberg 2006). Importantly, even among women with normal glucose tolerance at screening, increasing maternal glycaemia has been associated with a greater risk of obesity in their children (Hillier et al. 2007). Set against the rapid background changes occurring in body composition in many countries (see Section 1.5 and Chapter 3, Section 3.3.1), the long-term outcomes that are associated with variation in maternal body composition need further study (see Chapter 8).

1.4.4 Postnatal nutrition

We know little about the importance of current variations in postnatal diet for long-term function. Most studies of infant diet are limited largely to comparisons of breastfeeding and formula feeding in infancy and less is known about the role of weaning practice, and whether qualitative differences in diet in late infancy affect later health. Breastfeeding is associated with a number of beneficial long-term outcomes, including effects on a number of risk factors for cardiovascular disease (Martin, Ben-Shlomo et al. 2005; SACN 2011b). However, the confounding effects of social gradients in breastfeeding need to be considered, and recent studies from low- and middle-income countries, where influences on infant feeding practice vary, show some differences (Brion et al. 2011; Fall et al. 2011). While further data are needed from populations that differ in confounding structures, misclassification of nutritional exposures remains a...
particular challenge in infancy. Important data have therefore come from randomised controlled trials of infant feeding (Singhal et al. 2004) and the Promotion of Breastfeeding Intervention Trial (PROBIT) in Belarus (Kramer et al. 2001). Further follow-up of these children will be key in providing insights into the role of infant feeding, and its effects on lifelong health, in the future (see Chapter 8, Section 8.5.2).

1.5 Nutrition of young women today

Although there have been positive changes in the diets of adults in the UK over the past decades, there are huge inequalities in diet and nutrition across the population (SACN 2008). The diets of children and young adults have become a particular concern as, not only is the prevalence of obesity rising, but it is coupled with growing evidence of low micronutrient intakes and status in these age groups (see Chapter 3, Section 3.2). Additionally there are strong social patterning influences on diet, so that poor diets are more common in disadvantaged groups in the population, such as women who are food insecure (Nelson et al. 2007).

Thus, for many young women, not only could their current patterns of diet impact on their own nutritional status, they may also affect their ability to meet the nutrient needs of future pregnancies. Furthermore their dietary patterns are an influence on the way that they feed their children (Fisk et al. 2011), suggesting that inequalities in diet and nutrition will persist in the next generation. In the context of the long-term consequences of developmental effects of poor nutrition that this report presents, inequalities in early nutrition may be expected to translate into differences in risk of adult disease in the future. Intervention strategies to lower this risk will require a very clear understanding of the influence of current variations in diet and nutrition on growth and development in early life.

1.6 Key points

- An individual’s growth potential is determined by their genome, although adequate nutrient supply is required in early life to realise this growth potential.
- There is strong evidence that some nutrients have clear developmental effects, e.g. vitamin A (excess) and iodine and folate insufficiency, but the effects of more modest variations in maternal nutrition are less well understood.
- Fetal programming is defined as a process whereby a stimulus or insult acting at a critical phase of development results in long-term changes in the structure or function of the organism.
- Environmental conditions can impact on the genotype, resulting in more than one alternative form of structure, physiological state or behaviour developing. This is referred to as ‘developmental plasticity’.
- Epidemiological studies show a link between early experience and adult diseases such as diabetes, cardiovascular disease and cancer.
- Some individuals may be more vulnerable to the effects of stressors in adult life as a result of poor experiences in early life, such as inadequate nutrition.
- Experimental studies provide clear evidence of developmental influences of variations in early nutrition that may be key to the links between early life and adult disease, but our current understanding of how these experimental data inform optimal patterns of maternal and infant nutrition is limited.
- The poor diets of young women observed in the UK are of concern, and may impact on their ability to meet the nutrient needs of future pregnancies.
- Intervention strategies to lower future disease risk will require a clear understanding of the influence of current variations in diet and nutrition on growth and development in early life and on lifelong health.
1.7 Key references


