Associations of Perinatal Conditions with

Adult Body Size and Intelligence:

A Register-based Cohort Study in Norway

1967-1999

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CONTENTS

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LIST OF PAPERS

This thesis is based on the following four papers:

Paper I   MG Eide, N Øyen, R Skjærven, ST Nilsen, T Bjerkedal, GS Tell. Size at birth and gestational age as predictors of adult height and weight. Epidemiology; 2005;16(2):175-181.

Paper II   MG Eide, N Øyen, R Skjærven, T Bjerkedal. Association of birth size, gestational age, and adult height with intelligence: evidence from a cohort of 317 761 Norwegian men. (Under review)

Paper III   MG Eide, N Øyen, R Skjærven, LM Irgens, T Bjerkedal, ST Nilsen. Breech Delivery and Intelligence: A Population-Based Study of 8,738 Breech Infants. Obstet Gynecol 2005;105(1):4-11.

Paper IV   MG Eide, R Skjærven, LM Irgens, T Bjerkedal, N Øyen. Associations of birth defects with adult intellectual performance, disability and mortality: population-based cohort study. (Under review)

DEFINITIONS

Body mass index	Weight (kg)/height (m^2)
Preterm birth	Birth before 37 completed weeks of gestation.
Term birth	Birth from 37 to (and including) 41 completed weeks of gestation.
Post-term birth	Birth from 42 completed weeks of gestation.
Birth defect	Condition diagnosed at birth or the first seven days of life recorded in the Medical Birth Registry form according to the International Classification of Diseases, 8th Revision [ICD-8] codes: 740.0-759.9 for congenital anomalies and 551.1-9 for abdominal defects.
Neonatal period	Time period from birth through the 28th completed day of life
Neonatal mortality	Neonatal deaths per 1000 live births
Perinatal period	The time period including birth through the end of the seventh completed day (168 completed hours) of life
Perinatal mortality	Perinatal deaths per 1000 births (live and stillbirths)
Low birth weight	Birth weight below 2500 g
Infant mortality	Death within the first year of life (0-364 days) per 1000 live births

ABBREVIATIONS

CI   Confidence interval

cm   Centimeter

BMI   Body mass index

g   Grams

ICD-8   International Classification of Diseases, 8th Revision

IQ   Intelligence quotient

kg   Kilograms

m   Meters

MBRN   Medical Birth Registry of Norway

OR   Odds ratio

RR   Relative risk

SD   Standard deviation

SES   Socioeconomic status

WHO   The World Health Organization

INTRODUCTION

In perinatal epidemiological research, mortality has been a central outcome. Compared to later periods in life, perinatal mortality has been, and still is, considerable. However, as perinatal mortality has decreased to a gratifying extent, perinatal and neonatal morbidity, as well as long-term health outcomes and their possible perinatal origin have come into focus. The first period of life is increasingly thought to be important in the aetiology of adult health and disease. Recent evidence suggests that factors acting in foetal life, during critical periods of growth and development, may biologically 'programme' adult chronic disease.[1,2] Later experiences may modify these effects. Hence, adult chronic disease may also reflect cumulative lifetime unhealthy exposures.[3]

Health in early adulthood may be regarded as an intermediate factor on a causal pathway between intrauterine influences and adult disease development. Thus, elucidating influences of perinatal conditions on health in early adulthood may provide a better understanding of the "web of causation"[4] linking early life exposures and adult disease. This thesis is based on a nationwide historical cohort study assessing possible associations between perinatal conditions on one hand and adult body size and intelligence on the other.

Adult health

In 1948, The World Health Organization [WHO] defined health as "A state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity." In 1984, the definition of health was revised and expanded: "(…). Health is a resource for everyday life, not the objective of living; it is a positive concept, emphasizing social and personal resources as well as physical capabilities. (…)"

According to the WHO definition, health is an abstract and complex concept not easily measured. In epidemiologic research, mortality and broadly defined morbidity outcomes have been classical measures of adult health, or rather lack of health. However, lack of health is increasingly being considered more specific in terms of disease outcomes, as well as physiological, cognitive, and psychosocial malfunctioning. Health measures may be viewed as intermediate variables in the relationship between early life exposures and adult disease outcomes. Some selected anthropometric and functional measures of health associated with

chronic disease are listed in Table 1. These are the health measures of specific interest in this thesis. The impact of these health measures in relation to disease outcomes is described below.

Particularly during the last five decades, adult chronic disease has been a main public health concern of developed countries. Cardiovascular disease, cancers, chronic obstructive lung disease, and diabetes together contribute to about 50% of the global mortality burden and account for 19% of the global burden of disease.[5] In the developed world, the prevalence of obesity has risen dramatically, in both children and adults.[6,7] Obesity is a major risk factor for many chronic diseases, such as cardiovascular disease and type 2 diabetes.[8] Thus, obesity is an important cause of morbidity and mortality. Also, stature is related to health outcomes; for example, short stature in adulthood is associated with increased risk of longstanding illness and all-cause mortality.[9]

Table 1. Anthropometric and functional measures in adults which are associated with disease

Measure	Disease outcome	References
Height	Cancer	Bjørge, 2004 [10]
	Cardiovascular disease	Leon, 1995 [11]
	Obstructive lung disease	Leon, 1995 [11]
	Mortality	Waaler, 1984 [12]
Weight	Cancer	Calle, 2003 [13]
	Cardiovascular disease	Calle, 1999 [8]
	Diabetes	Willett, 1999 [14]
	Mortality	Calle, 1999 [8]
Cognitive function	Cardiovascular disease	Osler, 2003 [15]
	Mortality	Whalley, 2001 [16]

Height

Body height and weight are commonly used anthropometric measures. Height reflects both genetics and living conditions during the growth phase. Although little is known about the underlying genetics of adult stature, heritability of stature is reported to account for more than 80% of the variation.[17] Also, nutrition and infectious diseases in childhood are known to influence substantially adult height.[3] However, the relative contributions of genetics, intrauterine conditions, and childhood environmental factors to adult height are unknown.[18]

In Norway, as in most developed countries, mean height in adolescence and adulthood has been increasing through the last century.[19,20] The increase in height is viewed as an expression of generally improved living conditions, including the general nutritional status of the population.[20]

Adult height has been found to be predictive of all-cause mortality, as well as cardiovascular morbidity and obstructive lung disease.[12] These associations have been confirmed in several studies.[9,11,21] A similarity between secular trends in height and mortality has even been reported among 13-year old girls.[20] The height-mortality association appears to be rather strong, incremental, consistent across a number of study populations, and independent of socioeconomic circumstances in both childhood and adult life.[11] Waaler also reported that short stature was related to excess mortality from stomach and lung cancer.[12] On the other hand, tallness has been shown to be associated with high rates of kidney, breast, prostate, and colorectal cancers.[10,22] In one study, tallness appeared to be associated with good self-perceived health.[9]

Since height reflects an individual's childhood nutrition and growth, as well as socioeconomic conditions,[20] these findings may support the hypothesis that the early environment influences adult health. However, it has also been shown that tall stature is associated with better education and upward social mobility.[23] Therefore, height may influence health through its effect on adult socioeconomic position.[11] Other explanations for the positive association between stature and health may be a reverse pathway; that disease may lead to shorter height, or the possibility that genetic regulation of height and susceptibility to disease may be linked in some way,[12] e.g. by involving pleiotropic genes.

Weight
Weight is a modifiable risk factor since it is affected by environmental factors to a greater degree than height. Body mass index [BMI] is a widely used measure of weight adjusted for height, and, thus, of obesity. Weight, in terms of overweight and obesity, is a well known risk factor for poor adult health. There is an established association between excess body weight and overall mortality.[8] Obesity is a risk factor for many chronic diseases, such as coronary heart disease, stroke, respiratory disease, several orthopaedic disorders, gallbladder disease, infertility, and type 2 diabetes.[8,13,14,24] Obese women have a higher risk of obstetric complications.[25] Furthermore, overweight is associated with increased risk of developing

cancer at several specific sites, for example colorectal cancer and cancer of the endometrium in females.[13,14,25] Because age influences the risk, the relationship between breast cancer and body weight is unclear. However, at postmenopausal ages, high BMI is a risk factor for breast cancer.[3,25]

In addition to - and independent of - overall obesity, the distribution of fat is regarded as a potential risk factor for chronic diseases because centrally deposited fat is probably more metabolically active and more strongly associated with insulin resistance than peripheral fat.[25] Mechanisms underlying the association between obesity and poor health may be of both biological and social origin. For example, elevated blood pressure, hyperlipidemia and altered haemostatic factors are effects of excess fatness that are implicated in the association between obesity and coronary heart disease, whereas endocrine effects are infertility and type 2 diabetes.[25] However, being overweight may also have adverse socioeconomic consequences; it has been observed that fatter women are less likely to marry, have poorer job opportunities and lower incomes than other women.[24] Similar but weaker trends have been found among men. Finally, a genetic mechanism linked to both obesity and poor health due to chronic disease is also plausible.

Intelligence
Intelligence can be defined as "…a very general mental capability that, among other things, involves the ability to reason, plan, solve problems, think abstractly, comprehend complex ideas, learn quickly, and learn from experience."[26]

Intelligence can be measured by different tests. The obtained standardized measure of intelligence is termed intelligence quotient [IQ], and represents the individual's result in comparison to other people. The frequency distribution of IQ is Gaussian; the mean IQ is 100 and the standard deviation [SD] is 15. An IQ above 130 is considered very high, and 70 (-2 SDs) is considered the threshold of mental retardation.[26] Questions have been raised as to what intelligence test actually measure.[15,27,28] There is abundant evidence on the validity and reliability of intelligence tests.[29] Yet, they do not measure creativity, personality, or other important differences among individuals; nor are they intended to.[26] Nevertheless, the construct of intelligence is extremely useful, and, whatever intelligence tests measure, it is of great practical and social importance.[26] The use of intelligence tests is widespread in modern

society, especially for selection of applicants. In military services, intelligence tests have been used to allocate soldiers to various service branches.

Results of intelligence tests have been used as outcome measures when studying the effects on human development of special demographic events such as the Dutch famine during the winter of 1944-45. No effect of perinatal exposure to famine on intellectual performance was observed, and the authors suggested that postnatal influences have a more significant effect than prenatal conditions on intellectual abilities.[30] Still, the hypothesis that malnutrition in early foetal life may have adverse effects on the developing brain has been extensively studied by use of intelligence tests. Several studies have related different measures of size at birth to intellectual performance in childhood and adolescence.[30-42]

Recently, intelligence as a determinant of health outcomes has attracted much research attention. Studies have linked intelligence in childhood to mortality in later life,[15,16,43,44] although in one study the association was observed only in men.[43] Further, intelligence is associated with a number of important health outcomes, including cardiovascular disease,[15] suicide,[45] and some cancers.[46] The association between intelligence and mortality is inverse and incremental, implying a risk gradient across the distribution of IQ scores. Thus, this relates to the general population, rather than only to those with severe intellectual impairment. Moreover, the relation of poor health with intelligence remains following adjustment for early life socioeconomic position.[16,43]

Both social and genetic factors are likely to be important in determining the association between intelligence and health. Heritability of general intelligence is approximately 50% with estimates ranging from 40% to 80%; i.e. genetic variation accounts for approximately half of the variance.[29,47] High intelligence in childhood is likely to lead to educational success, well paid employment, and high social status; conditions that are strongly associated with later disease.[29,44] High intelligence promotes faster and more complete learning, resulting in better preventive self-care and better compliance with medication instructions.[48] Intellectual ability as a mediator between physical and social disadvantage in childhood and adult mortality would represent another mechanism accounting for the association. Finally, it has been hypothesized that intellectual ability may be an indicator of the effectiveness of information processing in the central nervous system and thus of the integrity of the body as a whole.[16]

Gottfredson and Deary have argued that technologic advances in modern societies make cognitive competence increasingly important for health.[49] They have proposed that inadequate health self-care is the principal mechanism by which intelligence is related to social inequalities in health. For example, diabetes, hypertension and many other chronic illnesses, require self-monitoring and frequent judgments to keep physiological processes within safe limits. The same authors have also claimed that differences in general intelligence is the "fundamental cause" of social inequalities in health, suggesting that cognitive ability is the driving force behind both socioeconomic attainment and health.[47] However, in a study by Singh-Maoux et al, although intelligence was found to have some independent association with health, it could not fully explain the relation between socioeconomic status [SES] and health.[48]

Perinatal conditions and adverse adult health

Until 1940, rates of all-cause mortality in children and young adults fell steeply in developed countries.[3] This was mainly due to the decline in mortality from infectious diseases, as bacteriological research had dominated the public health interest. After World War II, mortality rates from coronary heart disease and lung cancer rose rapidly.[3] Consequently, public health attention was shifted away from infectious disease and towards the aetiology of specific chronic diseases. It had been predicted that death rates in the middle-aged would begin to fall sharply as the cohorts who had experienced dramatic improvements in childhood survival during childhood reached this age. But apparently, health of adults worsened despite the improvements in child health. Therefore the search for aetiological factors focused on the adult environment and adult lifestyle, and risk factors like body size and various health behaviours were identified. Early life factors lost attention.

However, social and geographical variations in chronic disease risk could not simply be explained by the 'lifestyle model'. Interest in relations between early life and adult chronic disease was stimulated by findings that involved 'tracking' of risk factors such as blood pressure, cholesterol levels, and obesity from childhood to adult life.

In 1977, based on ecological analyses of official mortality statistics, the Norwegian researcher Anders Forsdahl hypothesized that poor living conditions in childhood and adolescence are

important risk factors for coronary heart disease, as well as all-cause mortality.[50] Poor childhood living conditions, particularly if followed by later affluence, were suggested as a possible mechanism. Thus, Forsdahl emphasized the accumulation of risk over the life course. Moreover, studies of adult height and adult mortality and morbidity provided support to the hypothesis that poor living conditions in childhood affects health in later life.[11,12]

More recently, research by David Barker and colleagues in Southampton, England, has gained much attention. Barker emphasized undernutrition during critical periods of development as the most important risk factor. Studies from his group have reported possible long-term associations between birth size and chronic adult diseases, such as coronary heart disease, stroke, respiratory disease, and type 2 diabetes, as well as intermediate conditions including hypertension, impaired lung function, and insulin resistance.[1,51,52] From these findings the so-called 'foetal origins hypothesis' emerged during the 1990s. The hypothesis is based on the concept of 'programming', by which is meant a general process whereby a stimulus or insult at a critical period of development have lasting or lifelong significance.[53] A critical period of development refers to a time window in which an exposure can have adverse (or protective) effects on development and subsequent morbidity.[54] The Barker group has interpreted the findings by suggesting that nutrition in foetal and early life is crucial; i.e. under-nutrition during critical periods of development is an important environmental risk factor. Thus, the foetal origins hypothesis holds that foetal vitality is a major determinant of health in adult life, and that foetal vitality is affected through foetal programming governed by maternal nutrition.[51] The nutritional basis for the foetal origins hypothesis is supported in a recent review.[55]

The term programming was first proposed by Alan Lucas in 1991. He initiated experimental studies to test the importance of early nutrition.[53] Programming is a well established biological concept, and, although most supporting evidence is derived from experimental studies in animals, the concept is biologically plausible. The effects of alterations in foetal nutrition may be direct, due to inadequate substrate availability, or indirectly mediated through endocrine hormonal effects. This may result in developmental adaptations with permanent changes in structure, physiology, and metabolism. Consequently, the individual may become susceptible to cardiovascular, metabolic or endocrine diseases later in life.

Coincident with the observations made by Forsdahl, follow-up studies evaluated human development after *in utero* exposure to the Dutch famine of 1944-1945.[56] These studies indicated that the intrauterine environment is an important determinant of adult health in terms of obesity[56] and cardiovascular and respiratory disease,[57] although as mentioned previously, no effects were observed for intelligence. On the other hand, almost two decades later, a study based on data from the Medical Birth Registry of Norway [MBRN] found no evidence that wartime conditions in Norway impaired perinatal survival, neither immediately nor in terms of perinatal survival in offspring of mothers born during the war.[58] As extreme maternal malnutrition was rare in Norway during World War II, the study indicates that maternal malnutrition probably affects perinatal survival when only caloric intake falls below a certain threshold.

The increasing literature on early origins of adult disease during the 1980s and 1990s challenged the aetiological model for adult disease that emphasized adult risk factors. Up to date, long-term outcomes such as obesity, mental health and cognitive function, as well as some cancers, are increasingly being studied in the light of the foetal origins hypothesis.

Nevertheless, criticism has been raised towards the foetal origins hypothesis. The major objections regard study design,[59] including loss-to follow-up,[60,61] and possible confounding factors, of which the influence of socioeconomic conditions[60,62] on adult health are the most important. Another major concern is the contributing roles of postnatal growth[63] and development, and how interactions between foetal and postnatal life influence on adult health.[64-66] Furthermore, the role is increasingly questioned of genetic factors and the interaction of genetic and environmental factors on developmental processes associated with adult chronic disease risk. This criticism has lead to a change in focus towards a 'life course approach',[3] rather than only early life experiences, as the possible pathway. That experiences in early life may have long-term effects on the development of chronic disease may be either due to their occurrence at some critical period of development (i.e. 'programming'), or because they contribute to a more gradual process of risk accumulation. The latter is referred to as the 'life course approach'. By studying physical or social exposures during pregnancy, childhood, adolescence, through adulthood, life course epidemiology is aimed at elucidating biological, behavioural, and psychological processes underlying long-term effects on health and disease risk.

There is currently much interest in size at birth and other perinatal variables as possible predictors of various health outcomes in later life. One such outcome is intelligence, and another is adult body size. The perinatal conditions associated with adult health outcomes of specific interest in this thesis are listed in Table 2. The impact of these conditions on disease outcomes is discussed below.

Table 2. Perinatal conditions associated with adult health outcomes

Perinatal condition	Adult health outcome	References
Birth weight	Height	Sørensen, 1997 [67]; Tuvemo, 1999 [68]
	Weight	Sørensen, 1997 [69]; Rasmussen 1998 [70]
	Cardiovascular disease	Barker, 1995 [51]
	Cognitive function	Sørensen, 1997 [32]; Richards, 2001 [34]
	Breast and testicular cancer	Michels, 1996 [71]; Møller, 1997 [72]
Birth length	Height	Sørensen 1999 [67]; Lundgren 2001 [73]
	Cognitive function	Lundgren, 2001 [31]
Gestational age	Neurological problems	Hack, 2002 [38]
	Testicular and prostate cancer	Weir, 2000 [74]; Ekbom, 2000 [75]
Breech delivery	Disability	Danielian, 1996 [76]
	Cognitive function	Sørensen, 1999 [77]
Birth defects	Disability	Mitchell, 1997 [78]
	Reproduction	Skjærven, 1999 [79]; Lie, 2001 [80]

The influence of perinatal conditions on adult health may be exerted through different pathways.[54] Figure 1 illustrates four pathways between poor intrauterine growth and adult health. The figure also indicates that a factor may modify (increase or decrease) the effect of another factor or act as a potential confounder. Path I is mainly biological in which poor intrauterine growth leads to impaired brain development which in turn has adverse effects on intellectual performance resulting in inefficient information processing in the central nervous system and poor health in adulthood. Path II is mainly a social pathway whereby adverse childhood SES influences educational attainment and adult SES. Path III is a socio-biological pathway whereby adverse childhood SES is associated with poor nutrition and environmental hazards in childhood leading to increased risk of childhood illness and subsequently poor intellectual performance. Path IV is a bio-social pathway in which childhood illness results in adverse educational attainment and lower adult SES. In addition, genetic factors may contribute both to intrauterine growth and intellectual performance, as well as health and disease later in life.
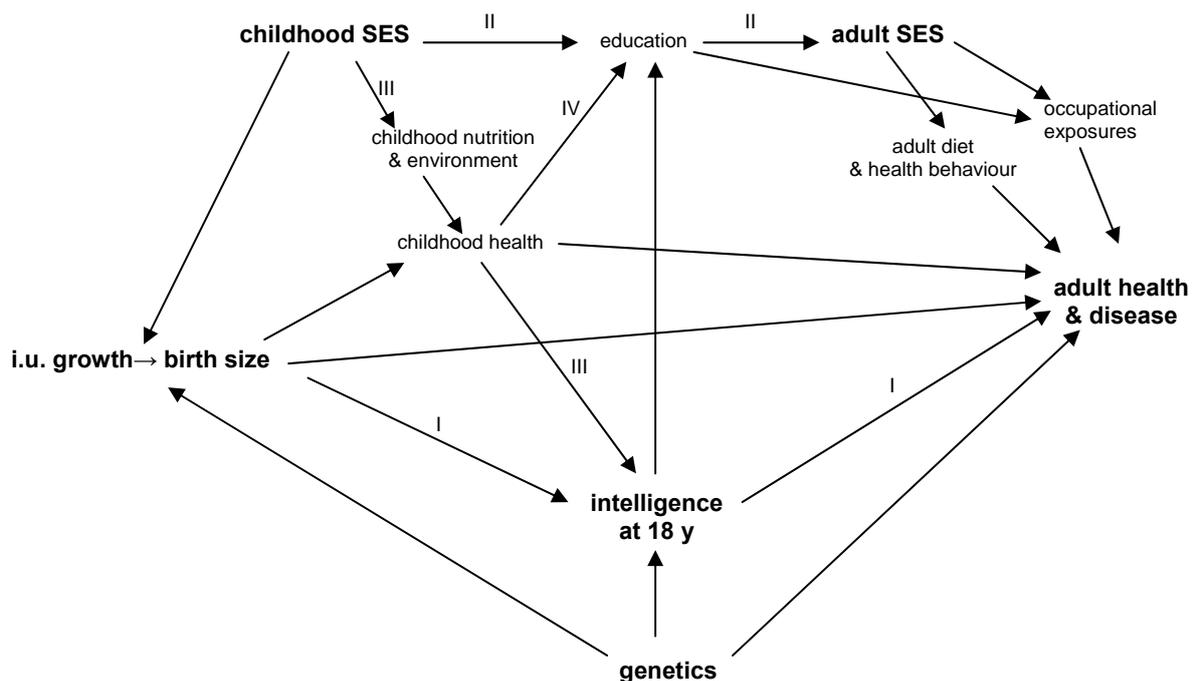
Figure 1. The potential pathways mediating the associations between perinatal conditions, intellectual performance and adult health outcome.

Birth weight

Birth weight is the most widely available routinely obtained measure of birth size. Since the late nineteenth century, weighing of newborns gradually has become a standard procedure in Norway. Traditionally, birth weight has been a practical indicator of the health of the newborns, and still is a key variable in perinatal epidemiology.

The frequency distribution of birth weight is normal with an extended lower tail.[81,82] The birth weight distribution can be described by three parameters; the mean, the SD of the predominant distribution, and the proportion of infants in the residual distribution.[81] The normal component of the distribution corresponds to the birth weight distribution of term births whereas the majority of births in the residual distribution are preterm.

Birth size is the result of foetal growth. Therefore, birth weight may be viewed as a product of foetal growth velocity, and the length of gestation. In turn, foetal growth is a proxy for a complex interplay of genetic and intrauterine environmental factors that include metabolic, endocrine, and vascular mechanisms, in addition to maternal nutrition.[64] Thus, birth weight is a convenient, although crude, summary of multiple influences on the developing foetus, and

serves as a marker i.a. of the intrauterine environment. Epidemiological studies have suggested that environmental influences account for about 25% and genetic factors 30-80% of birth weight variance.[83,84] Environmental factors associated with birth weight include nutrition, smoking, and even maternal health.[85] For example, women with cardiac or rheumatic disease have significantly higher rates of low birth weight,[86,87] and babies of obese mothers or mothers with gestational diabetes tend to be large at birth.[25,88,89] Observations from the Dutch famine have shown clear effects on birth weight (and to a lesser extent on birth length) of maternal famine exposure in third trimester.[90] Nevertheless, except at the extremes of intake, maternal dietary intake has relatively little impact on birth weight.[65,91]

Perinatal mortality is negatively associated with birth weight; however, with a slight increase for the largest birth weights.[92] Thus, low birth weight is strongly associated with high perinatal and infant mortality, as well as with overall and cause-specific childhood mortality.[93] Perinatal survival in low birth weight births has greatly increased during the last decades in Norway.[94] However, those who survive with a low birth weight have an increased risk of morbidity.[95]

Due to its availability from existing records (or recall in some instances), birth weight has been the most widely studied variable of birth size in retrospective studies regarding early origins of adult disease. The possible association between birth weight and subsequent blood pressure has been extensively studied; however, a recent review summarizes that birth weight is of little relevance to blood pressure in later life.[62] Birth weight has been found to be inversely associated with risk of type 2 diabetes,[60] as well as with future gestational diabetes risk in women.[96] Low birth weight in combination with high body mass index later in life is associated with the highest risk of cardiovascular disease and type 2 diabetes.[97,98] Insulin plays a central role in the regulation of foetal growth, and one foetal adaptation to undernutrition is alteration of insulin and glucose metabolism. Thus, foetal adaptation may involve insulin resistance found in patients with type 2 diabetes. Furthermore, several studies have demonstrated positive associations between birth weight and hormone-related cancers, including breast[71,99] and testicle,[72] whereas the association with prostate cancer risk is unclear.[75] The associations between birth weight and breast or testicular cancer have been hypothesized to be mediated through a high intrauterine oestrogen environment, or similar endocrine mechanisms.[71,99] However, the evidence of an association between birth weight and testicular cancer has been weakened by one study that showed no association.[74]

Birth weight is positively associated with height in adulthood.[68,69,100,101] Moreover, birth weight is positively associated with weight later in life.[68,70,73,100] Several studies have found that high birth weight is associated with increased risk of obesity in childhood and adulthood.[69,70,89] On the other hand, low birth weight is associated with central obesity.[102] Evidence exists that breastfeeding protects against adult obesity.[89] Children who are overweight tend to become overweight adults.[103] Thus, growth in foetal life, as well as in infancy, childhood and adolescence, may have a lasting influence on obesity in adulthood.[89,103,104] Both biological and social pathways may explain this relationship. Higher birth weight is linked to gestational diabetes and maternal obesity or weight gain during pregnancy. Gestational diabetes implies foetal exposure to hyperglycaemia and thus altered glucose-insulin metabolism, which in turn may lead to increased risk of obesity later in life. On the other hand, maternal obesity, which is associated with higher birth weight and also with later obesity in offspring,[104] may reflect a postnatal environment with unfavourable dietary and activity habits. Moreover, inherited genes for obesity could explain the association between maternal obesity, high birth weight and subsequent obesity in the offspring.

Malnutrition in early foetal life may have adverse effects on the developing brain.[105] Many studies have addressed this issue by use of birth weight as an indicator of foetal nutrition and intelligence tests at different ages as outcome measures. Most studies have found a positive association between birth weight and intellectual performance extending from the very low birth weights through the normal birth weight range,[30-42] whereas in some studies such an association has not been observed.[106-108] A major limitation in most studies evaluating birth size and intelligence is lack of control for current body size; this issue will be addressed in the discussion section.

Birth length

In addition to birth weight, measurements of birth length (cm) also characterize size at birth and provide a variable indicating prenatal growth. Birth weight and birth length are strongly interrelated variables. Generally, measurements of birth length seem to be considered only as a supplement to birth weight. For example, since birth weight is a crude marker of birth size, ponderal index (i.e.; birth weight (kg)/(birth length (m^3)) has been introduced to take birth length into account. Although the use of indices per se has been questioned,[109] the ponderal index has gained general support.

The frequency distribution of birth length is approximately Gaussian; however, its range is narrow, compared with the range of birth weight. Due to its wider range, birth weight possibly has been considered more precise than birth length.

The use of birth length as an indicator of perinatal risk has been limited. Still, birth length has been shown to be strongly inversely associated with both perinatal, neonatal and infant mortality.[110,111]

While birth weight has been focused in the association between size at birth and long-term outcomes, the literature is scarce on associations of birth length with adult health and disease. However, although not confirmed in later studies, shortness at birth was reported to be associated with adult high blood pressure in a study by Barker et al.[112] A Finnish study demonstrated an inverse association between length at birth and type 2 diabetes,[113] whereas a recent Norwegian study found an increased risk of colorectal cancer among men who were short at birth.[114] Further, birth length has been found to be a strong predictor of adult height; even stronger than birth weight.[67,68,73,100,101,115] Also, a positive association seems to exist between birth length and weight in later life, although hardly evaluated.[68,70,73,100] However, it is unclear whether length and weight at birth contribute independently to adult body size; i.e. if the strong correlation between the birth size variables can explain the associations. Some studies on the association between birth size and cognitive function have included measures of birth length.[31-33,106 37,116] In most studies[31,32,37,116] birth length has been positively associated with intellectual performance, whereas in two studies[33,106] birth length was not significantly related to intellectual performance. All these studies have limitations; either due to low numbers,[32,33,106] or due to lack of adjustment for gestational age[106] or SES.[31,37,116]

Gestational age
Earlier, small infants were believed to be small due to preterm delivery only, and low birth weight was used as a measure of preterm birth. Today, the two most common methods used to assess gestational age are either based on the mother's last menstrual period, or on ultrasound measurements of the foetus. Irrespective of method, gestational age is a continuous variable, and its frequency distribution is Gaussian.

Data on gestational age are of major importance in the interpretation of results in perinatal epidemiology. For example, Dutch famine studies have shown that the effects of prenatal exposure to famine depend upon its timing during gestation.[57] In previous literature, the possibilities to assess the effects of gestational age have been limited. Relatively few studies on the associations between perinatal risk factors and adult health outcomes have data on gestational age.[60] Further, gestational age has often been dichotomized into preterm or term. Because gestational age and birth weight, as well as birth length, are highly correlated, details of gestational age must be considered to disentangle possible effects of birth size from those of immaturity. In studies comprising data on gestational age, it appears that the association between being small at birth and coronary heart disease is independent of the length of gestation, and thus related to foetal growth rather than to premature birth.[60]

Preterm birth is a major cause of perinatal mortality and morbidity, and of long-term neurological problems.[38,95] Literature is scarce on associations of gestational age with adult health and disease, and most studies are from periods when relatively few preterm infants survived. Still, short gestational age has been associated with increased risk of both testicular[74] and prostate cancers,[75] whereas no consistent association with risk of breast cancer has been observed.[3,71]

A study of Swedish conscripts reported that mean height at conscription was positively associated with gestational age until term, and infants born at a gestational age below 32 weeks had a more than twofold increase in the risk for short adult stature compared to those born at term.[68] This study also found a positive association between gestational age and adult weight. These findings indicate that gestational age influences the association between birth size and adult size, and that gestational age must be adjusted for when evaluating these associations. The number of preterm births in the Swedish study allowed only three broad categories of gestational age. Thus, further research is required to further assess the influence of gestational age on these associations.

In a study from 1967, Barker and Edwards found that a shortened or prolonged period of gestation was associated with impaired intellectual performance in 11-year-old schoolchildren.[117] Comparisons between sibs in the same study made the authors suggest that in some cases, impaired performance might be a direct consequence of birth before or after term. Higher risks of impaired intellectual performance among pre- and post-term births have

also been suggested in more recent studies.[31,33,37,116] However, little is known about the independent effects of gestational age on intelligence because many studies on the association between birth size and intellectual performance suffer from lack of data on gestational age,[34,35,106,118] whereas others adjust for gestational age in regression models rather than evaluate its direct effects.[32,33,39]

Breech delivery

Breech presentation implies a longitudinal position of the foetus with its head at the uterine fundus. Breech presentation occurs in approximately 3% of all births.[119]

Factors predisposing to breech presentation include maternal factors (i.e. parity, maternal age, pelvic anomalies); mechanical factors reducing the available space *in utero* (for example uterine malformations); and finally, foetal factors, such as having a birth defect, might also be involved.[120]

Breech presentation per se appears to be a marker of adverse perinatal outcome.[121] Infants born after breech presentation have increased perinatal mortality and higher risk of neonatal complications.[122] Poorer outcomes may either result from underlying conditions that cause breech presentation,[123] or from damage to the infant during delivery.[121,122] Thus, breech presentation is a perinatal risk factor in its own right which may have possible long-term consequences.[120] Particularly, the increased risk of asphyxia during vaginal breech delivery may cause cerebral damage.

Breech presentation is associated with serious birth defects.[120,124] Infants born in breech presentation have considerably reduced birth weights and are more often born preterm compared with cephalic births.[119] Consequently, impaired postnatal growth and cognitive function may be possible adverse long-term outcomes after breech presentation.

Although there is an increasing amount of data available on the immediate perinatal outcomes, the long-term outcome after breech delivery has not been extensively studied. A few studies exist on outcomes in childhood, partly indicating an increased risk of handicap or health problems among breech infants,[76,125] whereas there is a paucity of information on long-term outcomes with follow-up until late adolescence and adulthood.

In this thesis, intellectual performance after breech birth is the outcome measure of particular interest. Intelligence tests may provide functional information about neurodevelopmental morbidity following cerebral damage after breech birth. Results on adult cognitive outcomes have been ambiguous.[77,124,126-128] Two studies failed to observe any effect of breech presentation or delivery method on intellectual performance,[126,128] whereas a third observed impaired cognitive function among breech infants.[77] One study found significantly better test scores in "noncephalic deliveries";[127] however, because the noncephalic group included both breech births and cephalic caesarean deliveries, comparison with other studies is difficult.

Birth defects

Birth defects may be defined as structural abnormalities of prenatal origin that are present at birth and that interfere with viability or physical well-functioning.[129] The prevalence of major birth defects is approximately 3%, depending on the definition used, and a similar proportion of defects is discovered later in life.[129] In registries that depend on routine examination at birth the prevalence is usually around 2-3%.[80,130]

Causes of birth defects include various genetic mechanisms, environmental exposures, and interactions between them.[78] However, for a large number of defects no cause can be identified.[78,131] Birth defects are a major cause of perinatal and infant mortality, and of childhood morbidity.[78] Due to medical conditions and sequelae associated with the specific disorders, birth defects also may have consequences for adult morbidity and disability.

Various long-term outcomes among infants with birth defects have been studied. For example, reproduction rate was the specific long-term outcome in two previous studies based on the MBRN.[79,80] These studies showed a reduced reproduction among individuals born with birth defects compared with those without such defects.

This thesis concentrates on variation in intellectual performance according to the presence of birth defects grouped on the basis of the ICD-classification. Intellectual performance has been sparsely studied in relation to several types of malformations; the majority of studies on cognitive function among infants with birth defects has concentrated on specific groups of defects such as heart defects,[132-135] neural tube defects,[136,137] and oral clefts.[138-140] No previous study on intellectual performance has followed all malformations registered in a very large cohort until death or cognitive testing in adulthood.

Socioeconomic factors and health

An individual's social environment may be as important to health outcomes as biological risk factors. Many risk factors for chronic disease are related to SES. Also, several socioeconomic factors are associated with pregnancy outcome. However, not all health outcomes show the same social patterning,[3] and not all measures of SES are similarly related to health.[141] Moreover, associations between SES and different diseases change over time.[3,49] What is considered to be appropriate social indicators may vary between populations, and within a population over time. SES is a complex construct generally used to elucidate social inequality. Income, education and occupation are the three basic aspects of SES.[142] In Scandinavia, the equality of income is high and material resources may thus be less important than education, occupation and social status.[3,141] Educational measures have a close relationship to living standards and social status as well as intellectual skills and knowledge.[16,142] Thus, education is a measure of both SES and individual resources. Education is the most commonly used measure of SES in epidemiological studies from North America and Europe including Scandinavia, while British literature has focused on occupational measures.[3,141]

There is a strong association between adult SES and health outcomes, and evidence exists that childhood SES has an effect which is additional to that of adult SES.[3,143,144] Both childhood and adult SES are associated with all-cause mortality and with cardiovascular mortality and morbidity.[143,145] Furthermore, adverse pregnancy outcomes such as perinatal and infant mortality, low birth weight, intrauterine growth restriction, and preterm birth are associated with socioeconomic disadvantage. [146,147]

There are at least three possible mechanisms for the social inequalities in health: first that health influences SES, second that SES influences health, and, third, that a common factor influence both health and SES. A reciprocal relationship between SES and health has been confirmed in a recent study, thus supporting both the health selection and social causation hypotheses.[144] Heredity may be a common factor which may influence both health and SES, for example through genetic contributions to intelligence. Consequently, a personal characteristic, such as intelligence, could determine both SES and health.

In the literature on health effects of SES, there has been a shift in focus from that of poverty towards more interest in socioeconomic gradients in health determinants.[3] Behavioural determinants such as smoking, physical activity, and diet, vary by SES, and access and response to health care services are affected by social and economic capacity. Behavioural determinants and psychosocial characteristics, as well as poor health, cluster in low socioeconomic groups.[148] Low SES is also associated with fewer educational opportunities, limiting the access to jobs and other social resources.[146] It is well known that conditions of work affect level of exposure to physical and psychological hazards.

The above mentioned associations between SES, perinatal risk factors and adult health outcomes imply that adjustment for socioeconomic factors is mandatory. The following factors are associated with SES and contribute to adverse pregnancy and health outcomes. Marital status and maternal education are proxies of SES available in this study. Also, in addition to being biological factors, maternal age and parity reflect social factors and thus serve as markers of social conditions. Smoking is an indicator of health damaging behaviour which is generally more frequent in the lower socioeconomic groups. However, data on smoking were unavailable in this study.

Marital status

Adverse pregnancy outcomes such as perinatal and neonatal mortality are more frequent among single mothers.[149,150] In Norway, marital status has frequently been used as a social indicator in studies of pregnancy outcome.[149,151] At the time the participants in the present study were born, only a small proportion of births was out-of-wedlock.

Links exist between marital status and health. It has been suggested that this link is associated with slow growth *in utero* and thus has its origin during foetal life.[152] Infants with birth defects reproduce less than those born without defects.[79,80] A possible explanation may be that having a birth defect implies difficulties in finding a partner; thus one may speculate on whether the lack of reproduction may be related to social rather than biological influences on reproduction. Healthier men tend to marry, and the social support offered by marriage is beneficial. This has been illustrated in a study showing that unmarried men have higher rates of cardiovascular disease and a shorter life span than married men.[153]

Maternal education

Neonatal and infant mortality are inversely associated with parental educational level.[154] This association may be due to nutritional deficiencies, infectious diseases, smoking, and other environmental factors that may be detrimental to the foetus and the newborn child. In Scandinavia, education seems to be a stronger predictor of pregnancy outcome than socio-economic status and income.[155] Educational attainment is also associated with health in later life, probably because it is a marker of personal capital in addition to reflecting material advantage during the life course.[142]

Maternal age

Perinatal mortality increases with increasing maternal age. Also, the risk of birth defects is influenced by maternal age. Some birth defects are associated with young maternal age (for example gastroschisis) and others, like Down syndrome, are associated with advanced maternal age.[156] Breech presentation is also associated with high maternal age.[119] Low maternal age is known to be a risk factor of sudden infant death syndrome.[157] Associations between maternal age and pregnancy outcome may arise from differences in life-style habits and socioeconomic conditions across age groups. In particular, teen-age mothers are more likely to be socially disadvantaged and have poorer health habits. Thus, in addition to being a biological factor, maternal age also represents a social variable.

Parity

In general, perinatal mortality is lower in second than in first births, and increases thereafter.[158] Other adverse pregnancy outcomes, for example low birth weight,[159] risk of intrauterine growth restriction[160] and preeclampsia,[161] and the proportion of breech births[119] are also associated with parity. As for maternal age, parity may influence pregnancy outcomes through differences in social conditions, i.e. maternal strain increases by number of children, as well as unfavourable conditions in the home environment for the youngest sibling. The latter may be particularly relevant in sudden infant death syndrome.[157]

Smoking

It has been proposed that smoking may affect foetal development through teratogenic effects and by causing foetal hypoxia. Maternal smoking during pregnancy is known to have a negative impact on foetal growth. Infants born to mothers who smoke during pregnancy are on average 200 g lighter than infants born to mothers who do not smoke,[162] and a dose-

response relationship between smoking and birth weight reduction has been observed.[163] Thus, short-term consequences of maternal smoking during pregnancy may be higher rates of morbidity and mortality which are associated with low birth weight. However, the long-term influence of maternal smoking on offspring's health is uncertain. A review from 1998 summarizes that there is evidence of a small decrease in children's height associated with prenatal exposure to smoking; however, the observed effects are small.[164] Smoking during pregnancy may affect foetal brain development and subsequently intellectual development. Although the evidence is somewhat unclear, an inverse association between prenatal exposure to smoking and intellectual function in childhood has been described.[164] A recent Danish study concluded that smoking during pregnancy may have long-term negative consequences on adult intelligence in offspring.[165]

Background of the present study

Early life influences on later abilities are of interest to psychologists, researchers, practitioners, policymakers, and the general public. Previous research has tended to focus on dichotomized perinatal risk factors, such as low birth weight and preterm birth, which may have obvious consequences for health and disease outcomes. However, the variation in risk of adult disease across the entire range of size at birth has been less characterized. Many epidemiological studies in this field are based on small numbers. Other studies suffer from designs and analysis that do not consider the normal range of birth size, or do not take account of important confounding factors, such as gestational age or SES. Another major problem in longitudinal studies is loss to follow-up. Also, the importance of modifiers working later in life needs to be recognized.

Having a clear picture of the early life determinants of health outcomes in young adulthood is important in developing our understanding of what mechanisms might explain the associations between the early life risk factors and adult disease and mortality. Numerous epidemiologic studies on early origins of adult disease have focused on morbidity among people in middle age or older. However, to understand the mechanisms involved, events occurring between birth and middle age must be taken into account. Thus, evaluation of intermediate health outcomes at younger ages will add to the existing knowledge.

Although Scandinavian studies on perinatal conditions and height, weight and intelligence at conscription exist, they have certain limitations. For example, in studies from Denmark, the study population was relatively small (*n* less than 4500).[32,67,69,77] Moreover, the description of eligible births in the cohort was unclear, implying a possible selection bias. The Swedish studies included larger samples, but suffered from inadequate control of confounding by SES when evaluating the association between birth size and intelligence.[31,37,116] Further, despite the relatively large sample sizes, the number of preterm births was relatively low.[68] Except from a study including less than 500 conscripts,[166] no large Norwegian study addressing perinatal conditions and health in early adulthood has been published.

In Norway, three national registries with compulsory notification are relevant. All births are registered in the Medical Birth Registry of Norway, and likewise all deaths are registered in the Cause of Death Registry. Further, all residents of Norway are insured in the National Health Insurance Office. Military service is mandatory for all male inhabitants, and draft board data are recorded by the Norwegian Conscripts Service. These registries provide a special opportunity to perform longitudinal studies and represent valuable sources for epidemiologic research. Every Norwegian citizen is identified by their national identification number, used in all registries, thus enabling record linkage of all four registries. This data set represents a unique opportunity for a longitudinal study of perinatal conditions and body size and intelligence at age 18 years.

AIMS OF THE STUDY

The overall aim of this thesis was to investigate, in a general population, influences of perinatal conditions on health measures in early adulthood. The four studies performed had the following specific aims:

Paper I. To examine birth length, birth weight, and gestational age as predictors of adult height and weight. In particular we wanted to focus on the effects of being born preterm.

Paper II. To explore the associations of birth weight, birth length, and gestational age with intellectual performance at age 18 years. We had a special emphasis on the contribution of attained height and maternal education to this association.

Paper III. To evaluate the effects of presentation at birth on intellectual performance at conscription. Next, to compare intellectual performance by delivery mode, and by methods of vaginal delivery.

Paper IV. To study the associations of various birth defects with adult intellectual performance, disability and mortality.

MATERIAL AND METHODS

In this section, the four databases used in this thesis will be presented; the Medical Birth Registry of Norway, Statistics Norway, the National Health Insurance Office, and the Norwegian Conscripts Service, before a thorough description of the study population and design of the present study is given.

The Medical Birth Registry of Norway

In this work, the Medical Birth Registry of Norway was the main data source together with the Norwegian Conscripts Service. The Medical Birth Registry was established in 1967 by the Directorate of Health, and run by the University of Bergen until 2002 when it was integrated into the Norwegian Institute of Public Health, to monitor maternal and perinatal health problems and to contribute to identification of their causes.[167] Since 1967, the Medical Birth Registry has collected data on all births (including stillbirths) from 16 weeks of gestation.[167] A standardized notification form (Appendix 1), which was principally unchanged from 1967 to 1998, has to be filled in after each delivery by the attending midwife or physician. The notification form comprises demographic variables, as well as data on maternal health, previous reproductive history, complications during pregnancy and delivery, and pregnancy outcome. The form is sent to the Medical Birth Registry within the ninth day post partum, or at discharge from the delivery department. All newborns undergo a medical examination (as well as screening blood tests) by a physician, usually a paediatrician, before hospital discharge. The diagnoses of birth defects are based on these examinations, as well as any additional diagnostic procedures during this stay.

Statistics Norway

The Population Registry. Since 1964, Norway has had a central registry of every inhabitant. The individuals are identified by the national identification number. The Medical Birth Registry is matched to the Population Registry providing complete ascertainment of all births.

The Cause of Death Registry. All births are routinely linked to computerized death certificates provided by Statistics Norway, for information on all deaths during the first year of life. The

underlying cause of death is coded in accordance with the International Classification of Diseases (ICD-8).

The Register of Level of Education covers all Norwegian inhabitants, and is continuously updated. Maternal educational level was registered as completed years of highest attained education in 1998, and grouped according to the Standard Classification of Education.

The National Health Insurance Office

Men registered in the National Health Insurance Office as being permanently disabled are exempted from military service. Their medical diagnoses were released by the National Health Insurance Office, and linked to the birth records.

The files of the National Health Insurance Office are updated regularly according to data on emigration and deaths in the Population Registry. In Norway, emigration is minimal, and the Population Registry makes it possible to trace an individual at any time.

The Norwegian Conscripts Service

The Norwegian Conscripts Service collects and stores the data from all examinations at the medical draft board. In Norway, military service is compulsory, and all men are required to register with the draft board at age 18 years for physical and mental examinations. Draft board examinations have followed the same standardized procedures over many decades, and data have consistently been collected under the supervision of health-care personnel. The drafted men are medically categorized as either fit or unfit for military service. The criteria for rejecting a conscript for military service are given in an armed services' catalogue of medical diagnoses.

The present study

Design

The studies in this thesis are population-based historical cohort studies, utilizing registry data. In all four studies, the unit of analysis is the infant examined at birth and age 18 years.

Record linkage

The national identification number assigned to all residents of Norway shortly after birth, enables identification and linkage between registries. The national identification number is composed by the date of birth plus five additional digits, and is unique to all Norwegian inhabitants. In the present study data on delivery, recorded by the Medical Birth Registry (1967-1979), were linked with data from the draft board, recorded by the Norwegian Conscripts Service (1984-1999). In addition, we added data from Statistics Norway (1967-1998) and the National Health Insurance Office (1967-1997), including information from the Population Registry. By use of these population-based registers the follow-up was almost complete; 94 percent of the birth cohort was traced through age 18 years.

Study population

All singleton male infants live born in Norway during the 13 year period from 1st January 1967 through 31st December 1979 and registered as Norwegian citizens, were included. Among the 393,570 male live births registered in this period, 4,833 (1.2%) died before age one, 3,550 (0.9%) died between age one and military draft, and 3,788 (1.0%) emigrated. In the birth cohorts included, 5,692 (1.4%) had at least one International Classification of Diseases, 9th Revision diagnosis indicating disability. Another 24,355 (6.2%) never appeared before the draft board for various reasons, including having a foreign citizenship. Altogether, 351,352 (89.3%) male conscripts with draft board medical data were identified in the Norwegian Conscripts Service during the period 1984-1999. In Paper I, analyses were restricted to conscripts with measurements of both weight and height (*n*=348,706 or 88.6% of the total birth cohort), while in Paper II-IV analyses were restricted to conscripts with data on intelligence testing and maternal educational level (*n*=317,761 or 80.7% of the birth cohort) (Figure 2).

```
Medical Birth Registry of Norway
            1967-79
          n=393,570
```

→ Dead before age 1 year
1.2%

→ Dead between age 1 year
and military draft
0.9%

→ Emigrated before
military draft
1%

→ Disabled & Not drafted
1.4%

→ Untraceable
6.2%

```
Drafted, 1985-99
     89.3%
```

→ Missing IQ-test or maternal
educational level
8.5%

```
Study cohort
   80.7%
 n=317,761
```
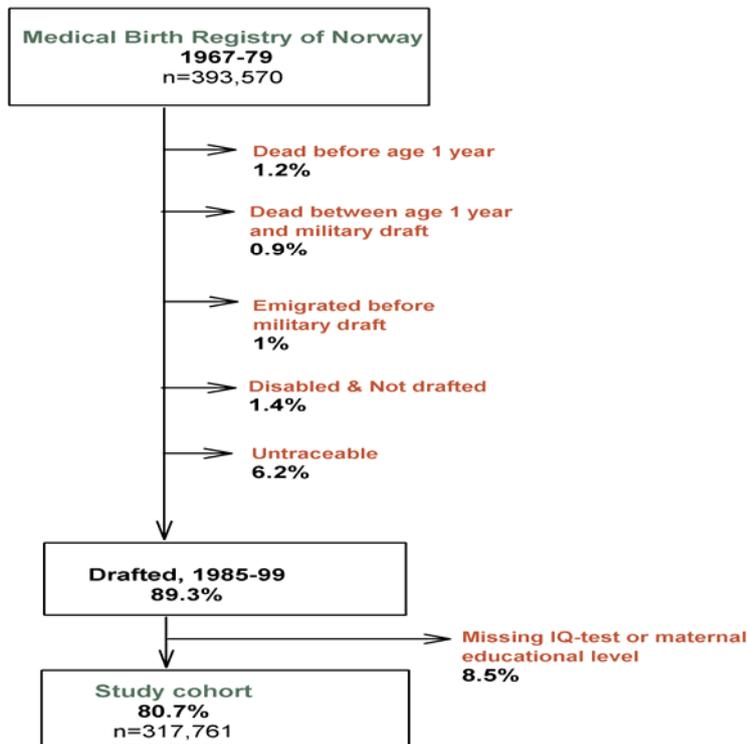
Figure 2. Follow-up diagram of singleton live male births in Norway, 1967-1979.

Outcome variables and classification

The draft board examinations comprise medical and psychological tests. For each conscript a health profile is established. The health profile is constructed for military use, in order to categorize the conscripts as either fit or unfit for military service. The profile is graded on a numerical scale with values from 1 to 9; value 1 means unfit for military service, values 2 to 8 reflect various degrees of functional impairment, whereas 9 indicates no functional impairment. In addition to measurements of height and weight, the profile consists of the functioning of ten organic systems, i.e. general physique, digestion, vision, hearing, arms, hands, gait, back, skin, and mental health (Appendix II).

Height and weight. The height and weight of every conscript were measured by standard methods, and the observations were noted to the nearest cm or kg. The conscripts were asked to take off their shoes, and to undress the upper body. Height was measured standing back to the measuring rod with the visual axis horizontal. The height was normally distributed, and ranged from 133 cm to 215 cm with a mean of 179.9 cm (SD 6.5 cm). Mean weight was 72.3 kg (SD 11.8 kg), and ranged from 36 kg to 181 kg.

Intellectual performance. General intellectual performance has been measured by a 53 minute validated group intelligence test, which was developed in 1953 for the Norwegian draft board, by the Psychological Services of the Norwegian Armed Forces, and revised in 1962. The test includes time-limited sub-tests covering 3 categories of items: verbal analogues, number series (calculation) and geometrical figures (an abbreviated version of Raven's Progressive Matrices).[168] Each sub-test is organized by increasing difficulty. The test questionnaire comprises a total of 120 questions. Three test scores are recorded, and the general ability score available in this thesis is obtained by a combination of the subtest scores (equally weighted). The result is presented as standard nine ("stanine") scores; i.e., single-digit standard scores (with values from 1 (low) to 9 (high)) based on a normal distribution, in which the mean is 5.0 and the SD is 1.96. The test is highly correlated with the Wechsler Adult Intelligence Scale (r =0.73-0.75).[168-170] All conscripts receive standard instructions prior to the time-limited tests. Standardized instruction of the personnel who undertake the tests as well as the use of a standard manual ensure validity and reliability.

The number who were assessed by the intelligence test is slightly lower than the total number of drafted, as some were obviously unfit due to the physical examinations, and others for unknown reasons, were not assessed in this way.

Exposure variables and classification
All exposure variables were obtained from the Medical Birth Registry.

Birth size, i.e. weight and length at birth, were the exposure variables in Paper I and II.

Birth weight is measured by the midwife attending the delivery. Birth weight is registered in grams in the Medical Birth Registry notification form. Birth weight data were missing for 657 births (0.17% of the total birth cohort). Birth weight was categorized as <1000 (<1500) g, 1000 (1500)-4999 g in 500-g categories, and >5000 g (Paper I-II). Standardization for birth weight within weeks of gestational age using z-scores was performed.

Birth length is measured by the midwife attending the delivery, and has mainly been registered as crown to heel (cm). However, during the period 1974-1978 certain hospitals measured crown to buttock length. Some of these measurements were mixed with the full length measurements, thereby introducing a subgroup with considerably shorter length. This

subgroup of infants were filtered out using a regression approach,[110] and were considered as having missing data on birth length. Thus, altogether birth length data were missing for 4,801 births (1.2%). Birth length was analyzed in categories of whole cm (Paper I-II), or categorized as <49 cm, 50 cm, 51 cm, 52 cm, or >53 cm (Paper II). Standardization for birth length within weeks of gestational age using z-scores was performed.

Gestational age. During the period 1967 through 1979, gestational age has consistently been estimated from the reported first day of the last menstrual period. Gestational age was missing for 13,544 births (3.4%). Due to uncertainty about the self-reported last menstrual period, early gestational bleeding or registration errors, some gestational ages may be inaccurate. To identify possible cases of misclassification we applied a method based on the assumption of normally distributed birth weights for each week of gestation.[171] In Paper I, a total of 3,194 (0.8%) infants with z-scores of birth weight by gestational age outside 3 SD were excluded in all analyses of gestational age. In Paper I-II, gestational age was divided in six categories (26-29, 30-33, 34-36, 37-38, 39-41, and 42-44 weeks). Gestational age less than 37 weeks was defined as preterm (26-33 weeks as early preterm, and 34-36 weeks as moderately preterm), 37-41 weeks as term, and 42-44 weeks as post-term.

Breech presentation and mode of delivery i.e. whether delivery was a caesarean or vaginal, were the main exposures in Paper III. If not otherwise stated, mode of delivery was categorized as vaginal. Presentation at birth was defined as either breech or cephalic. The validity of breech presentation and mode of delivery variables are very high. Breech vaginal deliveries were subdivided into assisted breech, forceps to aftercoming head, and breech extraction. Cephalic vaginal deliveries were categorised as uncomplicated, forceps delivery, vacuum extraction, or shoulder dystocia.

Birth defects that were diagnosed at delivery or during the initial hospitalisation (usually 5-7 days) have been recorded directly in the notification form. In Paper IV, we defined 26 categories of birth defects on the basis of ICD-8, as in previous studies.[79,80,172] For most infants, only a single defect was reported. When spina bifida was present with anencephaly, only anencephaly was counted, and when spina bifida was present with hydrocephalus, only spina bifida was counted. All other multiple defects were combined in a separate category. We defined a separate category for hip dysplasias, which were excluded from the category of limb defects. Also, we defined separate categories for isolated cleft lip and cleft palate, and

for combined cleft lip and palate. Likewise, Down syndrome was separated from other recognised syndromes. The categories were mutually exclusive, 25 containing isolated defects and 1 containing multiple defects.

Confounding variables and classification
All confounding variables, except maternal educational level, were obtained from the Medical Birth Registry.

Maternal age was categorized into 5-year groups. Maternal age was a confounder in all four studies. Data on maternal age were complete.

Parity i.e. number of previous births, including stillbirths, was categorized as 0, 1, 2, 3, 4+, or as primipara or multipara. In analyses of variance, multiparity was the reference. Parity was a confounder in all four studies. In Paper III and IV, however, this variable was termed "birth order", and categorized into 1, and 2 or more. Data on parity were complete.

Marital status was categorized as married or unmarried. Marital status was a confounder in all four studies. Data on marital status were complete.

Maternal educational level was obtained from Statistics Norway, and refers to the highest attained education in 1998. Maternal educational level was grouped according to revised official standards as low ($\leq$10 years), medium (11-14 years), or high ($\geq$14years).[173] This variable was an important confounder in Papers II-IV. Data on maternal education were missing for 20,966 births in the total cohort.

Year of birth was categorized into three periods; 1967-70, 1970-74, and 1975-79. Year of birth was considered as a potential confounder in Papers II and III. Data on year of birth were complete.

Birth weight is described above. Birth weight was considered as a potential confounder in Paper III.

Statistics

Crude odds ratios [OR] and relative risks [RR] with 95% confidence intervals [CI] were calculated using 2x2-tables. Chi square tests were performed to test differences between proportions.

To adjust for differences in the distributions of birth weight and length according to gestational age (Paper I and II) standardization of these variables was performed by use of z-scores (SD above or below the mean). Z-scores were calculated by subtracting the calculated mean from the observed value and divided by the SD. For term births in Paper I, standardization was also done on birth length within categories of birth weight, and vice versa. To allow for the comparison among the different predictors of intellectual performance (Paper II), z-scores for adult height were calculated based on data from the study cohort.

Analysis of variance and linear regression analyses were used to calculate regression coefficients and R squared (Paper I and II). Means were compared by analysis of variance (univariate analyses) and general linear models (adjusted analyses) (Paper II-IV).

Contingency tables, stratification (Paper I-IV), general linear models (Paper I-II) and logistic regression analysis (Paper III) were used to evaluate confounding and effect modification. Effect modification was first evaluated in stratified analyses and thereafter with specific interaction terms in the general linear or logistic regression models. General linear models (Paper I-IV) and logistic regression analysis (Paper III) were used to adjust for the confounders.

All tests were two sided, and $P < 0.05$ was chosen as level of statistical significance. SPSS software (version 11.0 and 12.0.1, SPSS, Chicago, Ill.) was used for statistical analyses.

Ethical approval

The study was cleared by the Regional Committee for Medical Research Ethics Review and approved by the Norwegian Board of Health and the Data Inspectorate.

MAIN RESULTS

Paper I.

Mean height at age 18 years increased linearly by increasing birth length from 46 cm. An increase in birth length from 46 to 56 cm corresponded to a 10.2 cm difference in final height. The association with height was weak for birth lengths below 46 cm. Also, birth length was positively associated with adult weight. Likewise, there was a clear linear relationship between birth weights above 2500 g and adult weight; increasing birth weight from 2500 to 3500 g yielded a 3.2 kg increase in adult weight. For birth weights below 2500 g the association with adult weight was weak. By use of stratified analyses, gestational age specific z-scores for birth length and birth weight, and standardization, we demonstrated that birth length and birth weight each contributed independently to adult stature and body weight. The effect of birth weight on adult weight was stronger for longer infants than for shorter; thus those who were both heavy and long at birth had the greatest increase in adult weight per relative birth weight category.

The R squared of adult height explained by birth length was 7-9%, whereas the R squared of adult weight explained by birth weight was <0.1%. Thus, the association between birth length and adult height was stronger than between birth weight and adult weight. Birth length and birth weight together explained 15% and 4.6% of the variance in adult height and weight, respectively.

Regarding gestational age, we found that the association between birth length and adult height was weaker among preterm than term births. This also applied to the birth weight-adult weight association. Moreover, preterm delivery itself was associated with lighter weight in adulthood. The strongest associations between birth size and adult size were seen among those born at gestational age 39-41 weeks.

Paper II.

The crude analyses showed that birth weight was positively associated with intelligence test score at conscription. Mean score increased by increasing birth weight up to 4500 g, after

which the scores declined. Adjustment for attained height resulted in a marked attenuation of the association. The association between birth length and intellectual performance showed a similar pattern to that observed for birth weight. However, there was no decline in scores for the longest birth lengths. Birth weight and birth length explained 0.2% and 0.1% of the variance in intellectual performance, respectively.

Intelligence test score at conscription also increased with increasing gestational age. At 28 weeks of gestation mean score was 4.40 compared with 5.10 at 40-41 weeks. At gestational age 40-41 weeks, there was a peak in performance followed by a significant decline in scores.

There was no evidence of interaction on intelligence between birth size and attained height. Attained height accounted for 1% of the variance in intellectual performance, whereas maternal education could explain 8.4% of the variance. Altogether, 10.9% of the variance in intellectual performance could be explained by birth size, height, maternal age, parity, and maternal education.

Even though the influence of maternal education influenced on intellectual performance was much stronger than that of attained height, the effects of birth size on intelligence were not attenuated by adjustment for maternal education to the same extent as adjustment for height.

Paper III.
Conscripts born in breech presentation were on average 263 g lighter at birth than those born in cephalic presentation. Based on birth weight alone, as indicated by the findings in Paper II, a lower intelligence score would be expected among breech births. However, the crude analyses showed that breech presented infants had a slightly higher mean intelligence test score compared with those in cephalic position (5.26 vs 5.22, P = 0.05). This difference was attenuated in analyses adjusted for birth order, maternal age, and maternal education (P = 0.3). The adjusted OR of having a low score (i.e. intelligence test score less than or equal to 3) was 1.02 (95% CI 0.96, 1.09) for breech compared with cephalic birth.

Comparing delivery mode in breech presentation, we found that intellectual performance was slightly lower among conscripts delivered by caesarean section than among those delivered vaginally (adjusted for birth order, maternal age, and maternal education; difference -0.13, P =

0.03). For caesarean as compared to vaginal breech birth, the OR of having a low score was 1.12 (0.92, 1.36), after adjustment for confounding factors.

Comparing delivery mode in cephalic presentation, males scored less if their mothers had a caesarean section instead of a vaginal delivery (adjusted as above; difference -0.11, P < 0.001). Among cephalic presented infants, the OR of having a low score was 1.10 (1.04, 1.16) for caesarean as compared to vaginal delivery, after adjustment for confounding factors.

Among breech vaginal births, intellectual performance was similar when comparing delivery by either forceps to the after-coming head or breech extraction to the assisted breech delivery (P = 0.06 and 0.2, respectively). Also, in analyses of vaginal cephalic births with birth weights 3000 g and above, there were no differences when comparing forceps, vacuum and shoulder dystocia with spontaneous delivery (P > 0.10 for all).

Paper IV.

The proportion of birth defects was 13.8% among those who died before military draft, and 11.3% among those who were disabled, whereas in the study cohort the proportion of birth defects was 1.9%. Among males with birth defects who survived to age 18 years, 8.0% were registered as disabled, compared with 1.3% in the group without defects.

Among males with birth defects the RR for mortality was 6.7 (6.3, 7.1) compared with males without defects. The RR for mortality was significantly increased for all categories of birth defects except for the cleft lip, genitalia, hip and skin/hair/nail categories.

Also, males with birth defects had a RR for disability of 6.0 (5.5, 6.5) compared with those without defects. With the exception of the cleft lip, skin/hair/nail, and respiratory defects, the RR for disability was significantly increased for all defect categories.

The RR for not being drafted due to any reason was 2.5 (2.4, 2.6) as compared to males with no birth defect. The RR for not being drafted was highest if maternal educational level was low (P < 0.05).

In analyses adjusted for maternal education, maternal age, marital status and birth order, there were no differences in mean intelligence test score for most categories of birth defects compared with those without defects. However, heart defects (P = 0.007) had slightly lower score than those without defects. Also, the lower score for cleft palate remained significant after adjustment (P = 0.045).

There was no difference in mean score for conscripts with multiple defects compared with men without defects (mean score 5.11 vs 5.22, P = 0.5). Moreover, after adjustment for confounding factors no significant difference was observed when comparing the overall score for multiple defects with the score for those who had a single defect (mean score 5.11 vs 5.22, P = 0.2). Comparisons between single and multiple defects among men with heart defects showed no significant difference (P = 0.6). Also, within the oral cleft categories, there were no significant differences in mean scores when comparing males having a single defect with those having additional defects (P > 0.05 for all).

DISCUSSION

Discussion of methods

In this section methodological strengths and limitations are summarized, and the extent to which the limitations have influenced the results is discussed.

The design

The design is that of a historical longitudinal cohort study. All male births are followed from delivery until age 18 years. The exposure is registered at delivery and the outcome at age 18 years. The design is well suited for evaluating the impact of foetal growth on adult health, and strengthens the evidence that the associations described in the study are causal.

However, the study comprises only two observations acting in a very specific time window, and no data on other periods of the life course were available. The possibility that some factors may cause both exposure and outcome cannot be ruled out. For example, genetic and socioeconomic factors are associated with both early life exposures and adult health outcomes. Below, confounding is further discussed.

Precision

The degree of precision of reported associations in a study may be reduced due to random error. Random error is variability in the data resulting from biological variation and unsystematic measurement errors. Precision can be improved by modifying the design of the study to reduce measurement errors, or by increasing the sample size. The latter is the principal way to increase precision in epidemiological studies.[174] The present study has a large sample size. All male singleton live births in Norway from 1967 to 1979 recorded by the MBRN were included. In most analyses, the numbers were large, and thus for most associations the estimates are precise (i.e., the CIs are narrow). However, small sample size was a problem in the subgroup analyses of birth defects and intellectual performance in Paper IV.

Internal validity

Internal validity may be reduced due to systematic errors. Selection bias, information bias and confounding are the main types of systematic errors.[174]

Selection bias results from procedures used to select subjects and from factors that influence study participation.[174] Selection bias implies that the association between exposure and disease is different for those who participate and those who don't. Consequently, the effect estimates among the included subjects may differ from the estimates one would get if those who did not participate were included. In cohort studies loss to follow-up implies a major source of selection bias.

The problem with loss to follow-up is reduced by using nationwide register data. Still, selection bias may affect the validity of the present study. Altogether, 89.3% of the birth cohort was identified with draft board data. Accordingly, such data were missing for 10.7% of the birth cohort due to deaths, permanent disability, or emigration before military draft. In addition, a number of men were untraceable. Of these, a small number probably were not drafted due to foreign citizenship, conscientious objection (although generally objection is taken at the draft board), or other unknown reasons. In 2005, the National Health Insurance Office, who carried out the record linkage, made an effort to further identify the untraceable group. It turned out that a technical problem had caused the lack of match of records as all individuals in the untraceable group were born on the 29th, 30th, or 31st of each month. Thus, the untraceable group is a random sample.

Selection bias would arise only if the association between perinatal risk and outcome differed between those studied and those lost to follow-up. The proportion of preterm and low birth weight infants was higher among those lost to follow-up as compared to those who made it to the draft board. If non-appearance before the draft board were associated with poor health, for example as measured by intelligence, the observed mean intelligence test scores would be higher than the true value. Hence, if data on those lost to follow-up had been available, the observed associations probably would have been strengthened; i.e. the true associations might be stronger than observed in our study. Likewise, if those drafted were taller as adults than those lost to follow-up, the observed mean height in our study would be higher than the true value. Also, a higher proportion of breech–presented infants never appeared before the draft

board. However, intelligence test score was available for the majority of breech births and equal to that of cephalic births despite a lower birth weight among the breech infants; thus, it is unlikely that selection bias may explain this finding.

Information bias occurs from errors in classification of the subjects selected for a study. Such bias may result in either non-differential or differential misclassification. If exposure or disease classification is incorrect for the same proportions of subjects in the groups compared, the misclassification is non-differential. If these proportions differ, misclassification depends on exposure or outcome status, and is termed differential. Differential misclassification may result in either an overestimate or an underestimate of the effect, whereas the bias introduced by non-differential misclassification is always directed towards the null value.

The use of pre-existing records is the most unbiased source of data, since the data were recorded prior to the onset of the outcome.[175] Nevertheless, there may be sources of information bias in this study. Firstly, although quality control is done regularly, registration errors are inevitable in such large databases as the MBRN and the Norwegian Conscripts Service, as well as the other registries used in this study. Registration errors may affect both exposure and outcome variables. However, any differential misclassification of the exposure variables is unlikely because this would imply that the recording of birth data relied on the result of the draft board examination. On the other hand, non-differential misclassification of birth data (i.e. independent of draft board examination) may be present and would reduce true associations.

Birth weight is considered to be a variable of good quality in the MBRN. Birth length measures, however, have been claimed to be less reliable than measurements of weight.[68] Trends have differed regarding to which extent an infant's hips should be stretched when measuring its length. Sick and floppy infants may have been falsely measured as too long because of a reduced muscle tonus. In this study, birth length represented a challenge with regard to the analytical approach due to its narrow range. Since birth length is registered in cm without decimals, 70% of the birth lengths were found at 5 discrete values; i.e. from 48 to 52 cm.

Gestational age in this study is based on self-reported data on the last menstrual period, because ultrasound dating was used during the period when our study infants were born. The

validity of the mother's last menstrual period as a basis for gestational age has been much debated, but is beyond the scope of this thesis. Misclassification of gestational age due to uncertainty about the self-reported last menstrual period is a recognized problem in registry-based epidemiological studies. Particularly this involves misclassification of preterm births. Gestational age may be misclassified as too short when bleeding early during pregnancy erroneously is reported as menstruation, and too long when conception follows an extended follicular phase.[176] Misclassification of gestational age could represent a bias in Paper I and II. To avoid such misclassification, birth weight was used as a corrective criterion and infants with z-scores for birth weight (or birth length) outside 3 and 4 SD, respectively, were excluded.[171] Besides, in Paper I, when infants in the residual distribution of birth weight were excluded from analyses of the association between birth weight and adult weight, the result was unaltered.

Breech presentation or cesarean section may in some cases have been classified as cephalic or vaginal deliveries, respectively. Presentation and caesarean section have always been considered critical variables in the medical registration of births, and misclassification is considered to be infrequent. The proportion of caesarean sections ascertained by the registry has been estimated at nearly 100%.[177]

Birth defects may be subject to information bias. During the period when our study infants were born, the MBRN collected birth defect data only from the notification form, which has been compulsory for all births. In case of unclear diagnoses, additional data have been routinely obtained from the hospital in charge. In general, birth defects are underreported. This may be because of inconsistency in filling out the forms but also because minor defects may not be detected early. Clinical manifestations of many heart defects and some urinary tract defects do not occur until after discharge from the maternity institution.[80] Misclassification of infants with multiple defects as having a single defect, as well as misclassification of syndromes may also be a problem. However, for neural tube defects and oral clefts, the proportions of cases ascertained by the registry have been estimated at approximately 90% and 80%, respectively.[178] Low ascertainment implies that there may be infants with undiagnosed birth defects in the reference group of individuals without malformations. Such misclassification of exposure would tend to deflate the effects of having a birth defect on intellectual performance. False positive cases may also represent a problem; however, in general false positive cases will reduce the effect of the diagnosis.

Any differential misclassification of the outcome variables is unlikely because this would imply that the draft board examination results was dependent of birth data; for example it is unlikely that the intelligence test result should differ with regard to presentation or delivery mode. On the other hand, non-differential misclassification of draft board examination (i.e. independent of birth data) cannot be ruled out. Height, weight, and intellectual performance may suffer from measurement errors if the standardized procedures were neglected. Most young men experience the examinations at the draft board as a control of their health status, and try to achieve as good score as possible. If conscripts for any reason tried to obtain poor scores on the intelligence test, such cases probably would not be more frequent among the subgroups at risk in this study compared with the reference groups.

Non-differential misclassification of confounders may also occur. Such misclassification may bias the results in either direction. The confounders considered were maternal age, parity, marital status and maternal educational level. Maternal age and parity are crucial variables in the registry and not likely misclassified. Data on maternal educational level were missing for a number of men, and may represent an information bias.

Confounding can be described as a mixing of effects, i.e. that the apparent effect of exposure is to some degree the effect of another variable. Therefore, the confounder must be imbalanced between the groups compared. Confounding can be controlled for in the study design by randomization or restriction of selected subjects. Also, if appropriate data on a confounder are available, a bias introduced by confounding may be dealt with in the analyses. There are two methods for control of confounding in the analyses; one is stratification and the other is the use of multivariable analyses.

In this thesis, the main issue was whether perinatal conditions are associated with adult health. However, there may be common causal factors influencing both the perinatal conditions and adult health. The possible confounding factors evaluated were maternal age, parity, marital status, and educational level, as well as the infant's year of birth. During the 13 years interval for this birth cohort, there were trends in intellectual performance at conscription according to year of birth. This variable was consistently evaluated as a confounder, but, due to its weak effect when other confounders were controlled for, it was ruled out in most analyses. In all papers, we included variables to measure aspects of SES. In Paper I, we used maternal age,

parity, and marital status as proxy variables for SES. In Paper II-IV data on maternal education were available and used as a proxy of SES together with maternal age, parity, and marital status. Additional measures of SES such as income and occupation were unavailable. However, in general, education is found to be more strongly and consistently associated with health and disease than is income or occupation, and may thus be the most judicious measure of SES in epidemiological studies.[142,147] Considering parental education jointly, maternal education appears to have the highest impact on perinatal conditions.[154,155,179] In our study, data on paternal education were available, but the proportion of missing cases was three times that of maternal education. We also had data on conscript's highest attained educational level in 1998. For the youngest cohorts this implies a follow-up period of 19 years, which is too short to achieve the highest level of education. Consequently, this variable was considered incomplete, and not used in the study. Thus, dependent on whether maternal education is a good proxy of SES or not, there may be residual confounding by SES.

There may be other confounders that we have not measured. Data on paternal body size were inaccessible. Also, a measure of maternal intelligence was unavailable, and although maternal educational level is a strong proxy of maternal intelligence, residual confounding may still be present. Data on smoking during pregnancy was not recorded in the MBRN during the period when our study infants were born. However, cigarette smoking is strongly associated with education.[148] Still, despite controlling for maternal educational level, residual confounding by smoking is possible.

Effect modification

Effect modification means that the effect of an exposure varies across levels of a third variable. Effect modification is a property of the effect under study, i.e. a result of biological variation, and is a finding to be reported rather than a bias to be avoided.[174] Stratified analysis is the preferable method for the evaluation of effect modification and in controlling for confounding.[174] Thus, large studies are needed to reliably evaluate effect modification. In Paper I we found a strong interaction between birth weight and length on adult weight, implying that infants who were heavy and long at birth became particularly heavy adults. In Paper II we did not find any interactions between birth size and height on intelligence.

Generalisability

Generalisability, or external validity, refers to whether the results and conclusions in a study are relevant also for other populations than those who are studied. Strong internal validity is required to achieve this quality. Generalisability also depends on whether the study population is representative for the question under investigation.

The present work is based on all drafted males who were live born in Norway during the 13-year period 1967-1979. Ethnically, Norway has a relatively homogenous, low-risk, white population. Thus, the results should be applicable to populations of white men outside Norway who survive until adulthood without serious disability. The observed associations between birth size and gestational age on the one hand, with height, weight and intelligence on the other, may have a biological basis. If so, the associations should be valid also for other populations. With regard to birth defects, our results cannot be transferred to countries where the social welfare and health care systems are much different from that in Norway during the study period.

Correlations among IQs from different test batteries tend to range between somewhat below 0.70 and 0.90.[29] Thus, the intelligence test (stanine) score used in the present study (r=0.73) is comparable to scores obtained on standard intelligence tests. Standard intelligence tests are constructed to yield equal IQ scores for males and females.[29] In studies controlling for gender, intelligence remains significantly associated with height.[46,180] Hence, it is plausible that our findings in Paper II apply to both sexes, although it cannot be ruled out that males and females might respond differently to prenatal insults due to different foetal growth rates.

Discussion of results

Plausibility and coherence are as important to the interpretation of epidemiological findings as internal validity. In this section, the results are discussed and compared with the results of other studies. In the two first papers we studied the influences of birth size and gestational age on adult height, weight, and intelligence. The exposure in these papers related to the general population. In the two last papers; however, we focused on exposures in two subgroups at

particular high perinatal risks, namely infants in breech presentation and those born with birth defects.

The overall picture in this thesis is that prenatal growth in terms of birth size had an impact, although weak, on later body size and intelligence, while the increased perinatal risks associated with breech birth and birth defects did not seem to be reflected in later intelligence among those who made it to the draft board.

Size at birth and adult body size (Paper I)

Previous studies have shown that there is an association between birth length and adult height.[67,100,115] This finding was repeated in the present study. A linear increase was observed in mean height at conscription by increasing birth length from 46 cm, whereas birth lengths below 46 cm represented mainly preterm births, and were only weakly associated with adult height. We also confirmed a positive association between birth length and adult weight, as has been shown in some studies.[68,70,73,100]

We observed an incremental increase in mean adult height by increasing birth weight, which is in agreement with previous studies.[68,69,100,101] Mean adult weight has been found to increase by birth weight.[68,70,73,100] Our results confirm this; although not for birth weights below 2500 g, which comprise a high proportion of preterm births.

The main question in this study was whether length and weight at birth contribute independently to adult height and weight, or if the observed isolated associations were due to the strong interrelations between the birth size variables and gestational age. This question requires that one birth size measure must be corrected for the other. The paper addresses this issue by use of stratified analyses, gestational age specific z-scores for birth length or birth weight, and standardization on birth length within categories of birth weight and vice versa. We demonstrated that length at birth contributed to adult height independent of birth weight and gestational age, and birth weight added to the effect of birth length. Likewise, birth weight contributed independently to adult weight. Birth length added to the effect of birth weight, except for a strong interaction between birth weight and length on adult weight among

the long infants. Thus, long and heavy infants became particularly heavy as adults. The latter finding is in agreement with Rasmussen and Johansson.[70] A Finnish study of twins found highest risk of being overweight among heavy infants of average length, but still they also observed an increased risk among those being both long and heavy.[100]

Our results suggested that the association between birth length and height was stronger than between birth weight and weight; i.e. 7-9% of the variation in adult height could be explained by birth length, whereas 0.1-2% of the variation of adult weight could be explained by birth weight. In comparison, a study evaluating effects of preeclampsia on growth into adulthood, estimated that birth length explained 12.6% of the variance in final height.[181] The variance in adult BMI explained by birth weight was clearly lower, but reported together with other factors. The result cannot be directly compared to our results, but is supportive of our interpretation; namely that the contribution of birth length to adult height was rather small, and the contribution of birth weight to adult weight was even smaller. Thus, assuming that height and weight in young adulthood are related to health outcomes later in life, prenatal factors may have influences on health outcomes; however there is reason to believe that other factors working through the life course are more critical.

The contribution of gestational age and preterm birth to the birth size-adult size association was an important concern in our paper. A noticeable feature when analyzing absolute birth size measures was that preterm infants appeared to be taller and heavier as adults than infants born at term, given the same size at birth. Whereas several studies have included only full term subjects,[21,101,115,182] some studies including preterms have had limited ability to evaluate gestational age effects due to low numbers of preterm births.[67,68,73] A few studies have investigated the effects of gestational age on the birth size-adult size association. Leger et al found,[115] as we did, that gestational age above 37 weeks had no effect on the association. The larger studies by Tuvemo et al[68] and Lundgren et al[73] have indicated that being short for gestational age was associated with short stature in adulthood. This was confirmed in our study. Tuvemo et al concluded that except in very preterm births, gestational age has a limited impact on final height, thus supporting our finding that gestational age had little effect on final height among term and post-term births. In our study, the relation between birth length and adult stature was weaker among preterm than term births. A possible interpretation is that birth size in preterm infants reflects the growth potential to a smaller extent than in term infants.

A novel finding in the present study was that preterm delivery was associated with lighter weight in adulthood. Similar results were reported in crude analyses in the studies by Tuvemo et al and Lundgren et al.[68,73] In contrast, a British study of 215 girls aged between 14 and 16 years, observed that gestational age hardly influenced the association between birth weight and body weight or body fat.[183]

In studies on early origins of adult diseases, BMI is commonly used to explore current body size as a modifying factor on the outcome. An example of such effect modification is that low birth weight in combination with high BMI is associated with the highest risk of cardiovascular disease or type 2 diabetes.[98] Low birth weight may be followed by compensatory growth, and an increased risk of high BMI later in life.[184] The idea that low birth weight in combination with high BMI increase the risk of health problems is relevant to our research but was not addressed in our paper. For the present discussion, some further analyses were performed. The proportion who became obese at 18 years (BMI>30) was significantly higher among infants with birth weight less than 2500 g compared with birth weights above 2500 g. Thus, our data support the findings that low birth weight is associated with high BMI.

While the methods used to investigate the association between birth size and adult size vary, the results consistently show that birth size influences on adult size, a finding supported by our study. As adult stature may be associated with disease, underlying shared factors predicting birth length, adult height, and disease later in life, are likely. Our study demonstrated that birth length was a stronger predictor of adult body size than birth weight which has been the key variable in studies on early origins of adult diseases. Therefore, when considering size at birth, birth length may be considered as a better predictor of adult morbidity and mortality than birth weight.

Size at birth and intelligence (Paper II)

A profound understanding of intelligence and its basic cognitive mechanisms is beyond the scope of this thesis as is a discussion of various controversies regarding intelligence. In this thesis, intelligence test score is regarded as a measure of important individual intellectual

abilities. And, despite its possible limitations, the intelligence test score reflects the variation across a normal population. The intelligence measure in this thesis is constructed for military use to classify the conscripts for duty, and is not designed to trace minor psychological impairments. However, it can be used to make a classification of the general intelligence. The various correlates of individual differences in intelligence have provoked many debates and controversies. However, these differences do not disappear, and as they apparently have significant health consequences, we should put some attention on their relevance.

Prenatal growth

That birth weight is associated with intelligence has been demonstrated in most,[30-42] but not all,[106-108] studies using somewhat different types of data and design. In our study, there was a slight dose-response association between birth weight and intellectual performance, even in term births, extending through the normal birth weight range; thus confirming that the association is not confined to the very low birth weights. The peak found around birth weight 4250 g in our study has been acknowledged in two previous studies with smaller samples,[32,34] whereas in one study the difference was not statistically significant.[33] However, our results indicated that the association of birth size with intelligence was weak. This is supported by a recent systematic review, which concluded that the effect of birth weight on intelligence is likely to be of a very small magnitude.[30]

The association between birth weight and intellectual performance is partly mediated by genetic factors,[185] but can also be influenced by common environmental factors. Furthermore, a pathway has been hypothesized, suggesting that malnutrition in early life affects brain development and later intellectual function.[15,32,33,105] Neurochemical influences, for example by insulin-like growth factor, which is associated with birth weight and also influences intellectual development, may play a role in this association.[34,186] Thus, a higher proportion of mothers with gestational diabetes among the highest birth weights may account for the lower score observed. Also, maternal obesity and type II diabetes may play a role.

Two previous studies[33,39] have estimated that birth weight explains 1% and 3.8% of the variation in cognition, respectively, which is more than in our study (0.2%). However, consistent with our findings, these studies found stronger effects of SES (explained variance up to 12% and 6.6%, respectively, against 8.4% in our study) on intelligence than that seen for birth weight.

Although focusing on birth weight, two relatively small studies on this topic including results for birth length did not find any association with intelligence,[33,106] whereas a large population-based Swedish study concluded similarly as we do; that shorter birth length is associated with lower scores.[31] In our study, birth length showed similar associations with intelligence as did birth weight, except that there was no decline in scores for the longest birth lengths. Also, attained height influenced slightly more on the birth length–intelligence association.

Gestational age is relevant in the interpretation of birth weight as an indicator of foetal growth. While some studies have not controlled for gestational age,[34,35,106] others have included only term births,[36,42,108] or stratified in broad categories,[31-33,41] and there has been relatively little focus on gestational age as a variable in its own right. The programming hypothesis has suggested that not only shortage of nutrients, as indicated by slow foetal growth, but also the timing of insults on the developing brain is important. More than three decades ago, a study by Barker et al suggested that children born at term had a higher mean score than children born after shorter or more prolonged gestation.[117] In a study by Shenkin et al, the association was not significant; however, the study included only 44 preterm births.[33] Two Scandinavian studies have indicated that intellectual performance is positively associated with gestational age.[31,32] Our results confirm these findings. We found a linear increase in mean score up to gestational ages 40-41 weeks, followed by a significant decline, as also observed by Barker et al.

Postnatal growth

It is important to consider whether postnatal factors may explain associations between birth size and later outcomes.[63] This can be done by adjusting for later size. Height is a measure of postnatal growth that has been consistently related to intelligence.[31,35,180,187-189] One might assume that intelligence may influence height through healthy behaviours, or the other way around, that height may affect intelligence through increased self-esteem.[187] However, the association is more likely to be due to independent factors affecting both height and intelligence; i.e. genetic or environmental factors such as nutrition, or a combination.[169,190]

Most previous studies on the association between birth weight and intelligence fail to consider postnatal growth,[32-34,36,39,41,42] whereas a few studies have taken attained height into consideration.[31,35,107] These studies have shown a continuous effect of growth during

childhood on later intellectual function. Lundgren et al showed that catch-up growth in height lowers the risk of intellectual impairment for those born very small for gestational age.[31] Richards et al demonstrated that the association between birth weight and intelligence is independent of postnatal growth.[35] Pearce et al concluded that postnatal growth may be more influential than foetal growth on intelligence.[107] In our study, the associations of birth size with intelligence were strongly reduced when adjusting for attained height. Thus, consistent with the previous studies,[31,35,107] postnatal growth in terms of height dominated over the effects of birth size on intelligence. Also, according to Lucas et al, if adjustment attenuates the effect of early size, later size is likely to be more relevant than early body size in the causal pathway.[63] We found no interactions between birth size and attained height, in agreement with Pearce et al.[107] Thus, birth size did not modify the effect of later body size on intellectual performance. Moreover, the association between attained height and intellectual performance was stronger than that of birth weight in terms of explained variance. Previously, it has been estimated that height explain 2% of the variation in intelligence,[187,189] compared with 1% in this study. Still, this is considerably lower than that explained by social class (14%) in one of these studies.[189]

Our data suggested that SES, in terms of maternal education, influenced more strongly on intelligence than did stature. In contrast, Pearce et al found that the relations between height or social class and intelligence were equally strong.[107] In that study, social class was based on parental occupation. It is possible that maternal education used in our study, may influence offspring's intelligence more strongly both through genetic and social pathways.

On the other hand, maternal education did not attenuate the effects of birth size on intelligence to the same extent as height. Despite height being influenced by postnatal factors, birth size and height are measures of growth that are strongly correlated (Paper I), while maternal education to a greater extent reflects social conditions. Thus, this finding indicates that the biological and social influences on intelligence follow different pathways.

In conclusion, most studies support the finding that, although the association is of a small magnitude, birth size and thus prenatal growth contribute to intellectual performance in later life, even when gestational age, height, and socioeconomic factors are considered. Postnatal growth may, however, have a greater influence on intelligence than prenatal growth. Future studies should be designed to evaluate how postnatal growth and environment may modify

this association and include biological samples aimed at identifying the underlying mechanisms.

Breech birth and intelligence (Paper III)

Presentation at birth

Prior to our study, only few and relatively small studies have focused on breech presentation and intelligence with conflicting results.[77,126,128] Our study did not show any difference in intellectual performance between male conscripts delivered in breech compared with cephalic presentation. This is in line with the findings in two studies, one Australian and one Norwegian, published in 1979 and 1985, respectively.[126,128] Neither of these observed any effect of breech presentation on intellectual performance. In contrast to our results, a study of Danish conscripts suggested impaired cognitive outcome after breech presentation.[77] A Finnish historical cohort study from 2004 evaluated long-term outcome in terms of need for special education at the age of 9 years. No difference between breech and cephalic births was observed.[124] Compared with these previous studies, strengths of the present study are its large sample size of breech births, the fact that it is nation-wide and also the high degree of follow-up.

Delivery mode

Some relatively small studies have compared intellectual outcomes after vaginal breech delivery and caesarean delivery.[77,124,128,191] In agreement with these studies, we could not demonstrate an adverse intellectual outcome after vaginal breech delivery compared with caesarean section. Since data on whether a caesarean delivery was elective or emergency were not recorded during the period our study infants were born, we could not disentangle possible hazards of emergency delivery. Cohort studies are criticized for being flawed by confounding by indication; i.e. that factors which influence the choice of mode of delivery may be more decisive as to the outcome for the baby than the mode of delivery.[123] Such data were unavailable in our study; however, since the vaginal breech group comprised the vast majority of births, confounding by indication probably would not change the results with regard to the lack of adverse effects of vaginal delivery.

For cephalic births in our study, caesarean section was associated with a significantly lower score, consistent with two previous studies.[77,192] However, the possibility of confounding by indication is particularly relevant when comparing delivery mode among cephalic births, and should be further evaluated.

Methods of vaginal delivery

Most studies focus on outcome differences in vaginal versus caesarean delivery, and I am not aware of any previous study comparing methods of breech vaginal births. We found that intellectual performance was similar when comparing delivery by either forceps to the after-coming head or breech extraction to the assisted breech delivery. In a study by Roemer et al such analyses could not be done because the birth records rarely differentiated between methods of vaginal delivery.[127]

Some studies have evaluated intellectual outcome in cephalic vaginal births.[127,192-194] In two of these studies instrumental vaginal delivery had higher intelligence test scores, [127,193] whereas in two studies there was no significant difference between spontaneous and instrumental delivery.[192,194] In analyses restricted to birth weights 3000 g and above, we found no differences when comparing forceps delivery, vacuum extraction or shoulder dystocia with uncomplicated delivery. In the study by Seidman et al, an advantage of instrumental delivery appeared in the crude estimates, consistent with our crude results.[192] Except for the study by Seidman et al, these studies include small samples, and may also suffer from biases due to selection and confounding factors.

Evaluation of confounding by birth weight was a major concern in our paper. Gestational age and birth length was evaluated as confounders, however, due to the high interrelation between these variables, controlling for birth weight turned out to be appropriate. Because breech delivery is associated with being small for gestational age and preterm delivery, the birth weight distribution for breech infants was shifted towards the left compared with cephalic births in the total birth cohort. This also applied to the study cohort of conscripts born in breech as compared to cephalic presentation. Because of their lower birth weights, infants in the left distribution should be at the highest risk of adverse perinatal outcomes. However, several studies have shown that these infants may fare better than would be expected due to their higher risk, a phenomenon recognized in perinatal epidemiology as the 'low birth weight

paradox'.[82,195] Consequently, adjusting for birth weight introduced an artefact resulting in a more favourable outcome for the breech group in which mean birth weight was lowest.

Birth defects and long-term outcomes (Paper IV)

Mortality

It is well acknowledged that infants with birth defects have increased perinatal and infant mortality.[78,79] Also, lower survival to adulthood has been reported in both males and females.[79,80] In these studies, mortality was higher at all ages up to 14 years for those with birth defects in both sexes.[79,80] The excess in risk relative to individuals without birth defects decreased with age, but was still more than 3-fold increased at age 14 among males.[80] Our finding was that the overall RR for mortality before military draft for infants with birth defects was increased more than six-fold compared with those without defects. The subgroup-analyses suggested that the RR for mortality was significantly increased for all categories of birth defects except for cleft lip, genitalia, hip, and skin/hair/nail. A Danish study that followed 5331 people with cleft lip and/or palate born between 1943 and 1987 to 1998, found that 7.5% had died.[196] This is comparable to 4.5% in our study, since the follow-up period is shorter. In the Danish study, mortality was not increased for cleft lip, whereas it was significantly increased for the cleft lip and palate and cleft palate only groups, which is all consistent with our results. A recent British follow-up study to age 35 years of 117 people with spina bifida born between 1963 and 1971,[197] found that 54% had died, thus supporting our finding for spina bifida-mortality.

Disability

Infants with birth defects also have an increased risk of childhood morbidity and disability.[78,198] We observed that the pattern of disability was similar to that of mortality. The risk of disability among surviving males with birth defects was six-fold increased compared with those born without defects. The subgroup-analyses showed significantly increased disability-risks for all categories, except cleft lip, skin/hair/nail, and respiratory defects. In the British study of spina bifida, 11% were in open employment.[197] Since appearance before the draft board may be regarded as an indicator of ability, this figure is comparable to the proportion being drafted in our study (17.7% of all males with spina bidifa).

Intellectual performance

Intellectual deficits have been reported among infants with heart defects.[132-135,199,200] In particular, these studies focus on cognitive development after cardiac surgery; a major issue is whether the intellectual impairment is a consequence of the primary disease or its treatment. Our study confirmed that males born with heart defects had significantly lower scores than those without defects. As data on surgical treatment were inaccessible, we could not evaluate whether the deficit was related to the disease or its treatment.

Cognitive dysfunction in children with oral clefts is well acknowledged.[138-140] Cognitive outcome in adults have been less studied, but evidence exists that the cognitive deficits reported among children persist until adulthood.[140] The aetiology of cognitive deficits is thought to be related to abnormal brain development alongside facial development, and may thus correlate to the severity of clefting. In our study, intellectual function was affected among those with cleft palate only, whereas intellectual deficits in those with cleft lip and combined cleft lip and palate were not confirmed. Moreover, we did not find any differences when comparing those having clefts as a single defect with those having additional defects; not even among those with cleft palate, which is associated with the highest proportion of additional defects.[201] In contrast, the study by Swanenburg de Veye et al[139] found that children with additional defects were disadvantaged with respect to their mental development. In that study, one-third of the total sample had additional defects. This is consistent with other reports,[201] and clearly higher than in our study; implying that misclassification of a proportion of multiple defects as single defects probably is present. Such misclassification may also have biased the overall analyses comparing single and multiple defects, in which no differences were observed.

In the follow-up study of spina bifida mentioned above,[197] 33% had an IQ equal to or more than 80 at age 5 to 15 years. In another British study, by Iddon et al, cognitive function was unaffected in patients with spina bifida alone.[137] Although not directly comparable, these studies support our finding that intellectual performance was not impaired in spina bifida. The study by Iddon et al showed that the majority of test scores was lower in patients with hydrocephalus (with or without spina bifida).[137] In our study, intelligence test score for hydrocephalus (without spina bifida) was low, although not statistically significant, when compared with men without defects. Given the relatively small number of men in this

category (*n*=21), there might be a possibility of type II error. In addition, some of the other subgroups of birth defects in our study were small in numbers.

Birth defects per se include a variety of abnormalities. In this paper, all birth defects were combined into one group in overall analyses of mortality, disability, and intellectual performance, whereas when performing more detailed analyses the defects were grouped. Grouping may be done either on the basis of the underlying mechanism or on the basis of which organ is involved. In this paper the latter approach was used, and birth defects were grouped on the basis of the ICD-classification. These organ-specific sub-groups are in accordance with four previous studies based on the MBRN,[79,80,172,202] except that in our study congenital hip dislocation was included in a separate category. This classification implies rather broad categories and the possibility of different causal pathways for the different types of birth defects within the same organ group. Also, some rare defects are merged into "other defects".

The persistence of mortality and disability risks among those with birth defects probably reflect ongoing complications related to the defects. Accordingly, loss to follow-up in this paper was clearly higher than in Paper I-III. This may affect the validity regarding intellectual performance. On the other hand, the above comparisons with mortality and disability in follow-up studies on oral clefts and spina bifida indicate that the losses to follow-up in our study for these two subgroups are not higher than in other studies. This may also apply to the other subgroups in our study. Moreover, despite loss to follow-up, we observed a significantly lower mean score in subgroups that could be expected to have lower scores according to previous literature; thus supporting our conclusions regarding the defect categories that have hardly been studied previously.

Socioeconomic factors

In Scandinavia, differences between social levels are small, and access to health care is practically independent of social class.[155,179] Nevertheless, socioeconomic differences do exist, and these differences have implications for perinatal health.[179] Also, inequalities in adult health are relatively large, despite an egalitarian policy.[141] A possible explanation may be that the egalitarian policy has had a stronger influence on income related inequalities of health

than in differences according to education.[141] Moreover, improvements in a country's overall health are often followed by larger social class inequalities in health.[47] This is probably because the improvements are smaller among those who have low education and low income than among those who have high education and better income. In Norway, for example, in 1990, there was a remarkable fall in SIDS incidence after the initiation of an intervention program to avoid prone sleeping. However, the RR of social factors (i.e. maternal age, parity, and marital status) increased with time and became stronger than before the program started.[203] Education reflects personal resources, such as knowledge and competence, and is not only a proxy for standard of living. Hence, education may influence health through differences in values, life-style behaviours, and problem-solving abilities.[142]

The association between intelligence and premature mortality may be mediated via attained level of education and social class.[27,43] Accordingly, a low intelligence test score at conscription would indicate reduced intellectual ability and subsequently lower educational attainment. Our data support this hypothesis; i.e. intelligence test score was highly correlated with educational attainment among those with the longest follow-up period after the military services.

During the last decades, there have been changes in educational attainment among women, with an increasing proportion attaining the highest educational level. In our study, some mothers who achieved their education after giving birth could not be identified. Resources and characteristics of these mothers were assumed to be similar to those who completed their education before having children. However, the use of maternal education as a proxy of SES did not allow us to distinguish between SES at birth and in adulthood.

In Paper I, adjustment for proxies of SES, i.e. maternal age, parity and marital status, did not substantially influence the associations between birth size and adult size. Supportive of this rather robust association, Emanuel et al[204] have argued, based on their findings in an intergenerational study, that the growth status of the individual is more important than the socioeconomic circumstances for the associations of birth size and adult height with chronic diseases. In Paper I, maternal education, which turned out to be the strongest confounder in Paper II, was not available. However, the association between height and social class is weaker than that between social class and intelligence.[189] Hence, although the confounding

factors included in Paper I have limitations as proxies of SES, there is reason to believe that adjustment for maternal education was not as important in Paper I as in Paper II.

In Paper II, we observed that increasing parity was negatively associated with intelligence, consistent with previous literature.[205] Although first born infants in general have lower birth weights then later born, this was not reflected in mean intelligence score. The extent to which this is a biological effect or rather a social effect of increasing family size needs to be further investigated.

In Paper III-IV, maternal education and other confounders accounted for the higher risks associated with breech delivery and birth defects. In Paper IV, the overall risk for not being drafted was highest if maternal education was low, thus indicating that ability was linked to SES. This may imply that the effects of increased perinatal risks on long-term outcomes are exceeded by influences of SES. Effect modification by SES has also been observed in other contexts. For example, a Finnish study found that growth had large effects on the risk of later hypertension in children living in poor social conditions, but only small effects in children in good living conditions.[184] Thus, since SES may modify the impact of early life exposures on adult health, adult diseases may be best focused on in a life course perspective.[54,66] Furthermore, this entails a potential for intervention programmes directed towards the social inequalities in health.

CONCLUSIONS

This nationwide study provides evidence for a minor contribution of prenatal growth to adult body size and intelligence.

The results of this thesis show that the positive associations between birth weight and length on one hand and adult weight and height on the other exist in a general population. The associations are weak, but extend through the normal range of birth size. The results further suggest an interaction between being long and heavy at birth on adult weight, with long and heavy infants becoming particular heavy as adults. Implications of our findings are that studies of birth size and adult size should take account of gestational age and the underlying birth weight distributions. The biological mechanisms that may be involved cannot be identified from the present study and need further investigation.

Our results support the evidence that prenatal growth in terms of birth size has an impact, although weak, on later intelligence. Postnatal growth and SES contribute to this association, and must be considered in studies of birth size and intelligence. Studies addressing the biological mechanisms underlying this association are required. Longitudinal studies with three or more observations, including data on SES, parental body size and intelligence, would give answers to questions regarding the role of effect modification and the impact of genetic factors.

Furthermore, this thesis weakens the hypothesis that breech birth could be associated with impaired intellectual performance in adulthood. Moreover, apart from a somewhat lower score among those with heart defects and cleft palate, intellectual performance is not adversely affected among infants in the majority of birth defect categories who survive without serious disability.

Other studies have suggested associations between intelligence and health outcomes. Our results suggest that SES, in terms of maternal education, has the strongest influence on offspring's intelligence. The causal mechanisms for these relations must be identified, and may form a knowledge basis for developing programs that can provide more effective health education and health care.

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Appendix 1

STATENS HELSETILSYN
Postboks 8128 Dep.
0032 OSLO

Medisinsk registrering av fødsel

Sendes 9. dag etter fødselen til fylkeslegen (stadsfysikus) i det fylket der moren er bosatt.

Merk: Det skal fylles ut blankett for hvert barn (foster). Dør barnet etter fødselen, skal det også fylles ut legeerklæring om dødsfall, og/eller dødsfallet meldes til skifteretten (lensmannen).

Barnet	Barnet var 1 ☐ Levende født 2 ☐ Dødfødt foster	Født dag, mnd., år	Klokkeslett	Personnr.	Skriv ikke her
	1 ☐ Enkel 2 ☐ Tvilling 3 ☐ Trilling 4 ☐ Firling		Kjønn 1 ☐ Gutt 2 ☐ Pike	
	Etternavn, alle fornavn (bare for levendefødte)			
	Fødested. Navn og adresse på sykehuset/fødehjemmet		Kommune	

Faren	Etternavn, alle fornavn	Født dag, mnd., år	Bostedskommune	

Moren	Etternavn, alle fornavn. Pikenavn	Født dag, mnd., år	
	Bosted. Adresse	Kommune	
	Ekteskapelig status 1 ☐ Ugift 6 ☐ Samboende 2 ☐ Gift 3 ☐ Enke 4 ☐ Separert 5 ☐ Skilt	Ekteskapsår (gifte)	
	Antall tidligere fødte (før denne fødselen) — Levende fødte — Av disse i live — Dødfødte		
	Er moren i slekt med faren? 1 ☐ Nei 2 ☐ Ja. Hvilket slektskapsforhold:		

Morens helse før svangerskapet	1 ☐ Normal 2 ☐ Sykdom (spesifiser):	
		Siste menstruasjons første blødningsdag	

Morens helse under svangerskapet	1 ☐ Normal 2 ☐ Komplikasjoner (spesifiser):	

Ble fødselen provosert	1 ☐ Nei 2 ☐ Ja	

Inngrep under fødselen	1 ☐ Nei 2 ☐ Ja (spesifiser):	
	Inngrepet utført av 1 ☐ Lege 2 ☐ Jordmor	

Komplikasjoner i forbindelse med fødselen	1 ☐ Nei 2 ☐ Ja (spesifiser):	

Fostervann, placenta og navlesnor	1 ☐ Normalt 2 ☐ Patologisk (spesifiser):	

Barnets tilstand	Bare for levende fødte. Tegn på asfyksi? 1 ☐ Nei 2 ☐ Ja	Apgarscore etter 1 min. — etter 5 min.	
	For levende fødte og dødfødte. Tegn på medfødt anomali, på skade eller sykdom? 1 ☐ Nei 2 ☐ Ja. Hvilke:		
	Lengde (i cm) — Hode-omkr. (i cm) — Vekt (i g) — For døde innen 24 timer Livet varte i — Timer — Min		
	For dødfødte. Døden inntrådte 1 ☐ Før fødselen 2 ☐ Under fødselen Dødsårsak:		
	Seksjon? 1 ☐ Nei 2 ☐ Ja		

Alvorlige arvelige lidelser i slekten	1 ☐ Nei 2 ☐ Ja Sykdommens art og hos hvilke slektninger:	

Sted (sykehusets stempel) — Dato — Jordmor — Lege

Appendix 2

FORSVARETS OVERKOMMANDO
SANITETSSTABEN

LEGEUNDERSØKELSE

1 PERSONDATA

Navn: .... VF ....

Fødselsnr .... Bostedskommune ....

Adresse ....

2 FYSISKE TESTER

STYRKE

Arm ☐ Rygg/mage ☐ Ben ☐

KONDISJON

Melkesyre ☐ Brutt ☐

3 PSYKOLOGISKE TESTER

ALMINNELIG EVNENIVA

U 4	U 5
0— 8=1 18—20=5 27—30=9	0—17=1 26—27=5 33—36=9

TEKNISK INNSIKT

U 6	U 3A
0—13=1 31—36=5 49—54=9	0— 6=1 12—13=5 20—27=9

4 MEDISINSK VURDERING

Undersøkelse ved *)	Dato	Kapasitet Høyde	Kapasitet Vekt	Fargesyn	Hørsel	Helseprofil 1 Alm.fysikk	2 Fordøyelse	3 Øyne	4 Ører	5 Armer	6 Hender	7 Gange	8 Rygg	9 Hud	10 Psyk.helse	Hoved-diagnose Kodetall -Kfr P-6	Kj.uts. / Midl. ud. Antall mndr.	Legens underskrift

*) 1-Sesjon, 2-Innrykk, 3-Innrykk uten tidl. sesjon, 4-Under 1 g. tjeneste, 5-Repetisjonsøvelse, 6-Heimvernet, 7-Utenom tjenestegjøring, 8-Sivilforsvaret og sivile tjenestepliktige, 9-Resttjeneste, 10-Befal, 11-Beredskap/Mob.

5 ANBEFALT FORDELING

Bør fordeles manuelt ☐   Anbefales fordelt ☐

Til våpenart	Til fagfelt	Til innkalling (Tidspkt)

Bør IKKE fordeles til:	Våpenart	Fagfelt

6 MERKNAD (til pkt 2—5)

BI 4212 B (Utg 7-89)