UNIVERSITY OF LONDON THESIS

Degree PhD Year 2007 Name of Author JEFFERIS, Barbara J. M. H

How do childhood cognition and life course health behaviours affect adult glucose homeostasis?

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July 2007

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I, Barbara J. M. H. Jefferis, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

Abstract

How do childhood cognition and life course health behaviours affect adult glucose homeostasis?

AIM To examine pathways from childhood cognitive ability, through adolescent and adult health behaviours to midlife glucose homeostasis.

SETTING Prospective, population-based 1958 British birth cohort with information about cognitive trajectories between 7 and 16 years, tobacco and alcohol use up to the forties, adult social position and educational qualifications and 45-year glucose homeostasis (indexed by HbA_{1c} level, elevated HbA_{1c} / type 2 diabetes status and metabolic syndrome).

RESULTS Poorer 7-year ability was associated with non-drinking, binge drinking and smoking in adulthood. Smoking was associated with poorer glucose homeostasis, with evidence of dose-response effects. There were graded associations between drinking frequency and glucose homeostasis; infrequent and non-drinkers had higher HbA_{1c} and greater risks of metabolic syndrome than more frequent drinkers. Poorer 7-year ability (rather than change in ability 7-16 years) was associated with poorer glucose homeostasis. These associations were mediated by lifecourse smoking and drinking frequency. Additionally adult social class and qualifications were important mediators of the associations. Adult adiposity was a strong mediator between cognition and glucose regulation and, when explored as an outcome, there were inverse associations between 7-year ability and 45-year BMI or waist circumference, and smoking and drinking trajectories were associated with adult adiposity. Adult smoking and drinking were associated with glucose regulation; after adjustment for confounding factors smoking and less frequent alcohol use were associated with poorer metabolic control.

CONCLUSIONS Poorer childhood cognitive development was modestly associated with poorer mid-adult glucose homeostasis. These associations were not due to confounding by early life factors, but were largely mediated by adult smoking and drinking and adult socio economic position. The same pathways similarly influenced adult adiposity which was an important mediator between cognitive ability and adult glucose regulation. Smoking and drinking into adult life are shaped by childhood cognition and both in turn shape adult glucose regulation.

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Acknowledgements

The data used in this study w as provided by Centre for Longitudinal Studies, Institute of Education. National Child Development Survey Composite File including selected Perinatal Data and sweeps one to five [computer file]. National Birthday Trust Fund, National Children's Bureau, City University, Social Statistics Research Unit [original data producers]. The Data Archive distributor, Colchester, Essex. SN:3148. 1994.

This work was supported by a Medical Research Council/Department of Health Special Training Fellowship in Health of the Public Research which allowed me to attend training courses and develop new skills. Also, research at the Institute of Child Health and Great Ormond Street Hospital for Children NHS Trust benefits from R&D funding received from the NHS Executive.

I would particularly like to thank my supervisors, Professors Chris Power and Catherine Law for all of their help and advice in the development and writing of this thesis.

I would also like to thank colleagues at ICH and elsewhere who helped me with both advice and moral support. In particular Orly Manor, Clyde Hertzman, Bryan Rodgers, Kate Atherton, Leah Li, Claudia Thomas, HuiQi Pan, Tessa Parsons and Tanya Caldwell.

Finally, I would especially like to thank my family and the many friends who provided consistent encouragement and support throughout the whole process of working on and writing this thesis.

Chapter 1, Introduction

This thesis examines pathways through life, from childhood through adolescence, to adult health in midlife. It tracks the influence of early social experiences and cognitive development on trajectories of health behaviours, including alcohol and tobacco use, across adulthood. Pathways from childhood cognitive ability to health behaviours are followed through to evaluate their impact on adult health status, specifically diabetes risk because of its increasing public health burden. Adult chronic diseases dominate the burden of disease in industrialized countries, and their contribution in low and middle-income countries is growing. The substantial population health impact of diabetes, alcohol and tobacco have long placed them on the public health agenda. Whilst diabetes, alcohol and tobacco use have been studied extensively, their treatment in this thesis differs from that of the classical post-war epidemiological model. The focus is on pathways operating across the lifecourse to these outcomes, so analyses are conducted within a lifecourse epidemiology framework. Pathways starting in childhood with cognitive development through to adult health behaviours and diabetes risk will be studied in order to contribute evidence to this rapidly emerging research area; cognitive epidemiology (Deary & Batty 2006).

Classical epidemiology focused on adult risk factors for adult disease outcomes and providing crucial baseline evidence for associations between behavioural practices, such as cigarette smoking with lung cancer, cardiovascular diseases and now diabetes. However, newer approaches explicitly acknowledge that adult health is influenced by exposures acting across the lifecourse: from birth through childhood and adolescence into adulthood. The accumulation and interplay of risks throughout life and not just in a short pre-morbid timeframe in adulthood, is increasingly recognised. Life course epidemiology has been defined as

> *"The study of long term effects on chronic disease risk of physical and social exposures during gestation, childhood, adolescence, young adulthood and later adult life. It includes studies of the biological, behavioural and psychosocial pathways that operate across an individual's life course ... to influence the development of chronic diseases" (Ben Shlomo & Kuh 2002).*

Life course epidemiology acknowledges the importance of exposures to biological, physical and social environments at different life stages. Sensitive and critical periods in early life may also shape later development by setting up individual trajectories of risks. Exposures may act cumulatively and have increasing effects over time, or exposures at particular time points may alter a developmental trajectory, changing risks of subsequent outcomes. The importance of exposures acting at different life stages will differ for contrasting health outcomes and evidence about the importance of different social and biological exposures already exists in diverse research literatures (Kuh & Ben-Shlomo 1997). Life-course epidemiology encourages integration of different perspectives as well as dialogue between disciplines in order to

understand pathways of accumulation of risk through life; this thesis draws on literature from diverse fields of epidemiologic research to inform analyses of pathways through the lifecourse.

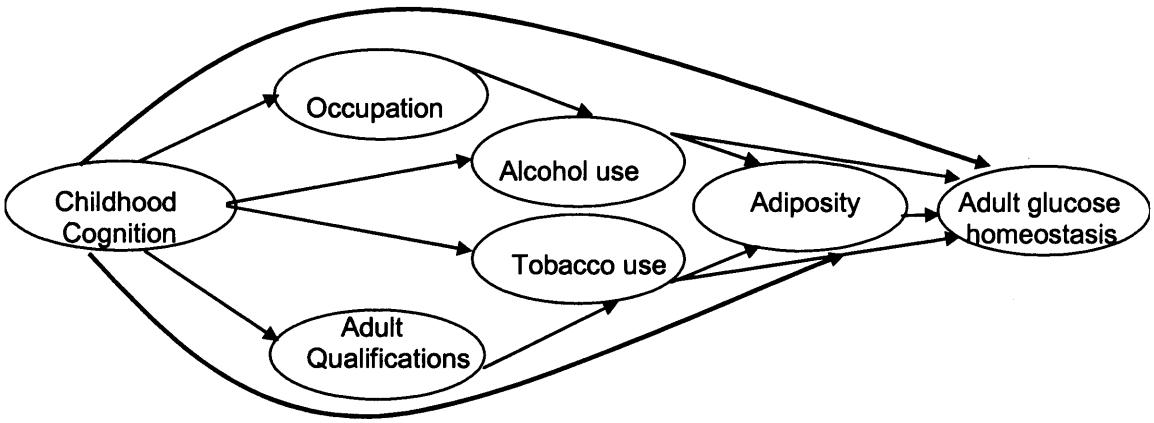


Figure 1 Conceptual outline of main relationships to be examined

Conceptual Framework and Aims

The conceptual framework looking at pathways of risks from childhood through the adolescent and early adult years, to mid-life is illustrated, moving from left to right across Figure 1. The arrows illustrate the pathways to adult glucose homeostasis and type 2 diabetes risk that will be examined. The pathways are broken down into distinct parts and addressed in different chapters, before pathways from child through to adulthood are brought together in the final analysis chapter. Starting from the left of Figure 1, associations between cognitive ability trajectories from mid-childhood to adolescence with health behaviours across adulthood will be investigated, along with the roles of attained adult social position and highest educational qualifications as mediators between childhood cognitive ability and adult behaviours (Chapter 4). Stability and change in health behaviours across the adult lifecourse will be investigated (Chapter 3). Building on this, associations between health behaviours over the lifecourse and mid-life glucose homeostasis (Chapter 5) and also associations between childhood cognitive ability and mid-life glucose homeostasis (Chapter 6) will be investigated separately. Analyses will be brought together to examine the pathways from childhood cognitive ability through adult health behaviours and social position to mid-life glucose homeostasis (Chapter 7).

Much research about diabetes onset and poor glucose tolerance has focused on events in adulthood, primarily the classic risk factors of obesity, central adiposity, physical inactivity and diet. The greater value of intensive lifestyle intervention, based on diet and physical activity over pharmacologic interventions to prevent diabetes onset is recognised in policy based on evidence from randomized control trials (Alberti et al. 2007). The focus on tobacco and alcohol use in relation to diabetes risk may seem surprising; but there is less evidence that they are associated with accumulation of risk for poor glucose regulation indexed by HbA_{1c} or metabolic

syndrome, and these behaviours are not classical risk factors diabetes as they are for cardiovascular diseases or stroke. Secondly, and importantly, the lifetime contribution of trajectories of health behaviours is poorly researched. The analytic approach taken here is different to previous studies of behavioural risk factors. Many studies of diabetes risk in relation to alcohol and tobacco use investigate single measures of behaviour and relate them to disease onset years later. However existing literature has not accounted for the role of continued and sustained alcohol and tobacco use over time, which a lifecourse perspective can address.

Terminology for lifecourse models

Lifecourse epidemiology necessitates the study of longitudinal data and few existing studies have prospective information about exposures over the lifecourse. This thesis uses data from a prospective British population-based birth cohort to explore pathways between exposures and outcomes, not just to establish associations between them. The terminology and lifecourse framework is now clarified. The analytic strategy is that each chapter examines one of a pair of associations (in Figure 1) and then a final chapter integrates analyses across the whole lifecourse evaluating pathways between early life and adult diabetes risk. In this thesis "pathways" are mediating variables on the causal chain between exposure and outcome and occur between the time of the exposure and the onset of the outcome. In contrast, common causes or confounders of an association are variables associated with both exposure and outcome but occur prior to, or at the same time as, the exposure. Confounders were identified *a priori* from the research literature and selected for inclusion in analyses, if they were associated with both exposure and outcome in this study. Because associations between variables at different stages of the life course are studied, a confounder of one association may be a mediator of another association. Comparing unadjusted analyses with analyses adjusted for factors hypothesized to be on the causal pathway indicates to what degree a pathway factor mediates between exposure and the outcome. Similarly comparison of unadjusted analyses and analyses adjusting for common confounders indicates to what degree an association is due to confounding.

Outcomes and exposures

The public health importance of the outcomes and exposures to be investigated is discussed here and specific details about the measures are in Chapter 2.

Glucose homeostasis, type 2 Diabetes and metabolic syndrome

The main outcome in this thesis is adult glucose homeostasis. Impaired glucose regulation affects increasing numbers of adults in the UK. Understanding the determinants of good or bad midlife glucose homeostasis is important in different population groups. In diabetic patients, serious and often irreversible complications can be prevented by good control (Stratton et al. 2000). In high risk groups, the silent onset of glucose dysregulation over many years may result in severe complications and progression to diabetes. However this can be prevented by

intervention through behavioural change or medication (Diabetes Prevention Program Research Group 2002). Finally, in the healthy population, evidence is mounting that incrementally poorer glucose regulation, well below the threshold of diabetes, is associated with increased mortality risks (Brunner et al. 2006; de Vegt et al. 1999; Khaw et al. 2001; Khaw et al. 2004). Therefore, three measures of midlife glucose homeostasis in a large population-based sample in the UK are investigated (Table 1.1). First, (self reported) diagnosed non insulin dependent (type 2) diabetes combined with undiagnosed diabetes, secondly, a high risk group with metabolic syndrome. Thirdly, in the whole population, glycosylated haemoglobin (HbA_{1c}) which indicates circulating glucose 2-3 months prior to measurement, reflecting longer-term status of glucose homeostasis rather than fluctuations in response to a glucose load. The three outcomes are collectively referred to as measures of adult glucose homeostasis.

A compelling reason to investigate glycosylated haemoglobin (HbA_{1c}) levels in a population sample is the accumulating evidence that the association between glucose levels and risks of morbidity and mortality extends across the population distribution of HbA_{1c}, fasting and post-load glucose, below blood-glucose levels defining diabetes. For example, in British men and women aged 45-79 years, all-cause mortality increased 28% per 1% increase in HbA_{1c} level and most of the population burden of mortality and cardiovascular events occurred in individuals with moderately raised HbA_{1c} (5-6.9%) (Khaw et al 2001; Khaw et al 2004).

The type 2 diabetes epidemic confers a very high burden of morbidity and mortality in the UK and world-wide. Approximately 4% or 1.8 million adults in the UK have diagnosed diabetes and 0.6 million more are undiagnosed, an estimated 90% of cases are type 2 diabetes (Diabetes UK 2004, p.8). Diabetes prevalence is increasing and expected to reach 3 million by 2010 (Forouhi et al. 2006). Prevalence estimates are complicated by silent onset of beta cell damage which can be present several years prior to diagnosis (Davies et al. 2004). At diagnosis, more than half of diabetes cases have cardiovascular disease; the most common macro-vascular end-point associated with diabetes. Cardiovascular disease risk is increased up to five fold and stroke two to three fold in diabetic populations. Progressively higher blood glucose is associated with progressively worsening risks for irreversible microvascular events, some macrovascular events and all cause mortality (Stratton et al 2000). In the UK diabetes costs some 5% of NHS budget which is projected to increase with increasing prevalence of diabetes expected in an ageing population where prevalence of obesity, a key risk factor of diabetes, is rising rapidly.

Metabolic syndrome, is to some a controversial endpoint. Syndrome X or metabolic syndrome represents a cluster of metabolic abnormalities which may be on the pathway to cardiovascular disease (Reaven 1988). Hypertension, hyperlipidaemia, obesity and poor glucose homeostasis

co-occur more frequently than expected by chance, and are classed as one metabolic disorder. Several definitions of metabolic syndrome have been proposed, with slightly differing cut-offs and components. Objections to the metabolic syndrome are based on uncertainty about pathogenesis, imprecision of the various definitions and its value as a marker for cardiovascular risk. Therefore whilst clustering of risk factors is acknowledged, critics of metabolic syndrome advocate treatment of patients on the basis of individual risk factors rather on based on metabolic syndrome status (Kahn et al. 2005).

Despite disagreements, metabolic syndrome is increasingly recognised; health care providers now recognize that it merits treatment, it has its own ICD 9 code and much research investigates the predictive value of metabolic syndrome for disease and mortality endpoints (Ford 2005; Hu et al. 2004; Park et al. 2003; Standl 2005; Sundstrom et al. 2006). A review of mortality associated with metabolic syndrome (defined by National Cholesterol Education Program (NCEP) criteria) found significantly increased risks of cardiovascular disease RR (Rate Ratio) 1.65(95%CI 1.38, 1.99) and diabetes onset 2.99(95%CI 1.96, 4.57). Using the WHO definition, estimates increased to 1.93(95%CI 1.39, 2.67) and 6.08(95%CI 4.76, 7.76) respectively (Ford 2005). Prevalence of metabolic syndrome is estimated to increase (in men and women respectively) from 10% and 15% in normal glucose tolerance, 42 and 64% in impaired fasting glucose or impaired glucose tolerance, and 78 and 84% in type 2 diabetes (Isomaa et al. 2001). Because individuals with metabolic syndrome suffer from increased risks of incident diabetes and cardiovascular disease, higher mortality rates and worse disease progression, it is an important end-point to investigate (Betteridge 2004).

Lifecourse health behaviours: alcohol and tobacco use

Health behaviours are the next major area of interest examined in this thesis as a potential pathway between cognitive ability and adult glucose homeostasis. Investigating the prevalence and changes in tobacco and alcohol use patterns over time is relevant to a broad range of health measures in addition to adult glucose regulation. Tobacco accounts for a very high burden of disease globally and in the UK, mainly from cancers and cardiovascular diseases (Peto et al. 1994). Half persistent smokers die from smoking related diseases, however quitting before middle age avoids most of the excess mortality risk (Doll et al. 2004). Tobacco use in pregnancy also increases risks of lower birthweight and higher infant mortality as well as longer term consequences on physical and cognitive growth of children (Butler et al. 1972; Fogelman & Manor 1988). In the UK, prevalence of cigarette smoking decreased, through the 1970s and 1980s from 50% men and 40% women, and the decrease slowed down and since the 1990s prevalence has been about 26-28% (Walker et al. 2001, p.121).

Heavy or episodic alcohol use results in a broader range of health and social consequences that range from direct health conditions such as liver cirrhosis and pancreatitis, injuries, accidents mental and behavioural disorders to the spectrum of antisocial and criminal behaviour (Department of Health 2001, pp.8-9). The benefits of alcohol for cardiovascular disease risk are debated; lower risks of myocardial infarction and ischaemic stroke are limited to men over 40 and postmenopausal women, with no additional benefit of consuming more than 1 to 2 units of alcohol per day (The Academy of Medical Sciences 2004, p.21). At present, alcohol consumption levels in the UK are greater than that which would result in net health benefits (The Academy of Medical Sciences 2004, p.15).

Alcohol use increases through adolescent years and peaks in the early 20s, with evidence of decline thereafter (Kuntsche et al. 2004; Naimi et al. 2003; Walker et al 2001, p.147). Alcohol consumption has increased over past decades to approximately 10 litres of pure alcohol per capita in the UK (British Beer and Pub Association 2001). The majority of adults in the UK regularly drink alcohol (75% men and 59% women report drinking in the past week) and consumption is high; 39% men and 22% women report exceeding daily drinking guidelines and this peaks in 16-24 year age group (Walker et al 2001, p.147). However few studies have followed individuals longitudinally through life, beyond early twenties or thirties to assess how trajectories of frequency and amount of alcohol consumed develop through adulthood. Lifecourse trajectories of binge and heavy drinking trajectories and smoking within individuals have not been investigated. Understanding stability and change in drinking patterns is important for evaluating accumulation of disease risks over the lifecourse.

The known pathological consequences of heavy alcohol use and smoking in addition to their role in reinforcing health inequalities (people in manual classes are more likely to smoke and drink heavily than those in non-manual classes), makes these health behaviours a worthy focus of investigation. Co-occurrence of smoking and different aspects of drinking is also of interest, because multiple unhealthy behaviours impose heavy health and social burdens; concurrent tobacco and alcohol use multiply disease risks, for example, cancers of oral cavity and respiratory tract (Bagnardi et al. 2001b). Further, the social processes affecting the uptake and persistence of these behaviours share common aspects (Room 2004).

Cognitive development in childhood

Building on accumulating evidence about associations between childhood cognition and morbidity (discussed below), cognitive ability will be examined as an antecedent to adult health behaviours and adult diabetes risk. The study of cognitive development investigates how individuals perceive, think, and understand their world, hence cognitive development includes, but is not limited to, the domain of intelligence, also encompassing reasoning, language and

memory development. Cognitive development acknowledges changes over the lifecourse, from infancy to adulthood and is not a static concept. By contrast, the study of intelligence has focused primarily on intellectual quotient (IQ) as measured by standardized psychometric tests and has been criticized for its narrowness of focus (testing only some aspects of intelligence) and for its cultural biases. It is now accepted that IQ tests measure only some types of abilities and that intelligence is not a measure of personality, creativity or other aspects of character and is not designed to be (Gottfredson 1997), after much debate a definition with general consensus of the research community was published:

> *"intelligence is 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. It is not merely book learning, a narrow academic skill, or test-taking smarts. Rather, it reflects a broader and deeper capability for comprehending our surroundings- "catching on," "making sense" of things, or "figuring out" what to do"* (Gottfredson 1997).

Intelligence testing scores individuals based on their rank in a normal distribution relative to a reference population. Standard IQ tests strongly predict school achievement, occupational and social outcomes. In essence, the results of different intelligence tests all correlate positively with each other, even when different dimensions of intelligence are tested eg spatial ability, comprehension or number ability. The underlying factor in intelligence tests is called "g" or the "general factor". There is not universal consensus about the nature of "g", however a hierarchical model conceptualizing different factors representing clusters of specialized abilities alongside each other with g at the apex has gained widespread acceptability (Neisser et al. 1996). It is not the place of this thesis to justify the use of "g". Rather, now that "g" is widely accepted this thesis uses evidence about it. The concept of an underlying factor and the correlations between tests of different domains of ability are an underlying principle for research into the associations between cognitive ability and later health and behavioural outcomes in this thesis. This thesis does not use psychometric IQ tests, so the terminology of cognitive ability rather than IQ is used to convey a broader concept of mental ability.

This thesis will investigate cognitive trajectories; both initial rank of cognitive ability in the early school years (age 7) and the change across childhood towards the end of school (age 16). Whilst absolute cognitive ability increases as children grow and gain additional knowledge, their rank in relation to other individuals of the same age may remain steady, or they may improve or decline relative to peers. Both initial level and changes in relative cognitive ability rank across childhood are expected to predict subsequent social and academic trajectories as well as behavioural and health outcomes. Level and change in ability rank will reflect the individual's cognitive developmental trajectories and closely related factors including social background and home environment, engagement with school, learning and socio-emotional

development. Change in ability rank may be a more sensitive measure of ability than initial level, if it reflects changes in home and school environment. Influences shaping cognitive ability early in the school years and change in ability throughout childhood are important to educational policy. Regardless of whether cognitive ability is also associated with adult health outcomes, many other important social reasons to promote education and develop cognitive abilities of children and adults exist. It is beyond the scope of this thesis to evaluate and discuss the relative importance of all the different influences on cognitive ability and change in ability in childhood. However some mention is warranted as context for the interest in level and change in ability during childhood.

Cognitive ability can be increased by schooling and by intensive programs, such as Head Start and the High Scope Perry Project which provided environmental interventions. However, gains in cognition faded out over time, although beneficial effects on antisocial behaviour were observed two decades later (Schweinhart et al. 1993; Weikart 1998). Cognitive ability is also influenced by genetic heritage, but it must be acknowledged that any genetic effect occurs in the context of an environment, albeit a cellular environment, which may be altered by other influences. Estimates of the heritability of "g" vary between 0.4 and 0.8 and are about 0.75 in white populations; 75% of the variability in IQ can be attributed to genetic influences (Neisser et al 1996). It has been argued that the effects of heritability on IQ increase with age: whilst environment importantly shapes cognitive ability in childhood, this effect reduces with increasing age (Neisser et al 1996). Therefore there may be large effects of home or school background on cognitive ability in childhood but these diminish with age. It has also been reported that intelligence is quite stable across the life course; correlations of 0.77 between IQ at age 7 and at age 18 years, with higher correlations of tests taken at closer time intervals are reported (Moffitt et al. 1993). If cognitive ability is stable across the lifecourse childhood cognitive ability should predict adult ability. Data from a small subsample of the 1932 Scottish mental surveys support this: the correlation between IQ at age 11 (in 1932) and in survivors traced at age 77 was 0.63 (n=93) (Deary et al. 2000). However this continuity implies that in the literature documenting associations between childhood cognitive ability and adult outcomes, it may be adult rather than childhood cognitive ability which is drives associations with adult health behaviours or health status.

Pathways

The background literature and the rationale for investigating pathways between cognition, health behaviours and adult glucose homeostasis are now discussed. Further detail will be given in the introduction to each chapter. It is acknowledged that not all possible influences on glucose metabolism will be studied, rather the focus is to contribute to existing knowledge about

the pathways from childhood cognition and adult health behaviours to adult glucose homeostasis.

Cognitive ability and adult morbidity and mortality

Cognitive epidemiology is a growing research field, investigating associations between pre-morbid IQ and later mortality (Deary & Batty 2006). Prospective and retrospective cohort studies have observed that childhood cognitive function is associated with adult morbidity (Martin et al. 2004) and mortality risks, into the 5th and even 7th decade of life (Hart et al. 2004; Whalley & Deary 2001). Adults who scored more highly on various tests psychometric tests of ability in childhood (for example around ages 8 or 11 years) had lower mortality risks from different causes of mortality (including cardiovascular and cancer deaths) (Batty et al. 2006a). For example, in a Scottish sample followed for 25 years, risk of death increased by 17% per standard deviation decline in IQ at age 10 or 11 years, this was reduced to 12% but not entirely explained on adjustment for adult social position and deprivation (Hart et al. 2003b). In addition many measures of morbidity and mortality including diabetes, are associated with highest adult educational qualifications (Acheson 1998). These noteworthy findings about childhood cognition build on earlier research demonstrating the greater risks of mortality and morbidity in older adults who perform worse in tests of cognitive ability in later life; indeed diabetic patients have greater cognitive decline than those with normal blood-sugar regulation. Adult cognitive ability is also associated with dementia, leading to the expectation that lower prior ability may be associated with dementia, but associations between childhood ability and many other causes of death are also seen (Kuh et al. 2004; Whalley & Deary 2001). Based on accumulating evidence that childhood cognitive ability is associated with mortality risks, including cardiovascular disease, and what little evidence specifically relates to diabetes risk (Martin et al 2004; Starr et al. 2000), it is expected that poorer childhood cognitive ability will be associated with elevated risks of poor adult glucose metabolism.

Health behaviours

It could be hypothesized that childhood ability directly affects adult health status, but it is more likely that other pathways are involved. This thesis particularly focuses on the role of health behaviours as pathways between childhood cognitive ability and adult diabetes risk. Childhood cognitive ability is just one of many exposures which influence uptake and persistence of health behaviours across adulthood, existing evidence suggests that school achievement and aspirations are associated with initiation of health behaviours, but their role in persistence of behaviour through adulthood is unclear. There is accumulating evidence for independent associations of tobacco and alcohol use on type 2 diabetes and HbA_{1c}, in addition to their influences on cardiovascular risk(Howard et al. 2004; Perry 2001). In diabetic patients, cigarette smoking is associated with the progression of diabetic complications such as

nephropathy (Baggio et al. 2002; Mehler et al. 1998). Very few studies examine influences on glycaemic control in non-diabetic populations (Boeing et al. 2000; Sargeant et al. 2001a), but several studies observed elevated risks of type 2 diabetes among smokers and heavy users of alcohol (Carlsson et al. 2000; Sairenchi et al. 2004; Wannamethee et al. 2001; Wannamethee et al. 2003). Because cognitive ability is associated with initiation of tobacco and alcohol use and these in turn are associated with diabetes risk, they are a valid pathway between cognition and diabetes risk. There is scope to investigate the importance of childhood cognitive ability in shaping trajectories of alcohol and tobacco use in more detail than the few studies to date that have accounted for behavioural factors as pathways from childhood cognition to adult health status (Hart et al 2004; Kuh et al 2004).

Several other mechanisms have been proposed and tested as explanations for the association between childhood cognition and adult health status and will be addressed in this thesis.

Confounding by childhood factors

Childhood cognition may reflect biological and physical injuries, such as poorer development *in utero*, birth risks, poor nutrition and physical illnesses accumulated prior to measurement of ability. Thus cognitive ability may mediate between early physical and social disadvantage and subsequent survival to adulthood. Poorer childhood social background is associated with poorer childhood cognitive ability (Hart et al. 2003a; Jefferis et al. 2002; Lawlor et al. 2005b; Lawlor et al. 2006a; Shenkin et al. 2004) and also with diabetes risk into mid-life (Langenberg et al. 2006; Lawlor et al. 2006b; Lidfeldt et al. 2007; Power et al. 2007). Adults from more manual class childhood backgrounds are more likely to develop poorer glucose tolerance than those from non-manual backgrounds, even after taking into account their adult circumstances(Lawlor et al. 2003a). At present it is not clear what particular aspects of childhood social circumstances are important on the pathway to influencing development of diabetes. Social position of origin is associated with a range of adult outcomes which may contribute to accumulation of diabetes risk, including trajectories of height and weight. Shorter stature and larger adult body size is associated with poorer early social position (Hardy et al. 2000; Li et al. 2004). There is evidence from the 1958 cohort and other studies that poorer social position in childhood is associated with smoking across the lifecourse, frequent consumption of alcohol and alcohol-related problems and physical inactivity (Caldwell et al. 2007; Graham & Hunt 1998; Jefferis et al. 2001; Lynch et al. 1997; Power et al. 2003; Wadsworth & Kuh 1997; Yang et al. 2007). Childhood social position is associated with adult health behaviours, even taking into account adult social status (Brunner et al. 1999; Power et al 2007). In addition to social class of origin, *intra uterine* growth, indexed by birthweight for gestational age may be important in understanding the associations cognition and diabetes risk. Across the range of normal birthweights, lower birthweight is consistently associated with small deficits childhood

cognitive function (whilst social class is more strongly associated with cognitive development, the birthweight effect is largely independent of social class) (Shenkin et al 2004). There is also evidence of a u-shaped association between birthweight and adult diabetes risk (Harder et al. 2007). Hence birthweight may be a common cause of childhood cognitive ability and adult diabetes risk, so birthweight will therefore be considered as a confounder. The hypothesis that childhood cognitive ability mediates between childhood socio-economic position and adult mortality risks has been tested, but it was not supported by data from the 1946 British birth cohort study (where the associations between childhood cognition and mid-life mortality risks were independent of childhood socioeconomic position and childhood illness), or a prospective Danish cohort where the mortality risks associated with cognitive ability remained elevated after adjustment for both birthweight and early socio-economic position (Kuh et al 2004; Osler et al. 2003).

Pathways through social trajectories

Higher childhood cognitive ability predicts higher educational achievements and more professional adult occupational position (Neisser et al 1996), both of which are associated with lower mortality risks from many outcomes. Hence educational qualifications and occupational social group are potential intermediate pathways between childhood cognitive ability and adult health outcomes. Material explanations of social inequalities in various health outcomes highlight social differences in quality of factors like housing, transport, tax and benefit policies, environmental exposures (such as air and soil pollution). Whilst there is differential exposure to these material conditions across the social spectrum which have demonstrable effects on health, gradients in health are seen right through the social spectrum and beyond levels at which extreme hardship exists. Alternative explanations of social gradients in adult health focus on differences in social status and social capital.

There is empirical support for pathways from cognitive ability through continued educational trajectories and social advantage to mortality risks. In a Scottish cohort IQ at 11 years (measured in 1932) was related to all cause mortality over a 25 year period from midlife into older age, and on adjustment for gender and occupation-based social position and area-based deprivation in midlife, the association was attenuated but still significant (Hart et al 2003b). A study of the 1946 British birth cohort (with fewer deaths) reported that the association between childhood cognitive ability and mid-life mortality was entirely mediated by adjustment for adult socioeconomic circumstances (Kuh et al 2004). However, the importance of social position as a pathway from childhood ability to health status may vary in time and space and with the type of health outcome studied. This is a feasible pathway between cognition and glucose homeostasis because social gradients in diabetes and impaired glucose metabolism are observed, using measures of either occupational class or education (Wamala et al. 1999). Individuals with the

least education or lower occupational status tend to have increased risks of diabetes (Kumari et al. 2004) and glucose dysregulation (Power et al 2007).

Non-linear effects

Cognition may reflect general integrity of the body, indicating how efficiently and reliably the brain processes information. Reaction time is believed to reflect brain processing speed and, in a large study of British adults, partly mediated the association between adult cognitive ability and mortality risks (Shipley et al. 2006). This hypothesis cannot be tested in this thesis because data on reaction time is lacking. There is some evidence that there is lower cognitive reserve and earlier cognitive decline in later life among people with lower IQ(Richards et al. 2004). Associations between childhood ability and poor adult health could be driven by the group with lowest scores of cognitive ability. Some support for non-linear associations comes from the 1946 study where highest mortality rates were seen in the lowest IQ quartile (Kuh et al 2004) and also in the Midspan cohort in Scotland (Hart et al 2003b). It is of interest to investigate non-linearity of associations between cognition and health behaviours and also between cognition and glucose homeostasis.

Gaps in literature: pathways from cognition to glucose homeostasis

Whilst the associations between childhood ability and adult morbidity have been replicated in different contexts, providing evidence for the robustness of an underlying association, there are unanswered questions about the pathways underlying the associations. Much research literature focuses on men, so evidence about women is weaker. It is not clear if the associations between childhood ability and later health and mortality outcomes are linear; if higher ability is always associated with improved outcomes, or whether there is a ceiling effect, after which there is no benefit to health. There is little research on the pathways through life which underlie the associations, both environmental and genetic. The research in this thesis can address some, but not all of the outstanding questions about the associations between childhood cognitive ability and adult health status.

To address gaps in existing literature this thesis will investigate whether childhood cognitive ability is associated with mid-life health status, specifically three indicators of diabetes risk. The research includes both sexes and will investigate whether there is evidence for any threshold in any association between cognitive ability and later health status. Importantly, it will also investigate more than one aspect of childhood cognitive ability in relation to adult health status: both ability level in mid-childhood and change in ability up to adolescence. Additionally, lifecourse models of specific pathways to mid-life glucose regulation will be tested. On the basis of the evidence discussed so far, it is hypothesized that higher levels of childhood cognitive ability will be associated with lower risks of diabetes. This association is expected to

be in part due to behavioural pathways through the initiation and persistence of alcohol and tobacco use through adult life (alongside markers of established risk factors physical activity and diet), as well as social pathways whereby higher childhood cognitive ability is associated with gaining higher educational qualifications and the allows entry into more professional occupations. The association between higher occupational status in adult life with diabetes risk may be due in part to its associations with health behaviours and adiposity as well as material factors and access to care. Because adult adiposity is a strong predictor of mid-life glucose dysregulation, factors influencing adult adiposity including tobacco and alcohol use, are expected to be associated with the onset of glucose dysregulation. The confounding roles of early social position and birthweight on the association between cognitive ability and later glucose dysregulation will also be tested.

The main aims of each of the different chapters are summarized in Table 1. To build on existing research, analyses presented in this thesis will focus first on understanding trajectories of tobacco and alcohol use through adolescence and into adult life (Chapter 3) and then on how drinking and smoking trajectories affect adult glucose metabolism (Chapter 5). The roles of tobacco and alcohol together with known influences on glucose regulation (obesity, diet and physical activity) will be considered (Chapter 7). The earlier chapters of the thesis focus on associations illustrated in Figure 1 and are, for the most part, limited to variables in the figure. The final analytical chapter focuses on the same associations but takes on board other confounding factors or common causes. Details of the data and methods are now described in Chapter 2.

Table 1.1 Summary of aims

The associations, and pathways underlying the associations, between the three following factors will be studied

(a) Cognitive ability trajectories	Relative rank in maths and reading ability in middle childhood and the trajectory of change to adolescence.
(b) Lifecourse health behaviours	Repeated measures of alcohol and tobacco use between early twenties and mid-forties.
(c) Midlife glucose homeostasis	(i) HbA1c level; (ii) high risk group (HbA1c ≥6% and type 2 diabetes) and (iii) metabolic syndrome

Subject area	Summary of aims
Lifecourse health behaviours (Chapter 3)	To examine the prevalence and co-occurrence of smoking and several dimensions of alcohol use. Cross-sectional associations and also trajectories of behaviours across adulthood will be examined.
Cognition and lifecourse health behaviours (Chapter 4)	To establish if childhood cognition is associated with adult health behaviours at single adult ages and as trajectories across adulthood. Further, to establish if associations between childhood cognitive ability and adult health behaviours are mediated by highest educational achievements and adult occupational position.
Lifecourse health behaviours and mid-life glucose homeostasis (Chapter 5)	To establish if mid-life glucose regulation is associated with tobacco and alcohol use at single adult ages and trajectories across adulthood? To further investigate whether associations are robust to adjustment for a priori confounding factors (diet and physical activity) or if they operate through adult adiposity.
Cognition and mid-life glucose homeostasis (Chapter 6)	To establish if childhood cognition is associated with mid-life glucose regulation and if associations are robust to adjustment for selected a priori confounders, if associations operate through adult social position, educational level or adiposity.
Cognition and mid-life glucose homeostasis (Chapter 7)	To establish if associations between cognition and mid-life glucose regulation are robust to adjustment for a variety of a priori confounders, and to investigate if associations operate through adult health behaviours.

Chapter 2, Methods and Measures

Introduction

This chapter describes data which will be analysed, including the sample size, losses to follow up and representativeness. Measures are described here, so descriptions are not repeated in subsequent analysis chapters. The measures are organised as exposures; pathways in childhood; pathways in adulthood; and health outcomes. Pathway variables are expected to mediate between an exposure and an outcome and understanding pathways is a main focus of the lifecourse framework adopted in this thesis. Cognitive ability measures are consistently used as exposures in this thesis, but other variables may be exposures or outcomes depending on the analysis. To illustrate, health behaviour trajectories across adulthood are used as outcomes in analyses investigating associations between childhood cognition and health behaviours (Chapter 4) and then used as exposures in analyses of associations between health behaviours and adult glucose regulation (Chapter 5), or used as pathways in analyses of cognition to health outcomes through health behaviours (Chapter 7). In addition to the measures listed in Figure 1.1 summarising the main pathways to be investigated in this thesis, other potential confounders are included. This is necessary in order to understand whether the associations studied are robust to confounders which are *a priori* expected to be associated with both exposures and outcome. The statistical methods and analytic strategy are also described.

Sample

This research uses data from the 1958 British birth cohort (National Child Development Study), a population-based prospective study, comprising approximately 98% of births in England, Scotland and Wales during one week in March 1958 (Power & Elliott 2006). Survivors of some 17,000 live births were contacted at birth or shortly afterwards, when the child's mother was asked to fill in a questionnaire. The children were followed-up at ages 7, 11 and 16 years through interviews with the child's parents, teachers and doctors. Additionally immigrants to the UK who were born in the study week were added to the sample at 7, 11 and 16 years. In adulthood, the cohort members filled in questionnaires at ages 23, 33 and 42 years (Power & Elliott 2006). At age 45 years (between September 2002 and March 2004) participants were interviewed by trained nurses. This thesis uses data from all of the surveys across the lifecourse of the cohort. A description of the historical context including social conditions in childhood, the school context, early adult employment transitions and partnership and parenting in the 1958 cohort is in Appendix 2.1.

Response to each survey is summarised in Table 2.1. By 45 years 6.7% of the cohort had died, the majority were perinatal deaths (Davie et al. 1972, pp.154-164). Emigration increased up to age 33 years and then decreased as emigrants returned to the UK. Loss to follow-up has

occurred at each survey, with a notable increase in the number of non-responders at 23 years. At 45 years only 59% of the eligible sample responded and sample attrition was mostly avoidable because contact was not attempted for 19% of the eligible sample. However, out of the contacted sample 72% participated which was a similar level to the other adult surveys. Response bias in the 45-year survey has been extensively studied; by 45 years there was under-representation (negative response bias) for the following groups of participants; born into manual social groups (-2%); no male head of household (-23%), children with internalising (-14%) and externalising (-17%) behaviour problems age 7 years, bottom decile of reading (-21%) and maths (-14%) scores age 7 years. Adult characteristics (age 42 years) associated with non-response to the 45-year survey were not being in work (-10%), manual social class (-3%), obesity (-5%), current smoking (-6%) and never drinking (-4%) (Atherton et al. 2007).

By 45-years only 2.0% of the sample classified themselves as non-white, less than census estimates of 7.5% in 45-49 year olds (Atherton et al 2007). Nearly half of the ethnic variation in the sample comes from the immigrants at ages 7 through 16 years. Hence the cohort is not ethnically representative of the current British population.

Ethics committee approval for the 45-year survey was obtained from the South East Multi-centre Research Ethics Committee (ref: 01/1/44). Approval for the 42-year survey was obtained from the North Thames Multi-centre Research Ethics Committee. For the 33 year survey ethical committee approval was not sought, but participants were asked for written consent to access medical records. Before the 23-year survey in 1981, ethics committee approval was not sought as it was not standard procedure at the time.

Measures

Childhood cognitive ability

Cognitive ability was tested in childhood; an age-appropriate maths test and reading test was taken at school at ages 7, 11 and 16 years and a general ability test at age 11 years. The fieldwork for each survey lasted several months, so analyses of test scores were adjusted for the child's age to the nearest month to account for increases in test scores with increasing age of the child. Maths and reading were the only ability measures tested at all three ages; other aspects of development were tested on single occasions. In order to study change in ability between 7 and 16 years, analyses therefore focus on maths and reading.

At age 7 the maths test included ten arithmetic problems of graded levels of difficulty (score range 0-10). If necessary teachers read questions for poor readers. At age 11, the test (range 0-40) comprising problem and mechanical questions was a modified version of the Vernon graded arithmetic test, constructed by the National Foundation for Educational Research in England

and Wales(Goldstein & Fogelman 1974). For the 16-year survey, a maths comprehension test (range 0-31) was constructed at University of Manchester specifically for use with this age group. The scores for the maths tests were approximately normally distributed.

At age 7 the Southgate reading test was used which is a standardised test of word recognition and it identified poor readers (Southgate 1962). Children selected one word corresponding to a picture from a list of several words, then teachers read out words that the children had to identify from a printed list. The reading comprehension test used at 11 years was constructed specifically for this study by the National Foundation for Educational Research in England and Wales and was parallel to the Watts Vernon reading comprehension test, a test of sentence completion with a ten minute time limit. The same test was also used at 16 years. The distributions of the 7 and 16 year test results were skewed (most children scored highly) so power transformations were used to improve the distribution and symmetry of the scores. The 7 year scores were raised to power 4 and 16 year scores to power 3.

Additionally a general ability test approximating the conventional intelligence test, with verbal and non-verbal components (score range 0-80) was taken at age 11years. The two parts of this test are summed to give an overall IQ measure (Douglas 1964, pp.34-35, 161-164).

Because different (age-appropriate tests) were used at the three childhood ages, it was not appropriate to look at absolute changes in the raw test scores over time. Therefore, test scores were converted to standard deviation scores (z-scores) (mean=0, standard deviation=1) to allow comparison across ages. The z-scores were calculated with genders together for the sample with available data. Coding of z-scores was reversed; a negative z-score corresponds to a high test result and a positive score to a low test result.

The z-scores of maths and reading indicate rank relative to peers. Change in z-score between 7 and 16 years indicates changes in relative ranking of participants. If a child remains in the same position relative to their peers, this does not imply that they have the same absolute ability level at the two test-points; general learning relating to for example mathematical and reading ability and vocabulary will have occurred during this period.

Trajectories of maths and reading between 7 and 16 years

To summarise an individual's maths z-score trajectory between 7 and 16 years, repeated measures multilevel models (in MLwiN 2.0)(Goldstein 1995) were used to estimate an intercept and slope of the maths z-scores for each participant. The maths z-scores at ages 7, 11 and 16 years were entered as the dependent variables in a model with age (centred at 7, the age at the first maths test) and allowing for level 2 (between person) variation but not level 1 (within-

person) variation. Model predictions (illustrated in Figure 2.1) were made for participants with complete or incomplete data. An intercept representing 7-year z-score (or initial level) was predicted from the model. The intercept was the sum of a fixed constant (the group average ability at 7 years) plus a level 2 term representing the individual's deviation from the constant. A slope of z-score between 7, 11 and 16 years was also predicted, indicating the change in rank to age 16. Because there are only three time points, it is not possible to model a non-linear association so a linear association was assumed. The change coefficient was the sum of a fixed constant (group average change in ability rank between 7 and 16 years) and the person-specific deviation from the constant. The slope term was multiplied by 9 (16-7=9 years) so that the estimates of change in ability related to the entire period rather than one year in the period. The predicted slope (ie change in z-score between age 7 and 16 years) represents the change in rank of ability relative to peers, rather than the absolute change in ability level between 7 and 16 years. The process was repeated for reading z-scores.

The predicted level and slope of the z-scores were used as independent variables in subsequent analyses. Predicted z-scores were coded inversely so that a high test score was represented by a negative predicted z-score and a low test score by a positive predicted z-score. An improvement in rank between 7 and 16 years was indicated by a negative value for the slope. Because the test scores are coded inversely, in order to be clear about the direction of associations reported in the results sections, the direction of association with reading and maths test results is reported as the association with "ability" although it is acknowledged that whilst reading and maths are key skills, they do not reflect all dimensions of childhood cognitive ability. Appendix 2.2 contains further information about the validation of the maths and reading scores.

Confounding factors from childhood

Birthweight was recorded by the midwife at delivery in pounds and ounces and converted to Kilograms. Gestational age was recorded as days since last menstrual period and checked against GP records. Analyses of birthweight were adjusted for gestational age.

Maternal smoking was reported at birth as smoker or non-smoker after the fourth month of gestation.

Infant feeding was reported at the 7-year survey and coded as not breast fed; breast fed for less than one month; more than one month.

Family history of diabetes in parents or siblings was reported at age 7 years by the cohort member's parents

Childhood behavioural adjustment is indicated by the Bristol Social Adjustment Guide at age 7 and 11 years and by the Rutter scale at age 16. In each case, a list of statements about the child were selected from a range of options and the sum of the scores from the list of syndromes

identified were grouped. The bottom 50% were categorized as "normal", a middle group as "borderline" and the top 13% as "maladjusted" (Ghodsian 1983).

Parental smoking; A parent completed the 16-year questionnaire and reported parental smoking in the home separately for each parent; non-smoking, smoking 1-10, 11-20, >21 cigarettes/ day and smoking pipe or cigar.

16-year smoking was reported by the cohort member and coded as; non-smoker or < 1 cigarette/ week; 1-19 cigarettes /week and ≥20 cigarettes/ week.

16-year drinking was reported by the cohort member and coded as; had an alcoholic drink in the past week; in the past month; infrequently/ can't remember; never had an alcoholic drink.

Pathways in adulthood: Health behaviours

Cigarette Smoking .

Adult cigarette smoking was self-reported at 23, 33 and 42 years; whether the person currently smoked, and if so, number of cigarettes smoked. One cigarette is assumed to be equivalent to 1 gram of tobacco. Number of cigarettes smoked /day was reported; smokers of ≥ 1cigarette/ day were coded as current smokers. At 23, 33 and 42 years cohort members were asked if they had smoked in the past. Smoking data were cleaned, removing inconsistencies in responses given at any one age as well as using data from previous ages. For example, if a cohort member reported daily smoking at 23 years but reported they were a never smoker at 33 or 42 years, they were recoded to ex-smokers for each time after the daily smoking report. Cohort members were categorised as never smokers, ex-smokers and current smokers (split into "light" 1-19 cigarettes/day and "heavy" ≥20 cigarettes/day). Yearly quit rates were calculated between 23-33 years and 33-42years. The number of quitters between, eg 23-33y was divided by the number of ever smokers between 23-33y. This estimate was then averaged over the number of years between the two follow-up points to obtain a yearly rate.

Alcohol consumption

Adult alcohol consumption was self reported at 23, 33, 42 and 45 years. Cohort members were asked if they consumed alcohol and how often they usually drank (Table 2.3). A series of questions asked about the amount consumed in the past week; the number of glasses of wine; pints of beer; measures of spirits; and measures of martini/ vermouth/ sherry/ port. At 42 years, to keep pace with changing drinking patterns, the number of bottles of alcopops was also asked. The number of drinks of each type of alcohol was converted into standard units; (8g or 10ml of ethanol), equivalent to half a pint of beer, one small glass of wine or one measure of spirits (Dight 1976). Units were grouped into categories published by the Royal College of Physicians (Marmot et al. 1995).

Table 2.3 summarises the categorisation of usual drinking frequency, non-drinking, sensible, heavy and binge drinking. Binge drinking at 23, 33 and 42 years is calculated by dividing total units consumed in the past week by (usual) drinking frequency, to get an index of usual number of drinks per occasion. Binge drinkers consumed ≥10 units/occasion (men) and ≥7 (women). More recently sensible drinking limits have shifted the emphasis from weekly to daily recommendations so drinkers consuming most of their weekly units on one occasion could no-longer be classified "sensible drinkers". Binge drinking is now defined exceeding twice the daily limits of 3-4 units/day (men) or 2-3 units/day (women) (Department of Health 1995, p.25). Because of the time span that the 1958 cohort data covers, the analyses presented will for the most part relate to the cut points of 7 and 10 units because they relate to the time period that the cohort were living most of their adult years. Because binge drinking has only recently become such an important policy and research focus, only t he most recent 45-year survey asked questions directly about the number of drinks consumed on one occasion. Because the format of the 45-year binge drinking and also heaviness of drinking questions are different, the 45-year data is not directly comparable to that at earlier ages, so continuities most aspects of drinking cannot be compared between 45 years and the 23, 33 and 42 year surveys.

Diet at 33 and 42 years

Summary measures of diet at 33 and 42 years were constructed from food frequency questionnaires and coded to be comparable across surveys. Frequency of consuming key dietary items were asked separately; fruit, salads, chips, sweets, cakes and food fried in oil or animal fat. The frequency of consuming each item was summed to produce a score, with more points for more frequent consumption of fruits and salad and less points for more frequent consumption of fried foods, cakes and sweets. The score was split into quartiles and used as a categorical variable, with the healthiest group as baseline. Further details presented elsewhere (Parsons et al. 2005).

Physical activity at 33, 42 and 45 years

Frequency of leisure time physical activity at 33 and 42 years was grouped into ≤2-3/ month (included cohort members not reporting any regular exercise); 1/week; 2-3/week; 4-7/ week. Physical inactivity at 45 years was indexed by number of hours per week spent watching television and number of hours per day spent using a personal computer.

Socioeconomic position

Social position was categorised using Registrar General's occupation-based scale (Office of Populations Censuses and Surveys and Employment Department Group 1990) which is available from childhood to age 42. The occupational categories have been updated reflecting

the evolving labour market. Social class at birth and 7 years was classified by occupation of the participant's father, if there was no male head of household, the participant was classified with groups IV&V based on similarities between the groups. Childhood social class was based on class at birth, or class at 7 years if information was missing. Adult social class was based on the cohort member's own current or most recent occupation at 33 years (occupation at 23 years was used if 33-year data was missing). Occupational groups were collapsed into four categories (Table 2.3). Social position was more strongly correlated between childhood surveys than adult surveys, Spearman's r= 0.61 0-7 years and r=0.53 23-33 years. Social class was used as a categorical or as a continuous variable, depending on analyses.

Educational qualifications

Highest academic qualifications achieved by 33 years are scored using the Burnham scale (Department of Education and Science 1972) in five categories (Table 2.4). Data were gathered when participants left school and also at the 23 and 33-year surveys, filling in missing data at 33 years with information from the previous survey if necessary. Educational level was moderately correlated with occupation-based social group (Spearman's r=0.50), it was investigated separately to adult occupational position. Using qualifications up to 33 rather than 23 years, includes qualifications taken after the first available opportunity (in the early 20s) to be included. Highest educational qualifications are available for both sexes, whether or not they are in employment, are stable through adulthood and have high validity and reliability. Highest educational qualifications broadly classify the population according to a measure of ability and are a superior measure of ability to number of years spent in education.

Adult health outcomes

42 years

Type 2 (non-insulin dependent) diabetes diagnosed by a doctor and controlled by controlled by diet or tablets was self-reported. Insulin-dependent, controlled by injection and "other" kinds of diabetes were excluded from analyses.

45 years

Measures and assays for the biological specimens.

A trained nurse measured body size and took biological samples during a home interview at 45 years. If the cohort member consented to give blood, four tubes were taken and posted to laboratories for processing, if time between sample collection and receipt at the laboratory exceeded five days (or the dates were missing), test results were recorded as missing. If the samples were insufficient, unsuitable, or the laboratory procedures were unsuccessful, this was recorded.

HbA_{1c} (glycosylated haemoglobin) reflects mean blood glucose concentration over preceding 60 days (the half-life of a red blood cell). HbA_{1c} is formed by non-enzymatic glycation of haemoglobin during red blood cell circulation. The unit of measurement for HbA_{1c} is percentage (of total haemoglobin A which is glycosylated).

HbA_{1c} was measured using ion exchange high performance liquid chromatography (TOSOH HLC-723 Ghb V, A_{1c}2.2) for automatic separation of HbA_{1c}. The analyser is certified as DCCT traceable by the National Glycohemoglobin standardisation program. Each chromatogram was inspected for correct separation and results repeated if necessary. Unusual patterns and results outside the normal range (3.5-18%) were recorded as missing. Laboratory reference ranges were; non-diabetic subjects <6.1% and inadequate control of diabetes >7.5%. Measures of imprecision of the method are reported between and within batch. At high and low levels of HbA_{1c} the within batch coefficient of variation varied between 0.42% and 0.76%. The between batch coefficient of variation was 1.99% at both low (5.14) and high (9.22) values of HbA_{1c}. This is lower than the practical working coefficient of variation of 2.1% which has been proposed (Gibb et al. 1999).

Exclusions

Participants with type 1 (insulin-dependent) diabetes and those taking oral anti-diabetics (BNF code 6.1.2; sulphonureas, biguanides and other antidiabetics, n=92), or other medications believed to alter HbA_{1c} levels were excluded from analyses of HbA_{1c}, n=45 (Appendix 2.3).

Elevated HbA_{1c} / type 2 diabetes group included participants who reported type 2 diabetes (42-year survey) or were taking oral anti-diabetic medications at 45 years (as above). Participants with HbA_{1c} levels ≥ 6% were included in the higher risk group, as they are at elevated risk of type 2 diabetes. The high risk group is contrasted with cohort members with HbA_{1c} <6%. For comparison analyses were also run with ≥7% HbA_{1c}.

Exclusions: participants with type 1 diabetes and those taking medication other than oral anti-diabetics, believed to alter HbA_{1c} levels, n=45 (Appendix 2.3).

Triglycerides were measured by autoanylser from non-fasting venous blood samples.

HDL cholesterol was measured by autoanylser from non-fasting venous blood samples.

Blood pressure was recorded using an Omron 705CP automated sphygmomanometer when the participant was seated and had rested for five minutes. Mean blood pressure was calculated from three measures of systolic and diastolic readings (mmHg). Hypertension was defined as taking antihypertensive medications or systolic blood pressure ≥140 mmHg, or diastolic blood pressure ≥90 mmHg.

Standing Height was measured in metres using a Leicester portable stadiometer; participants were unshod and stood upright with their head in the Frankfort plane. If a measure could not be taken or was declined, participants reported estimated height (n=84).

Body weight was measured using Tanita weighing scales to the nearest 0.1kg, with shoes removed and wearing light clothing. If a weight measurement was refused (n=100), the participant reported estimated weight.

Body Mass Index (BMI) was calculated in Kg/m^2

Waist circumference was measured to the nearest millimetre, midway between the costal margin and iliac crest.

Metabolic Syndrome is scored using an adaptation of the National Cholesterol Education Program (NCEP) Adult Treatment Panel (ATP) III criteria; presence of 3 of 5 risk factors defines metabolic syndrome (Table 2.5). As in many other studies of metabolic syndrome, cut points for defining metabolic syndrome were altered to reflect the data available and the population under study. In the absence of fasting plasma glucose level other larger population-based studies have used HbA_{1c} ≥6.1% (Ferreira et al. 2005). In this thesis two HbA_{1c} cut points are investigated; ≥6% and ≥7% resulting in two groups labelled metabolic syndrome. The group with HbA_{1c} ≥6% are presented; the ≥7% group were used for confirmatory analyses. Both groups are at elevated risk of subsequent diabetes onset or may have undiagnosed diabetes as there is often a long time-lag between disease onset and diagnosis. Data from the 45-year survey is used to define metabolic syndrome, the sample is younger than many other study populations. Large proportions of the cohort met the standard NCEP criteria so more conservative cut points drawn from other clinical standards were used.
Exclusions: participants with type1 diabetes, those taking medication other than oral anti-diabetics (n=45), believed to alter HbA_{1c} levels (see Appendix 2.3) and one woman who was pregnant at the 45-year survey.

Statistical methods:

The lifecourse framework for analyses was outlined in Chapter 1. Repeated measures data is a strength of the prospective cohort study design, and helps to clarify chains of causality that cannot be addressed with cross-sectional data. However, it complicates data analysis because many classic tools of data analysis assume data are uncorrelated and independent which is not the case. Analysis of repeated measures data requires methods which explicitly take account of

the correlation between repeated measurements on individual cohort members; such methods include generalised estimating equations and random effects models which allow individual level error terms to be estimated. This thesis uses a two stage analysis approach to analyses of repeated measures data at different stages of lifecourse because of the different types of data. In childhood, repeated measures of continuous test scores are the main exposure of interest, modelling continuous and reasonably normally distributed data is possible using repeated measures multilevel models in MLwiN. From these models, individual-level summary statistics about the relative rank of the 7 year maths score and change in rank to 16 years were estimated (see Appendix 2.2). Estimates were used as predictors in analyses of adult outcomes. For outcomes at one time point, linear or logistic regression models were used, as appropriate. However, for analyses of repeated measures categorical data in adulthood (eg drinking or smoking trajectories 23-42 years) logistic repeated measures multilevel models in MLwiN were used with outcomes of, for example, heavy drinking at 23, 33 and 42 years. Because the repeated measures multilevel models are complex to present, alternative summary statistic measures were also used for simplicity. Count variables indicating the number of occasions that an adult was, for example, a heavy drinker (0-3, between 23, 33 and 42 years) were also used to summarise trajectories of adult health behaviours.

Gender

Analyses were performed separately by gender because there are marked gender differences in the patterns of health behaviours over the lifecourse and also in the prevalence of glucose regulation measures. This thesis focuses on understanding pathways between cognitive ability and health behaviours and in turn health outcomes; therefore gender differences in the exposures and in the pathway variables mean that it is appropriate to analyse data separately by gender.

Analyses of HbA_{1c}

The methods for analyses in each chapter are given separately, but treatment of HbA_{1c} is explained here because it is used in several chapters. The distribution of HbA_{1c} is positively skewed, with a long tail of high values. High values indicate participants at elevated risk of metabolic syndrome or developing diabetes. To deal with the skewness, geometric mean HbA_{1c} values are presented in descriptive analyses. When HbA_{1c} was used as a dependent variable, linear regression analyses with robust standard errors were used to evaluate the associations between untransformed HbA_{1c} as a continuous outcome and independent variables. The robust standard errors provide conservative estimates of the standard errors even though the probability model for HbA_{1c} may not fit well because of the skewed distribution. The units for HbA_{1c} level are percentage points (of haemoglobin bound to glucose) so coefficients from linear regression analyses refer to an additive increase in HbA_{1c} level (measured in percent) rather than a

percentage change in the level; for example a coefficient of 0.2 % corresponds to the move from a baseline of say 5%, to 5.2%, rather than 2% of 5% ie 0.1% therefore moving from 5.0% to 5.1%.

Sample numbers at 45 years

Of the 9377 participants who provided information at 45 years, 9348 had valid 45-year body mass index, 9291 had valid waist circumference, 9297 had valid blood pressure and 9308 participants reported information about frequency of drinking alcohol at 45 years. Not all of the 9377 respondents consented to have blood taken by the nurse at the 45-year home visit. Of the participants who consented to have blood taken, 8209 were considered eligible for analysis as they had valid data for the following: date when the blood was taken, short enough delay until the sample was received at the laboratory in Newcastle for analysis, and the sex and date of birth variables were correct. Of the 8209 participants with any valid blood samples, numbers with completed assays with plausible values (within limits set by the laboratory) for each of the blood analytes were: HbA_{1c}; 7916, HDL cholesterol; 7801, triglycerides; 7792.

In the 7916 participants with valid HbA_{1c}, 56 cohort members reported Type 1 diabetes (and were excluded from analyses of HbA_{1c}, elevated HbA_{1c} /type 2 diabetes or metabolic syndrome). 7860 participants remained, of whom 111 reported type 2 diabetes and 7688 were without known diabetes. A further 61 had HbA_{1c} reading but unknown diabetes status (excluded from analyses). The analysis sample for HbA_{1c} was therefore 7688 +111= 7799. From 7799 a further 111 were excluded as they were taking oral antidiabetics and 45 were taking medications thought to alter their HbA_{1c} (see Appendix2.3).

Missing data

The strength of the repeated measures data in the 1958 cohort also brings the problems of missing data as the length of follow-up time of the cohort increases (Table 2.1). Missing data may be problematic if losses to follow-up are related to variables of interest to the analyses. Analysis samples in different chapters vary according to the number of people with complete data on the necessary covariates. In an appendix to each chapter sample attrition will be addressed; the distribution of social class at birth of the analysis sample will be compared to the original birth sample to assess any biases. Strategies used to deal with missing data include using repeated measures models which take account of missingness and also in the final chapter of the thesis where attrition is greatest as the models contain variables from across the lifecourse, multiple imputation using iterated chained equations is employed. These issues will be expanded on in later chapters.

Next stages

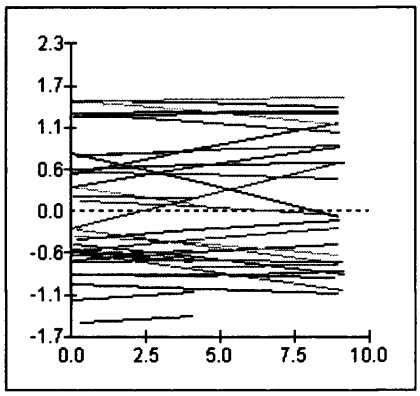
The following chapters investigate the associations illustrated in Figure 1.1, breaking down the pathways from childhood cognitive ability through to adult glucose regulation into separate chapters. The left hand side of Figure 1.1 starts with the associations between childhood cognition and health behaviours which are addressed in Chapter 4. However, for ease of interpretation, the basic patterns of health behaviours are investigated in Chapter 3, before moving on to the associations between cognitive ability and health behaviour in Chapter 4 and health behaviours and glucose homeostasis in Chapter 5. The pathways from cognition to adult glucose homeostasis will then be investigated in Chapters 6 and 7. The strengths and weaknesses of the measures used will be discussed as they occur in the discussion of each chapter. The relative merits of the analysis strategy will be discussed in Chapter 8.

Table 2.1.Response and sample loss in 1958 British birth cohort surveys from birth to 45 years

	Age at contact (years)							
	Birth	7	11	16	23	33	42	45
Total cohort	17638	18016	18287	18558	18558	18558	18558	18558
Dead	0	812	829	862	888	992	1120	1245[a]
Emigrant	0	475	702	800	1198	1337	1320	1300[b]
Eligible sample	17638	16729	16756	16896	16472	16229	16118	16013
No contact attempted	-	-	-	-	-	479	479	3004
Contact attempted								
Non-responders	223	1304	1419	2242	3935	4282	4220	3632[c]
Participants	17415	15425	15337	14654	12537	11468	11419	9377
(% of eligible sample)	98.7	92.2	91.5	86.7	76.1	70.7	70.8	58.6
(% of contacted sample)	98.7	92.2	91.5	86.7	76.1	72.8	73.0	72.1

[a] includes 33 deaths identified after commencement of fieldwork, figure is updated from the 28 deaths stated previously.(Strachan et al. 2007)
[b] includes 65 emigrants identified after commencement of fieldwork
[c] includes 1038 permanent refusals (for whom no contact was attempted) to facilitate comparison with previous surveys in which permanent refusals could not be distinguished from temporary refusals, figure is updated from the 1041 permanent refusals stated previously.(Strachan et al 2007)
[d] table source (Atherton et al 2007)

Figure 2.1 Estimated trajectories of maths ability 7-16 years from repeated measures model, for a sample of cases[a]



[a]Age (x axis) is centred on zero because the first estimate is taken at 7-years and the estimates are for the time span for which data are available, rather than extrapolating back to birth (which would be -7 on this scale).

Table 2.2 Alcohol use categories

Group	Cut Off [a]	Derivation of variable
Usual drinking frequency	5-6 days a week "daily;" 1-3 / week "weekly" 1-3/month "monthly"; "infrequently or on special occasions"; "never" drinking.	Usual drinking frequency was reported at 23, 33, 42 and 45 years. Whilst categories varied slightly between the surveys, groups which were comparable across the surveys were formed.
Non- drinkers	Never drinkers and those who drank infrequently or on special occasions	Using usual weekly consumption habit, CMs who reported usually drinking "infrequently or on special occasions" were classified with the "never drinkers" as a "non-drinker" group. Most "never" drinkers reported drinking at other surveys, so the number of true abstainers by 45 years was very low and too small to analyse meaningfully.
Sensible drinkers	≤1 units/ week men ≤4 units/ week women	CMs classified according to number of units consumed in the past week. CMs who did not report usual drinking habit but who reported number of units in the past week were categorised based on their intake. CMs who reported a weekly drinking but did not answer questions about amount consumed are assumed to have consumed no units in the past week.
Heavy drinkers	≥36 units/ week men ≥22 units/ week women	
Binge drinkers	≥10 units/ session men ≥7 units/ session women	Index of drinks per occasion derived by dividing last week's alcohol consumption (in units) by the frequency of usual drinking (eg assume "most days"= 5 times per week), for CMs who reported drinking at least twice a month. If CM reports zero units or question about units not answered, assume zero and non binge drinker.

CM = cohort member

[a]Group selected from whole population with information on drinking habits

Table 2.3 Distribution [%(n)] of social class in child and adulthood.

Social position[a]	Birth	Birth + 7 years	33 years	33 years + 23 years
Men				
I & II	17.0 (1488)	17.2 (1585)	39.8 (2101)	34.6 (2393)
IIINM	9.5 (835)	9.5 (869)	10.7 (562)	11.5 (794)
IIIM	49.5 (4334)	49.1 (4507)	33.2 (1753)	34.9 (2417)
IV& V & single	23.9 (2096)	24.2 (2223)	16.3 (857)	19.0 (1314)
Total	100.0 (8753)	100.0 (9184)	100.0 (5273)	100.0 (6918)
Women				
I & II	16.9 (1391)	17.2 (1474)	32.5 (1726)	28.9 (1984)
IIINM	9.2 (758)	9.3 (758)	36.5 (1937)	38.8 (2665)
IIIM	49.2 (4037)	48.7 (4179)	7.4 (391)	8.1 (557)
IV& V & single	24.7 (2025)	24.9 (2140)	23.6 (1253)	24.2 (1665)
Total	100.0 (8211)	100.0 (8589)	100.0 (5307)	100.0 (6871)

[a] Based on Registrar General's occupation classification

Table 2.4 Distribution [n (%)] of highest educational qualification age 33 years.

Qualification 33 years	*Men* n (%)	*Women* n (%)
Higher	1593 (29.2)	1470 (25.9)
A Level	1317 (24.1)	588 (10.3)
O Level	1302 (23.9)	2059 (36.2)
< O Level	742 (13.6)	957 (16.8)
None	502 (9.2)	611 (10.7)
Total	5455 (100.0)	5685 (100.0)

Table 2.5 Definition of metabolic syndrome

	NCEP ATP III	1958 cohort
Central obesity (waist circumference)	Men ≥102 cm Women ≥88 cm	Men ≥102 cm Women ≥88 cm
High triglyceride	Fasting triglyceride >150 mg/dL (1.7 mMol/L)	Non-fasting triglyceride ≥2.3 mMol/L [a]
Low HDL cholesterol	Men: <40 mg/dL (1.0 mMol/L) Women: <50 mg/dL (1.3 mMol/L)	Men: <1.0 mMol/L Women: <1.3 mMol/L
High blood pressure	Systolic BP ≥130 mmHg and / or Diastolic BP ≥85 mmHg	Systolic BP ≥140 mmHg or Diastolic BP ≥90 mmHg or on antihypertensive medication [b]
Poor glucose regulation	Fasting plasma glucose 110 mg/dL (6.1 mMol/L)	(i) HbA1c ≥6% or (ii) pre-existing self-reported type 2 diabetes (42 years) or (iii) taking oral anti-diabetics (BNF 6.1.2; sulphonureas, biguanides and other antidiabetics).[c]

[a] ATPIII definition of "very high" triglycerides; this cut-point was used because the blood sample was non-fasting (Expert Panel on Detection Evaluation and Treatment of High Blood Cholesterol in Adults 2001)
[b] WHO cut-points
[c] Analyses were repeated with HbA_{1c} ≥7%. IDF definition also includes treated diabetics.

Table 2.6 Prevalence [(n, %)] of each of the constituent risk factors for metabolic syndrome measured at 45 years, and frequency of the co-occurrence of risk factors, by gender.

45-year outcome[a]	N	*Men* % or mean (SD)	N	*Women* % or Mean (SD)	N	*Both* % or Mean (SD)
HbA_{1c}	3912	5.264[b]	3896	5.147[b]	7808	5.206[b]
HbA_{1c} >6%	182	4.7%	113	2.9%	295	3.8%
HbA_{1c} >7%	81	2.1%	40	1.0%	121	1.5%
High HbA_{1c} (≥6% & Type 2 Diabetes)	190	4.9%	129	3.3%	319	4.1%
High HbA_{1c} (≥7% & Type 2 Diabetes)	98	2.5%	62	1.6%	160	2.1%
Systolic	4632	132.87 (14.98)	4665	120.32 (15.54)	9297	126.57 (16.51)
Diastolic	4632	82.05 (10.37)	4665	75.63 (10.23)	9297	78.83 (10.81)
Hypertension	1604	34.6%	761	16.3%	2365	25.4%
Triglycerides	3912	2.09[a]	3887	1.36[a]	7799	1.69[a]
High triglycerides	1731	44.2%	691	17.8%	2422	31.1%
HDL	3914	1.43 (0.34)	3894	1.69 (0.41)	7808	1.56 (0.39)
Low HDL	160	4.1%	761	19.5%	921	11.8%
Waist circumference	4626	98.47 (0.17)	4665	85.59 (0.19)	9291	92.00 (0.14)
Large waist	1515	32.8%	1722	36.9%	3237	34.8%
Number of risk factors		HbA_{1c} >6%				
0	1,196	31.3	1,806	47.6	3,002	39.4
1	1,292	33.8	1,004	26.5	2,296	30.1
2	847	22.1	600	15.8	1,447	19.0
3	399	10.4	276	7.3	675	8.9
4	77	2.0	98	2.6	175	2.3
5	14	0.4	11	0.3	25	0.3
Total	3825	100	3795	100	7620	100
>=3 risk factors	490	12.8%	385	10.4%	875	11.5%
Number of risk factors		HbA_{1c} >7%				
0	1,212	31.7	1,814	47.8	3,026	39.7
1	1,299	34.0	1,011	26.6	2,310	30.3
2	862	22.5	607	16.0	1,469	19.3
3	381	10.0	275	7.3	656	8.6
4	64	1.7	81	2.1	145	1.9
5	7	0.2	7	0.2	14	0.2
Total	3825	100	3795	100	7620	100
>=3 risk factors	452	11.8%	363	9.6%	815	10.7%

[a] cut-offs from table 2.5 are used
[b] geometric mean HbA_{1c}

Appendix 2.1 *Social context of the 1958 cohort*

The analyses presented in this thesis are based on the 1958 British birth cohort, a prospective population-based sample from England, Scotland and Wales followed-up since birth. Although immigrants born in the same original week were added to the sample during the childhood follow-ups, the sample is primarily Caucasian. Most participants were born in England and fewer from Scotland and Wales. When the cohort were born in 1958, post-war rationing had ended, but they experienced material hardships; at age 7 years 15% lived in homes defined as crowded (with more than 1.5 person per room)(Davie et al 1972, p.51) and three quarters of the cohort were born into manual class families. Few cohort members attended any kind of nursery or kindergarten prior to formal education which started at age 5 years. Primary education has been free since before 1900. The childhood cognition tests which will be investigated were age-appropriate tests taken in school. The first follow-up of the cohort was at age seven years, at the time of transition from infant school to junior school. The majority of schools were maintained by the local education authority. Whilst it was a policy objective to reduce class sizes, in 1965 (when cohort members were aged 7 years) 58% of children were in over-sized classes, with 36 or more pupils (Davie et al 1972, p.122). The second follow-up was when children were finishing junior school and taking the 11-plus examination which determined what type of secondary school they could attend. The third follow-up was at age 16 when the children were in the final year of compulsory schooling; they were in the first year group required to stay at school until age 16 years. In Scotland and Wales the majority of children attended comprehensive schools, whereas only half of the cohort members in England did. A small minority were in special needs schools or had been statemented. Much learning takes place outside the school and attainment is importantly shaped by the home environment. As an indicator of home environment, more mothers (49%) reported reading weekly to their children at age 7 compared to fathers (36%).

The 1958 cohort was born into a society dominated by manual occupational groups: half were born into social class 3 manual, but the non-manual groups including service industries now dominate. Cohort members gained more educational qualifications than their parents' generation; 27% gained graduate qualifications. However, more than half the men passed A levels or gained a degree compared to one third of the women. When the cohort left school they faced a labour market with rising unemployment due to collapse of manufacturing industries. Whilst equal opportunities legislation was introduced in the 1970s and 1980s, many women were still in low-paid part-time jobs with poor promotion prospects. Women's participation in the labour market declined at the birth of the first child and subsequently rose with return to part-time and later to full-time work. By the 33-year follow-up 80% of the cohort were married or cohabiting. At age 23 years 15% were parents and by 33 years, two thirds were parents. Women became parents earlier and had more children than men. Childbearing was socially patterned; the less-educated women had children earlier than their more educated counterparts.

Appendix 2.2

Maths and Reading tests

Correlations between the maths and reading tests are moderately strong between ages 7, 11 and 16 (Pearson's ρ range 0.47 to 0.8) and slightly greater between 11 and 16 years than 7 and 11 years. The maths and reading tests are also positively correlated with each other and with the scores for the 11-year general ability test.

Table A2.2.1 Pearson's correlation coefficients (ρ)[a] for z-scores of reading and maths at 7, 11 and 16 years. Males above diagonal, females below.

		Maths			Reading			General Ability
Maths		7 years	11 years	16 years	7 years	11 years	16 years	11 years
7 years	ρ		0.58	0.49	0.56	0.49	0.48	0.54
	N		6527	5344	7619	6529	5366	6528
11 years	ρ	0.56		0.78	0.63	0.75	0.69	0.82
	N	6202		5265	6557	7255	5289	7253
16 years	ρ	0.48	0.75		0.55	0.66	0.67	0.72
	N	5142	5047		5361	5265	6103	5264
Reading								
7 years	ρ	0.53	0.59	0.47		0.64	0.63	0.65
	N	7219	6212	5150		6559	5382	6558
11 years	ρ	0.48	0.74	0.64	0.61		0.79	0.75
	N	6205	6873	5048	6215		5289	7255
16 years	ρ	0.48	0.71	0.64	0.62	0.80		0.71
	N	5175	5079	5817	5183	5080		5288
General Ability								
11 years	ρ	0.51	0.80	0.66	0.63	0.74	0.74	
	N	6207	6873	5050	6217	6876	5082	

[a]all correlation coefficients $p < 0.01$ (1-tailed).

Validation of the estimated maths and reading trajectories

The intercept or 7 year level of maths or reading is very highly correlated with the z-score for 7 year maths or reading (Table A.2.2.2). The estimated change in z-scores between 7 and 16 years from the multilevel model is very highly correlated with the change in ability rank indicated by the simple difference in z-scores between 7 and 16 years. The Pearson correlation coefficients for the estimated change with the simple difference between 7 and 11 and also with difference in ability between 11 and 16 years are all strong and positive.

Table A2.2.2 Pearson's correlation coefficients [ρ(n)] for the raw and estimated z-scores between ages 7 and 16 years for men and women.

	Maths		Reading	
	Men	Women	Men	Women
7 year z-score Raw score and estimated intercept	0.93 (7635)	0.92 (7241)	0.88 (7662)	0.88 (7246)
Change in z-score 7-16 years Raw score and Model estimate	0.99 (5343)	1.00 (5142)	0.88 (5381)	0.90 (5183)

A key difference between the simple difference measure and the estimated scores is that the differences are only available for people with data at both time-points whereas the model estimates are available for subjects with incomplete data. The increase in sample size improves the power of the study, an extra 6311 participants have estimated maths scores and 6235 have reading scores (Table A.2.2.3). Additionally, the model estimates take the 11-year score into account as well and the 7 and 16 year scores which are used in the simple difference estimate.

Table A2.2.3 Numbers available for the analysis of raw and estimated ability scores at ages 7, 11 and 16 years for men and women.

	Maths		*Reading*	
	Men	Women	Men	Women
7 year z-score				
Raw score	7644	7253	7673	7257
Model estimate	8643	8153	8644	8155
Change in z-score 7-16 years				
Raw score	5343	5142	5381	5183
Model estimate	8643	8153	8644	8155
N gained using model estimate	3300	3011	3263	2972

The distribution of level and change in maths and reading z-scores are described in Table A2.2.4. 7-year z-scores were similar between sexes for maths, although girls fared better at reading (lower z-scores). With respect to change between 7 and 16 years, more girls than boys declined in relative rank (positive z-scores for change). The same word recognition test to identify poor readers was used at both 11 and 16 years, so many participants scored highly at 16 years. The ceiling effect in the 16-year test may explain why many participants (especially men) increased relative rank of reading ability between 7 and 16 years. Given that the maths tests did not suffer from ceiling effect and had superior discriminatory ability at each age, results of analyses using maths tests are the primary focus in later chapters.

Table A2.2.4 Distribution of the level and change in maths and reading scores between 7 and 16 years[a]

		Men			Women	
	Total N	N	%	Total N	N	%
Maths z-score 7 years						
< -1.0	8643	1665	19.3	8153	1402	17.2
> -1.0, < 0		2585	29.9		2313	28.4
> 0, < 1.0		2919	33.8		2913	35.7
> 1.0		1474	17.1		1525	18.7
Change in maths z-score 7-16 years						
< -1.0	8643	1353	15.7	8153	832	10.2
> -1.0, < 0		3078	35.6		2579	31.6
> 0, < 1.0		3033	35.1		3179	39.0
> 1.0		1179	13.6		1563	19.2
Reading z-score 7 years						
< -1.0	8644	1297	15.0	8155	1936	23.7
> -1.0, < 0		2650	30.7		2733	33.5
> 0, < 1.0		2460	28.5		2104	25.8
> 1.0		2237	25.9		1382	16.9
Change in reading z-score 7-16 years						
< -1.0	8644	2622	30.3	8155	456	5.6
> -1.0, < 0		3758	43.5		1541	18.9
> 0, < 1.0		1797	20.8		3595	44.1
> 1.0		467	5.4		2563	31.4

[a] Z-scores coded negatively. Z-scores are estimates from multilevel models of maths (or reading) trajectories 7-16 years.

As an indication of the validity the correlation matrix between the estimated reading and maths scores with the general ability scores are presented (Table A2.2.5). The correlation between the maths z-score at 7 years and the estimated maths z-score at 7 years is strong: 0.93 (0.88 for reading).

Table A2.2.5 Pearson's correlation coefficients (ρ)[a] for predicted intercept and slope of z-scores of reading and maths and general ability test at 11 years. Males above diagonal, females below.

		Maths z-score			Reading z-score		
Maths z-score		7-year level	Change 7-16 years	11-year general ability	7-year level	Change 7-16 years	11-year general ability
7-year level	ρ	-	-0.014[b]	-0.752	0.734	0.150	-
	N		8643	7254	8641	8641	
Change 7-16 years	ρ	-0.216	-	-0.303	0.239	0.270	-
	N	8153		7254	8641	8641	
11-year general ability	ρ	-0.733	-0.118	-	-	-	-
	N	6875	6875				
Reading z-score							
7-year level	ρ	0.717	0.048		-	0.122	-0.775
	N	8150	8150			8644	7254
Change 7-16 years	ρ	0.051	0.254	-	-0.098	-	-0.224
	N	8150	8150		8155		7254
11-year general ability	ρ	-	-	-	-0.761	-0.122	-
	N				6975	6875	

[a] all correlation coefficients $p < 0.01$ (1-tailed).
[b] $p=0.20$

Standard IQ tests predict highest educational qualifications and adult occupational status. As a means of validating the estimated reading and maths trajectories, the associations between the intercept and slope of the maths and reading trajectories and highest educational qualifications and social class were estimated. Previous work on the 1958 cohort using trajectories of maths and reading between 7 and 16 years reported that trajectories were strongly associated with childhood social position; trajectories diverged between 7 and 16 years in the across the social spectrum, and lower birthweights were associated with a constant but consistently lower intercepts. The association between trajectories and adult educational qualifications were in the expected direction (Jefferis et al 2002). Table A2.2.6 presents increasing relative rate ratios (RRRs) for educational qualifications and social position associated with one standard deviation increase in the estimated intercept and slope of reading and maths (ie decrease in 7-year ability

and reduction in rank between 7 and 16 years). Associations are similar for maths and reading. Associations between 7-year z-score and qualifications are stronger than with social class. 7-year z-score is more strongly associated with adult class and qualifications that the change in z-score 7-16 years. Other research reports that the 11-year verbal and non-verbal ability test scores are associated with adult outcomes (Maughan et al. 1999)

Table A2.2.6 Association [RRR (95% CI)] [a] between reading and maths intercept and slope and highest educational qualifications and adult social class.

	Men		Women	
33-year outcome	7-year z-score	7-16 year z-score change	7-year z-score	7-16 year z-score change
Qualifications		*Maths*		
Higher Qualifications	1	1	1	1
A Level	2.27 (2.07, 2.49)	1.75 (1.61, 1.89)	1.40 (1.25, 1.56)	1.12 (1.02, 1.24)
O Level	2.77 (2.52, 3.04)	2.19 (2.01, 2.37)	2.63 (2.41, 2.87)	1.77 (1.65, 1.91)
< O Level	6.87 (6.02, 7.85)	3.63 (3.23, 4.07)	7.69 (6.76, 8.75)	3.01 (2.71, 3.35)
None	20.39 (16.30, 25.50)	6.09 (5.17, 7.17)	19.93 (16.10, 24.68)	4.47 (3.87, 5.17)
		Reading		
Higher Qualifications	1	1	1	1
A Level	2.23 (2.03, 2.46)	1.42 (1.32, 1.52)	1.41 (1.23, 1.61)	1.22 (1.10, 1.34)
O Level	2.62 (2.38, 2.88)	1.49 (1.39, 1.61)	2.75 (2.49, 3.04)	1.58 (1.48, 1.70)
< O Level	5.17 (4.59, 5.82)	1.86 (1.69, 2.06)	7.23 (6.37, 8.21)	2.22 (2.01, 2.44)
None	13.22 (11.00, 15.89)	2.80 (2.43, 3.23)	19.65 (16.14, 23.92)	3.78 (3.31, 4.31)
Occupational class		*Maths*		
I & II	1	1	1	1
IIINM	1.33 (1.23, 1.45)	1.23 (1.14, 1.34)	1.76 (1.65, 1.87)	1.32 (1.24, 1.40)
IIIM	2.74 (2.55, 2.94)	2.05 (1.92, 2.19)	2.81 (2.50, 3.17)	1.74 (1.56, 1.93)
IV & V	3.67 (3.34, 4.03)	2.16 (1.99, 2.34)	3.71 (3.39, 4.06)	1.87 (1.73, 2.02)
		Reading		
I & II	1	1	1	1
IIINM	1.26 (1.15, 1.38)	1.11 (1.02, 1.20)	1.71 (1.59, 1.83)	1.37 (1.29, 1.45)
IIIM	2.83 (2.63, 3.04)	1.54 (1.45, 1.63)	2.74 (2.45, 3.07)	1.74 (1.57, 1.93)
IV & V	3.73 (3.40, 4.10)	1.65 (1.53, 1.77)	3.55 (3.26, 3.86)	1.73 (1.61, 1.86)

[a] estimates from multinomial regression analyses

As a sensitivity analysis for the predicted maths z-scores, the same analyses were run with the raw difference scores (maths z-score at 7 and maths z-score at 7- maths z-score at 16) and the results are compared (Tables A2.2.7a and b). The models using the raw data include fewer participants (ns in footnotes), but the effect estimates from on the raw data are stronger, although the confidence intervals are slightly wider. The patterns of associations and conclusions remain unchanged using the predicted estimates or the raw data. If drop-out over time is non-random then estimates may be biased and using the predicted maths or reading scores doesn't correct bias, but only increases the power.

Table A2.2.7a. Odds ratio (95% CI) for current smoking by childhood maths trajectories (raw data), adult qualifications and social position.

	Adjusted[d]	Adjusted + childhood social class[e]	Adjusted +behavioural problems[f]	Adjusted + adult social class[g]	Adjusted + adult qualifications[h]	Adjusted +all[i]
			Men			
			23 year Current smoking [bc]			
Maths z-score[a]						
7 years	1.44	1.43	1.29	1.30	1.21	1.09
	(1.31, 1.57)	(1.30, 1.58)	(1.16, 1.42)	(1.17, 1.44)	(1.08,1.36)	(0.97,1.23)
Change	1.50	1.50	1.34	1.38	1.29	1.16
7-16 years	(1.37, 1.64)	(1.37, 1.64)	(1.21, 1.47)	(1.24, 1.52)	(1.16,1.44)	(1.03,1.29)
			33 year Current smoking [bc]			
Maths z-score[a]						
7 years	1.50	1.46	1.30	1.31	1.16	1.04
	(1.36,1.64)	(1.33,1.61)	(1.18,1.44)	(1.18,1.46)	(1.03,1.30)	(0.92,1.17)
Change	1.55	1.52	1.35	1.38	1.24	1.11
7-16 years	(1.42,1.70)	(1.38,1.67)	(1.22,1.49)	(1.25,1.53)	(1.11,1.38)	(0.99,1.24)
			42 year Current smoking [bc]			
Maths z-score[a]						
7 years	1.67	1.59	1.43	1.42	1.27	1.14
	(1.49,1.86)	(1.42,1.78)	(1.27,1.61)	(1.25,1.61)	(1.11,1.45)	(0.99,1.31)
Change	1.73	1.65	1.48	1.50	1.36	1.22
7-16 years	(1.55,1.93)	(1.48,1.85)	(1.32,1.67)	(1.33,1.69)	(1.20,1.55)	(1.06,1.39)
			Women			
			23 year Current smoking [bc]			
Maths z-score[a]						
7 years	1.57	1.54	1.35	1.43	1.25	1.14
	(1.43,1.73)	(1.39,1.7)	(1.21,1.50)	(1.28,1.59)	(1.11,1.40)	(1.01,1.28)
Change	1.87	1.84	1.64	1.73	1.56	1.44
7-16 years	(1.70,2.06)	(1.66,2.03)	(1.48,1.82)	(1.56,1.92)	(1.40,1.74)	(1.28,1.61)
			33 year Current smoking [bc]			
Maths z-score[a]						
7 years	1.83	1.76	1.50	1.62	1.35	1.21
	(1.66,2.03)	(1.59,1.96)	(1.35,1.67)	(1.45,1.81)	(1.19,1.52)	(1.07,1.37)
Change	2.03	1.95	1.70	1.83	1.59	1.44
7-16 years	(1.84,2.24)	(1.76,2.16)	(1.53,1.89)	(1.64,2.04)	(1.42,1.78)	(1.28,1.62)
			42 year Current smoking [bc]			
Maths z-score[a]						
7 years	1.88	1.76	1.51	1.63	1.38	1.25
	(1.68,2.11)	(1.56,1.98)	(1.33,1.71)	(1.44,1.85)	(1.20,1.58)	(1.09,1.44)
Change	2.06	1.93	1.69	1.83	1.60	1.47
7-16 years	(1.84,2.31)	(1.72,2.18)	(1.50,1.91)	(1.62,2.06)	(1.41,1.82)	(1.29,1.68)

[a] z-scores are reversed, ie an increase represents a decline in ability.
[b] sample with information on drinking, maths score, social class at birth, Rutter score at 16 years, highest qualifications and social class. 2895 men and 3178 women at 23 years; 3265 men and 3475 women at 33 years; 2849 men and 3151 women at 42y
[c] current smokers compared to non-smokers (including ex-smokers)
[d] model 1= 7-year maths score + change in maths 7-16 years
[e] model 2 = model 1 + social class of origin
[f] model 3 = model 2 + behavioural problems (16 years, Rutter score)
[g] model 4 = model 2 + adult social class
[h] model 5= model 2 + adult qualifications
[i] model 6 = model 2 + behavioural problems (16 years, Rutter score) + adult qualifications + adult social class

Table A2.2.7b. Odds ratio (95% CI) for current smoking by childhood maths trajectories (model estimates), adult qualifications and social position.

	Adjusted[d]	Adjusted + childhood social class[e]	Adjusted + behavioural problems[f]	Adjusted + adult social class[g]	Adjusted + adult qualifications[h]	Adjusted +all[i]
			Men			
			23 year Current smoking [bc]			
Maths z-score[a]						
7 years	1.32	1.31	1.19	1.19	1.13	1.02
	(1.22, 1.42)	(1.21, 1.42)	(1.10, 1.29)	(1.10, 1.30)	(1.03, 1.23)	(0.93, 1.12)
Change	1.28	1.28	1.19	1.21	1.17	1.08
7-16 years	(1.20, 1.37)	(1.20, 1.37)	(1.11, 1.27)	(1.13, 1.30)	(1.09, 1.26)	(1.00, 1.17)
			33 year Current smoking [bc]			
Maths z-score[a]						
7 years	1.35	1.33	1.19	1.19	1.09	0.98
	(1.26, 1.46)	(1.23, 1.43)	(1.10, 1.29)	(1.09, 1.29)	(0.99, 1.19)	(0.89, 1.07)
Change	1.32	1.30	1.20	1.22	1.16	1.07
7-16 years	(1.24, 1.41)	(1.22, 1.39)	(1.12, 1.29)	(1.14, 1.31)	(1.08, 1.25)	(0.99, 1.15)
Maths z-score[a]			*42 year Current smoking* [bc]			
7 years	1.48	1.43	1.29	1.27	1.19	1.07
	(1.36, 1.62)	(1.30, 1.56)	(1.18, 1.42)	(1.15, 1.41)	(1.07, 1.33)	(0.96, 1.20)
Change	1.41	1.38	1.28	1.29	1.24	1.14
7-16 years	(1.31, 1.53)	(1.27, 1.49)	(1.18, 1.39)	(1.19, 1.40)	(1.14, 1.35)	(1.05, 1.25)
			Women			
			23 year Current smoking [bc]			
Maths z-score[a]						
7 years	1.42	1.38	1.22	1.28	1.13	1.04
	(1.32, 1.53)	(1.27, 1.49)	(1.13, 1.33)	(1.18, 1.40)	(1.03, 1.23)	(0.94, 1.14)
Change	1.48	1.46	1.37	1.42	1.34	1.28
7-16 years	(1.38, 1.58)	(1.36, 1.56)	(1.28, 1.47)	(1.32, 1.52)	(1.24, 1.44)	(1.19, 1.38)
			33 year Current smoking [bc]			
Maths z-score[a]						
7 years	1.65	1.59	1.38	1.48	1.25	1.15
	(1.52, 1.78)	(1.46, 1.72)	(1.27, 1.51)	(1.36, 1.61)	(1.14, 1.38)	(1.04, 1.27)
Change	1.51	1.48	1.38	1.44	1.34	1.28
-16 years	(1.41, 1.62)	(1.38, 1.59)	(1.28, 1.48)	(1.34, 1.55)	(1.25, 1.45)	(1.18, 1.38)
			42 year Current smoking [bc]			
Maths z-score[a]						
7 years	1.68	1.59	1.39	1.48	1.27	1.17
	(1.54, 1.84)	(1.45, 1.75)	(1.26, 1.54)	(1.34, 1.64)	(1.14, 1.41)	(1.04, 1.31)
Change	1.52	1.48	1.38	1.44	1.34	1.28
7-16 years	(1.41, 1.64)	(1.37, 1.60)	(1.27, 1.49)	(1.33, 1.56)	(1.23, 1.46)	(1.17, 1.39)

[a] Z-scores are reversed, ie an increase represents a decline in ability.
[b] sample with information on drinking, maths score, social class at birth, Rutter score at 16 years, highest qualifications and social class. 3265 men and 3584 women at 23 years; 3700 men and 3939 women at 33 years; 3206 men and 3552 women at 42y
[c] current smokers compared to non-smokers (including ex-smokers)
[d] model 1= 7-year maths score + change in maths 7-16 years
[e] model 2 = model 1 + social class of origin
[f] model 3 = model 2 + behavioural problems (16 years, Rutter score)
[g] model 4 = model 2 + adult social class
[h] model 5= model 2 + adult qualifications
[i] model 6 = model 2 + behavioural problems (16 years, Rutter score) + adult qualifications + adult social class

Appendix 2.3

Medication exclusions

About 500 people were taking steroids, the majority for respiratory problems. Information is recorded consistently on the indication for treatment (but only at a system level eg for skin disease, for respiratory disaease) and on the type of steroid in the medication. Information on dose is recorded infrequently. Information on route is recorded for some indications but not for others.

Main analyses are run excluding people who are expected to have altered glycaemic function as a result of their steroid medication and including people who are expected to have unaltered glycaemic function even though on steroid medication (n=59). These people are identified based on the indication and the route (where recorded). Main analyses will then be re-run with additional exclusions where there is uncertainty whether glycaemic function is likely to be affected by steroid medication (n=423). Not all people with medications had valid HbA_{1c} so numbers excluded from the HbA_{1c} sample are lower than in the table.

Table A2.3.1 Exclusion criteria based on medications

BNF code	BNF group	N	Include / Exclude
010500	Chronic bowel disorders	12	EXCLUDE. Likely to be taking systemic steroids and have altered glycemia
030200	Respiratory system;	423	INCLUDE BUT EXCLUDE ON A FINAL RE-RUN. The respiratory group are the majority of the people on steroids. It was not always coded if people were taking tablets or inhalers and we do not know dose, so we can't say which members of this group should be excluded, so this group could stay in analysis and be excluded for a final re-run as a check.
060301	Replacement endocrine therapy	2	INCLUDE. The group on replacement endocrine therapy are fine to include as they have steroids as replacement therapy
060302	Endocrine system	36	EXCLUDE. This group are likely to have altered glycemia
080202	Malignant diseases	1	EXCLUDE. This person is likely to have altered glycemia
100102	Corticosteroids for musculoskeletal and joint diseases	11	EXCLUDE prednisolone (n=10) INCLUDE local injections (n=1)
110401	Eye diseases		INCLUDE. Mostly on drops (occasional ointments). topical treatment will not affect glycemia
120101	Ear (otitis externa)		INCLUDE. The route is spray, drops or ointment. Topical treatment will not affect glycemia
120201	Nose		INCLUDE. For nasal allergy, the route is drops or nasal spray. Topical treatment will not affect glycemia
130400	Skin (topical corticosteroids)		INCLUDE. Topical treatment will not affect glycemia

Chapter 3, Trajectories of health behaviours

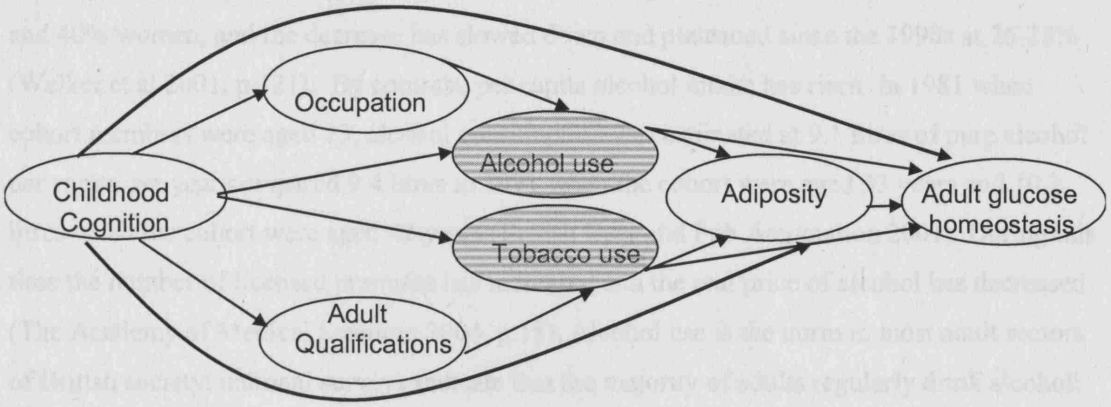


Figure 3.1 Conceptual Framework

Introduction

As indicated by the shading in the conceptual framework (Figure 3.1), the focus of this chapter is on health behaviours across adulthood, specifically alcohol and tobacco use; the two most commonly used drugs in Western societies. Other behaviours namely diet and physical activity are clearly important to understanding pathways to adult glucose homeostasis but have already been much researched. This thesis therefore focuses on alcohol and tobacco use to address the aim in Table 1.1 (Chapter 1) of understanding pathways to adult glucose homeostasis. Daily cigarette smoking, usual frequency of drinking, non-drinking, binge (or heavy episodic drinking) and heavy drinking and the type of alcohol consumed will be investigated because, as discussed in Chapter 1, they are expected to be associated both with cognitive ability and adult glucose homeostasis. Trajectories of smoking and drinking across the adult lifecourse are studied first, to inform subsequent analyses of associations illustrated in Figure 3.1 between (i) childhood cognitive ability and health behaviours (Chapter 4) and also (ii) health behaviours and adult glucose homeostasis (Chapter 5) and thereby (iii) the role of health behaviours as mediators between childhood cognitive ability and adult glucose homeostasis (Chapter 7).

Health behaviours are behaviours which have health consequences, and may be protective (taking exercise, healthy diet, brushing teeth) or risky (smoking tobacco, binge drinking, taking drugs). However "health-behaviours" are not just directed by desire for health; health concerns are unlikely to be the immediate prompts for when and where individuals smoke or drink. Many other factors including the social setting and cultural norms influence location and timing of behaviours. At the macro-level economic and legal policies regulate sales, taxation and access and at the individual level, gender, age and social background differences in individual health behaviours are well documented in various populations and subgroups (Agudo et al. 2004; Berrigan et al. 2003; Walker et al 2001, pp.115-162). Over the lifetime of the cohort, the

distributions of cigarette smoking and alcohol use have changed in the United Kingdom. Tobacco use peaked, first among men and then among women, and adult smoking prevalence is now lower than historically; prevalence decreased through the 1970s and 1980s from 50% men and 40% women, and the decrease has slowed down and plateaued since the 1990s at 26-28% (Walker et al 2001, p.121). By contrast, per capita alcohol intake has risen. In 1981 when cohort members were aged 23, alcohol consumption was estimated at 9.1 litres of pure alcohol per capita per year compared 9.4 litres in 1991 when the cohort were aged 33 years and 10.2 litres when the cohort were aged 42 years (British Beer and Pub Association 2001). During this time the number of licensed premises has increased and the real price of alcohol has decreased (The Academy of Medical Sciences 2004, p.18). Alcohol use is the norm in most adult sectors of British society; national surveys indicate that the majority of adults regularly drink alcohol; 75% men and 59% women report drinking in the past week (Walker et al 2001, p.146). Per capita alcohol consumption is high compared to other European countries (British Beer and Pub Association 2001). In cross-sectional studies, tobacco and alcohol use is reported to be greater in men than in women and also in younger age groups (Bridgwood et al. 2000,pp.123, 151).

Initiation and persistence of cigarette smoking and alcohol use.

Most smokers start smoking in adolescence and early initiation and heavier adolescent smoking is associated with persistent smoking into adulthood (Janson 1999). Nicotine dependence starts in adolescence and 14-15 year-olds report nicotine withdrawal effects (McNeill 1991). Adolescence and early adulthood is also the stage in life when purchasing alcohol becomes legal in the UK and many other European countries. Exceeding sensible drinking limits is most prevalent and mean alcohol consumption is highest in early adulthood (Lader & Meltzer 2001, p.12). Early age at first alcoholic drink is also reported associated with adult drinking (Prescott & Kendler 2001), although the associations are not as consistent as for cigarette smoking. An extensive literature exists about uptake of smoking and drinking (Donovan 2004; Tyas & Pederson 1998) and transitions in smoking and drinking from adolescence into early adult life (Bennett et al. 1999; Schulenberg & Maggs 2002; White et al. 2002). Previous work on the cohort has demonstrated continuities in binge drinking and non-drinking between adolescence and adulthood to 42 years, and also continuities between adolescent and adult smoking (Jefferis et al. 2003; Jefferis et al. 2005). Literature about stability and change across adulthood into mid-life is much sparser.

Studying trajectories of change or stability in health behaviours throughout adulthood is important because persistence of different patterns of alcohol use and cigarette smoking have longer-term health consequences than short-lived behaviour after initiation. It is well-documented that heavier smoking has negative health consequences and smoking exhibits strong tracking (Janson 1999), as expected from the addictive nature of nicotine (Royal College

of Physicians of London 2000; US Department of Health and Human Services 1998). Stability of alcohol use has been less studied. Drinking is reported to be more stable after adolescence and early adulthood (Mulder et al. 1998). There is some evidence that stability of non-drinking is greater than light or heavy drinking (Doll et al. 1994a; Emberson et al. 2005). Associations between different patterns of alcohol consumption and health are not as clear-cut as for smoking and if alcohol use is unstable over time, studies relating single measures of drinking to subsequent morbidity may estimate associations poorly.

Studies of intra-individual trajectories of health behaviours are rarer than cross-sectional studies (Kemm 2003; Kemm 2001). Existing longitudinal studies are limited by either covering short time period (Tucker et al. 2003), specific sub-populations or use different measures of alcohol use at the different time points (Wennberg et al. 2000). Also they tend to be focused on measures of problem drinking or alcohol dependence rather than measures of binge or heavy drinking which are more common (Bennett et al 1999). Different dimensions of alcohol use have public health relevance; much literature about physical health consequences of alcohol has focused on heaviness of drinking, for example in relation to cardiovascular risk. Frequency of alcohol intake (Howard et al 2004) and heaviness of drinking on single occasions (bingeing) are increasingly recognised in alcohol epidemiology as areas needing further study (Rehm et al. 1996). The negative (or positive) health consequences of trajectories of particular smoking and alcohol use patterns make them worthy of investigation.

Usual drinking frequency

To date, little evidence about intra-individual stability or change in drinking frequency over time exists. Cross-sectional data indicate that men drink more frequently than women and that drinking is more frequent in middle age than in early adulthood (Bennett et al. 1991; Bridgwood et al 2000, p.146).

Binge drinking

Early adult binge drinking is a particular policy concern both for its associations with accident and violence related morbidity as well as potential for subsequent chronic health outcomes and establishment of drinking patterns that last into adult life (Kuntsche et al 2004). Current prevalence of binge drinking (≥8/6 units /occasion) during the past week is estimated at 22% in men and 10% in women, with higher prevalences in 16-24 year age group; 37% men and 27% women (Walker et al 2001, p.154). Longitudinal studies suggest that binge drinking at one time increases chances of later binge drinking. Most literature focuses on the transition from adolescence to early adult years, when modest continuity in binge drinking is reported (McCarty et al. 2004).

Heavy drinking

Prevalence of heavy drinking is expected to be greater in men than women and to vary with age; population data indicate that exceeding sensible limits is more common in early adulthood and less so in mid-life (Walker et al 2001, p.147). Age-related decline in very heavy drinking; (>50 units/week (men), >35 units/week (women)) is clearer cut than for lighter drinking, as heaviest consumption is concentrated in younger adults (Walker et al 2001, pp.152-153). From existing data it is expected that stability of heavy drinking will be lower than for lighter drinking (Doll et al 1994a; Emberson et al 2005; Zins et al. 1999).

Non-drinking

Non-drinkers are worthy of investigation because of their reported elevated risks of diabetes in comparison to moderate drinkers. However the low prevalence of lifetime abstainers makes true never-drinkers hard to study. It is expected that more women than men will be non-drinkers and that prevalence will increase with age. Existing studies report some change in non-drinking over time but moderately strong stability (Doll & Peto 1995; Emberson et al 2005; Kerr et al. 2002).

Clustering of smoking and drinking patterns

Co-occurrence of behaviours is important because the social and behavioural processes affecting the uptake and persistence of smoking and drinking share some common aspects (Room 2004). Also tobacco and alcohol use act synergistically to modify risk of chronic disease outcomes in later life (Bagnardi et al. 2001a). It is expected that smokers will drink more often and more heavily than non-smokers. Likewise, heavier smokers are expected drink more heavily (Istvan & Matarazzo 1984). For example, smokers are two to three times more likely to drink than non-smokers (Jackson et al. 2003; Schuit et al. 2002). There are many permutations of smoking and drinking behaviours, so a few which are expected to be associated with glucose homeostasis are selected for investigation. It is expected that cigarette smoking (and in particular heavy smoking) and both heavy drinking and non-drinking will be associated with poorer glucose regulation. Therefore co-occurrence between smoking and non-drinking or heavy drinking will be examined.

Most studies examining overlap between health behaviours are cross-sectional and therefore cannot investigate whether behaviour at one point in time shapes behaviour in later life. The availability of prospective data enables investigation of the role of smoking in predicting later drinking. Of particular interest in public health terms is investigating whether the beneficial health effects of quitting smoking are accompanied by changes in alcohol use. Some studies report that quitters decrease their alcohol intake as a coping mechanism to deal with quitting smoking (Zacny 1990), whereas it is also possible that ex-smokers increase their alcohol to

substitute for smoking. Few studies to date have investigated these questions (Jensen et al. 2003).

Aims

This aims of this chapter are:

1. to examine the cross-sectional patterns of (i) alcohol and (ii) tobacco use, at successive surveys from adolescence through to mid-adult life;
2. to examine the trajectories of stability or change in (i) alcohol and (ii) tobacco use between adolescence and mid-adult life;
3. to examine if alcohol and tobacco use overlap (or cluster) at each survey, whether this varies over time or is associated with the amount of alcohol or tobacco consumed;
4. to examine whether quitting smoking influences drinking habits at later surveys.

In addition to the aims above, social gradients in cigarette smoking and the different measures of alcohol use are investigated because these associations need to be understood for analyses in the next chapter where social class is proposed as a mediator between childhood cognitive ability and health behaviours, or between health behaviours and adult glucose regulation. Much literature about social gradients exists, so this is not a main focus here, results are presented in Appendix 3.1 and used as confirmation of existing knowledge from other studies.

Methods

Measures of alcohol consumption (frequency and amount) and cigarette consumption at ages 16, 23, 33 and 42, with additional information about alcohol use at 45 years are described in Chapter 2. Samples with data for analysis vary for cross-sectional and longitudinal analyses; analyses are based on the maximum sample with complete data available (numbers reported in tables). There is some evidence that analysis samples under-represent cohort members from manual social origins compared to the full dataset. In the sample with full smoking (or drinking) data 16-42 years, the distribution of both smokers and drinkers at 16 years is similar to distribution in the full 16-year sample (Appendix 3.2).

Statistical analyses

For aim one, prevalences of alcohol and tobacco use at each age were calculated. For aim two, trajectories of alcohol and tobacco use were investigated. Longitudinal analyses use data from 23, 33 and 42-year surveys as this was most comparable. Associations between repeated measures of either tobacco or alcohol were estimated. Cohen's kappa was used as a simple measure of association between ordinal grouped measures at different ages. Logistic regression was used to estimate associations between binary variables across two time points. Repeated

measures multilevel models were used to investigate associations across more than two time points, the outcome in the repeated measures models was the behaviour of interest, eg current smoking at 23, 33 and 42 years. The change in odds of smoking at 23 vs 33 and 23 vs 42 years was then tested. Additionally, Pearson's correlation coefficients were calculated for continuous variables (including number of cigarettes smoked or number of units of alcohol consumed).

To evaluate co-occurrence of tobacco and alcohol use for aim 3, observed overlap of smoking and drinking was compared to expected overlaps. The observed overlap at each age is the percentage of cohort members reporting both behaviours, out of all cases with full data on smoking and drinking data at that survey. The expected overlap was calculated assuming statistical independence between each pair of variables, by multiplying the observed prevalence of the two separate measures. The ratio between observed and expected frequencies was calculated, to assess whether each pair of behaviours was more likely to occur together than if they were independent (ratio >1). To examine change in overlap over time, the ratios were compared across time-points. To investigate whether heaviness of smoking or drinking was associated with overlap, the overlap ratios were examined and the prevalence of smoking based on heaviness of drinking was plotted (and vice versa).

For aim 4, logistic regression analyses summarised associations between quitting smoking and drinking status at a later survey. OR for drinking status (binge, heavy daily and non-drinking) at a follow-up was estimated for participants who smoked at baseline, comparing the odds of drinking in quitters to odds of drinking in persistent smokers.

Results

Cross-sectional prevalence and stability and change in smoking and drinking

Smoking

Prevalence

One in three adolescents smoked ≥1 cigarette/ week (Table 3.1). Of these, 74% boys and 62% girls smoked ≥20 cigarettes/ week. Between the ages of 23 and 42 years approximately half of the cohort were ever regular smokers. Prevalence peaked at 23 years and declined to 26% (Table 3.1). 1.5% (n=144) started smoking after 23 years, whilst increasing numbers quit smoking. Men consistently smoked more than women (at 42 years, mean 18.7 cigarettes/ day for men and 16.2 for women). Amount smoked at each survey varied considerably (standard errors are large) and was positively correlated between surveys; Pearson's ρ=0.54 (23-33 years) and ρ=0.60 (33-42 years). Mean amount smoked differed little over time. Persistent smokers smoked more heavily than other smokers at each survey. Persistent smokers who were smoking

at 16 years smoked more at 42 years than the smokers who started later (at 23 years). Cohort members who smoked at only one survey tended to smoke less than (i) those smoking at more surveys and (ii) those who continued smoking for longer (data not presented).

Stability 23-42 years

Non-smoking was more stable than smoking; over 90% non-smokers at one age were still non-smokers at the next survey (Table 3.2). Smoking at baseline strongly predicted smoking at the next survey; nearly 3 in 4 smokers persisted. Kappa provides a measure of the association between smoking status at the successive ages: the coefficients show strong associations of smoking at 23-33 and indicate that the association strengthened 33-42 years.

Profiles of smoking 16-42 years (Figure 3.2) illustrate the different trajectories of smoking over age. The two largest groups were the non-smokers (about half of the cohort) and the persistent smokers (approximately one in six cohort members). Other common patterns were smoking at one or both of the 16 and 23 year surveys, or at three consecutive surveys; 16-33 and 23-42. Counting smoking habits from 23 years onwards, the persistent smokers (23, 33 and 42 year smokers) accounted for one in five of the cohort members. A summary measure of smoking history between 23 and 42 years was constructed (Figure 3.4); nearly half of the cohort ever smoked and more (16%) quit smoking prior to 33 years compared to after (12%). More men than women were heavy smokers at 42 years; 12% smoked 1-19 cigarettes/day and 14% smoked more; whilst in women 15% smoked 1-19 cigarettes/day and 11% smoked more. Average annual quit rates between surveys were 3.1%/ year between 23-33 years and 3.6% between 33-42 years for men and 3.0% for both periods for women.

In summary smoking prevalence peaked at 23 years and declined thereafter, by 42 years half of the cohort had ever smoked and one quarter were still smokers. There was evidence for strong stability of smoking across the adult surveys.

Alcohol

Non-drinking

By age 16 only 5% men and 8% women reported that they had "never had a drink" (Table 3.3). From age 23 onwards, prevalence of "never drinking" was low; about 4% for men and 6% for women and infrequent and special occasion drinking varied from 7 to 11% in men and 17 to 23% in women.

Most "never" drinkers reported consuming alcohol at previous surveys: 147 cohort members reported "never" drinking at 45 years of whom 87 had not drunk at previous surveys. The

"special occasion" drinkers were combined with the "never drinkers" to form a group termed "non-drinkers". Compared to drinkers, non-drinkers at 45 years had lower levels of heavy or binge drinking at each previous survey; in men the prevalence of heavy drinking at 23, 33 and 42 years was 6%, 2% and 1% compared to 16%, 9% and 17% in men who were drinkers age 45. In men prevalence of non-drinking increased from 10% at 23 years to 15% at 45 years, whereas prevalence remained at 28% in women. Repeated measures models of non-drinking 23-42 years confirmed that in men, non-drinking was more prevalent at 33 years (OR 1.54 $p<0.001$) and 42 years (OR 1.44 $p<0.001$) than 23 years. Whilst in women, non-drinking at 33 years did not differ from 23 ($p=0.53$) but was less common at 42 years; OR 0.79, $p<0.001$.

Stability of drinking and non-drinking 23-45 years

Most drinkers at a given adult survey drank at the next survey (>80%) and approximately half of the non-drinkers at one survey were non-drinkers at the next survey, rising to three quarters between 42 and 45 years (Table 3.4). Kappa, was greater between 42-45 years and 33-42 years than 23-33 years suggesting stronger tracking of the non-drinking at older ages. Figure 3.3 illustrates profiles of drinking 16-42 years; most of the cohort were drinkers; 61 % of men between 16 and 42 years, and a further 19% 23-42 years (equivalent proportions for women were 37% and 17%). The trajectories of non-drinking at ages 23-42 years (rather than 16-42 years), show that stability of non-drinking was higher in women than in men; nearly 10% women were consistently non-drinkers 23-42 years (Figure 3.5).

Frequency of drinking

At 16-years 52% of boys and 40% of girls drank in the past week (Table 3.3), and a further 19% boys and 18% girls drank in the past month. In adulthood prevalence of drinking at least weekly ranged from 71% to 81% in men and 43% to 63% in women. At each age "daily drinking" (drinking on most days) was more common in men than women. Nearly one in three men were daily drinkers at 23 years, and similarly at 45 years, however there was not a linear trend with age in men (tested using multilevel model of daily drinking 23- 42 years). For women, daily drinking increased from one in ten women at 23 years to one in five women at 45 years. Drinking 1-3 times a week (termed weekly drinking) was the modal category in both sexes, accounting for up to half of the cohort at each survey.

Stability of usual drinking frequency

16-year drinking frequency was weak to moderately correlated with adult drinking frequency; ρ between 0.22 and 0.17 (Table 3.5). Correlation between drinking frequency in adulthood was stronger; $\rho=0.73$ in men and $\rho=0.68$ for women between 42 and 45-year surveys which were closest in time. Tracking of daily drinking was low between 23 and 33 years but moderately high at the later surveys. 32% daily drinkers at 23 years were still daily drinkers at 33 years,

whilst 63% daily drinkers at 33 years were also daily drinkers at 42 years and similar percentage between 42 and 44 years (Table 3.6). The number of occasions that a cohort member was a daily drinker was summed for those with complete data 23-42 years. More men than women reported repeated daily drinking; 25% men at one adult survey and 14% at two surveys and 7% at all three surveys. For women equivalent proportions were 15%, 5% and 2% (Figure 3.6). Including 45-year drinking frequency gives a similar pattern with 23% men and 15% women reporting daily drinking on one occasion and smaller proportions reporting more frequent daily drinking. The most stable drinking frequency category was weekly drinking: 57% of weekly drinkers age 23 years remained so at 33 years and 66% weekly drinkers at 33 years also drank weekly at 42 years.

In summary most of the cohort were drinkers and the prevalence peaked at 23 years. There was evidence for strong stability of drinking across the adult surveys. Men drank more frequently than women. Weekly drinking was the most common drinking frequency in adulthood and frequency was positively correlated between surveys although there were not linear trends in frequency with increasing age. 7% men and 2% women were daily drinkers at 23, 33 and 42 years.

Amount of alcohol consumed

At 16 years, only cohort members who drank during the past week reported how much alcohol they consumed in the last week. Of these, 48% of boys drank ≥5 units compared to only 14% of girls (Table 3.7). In adulthood, men consistently drank more heavily than women and more often exceeded sensible limits; at 42 years 36% men exceeded 21 units/week whilst 15% women exceeded 14 units/week (Table 3.8). There were not clear age trends in the number of units consumed. Mean amount of alcohol consumed increased with increasing frequency of drinking (Table 3.9). Among men at 42 years, daily drinkers consumed 43 units of alcohol in the past week an average, compared to 18 units in the weekly drinkers and 5 units in the monthly drinkers, equivalent means for women were 21, 8 and 3 units.

In summary men drink more heavily than women and more frequent drinkers consumed more alcohol than less frequent drinkers.

Prevalence of heavy drinking

Despite the lower limit for women than men, approximately four times as many men as women report heavy drinking. Approximately 20% of male and 5% of female cohort members were heavy drinkers at any one survey (Table 3.8). There was not a linear trend in prevalence with increasing age; in a repeated measures multilevel model with the outcome heavy drinking 23-42 years, the prevalence of heavy drinking was significantly lower at 33 years than at 23 years

($p<0.01$ for men and for women), but did not differ between 23 and 42 years ($p=0.197$ men; $p=0.974$ women).

Stability of heavy drinking 23-42 years

Continuity of heavy drinking was modest; kappa (Table 3.10) indicated that continuity was lower than for drinking status (Table 3.4) or smoking status (Table 3.2). Continuity was stronger between 33-42 years compared to between 23-33 years; 31% of men who were heavy drinkers at 23 were also heavy drinkers at 33 but 52% heavy drinkers at 33 were also heavy drinkers at 42. For women, prevalence of heavy drinking was lower, but equivalent percentages were 13% 23-33 years and 42% 33-42 years.

Most participants (62% men and 87% women) were never heavy drinkers in adulthood (Figure 3.7). 24 % men and 10% women were heavy drinkers at one age (mostly 23 or 42 years), and only 4% men and 0.4% women were repeatedly heavy drinkers at 23, 33 and 42 years.

In summary heavy drinking was more prevalent at 23 years than 33 years but rose again at 42 years. More men than women were heavy drinkers. There was evidence for modest stability of heavy drinking across the adult surveys. 4% men and 0.4% women were heavy drinkers at 23, 33 and 42 years.

Prevalence of binge drinking

Using either high (≥7/10 units/ week) or lower (≥6/8 units/ week) cut points, binge drinking was more common than heavy drinking, but less differentiated by gender. Approximately twice as many men as women were identified as binge drinkers at each age using the 10/7 unit cut-points, e.g. 37% (men) and 18% (women) at 23 years (Table 3.8). Binge drinking declined with age in non-linear fashion; prevalence was greatest at 23 years and lower at 33 and 42 years (difference between surveys confirmed with repeated measures multilevel model of binge drinking 23-42 years).

Stability of binge drinking 23-42 years

There were modest continuities in binge drinking through adulthood: 40% men who were binge drinkers at 23 years were also binge drinkers at 33 years and 48% of binge drinkers at 33 years continued at 42 years. Equivalent proportions for women are 21% and 25% (Table 3.11). Kappa provides weak evidence for tracking in binge drinking across the ages. Kappa was similar using the high or lower classifications (data not presented). At each age, the majority of cohort members changed their consumption relative to the previous age by more than five units of alcohol. Approximately one third of cohort members were binge drinkers at only one survey

(Figure 3.8). More men than women were classified as binge drinkers repeatedly: 8% men and 1% women at all 3 adult surveys.

In summary binge drinking was more prevalent at 23 years than 33 years but rose again at 42 years. About twice as many men as women were binge drinkers. There was evidence for moderate stability of binge drinking across the adult surveys. 8% men and 1% women were binge drinkers at 23, 33 and 42 years.

Cross sectional association between smoking and drinking habits.

The observed prevalence of each smoking and drinking measure in the cross-sectional sample with complete data is in column 1 in Table 3.12. To illustrate, at 23 years 10.0% of men were non-drinkers and 39.8% were smokers. Columns 2-6 present the observed (below the diagonal) and expected (in italics, above the diagonal) prevalences of the co-occurrence of drinking and smoking. Observed prevalence of smoking and non-drinking was 3.3%. In brackets below the prevalence of overlap is the percentage of non-drinkers who were smokers; 8% of non-drinkers were smokers whilst 39.8% of the whole population smoked. The expected prevalence of smoking and non-drinking co-occurring if they were independent would be 0.1*0.398=0.398 ie 4.0% (in italics in the "expected" section of the table, above the diagonal). The ratio of observed prevalence of co-occurrence of smoking and drinking compared to expected prevalence, if the behaviours were statistically independent is in brackets. A ratio of greater than 1 indicates that a pair of behaviours co-occur more often than if they were statistically independent. The ratio of observed and expected prevalence of smoking and non-drinking was 3.3/3.9=0.84, indicating that smoking prevalence is lower in non-drinkers than in drinkers. At 23 in women and at 33 years in both sexes, observed smoking prevalence in non-drinkers was not different to drinkers, however at 42 years, the prevalence of smoking was higher than expected in non-drinkers; ratios of 1.36 (men) and 1.30 (women). Heavy drinking was the drinking measure most strongly related to current smoking: ratios around 1.3-1.5 in men and 1.6-1.7 in women. At each age the prevalence of smoking in heavy drinkers was high; 53% compared to 40% in the whole sample of men at 23 years. Smoking and binge drinking co-occurred in a significant minority of the cohort; 18% of men and 9% women at 23 years, and 11% men and 6% women at 33 and 42 years.

More overlap was seen within drinking measures rather than between smoking and drinking measures. The ratios of observed to expected prevalence of heavy and binge drinking co-occurring were between 2 and 2.6 in men and 3.4 to 5.1 in women, and the ratios of heavy and daily drinking were 2.3-3.1 in men and 4-6 in women.

The prevalence of co-occurrence of each pair of smoking and drinking patterns was higher in men than women. However, in contrast, the ratios of observed to expected prevalence of the smoking and drinking behaviours were higher for women, indicating greater overlap than expected. For example, less women than men smoke or drink heavily but among women smokers, there are more heavy drinkers than expected than in men. Prevalence of co-occurrence of drinking behaviours were greater in men, but overlap was stronger in women.

Comparing the observed prevalence in the first column with the observed overlaps below the diagonal in columns 2-6, the overlaps between the smoking and drinking can be summarised as follows:

- Most heavy drinkers were binge drinkers or daily drinkers.
- Most binge drinkers were not heavy or daily drinkers.
- Most daily drinkers were not binge or heavy drinkers, although in men at 23 years half were heavy drinkers.
- Most smokers were not binge, heavy or problem drinkers.

Change in clustering with age

Comparing the ratios indicating clustering between each pair of behaviours over the three surveys, indicated that some ratios differed consistently between surveys. The co-occurrence of smoking and non-drinking (of particular interest for diabetes risk), changed with age. In both sexes the clustering ratio between smoking and non-drinking changed from below one at 23 years (0.83 in men) to greater than one at 42 years (1.36 in men). The people who stopped drinking between 33 years and 42 years were more likely to smoke at 33 and at 42 than those who continued drinking. To illustrate, 33-year smoking prevalence in people who stopped drinking 33-42 years was 43%, compared to 29% among continued drinkers. This pattern is very similar in both sexes. Comparing the observed to expected ratios over the ages, the overlap between daily drinking and current smoking decreased between 23 and 42 years. In women the overlap between daily drinking and binge drinking declined with age (from 0.59 to 0.78) and the overlap between binge drinking and smoking increased (1.20 to 1.55). In men the overlap between binge drinking and heavy drinking increased from 2.01 to 2.56.

The overlap between smoking and heavy drinking is also of particular interest in relation to risk of poor glucose regulation. The observed to expected ratios indicating clustering of smoking and heavy drinking in Table 3.12 do not suggest a strengthening of clustering with increasing age. Logistic regression analyses indicated that the odds of heavy drinking were twice as great in smokers compared to non-smokers and were similar at 23 and 42 years. Additionally, heavy smokers are more likely to drink heavily than lighter and non-smokers (data not presented).

In summary the overlap between smoking and each of the drinking measures was lower than the overlap within the drinking measures. Although most smokers are not binge, heavy or daily drinkers, there are consistently more heavy, binge and daily drinkers among the smokers and ex-smokers than the never smokers, in both men and women.

Dose dependence in the cross-sectional association between smoking and drinking habits

To examine if there was any evidence of dose-dependence in the overlap between smoking and drinking, Figures 3.9a-c illustrate how the number of cigarettes smoked varied by heaviness of drinking at each adult age. Heavy drinkers smoked more cigarettes per day than light drinkers at each age. Never and special occasion drinkers smoked more than sensible drinkers at 23 and 33 years, but the amount smoked was similar in non and moderate drinkers at 42 years. Looking at the overlap from the other perspective (Figures 3.10a-c), the number of units of alcohol consumed in the past week was greater on average in heavy than in light smokers. Ex-smokers consumed more units of alcohol than non-smokers at each age. However the major difference in alcohol consumption levels was between genders rather than by smoking status.

In summary smoking prevalence was greater in heavier drinkers and non-drinkers than in moderate drinkers. Smokers drank slightly more alcohol than ex-smokers or never smokers.

Association of smoking with drinking habits across adult surveys.

Table 3.13 presents ORs for drinking status at one survey for participants who smoked at the previous survey. ORs for binge, heavy, daily and non-drinking at the second survey, contrast the odds of drinking in ex-smokers to odds of drinking in persistent smokers. In men who quit smoking before the 33 or 42-year surveys, the odds of subsequent binge and heavy drinking were reduced; OR for binge drinking at 33 years was 0.63 (95%CI 0.50, 0.78) and OR for heavy drinking at 33 years was 0.63 (0.47, 0.83). However among women there was only evidence to suggest that quitting smoking before the 42-year survey was associated with 42-year drinking; OR for binge drinking was 0.57 (0.42, 0.79), OR for heavy drinking was 0.44 (0.28, 0.70). There was no evidence in either sex to suggest that quitting smoking was associated with becoming a daily drinker or a non-drinker at a subsequent age. The exception to this was the lower odds of being a non-drinker at 42 years among women who quit smoking by 42 years (OR=0.63, 95% CI 0.48, 0.83).

The serial measures of alcohol and tobacco use record at how many surveys a participant reports the behaviour in question (Figures 3.5-3.8), correlations between the serial measures of smoking with each measure of serial drinking were all weak (Pearson's r <0.25). Persistent smokers were more likely to report repeated binge or heavy drinking than less frequent smokers. Serial

measures of drinking were more strongly correlated with each other than with smoking; repeatedly heavy drinking was positively correlated with repeatedly binge drinking: ρ=0.56 (men), ρ=0.39 (women).

Profiles summarise the number of cohort members in each of the possible combinations of smoking or of drinking between 16 and 42 years (Figures 3.2 and 3.4). Crosstabulating the profiles of smoking and drinking between 16 and 42 years indicate that nearly all persistent smokers drank at some point in adulthood. The majority (62%) of male persistent smokers were also persistent drinkers 16-42 years, less so for women (36%). Very few persistent smokers never drank throughout adulthood (0.7% men and 3% women). Whereas, half of the persistent drinkers smoked at some point in adulthood and a minority (12%) of persistent drinkers were persistent smokers (genders were very similar).

In summary quitting smoking was not associated with becoming a daily drinker, but was associated with lower odds of starting heavy or binge drinking. Only in women was there evidence that quitting smoking was associated with giving up drinking. The number of occasions that a person smoked was weakly associated with the number of occasions that they drank. The number of occasions that a person was a heavy drinker was associated with the number of occasions that they were a daily or binge drinker.

Discussion

These results give insights into changes over time in separate and co-occuring health behaviours within individuals. By their mid-forties half of this cohort of British men and women had regularly smoked cigarettes, and of these, half had quit. Over 95% reported usually drinking alcohol on at least one survey, and half of the cohort drank at each survey between 16 and 42 years. Half of the men and 60% of the women drank "sensibly". Smoking and drinking were more common among men than women, peaking at 23 years and declining thereafter. However, there were sustained levels of smoking and binge or heavy drinking into the mid forties. The overlap between smoking and non-drinking increased with increasing age and the overlap between smoking and heavier drinking also increased with increasing age. Overlap between binge and heavy drinking was strong; most heavy drinkers binge drink.

What this study adds

The study of intra-individual smoking and drinking trajectories spanning two decades in adulthood, in a population-based sample is novel. Few studies have examined stability of smoking and different patterns of drinking together over such a long time period. Whilst some studies have addressed the co-occurrence of alcohol and tobacco use at single time points, changes over the lifecourse in overlap of smoking and drinking are less studied. Previous work

on alcohol and tobacco use has mostly focused on the transition between adolescence and early adulthood (Orlando et al. 2004; Schulenberg et al. 1996; White et al 2002) and few studies address uptake and stability through into mid adulthood. Few studies investigating the inter-relationships of health behaviours over time use population-based samples; many studies of co-morbidity between alcohol and tobacco use are based, for example, on alcohol-dependent populations with high levels of substance use. Much literature about drinking patterns in early adult life relates specifically to the college environment in the USA (Hill et al. 2000; Kuntsche et al 2004; Tucker et al 2003), but context differs from the UK in several respects: the legal age for purchasing alcohol is older, standard drink sizes differ and drinking culture differs.

Strengths and weaknesses

The 1958 cohort provides a rare opportunity to assess stability and change in smoking, drinking frequency, heaviness and binge drinking over time within individuals. Comprehensive data in a large prospective population-based cohort is a considerable strength. The prevalences of alcohol and tobacco use were found to be similar to other British population-based studies (unless indicated otherwise below) which suggests greater validity.

Smoking is self-reported, but is found to be reliable in population-based studies (Patrick et al. 1994; Rebagliato 2002), and validation by cotinine measures, did not find evidence of differential reporting of smoking by social class (Erens & Primatesta 1999, Chapter 3.3). Alcohol use is complex to assess because frequency and amount must be taken into account. Self-reported drinking incurs some error, but no gold standard method exists for assessing usual alcohol intake in population surveys. Frequency, amount and type of alcohol vary over time and a "usual" measure of alcohol consumption can be hard to estimate. Several types of questionnaires or diaries exist, but using a quantity and frequency approach with separate questions for intake of each different type of alcoholic beverage improves recall of amount consumed (Feunekes et al. 1999). The present study benefits from a "usual" drinking frequency measure and the amount consumed is based on past week's intake. Some questionnaires use longer reference periods to minimise fluctuations in consumption over a week, but are limited by accuracy of recall over longer time-periods. Because binge drinkers were identified using the usual drinking frequency combined with amount consumed, both binge and heavy drinking measures may be affected by short term fluctuations in amount consumed. However a strength of the dataset is having comparable measures on the same population over two decades.

Definitions of binge drinking are inconsistent across existing literature in respect of both unit size and cut-offs to categorise binge; some studies use as few as 5 units per occasion to define binge drinking (Casswell et al. 2003; Kuntsche et al 2004). The measure of binge drinking used here ($\geq$7 units per occasion for women and $\geq$10 for men) is higher than in other studies because

the data are based on usual weekly consumption (Marmot et al 1995). However, more recent recommendations about binge drinking are based on daily consumption guidelines, which would be equivalent to 6 and 8 units per occasion, thus the measure used here is a conservative estimate of binge drinking (Department of Health 1995, p.25). There is also inconsistency in how non-drinking is operationalised in the literature (International Center for Alcohol Policies 2000). A broad definition for non-drinking (drinking on special occasions or "never") was used to indicate habitual non-consumption rather than a more restrictive definition "never" having drunk. A study of "never" drinkers based on this population, demonstrates that this group includes many past drinkers and the true prevalence of abstention is likely to be exceedingly low in the UK (Caldwell et al. 2006).

Reporting of alcohol consumption may be biased towards lower consumption at home because measures in the home are not standardised as in places of public consumption. Additionally, conscious under-reporting of intake is likely. Participants are too young to have yet suffered extensive smoking or alcohol-related mortality so differential mortality is unlikely to bias the results.

Data about attitudes and intentions towards particular health behaviours was not available, so whilst behavioural change was studied, theories of change could not be tested. Although it has been acknowledged that the predictive value of models of behavioural change is limited in practice(Conner & Norman 2005).

An important dimension of alcohol use that was not studied is abuse and dependence. Whilst it has serious public health implications, particularly in the overlap with some physical and mental health outcomes, there are not *a priori* reasons to expect associations between adult problem drinking behaviour and mid-life glucose homeostasis.

Generalisability of findings

The associations reported here are specific to this cohort of British men and women. Variations in drinking culture and alcohol or tobacco availability in different geographic and temporal settings are expected to influence stability and change in drinking frequency and amount of alcohol and tobacco use over time. The data analysed here span several decades, during which time both period and age effects have shaped drinking and smoking behaviour, both in terms of changing social acceptability and availability of alcohol and tobacco. The increase in per capita consumption of alcohol in the UK has increased in line with decreasing real price of alcohol is a period effect (The Academy of Medical Sciences 2004, p.14). However, it is not possible to separate period effects from age effects in the 1958 cohort as it is a study of a single generation. In order to separate period and age effects, it is necessary to

compare the results of this study with comparable results from cohorts born at different times. Extrapolation of the results for the 1958 cohort to other populations must take into account the different social setting as well as potential differences in drinking and smoking levels.

How the 1958 cohort data compares to other British data

Adolescent smoking in the 1958 cohort was somewhat higher than in contemporary studies. Regular smoking (>1 cigarette per week) increases sharply with age in contemporary surveys; by 15 years 20% boys and 26% girls were regular smokers and an additional 9% were occasional smokers (Blenkinsop et al. 2003, p.25). Prevalence of adolescent smoking was similar to other surveys at the time (Pearson & Richardson 1978). Further, adult smoking patterns were very similar to the age-specific estimates of smoking in the General Household Survey (Bridgwood et al 2000, p.123).

Comparing the adolescent drinking with contemporary measures, the frequency of drinking in the 1958 cohort has a similar distribution to today's 15 year olds, however there has been a secular increase in the number of units consumed. Between 1992 and 2002 the mean number of units consumed per week increased from 8.1 to 12.9 among 15 year olds (Blenkinsop et al 2003, p.86).

Usual drinking frequency

Recently there has been a return to an earlier focus in epidemiological studies on alcohol use which emphases drinking frequency in addition to average volume consumed (Rehm et al 1996). Drinking frequency gives some indication of the social aspects of alcohol use that is not captured in average volumes.

The prevalence of true lifetime abstainers was too low to analyse meaningfully. Given that the effects of drinking alcohol on "special occasions" compared to "never" on mid-life glucose regulation were not expected to differ *a priori*, "special occasion" drinkers were categorised with "never drinkers" to create a group who did not habitually drink. Prevalence of non-drinking in the 1958 cohort was higher than in the General Household Survey (GHS), although definitions of non-drinkers may differ (Bridgwood et al 2000). Usual drinking frequency in 1958 cohort fits with other British cross-sectional data. In line with expectations, men drank more frequently than women. The prevalence of daily drinking in the 1958 cohort at age 23 years is slightly higher than in more recent British national surveys, but frequency of daily drinking at the later ages is similar (although somewhat higher) than in the relevant age groups in national surveys (Bridgwood et al 2000, p.151). The increase in drinking frequency with increasing age fits with GHS data. Younger adults were less likely to have drunk in the past

week than older adults; 69% 16-24 year old men compared to 78% of 25-64 year olds (45% and 65% respectively in women).

Heavy drinking

The prevalence of women exceeding sensible limits (14 units/ week) in the 1958 cohort was slightly lower than in national survey data, although prevalence among men was similar. The GHS reports little change in the proportion of men exceeding the sensible limits (21 units /week) between 1988 and 2001, although the proportion of women exceeding sensible limits increased in that time. The 1991 GHS reported a prevalence of 34% men (and 14% women) in 25-45 year olds, compared to 33-year cohort data from 1991 (28% men and 8% women, Table 3.5)(Walker et al 2001). Prevalence of heavy drinking at 42 years was similar to national survey data (Bridgwood et al 2000, p.160). It was expected that prevalence of heavy drinking would decrease with increasing age, as seen elsewhere (Bennett et al 1991; Bridgwood et al 2000, p.160), however there was no clear trend with age in the 1958 cohort, although with only three time points a trend is harder to establish. Studying other age cohorts at the same time would help to identify whether secular trends in heavy drinking obscured the expected decline with increasing age.

Recent national data on binge drinking is collected as the number of drinks per day and is therefore not strictly comparable to the index of binge drinking calculated at 23,33 and 42 years. Binge drinking remained prevalent in the 1958 cohort throughout adulthood and was not confined to the early twenties; at 42 years approximately 1 in 3 men and 1 in 7 women were identified as binge drinkers. Few studies have repeated measures of drinking over such a long follow-up time as the 1958 cohort, although other studies support the general pattern that binge drinking is most prevalent in early adulthood, declining thereafter, whilst remaining at substantial levels into later adulthood (Bennett et al 1991; Fillmore 1987; Kuntsche et al 2004; Naimi et al 2003; Walker et al 2001, p.148).

Continuity of smoking and drinking across adulthood

Whilst the strong tracking of smoking over time is well established, less longitudinal population-level data exists on drinking. Repeated cross-sectional studies such as the GHS indicate sustained levels of alcohol use across adulthood, but cannot assess individual-level changes in behaviour. Assessing the relative strengths of tracking in health behaviours across different study samples and populations is problematic; differing methodology is used and measures of tracking are sensitive to the categorisation of data (Twisk et al. 1994). Further, stability and change may differ between locations and time periods.

Cigarette smoking

Continuity was high; 70% of smokers at one survey smoked ten years later; an estimate similar to other studies (Mulder et al 1998). As expected from existing literature, and the addictive nature of nicotine, the stability of tobacco use is greater than for alcohol use (Merline et al. 2004; Mulder et al 1998). One quarter of the cohort smoked at 42 years, the majority of whom were persistent smokers over two decades in adulthood. These persistent smokers are important in public health terms because they will have a high burden of morbidity and mortality (Doll et al 2004).

Non-drinking

In the 1958 cohort non-drinking was less stable over time than smoking, but more stable than heavy and binge drinking. This concurs with analyses of middle-aged men in the British Regional Heart study indicating less variation over time in non-drinkers compared to progressively heavier drinkers. Using average alcohol exposure over a follow-up period between 5 and 20 years, 78% of non-drinkers at baseline, were still on average classified as non-drinkers at the end of follow up. 65% of light drinkers at baseline (1-2 drinks/day or weekend-only drinkers of 1-6 drinks/day) were still on average light drinkers compared to only 28% of heavier drinkers at baseline (>6 drinks/day) (Emberson et al 2005). Greater stability of non-drinking compared to heavier daily drinking was also reported over a 3-year (Zins et al 1999) and a thirteen-year follow-up period (Doll et al 1994a). The greater continuity in non-drinking than in heavier drinking over time may be because non-drinkers have strong reasons for abstaining from alcohol, such as religious beliefs, health status or because they dislike alcohol; factors which may be less likely to change over time. In contrast, drinking alcohol is the norm in current British society as was seen in the 1958 cohort; at each age the majority of cohort members were drinkers. Alcohol use is influenced by many individual-level factors and may fluctuate in the short-term accounting for the greater changes over time in heavy and binge drinking seen in the cohort. Additionally changes in heavy drinking may be due to health, social and financial consequences which make it unsustainable over long periods.

The greater stability of non-drinking relative to heavier drinking is important for debates about the raised risks of health problems in non-drinkers relative to moderate drinkers. It has often been argued that the non-drinkers are at raised risk of poor health outcomes because of their past heavy drinking histories (Shaper et al. 1988). However non-drinkers at age 45 had mostly consumed some alcohol in the past, but their rates of heavy drinking at previous surveys were very low, much lower than among the drinkers at 45 years. The relative instability of heavy drinking challenges the association between heavy drinking and health risks; if heavy drinking is unstable and most of the heavy drinkers at a given time are in fact more moderate drinkers on other occasions (as is seen in the low number of cohort members who were heavy drinkers on two or three adult surveys), then morbidity risks of heavy drinking may be greater than

assumed, as exposure to heavy drinking over a short time period may increase disease risks. Alternatively, there may be an overestimation of risk if heavy drinkers may be socially more deprived and have poorer health outcomes because of confounding by other factors.

Daily drinking

Daily drinking was moderately stable within individuals between the adult surveys, although continuity 23-33 years was much lower than 33-42 or 42-45 years (approximately 30%, compared to over 60%), and this may be due to maturing out of the heavy and frequent drinking patterns often reported in younger age groups. A meta-analysis of drinking frequency across the lifecourse reported greater changes in drinking frequency prior to age 30 and greater stability in later life (Johnstone et al. 1996).

Binge drinking

There was evidence for moderate tracking of binge drinking within individuals between 23, and 42 years. Most binge drinkers in adulthood changed their behaviour during the study, although for a significant minority of men, binge drinking was identified at two or all three surveys (19% at two surveys and 8% at three surveys). The modest tracking in binge drinking fits with studies of stability of alcohol use in US and European populations, which document change and stability in adult drinking (McCarty et al 2004; Wennberg et al 2000)

Heavy drinking

Heavy drinking tracked modestly across the adult surveys; whilst heavy drinking at one adult age was associated with greater prevalence of heavy drinking at the next age, most heavy drinkers changed their behaviour. Only 10% of men were heavy drinkers at two surveys in adulthood and 4% were heavy drinkers at three surveys. Very few women were heavy drinkers at two or more surveys (<3%). There was more change in heavy drinking than in binge drinking. This modest tracking of heavy drinking in the 1958 cohort fits with other literature. In the British Doctor's study; one third of heavy drinkers at baseline were heavy drinkers at follow-up 14 years later (Doll et al 1994a). An American study of men and women aged up to 35 years reported that the odds of heavy drinking up to 16 years after a baseline survey were 3 times greater in those who were baseline heavy drinkers compared to non-drinkers (Merline et al 2004).

Cross-sectional overlap of smoking and drinking

The importance of studying the overlap of health behaviours has long been recognised (Wiley & Camacho 1980), and many studies have investigated co-occurrence of multiple behaviours or pairs of behaviours. One of the most consistent findings is co-occurrence of tobacco and alcohol use; drinkers are more likely to smoke than non-drinkers, and smokers more likely to

drink alcohol than non-smokers (Doll et al 1994a; Schuit et al 2002). It is now well established that health behaviours cluster, with people engaging in multiple healthy or, conversely, unhealthy practices (Rosal et al. 2001). Smokers are reported to have lower intake of fresh fruits and vegetables or fibre intake, higher saturated fat intake and are less physically active (Berrigan et al 2003; Burke et al. 1997; Raitakari et al. 1995; Schuit et al 2002), although these associations may be weaker than associations between alcohol and tobacco use. Studies in alcohol-dependent populations report poorer diets than in those not dependent on alcohol. At a population level, data on alcohol use in relation to other health behaviours are more scarce, although there is some evidence relating alcohol use to poorer diet (Raitakari et al 1995) and increased risks of illicit drug use, although these other behaviours are not studied here.

One quarter of the cohort were smokers at 42 years and of these significant numbers had concurrent drinking habits which are expected to have health consequences. Between one fifth and one third of the cohort both smoked and usually drank alcohol, fitting with other reports that drinkers are more likely to smoke than non-drinkers and smokers are more likely to drink than to abstain (Burke et al 1997; Doll et al 1994a; Milligan et al. 1997; Schuit et al 2002). However the overlap varied with age; at 23-years smoking prevalence was higher in drinkers than in non-drinkers, but by 42 years the association had reversed and smoking prevalence was greater in non-drinkers than in drinkers. This challenges previous research which has consistently shown that drinkers are more likely to smoke than non-drinkers. However, few previous studies of overlap take age into account, one such study reported a slightly greater overlap between smoking and drinking in younger adulthood than later adulthood. The prevalence odds ratio of for smoking and drinking was 3.78 at 20-29 years compared to 2.15 at 40-49 years (Schuit et al 2002).

The overlap between smoking and non-drinking reversed over time; cohort members who stopped drinking were more likely to smoke at 33 and at 42 years than those who continued drinking, so smoking prevalence among non-drinkers was greater at later ages than at earlier ages. However there were not clear trends in clustering of smoking with other drinking measures with increasing age.

Overlap between different drinking patterns

The overlap between binge and heavy drinking was the strongest overlap seen between drinking patterns, for example at 23 years 16% of men and 4% of women were both binge and heavy drinkers. This may in part be an artefact of the way in which binge drinking was defined based on average drinks per usual drinking day. However it is likely that heavy drinkers (>21 or 36 units per week respectively for women and men) consume heavily on single occasions. A

Welsh study which used the same cut-points for binge drinking as this study, reported that men and women who drank heavily were more likely to be binge drinkers than not. Also heavier drinkers reported binge drinking more often than lighter drinkers. To illustrate, 14% men who drank <21 units/week were weekly binge drinkers compared to 63% men who drank 22-49 units per week and 51% men who drank >50 units per week (Bennett et al 1991). Binge drinking was more common in monthly or weekly drinkers than in daily drinkers, although again this may be in part due to the use of drinking frequency measure to calculate binge drinking and those who were daily drinkers had to report heavier total consumption than weekly or monthly drinkers in order to be classified as binge drinkers.

By examining smoking with different dimensions of alcohol use, this study adds to previous research literature, which has mostly investigated single health behaviours or associations between pairs of behaviours. More recently, studies have started to take a wider view by encompassing more health behaviours. Some studies of the overlap of drinking and smoking and other behaviours including physical activity and measures of diet count the numbers of healthy or unhealthy behaviours that a person engages in, for the purpose of documenting clustering (Laaksonen et al. 2003; Pronk et al. 2004). However, preserving the different types of drinking behaviours allows greater insight into the overlap between specific drinking patterns rather than generic clustering of healthy or unhealthy behaviour.

The overlap of drinking and smoking is particularly relevant to public health, firstly because they act synergistically to alter disease risk (Bagnardi et al 2001a), and secondly, relevant to behavioural change, they may share common social cues or functions (sociability, relaxation, alleviating boredom, rewards and so forth)(Room 2004). Several theories exist to explain the co-occurrence of smoking and drinking: nicotine and alcohol may act by a common pathway, each promoting desire for the other either, or each may dampen the unpleasant effects of withdrawal from the other. Or according to the associative learning model, tobacco and alcohol use become conditional stimuli for each other because they are frequently consumed together (Istvan & Matarazzo 1984). Alternatively, the behavioural association between smoking and drinking may be due to the chronic use of one substance resulting in tolerance to the effects of the other substance. This would offer an explanation for chronic use of alcohol resulting in increased consumption of tobacco if ethanol resulted in cross-tolerance to the effects of smoking. Similarly the effect might work in reverse. Another possibility is that the co-occurrence could be due to metabolism of one substance affecting the rate of metabolism of the other. Thus if tobacco users experienced an increase in alcohol metabolism, they might drink more. There is some animal evidence suggesting that alcohol does increase nicotine metabolism, although this evidence is not all consistent. Alternatively co-occurrence could be expected if the adverse effects of one drug were counteracted by the other; for example if

sedation by alcohol was counteracted by smoking. Also if the positive effects of smoking (such as increased concentration) were reduced by alcohol use then tobacco use might be expected to be greater among drinkers.

Smoking predicting drinking at later life stages

A strength of repeated measures data on smoking and drinking in the same individuals is the ability to examine how changes in one behaviour are associated with changes in another. Although there are many potential changes that could be investigated in this dataset, the analyses of change were limited to one policy-relevant issue which is whether quitting smoking at one time increases the odds that a person becomes a heavier drinker or binge drinker or changes drinking frequency at a later age. There was some evidence that men who had quit smoking before the 33 or 42-year surveys were less likely to binge or heavy drink at later ages, however among women there was only evidence to suggest that quitting smoking before the 42-year survey was associated with lower risks of binge or heavy drinking. This fits with reports from other studies that quitting smoking is associated with reduced odds of initiating heavy drinking (Karlamangla et al. 2006). However not all studies report that quitting smoking was associated with change in odds of heavy drinking (Jensen et al 2003; Kranzler et al. 2002) or alcohol use at follow-up (Perkins et al. 1993). In the 1958 cohort there was not evidence to suggest that quitting smoking was associated with becoming a daily drinker or a non-drinker at a subsequent age. The exception to this was the lower odds of non-drinking at 42 years among men who quit smoking by 42 years. Hence there was not evidence that one harmful behaviour was substituted for another. A 7-year follow-up study of Finnish men and women reported that smoking cessation was not associated with onset of heavy alcohol use (defined as >10 units/week in men and >4 units/week in women), however only among women, smoking cessation was associated with decreased alcohol use at follow up (Laaksonen et al. 2002). In the 1958 cohort, current smoking predicted heavier and binge drinking at subsequent surveys, in line with evidence from USA that teenage smoking and marijuana use increase risks of harmful and binge drinking at 30 years (McCarty et al 2004). Although smoking and drinking are associated at successive surveys in the 1958 cohort, associations between behaviours at surveys as much as ten years later may not be causal. There is strong inter-relation of smoking and drinking habits, because drinking predicts smoking and smoking predicts later drinking it is hard to definitively disentangle whether these are chains of causality. Studies with surveys which are closer together in time and ask about attitudes towards behaviours may help progress this line of research further. The associations between tobacco and alcohol use may run in either direction, or may be due to a third common factor. The close association between smoking and drinking is nevertheless useful to note in terms of identifying groups who are at increased risk of poorer physical and mental health or potential substance abuse, given the reported associations between early or repeated use of alcohol, and subsequent alcohol problems.

Health burden

One quarter of this cohort smoked in their forties and are likely to bear a burden of disease from their smoking habit, whereas the quarter who had quit smoking should avoid most of the mortality risk (Doll et al. 1994b). Most cohort members were habitual drinkers in adulthood and at each survey more men than women were daily, binge or heavy drinkers. There were not clear linear age trends in daily, binge or heavy drinking; although they were most frequent at age 23 years and lower at ages 33 and 42 years. Continuity in drinking patterns was lower than for smoking and the continuity in non-drinking was greater than for binge or heavy drinking. Whilst continuity in binge and heavy drinking is low, there were still significant minorities of men in particular who were repeatedly reporting binge (and to a lesser degree) heavy drinking. Repeatedly reporting these harmful drinking patterns across extended periods of time is likely to confer raised risks of health and social consequences as well as raising the risks of problem drinking in later life. This longitudinal study suggests that interventions are justified at earlier life stages in order to prevent initiation of smoking which tracks strongly through adulthood, although the change in heavy and binge drinking that continues through into adulthood suggests that policies should be concentrated throughout the lifecourse rather than only in the high risk early adult years.

The age-related change in co-occurrence of smoking and non-drinking was a novel finding and it will have health consequences for outcomes related to non-drinking and smoking, including diabetes and cardiovascular risk. Overall, the prevalence of unhealthy behaviours was greater in men than women, but clustering of drinking patterns was slightly stronger for women than men. Clustering of health behaviours did not however show clear trends over age. The co-occurrence of behaviours provides evidence supporting the multidimensional nature of health behaviours. This suggests that health promotion messages should encompass healthy lifestyles overall rather than single out specific behaviours. The need for these messages appears to be greater in men than in women based on higher observed prevalences of unhealthy smoking and drinking patterns and is also sustained through adulthood.

Table 3.1 Smoking status and cigarette consumption at 16, 23, 33 and 42 years.

	Male						Female					
		Non-smoker	Ex	Current Smoker	Cigarettes /day			Non-smoker	Ex	Current Smoker	Cigarettes /day	
Age at survey (years)	Total N[a]	%	%	%	Mean	SE	Total N[a]	%	%	%	Mean	SE
16[b]	6114	65.4	-	34.6	-	-	5855	69.5	-	30.5	-	-
23	6237	49.9	10.3	39.8	17.3	0.2	6245	52.7	9.3	38.1	15.0	0.2
33	5502	46.3	21.9	31.8	18.5	0.3	5710	48.4	20.1	31.5	16.2	0.2
42	5594	45.7	28.7	25.6	18.7	0.2	5764	47.7	26.3	26.0	16.2	0.2
Persistent smoker												
16-42 years	3088			13.5	19.3[c]	0.4[c]	3453			12.5	16.9[c]	0.3[c]
23-42 years	3088			4.5	17.8[c]	0.7[c]	3453			6.6	15.8[c]	0.5[c]

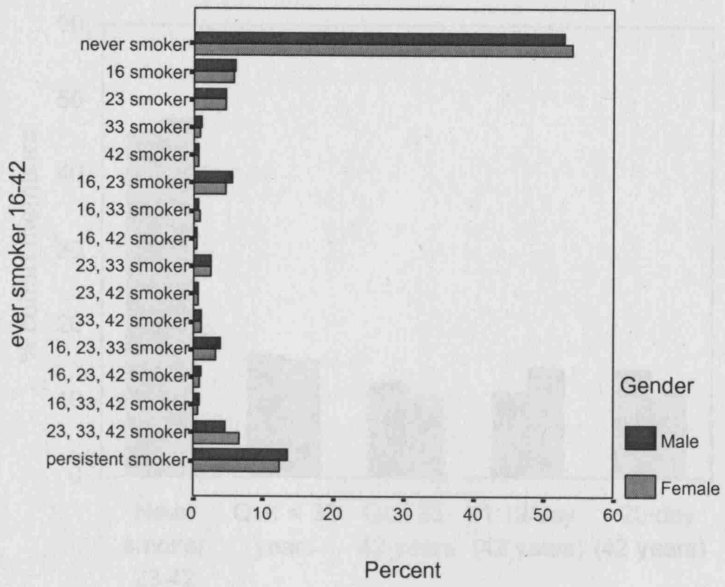
[a]N varies by survey
[b]≥1 cigarette/week
[c]at 42 years

Table 3.2 Association between smoking at 23-33 and 33-42 years.

	Men			*Women*		
	Kappa[a]	% (n) Non-smoker	% (n) Smoker	Kappa[a]	% (n) Non-smoker	% (n) Smoker
23 years	0.65	*33 years*		0.68	*33 years*	
Non –		93.2	6.8		95.9	4.1
Smoker		(2675)	(196)		(3115)	(132)
Smoker		30.0	70.0		29.6	70.4
		(526)	(1226)		(414)	(984)
33 years	0.70	*42 years*		0.74	*42 years*	
Non –		93.9	6.1		96.3	3.7
smoker		(2914)	(188)		(3357)	(129)
Smoker		28.2	71.8		25.9	74.1
		(518)	(1321)		(395)	(112)

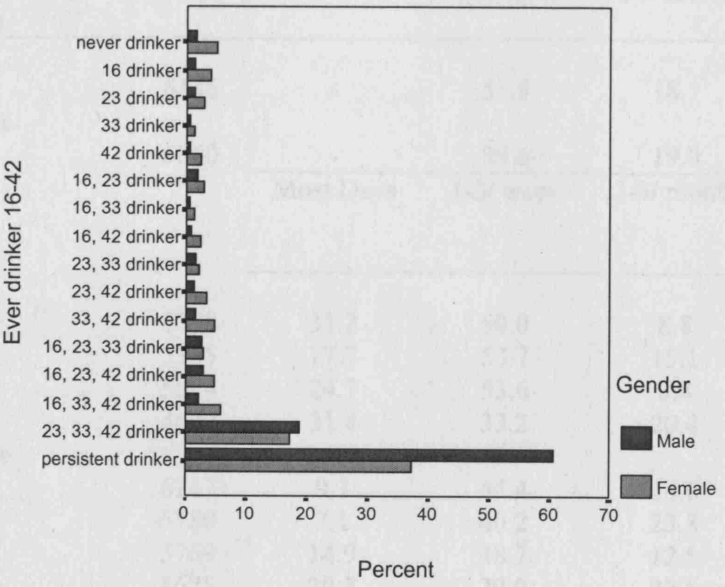
[a]Cohen's kappa (measure of association, all $p<0.001$).

Figure 3.2 Profiles (n and %) of smoking[a] habits between 16 and 42 years.



[a]Smoking defined as ≥1 cigarette/ week 16 years, and ≥1 cigarette/ day 23, 33 and 42 years.

Figure 3.3 Profiles (n and %) of drinking[b] habits between 16 and 42 years.



[b]Drinking defined as drinking in the past month or less at 16 years, and drinking more often than "infrequently" or on special occasions at 23, 33 and 42 years.

Figure 3.4 Smoking history 23-42 years, in cohort members with complete data (n=11360)

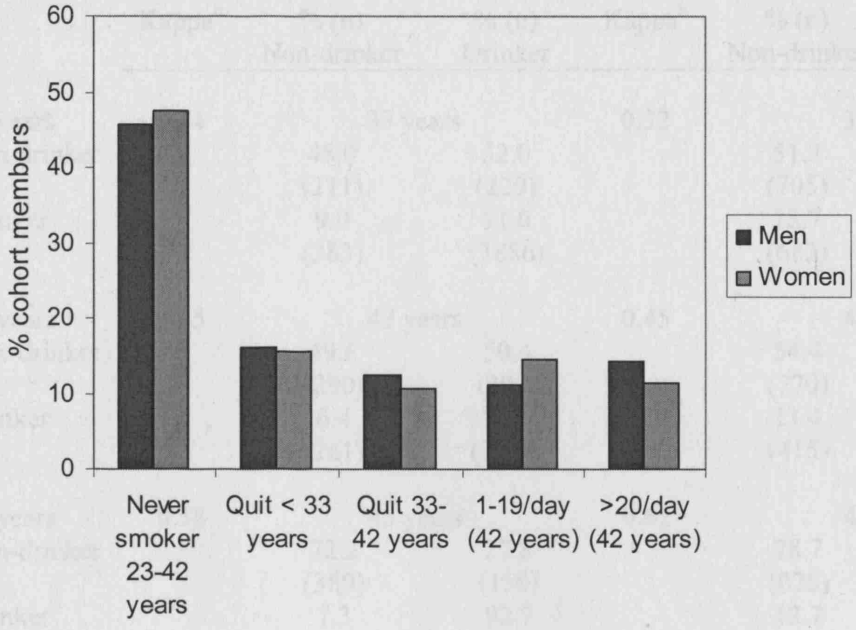


Table 3.3 Frequency (%) of alcohol consumption at 16, 23, 33, 42 and 45 years.

Age at survey (years)	Total N	-	≥1/week	≥1/ month	Infrequent	Never had a drink
Male						
16	6146	-	51.9	18.1	24.8	5.2
Female						
16	5860	-	39.6	19.0	33.4	8.0
		Most Days	1-3/ week	2-3/ month	Infrequent/ special occasions	"Never" drinker
Male						
23	6258	31.2	50.0	8.8	6.5	3.5[a]
33	5585	17.7	53.7	15.1	10.5	3.0[b]
42	5604	24.7	53.6	8.8	8.8	4.2[c]
45	4607	31.4	33.2	20.4	10.0	5.0[d]
Female						
23	6267	9.7	45.4	16.6	22.0	6.2[a]
33	5780	7.1	40.2	23.8	22.9	5.9[b]
42	5769	14.9	48.7	12.5	17.5	6.5[c]
45	4675	20.7	29.0	22.5	19.1	8.7[d]

[a] non-drinker = never drink
[b] non-drinker = never
[c] non-drinker = never nowadays + never had an alcoholic drink
[d] non-drinker = not in the last 12 months (including those who have ever drunk alcohol)

Table 3.4 Association between drinking status[a] at 23-33; 33-42 and 42-45 years.

	Men			Women		
	Kappa[b]	% (n) Non-drinker	% (n) Drinker	Kappa[b]	% (n) Non-drinker	% (n) Drinker
23 years	0.34	33 years		0.32	33 years	
Non-drinker		48.0 (211)	52.0 (229)		51.2 (705)	48.8 (672)
Drinker		9.0 (383)	91.0 (3886)		18.7 (682)	81.3 (2960)
33 years	0.45	42 years		0.45	42 years	
Non-drinker		49.6 (290)	50.4 (303)		54.4 (770)	45.6 (646)
Drinker		6.4 (261)	93.6 (3848)		11.4 (415)	88.6 (3241)
42 years	0.58	45 years		0.62	45 years	
Non-drinker		72.2 (389)	27.8 (150)		78.7 (825)	21.4 (224)
Drinker		7.3 (287)	92.7 (3623)		12.7 (446)	87.3 (3064)

[a] drinkers defined as drinking more often than on special occasions or infrequently
[b] Cohen's kappa (measure of association, all $p<0.001$)

Figure 3.5 Number of adult surveys (23, 33 and 42 years) that a cohort members was classified as a non drinker, by gender.

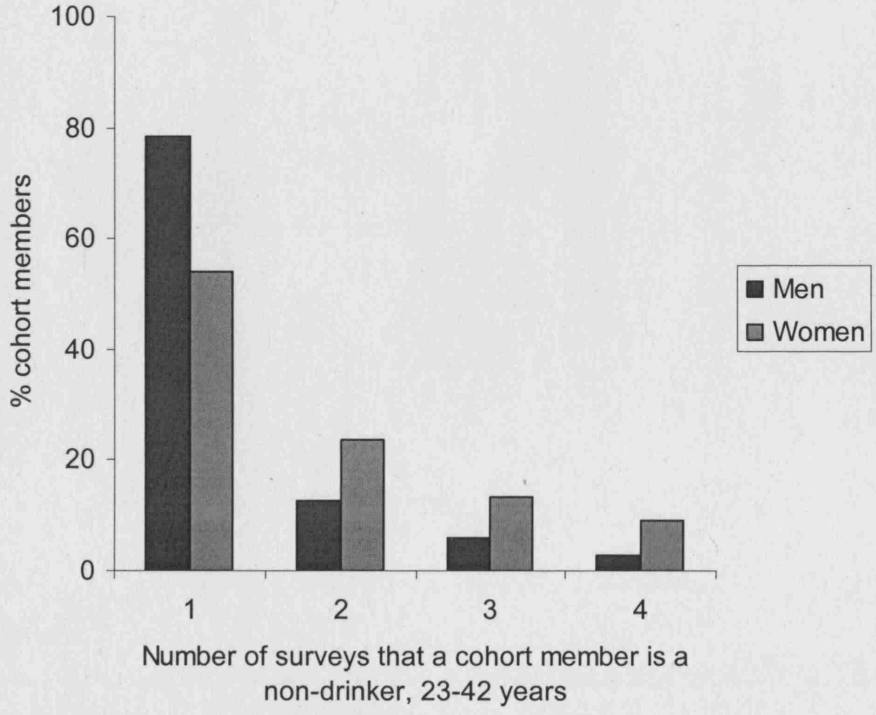


Table 3.5. Spearman's correlation (ρ) coefficients between usual frequency of alcohol consumption at 16, 23, 33 and 42 years[a]

Men	16 years	23 years	33 years	42 years	45 years
Women					
16 years		0.223	0.175	0.167	0.192
		(4747)	(4210)	(4214)	(3540)
23 years	0.217		0.416	0.335	0.328
	(4780)		(4709)	(4654)	(3920)
33 years	0.184	0.428		0.527	0.511
	(4411)	(5024)		(4718)	(4023)
42 years	0.174	0.395	0.576		0.678
	(4403)	(4965)	(5080)		(4456)
45 years	0.189	0.405	0.548	0.733	
	(3650)	(4110)	(4243)	(4564)	

[a] drinking frequency at 16 years: in the past week; in the past month; not in the past month & can't remember; never had a drink. Drinking frequency at 23, 33, 42 and 45 years: most days; 1-3/week; 1-3/month; infrequent & special occasions & never

Table 3.6 Association between daily drinking status[a] at 23-33; 33-42 and 42-45 years.

		Men			*Women*	
	Kappa[b]	% (n) Daily drinker	% (n) Other Drinker	Kappa[b]	% (n) Daily drinker	% (n) Other Drinker
23 years	0.27	*33 years*		0.26	*33 years*	
Daily drinker		34.0 (506)	66.6 (982)		28.8 (138)	72.2 (359)
Other Drinker		9.9 (318)	90.1 (2903)		5.0 (225)	95.0 (4302)
33 years	0.40	*42 years*		0.34	*42 years*	
Daily drinker		63.6 (530)	36.4 (304)		62.6 (226)	37.4 (135)
Other Drinker		16.9 (657)	83.1 (3227)		11.1 (526)	88.9 (4193)
42 years	0.55	*45 years*		0.57	*45 years*	
Daily drinker		61.5 (859)	38.3 (532)		55.0 (518)	45.0 (424)
Other Drinker		7.9 (243)	92.1 (2822)		5.0 (181)	95.0 (3441)

[a] daily drinkers defined as drinking more often than 5 days a week
[b] Cohen's kappa (measure of association, all $p<0.001$)

Figure 3.6 Number of adult surveys (23, 33 and 42 years) that a cohort member was classified as a daily drinker, by gender.

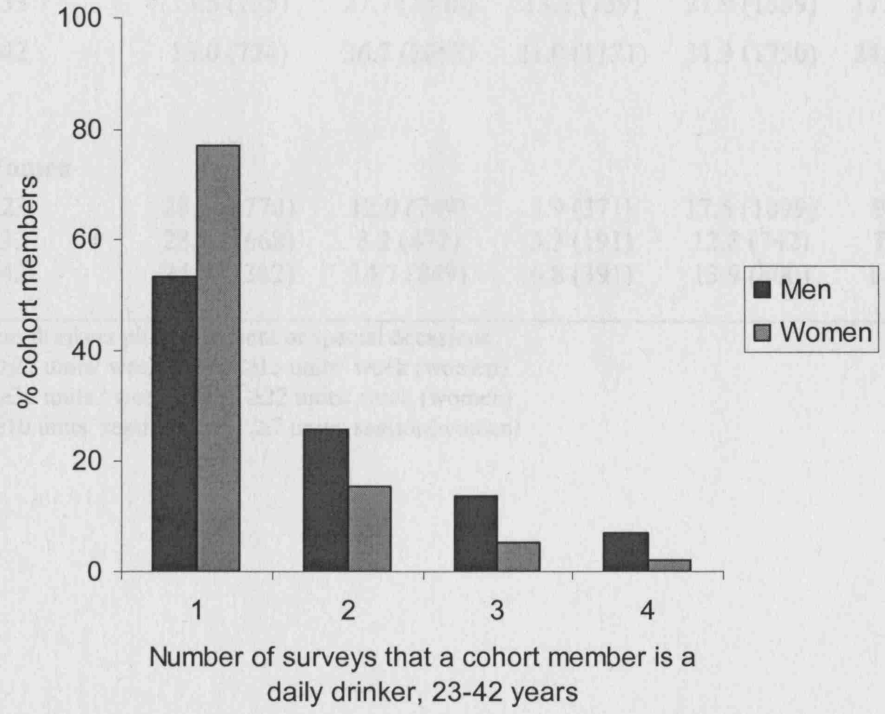


Table 3.7 Usual alcohol consumption (% and n) among drinkers ages 16 to 42 years, by gender[a].

	Units per week						Total
	<1 unit	1-2	3-4	5-6	7-8	>8	
16 years							
Men	128 (4.0)	1013 (31.7)	527 (16.5)	383 (12.0)	763 (23.9)	377 (11.8)	3191
Women	79 (3.4)	1397 (60.3)	529 (22.8)	173 (7.5)	140 (6.0)		2318

	<1 unit	1-10	11-14	15-21	22-35	≥36	Total
Men							
23 years	304 (5.4)	2073 (36.8)	846 (15.0)	1005 (17.8)	657 (11.7)	746 (13.2)	5631
33 years	355 (7.3)	2175 (45.0)	754 (15.6)	787 (16.3)	424 (8.8)	335 (6.9)	4830
42 years	291 (6.0)	1877 (38.6)	645 (13.3)	846 (17.4)	567 (11.7)	639 (13.1)	4865
Women	<1 unit	1-7	8-14	15-21	22-35	≥ 36	Total
23 years	538 (12.0)	2125 (47.3)	1085 (24.1)	378 (8.4)	263 (5.8)	108 (2.4)	4497
33 years	581 (14.1)	2157 (52.4)	903 (22.0)	281 (6.8)	137 (3.3)	54 (1.3)	4112
42 years	370 (8.4)	2032 (46.4)	1127 (25.7)	458 (10.5)	245 (5.6)	146 (3.3)	4380

[a]Adult ages: all consumption reported for the past week and censored above 250 units (5 men censored at 42 years).

Table 3.8 Prevalence (%, n) of drinking habits in the whole cohort.

Age at survey (years)	Non-drinkers[a]	Above sensible limits[b]	Heavy drinkers[c]	Binge drinkers[d]	Daily drinkers[e]	Total
Men						
23	10.0 (627)	38.5 (2408)	22.1 (1380)	37.1 (2302)	31.2 (1954)	6258
33	13.5 (755)	27.7 (1546)	13.2 (739)	27.9 (1559)	17.7 (989)	5583
42	13.0 (724)	36.7 (2052)	21.0 (1171)	31.3 (1750)	24.6 (1375)	5587
Women						
23	28.2 (1770)	12.0 (749)	5.9 (371)	17.5 (1099)	9.7 (610)	6267
33	28.8 (1668)	8.2 (472)	3.3 (191)	12.8 (742)	7.1 (411)	5784
42	24.0 (1382)	14.7 (849)	6.8 (391)	13.9 (800)	14.9 (858)	5766

[a]non-drinkers plus infrequent or special occasions
[b] ≥22 units/ week (men) ≥15 units/ week (women)
[c] ≥36 units / week (men) ≥22 units/ week (women)
[d] ≥10 units/ session (men) ≥7 units/ session(women)

Table 3.9 Number of units of alcohol consumed in the past week [mean (n)] classified by usual frequency of drinking, in the whole cohort.

Age at survey (years)	Daily	1-3/ Week	2-3/month	Mean (Total n)
Men				
23	43.0 (1954)	18.1 (3127)	5.1 (550)	25.5 (5631)
33	37.4 (989)	17.5 (2997)	5.7 (843)	19.5 (4829)
42	43.6 (1375)	20.5 (2998)	7.3 (492)	25.7 (4865)
Women				
23	20.6 (610)	8.3 (2847)	2.9 (1040	8.7 (4497)
33	18.0 (411)	7.6 (2325)	2.7 (1378)	7.0 (4114)
42	19.7 (858)	8.4 (2805)	2.9 (719)	9.7 (4382)

Table 3.10 Association between heavy drinking at 23-33 and 33-42 years.

		Men			*Women*	
	Kappa[a]	% (n) Non/ Lighter drinker	% (n) Heavy Drinker	Kappa[a]	% (n) Non/ Lighter drinker	% (n) Heavy Drinker
23 years	0.26	*33 years*		0.13	*33 years*	
Non/ Lighter drinker		91.5 (3376)	8.5 (312)		97.3 (4599)	2.7 (126)
Heavy Drinker		69.2 (707)	30.8 (314)		86.7 (255)	13.3 (39)
33 years	0.28	*42 years*		0.24	*42 years*	
Non/ Lighter drinker		83.6 (3435)	16.4 (674)		94.4 (4635)	5.6 (274)
Heavy Drinker		47.8 (287)	52.2 (314)		57.7 (94)	42.3 (69)

[a] Cohen's kappa (measure of association, all $p<0.001$)

Figure 3.7 Number of adult surveys (23, 33 and 42 years) that cohort members were classified as heavy drinkers, by gender.

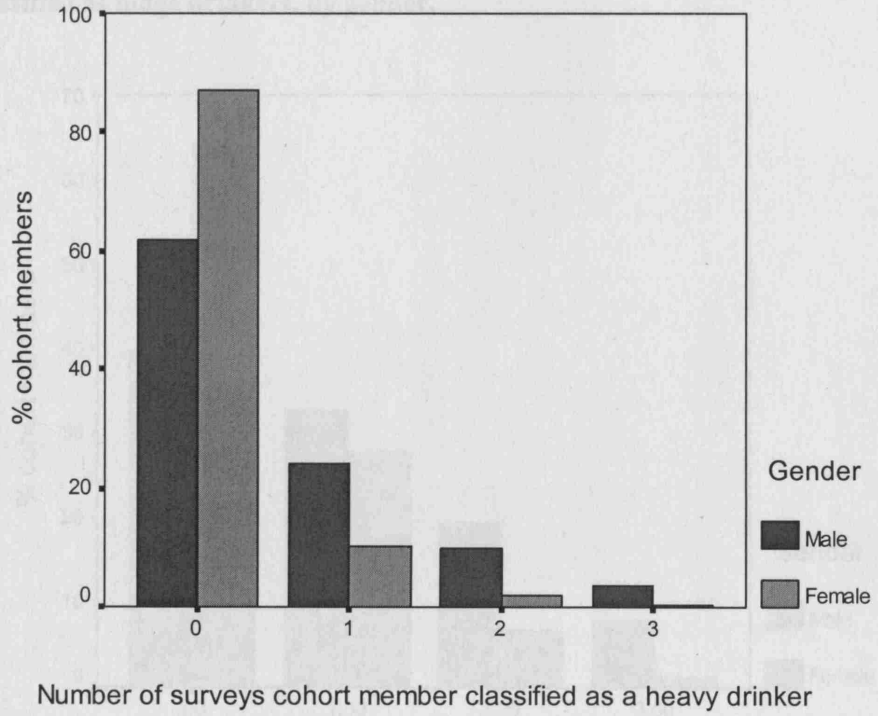


Table 3.11 Association between binge drinking at 23-33 and 33-42 years.

		Men			*Women*	
	Kappa[b]	% (n) Non binge[a]	% (n) Binge	Kappa[b]	% (n) Non binge[a]	% (n) Binge
23 years	0.20	*33 years*		0.11	*33 years*	
Non binge[a]		79.2 (2373)	20.8 (624)		88.9 (3399)	11.1 (458)
Binge		59.9 (1026)	40.1 (686)		79.0 (707)	21.0 (188)
33 years	0.23	*42 years*		0.12	*42 years*	
Non binge[a]		75.4 (2565)	24.6 (839)		87.7 (3976)	12.3 (543)
Binge		51.8 (677)	48.2 (629)		75.7 (493)	24.5 (160)

[a] non binge includes non-drinkers here.
[b] Cohen's kappa (measure of association, all $p<0.001$)

Figure 3.8 Number of adult surveys (23, 33 and 42 years) that cohort members were classified as binge drinkers, by gender.

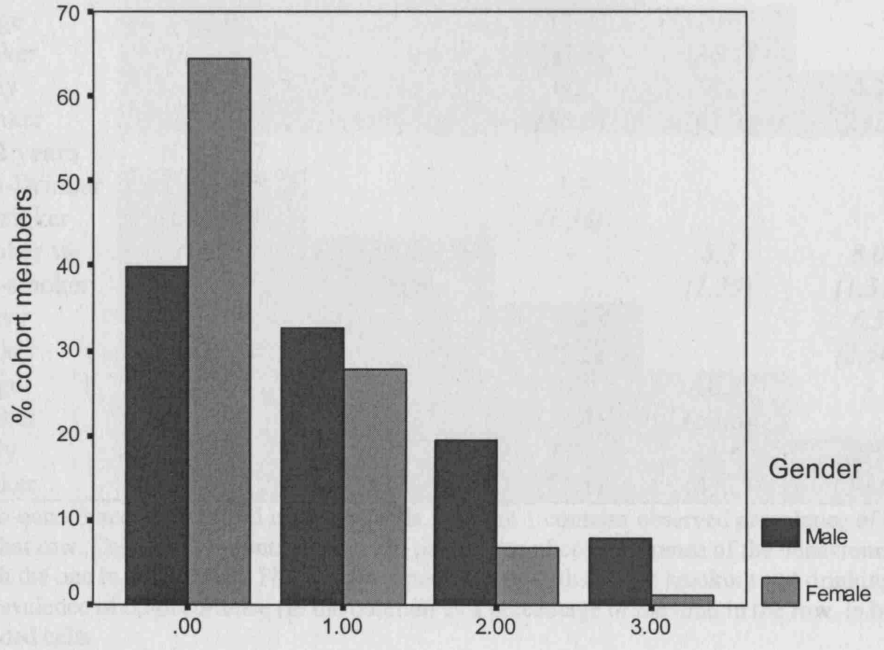


Table 3.12 Co-occurrence [observed prevalence (%)] and clustering [ratio of observed: expected prevalences] of smoking habits and drinking habits at 23, 33 and 42 years.

a) Men

	Observed Prevalence[a] (column as % of row)[b]	*Expected Prevalence[c] (Ratio Observed: Expected)[d]*				
		Non-drinker	Smoker	Heavy drinker	Binge drinker	Daily drinker
23 years	N = 6234					
Non-Drinker vs drinker	10.0	-	*3.9 (0.84)*			
Smoker vs non-smoker	39.8	3.3 (8.2)	-	*8.8 (1.32)*	*14.7 (1.20)*	*12.4 (1.15)*
Heavy drinker	22.1		11.6 (52.5)	-	*8.1 (2.01)*	*6.9 (2.34)*
Binge drinker	37.0		17.6 (47.6)	16.4 (44.4)	-	*11.6 (0.91)*
Daily drinker	31.2		14.2 (45.6)	16.1 (51.7)	10.5 (33.7)	-
33 years	N =5499					
Non-Drinker vs drinker	13.5	-	*4.3 (1.05)*			
Smoker vs non-smoker	31.8	4.5 (14.2)	-	*4.2 (1.50)*	*8.9 (1.34)*	*5.6 (1.11)*
Heavy drinker	13.1		6.3 (47.6)	-	*3.7 (2.40)*	*2.3 (3.13)*
Binge drinker	28.0		11.9 (42.5)	10.1 (36.1)	-	*4.9 (0.85)*
Daily Drinker	17.6		6.2 (35.0)	7.2 (41.2)	4.2 (23.7)	-
42 years	N = 5577					
Non-Drinker vs drinker	13.0	-	*3.3 (1.36)*			
Smoker vs non-smoker	25.5	4.5 (17.6)	-	*5.3 (1.39)*	*8.0 (1.31)*	*6.3 (1.06)*
Heavy drinker	21.0		7.4 (35.5)	-	*6.5 (2.56)*	*5.2 (2.26)*
Binge drinker	31.3		10.5 (33.4)	16.8 (53.6)	-	*7.7 (0.97)*
Daily drinker	24.6		6.7 (27.1)	11.6 (47.3)	7.5 (30.4)	-

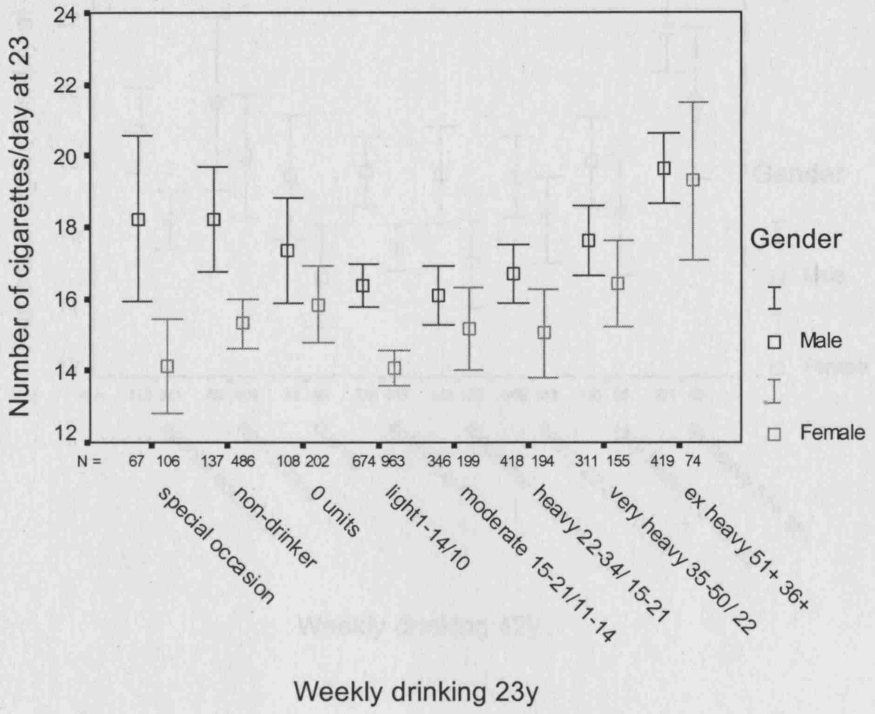
[a] Co-occurrence summarised in shaded cells. Column 1 contains observed prevalence of behaviour listed in that row. Columns 2-5 contain observed prevalence of co-occurrence of the behaviours listed in row with the one in the column. The sample is participants with data on smoking and drinking at one age.
[b] prevalence of co-occurrence (in the column) as a percentage of the total in the row, in brackets in the shaded cells.
[c] expected prevalence of co-occurrence both behaviours listed in row i and column j (expected prevalence of i and j= observed prevalence i*observed prevalence j). Top line of unshaded cells.
[d] Clustering presented in brackets in the unshaded cells. Ratio of observed:expected co-occurrence = observed prevalence of co-occurrence both behaviours / expected prevalence of co-occurrence both behaviours

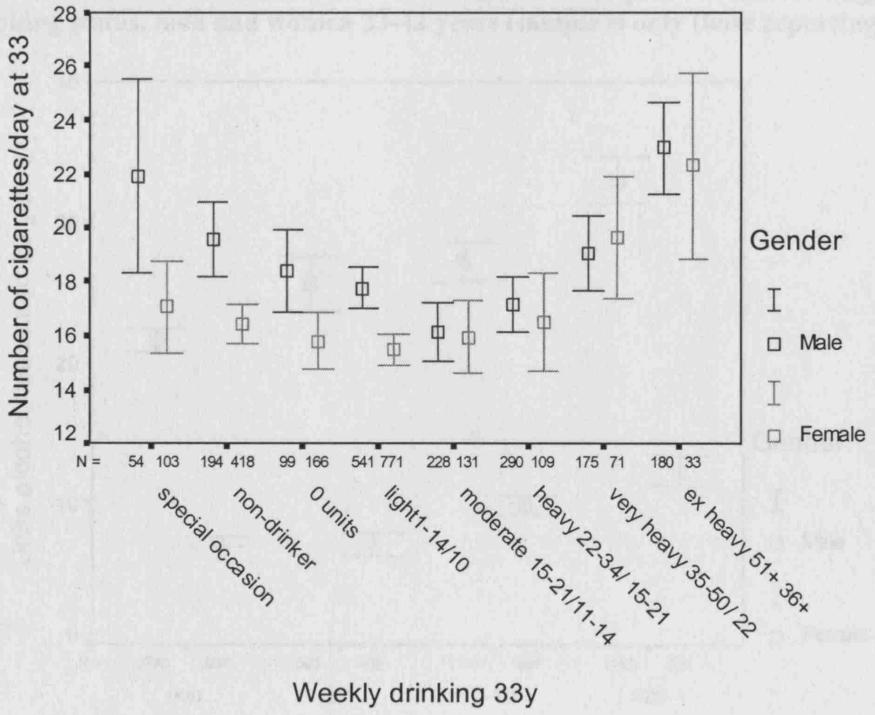
b) Women

	Observed Prevalence[a] (column as % of row)[b]	*Expected Prevalence[c] (Ratio Observed: Expected)[d]*				
		Non-drinker	Smoker	Heavy drinker	Binge drinker	Daily drinker
23 years	N = 6244					
Non-Drinker vs drinker	28.2		*10.2 (0.93)*			
Smoker vs non-smoker	38.1	9.5 (24.9)	-	*2.2 (1.63)*	*6.7 (1.20)*	*3.7 (1.34)*
Heavy drinker	5.9		3.7 (62.2)	-	*1.0 (3.40)*	*0.6 (5.90)*
Binge drinker	17.5		8.6 (48.9)	3.5 (20.0)	-	*1.7 (0.59)*
Daily drinker	9.7		5.0 (51.2)	3.4 (34.9)	1.0 (10.3)	-
33 years	N = 5712					
Non-Drinker vs drinker	28.8		*9.1 (1.00)*			
Smoker vs non-smoker	31.5	9.1 (28.9)	-	*1.0 (1.74)*	*4.0 (1.36)*	*2.2 (1.08)*
Heavy drinker	3.3		1.8 (55.0)	-	*0.4 (5.06)*	*0.2 (7.40)*
Binge drinker	12.8		5.5 (42.9)	2.2 (16.9)	-	*0.9 (0.64)*
Daily drinker	7.1		2.4 (34.2)	1.8 (24.9)	0.6 (8.4)	-
42 years	N=5761					
Non-Drinker vs drinker	24.0		*6.0 (1.30)*			
Smoker vs non-smoker	26.0	7.8 (30.1)	-	*1.8 (1.72)*	*3.6 (1.55)*	*3.9 (1.04)*
Heavy drinker	6.8		3.0 (44.9)	-	*1.0 (4.58)*	*1.1 (4.02)*
Binge drinker	13.9		5.6 (40.5)	4.3 (31.2)	-	*2.1 (0.78)*
Daily drinker	14.9		4.0 (27.0)	4.1 (27.2)	1.6 (10.8)	-

[a] Co-occurrence summarised in shaded cells. Column 1 contains observed prevalence of behaviour listed in that row. Columns 2-5 contain observed prevalence of co-occurrence of the behaviours listed in row with the one in the column. The sample is participants with data on smoking and drinking at one age.
[b] prevalence of co-occurrence (in the column) as a percentage of the total in the row, in brackets in the shaded cells.
[c] expected prevalence of co-occurrence both behaviours listed in row i and column j (expected prevalence of i and j= observed prevalence i*observed prevalence j). Top line of unshaded cells.
[d] Clustering presented in brackets in the unshaded cells. Ratio of observed:expected co-occurrence = observed prevalence of co-occurrence both behaviours / expected prevalence of co-occurrence both behaviours

Figure 3.9a-3.9c Amount of alcohol consumed in the past week according to heaviness of smoking, men and women 23-42 years (sample is only smokers)





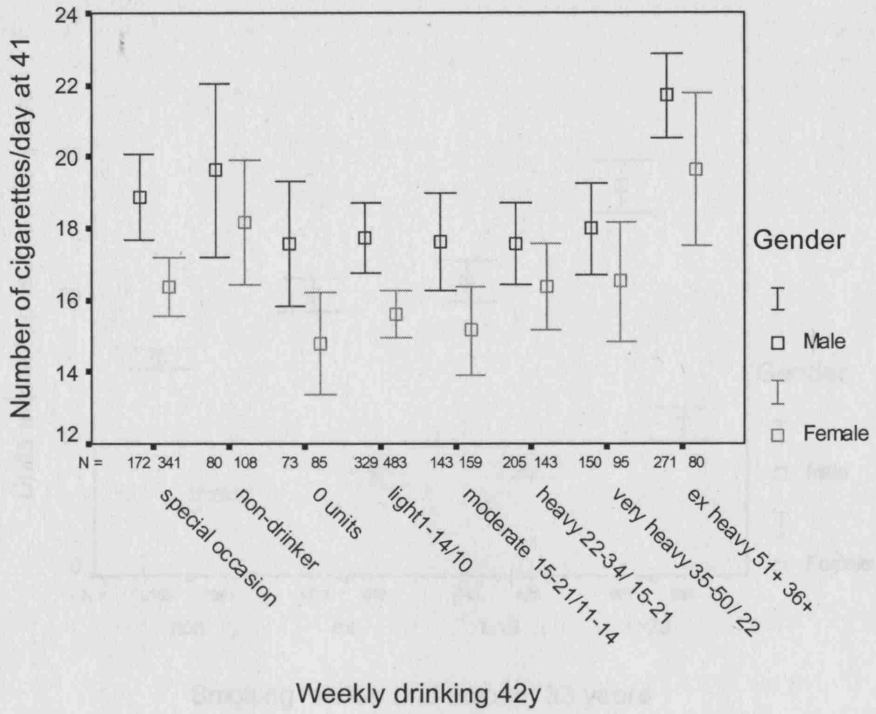
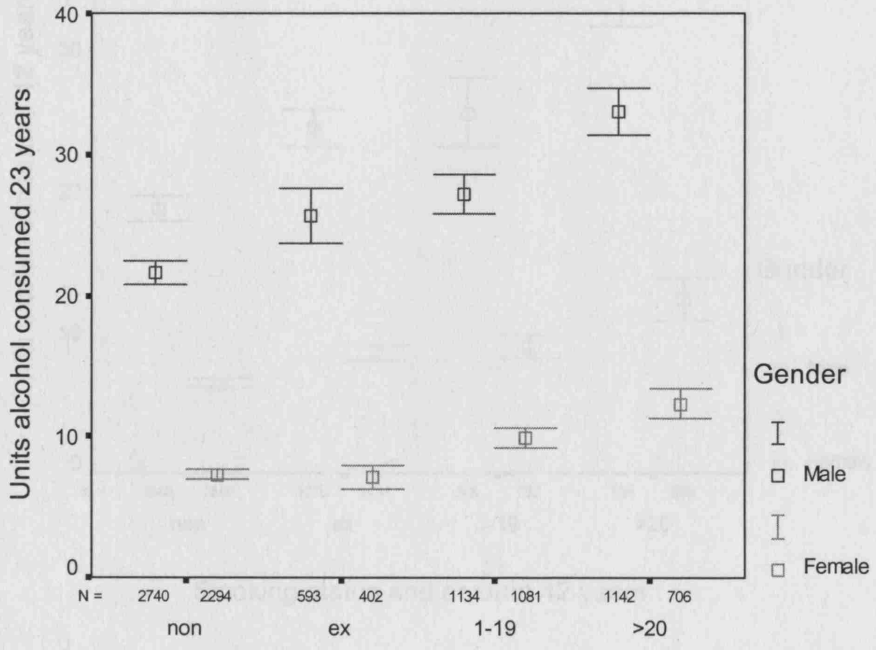
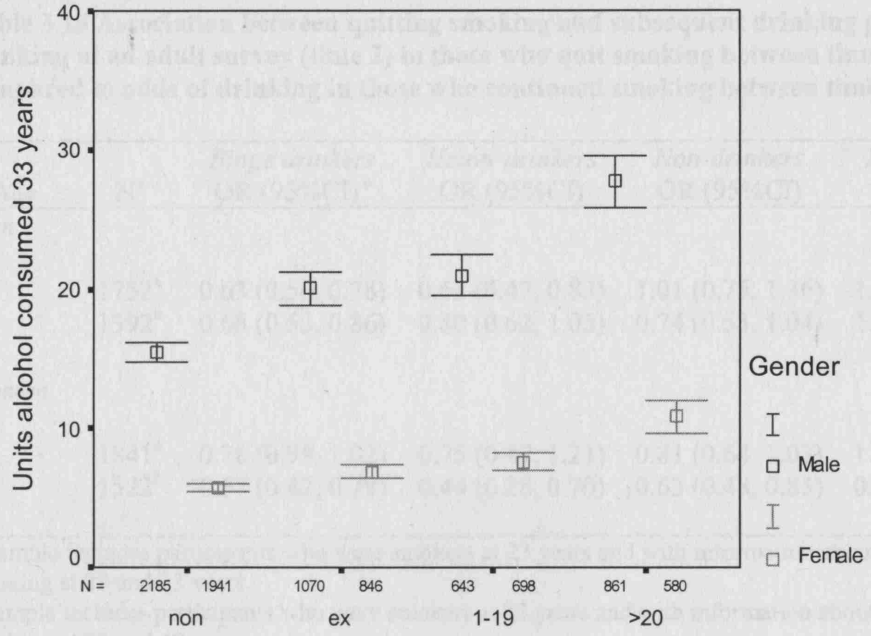
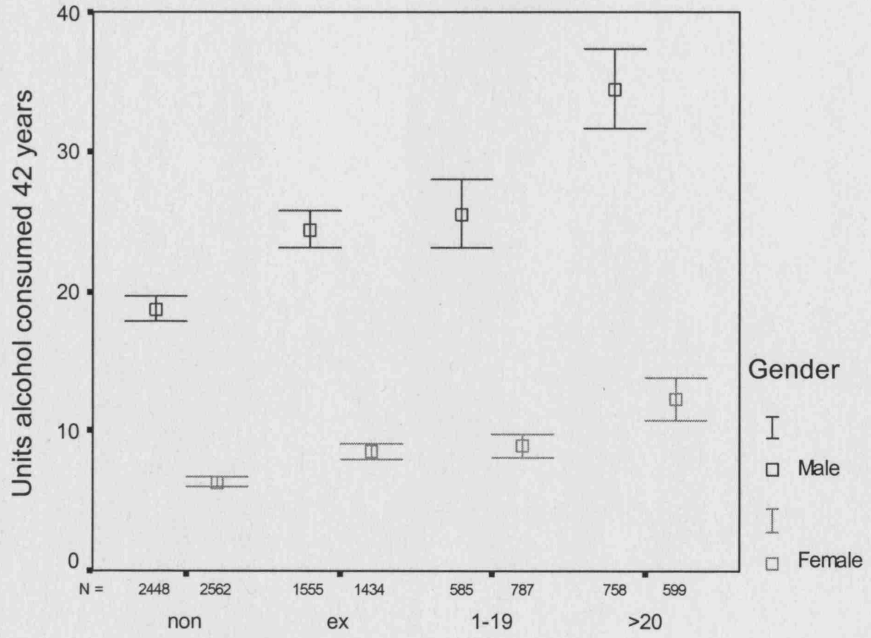


Figure 3.10a-3.10c Amount of alcohol consumed in the past week according to concurrent smoking status, men and women 23-42 years (sample is only those reporting alcohol use)





Smoking status and amount 33 years



Smoking status and amount 42 years

Table 3.13 Association between quitting smoking and subsequent drinking patterns. OR of drinking at an adult survey (time 2) in those who quit smoking between time 1 and time 2 compared to odds of drinking in those who continued smoking between time 1 and time 2.

Age	N[a]	*Binge drinkers* OR (95%CI)[c]	*Heavy drinkers* OR (95%CI)	*Non-drinkers* OR (95%CI)	*Daily drinkers* OR (95%CI)
Men					
33	1752[a]	0.63 (0.50, 0.78)	0.63 (0.47, 0.83)	1.01 (0.75, 1.36)	1.16 (0.90, 1.49)
42	1392[b]	0.68 (0.53, 0.86)	0.80 (0.62, 1.03)	0.74 (0.53, 1.04)	1.25 (0.97, 1.61)
Women					
33	1841[a]	0.78 (0.59, 1.02)	0.75 (0.47, 1.21)	0.81 (0.64, 1.03)	1.29 (0.91, 1.83)
42	1522[b]	0.57 (0.42, 0.79)	0.44 (0.28, 0.70)	0.63 (0.48, 0.83)	0.91 (0.66, 1.26)

a Sample includes participants who were smokers at 23 years and with information about drinking and smoking at 23 and 33 years.

[b] Sample includes participants who were smokers at 33 years and with information about drinking and smoking at 33 and 42 years.

[c] Binge drinkers vs other drinkers and non-drinkers. OR comparing odds of binge drinking in participants who quit smoking between 23 and 33 years compared to odds of binge drinking in participants who continued smoking between 23 and 33 years.

Appendix 3

Appendix 3.1 **Social gradients in tobacco and alcohol use**

Appendix 3.2 **Sample representativeness**

Appendix 3.1

Social gradients in smoking and drinking

There are social gradients in smoking with cigarette use being more concentrated in manual social groups and in particular heavy smoking in more manual groups (Power et al. 2004). Social gradients in alcohol use are less studied, although there is evidence that both non-drinking and heavy drinking are concentrated in more manual socio-economic groups (Marmot 1997).

Logistic regression models summarised associations between adult social class and (i) smoking and (ii) each measure of drinking. Changes in social gradients across adult surveys were tested using repeated measures multilevel models. The outcome was eg current smoking at 23, 33 and 42 years and the change over time in the social gradients was tested in models with interactions between time point and social class.

Social gradients in smoking

Strong social gradients in smoking status are evident in this cohort: at each adult age men and women in more professional and managerial occupations are less likely to smoke and less likely to smoke heavily than their counterparts from manual social groups (Table A3.2.2).

Social gradients in drinking

Social gradients in drinking vary both according to the age at which drinking is measured and also the life stage in which social position is measured. There are clear social gradients in non-drinking at each adult age; prevalence of non-drinking was higher in participants in manual than professional classes at each age in both sexes, and social gradients strengthened in men from OR1.18 (95% CI 1.10, 1.27) at 23 years to OR1.34 (95% CI 1.24, 1.44) at 42 years. ORs did not change between 23 and 42 years for women OR1.33 (95% CI 1.26, 1.39) at 23 years (Table A3.2.1). An inverse gradient was seen for daily drinking; prevalence of daily drinking among professional and managerial classes was greater than in unskilled manual groups, in men the social gradient strengthened to age 42 years, but the gradient remained stable in women. Similar patterns of social gradients are seen with social class of origin (data not presented).

Sensible drinking

Sensible drinking was associated with own social position; adults in professional occupations were more likely to be sensible drinkers than those with manual occupations. Similarly, there was a shallow social gradient by social position at birth.

Binge drinking

Own adult social position was consistently associated with binge drinking in men across the adult surveys in men: at 42 years the OR of binge drinking associated with each change in social group from manual to professional occupational group was 1.25 (95% CI 1.19, 1.32). However for women, the social gradient in binge drinking reversed from higher prevalence in the more professional social groups at 23 years OR 0.91 (0.86, 0.97) to lower prevalence in the more professional social groups at 42 years OR 1.21 (1.13, 1.21). In a repeated measures multilevel model with binge-drinking 23-42 years as the outcome, there were significant interactions between time point and social class in the women (both $p<0.05$), indicating that the association between binge drinking and social class differed between 23 and 33 years and also between 23 and 42 years. Among the men, interactions were not significant as the social gradient remained similar 23-42 years. Adults born into professional households are also less likely to binge drink or to drink heavily than those from manual households (data not presented).

Heavy drinking

Social gradients in heavy drinking in men and were stable between 23 and 42 years; OR1.16 (95% CI 1.09, 1.22) at 23 years, the prevalence of heavy drinking was higher in the manual than non-manual groups at all ages in men, but only at 23 years in women. At 33 and 42 years there were not significant trends in heavy drinking by adult social position in women (Table A3.2.1). There was not a significant change over age in the social gradients in heavy drinking in men or women. In contrast, Social gradients in heavy drinking by social class of origin were seen at 33 and 42 years in men when the prevalence of heavy drinking was greatest in the men born into manual social groups. Among women, however there was an inverse gradient with women born into professional and managerial homes more likely to be heavy drinkers at 23 and 33 years but there was no social gradient in heavy drinking at 42 years (data not presented).

Social gradients in drinking and smoking

Social gradients in never, ex and heaviness of smoking favouring the more professional social groups at each time point were seen in the 1958 cohort. This was the expected direction of associations based on other literature (Bridgwood et al 2000, p.119; Cavelaars et al. 2000; Giskes et al. 2005; Jarvis & Wardle 1999; Osler et al. 2000; Romelsjo 1989). More detailed analyses of social gradients in smoking status in the cohort are presented elsewhere; in men and women smoking status was clearly graded by social class at each age in childhood and

throughout adulthood (Jefferis et al. 2004a). Men and women from manual social groups were more likely to take up smoking, and less likely to quit smoking between 23 and 42 years than their non-manual counterparts (Jefferis et al. 2004b). There were gradients in persistent smoking (smoking at 23, 33 and 42 years) by social position in childhood and in adulthood. This relationship was similar between the genders, but for early social position was slightly stronger in women than in men and in women there was an effect of early social position after taking account of adult social position (Jefferis et al 2004a).

Social gradients in frequency and amount of alcohol use were seen in the 1958 cohort, but existing literature about social gradients in different dimensions of drinking habits is less consistent than literature about smoking habits. In the 1958 cohort, daily drinking was more common in adults in professional and managerial groups and infrequent drinking was more common in adults from manual and unskilled groups, which fits with data from national surveys (Bridgwood et al 2000, p.154). Changes over time in the social gradients in drinking frequency have been reported in a young New Zealand population. Adults with higher incomes drank more frequently as they aged from 18 to 26 years. Education level was also associated with drinking frequency at age 18 among men; more highly educated men were more likely to drink less frequently, but this gradient did not persist to age 26 years (Casswell et al 2003).

Social gradients in adult heavy drinking were seen in men but not in women in whom the prevalence of heavy drinking was lower. The literature about social gradients in heavy drinking is mixed. Some other studies have also reported that excessive drinking is more common in less educated men but that there are no gradients in women (Van Oers et al. 1999). Other studies also report heavier drinking in less educated men (Karlamangla et al 2006). Heavy drinking has also been reported to be more common in women with more professional social position while there was little social gradient in heavy drinking in men (Marmot 1997).

In the 1958 cohort, there was a social gradient in binge drinking in men at each adult age and in women at 42 years, whereby binge drinking was more prevalent in more manual social groups. This direction of this gradient fits with some other data, for example a Dutch study reported higher levels of binge drinking in less educated men and women(Droomers et al. 1999). In a younger cohort from New Zealand less-well educated men and women were more likely to drink heavily on one drinking occasion as they aged (Casswell et al 2003). However the social gradient in binge drinking in women was not consistent over time: the women from more professional social groups had elevated odds of binge drinking in their twenties, but by the time they were in their forties they had lower odds of binge drinking so the social gradient had reversed. In relation to other literature, not all studies report significant social gradients in binge

drinking (Blake et al. 2004; Lader & Meltzer 2001, p.17; Rickards et al. 2004, p.164). Indeed, inconsistencies in existing literature about social gradients in binge drinking may in part be due to changes in the gradients with increasing age (as seen in women in the 1958 cohort) and also that there are differences between studies in the drinking measures used (Casswell et al 2003). Further analysis of the social gradients in binge drinking over the adult years are presented in a separate publication (Jefferis et al. 2007).

Additionally, gradients in drinking status vary according to the stage in the life course when social class was measured. Sensible, binge and heavy drinking were more clearly socially graded according to social class of origin than adult social class. Adults born into professional and managerial household were more likely to drink sensibly and less likely to drink heavily or binge drink than their manual origin counterparts.

Previous work on the 1958 cohort has investigated other demographic characteristics of smokers and drinkers. Men and women who are married were more likely to smoke than people who live alone. However, previously separated divorced or widowed were even more likely than others to smoke, whether they were currently cohabiting or single. At each age more women than men had children. Men and women with children by 23 years were more likely to smoke than those without children, this difference decreased by 33 years when more people have dependent children; two thirds had children at 33 years compared to one quarter at 23 years (Ferri 1993). Marital status is related to early adult drinking habits; single and divorced men and women drink more units of alcohol at 23 and 33 years and their married counterparts (Power et al. 1999). They are also more likely to be heavy drinkers. Past employment histories are also related to heavy drinking; cohort members were unemployment history of more than six months are at increased risk of heavy drinking compared to those with shorter periods of unemployment (Power & Estaugh 1990).

Table A3.1.1 Association between alcohol use and adult social class at 33 years (OR, 95%CI) at 23, 33 and 42 years.

Age	N[a]	*Binge drinkers* Prevalence (%)	OR (95%CI)[c]	*Heavy drinkers* Prevalence (%)	OR (95%CI)[d]
Men					
23	6094	37.2	1.18 (1.13, 1.24)	22.0	1.16 (1.09, 1.22)
33	5466	28.0	1.23 (1.16, 1.29)	13.2	1.19 (1.11, 1.28)
42	5174	31.3	1.25 (1.19, 1.32)	21.0	1.12 (1.06, 1.19)
Test for trend					
(23 vs 33)[d]			p=0.291		p=0.407
(23 vs 42)[d]			p=0.119		p=0.555
Women					
23	6186	17.6	0.91 (0.86, 0.97)	5.9	0.90 (0.82, 0.99)
33	5668	12.9	1.09 (1.02, 1.16)	3.4	0.91 (0.80, 1.04)
42	5463	13.9	1.21 (1.13, 1.29)	6.9	1.02 (0.93, 1.12)
Test for trend					
(23 vs 33)[d]			p<0.001		p=0.550
(23 vs 42)[d]			p<0.001		p=0.974
Age	N[a]	*Non-drinkers* Prevalence (%)	OR (95%CI)[b]	*Daily drinkers* Prevalence (%)	OR (95%CI)[c]
Men					
23	6094	9.8	1.18 (1.10, 1.27)	31.3	0.90 (0.86, 0.95)
33	5466	13.2	1.33 (1.24, 1.43)	17.8	0.74 (0.69, 0.78)
42	5174	12.4	1.34 (1.24, 1.44)	25.1	0.76 (0.72, 0.81)
Test for trend					
(23 vs 33)[d]			p=0.026		P<0.05
(23 vs 42)[d]			p=0.021		P<0.05
Women					
23	6186	27.9	1.33 (1.26, 1.39)	9.8	0.72 (0.67, 0.78)
33	5668	28.5	1.25 (1.19, 1.31)	7.2	0.68 (0.62, 0.76)
42	5463	23.5	1.33 (1.25, 1.40)	15.1	0.72 (0.67, 0.77)
Test for trend					
(23 vs 33)[d]			p=0.121		p>0.05
(23 vs 42)[d]			p=0.102		p>0.05

a Sample includes participants with social class at 33 years (or 23 years if missing) (n=12229) plus alcohol data at any one of the 3 time-points.

[b] Non-drinkers vs drinkers, OR per unit change in 33-year occupational class, grouped into 4 categories. Professional and managerial (RG I&II) are baseline.

[c] Binge drinkers vs other drinkers and non-drinkers, OR per unit change in 33-year occupational class, grouped into 4 categories. Professional and managerial (RG I&II) are baseline.

[d] Heavy drinkers vs other drinkers and non-drinkers, OR per unit change in 33-year occupational class, grouped into 4 categories. Professional and managerial (RG I&II) are baseline.

e The change in social gradient for drinking from 23 to 42 years was tested using the interactions of qualifications with 33-year time point and also qualifications with 42-year time point in a repeated measures model

Appendix 3.2

Sample representativeness

Table A.3.2.1 Distribution [%(n)] of social class at birth in the original birth sample compared with the distribution in the sample with smoking data 23-42 years

	Birth sample		42-year sample with full smoking and drinking frequency[a]		Analysis sample for 45-year smoking and drinking models[b]	
	N	% (95%CI)	N	% (95%CI)	N	% (95%CI)
Total N	16,966		7968		6654	
Men						
Class I&II professional	1488	17.0 (16.2,17.8)	741	19.7 (18.4,21.0)	639	20.3 (18.9,21.7)
Class IV&V & no head of household	2096	23.9 (23.0,24.8)	797	21.2 (19.9,22.5)	645	20.5 (19.1,21.9)
Women						
Class I&II professional	1391	16.9 (16.1,17.8)	756	18.0 (16.8,19.2)	633	18.3 (17.0,19.7)
Class IV&V & no head of household	2025	24.7 (23.7,25.6)	936	22.3 (21.0,23.6)	748	21.6 (20.3,23.1)

[a] Sample at 42 years with smoking and drinking data 23-42 years=8515. The total N with data on social class at birth is 7968/8515

[b] Analysis sample at 45 years with data for smoking and drinking data 23-45 years =7072. The total N with data on social class at birth is 6654.

There is some evidence that the sample with complete data on smoking 23-42 years and drinking 23-42 years or 23-45 years over-represents those in more professional social classes and under-represents those in more manual social classes. However, most analyses presented in this chapter use fewer measures of smoking and drinking and do not require full data on smoking and drinking between 23 and 45 years and the sample is more representative of the sample at birth.

Adolescent smoking and drinking

In the sample with full smoking data 16-42 years, the distribution of smokers at 16 years is 32% (n=990) men and 29% (n=999) women, this is similar to the full cross sectional sample at 16 years 35% (n=2118) men 31% (n=1783) women. In the sample with full alcohol use data, the prevalence of drinking at least weekly age16 years is 54% (n=1697) men 42% (n=1479) women, which is similar to the full cross sectional sample at 16 years 52% (n=3191) men 40% (n=2318) women.

Chapter 4, Childhood Cognitive Ability and Adult Health Behaviours

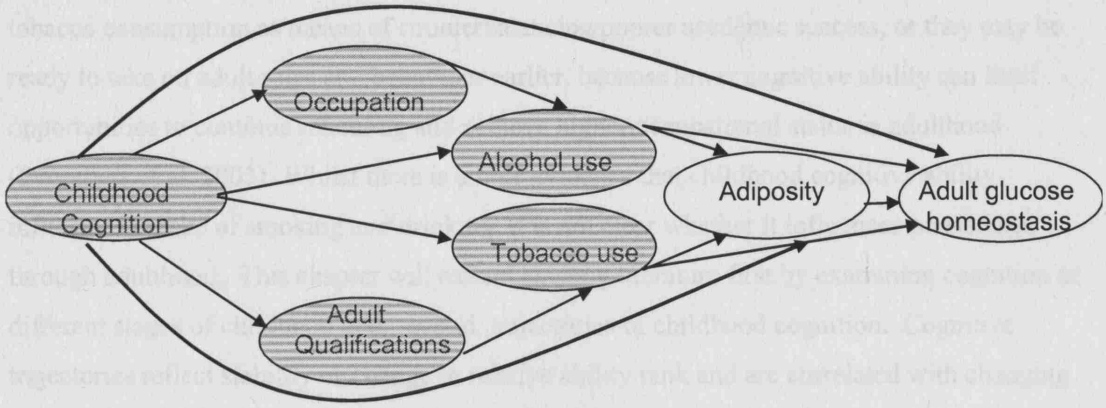


Figure 4.1 Conceptual framework

Introduction

The increasing importance of a lifecourse perspective to understanding the development of adult disease has broadened the focus of epidemiological research to include early as well as adult experiences. An emerging body of literature demonstrates associations between higher childhood cognitive ability and lower risks of adult morbidity (Martin et al 2004) and mortality risks many decades later (Hart et al 2004; Whalley & Deary 2001) (Chapter 1). Associations between cognitive ability and adult morbidity or mortality may be mediated by several pathways including greater receptiveness to health behaviour messages (preventive health) in individuals with higher cognitive ability. To date little literature exists about associations between childhood cognitive ability and smoking or drinking across adulthood and, as highlighted in Figure 4.1, these associations are investigated in this chapter. Pathways from childhood cognitive ability through adult social position and educational level will also be investigated. Subsequent chapters build on these analyses to investigate other pathways between early ability and adult morbidity (Figure 4.1).

There is a large literature about initiation of heath behaviours in adolescence and early adulthood. This is the life stage when smoking is initiated (Chassin et al. 1990), purchasing alcohol use becomes legal, drinking more than sensible limits is most prevalent and mean consumption is highest (Lader & Meltzer 2001, p.12). It is also when highest educational qualifications are mostly achieved. Prior research indicates that lower achieving and lower aspiring children are more likely to take up cigarette smoking (Conwell et al. 2003) and poor school performance predicts drinking status, and frequency and amount of alcohol use (Bucholz 1990; Casswell et al. 2002). Ability and educational achievement also predict problem drinking

between adolescence and early adulthood (Fergusson et al. 2005). Thus cognitive growth and development throughout childhood, not just at adolescence or in early adulthood may influence persistence of health behaviours. Adolescents with lower cognitive ability may use alcohol or tobacco consumption as means of counterbalancing poorer academic success, or they may be ready to take on adult roles and behaviour earlier, because lower cognitive ability can limit opportunities to continue schooling and achieve higher occupational status in adulthood (Droomers et al. 2003). Whilst there is ample evidence that childhood cognitive ability influences uptake of smoking and drinking, it is not clear whether it influences persistence through adulthood. This chapter will extend existing literature first by examining cognition at different stages of childhood and, second, trajectories of childhood cognition. Cognitive trajectories reflect stability or change in relative ability rank and are correlated with changing social circumstances(Jefferis et al 2002), engagement with school, self-efficacy and self-esteem. Health psychology literature indicates that self-efficacy about a behaviour is strongly associated with that behaviour (for example feeling capable of quitting smoking). In contrast, specific knowledge about the positive or negative effects of a particular behaviour (that for example, smoking causes many diseases) is a poor predictor of that behaviour (Conner & Norman 2005).

Childhood cognitive ability may be independently associated with adult health behaviours or simply be a marker for a trajectory to later qualifications and occupational status which then act directly or indirectly on health behaviours and health status (Figure 1). Adult educational qualifications and occupational opportunities may both shape social experiences and influence attitudes, and opportunities to engage in health behaviours. In the UK, northern Europe and USA, more highly educated people are less likely to engage in health-harming behaviours (particularly smoking and heavy drinking, poor diet and low levels of physical activity)(Lynch et al 1997). Educational gradients in health behaviours mirror gradients based on occupational position or housing tenure. Whilst the size of the educational gradients differs between behaviours and by gender and time period, the overall pattern in that region is similar. Most studies of educational gradients use a measure of highest attained qualifications which reflects accumulated effects of childhood cognitive development as well as social and cultural norms from earlier in life. Highest attained qualifications are also correlated with adult life circumstances; being employed, occupational level and domestic roles including partnership and parenting (Ferri1993, pp.45-46; Randall et al. 2005).

Very few studies have investigated pathways from childhood ability to adult health outcomes through health behaviours and adult educational level and social position. A Danish study reported that lower cognitive ability in young men was associated with higher risk of non-drinking, but this was mediated by adult socioeconomic status, whereas no significant association between cognitive ability and heavy drinking was found. Smoking was associated

with lower cognitive ability but the pathways from ability to adult smoking or heavy drinking were not tested (Mortensen et al. 2005). In a Scottish study, quitting smoking during adulthood was associated with lower 11-year cognitive ability but that the association was entirely mediated by adjustment for adult socioeconomic status and deprivation measures (Taylor et al. 2003). A New Zealand birth cohort study reported that smoking and nicotine dependence at age 25 years were associated with lower cognitive ability at ages 8 and 9 years, but did not examine pathways between childhood ability and adult smoking (Fergusson et al. 2007). In the same cohort, associations between childhood cognitive ability and alcohol abuse and dependence at age 25-years were studied, but dependence was not associated with cognitive ability (Fergusson et al 2005).

This chapter will examine associations between cognitive development and health behaviours, extending current literature to include childhood cognitive development earlier in the lifecourse and health behaviours at later stages of the lifecourse than previously studied. A large literature exists about factors associated with initiation of health behaviours, including male gender, increasing age at initiation, perceptions of family approval and modelling behaviour on parents and peers, coping with anxiety and depression, problem behaviour, aggressiveness, sensation-seeking, as well as lower engagement with school and poorer school performance (Donovan 2004; Tyas & Pederson 1998). Many risk factors are associated with cognitive ability or academic aspirations and may be pathways through which cognitive trajectories influence persistence of adult health behaviours. As it is not possible to study all of these factors, the focus here is on understanding associations between childhood cognitive ability and adult health behaviours.

Social position of origin may confound associations between childhood cognitive ability and adult health behaviours. Manual social origins are consistently associated with poorer childhood cognitive ability, in this cohort (Jefferis et al 2002) and others (Lawlor et al 2005b; Lawlor et al 2006a). Additionally, manual social origins are associated with elevated risks of smoking, non-drinking and binge drinking in adult life (Lawlor et al. 2005a; Power et al 2004; van de Mheen et al. 1998; Yang et al 2007). Social position in childhood is therefore considered as a confounder in analyses of childhood cognitive ability and health behaviours.

Childhood cognitive ability is but one of many potential influences on adult health behaviours. Another important factor associated with adult health behaviours is childhood and adolescent problem behaviours. Children with problem behaviours are at increased risk of initiating cigarette or alcohol use (and other health behaviours) (Conwell et al 2003; Donovan 2004). Associations between problem behaviours and poor childhood ability have been repeatedly documented (Conwell et al 2003; Fergusson & Horwood 1995; Hinshaw 1992). The direction

of causality between childhood ability and problem behaviours is not clear: problem behaviour may predict poor school achievement or poor school achievement may predict problem behaviour. Hence, the role of childhood problem behaviours as either mediators or confounders of associations between childhood cognitive ability and adult cigarette and alcohol use patterns will be tested.

As illustrated in Figure 4.1, it is hypothesised that poorer childhood cognitive ability will be associated with poorer adult glucose regulation, and that this may operate through uptake and persistence of adult health behaviours, which are the main focus of this chapter. It is hypothesised that poorer childhood cognitive ability trajectories will be associated with smoking, heavy and binge drinking and non-drinking. These associations may operate through the pathways of attainment of adult qualifications and social position, illustrated in Figure 4.1. Hence this chapter aims to investigate whether:

1. cognitive trajectories, ie initial (7-year) level of ability and change in ability rank (between 7 and 16 years) are associated with smoking (or drinking)?

2. associations between childhood cognitive ability and adult health behaviours confounded by childhood social position or behavioural problems?

3. associations between childhood cognitive ability and adult health behaviours mediated by highest educational achievements and adult occupational position?

As discussed in Chapter 2, childhood cognitive ability measures are age-specific reading and maths ability tests. The tests are strongly correlated with each other (and with verbal and non-verbal ability), Pearson's r varies between 0.47 and 0.75 (Table A2.2.1). Whilst individuals can be discordant on their ability levels in the two domains, the correlations give rise to the expectation that adult health behaviours will be similarly associated with reading and maths tests.

Methods

A full description of measures and how they are treated in analyses is given in Chapter 2. Maths and reading test scores and were converted to z-scores (genders together) so relative position, or rank, of individuals could be compared across the three childhood ages (7, 11 and 16 years). The maths and reading z-scores were coded negatively in the analyses; ie a unit increase in z-score is a standard deviation decrease in raw maths or reading ability test score. Improvement in rank relative to peers is indicated by a negative value of change in z-score between 7 and 16 years. Inverse coding was used so that regression coefficients are (for the most part) positive and odds ratios are greater than 1, and easier to interpret. Chapter 3 (Tables

3.1 and 3.8) describe adult cigarette and alcohol use patterns.

As a preliminary step, logistic regression models were used to assess the association between maths (or reading) z-scores separately at each childhood age with adult drinking and smoking. Graphs of drinking and maths z-scores were examined, to investigate the linearity of associations between maths or reading z-scores and drinking or smoking measures.

For aim 1, individual maths or reading trajectories from age 7, 11 and 16 years, were summarised using repeated measures multilevel models (in MLwiN). The intercept corresponds to the initial z-score at age 7, and the slope to the change in rank of maths (or reading) between 7 and 16 years. The estimates from the multilevel model for predicted intercept and slope for cognitive ability scores were used as dependent variables in logistic regression models to estimate the odds of drinking or smoking at each survey (time-point) in adulthood (23, 33 and 42 years).

Analyses were run to estimate odds ratios (ORs) separately for (i)current smoking, (ii)non-drinking, (iii)binge drinking and (iv)heavy drinking at 23, 33 and 42 years in turn. Likewise Relative Rate Ratios (RRRs) for usual drinking frequency at 23, 33, 42 and 44 years associated with maths (or reading) z-scores were estimated in multinomial regression models. First, ORs or RRRs from unadjusted models with initial level and change in maths or reading rank are reported. For aim 2, to establish whether the associations between maths (or reading) level and change 7 to 16 years, are confounded by social position of origin, models were adjusted for class of origin. Models were next adjusted for behavioural problems in childhood to investigate whether behaviour problems confound or mediate the associations between childhood cognitive ability and adult smoking or drinking. Finally for aim 3, models were adjusted for adult educational qualifications and occupational position to see if these factors were mediators.

A summary measure approach was used for the trajectories of health behaviours; a smoking history variable was constructed and the number of adult time-points that individuals were drinkers was summed across 23, 33 and 42 years, producing a score (range 0 to 3) (Chapter 3). Associations between maths trajectories and the summary drinking and smoking measures were investigated using ordered polytomous regression models. The final stage of analyses investigated whether the initial level (age 7) and change (between 7 and 16 years) in maths z-scores were associated with the change in either drinking or smoking across the adult survey ages (23, 33 and 42 years), using repeated measures multilevel models. Models were adjusted for potential mediators educational qualifications or occupational position.

Results

The analysis samples are similar to the birth sample, but at 42 years somewhat under-represent groups from manual social origins (Appendix4.1, Table A4.1.1).

Cross-sectional analyses of maths and reading z-scores at 7,11 and 16 years are presented as a preliminary step in Appendix 4.2, before analyses of cognitive trajectories.

Cigarette smoking and childhood cognition

Children who performed worse in maths tests at ages 7, 11 or 16 years were more likely to smoke in adulthood, and if they did smoke, less likely to quit. Appendix 4.2, Table A4.2.1 presents ORs for associations between maths z-scores at each childhood age and adult smoking or quitting smoking. At each adult age ORs for smoking were significant; decreasing ability level (ie increasing z-score) was associated with higher odds of current smoking and lower odds of quitting smoking. The OR for smoking at 23 years was 1.15 (95%CI 1.09. 1.21) per standard deviation (SD) increase in 7-year maths z-score and strengthened somewhat to 1.48 (95%CI 1.39, 1.57) for 16-year maths z-score (Table A4.3.2). The ORs increase progressively with increasing age of smoking; to 1.69 (95%CI 1.57, 1.83) for 42-year smoking per SD increase in 16-year maths z-score. The pattern is mirrored by the ORs for quitting smoking. Among smokers, participants with lower maths ability (higher z-scores) were less likely to quit, and associations with 16-year z-scores were stronger than with 7-year z-scores. Further, the ORs were stronger for later quitting (by 42 years) than earlier quitting (by 23 years). Thus childhood ability discriminated increasingly between groups with different smoking habits later in life.

Alcohol drinking and childhood cognition.

Several categories of alcohol use were investigated: drinking frequency, non-drinking, binge drinking and heavy drinking. Poorer ability was associated with increased odds of non-drinking compared to drinking; one SD increase in maths z-score was associated with about 40% increased odds of non-drinking (Appendix 4.3 Table A4.3.2).

Associations between childhood ability and binge drinking differed by gender. In men, 7-year maths z-score was not associated with binge drinking. However poorer ability (higher z-scores) at 11 and 16 years were associated with elevated odds of binge drinking at each adult age; OR 1.25 (95%CI 1.17, 1.33) at 42 years, per SD increase in 16-year z-score (Table A4.3.2). In contrast, girls with poorer maths ability at 7, 11 and 16 had lower odds of binge drinking at 23 years than girls with higher ability (ie girls with lower z-scores); for example OR 0.90 (95%CI 0.84, 0.98) for 16-year maths. Maths z-scores were not associated with binge drinking at 33 years, but the association between 42-year binge drinking and childhood maths z-scores was reversed. The OR for binge drinking was 1.41 (95% CI 1.28, 1.56) per SD increase in 16-year maths z-score.

Associations between heavy drinking and maths z-scores were weaker and less consistent than for binge drinking. In men 7 and 11 year maths z-scores were not associated with heavy drinking, but ORs of around 1.10 were seen for 16-year maths z-scores (Table A4.3.2); boys with lower 16-year maths ability had higher odds of adult heavy drinking. In contrast, women with poorer 7 or 11 year maths ability had lower odds of heavy drinking at 23 or 33 years but not at 42 years.

Decreased drinking frequency was associated with lower maths ability (higher z-scores) and associations were stronger at later adult ages (data not presented).

In summary, maths z-scores at each age in childhood were associated with current and ex-smoking and drinking frequency, associations were strongest with later childhood ability. Maths ability in later childhood was associated with binge and heavy drinking.

Are trajectories of cognitive ability associated with adult smoking and drinking?

The cognitive trajectories (7-year z-score and change 7-16 years) were described in Chapter 2, z-scores were coded inversely so a high 7-year z-score corresponds to lower ability and a positive 7-16 year change z-score corresponds to a decline in ability rank 7-16 years. Results for reading z-scores are mostly similar to those reported here for maths z-score (unless specifically noted) and are therefore presented in Appendix 4, Tables 4.1a-4.1f.

Smoking and cognition through childhood

The first column of Table 4.1a presents ORs for the association between (i) 7-year maths z-score and (ii) 7-16 year change in z-score (adjusted for each other) with current smoking at 23, 33 and 42 years. Lower initial ability and declining ability rank (ie increased 7-year z-score and 7-16 year change) were associated with elevated odds of adult smoking.

Drinking and cognition through childhood

Table 4.1b presents equivalent results for adult non-drinking (never and "special occasion" drinkers compared to drinkers). Lower maths ability rank (higher 7-year maths z-scores) was associated with increased odds of non-drinking at 23, 33 and 42 years. Decline in maths ability rank (higher 7-16 year z-score) was only associated with elevated odds of non-drinking at 42 years. Repeating analyses using only the "never" drinkers at each age, poorer 7-year ability was associated with raised odds of "never" drinking at each adult age.

The ORs in the first column of Table 4.1c indicate that for men lower ability (higher 7-year

maths z-score) was associated with raised odds of binge drinking at 23 and 42 years. Decline in ability rank (increase in 7-16 year z-score) was consistently associated with higher odds of binge drinking at each adult age. The results for women's binge drinking differed. As in Table A4.2.2, the association between 7-year maths z-score and binge drinking changed with increasing age; from a negative association for 23-year binge drinking to a positive association for 42-year binge drinking. There were raised odds of binge drinking only at 33 and 42 years associated with 7-16 year change in maths z-score.

Associations between maths z-scores and heavy drinking were less consistent. Among men, 7-year z-score was not associated with heavy drinking but declining ability rank (increasing 7-16 year z-score) was associated with elevated odds of heavy drinking at each adult age (Table 4.1d). In contrast, among women, poorer 7-year ability was associated with lower odds of heavy drinking at 23 and 33 years and there were no associations with the 7-16 year change in ability rank. Results using reading test scores differed; lower 7-year ability (higher z-score) was associated with elevated odds of heavy drinking at 23 years in men and associations with change in reading rank 7-16 years were not seen (Appendix 4.4, Table A4.4.1d). In contrast, for women, lower reading ability (higher 7-year z-score) but not change in rank 7-16 years was associated with lower odds of heavy drinking at 23 and 33 years. This mirrors the association seen for 7-year ability and women's binge drinking at 23 years (Table A4.4.1c)..

Lower usual drinking frequency was associated with lower 7-year maths ability; with each SD increase in 7-year maths z-score, the relative rate ratio (RRR) of drinking less frequently compared to daily drinking increased at each adult age. In men, the RRR for 23-year weekly drinking compared to daily drinking was 1.15 (95% CI 1.07, 1.25) and increased to 1.55 (95% CI 1.34, 1.81) for infrequent or never drinking. The RRR of drinking weekly and monthly compared to daily, did not increase systematically with declining 7-16 year maths rank, although infrequent and never drinking compared to daily drinking was associated with lower 7-16 year maths rank. Lower 7-year reading ability was consistently associated with increased RRR of drinking less frequently. However, in contrast to the maths scores, change in reading z-scores 7-16 years was more consistently associated with drinking frequency. Decline in reading ability 7-16 years was associated with drinking less frequently.

In summary, lower 7-year maths ability and decline in maths rank7-16 years were associated with higher odds of current and lower odds of quitting smoking. Lower 7-year ability was more consistently associated with raised odds of non-drinking, binge and less frequent drinking. Heavy drinking was less consistently associated with maths trajectories.

Are associations between childhood ability and adult health behaviours confounded by social position of origin?

Social position was associated with both the 7-year z-score and 7-16 year change in z-score of maths and reading; manual social groups had lower 7-year maths or reading ability and poorer trajectories to 16 years (Appendix 4.3, Tables A.4.3.1-4.3.4). Manual social class at birth was also associated with greater risks of smoking at each adult time point and lower risks of quitting smoking, higher risks of non-drinking, binge drinking, lower frequencies of daily drinking and there were weaker associations with heavy drinking.

Despite associations described above, the adjusted models in column 2 of Tables 4.1a- 4.4f provide little evidence that social position of origin confounded the associations between (i) initial level or (ii) change in maths and reading rank between 7 and 16 years and any of the smoking or drinking measures. Hence, the associations between maths and reading ability and drinking or smoking are largely independent of social origins.

In summary, social position of origin did not confound associations between (i) 7-year or (ii) 7-16 year change in maths and reading z-scores and any of the smoking or drinking measures.

Are associations between childhood ability and adult health behaviours confounded or mediated by childhood behavioural problems?

At each age, the groups with borderline and problem behaviour had poorer 7-year ability and poorer trajectories to 16 years than the "normal" group (Tables A4.2.1-A4.2.4, Appendix 4.2). Further the "problem" groups had higher prevalence of smoking, binge or heavy drinking and lower prevalence of quitting smoking or daily drinking in adulthood. From existing literature it was not clear whether behavioural problems would confound or mediate between childhood maths (and reading) trajectories and drinking or smoking in adulthood. Therefore logistic regression models of each of the smoking or drinking outcomes were run in turn with adjustment for behavioural problems at 7 years, at 11 years and finally at 16 years. The degree of attenuation of the coefficient estimates on adjustment for each of the behavioural scores was then examined; if 7-year behavioural problems were acting as a confounder and influencing 7-year z-scores and 7-16 year change (as well as adult smoking or drinking) then the coefficients for maths and reading would be expected to attenuate after adjustment for 7-year behavioural problems. Adjusting models of smoking and drinking for 7-year behavioural problems had negligible impact on the coefficients for 7-year maths z-score or 7-16 change in z-score. Typically the second decimal place of the OR was changed by 1-2 points (data not presented). Therefore behavioural problems at the start of the cognitive trajectories were not acting to confound the association between ability and later smoking or drinking. However, the models adjusted for 16-year behavioural problems showed more substantial attenuation of the

association between childhood ability and adult smoking and drinking. The attenuation of the ORs in these models was interpreted as indicating mediating effect of 16-year behaviour because the 16-year behavioural problems occur in time after most of the childhood cognitive trajectory has occurred.

The models in the third column of Table 4.1a adjusted for 16-year behavioural problems age (and social class at birth) indicated that 16-year behavioural problems mediate associations between childhood maths z-score and smoking in adulthood. For example, the OR for smoking at age 42 years in men (adjusted for social class at birth) was 1.43 (95%1.30, 1.56) which was attenuated to 1.29 (95%CI 1.18, 1.42). Among women the equivalent attenuation was from 1.59 (95%1.45, 1.75) to 1.39 (95%1.26, 1.54). The associations between 7-16 year change in maths z-score with smoking were also attenuated on adjustment for 16-year behavioural problems in both men and women.

Associations between 7-year maths z-score and also 7-16 year change in maths z-score and non-drinking at 33 and 42 years in men and at 23 and 42 years in women were partly mediated by 16-year behavioural problems (Table 4.1b, column 3). Among men, adjustment for 16-year behavioural problems entirely mediated the association between 7-year z-score and binge drinking, and partly mediated the association between 7-16 year change in maths z-score and binge drinking. Among women, 16-year behavioural problems were not a strong mediator of the association between either 7-year or 7-16 year change in maths z-score and binge drinking (adjusted for social class at birth), with the exception of binge drinking at 42 years which was partly mediated (Table 4.1c). For men, 16-year behavioural problems were not a strong mediator of associations between 7-16 year change in maths z-score and heavy drinking, except at 33 years where the association was partly mediated. Among women, 16-year behavioural problems were not a strong mediator between either 7-year or 7-16 year change in maths z-score and heavy drinking (Table 4.1d). Neither were 16-year behavioural problems a mediator of associations between either 7-year or 7-16 year change in maths z-score and drinking frequency (Table 4.1e and f).

In summary, early childhood behaviour problems did not confound associations between (i) initial level or (ii) change in maths and reading rank between 7 and 16 years and smoking or drinking. However behavioural problems in adolescence did mediate between maths ability and adult smoking, non-drinking and binge drinking.

Are associations between childhood ability and adult health behaviours mediated by adult educational level or occupational status?

Occupational social position and educational qualifications by 33 years were positively correlated; spearman ρ=0.50. Adult social position and educational qualifications were associated with both 7-year or 7-16 year change in maths (and reading) z-score; individuals with lower 7-year maths or reading and poorer trajectories of change to 16 years were more likely to have lower educational qualifications and manual occupations than those with higher childhood test scores (Appendix 4.2 and Appendix A2, Table 2.2.6).

Smoking and cognition through childhood

Associations between 7-year maths z-score or change in maths z-score 7-16 years and adult smoking were attenuated on adjustment for adult social position and highest educational qualifications (Table 4.1a, columns 4 and 5). Highest qualifications were a stronger mediator between maths z-scores and smoking than social position. However the ORs of smoking associated with poorer childhood maths ability remained significantly elevated.

Drinking and cognition through childhood

On adjustment for adult educational level or educational qualifications, the associations between non-drinking and poorer 7-year maths (higher z-score) were somewhat attenuated, but still positive and significant (Table 4.1b). The association between decline in 7-16 year rank (increase in z-score) and 42-year non-drinking was entirely mediated by adult qualifications (and also by occupational class in women). Repeating analyses using the "never" drinkers at each age, the association between higher intercept (lower initial ability) with raised odds of never drinking at each age was attenuated by social class and higher qualifications adjusted separately.

For binge drinking, among men 7-years maths z-score was associated with binge drinking only at 42 years and this was reduced to null on adjustment for either highest educational qualifications or occupational position (Table 4.1c). However, the OR for binge drinking by 7-16 year decline in maths rank (increase in z-score) was positive and significant although somewhat attenuated on adjustment at each adult age. Thus change in maths z-score across childhood had a lasting association with men's binge drinking; decreasing rank increased odds of binge drinking at successive adult ages. Among women, the patterns of associations between 7-year maths z-score and 7-16 year change in maths z-scores and binge drinking were attenuated somewhat, but still positive and significant at 23 years and negative and significant at 42 years with separate adjustments. However adjustment for both highest educational qualifications and occupational position mostly reduced associations to null.

The associations between 7-16 year change in maths z-score and heavy drinking in men were attenuated but robust to adjustment for both educational qualifications and occupational class. Similarly the associations between 7-year maths z-score and heavy drinking in women at 23 and 33 years were also robust to adjustment and little changed (Table 4.1d).

The associations between drinking frequency at each adult age and 7-year maths z-score were attenuated but not removed on adjustment for either adult educational level, social class, or both adult exposures (Table 4.1e and f).

In summary, educational qualifications were partial mediators of associations between cognition and (i)smoking (ii) non-drinking (iii)heavy drinking (iv) drinking frequency. However they entirely mediated some of the associations between 7-year maths ability and adult binge drinking.

Are associations between childhood maths and reading trajectories and adult smoking and drinking entirely mediated in adjusted models?

Childhood cognition and smoking

Among men, the associations between 7-year maths z-score and adult smoking were entirely mediated, whereas 7-16 year change in maths z-score was still associated with elevated odds of adult smoking (Table 4.1a, columns 4 and 5). Among women poorer ability indicated by both increasing 7-year maths z-score and change in maths z-score were associated with attenuated but still significantly elevated odds of smoking at each adult age.

Childhood cognition and non-drinking

Among men and women, associations between 7-year maths z-score and non-drinking were attenuated but not entirely mediated on adjustment for all the pathways (Table 4.1b). Whereas weaker associations between 7-16 year change in maths z-score and non-drinking were entirely mediated by adult education level.

Childhood cognition and binge drinking

Associations between 7-16 year change in maths z-score and adult binge drinking were mostly entirely mediated (Table 4.1c). However, associations between increase 7-16 year change in maths z-score (ie decline in maths ability 7-16 years) and binge drinking were still somewhat elevated at 23 years (men) and at 42 years (women).

Childhood cognition and heavy-drinking

In women adjusted associations between 7-year maths z-score and heavy drinking were attenuated but still significant at 23 years, but entirely mediated at 33 years (Table 4.1d). In

men, weak inverse associations between 7-year maths z-score and heavy drinking became apparent at 33 and 42 years after adjustment for all the pathways (ie higher ability was associated with increased risks of heavy drinking). Adjusted associations between 7-16 year change in maths z-score and heavy drinking in men were attenuated; the OR was still significant at 23 years, but not at 33 and 42 years.

Childhood cognition and usual drinking frequency

Adjusted associations between poorer 7-year maths (higher z-score) and less frequent usual drinking were partly mediated but still significant (Tables 4.1e and f). Adjusted associations between 7-16 year change in maths z-score and infrequent drinking were seen in women at 42 years.

Smoking trajectories and cognition through childhood

Next adult smoking history (see Chapter 3, Figure 4) was used as the dependent variable in a multinomial regression analysis. Relative risk ratios (RRRs) for (i) early and (ii) late quitting smoking, or 42-year (iii) light or (iv) heavy smoking were contrasted with the never smoker 23-42 years baseline group. RRR are per SD increase in 7-year maths z-score and 7-16 year maths z-score. Table 4.2a, column 1 shows that lower 7-year maths ability (higher z-score) was associated with higher RRR of light and heavy 42-year smoking, and additionally in women, with quitting smoking. Decline in maths rank 7-16 years was associated with increased RRR of quitting smoking and current smoking. Associations between smoking and maths z-scores were not much changed by adjustment for social position of origin but were mediated by 16-year behavioural problems and adult qualifications, but less by adult class. Adjusted associations were all significant, apart from 7-year maths z-score with quitting smoking in men.

Drinking trajectories and cognition through childhood

Drinking trajectories are first investigated with a summary statistics approach (Tables 4.2b-d); the number of occasions (0-4) that a person is a drinker on the 23, 33 and 42-year surveys is the dependent variable in multinomial regression (distributions of the summary outcome variables in Chapter 3, Figures 3.5-3.8). Lower 7-year maths ability (higher z-score) was associated with non-drinking on more occasions in adulthood (Table 4.2b). Change in maths z-score 7-16 years was less consistently associated with repeated non-drinking. Associations were not much confounded by social position of origin, but attenuated somewhat by 16-year behavioural problems and more so by adult qualifications and social class. Fully adjusted associations were significant between 7-year maths z-score and being a non-drinker on one or two occasions compared to none in men and between being a non-drinker on three occasions compared to none in women.

Lower 7-year maths ability (higher z-score) and decline in maths rank (higher 7-16 year change z-score) in men were both associated with repeated binge drinking (Table 4.2c). Adjustment for educational qualifications and to a lesser degree, behavioural problems and adult social class completely attenuated associations with 7-year maths z-score but not 7-16 year maths z-score.

7-year maths ability was not associated with repeated heavy drinking. Among men heavy drinking on three occasions compared to never, was only associated with higher 7-year maths ability (lower z-score) in the fully adjusted model. In contrast, associations between declining ability rank 7-16 years (increasing maths z-score) and increased repeated heavy drinking were robust to adjustment (Table 4.2d). Repeated heavy drinking in women was not associated with 7-year z-score except after adjustment for educational level, nor was it associated with change in z-score 7-16 years.

In summary, associations between cognitive trajectories and smoking were partly mediated and associations between cognitive trajectories and binge drinking were fully mediated by adult class and educational level. Repeated heavy drinking was not consistently associated with cognitive trajectories.

The association between childhood ability and persistence of health behaviours was next addressed using multilevel models with smoking (or drinking) at three adult occasions as the outcome and the 7-year maths (or reading) z-score and change 7-16 years as predictors. The models tested whether the associations between initial ability and change in ability rank on smoking (or drinking) differed between the adult surveys, as indicated by interactions between time-point and the intercept or the slope of maths ability. Models were next adjusted for educational qualifications and social class, and then the process was repeated for reading scores.

In repeated measures models of smoking across adulthood, men and women with lower 7-year maths ability (higher z-scores), compared to those with higher ability (lower z-scores) were more likely to smoke at either 33 or 42 years compared to 23 years. Men and women with lower 7-year maths ability (higher z-scores) were more likely to quit at 33 or 42 than 23 years (interactions between (i) age 33 and 7-year maths z-score and (ii) age 42 and 7-year maths z-score, $p<0.05$ for current smoking and for quitting). There were not significant interactions between maths trajectories and change in non-drinking or heavy drinking across adulthood for men or women. Whereas women with lower 7-year maths ability (higher z-scores) were more likely to binge drink at 33 or 42 years than 23 years (interactions between (i) age 33 and 7-year maths z-score and (ii) age 42 and 7-year maths z-score were both $p<0.05$ for binge drinking). 7-16 year change in maths ability was associated with change in binge drinking between 23 and 42 years; women whose ability rank decreased were more likely to binge drink at either 33 or 42

than 23 years compared to those whose rank remained stable or increased. To illustrate, among women whose maths rank decreased (eg 0.25 increase in z-score), prevalence of binge drinking at later ages was higher; 16% at 33 and 18% at 42 years compared to 12% at both 33 years and 42 years among women whose rank increased (0.25 decrease in z-score), and 14% at 33 and 15% at 42 years among those who remained the same rank between 7 and 16 years. These differences persisted after adjustment for later social position or educational qualifications. Interactions between (i) age 33 and 7-16 year maths z-score and (ii) age 42 and 7-16 year maths z-score were both $p<0.05$ for binge drinking. For men, neither the 7-year maths z-score nor the change in z-score to age 16 was associated with changes in binge drinking over the three adult time-points.

In summary, cognitive trajectories were associated with changes in smoking across adulthood. There was not evidence that change in non-drinking or heavy drinking was associated with childhood cognitive trajectories. Stopping binge drinking with increasing adult age was associated with both lower 7-year ability and a decline in ability level to 16 years.

Discussion

Main findings

Childhood cognitive ability trajectories across childhood were consistently and significantly associated with adult smoking. Children with higher 7-year cognitive ability rank and those who increased ability rank relative to their peers were less likely to smoke at each adult age. Childhood ability was more strongly associated with smoking at older ages (age 42 compared to 23) and associations were not confounded by social position of origin or mediated by either highest qualifications or adult occupational status. Childhood ability trajectories were also associated with adult smoking history 23- 42 years. Drinking status (non-drinker or drinker), binge drinking and usual drinking frequency throughout adult life were associated with childhood ability levels. Men and women with lower 7-year ability relative to their peers were more likely to be non-drinkers than drinkers in their twenties and forties. Decreases in relative ability rank 7-16 years were associated with higher odds of binge drinking at each adult age in men. In women however, the associations between declining ability rank and binge drinking reversed between 23 and 42 years. Women with increased ability rank in maths or reading ability 7-16 years were more likely to binge drink in their twenties than women with declining ability rank, but the reverse was true in their forties when the women with declining ability 7-16 years were more likely to binge drink. These associations were largely mediated by adult social position and educational level. Associations between ability and heavy drinking were weaker and less consistent. Decline in maths ability rank 7-16 years was associated with increased odds of heavy drinking in men, although associations were mediated by behaviour problems, adult social class and qualifications. In women, the associations between lower 7-year ability and

increased odds of heavy drinking at 23 and 33 years, were also mostly mediated by adolescent behavioural problems and adult social position, although the association with 23-year drinking remained significant. Drinking frequency was most consistently associated with 7-year maths and reading levels and less so with 7-16 year change in ability rank. The association between lower 7-year maths ability and less frequent drinking was partly mediated by adult social class (men) and highest qualifications (women).

Non-drinking on more occasions 23-42 years was associated with lower 7-year ability and was partly mediated by adult qualifications, but not consistently associated with change in ability 7-16 years. Repeated heavy drinking 23-42 years was not consistently associated with 7-year ability and only in men was associated with decline in ability 7-16 years. Repeated binge drinking was associated with lower 7-year ability and was entirely mediated by adjustments, and also associated with decline in ability 7-16 years after adjustment. The number of occasions that a woman was a binge drinker was not associated with maths ability. However, taking account of the timing of binge drinking in multilevel models, both initial ability and decreasing ability rank were significantly associated with change in binge-drinking 23-33 and 23-42 years. Women with lower initial sores were less likely to binge drink at 23 than those with higher scores, they were also more likely to change habits 23-33 years or 23-42 years to initiate binge drinking.

To date, this is the first study to examine associations between childhood cognitive trajectories, and lifecourse measures of smoking and drinking as well as investigating confounders and pathways. These results augment existing literature about childhood cognition and adult health and mortality outcomes. Of course, cognition is just one of many influences on drinking and smoking behaviour, including macro-level influences such as price, availability and advertising as well as individual-level influences, including ethnicity, demographic and psychosocial factors (Yang et al 2007). The particular focus on cognitive ability is justified because of the need to understand how the recently documented link between childhood cognition and adult health outcome arises (Hart et al 2004; Martin et al 2004).

Strengths and weaknesses

General strengths identified in previous chapters include: (i) the prospective population-based cohort design of the 1958 study; it is not a sub-study, for example, based on high-achievers, the cohort also benefits from large sample size (Chapter 3); (ii) the benefit of studying both men and women (iii) the maths and reading tests are non-standard but were age-appropriate and were correlated with 11-year general ability (iv) trajectories of cognitive ability can be estimated for individuals with incomplete data (v) including change in childhood ability adds to previous work on ability at single points in childhood with health behaviours (Chapter 2) (vi) measures of social class and highest educational qualifications were derived from information gathered at

different ages across the lifecourse and made the most of data from other surveys to fill in missing data where appropriate (Chapter 2) (vii) however a weakness is that self-reported smoking and drinking measures may incur error (Chapter 3). Further strengths and weaknesses relate specifically to the analyses and the statistical approach taken in this chapter. Using tests of two different domains of cognitive ability has the advantage that both expected to be correlated with underlying general ability 'g', but each gives some additional information. The long-term follow-up of the cohort confers the strength of prospective data but also brings the weakness of possible bias due to selective drop-out of the participants with poorer cognitive scores which would result in underestimates of the strength of association between cognitive ability and the adult outcomes. Appendix 4.1 suggests some under-representation of cohort members from manual social origins in the analyses. Reporting of alcohol or tobacco intake may be biased in relation to cognition; if individuals with greater cognitive ability are more likely to report what is expected (i.e. more moderate consumption) and less binge or heavy drinking and less smoking then associations between cognitive ability and drinking or smoking may be underestimated. However, the possibility cannot be investigated in this dataset as alternative measures of adult drinking and smoking are not available.

Generalisabilty of the findings

Associations reported here may not be generalisable to other settings. As discussed in chapter 3, patterns of smoking and drinking in this cohort as they aged may be specific to the particular geographical and cultural setting and time period. Changing educational (as opposed to social) gradients in alcohol use over time are not well documented in the UK, although a study in the Netherlands reports increasing educational gradients in heavy drinking over time (Droomers et al. 2004a). Secular changes in drinking cultures may affect the educational gradients in drinking frequency in other generations and differential changes by educational level will mean that the associations between cognitive ability and health behaviours seen here are not valid in other settings. Further, the cohort is primarily ethnically Caucasian and therefore not representative of other ethnic groups where different attitudes to cigarette and alcohol use may result in different educational distribution of use.

How these results fit with current knowledge

Previous research about cognitive development and alcohol and tobacco use has focused on firstly, the association between initiation of health behaviours and concurrent ability and secondly the association between adult or mid life ability and persistence of behaviours. Most studies are cross sectional and few use repeated measures of ability. Results presented here build on literature indicating that initiation of health behaviours is strongly related to educational success or failure; children with lower ability or low aspirations at school are much more likely to start to drink and engage in other health risky behaviours (Donovan 2004; Kuntsche et al 2004). Individuals with greater cognitive skills may be more averse to health

damaging behaviours if they are more forward-looking, motivated to invest in themselves, and more receptive to health promotion messages. For example less-educated smokers were more likely to discount future rewards than more educated smokers (Jaroni et al. 2004). Further, more educated individuals are more likely to possess the material and personal resources which allow them to avoid health damaging behaviours, or to overcome barriers to change and adopt healthier behaviours.

Predictors of persistence or quitting health behaviours are not necessarily the same as the predictors of initiation and these analyses extend the study of childhood ability to persistence of health behaviours through adulthood. Two studies investigate childhood ability and adult smoking and one investigates drinking (Kuh et al. 2002; Mortensen et al 2005; Taylor et al 2003), however they do not examine change in ability, or have limited measures of pathways such as adult education and occupation. By studying trajectories of binge and heavy drinking further into adulthood than most other studies these analyses extend the literature about precursors of adult drinking which is mainly focused on adolescence and early adulthood and focuses on problem drinking outcomes. The relative importance of social position at different life stages in shaping health behaviours is increasingly appreciated, for example with evidence that adult smoking and drinking are influenced by social position in early as well as later life (Blane et al. 1996; Brunner et al 1999; Graham & Der 1999; Graham & Hunt 1998; Jefferis et al 2004a; Lynch et al 1997). In contrast to socio-economic position, the relative contributions of cognitive ability across the lifecourse to shaping health behaviours have not been evaluated.

Theory of health behaviour change

From a theoretical perspective models of behaviour can inform our understanding of why cognitive ability would influence health behaviours. As mentioned in Chapter 3, theories of behaviour change could not be tested; although the main theories are discussed to inform the interpretation of associations between cognitive ability and health behaviours.

Social cognitive models propose that attitudes and norms shape intentions and intentions are the proximate determinants of behaviour change. One relevant model from this group is the theory of planned behaviour; attitudes towards behaviour, subjective norms and perceived behavioural control (a concept similar to self efficacy) all shape intentions which then in turn shape behaviour. Behaviour change research indicates that specific knowledge of risks associated with certain behaviours is not a good predictor of behaviour change (for example knowing that smoking causes lung cancer). However practical advice and high self efficacy in addition to knowledge of risks are more successful in predicting behavioural intentions, which in turn predict behaviour (for example access to nicotine patches and feeling able to quit smoking). A study examining changes in binge drinking found that perceptions of control over drinking and

perceiving many facilitators of drinking were important (Norman et al. 1998). If childhood ability and change in relative ability are associated with development of self-efficacy, attitudes, norms or intentions, we can say that the results seen here are compatible with this type of model operating. There is some support for this from existing literature. In a sample of British adults, social gradients (using Registrar General measure) in smoking, diet and physical activity as well as in attitudes and expectancies about health were reported (Wardle & Steptoe 2003). Men and women from manual social groups had worse expectancies about their future health and thought about health-enhancing behaviours less often and were more likely to believe that health is influenced by chance. As occupation and education are correlated, we can expect educational gradients in these measures. Indeed a study of Norwegian women reported educational gradients in intentions towards health behaviours and also self-efficacy, response-efficacy beliefs and belief in the importance of chance on influencing health (Leganger & Kraft 2003).

Childhood cognitive ability

Cognitive ability was discussed in Chapter 1 and is indexed by maths and reading abilities which are key skills, widely used in daily life and were assumed to reflect general ability. Different dimensions of early ability and change in ability may reflect the accumulation of subtly different exposures through childhood. Initial ability reflects genetic potential for maths and reading, as well as the learning experience and social background which are known influences on childhood ability. Trajectories of change in ability rank reflect not only the changes in ability relative to peers but will be influenced by the changing social circumstances of the home as well as the type of schooling and engagement with school. Educational trajectories through life contribute not only to the occupational opportunities that an individual subsequently encounters but they shape the social experiences which in turn influences the attitudes to opportunities to engage in health behaviours. Change in ability may indicate cumulated exposure to social environment; previous studies of the 1958 and 1946 British birth cohorts both identify the increasing influence of social background on changes in ability scores over childhood (Fogelman & Goldstein 1976; Jefferis et al 2002).

Adjustment for social class of origin and behavioural problems

Other studies of the link between cognition and mortality have suggested that the association may reflect the importance of childhood socioeconomic position on later mortality (Kuh et al 2004). When models of cognitive ability and adult smoking or drinking were adjusted for childhood social position the associations were little changed in this study. Effect estimates were somewhat reduced (by at most five points in the first decimal place, but mostly in the second decimal place), but the main effects were never abolished on adjustment for childhood social position. Therefore there is not evidence that effects of social position on cognitive trajectories and also on later health behaviours are the common cause of both cognitive ability

and later health behaviours.

Adolescent behavioural problems are also reported to be associated with both childhood cognitive ability and smoking and drinking uptake and were expected to potentially confound or mediate between childhood ability and adult smoking. The associations between behavioural problems at 16 years and adult smoking and drinking were stronger than at the earlier ages in childhood. This was interpreted as evidence that 7 and 11-year behavioural problems were not acting as confounders of associations between cognitive ability and adult smoking. Because 16-year problems occur later in the temporal sequence, these were conceptualised as mediators between childhood ability level and adult smoking rather than as confounders. When the associations between cognitive ability and adult smoking or drinking were adjusted for 16-year behavioural problems, associations were somewhat attenuated for smoking, drinking frequency and heavy drinking and much attenuated for binge drinking. Other studies of the association between childhood cognitive ability and adult smoking (Taylor et al 2003) or drinking (Mortensen et al 2005) do not take account of childhood social position or behavioural problems. A study based on a younger New Zealand cohort reported associations between 7-year cognitive ability and a range of measures of substance dependence (in contrast to the measures of regular alcohol use investigated in this chapter) which were mainly mediated by childhood conduct problems and to a lesser degree social position in childhood(Fergusson et al 2005).

Adjustment for occupation and educational qualifications

As discussed in chapter 1, childhood cognition predicts level of educational qualifications attained (Fergusson et al 2005) and adult social position (Fergusson & Horwood 1995; Hart et al 2003a; Neisser et al 1996), and there is evidence that the associations are independent of childhood social position and adolescent conduct problems (Fergusson et al 2005). To investigate whether associations between childhood cognitive ability and adult smoking and drinking were mediated by adult social position and educational level, analyses were adjusted for these factors. Both adult qualifications and social position are associated with adult cigarette and alcohol use; manual occupations and lower levels of education are associated with higher risks of non-drinking and also with heavier drinking as well as with higher risks of cigarette smoking. The social gradients may reflect adult circumstances (deriving from work and home conditions for example, (un)employment, job stress and control, partnership and parenthood transitions (Chilcoat & Breslau 1996)) or longer-term accumulated material experiences and cultural norms or expectations. Acquisition of highest qualifications reflects success in ability as well as the social aspect of attending and completing school or higher education. Qualifications will arguably be influenced to a greater degree than maths scores by behavioural and social factors. In the 1958 cohort, men gained higher levels of educational qualifications

than women by 33 years, also compared to married men and women, divorcees were more likely to have lower qualifications and single people to have higher qualifications. Having children by 33 years was more common in the cohort members with lower levels of qualifications and having higher numbers of children in the household by 33 years was associated with lower levels of educational qualifications(Ferri 1993, p.46). A Dutch study of educational gradients in adult smoking found that cultural and material factors (including financial situation and locus of control) were relatively more important than psychosocial factors (such as neuroticism and coping styles) in explaining the education gradient (Stronks et al. 1997). A study of educational gradients in quitting smoking found that education had a unique contribution to predicting quitting beyond the effects of demographic and environmental factors as well as nicotine dependence (Wetter et al. 2005). Investigating educational gradients in heavy adult alcohol use, financial problems, deprivation and income were all found to have good explanatory power whilst psychosocial factors (life events, own poor health, difficulties with relationships and other people's health) were not (Droomers et al 1999).

In this study, qualifications and occupational class were moderately correlated and were used to indicate different exposures. The main focus in these analyses is what the adjustment for occupation and education implies about the association between early ability and health behaviours, rather than the main effects of occupation and education on health behaviours. When the associations between early cognitive ability and change in ability across childhood and health behaviours were adjusted for educational level, there were substantial mediating effects of education, compared to occupational social position.

Briefly, many studies have examined the different associations of occupation and education and with health behaviours and health outcomes and the associations are expected to differ for different types of health outcomes and different types of health behaviours. For example, a study of the associations between education, occupation-based class and income with adult self-rated health reported that associations between education and self rated health were mediated by occupational class and income (Lahelma et al. 2004). A study of British adults comparing the associations between occupation or education with smoking behaviour and with mortality risk reported stronger associations with occupational class than educational qualifications (Davey Smith et al. 1998). Adjusting associations between childhood ability and health behaviours presented in this chapter for educational qualifications and social class takes into account own attained social position in addition to social position and experiences of the family during childhood. Although own social class is influenced by parental class (Blanden & Gregg 2004), there is evidence from the literature that measures of own social background are more important than those of family background in explaining health behaviours (Glendinning et al. 1994). Indeed adolescent smoking status is a strong predictor of later social position; it has been argued

that health behaviours can themselves shape subsequent social trajectories (Glendinning et al 1994; Koivusilta et al. 2003). There is also evidence to suggest that adolescent alcohol use may influence subsequent levels of educational qualifications achieved in early adulthood (King et al. 2006).

Childhood ability and adult cigarette use

Adult cigarette smoking and quitting was associated with each of the cognitive measures cross sectionally at 7, 11 and 16 years, and also both the initial level and change in ability trajectories were associated with smoking in women and men, apart from initial ability for men. This fits with other evidence of association of childhood cognition on adult smoking; a prospective study of Czech men and women reported that low childhood IQ and also low conscientiousness were associated with adult smoking in men and women aged 32-35 years (Kubicka et al. 2001). Data from the Scottish Mental Survey carried out in 1932 and the Renfrew & Paisley study follow-ups reported that higher childhood IQ was associated with increased risks of quitting smoking in adulthood (Taylor et al 2003).

Social position of origin is associated with adult smoking in this cohort and others (Power et al 2004) and was expected to confound associations between childhood ability and adult smoking. However there was little evidence of confounding of the associations with smoking at separate adult time-points, or across adulthood. Adjusting the associations between cognitive ability and adult smoking for 16-year behavioural problems attenuated associations, in line with literature about smoking uptake being greater in children with behavioural problems (Storr et al. 2004; Tyas & Pederson 1998), although to date studies of cognitive ability and adult smoking have not tested the role of either social position or behavioural problems as confounders or mediators (Mortensen et al 2005; Taylor et al 2003).

Associations between childhood maths (or reading) and adult smoking were mostly not mediated by highest attained qualifications; childhood ability was attenuated and non-significant in some cases at 7 years, but ability later in childhood remained robust to adjustment. In models of ability trajectories of men and women, both the initial level and change in ability were associated with smoking and, apart from initial ability for men, these effects were robust to adjustment for qualifications and social class, with greater mediation through qualifications than occupation. A study of Danish men found that lower IQ in young adulthood was associated with adult smoking but the relative importance of later SES was not tested (Mortensen et al 2005). Whilst a Scottish study found that quitting smoking in midlife, but not current smoking was associated with lower IQ at 11 years, but adjustment for adult SES and deprivation measures eliminated the association (Taylor et al 2003).

The findings that declining ability was strongly associated with adult smoking (both at single ages and across adulthood) fit with data from the 1970 British birth cohort study; persistently low ability at age 5 and 10 years in men and persistently high ability at 5 and 10 years in women was associated with respectively higher and lower risks of smoking at age 30 compared to children in the middle range ability at age 5 (Feinstein & Bynner 2004). Low measured ability and persistently low perceived ability in school years are reported to be associated with increased risks of cigarette, alcohol and marijuana use in adolescence (Bergen et al. 2005).

Adult circumstances and adult cigarette use

The associations between adult education and persistent smoking are not the main interest here (rather the associations between childhood ability and persistent smoking). However studies of the pathways from adult education to smoking may help to illuminate mechanisms underlying some of the associations between early ability and later smoking status. In the GLOBE longitudinal study in the Netherlands (including adults aged over 20) smoking was assessed at baseline and 6.5 years later. About half of the variance in educational gradients in persistent smoking was accounted for by differences in the prevalence of chronic illness, perceived control, neuroticism and emotional social support. Educational gradients in self-efficacy in relation to smoking cessation were found, but no gradients in intention to quit smoking (Droomers et al. 2004b). A 4-year follow-up study of quitting smoking reported that educational gradients in quitting smoking were not explained by job-related, demographic, environmental and tobacco dependence measures (Wetter et al 2005) suggesting that pathways between educational level and cigarette smoking status are not completely understood.

In both the models with cognition at single ages and also the trajectories, the association between childhood ability and adult smoking was stronger later in adulthood (confirmed by the multilevel models of smoking status across adulthood). This may reflect different types of smokers who persist in smoking or quit. Smokers at 42 years are mostly long-term smokers and more predominantly of lower social origins than the smokers at 23 years. Adult education is related to adult smoking in this setting and in others (Barbeau et al. 2004; Jefferis et al 2004a) and social gradients in smoking in this cohort derive from early smoking habits(Jefferis et al 2004b).

Alcohol use and cognitive ability

Men and women with lower childhood ability scores relative to their peers were more likely to abstain from drinking in adulthood between their twenties and forties. Men with lower scores in childhood were more likely to binge drink in adulthood, whereas women with lower scores were less likely to binge drink in their twenties but more likely to binge drink by their forties. Increases in relative ability rank across childhood were associated with lower odds of binge drinking in men at each adult age. In contrast to men, the associations between improved ability

scores and binge drinking in women reversed from a positive association with binge drinking in the twenties to a negative association in the forties. Lower 16-year ability was associated with higher risk of heavy drinking at each adult age in men whereas for women lower ability was associated with lower odds of heavy drinking at 23 and 33 years. In relation to ability change, men with declining ability scores were more likely to be heavy drinkers whereas women with lower initial scores were more likely to be heavy drinkers.

Lower ability each point in childhood was associated with greater risk of non-drinking in men and women through adult life. Initial ability rather than change between 7 and 16 years consistently conferred the higher risk of non-drinking and also drinking less frequently than daily. In contrast, for binge drinking, the effects of initial ability were mostly accounted for by behavioural problems at 16 years, adult social position and educational qualifications. Change in ability was more consistently associated with binge drinking at separate ages in men and women and heavy drinking in men, but less with drinking frequency. As discussed earlier, change in ability may be more associated with the longer term social, economic and demographic pathways into adult life and is associated with decisions about health behaviour throughout adulthood. Persistent binge and heavy drinking through adulthood is an important issue because of health and social harms that accrue to heavier drinkers and those around them. For women, improved ability was associated with change in binge drinking trajectories (to a healthier pattern of non-bingeing in later life), rather than a change in the total number of adult time points that binge drinking was identified. For men the pattern of change in individual trajectories in binge drinking across adulthood was not affected by early initial ability or change in ability. However there was a robust association between improved ability and being a binge or heavy drinker on fewer numbers of adult time-points in men. Adult circumstances explained some, but not all of the decreased risk of persistent binge or heavy drinking conferred by improving ability. In men decline in ability rank 7-16 years was associated with being a heavy drinker more often in adult life, although this was mediated by adult qualifications.

The higher prevalence of adult drinking in individuals with higher childhood cognitive ability contrasts with the higher prevalence of alcohol teenage initiation among less educated. However if early initiation of alcohol predicts more harmful patterns of alcohol use in later life such as binge or problem drinking, then this might explain the increased odds of early adult binge drinking among those with lower (later) childhood cognitive ability. There is mixed evidence from other studies that early onset of drinking alcohol predicts harmful patterns of alcohol use in later life(Bonomo et al. 2004; DeWit et al. 2000; Grant & Dawson 1997). However, in the 1958 cohort when analyses of early ability and change in ability were additionally adjusted for either frequency or amount of alcohol use at 16 years, associations between childhood ability and adult drinking were little changed (data not presented).

Adjusting the associations between childhood ability and adult drinking for childhood social position did not provide evidence for confounding by social position, despite expectations that this might be the case. There was evidence of some mediating effect of child behaviour problems on the drinking measures, and this was most notable for binge drinking. It may be that a binge drinking pattern is more strongly associated with problem behaviours in adolescence than heavy drinking or usual drinking frequency. However studies of childhood ability and drinking have neither studied the range of outcomes investigated here, nor investigated the role of social position of origin and behavioural problems (Mortensen et al 2005).

Adult circumstances and adult alcohol use

To investigate whether associations between childhood ability and adult drinking were acting through highest adult qualifications and occupational status, analyses were adjusted for these variables. The adult measures mediated between childhood ability and binge-drinking, suggesting that adult circumstances importantly influence binge-drinking. Associations between other drinking patterns and childhood cognitive ability were partly mediated by adult circumstances; drinking patterns were still associated with childhood ability in the full models (including drinking frequency and men's binge and heavy drinking). A Danish prospective study of IQ measured after age 18 years and adult drinking in men reported that lower IQ was related to non-drinking; OR 0.5 (0.31,0.83) per 2 SD increase in IQ. However the association was entirely mediated by adult socio-economic position; OR 0.88 (0.53, 1.44) (Mortensen et al 2005), as with the association between 7-16 year change in maths and non-drinking, although 7-year maths was still associated with non-drinking after adjustment. The Danish study did not find an association between childhood IQ and heavy drinking; similarly the 1958 data indicated weak associations. A Czech study did not find associations between childhood ability and adult binge drinking, but reported low conscientiousness and extroversion in childhood were predictors of adult drinking(Kubicka et al 2001).

Results from 1958 cohort fit with non-linear associations observed between adult ability levels and alcohol use; adult non-drinkers and heavier drinkers have lower adult ability scores (Rodgers et al. 2005) education(Van Oers et al 1999) or occupational position(Lynch et al 1997; Marmot 1997) than moderate drinkers.

Contrasting the associations between cognition and drinking compared to smoking

There are strong occupation-based social gradients in adult smoking in this cohort(Jefferis et al 2004b) which fits with data from many other studies. However social gradients in adult drinking are weaker and less consistent over age (Marmot 1997). The differences in associations may stem from several issues. Whilst health messages are strong and consistent about the

universally negative consequences of cigarettes for smokers, those around them and their unborn children, health messages about alcohol are more equivocal. Some health benefits are associated with alcohol consumption, although knowledge of the recommended daily safe limits and the amount of a favourite drink that constitutes the relevant number of units is poor, especially among older adults and those who drink less(Lader & Goddard 2004, p.12). In the general population knowledge of units is often erroneous; recall may be poor because larger servings contain more than one standard unit also alcohol content of drinks may be higher now than when standard units were introduced, and recall may impaired by heavy consumption. Alcohol has positive symbolism for celebrations and hospitality and the social acceptability of alcohol consumption is greater than smoking in the UK. However in some social and religious groups, temperance is socially desirable and abstinence from alcohol use would not show educational gradients.

Health behaviours and cognition in later life

Positive, albeit weak, associations between lower childhood cognitive ability and higher risks of either abstaining or heavy drinking in adulthood may confound the results of previously published studies reporting associations between moderate alcohol use in midlife with increased midlife cognitive ability. To date most studies investigating cognitive ability in midlife associated with alcohol intake lack the initial cognitive status information (Elwood et al. 1999; Kalmijn et al. 2002). One exception is the small Wisconsin longitudinal study which, in line with the direction of associations reported here, found the apparent benefits of alcohol consumption on later cognitive ability disappear when childhood ability is accounted for (Krahn et al. 2003). Equivalently, higher smoking rates in less able children may affect estimates of the association between smoking and declining adult cognitive function (Cervilla et al. 2000; Kalmijn et al 2002; Whalley et al. 2005). Few studies can control for early life cognitive ability prior to onset of smoking, although one longitudinal study has done so, and reported that independent of adolescent ability, smokers still had greater cognitive decline in their fifties (Richards et al. 2003).

Gender

Analyses were run separately by gender; as more men than women smoke and smoke heavily (Rickards et al 2004, p.121), drink alcohol, drink heavily and suffer alcohol related problems (Wilsnack et al. 2000). Persistence of health behaviours may have different predictors in men and women, due to biological differences including different rates of alcohol uptake and metabolism, or differences in social roles and expectations about alcohol and tobacco use (Wilsnack et al 2000). If reasons for drinking and smoking differ by gender, then associations between cognition and health behaviours may differ by gender. The main gender difference was in the association between cognitive ability and binge drinking. The consistent association between binge drinking and poor ability in men contrasted with the change in the association for

women. Adult circumstances were on the pathway between cognition and binge drinking, suggesting that explanations may lie with gender differences in adult domestic and employment trajectories, social roles or acceptability of binge drinking.

Conclusions

There is evidence of associations between childhood and adolescent ability to adult health behaviours between twenties and forties that were not confounded by social class of origin. This builds on knowledge about associations between educational level and adolescent initiation of health behaviours. Choices about adult health behaviours may be more influenced by childhood exposures than we have understood to date. The associations between ability and smoking and also binge drinking were strongest and most consistent and were partly mediated by adolescent behaviour and adult circumstances.

Table 4.1a. Odds ratio (95% CI) for current smoking by childhood maths trajectories, adult qualifications and social position.

	Adjusted[d]	Adjusted + childhood social class[e]	Adjusted + behavioural problems[f]	Adjusted + adult social class[g]	Adjusted + adult qualifications[h]	Adjusted +all[i]
			Men			
Maths z-score[a]			*23 year Current smoking* [bc]			
7 years	1.32	1.31	1.19	1.19	1.13	1.02
	(1.22, 1.42)	(1.21, 1.42)	(1.10, 1.29)	(1.10, 1.30)	(1.03, 1.23)	(0.93, 1.12)
Change 7-16 years	1.28	1.28	1.19	1.21	1.17	1.08
	(1.20, 1.37)	(1.20, 1.37)	(1.11, 1.27)	(1.13, 1.30)	(1.09, 1.26)	(1.00, 1.17)
Maths z-score[a]			*33 year Current smoking* [bc]			
7 years	1.35	1.33	1.19	1.19	1.09	0.98
	(1.26, 1.46)	(1.23, 1.43)	(1.10, 1.29)	(1.09, 1.29)	(0.99, 1.19)	(0.89, 1.07)
Change 7-16 years	1.32	1.30	1.20	1.22	1.16	1.07
	(1.24, 1.41)	(1.22, 1.39)	(1.12, 1.29)	(1.14, 1.31)	(1.08, 1.25)	(0.99, 1.15)
Maths z-score[a]			*42 year Current smoking* [bc]			
7 years	1.48	1.43	1.29	1.27	1.19	1.07
	(1.36, 1.62)	(1.30, 1.56)	(1.18, 1.42)	(1.15, 1.41)	(1.07, 1.33)	(0.96, 1.20)
Change 7-16 years	1.41	1.38	1.28	1.29	1.24	1.14
	(1.31, 1.53)	(1.27, 1.49)	(1.18, 1.39)	(1.19, 1.40)	(1.14, 1.35)	(1.05, 1.25)
			Women			
Maths z-score[a]			*23 year Current smoking* [bc]			
7 years	1.42	1.38	1.22	1.28	1.13	1.04
	(1.32, 1.53)	(1.27, 1.49)	(1.13, 1.33)	(1.18, 1.40)	(1.03, 1.23)	(0.94, 1.14)
Change 7-16 years	1.48	1.46	1.37	1.42	1.34	1.28
	(1.38, 1.58)	(1.36, 1.56)	(1.28, 1.47)	(1.32, 1.52)	(1.24, 1.44)	(1.19, 1.38)
Maths z-score[a]			*33 year Current smoking* [bc]			
7 years	1.65	1.59	1.38	1.48	1.25	1.15
	(1.52, 1.78)	(1.46, 1.72)	(1.27, 1.51)	(1.36, 1.61)	(1.14, 1.38)	(1.04, 1.27)
Change 7-16 years	1.51	1.48	1.38	1.44	1.34	1.28
	(1.41, 1.62)	(1.38, 1.59)	(1.28, 1.48)	(1.34, 1.55)	(1.25, 1.45)	(1.18, 1.38)
Maths z-score[a]			*42 year Current smoking* [bc]			
7 years	1.68	1.59	1.39	1.48	1.27	1.17
	(1.54, 1.84)	(1.45, 1.75)	(1.26, 1.54)	(1.34, 1.64)	(1.14, 1.41)	(1.04, 1.31)
Change 7-16 years	1.52	1.48	1.38	1.44	1.34	1.28
	(1.41, 1.64)	(1.37, 1.60)	(1.27, 1.49)	(1.33, 1.56)	(1.23, 1.46)	(1.17, 1.39)

[a] z-scores (from models of trajectories 7-16 y) are reversed; increase in score represents decline in ability rank.
[b] sample with data on drinking, maths and all covariates; 3265 men and 3584 women at 23 years; 3700 men and 3939 women at 33 years; 3206 men and 3552 women at 42y
[c] current smokers compared to non-smokers (including ex-smokers)
[d] model 1= 7 years maths score + change in maths 7-16 years
[e] model 2 = model 1 + social class of origin
[f] model 3 = model 2 + behavioural problems (16 years, Rutter score)
[g] model 4 = model 2 + adult social class
[h] model 5= model 2 + adult qualifications
[i] model 6 = model 2 + behavioural problems (16 years, Rutter score) + adult qualifications + adult social class

Table 4.1b Odds ratio (95% CI) for non-drinking (vs drinking) associated with maths z-score at age 7 and with change in maths z-score 7-16 years.

	Adjusted[d]	Adjusted + childhood social class[e]	Adjusted +behavioural problems[f]	Adjusted + adult social class[g]	Adjusted + adult qualifications[h]	Adjusted +all[i]
			Men			
Maths z-score[a]			*23 year Non-drinking* [bc]			
7 years	1.39	1.41	1.40	1.45	1.35	1.38
	(1.22, 1.59)	(1.23, 1.61)	(1.21, 1.61)	(1.25, 1.68)	(1.15, 1.58)	(1.17, 1.62)
Change 7-16 years	0.98	0.98	0.98	1.00	0.96	0.96
	(0.87, 1.10)	(0.87, 1.11)	(0.86, 1.10)	(0.88, 1.13)	(0.84, 1.09)	(0.84, 1.10)
Maths z-score[a]			*33 year Non-drinking* [bc]			
7 years	1.54	1.52	1.44	1.40	1.38	1.29
	(1.38, 1.70)	(1.37, 1.70)	(1.29, 1.62)	(1.25, 1.58)	(1.21, 1.56)	(1.14, 1.47)
Change 7-16 years	1.05	1.04	0.99	0.99	0.98	0.93
	(0.95, 1.15)	(0.95, 1.14)	(0.90, 1.09)	(0.90, 1.09)	(0.88, 1.08)	(0.84, 1.03)
Maths z-score[a]			*42 year Non-drinking* [bc]			
7 years	1.56	1.52	1.44	1.40	1.42	1.33
	(1.38, 1.76)	(1.34, 1.72)	(1.26, 1.64)	(1.22, 1.60)	(1.23, 1.64)	(1.15, 1.55)
Change 7-16 years	1.14	1.12	1.07	1.07	1.08	1.02
	(1.03, 1.27)	(1.01, 1.25)	(0.96, 1.19)	(0.96, 1.20)	(0.96, 1.21)	(0.91, 1.15)
			Women			
Maths z-score[a]			*23 year Non-drinking* [bc]			
7 years	1.47	1.40	1.34	1.28	1.23	1.17
	(1.36, 1.60)	(1.29, 1.52)	(1.23, 1.46)	(1.17, 1.41)	(1.12, 1.36)	(1.06, 1.30)
Change 7-16 years	1.10	1.07	1.04	1.03	1.01	0.98
	(1.03, 1.18)	(0.99, 1.15)	(0.97, 1.12)	(0.95, 1.11)	(0.93, 1.09)	(0.91, 1.06)
Maths z-score[a]			*33 year Non-drinking* [bc]			
7 years	1.39	1.35	1.32	1.29	1.26	1.23
	(1.29, 1.50)	(1.25, 1.46)	(1.21, 1.43)	(1.19, 1.40)	(1.15, 1.39)	(1.12, 1.35)
Change 7-16 years	1.05	1.04	1.02	1.02	1.00	0.99
	(0.99, 1.13)	(0.97, 1.11)	(0.95, 1.09)	(0.95, 1.09)	(0.93, 1.08)	(0.92, 1.07)
Maths z-score[a]			*42 year Non-drinking* [bc]			
7 years	1.47	1.43	1.33	1.32	1.24	1.17
	(1.34, 1.60)	(1.31, 1.57)	(1.21, 1.46)	(1.20, 1.46)	(1.12, 1.38)	(1.05, 1.30)
Change 7-16 years	1.16	1.14	1.09	1.11	1.07	1.03
	(1.08, 1.25)	(1.06, 1.23)	(1.01, 1.18)	(1.02, 1.20)	(0.99, 1.16)	(0.95, 1.12)

[a] z-scores (from models of trajectories 7-16 y) are reversed; increase in score represents decline in ability rank.
[b] sample with data on drinking, maths and all covariates; 3275 men and 3597 women at 23 years; 3752 men and 3990 women at 33 years; 3205 men and 3552 women at 42y.
[c] non-drinkers compared to those drinking more often than on special occasions
[d] model 1= 7 years maths score + change in maths 7-16 years
[e] model 2 = model 1 + social class of origin
[f] model 3 = model 2 + behavioural problems (16 years, Rutter score)
[g] model 4 = model 2 + adult social class
[h] model 5= model 2 + adult qualifications
[i] model 6 = model 2 + behavioural problems (16 years, Rutter score) + adult qualifications + adult social class

Table 4.1c. Odds ratio (95% CI) for binge drinking by childhood maths trajectories, adult qualifications and social position.

	Adjusted[d]	Adjusted + childhood social class[e]	Adjusted+ behavioural problems[f]	Adjusted + adult qualifications[g]	Adjusted + adult social class[h]	Adjusted +all[i]
			Men			
Maths z-score[a]			*23 year Binge-drinking* [bc]			
7 years	1.08	1.06	1.02	0.97	1.00	0.93
	(1.00, 1.16)	(0.98, 1.14)	(0.94, 1.10)	(0.89, 1.06)	(0.92, 1.09)	(0.85, 1.02)
Change 7-16 years	1.26	1.24	1.21	1.19	1.20	1.15
	(1.18, 1.34)	(1.16, 1.33)	(1.13, 1.29)	(1.10, 1.27)	(1.12, 1.29)	(1.06, 1.24)
Maths z-score[a]			*33 year Binge-drinking* [bc]			
7 years	1.07	1.03	1.01	0.93	0.97	0.90
	(0.99, 1.15)	(0.95, 1.11)	(0.93, 1.10)	(0.85, 1.01)	(0.89, 1.06)	(0.82, 0.99)
Change 7-16 years	1.22	1.19	1.18	1.11	1.15	1.10
	(1.14, 1.30)	(1.11, 1.27)	(1.10, 1.26)	(1.04, 1.20)	(1.07, 1.23)	(1.02, 1.18)
Maths z-score[a]			*42 year Binge-drinking* [bc]			
7 years	1.15	1.10	1.04	1.03	1.05	0.97
	(1.06, 1.24)	(1.01, 1.19)	(0.96, 1.14)	(0.93, 1.13)	(0.96, 1.15)	(0.88, 1.07)
Change 7-16 years	1.17	1.14	1.09	1.09	1.10	1.04
	(1.09, 1.25)	(1.06, 1.22)	(1.02, 1.17)	(1.01, 1.17)	(1.02, 1.19)	(0.96, 1.13)
			Women			
Maths z-score[a]			*23 year Binge-drinking* [bc]			
7 years	0.88	0.88	0.88	0.94	0.92	0.95
	(0.81, 0.96)	(0.80, 0.97)	(0.80, 0.97)	(0.85, 1.05)	(0.83, 1.01)	(0.85, 1.06)
Change 7-16 years	0.99	0.99	0.99	1.02	1.00	1.02
	(0.91, 1.06)	(0.91, 1.07)	(0.91, 1.07)	(0.94, 1.11)	(0.92, 1.09)	(0.93, 1.11)
Maths z-score[a]			*33 year Binge-drinking* [bc]			
7 years	1.01	1.01	0.99	0.92	0.96	0.89
	(0.92, 1.11)	(0.92, 1.12)	(0.90, 1.10)	(0.82, 1.04)	(0.86, 1.06)	(0.79, 1.01)
Change 7-16 years	1.11	1.11	1.10	1.06	1.08	1.05
	(1.02, 1.20)	(1.02, 1.21)	(1.01, 1.20)	(0.97, 1.16)	(0.99, 1.18)	(0.95, 1.15)
Maths z-score[a]			*42 year Binge-drinking* [bc]			
7 years	1.31	1.24	1.21	1.10	1.19	1.08
	(1.18, 1.45)	(1.12, 1.39)	(1.08, 1.35)	(0.97, 1.25)	(1.06, 1.33)	(0.94, 1.22)
Change 7-16 years	1.22	1.19	1.17	1.13	1.16	1.11
	(1.12, 1.33)	(1.08, 1.30)	(1.06, 1.28)	(1.02, 1.24)	(1.06, 1.27)	(1.01, 1.23)

[a] z-scores (from models of trajectories 7-16 y) are reversed; increase in score represents decline in ability rank.
[b] sample with data on drinking, maths and all covariates; 3275 men and 3597 women at 23 years; 3752 men and 3990 women at 33 years; 3205 men and 3552 women at 42y
[c] binge drinkers compared to light drinkers plus non-drinkers
[d] model 1= 7 years maths score + change in maths 7-16 years
[e] model 2 = model 1 + social class of origin
[f] model 3 = model 2 + behavioural problems (16 years, Rutter score)
[g] model 4 = model 2 + adult qualifications
[h] model 5 = model 2 + adult social class
[i] model 6 = model 2 + behavioural problems (16 years, Rutter score) + adult qualifications + adult social class

Table 4.1d. Odds ratio (95% CI) for heavy drinking by childhood maths trajectories, adult qualifications and social position.

	Adjusted[d]	Adjusted + childhood social class[e]	Adjusted + behavioural problems[f]	Adjusted + adult social class[g]	Adjusted + adult qualfications[h]	Adjusted +all[i]
			Men			
Maths z-score[a]			*23 year Heavy-drinking* [bc]			
7 years	1.03	1.03	1.00	0.97	0.97	0.93
	(0.94, 1.12)	(0.95, 1.13)	(0.91, 1.10)	(0.88, 1.07)	(0.88, 1.08)	(0.84, 1.04)
Change 7-16 years	1.21	1.21	1.18	1.17	1.17	1.12
	(1.12, 1.30)	(1.12, 1.31)	(1.09, 1.28)	(1.08, 1.27)	(1.07, 1.27)	(1.03, 1.22)
Maths z-score[a]			*33 year Heavy-drinking* [bc]			
7 years	1.01	0.97	0.92	0.92	0.85	0.81
	(0.92, 1.11)	(0.88, 1.07)	(0.82, 1.02)	(0.82, 1.02)	(0.75, 0.95)	(0.71, 0.91)
Change 7-16 years	1.18	1.15	1.10	1.11	1.05	1.01
	(1.08, 1.28)	(1.05, 1.25)	(1.01, 1.21)	(1.01, 1.21)	(0.95, 1.15)	(0.92, 1.11)
Maths z-score[a]			*42 year Heavy-drinking* [bc]			
7 years	0.97	0.94	0.92	0.92	0.86	0.84
	(0.89, 1.06)	(0.86, 1.03)	(0.83, 1.01)	(0.84, 1.02)	(0.78, 0.96)	(0.76, 0.94)
Change 7-16 years	1.23	1.21	1.18	1.19	1.14	1.12
	(1.14, 1.33)	(1.12, 1.30)	(1.09, 1.28)	(1.09, 1.29)	(1.04, 1.24)	(1.02, 1.22)
			Women			
Maths z-score[a]			*23 year Heavy-drinking* [bc]			
7 years	0.78	0.79	0.76	0.79	0.75	0.73
	(0.68, 0.90)	(0.68, 0.91)	(0.65, 0.89)	(0.67, 0.92)	(0.63, 0.89)	(0.61, 0.87)
Change 7-16 years	0.93	0.93	0.91	0.92	0.90	0.88
	(0.82, 1.05)	(0.82, 1.05)	(0.80, 1.03)	(0.81, 1.05)	(0.79, 1.04)	(0.77, 1.01)
Maths z-score[a]			*33 year Heavy-drinking* [bc]			
7 years	0.81	0.90	0.82	0.90	0.85	0.82
	(0.67, 0.98)	(0.74, 1.10)	(0.67, 1.02)	(0.73, 1.12)	(0.67, 1.08)	(0.64, 1.04)
Change 7-16 years	1.12	1.20	1.14	1.21	1.18	1.14
	(0.96, 1.32)	(1.02, 1.42)	(0.96, 1.35)	(1.02, 1.43)	(0.99, 1.41)	(0.95, 1.36)
Maths z-score[a]			*42 year Heavy-drinking* [bc]			
7 years	0.93	0.97	0.93	0.97	0.91	0.89
	(0.81, 1.07)	(0.84, 1.12)	(0.80, 1.08)	(0.83, 1.12)	(0.77, 1.07)	(0.75, 1.05)
Change 7-16 years	1.07	1.09	1.07	1.10	1.06	1.05
	(0.95, 1.20)	(0.97, 1.23)	(0.94, 1.21)	(0.97, 1.24)	(0.94, 1.21)	(0.92, 1.19)

[a] z-scores (from models of trajectories 7-16 y) are reversed; increase in score represents decline in ability rank.
[b] sample with data on drinking, maths and all covariates; 3295 men and 3597 women at 23 years; 3752 men and 3990 women at 33 years; 3205 men and 3552 women at 42y
[c] heavy drinkers compared to light drinkers plus non-drinkers
[d] model 1= 7 years maths score + change in maths 7-16 years
[e] model 2 = model 1 + social class of origin
[f] model 3 = model 2 + behavioural problems (16 years, Rutter score)
[g] model 4 = model 2 + adult social class
[h] model 5= model 2 + adult qualifications
[i] model 6 = model 2 + behavioural problems (16 years, Rutter score) + adult qualifications + adult social class

Table 4.1e RRR of drinking frequency (baseline is daily drinking) per SD decrease in maths intercept and slope, men

Drinking frequency	*7-year maths z-score + change*[b]	*+ social class at birth*[c]	*+ behavioural problems (16y)*[d]	*+ Adult qualifications*[e]	*+ Adult social class*[f]	*+ All*[g]
23 years			*7-year maths z-score*[a]			
Daily	1	1	1	1	1	1
Weekly	1.15 (1.07, 1.25)	1.13 (1.04, 1.22)	1.15 (1.05, 1.25)	1.16 (1.06, 1.28)	1.12 (1.03, 1.23)	1.16 (1.06, 1.28)
Monthly	1.37 (1.19, 1.57)	1.34 (1.16, 1.55)	1.35 (1.16, 1.57)	1.30 (1.10, 1.54)	1.32 (1.13, 1.54)	1.30 (1.09, 1.54)
Infrequent/ Never	1.55 (1.34, 1.81)	1.55 (1.32, 1.81)	1.55 (1.32, 1.82)	1.49 (1.25, 1.78)	1.58 (1.33, 1.88)	1.53 (1.27, 1.84)
			Change 7-16 years			
Daily	1	1	1	1	1	1
Weekly	1.05 (0.98, 1.13)	1.04 (0.97, 1.11)	1.05 (0.98, 1.13)	1.06 (0.98, 1.14)	1.03 (0.96, 1.11)	1.06 (0.98, 1.15)
Monthly	0.91 (0.81, 1.04)	0.90 (0.80, 1.02)	0.91 (0.80, 1.03)	0.88 (0.77, 1.01)	0.89 (0.78, 1.02)	0.88 (0.77, 1.02)
Infrequent/ Never	1.00 (0.88, 1.12)	0.99 (0.88, 1.12)	0.99 (0.88, 1.13)	0.97 (0.85, 1.11)	1.00 (0.88, 1.14)	0.98 (0.86, 1.13)
33 years			*7-year maths z-score*[a]			
Daily	1	1	1	1	1	1
Weekly	1.31 (1.20, 1.44)	1.29 (1.18, 1.42)	1.32 (1.20, 1.46)	1.34 (1.21, 1.49)	1.19 (1.07, 1.31)	1.28 (1.15, 1.43)
Monthly	1.45 (1.29, 1.62)	1.43 (1.27, 1.61)	1.46 (1.29, 1.65)	1.45 (1.26, 1.66)	1.32 (1.16, 1.50)	1.39 (1.20, 1.61)
Infrequent/ Never	1.94 (1.70, 2.22)	1.91 (1.66, 2.19)	1.83 (1.59, 2.11)	1.78 (1.52, 2.08)	1.64 (1.41, 1.90)	1.60 (1.36, 1.88)
			Change 7-16 years			
Daily	1	1	1	1	1	1
Weekly	1.04 (0.97, 1.13)	1.03 (0.96, 1.12)	1.05 (0.97, 1.14)	1.06 (0.97, 1.15)	0.98 (0.9, 1.06)	1.03 (0.94, 1.12)
Monthly	1.00 (0.90, 1.10)	0.99 (0.89, 1.10)	1.01 (0.90, 1.12)	1.00 (0.89, 1.11)	0.94 (0.84, 1.05)	0.98 (0.87, 1.10)
Infrequent/ Never	1.07 (0.96, 1.19)	1.06 (0.95, 1.18)	1.03 (0.92, 1.15)	1.02 (0.90, 1.14)	0.96 (0.86, 1.08)	0.95 (0.84, 1.07)

[a] Maths z-scores are negatively coded (ie an increase represents a decrease in rank). Z-score are estimates from multilevel models of maths trajectories 7-16 years. Analysis sample is fixed, based on maximum number with information on drinking at one adult age plus, maths score highest qualifications and social class.

[b] model 1 = 7-year z-score + 7-16 year change in z-score

[c] model 2= model 1 + social class at birth

[d] model 3= model 1 + 16-year behavioural problems

[e] model 4= model 1 + qualifications achieved by 33 years

[f] model 5= model 1 + social class at 33 years

[g] model 6= model 2 + 16-year behavioural problems + 33-year qualifications + 33-year social class

Table 4.1e RRR of drinking frequency (baseline is daily drinking) per SD decrease in maths intercept and slope, men (continued)

Drinking frequency	*7-year maths z-score + change*[b]	*+ social class at birth*[c]	*+ behavioural problems (16y)*[d]	*+ Adult qualifications*[e]	*+ Adult social class*[f]	*+ All*[g]
42 years			*7-year maths z-score*[a]			
Daily	1	1	1	1	1	1
Weekly	1.28 (1.18, 1.40)	1.24 (1.13, 1.35)	1.22 (1.12, 1.34)	1.23 (1.11, 1.36)	1.16 (1.06, 1.28)	1.17 (1.06, 1.30)
Monthly	1.39 (1.19, 1.61)	1.32 (1.13, 1.54)	1.25 (1.06, 1.47)	1.25 (1.04, 1.49)	1.23 (1.04, 1.46)	1.17 (0.97, 1.41)
Infrequent/ Never	1.88 (1.63, 2.15)	1.78 (1.55, 2.05)	1.66 (1.43, 1.92)	1.65 (1.40, 1.94)	1.55 (1.33, 1.81)	1.46 (1.23, 1.73)
			Change 7-16 years			
Daily	1	1	1	1	1	1
Weekly	0.99 (0.92, 1.07)	0.97 (0.90, 1.04)	0.96 (0.89, 1.04)	0.96 (0.89, 1.04)	0.93 (0.86, 1.01)	0.93 (0.86, 1.01)
Monthly	1.09 (0.96, 1.23)	1.06 (0.93, 1.20)	1.01 (0.89, 1.15)	1.02 (0.89, 1.17)	1.01 (0.89, 1.15)	0.97 (0.84, 1.11)
Infrequent/ Never	1.14 (1.02, 1.28)	1.10 (0.98, 1.24)	1.04 (0.92, 1.17)	1.05 (0.93, 1.19)	1.01 (0.90, 1.15)	0.96 (0.85, 1.10)

[a] Maths z-scores are negatively coded (ie an increase represents a decrease in rank). Z-score are estimates from multilevel models of maths trajectories 7-16 years. Analysis sample is fixed, based on maximum number with information on drinking at one adult age plus, maths score highest qualifications and social class.
[b] model 1 = 7-year z-score + 7-16 year change in z-score
[c] model 2= model 1 + social class at birth
[d] model 3= model 1 + 16-year behavioural problems
[e] model 4= model 1 + qualifications achieved by 33 years
[f] model 5= model 1 + social class at 33 years
[g] model 6= model 2 + 16-year behavioural problems + 33-year qualifications + 33-year social class

Table 4.1f RRR of drinking frequency (baseline is daily drinking) per SD decrease in maths intercept and slope, women

Drinking frequency	*7-year maths z-score + change*[b]	*+ social class at birth*[c]	*+ behavioural problems (16y)*[d]	*+ Adult qualifications*[e]	*+ Adult social class*[f]	*+ All*[g]
23 years			*7-year maths z-score*[a]			
Daily	1	1	1	1	1	1
Weekly	1.40 (1.25, 1.58)	1.31 (1.16, 1.49)	1.31 (1.15, 1.50)	1.25 (1.08, 1.44)	1.31 (1.15, 1.49)	1.26 (1.09, 1.45)
Monthly	1.70 (1.49, 1.95)	1.53 (1.33, 1.77)	1.50 (1.29, 1.74)	1.42 (1.20, 1.68)	1.50 (1.29, 1.74)	1.40 (1.19, 1.66)
Infrequent/ Never	2.06 (1.81, 2.35)	1.84 (1.60, 2.12)	1.76 (1.52, 2.03)	1.57 (1.34, 1.84)	1.68 (1.45, 1.94)	1.50 (1.28, 1.76)
			Change 7-16 years			
Daily	1	1	1	1	1	1
Weekly	1.06 (0.96, 1.17)	1.02 (0.92, 1.13)	1.02 (0.92, 1.13)	0.99 (0.89, 1.10)	1.02 (0.92, 1.13)	0.99 (0.89, 1.11)
Monthly	1.16 (1.03, 1.30)	1.09 (0.96, 1.22)	1.07 (0.95, 1.21)	1.04 (0.92, 1.19)	1.07 (0.95, 1.21)	1.04 (0.91, 1.18)
Infrequent/ Never	1.18 (1.06, 1.31)	1.10 (0.99, 1.23)	1.76 (1.52, 2.03)	1.02 (0.90, 1.14)	1.06 (0.94, 1.18)	0.99 (0.88, 1.12)
33 years			*7-year maths z-score*[a]			
Daily	1	1	1	1	1	1
Weekly	1.53 (1.34, 1.75)	1.43 (1.24, 1.66)	1.49 (1.29, 1.74)	1.39 (1.18, 1.63)	1.35 (1.16, 1.56)	1.39 (1.19, 1.64)
Monthly	1.72 (1.50, 1.99)	1.56 (1.34, 1.82)	1.65 (1.41, 1.93)	1.48 (1.25, 1.76)	1.50 (1.28, 1.75)	1.51 (1.27, 1.80)
Infrequent/ Never	2.13 (1.85, 2.46)	1.93 (1.66, 2.25)	1.96 (1.67, 2.30)	1.75 (1.48, 2.07)	1.74 (1.49, 2.04)	1.71 (1.45, 2.03)
			Change 7-16 years			
Daily	1	1	1	1	1	1
Weekly	1.01 (0.90, 1.13)	0.97 (0.86, 1.09)	0.99 (0.89, 1.12)	0.95 (0.85, 1.07)	0.94 (0.84, 1.06)	0.96 (0.86, 1.09)
Monthly	1.11 (0.98, 1.25)	1.04 (0.92, 1.18)	1.08 (0.95, 1.22)	1.02 (0.89, 1.15)	1.02 (0.90, 1.16)	1.04 (0.91, 1.18)
Infrequent/ Never	1.09 (0.97, 1.23)	1.03 (0.91, 1.16)	1.04 (0.92, 1.17)	0.98 (0.87, 1.11)	0.98 (0.87, 1.11)	0.98 (0.87, 1.11)

[a] Maths z-scores are negatively coded (ie an increase represents a decrease in rank). Z-score are estimates from multilevel models of maths trajectories 7-16 years. Analysis sample is fixed, based on maximum number with information on drinking at one adult age plus, maths score highest qualifications and social class.

[b] model 1 = 7-year z-score + 7-16 year change in z-score

[c] model 2= model 1 + social class at birth

[d] model 3= model 1 + 16-year behavioural problems

[e] model 4= model 1 + qualifications achieved by 33 years

[f] model 5= model 1 + social class at 33 years

[g] model 6= model 2 +16-year behavioural problems + 33-year qualifications + 33-year social class

Table 4.1f RRR of drinking frequency (baseline is daily drinking) per SD decrease in maths intercept and slope, women

(Continued)

Drinking frequency	*7-year maths z-score + change*[b]	*+ social class at birth*[c]	*+ behavioural problems (16y)*[d]	*+ Adult qualifications*[e]	*+ Adult social class*[f]	*+ All*[g]
42 years			*7-year maths z-score*[a]			
Daily	1	1	1	1	1	1
Weekly	1.30 (1.17, 1.43)	1.21 (1.09, 1.35)	1.24 (1.11, 1.39)	1.18 (1.04, 1.33)	1.16 (1.04, 1.3)	1.18 (1.04, 1.34)
Monthly	1.65 (1.45, 1.88)	1.49 (1.30, 1.71)	1.53 (1.32, 1.76)	1.38 (1.18, 1.62)	1.41 (1.22, 1.63)	1.39 (1.18, 1.63)
Infrequent/ Never	1.88 (1.67, 2.12)	1.73 (1.52, 1.96)	1.63 (1.43, 1.86)	1.46 (1.27, 1.69)	1.54 (1.35, 1.76)	1.38 (1.19, 1.59)
			Change 7-16 years			
Daily	1	1	1	1	1	1
Weekly	1.07 (0.98, 1.16)	1.03 (0.94, 1.12)	1.04 (0.95, 1.14)	1.01 (0.92, 1.11)	1.00 (0.92, 1.10)	1.18 (1.04, 1.34)
Monthly	1.05 (0.93, 1.19)	0.99 (0.88, 1.12)	1.00 (0.89, 1.13)	0.95 (0.84, 1.08)	0.96 (0.85, 1.09)	1.39 (1.18, 1.63)
Infrequent/ Never	1.22 (1.10, 1.35)	1.16 (1.04, 1.28)	1.12 (1.01, 1.25)	1.07 (0.95, 1.19)	1.10 (0.99, 1.22)	1.38 (1.19, 1.59)

[a] Maths z-scores are negatively coded (ie an increase represents a decrease in rank). Z-score are estimates from multilevel models of maths trajectories 7-16 years. Analysis sample is fixed, based on maximum number with information on drinking at one adult age plus, maths score highest qualifications and social class.

[b] model 1 = 7-year z-score + 7-16 year change in z-score

[c] model 2= model 1 + social class at birth

[d] model 3= model 1 + 16-year behavioural problems

[e] model 4= model 1 + qualifications achieved by 33 years

[f] model 5= model 1 + social class at 33 years

[g] model 6= model 2 + 16-year behavioural problems + 33-year qualifications + 33-year social class

Table 4.2a. Association between maths trajectory 7-16 years and smoking history 23-42 years [RRR (95% CI)]

Smoking 23-42 years	*7-year maths z-score + change*[c]	*+ social class at birth*[d]	*+ behavioural problems (16y)*[e]	*+ Adult qualifications*[f]	*+ Adult social class*[g]	*+ All*[h]
Men N=3206[b]			*7-year maths z-score*[a]			
Never	1	1	1	1	1	1
quit 23-33	1.03 (0.93, 1.14)	1.05(0.94,1.17)	0.99(0.88,1.11)	1.00(0.89,1.13)	1.03(0.91,1.16)	0.96(0.84,1.09)
quit 33-42	1.04 (0.92, 1.17)	1.07(0.94,1.20)	0.96(0.85,1.09)	0.96(0.83,1.10)	1.00(0.88,1.13)	0.87(0.75,1.01)
1-19/day	1.35 (1.19, 1.53)	1.31(1.14,1.49)	1.17(1.02,1.34)	1.11(0.96,1.29)	1.20(1.04,1.39)	1.01(0.86,1.17)
>20/day	1.64 (1.46, 1.85)	1.59(1.41,1.80)	1.38(1.22,1.56)	1.30(1.13,1.49)	1.36(1.19,1.55)	1.10(0.95,1.27)
			Change 7-16 years			
Never	1	1	1	1	1	1
quit 23-33	1.21 (1.11, 1.32)	1.23(1.12,1.34)	1.17(1.07,1.29)	1.19(1.08,1.31)	1.21(1.10,1.33)	1.15(1.04,1.27)
quit 33-42	1.23 (1.11, 1.36)	1.25(1.13,1.38)	1.16(1.04,1.28)	1.17(1.05,1.30)	1.20(1.08,1.34)	1.09(0.97,1.22)
1-19/day	1.52 (1.36, 1.71)	1.49(1.33,1.68)	1.38(1.23,1.55)	1.35(1.19,1.53)	1.42(1.26,1.60)	1.26(1.11,1.42)
>20/day	1.53 (1.38, 1.70)	1.50(1.35,1.67)	1.35(1.21,1.51)	1.33(1.18,1.49)	1.37(1.22,1.54)	1.18(1.05,1.33)
Women N=3551[b]			*7-year maths z-score*[a]			
Never	1	1	1	1	1	1
quit 23-33	1.13(1.02,1.24)	1.14(1.03,1.26)	1.10(0.99,1.22)	1.10(0.98,1.24)	1.12(1.01,1.25)	1.08(0.95,1.22)
quit 33-42	1.40(1.24,1.57)	1.40(1.24,1.59)	1.25(1.10,1.43)	1.26(1.09,1.45)	1.36(1.19,1.55)	1.17(1.01,1.35)
1-19/day	1.68(1.49,1.89)	1.59(1.41,1.80)	1.41(1.24,1.60)	1.29(1.12,1.49)	1.50(1.32,1.71)	1.19(1.03,1.38)
>20/day	2.04(1.78,2.34)	1.91(1.66,2.20)	1.55(1.34,1.80)	1.44(1.23,1.69)	1.70(1.47,1.97)	1.25(1.07,1.47)
			Change 7-16 years			
Never	1	1	1	1	1	1
quit 23-33	1.23(1.13,1.35)	1.24(1.13,1.36)	1.22(1.11,1.33)	1.22(1.11,1.34)	1.23(1.13,1.35)	1.20(1.1,1.32)
quit 33-42	1.37(1.23,1.52)	1.37(1.23,1.53)	1.29(1.15,1.43)	1.30(1.16,1.45)	1.35(1.21,1.51)	1.24(1.11,1.39)
1-19/day	1.54(1.39,1.70)	1.49(1.35,1.65)	1.40(1.26,1.55)	1.35(1.21,1.51)	1.45(1.31,1.61)	1.30(1.16,1.45)
>20/day	1.90(1.68,2.14)	1.83(1.62,2.07)	1.65(1.46,1.86)	1.61(1.42,1.83)	1.75(1.54,1.98)	1.50(1.32,1.70)

[a] Maths z-scores are negatively coded (ie an increase represents a decrease in rank). Z-score are estimates from multilevel models of maths trajectories 7-16 years.
[b] analysis sample is fixed, based on maximum number with information on smoking at 3 adult ages plus, maths score highest qualifications and social class.
[c] model 1=7-year z-score + 7-16 year change in z-score
[d] model 2= model 1 + social class at birth
[e] model 3= model 1 + 16-year behavioural problems
[f] model 4= model 1 + qualifications achieved by 33 years
[g] model 5= model 1 + social class at 33 years
[h] model 6= model 2 + 16-year behavioural problems + 33-year qualifications + 33-year social class

Table 4.2b. Association between maths trajectory 7-16 years and the number of adult surveys (0, 1, 2, 3) a person is a non-drinker[a] [RRR (95% CI)]

	7-year maths z-score + change[d]	*+ social class at birth[e]*	*+ behavioural problems (16y)[f]*	*+ Adult qualifications[g]*	*+ Adult social class[h]*	*+ All[i]*
Number of occasions non-drinker						
Men N=2830[c]			*7-year maths z-score[b]*			
Never	1	1	1	1	1	1
1	1.50 (1.33, 1.70)	1.44 (1.27, 1.64)	1.44 (1.26, 1.65)	1.36 (1.18, 1.58)	1.41 (1.23, 1.62)	1.36 (1.17, 1.58)
2	1.67 (1.39, 2.00)	1.63 (1.35, 1.97)	1.52 (1.25, 1.85)	1.51 (1.21, 1.88)	1.48 (1.20, 1.83)	1.37 (1.08, 1.73)
3	1.48 (1.13, 1.94)	1.50 (1.14, 1.97)	1.35 (1.03, 1.78)	1.34 (1.00, 1.79)	1.44 (1.06, 1.95)	1.25 (0.92, 1.70)
			Change 7-16 years			
Never	1	1	1	1	1	1
1	1.11 (1.00, 1.24)	1.09 (0.97, 1.21)	1.09 (0.97, 1.22)	1.05 (0.93, 1.18)	1.07 (0.96, 1.20)	1.05 (0.92, 1.18)
2	1.08 (0.93, 1.24)	1.06 (0.92, 1.22)	1.00 (0.86, 1.16)	1.01 (0.86, 1.18)	1.00 (0.86, 1.16)	0.94 (0.80, 1.11)
3	0.97 (0.79, 1.21)	0.98 (0.79, 1.22)	0.89 (0.72, 1.11)	0.91 (0.73, 1.15)	0.96 (0.76, 1.20)	0.85 (0.67, 1.08)
Women N=3228[c]			*7-year maths z-score[b]*			
Never	1	1	1	1	1	1
1	1.39 (1.27, 1.52)	1.31 (1.19, 1.44)	1.27 (1.16, 1.41)	1.27 (1.14, 1.41)	1.25 (1.13, 1.38)	1.14 (0.98, 1.32)
2	1.67 (1.49, 1.88)	1.59 (1.41, 1.80)	1.50 (1.31, 1.70)	1.31 (1.14, 1.5)	1.45 (1.27, 1.64)	1.25 (1.05, 1.49)
3	1.70 (1.46, 1.98)	1.62 (1.38, 1.90)	1.49 (1.27, 1.75)	1.37 (1.14, 1.63)	1.42 (1.20, 1.67)	1.37 (1.12, 1.67)
			Change 7-16 years			
Never	1	1	1	1	1	1
1	1.12 (1.04, 1.21)	1.08 (1.00, 1.17)	1.07 (0.99, 1.15)	1.07 (0.98, 1.16)	1.06 (0.98, 1.14)	1.01 (0.92, 1.11)
2	1.06 (0.96, 1.17)	1.03 (0.94, 1.14)	0.99 (0.90, 1.10)	0.93 (0.84, 1.04)	0.99 (0.89, 1.09)	0.81 (0.72, 0.91)
3	1.22 (1.07, 1.38)	1.18 (1.04, 1.34)	1.13 (0.99, 1.28)	1.09 (0.95, 1.24)	1.11 (0.97, 1.27)	0.88 (0.76, 1.02)

[a] non-drinkers compared to drinkers

[b] Maths z-scores are negatively coded (ie an increase represents a decrease in rank). Z-score are estimates from multilevel models of maths trajectories 7-16 years.

[c] analysis sample is fixed, based on maximum number with information on drinking at 3 adult ages plus, maths score highest qualifications and social class.

[d] model 1 = 7-year z-score + 7-16 year change in z-score

[e] model 2= model 1 + social class at birth

[f] model 3= model 1 + 16-year behavioural problems

[g] model 4= model 1 + qualifications achieved by 33 years

[h] model 5= model 1 + social class at 33 years

[i] model 6= model 2 + 16-year behavioural problems + 33-year qualifications + 33-year social class

Table 4.2c. Association between maths trajectory 7-16 years and the number of adult surveys (0, 1, 2, 3) a person is a binge drinker[a] [RRR (95% CI)]

	7-year maths z-score + change[d]	*+ social class at birth[e]*	*+ behavioural problems (16y)[f]*	*+ Adult qualifications[g]*	*+ Adult social class[h]*	*+ All[i]*
Number of occasions binge drinking[a]						
Men N=2830[c]			*7-year maths z-score[b]*			
Never	1	1	1	1	1	1
1	1.11 (1.02, 1.22)	1.08 (0.98, 1.18)	1.07 (0.97, 1.18)	1.06 (0.95, 1.18)	1.06 (0.96, 1.17)	1.05 (0.94, 1.17)
2	1.16 (1.04, 1.28)	1.10 (0.99, 1.22)	1.07 (0.96, 1.20)	1.04 (0.92, 1.17)	1.05 (0.93, 1.18)	1.00 (0.88, 1.14)
3	1.24 (1.07, 1.42)	1.18 (1.02, 1.37)	1.08 (0.93, 1.27)	1.01 (0.86, 1.20)	1.08 (0.92, 1.27)	0.93 (0.78, 1.11)
			Change 7-16 years			
Never	1	1	1	1	1	1
1	1.11 (1.02, 1.20)	1.09 (1.00, 1.18)	1.08 (0.99, 1.18)	1.08 (0.99, 1.18)	1.08 (0.99, 1.17)	1.07 (0.98, 1.17)
2	1.27 (1.16, 1.40)	1.23 (1.12, 1.36)	1.21 (1.10, 1.34)	1.19 (1.07, 1.32)	1.20 (1.09, 1.32)	1.16 (1.05, 1.29)
3	1.63 (1.43, 1.86)	1.59 (1.38, 1.82)	1.48 (1.29, 1.70)	1.44 (1.24, 1.67)	1.50 (1.30, 1.73)	1.35 (1.16, 1.58)
Women N=3228[c]			*7-year maths z-score[b]*			
Never	1	1	1	1	1	1
1	1.06 (0.98, 1.15)	1.05 (0.96, 1.14)	1.02 (0.94, 1.12)	1.04 (0.94, 1.15)	1.06 (0.97, 1.16)	1.03 (0.93, 1.14)
2	1.02 (0.88, 1.18)	1.00 (0.86, 1.16)	1.02 (0.87, 1.19)	0.90 (0.75, 1.08)	0.94 (0.80, 1.10)	0.90 (0.74, 1.08)
3	1.12 (0.81, 1.55)	1.13 (0.79, 1.61)	1.02 (0.74, 1.40)	0.91 (0.61, 1.38)	1.16 (0.79, 1.70)	0.90 (0.61, 1.33)
			Change 7-16 years			
Never	1	1	1	1	1	1
1	1.06 (0.99, 1.14)	1.05 (0.98, 1.13)	1.04 (0.97, 1.12)	1.05 (0.97, 1.13)	1.06 (0.98, 1.14)	1.04 (0.97, 1.12)
2	1.12 (0.99, 1.28)	1.11 (0.98, 1.26)	1.12 (0.99, 1.28)	1.05 (0.92, 1.21)	1.08 (0.95, 1.23)	1.06 (0.92, 1.21)
3	1.21 (0.85, 1.72)	1.21 (0.84, 1.75)	1.14 (0.79, 1.65)	1.09 (0.74, 1.61)	1.23 (0.85, 1.78)	1.07 (0.73, 1.58)

[a] binge drinkers compared to light drinkers plus non-drinkers

[b] Maths z-scores are negatively coded (ie an increase represents a decrease in rank). Z-score are estimates from multilevel models of maths trajectories 7-16 years.

[c] analysis sample is fixed, based on maximum number with information on drinking at 3 adult ages plus, maths score highest qualifications and social class.

[d] model 1 = 7-year z-score + 7-16 year change in z-score

[e] model 2= model 1 + social class at birth

[f] model 3= model 1 + 16-year behavioural problems

[g] model 4= model 1 + qualifications achieved by 33 years

[h] model 5= model 1 + social class at 33 years

[i] model 6= model 2 + 16-year behavioural problems + 33-year qualifications + 33-year social class

Table 4.2d. Association between maths trajectory 7-16 years and the number of adult surveys (0, 1, 2, 3) a person is a heavy drinker[a] [RRR (95% CI)]

	7-year maths z-score + change[d]	*+ social class at birth*[e]	*+ behavioural problems (16y)*[f]	*+ Adult qualifications*[g]	*+ Adult social class*[h]	*+ All*[i]
Number of occasions heavy drinking						
Men N=2830[c]			*7-year maths z-score*[b]			
Never	1	1	1	1	1	1
1	1.02 (0.93, 1.12)	1.00 (0.91, 1.09)	0.98 (0.89, 1.09)	0.93 (0.83, 1.04)	0.97 (0.87, 1.07)	0.92 (0.82, 1.03)
2	1.13 (0.99, 1.29)	1.10 (0.96, 1.25)	1.04 (0.91, 1.20)	1.04 (0.89, 1.21)	1.05 (0.91, 1.21)	0.99 (0.84, 1.15)
3	0.91 (0.76, 1.10)	0.93 (0.77, 1.13)	0.86 (0.71, 1.04)	0.80 (0.64, 1.00)	0.89 (0.73, 1.08)	0.75 (0.60, 0.95)
			Change 7-16 years			
Never	1	1	1	1	1	1
1	1.23 (1.13, 1.33)	1.21 (1.11, 1.31)	1.20 (1.10, 1.30)	1.16 (1.06, 1.26)	1.19 (1.09, 1.29)	1.15 (1.05, 1.25)
2	1.44 (1.28, 1.62)	1.41 (1.25, 1.60)	1.36 (1.20, 1.54)	1.36 (1.20, 1.56)	1.38 (1.21, 1.56)	1.31 (1.15, 1.50)
3	1.26 (1.07, 1.50)	1.28 (1.07, 1.53)	1.20 (1.00, 1.43)	1.16 (0.95, 1.42)	1.24 (1.03, 1.50)	1.11 (0.90, 1.36)
Women N=3228[c]			*7-year maths z-score*[b]			
Never	1	1	1	1	1	1
1	0.89 (0.79, 1.00)	0.89 (0.79, 1.01)	0.88 (0.77, 1.00)	0.85 (0.73, 0.99)	0.88 (0.77, 1.01)	0.84 (0.73, 0.98)
≥2	0.79 (0.61, 1.02)	0.88 (0.67, 1.15)	0.79 (0.60, 1.04)	0.81 (0.61, 1.09)	0.87 (0.67, 1.14)	0.77 (0.57, 1.02)
			Change 7-16 years			
Never	1	1	1	1	1	1
1	0.93 (0.84, 1.03)	0.93 (0.84, 1.03)	0.92 (0.83, 1.02)	0.91 (0.81, 1.01)	0.92 (0.83, 1.02)	0.90 (0.81, 1.01)
≥2	1.16 (0.95, 1.42)	1.24 (1.00, 1.53)	1.16 (0.94, 1.44)	1.19 (0.96, 1.47)	1.23 (1.00, 1.53)	1.14 (0.92, 1.42)

[a] heavy drinkers compared to light drinkers plus non-drinkers
[b] Maths z-scores are negatively coded (ie an increase represents a decrease in rank). Z-score are estimates from multilevel models of maths trajectories 7-16 years.
[c] analysis sample is fixed, based on maximum number with information on drinking at 3 adult ages plus, maths score highest qualifications and social class.
[d] model 1 = 7-year z-score + 7-16 year change in z-score
[e] model 2= model 1 + social class at birth
[f] model 3= model 1 + 16-year behavioural problems
[g] model 4= model 1 + qualifications achieved by 33 years
[h] model 5= model 1 + social class at 33 years
[i] model 6= model 2 + 16-year behavioural problems + 33-year qualifications + 33-year social class

Appendix Chàpter 4 Cognitive development and health behaviours

Appendix 4.1 Sample representativeness

Table A4.1.1 Distribution [%(n)] of social class at birth in the original birth sample compared with the distribution in the sample with valid smoking and drinking variables and the analysis sample

	Birth sample		Sample with 42-year smoking and drinking [a]		Analysis sample for smoking and drinking models[b]	
	N	% (95%CI)	N	% (95%CI)	N	% (95%CI)
Total N	16,966		11013		6757	
Men						
Class I&II professional	1488	17.0 (16.2,17.8)	1013	18.7 (17.7,19.8)	659	20.6 (19.2,22.0)
Class IV&V & no head of household	2096	23.9 (23.0,24.8)	1230	22.7 (21.6,23.9)	656	20.5 (19.1,21.9)
Women						
Class I&II professional	1391	16.9 (16.1,17.8)	1011	18.0 (17.0,19.1)	682	19.2 (17.9,20.5)
Class IV&V & no head of household	2025	24.7 (23.7,25.6)	1318	23.5 (22.4,24.7)	782	22.0 (20.7,23.4)

[a] Sample with smoking / drinking data at 42 years =11359. From this sample, the total N with data on social class at birth is 11013.

[b] Analysis sample at 42 years with data for cognition and smoking / drinking models and all the pathway factors=6757

There is some evidence that the 42 year sample under-represents those in more manual social classes. Further there is evidence that the analysis sample for the smoking and drinking models (with full data on all of the pathway factors presented in the regression analyses) is more biased towards the professional classes and less representative of those with manual origins, particularly among men.

Appendix 4.2: Associations between observed maths z-scores at 7, 11 and 16 years with adult smoking and drinking at 23-42 years

Table A4.2.1 Unadjusted odds ratio (95%CI) for (a) smoking and (b) quitting smoking at 23, 33 and 42 years, per unit decrease in maths z-score at 7, 11 and 16 years[a]

Age (years) at maths test	MEN	WOMEN	MEN	WOMEN
	23 year Current smoking		*23 year quit smoking*	
7	1.15	1.10	0.84	0.96
	(1.09, 1.22)	(1.04, 1.17)	(0.77, 0.93)	(0.87, 1.06)
11	1.35	1.41	0.80	0.76
	(1.28, 1.43)	(1.33, 1.49)	(0.73, 0.88)	(0.68, 0.84)
16	1.48	1.65	0.78	0.76
	(1.39, 1.57)	(1.54, 1.76)	(0.70, 0.86)	(0.68, 0.85)
	33 year Current smoking		*33 year quit smoking*	
7	1.19	1.17	0.81	0.86
	(1.12, 1.27)	(1.10, 1.25)	(0.74, 0.87)	(0.79, 0.94)
11	1.42	1.54	0.73	0.68
	(1.33, 1.51)	(1.44, 1.65)	(0.67, 0.79)	(0.62, 0.74)
16	1.57	1.87	0.69	0.62
	(1.46, 1.69)	(1.72, 2.02)	(0.63, 0.76)	(0.56, 0.68)
	42 year Current smoking		*42 year quit smoking*	
7	1.22	1.21	0.80	0.86
	(1.14, 1.30)	(1.13, 1.29)	(0.74, 0.87)	(0.79, 0.93)
11	1.48	1.62	0.71	0.67
	(1.38, 1.58)	(1.51, 1.74)	(0.66, 0.77)	(0.62, 0.73)
16	1.69	1.94	0.65	0.61
	(1.57, 1.83)	(1.78, 2.11)	(0.59, 0.71)	(0.55, 0.67)

[a] n varies by model; includes the maximum number of cohort members with individual test score and smoking data available.

Table A.4.2.2 Unadjusted odds ratio (95%CI) for (a) non-drinking and (b) binge (c) heavy drinking at 23, 33 and 42 years, per standard deviation decrease in maths z-score at 7, 11 and 16 years.[a]

Age (years) at maths test	MEN	WOMEN	MEN	WOMEN	MEN	WOMEN
	23 year Non-drinking		*23 year Binge drinking*		*23 year Heavy drinking*	
7	1.47	1.32	0.96	0.87	0.96	0.80
	(1.33, 1.61)	(1.24, 1.40)	(0.90, 1.01)	(0.81, 0.93)	(0.90, 1.02)	(0.71, 0.90)
11	1.46	1.57	1.07	0.83	1.03	0.80
	(1.32, 1.61)	(1.47, 1.68)	(1.02, 1.13)	(0.78, 0.89)	(0.96, 1.09)	(0.70, 0.88)
16	1.27	1.43	1.22	0.90	1.12	0.78
	(1.15, 1.40)	(1.33, 1.53)	(1.15, 1.29)	(0.84, 0.98)	(1.05, 1.20)	(0.69, 0.88)
	33 year Non-drinking		*33 year Binge drinking*		*33 year Heavy drinking*	
7	1.48	1.32	0.99	0.93	0.92	0.83
	(1.36, 1.62)	(1.24, 1.40)	(0.93, 1.06)	(0.86, 1.02)	(0.84, 1.00)	(0.71, 0.97)
11	1.47	1.41	1.12	0.97	1.07	0.84
	(1.34, 1.61)	(1.32, 1.51)	(1.05, 1.20)	(0.89, 1.05)	(0.98, 1.16)	(0.72, 0.98)
16	1.39	1.36	1.24	1.07	1.16	0.85
	(1.26, 1.53)	(1.27, 1.47)	(1.15, 1.32)	(0.98, 1.18)	(1.06, 1.27)	(0.71, 1.01)
	42 year Non-drinking		*42 year Binge drinking*		*42 year Heavy drinking*	
7	1.40	1.31	1.06	1.09	0.90	0.94
	(1.28, 1.53)	(1.22, 1.40)	(0.99, 1.12)	(1.01, 1.19)	(0.83, 0.96)	(0.85, 1.06)
11	1.51	1.49	1.15	1.21	0.99	0.96
	(1.38, 1.65)	(1.38, 1.60)	(1.08, 1.22)	(1.21, 1.31)	(0.93, 1.06)	(0.86, 1.08)
16	1.48	1.49	1.25	1.41	1.08	1.01
	(1.34, 1.64)	(1.37, 1.61)	(1.17, 1.34)	(1.28, 1.56)	(1.01, 1.17)	(0.89, 1.14)

[a] n varies by model; includes the maximum number of cohort members with individual test score and drinking data available.

Appendix 4.3 Associations between 7-year z-score and change in z-score 7-16 years with confounders and pathway variables

Table A4.3.1 Distribution (%) of the 7-year maths z-score by the pathway variables

	Quintiles of 7-year maths z-score					*Total*		
	Highest ability	2	3	4	Lowest Ability	*%*	*n*	linear trend[a]
				Men				
7y z-score	21.0	20.4	20.0	19.7	18.9	*100*	*8643*	
				Class at birth (%)				
I&II	32.0	18.8	15.5	10.3	7.4	*17.1*	*1425*	P<0.001
IIINM	12.0	11.2	9.6	8.0	6.7	*9.6*	*797*	
IIIM	41.4	50.5	51.5	52.2	49.7	*49.0*	*4071*	
IV&V&S	14.6	19.6	23.4	29.5	36.1	*24.3*	*2020*	
				Rutter score 16 years (%)				
Normal	70.5	57.1	47.4	39.4	28.5	*49.8*	*2924*	P<0.001
Borderline	24.9	31.7	36.3	39.7	42.8	34.6	*2033*	
Case	4.6	11.2	16.3	20.9	28.6	15.7	*922*	
				Class at 33 years (%)				
I&II	60.0	42.8	30.3	20.8	12.6	*34.5*	*2346*	P<0.001
IIINM	14.6	14.8	12.0	9.4	5.5	*11.5*	*784*	
IIIM	17.6	30.9	38.2	45.5	46.8	*35.1*	*2387*	
IV&V	7.9	11.5	19.5	24.4	35.2	*19.0*	*1291*	
				Qualifications at 33 years (%)				
None	0.7	2.6	6.4	12.9	28.1	*9.0*	*480*	P<0.001
< O level	2.0	8.5	15.0	21.4	24.7	*13.6*	*728*	
O level	16.8	26.0	29.1	26.2	21.4	*23.9*	*1280*	
A level	22.9	25.9	26.9	25.6	19.3	*24.3*	*1304*	
Higher	57.0	37.1	22.0	13.9	6.5	*29.3*	*1568*	
				Women				
7y z-score	19.0	19.5	19.5	20.3	21.2	*100.0*	*8643*	
				Class at birth (%)				
I&II	33.6	21.1	14.7	11.2	6.8	*17.2*	*1425*	P<0.001
IIINM	12.0	10.4	10.4	8.6	6.1	*9.4*	*797*	
IIIM	41.0	48.0	49.7	52.3	51.6	*48.6*	*4071*	
IV&V&S	13.5	20.4	25.2	28.0	35.5	*24.7*	*2020*	
				Rutter score 16 years (%)				
Normal	74.9	65.02	58.64	50.23	33.36	56.42	*3189*	P<0.001
Borderline	21.7	28.3	32.3	35.5	43.8	32.3	*1827*	
Case	3.4	6.7	9.1	14.3	22.8	11.3	*636*	
				Class at 33 years (%)				
I&II	51.6	34.5	26.8	20.5	11.7	*29.1*	*2346*	P<0.001
IIINM	34.7	42.0	43.2	41.0	33.0	*38.8*	*784*	
IIIM	4.2	6.8	7.8	9.5	12.0	*8.1*	*2387*	
IV&V	9.5	16.7	22.3	28.9	43.3	*24.0*	*1291*	
				Qualifications at 33 years (%)				
None	1.1	4.1	6.5	13.2	29.5	*10.4*	*480*	P<0.001
< O level	3.3	9.9	18.2	24.2	30.5	*16.8*	*728*	
O level	28.9	38.6	44.0	40.6	29.4	*36.4*	*1280*	
A level	15.2	13.6	11.2	7.6	3.8	*10.4*	*1304*	
Higher	51.6	33.8	20.2	14.5	6.8	*26.0*	*1568*	

[a] Tests for linear trend use 7-year z-score as a continuous variable

Table A4.3.2 Distribution (%) of the 7-16 year change in maths z-score by pathway variables

	Quintiles of 7-16 year change in maths z-score					*Total*		
	Highest ability	2	3	4	Lowest Ability	*%*	*n*	Linear trend[a]
				Men				
7-16 z-score	23.2	21.0	19.8	19.3	16.8	*100.0*	*8643*	
			Class at birth (%)					
I&II	26.6	18.5	15.1	13.6	8.7	*17.1*	*1425*	P<0.001
IIINM	11.0	9.0	10.0	9.0	8.0	*9.6*	*797*	
IIIM	44.4	48.6	48.7	51.8	53.0	*49.0*	*4071*	
IV&V&S	17.8	23.4	26.4	25.8	30.5	*24.3*	*2020*	
			Rutter score 16 years (%)					
Normal	67.9	53.2	43.2	40.9	33.6	*49.7*	*2924*	
Borderline	27.1	33.1	39.3	39.2	38.7	*38.7*	*2033*	
Case	5.0	13.7	17.5	19.9	27.8	*27.8*	*922*	
			Class at 33 years (%)					
I&II	53.3	35.3	30.5	26.5	18.8	*34.5*	*2346*	P<0.001
IIINM	14.4	11.9	11.3	9.2	9.6	*11.5*	*784*	
IIIM	21.6	30.9	38.9	43.2	46.5	*35.1*	*2387*	
IV&V	10.6	21.9	19.4	21.1	25.1	*19.0*	*1291*	
			Qualifications at 33 years (%)					
None	2.9	9.7	11.5	9.9	14.1	*9.0*	*480*	P<0.001
< O level	6.6	12.6	13.3	18.3	21.6	*13.6*	*728*	
O level	17.5	23.0	25.2	29.4	27.8	*23.9*	*1280*	
A level	24.5	24.0	25.0	23.2	25.0	*24.3*	*1304*	
Higher	48.5	30.7	24.9	19.3	11.5	*29.3*	*1568*	
				Women				
7-16 year z-score	16.6	16.6	20.3	20.8	23.4	*100.0*	*1908*	
			Class at birth (%)					
I&II	27.9	17.9	14.9	16.0	11.9	*17.2*	*1353*	P<0.001
IIINM	10.2	10.5	8.5	8.5	9.6	*9.4*	*743*	
IIIM	41.5	47.7	50.0	51.6	50.7	*48.6*	*3826*	
IV&V&S	20.5	23.9	26.5	23.9	27.8	*24.7*	*1947*	
			Rutter score 16 years (%)					
Normal	69.6	58.7	56.3	51.5	48.5	*56.4*	*3189*	
Borderline	25.0	31.5	30.6	36.0	36.9	*32.3*	*1827*	
Case	5.4	9.8	13.1	12.6	14.6	*11.3*	*636*	
			Class at 33 years (%)					
I&II	41.7	28.0	25.3	26.9	25.5	*29.1*	*1967*	P<0.001
IIINM	36.8	38.7	40.3	40.2	38.1	*38.8*	*2628*	
IIIM	5.2	8.4	8.9	8.0	9.3	*8.1*	*545*	
IV&V	16.3	24.9	25.5	25.0	27.1	*24.0*	*1627*	
			Qualifications at 33 years (%)					
None	6.2	11.1	11.2	11.2	11.7	*10.4*	*583*	P<0.001
< O level	10.1	14.0	19.0	19.3	20.1	*16.8*	*941*	
O level	28.4	36.5	37.5	37.8	40.1	*36.4*	*2036*	
A level	14.5	11.3	10.3	8.7	8.2	*10.4*	*584*	
Higher	40.9	27.0	21.9	23.0	19.8	*26.0*	*1456*	

[a] Tests for linear trend use 7-year z-score as a continuous variable

Table A4.3.3 Distribution (%) of the 7-year reading z-score by the pathway variables

	Quintiles of 7-year reading z-score					*Total*		
	Highest ability	2	3	4	Lowest Ability	*%*	*N*	linear trend[a]
				Men				
7y z-score	15.5	18.6	20.3	21.4	24.1	*100.0*	*8644*	
				Class at birth (%)				
I&II	35.4	22.4	16.3	11.0	7.0	*17.1*	*1425*	P<0.001
IIINM	13.3	11.4	10.6	7.7	6.5	*9.6*	*798*	
IIIM	37.8	48.7	53.1	52.4	50.0	*49.0*	*4071*	
IV&V &S	13.5	17.5	20.1	28.9	36.5	*24.3*	*2020*	
				Rutter 16 years (%)				
Normal	72.6	61.2	52.4	44.5	25.5	*49.7*	*2924*	P<0.001
Borderline	23.7	29.7	35.4	36.4	44.4	*34.6*	*2034*	
Case	3.7	9.2	12.2	19.1	30.1	*15.7*	*922*	
				Class at 33 years (%)				
I&II	66.0	46.9	34.8	23.2	12.0	*34.5*	*2347*	P<0.001
IIINM	15.0	16.5	13.4	9.4	5.0	*11.5*	*783*	
IIIM	13.1	25.2	36.3	47.5	46.0	*35.1*	*2386*	
IV&V &S	6.0	11.4	15.6	19.9	37.0	*19.0*	*1291*	
				Qualifications at 33 years (%)				
None	0.3	1.5	4.0	9.4	28.5	*9.0*	*480*	P<0.001
< O level	2.4	6.3	12.4	20.2	24.6	*13.6*	*728*	
O level	15.4	25.5	26.4	27.6	22.7	*23.9*	*1279*	
A level	20.2	27.1	28.1	27.3	18.0	*24.3*	*1304*	
Higher	61.7	39.6	29.2	15.6	6.2	*29.3*	*1569*	
				Women				
7y z-score	24.8	21.5	21.5	18.5	15.6	*100.0*	*8,155*	
				Class at birth (%)				
I&II	32.8	18.3	13.1	9.0	5.3	*17.2*	*1354*	P<0.001
IIINM	12.6	10.5	9.7	6.9	5.4	*9.4*	*742*	
IIIM	40.6	50.6	51.7	53.2	49.6	*48.6*	*3827*	
IV&V &S	14.1	20.6	25.5	30.9	39.6	*24.7*	*1947*	
				Rutter score 16 years (%)				
Normal	72.9	62.9	55.9	46.9	28.8	*56.4*	*3189*	P<0.001
Borderline	24.1	29.6	34.6	35.0	45.3	*32.4*	*1830*	
Case	3.0	7.5	9.5	18.2	25.9	*11.3*	*636*	
				Class at 33 years (%)				
I&II	48.0	32.4	23.2	18.6	10.3	*29.1*	*1966*	P<0.001
IIINM	37.9	42.4	44.0	38.9	27.8	*38.8*	*2628*	
IIIM	4.4	7.4	9.6	9.5	12.1	*8.1*	*546*	
IV&V &S	9.8	17.9	23.2	33.0	49.8	*24.1*	*1628*	
				Qualifications at 33 years (%)				
None	0.5	4.9	7.4	14.2	39.6	*10.4*	*584*	P<0.001
< O level	2.5	12.3	20.9	30.2	29.4	*16.8*	*941*	
O level	31.7	39.8	46.7	37.2	23.3	*36.4*	*2035*	
A level	15.6	13.7	8.7	6.1	2.6	*10.4*	*583*	
Higher	49.7	29.3	16.4	12.2	5.2	*26.0*	*1456*	

[a]Tests for linear trend use 7-year z-score as a continuous variable

Table A4.3.4 Distribution (%) of the 7-16 year change in reading z-score by pathway variables

	Quintiles of 7-16 year change in reading z-score					*Total*		
	Highest ability	2	3	4	Lowest ability	*%*	*n*	linear trend[a]
				Men				
7-16 year z-score	32.8	29.7	20.9	10.8	5.8	*100.0*	*8644*	
				Class at birth (%)				
I&II	23.2	17.3	11.3	12.1	11.7	*17.1*	*1425*	P<0.001
IIINM	11.1	10.1	8.2	7.3	7.7	*9.6*	*798*	
IIIM	45.3	49.7	51.9	51.2	51.8	*49.0*	*4071*	
IV&V&S	20.4	22.9	28.6	29.5	28.8	*24.3*	*2020*	
				Rutter score 16 years (%)				
Normal	62.0	48.7	39.8	38.7	42.1	*49.7*	*2924*	P<0.001
Borderline	28.7	34.7	38.6	41.4	39.3	*34.6*	*2034*	
Case	9.3	16.6	21.7	20.0	18.6	*15.7*	*922*	
				Class at 33 years (%)				
I&II	46.5	34.1	24.0	23.9	22.1	*34.5*	*2347*	P<0.001
IIINM	14.1	11.5	8.8	8.6	10.7	*11.5*	*783*	
IIIM	27.0	35.8	40.2	43.3	45.5	*35.1*	*2386*	
IV&V	12.4	18.6	27.0	24.2	21.7	*19.0*	*1291*	
				Qualifications at 33 years (%)				
None	3.1	8.3	17.3	12.7	13.2	*9.0*	*480*	P<0.001
< O level	9.4	14.1	16.1	19.1	18.6	*13.6*	*728*	
O level	22.2	23.7	23.0	27.6	30.2	*23.9*	*1279*	
A level	23.9	23.5	25.5	25.9	24.0	*24.3*	*1304*	
Higher	41.5	30.4	18.1	14.8	14.1	*29.3*	*1569*	
				Women				
7-16 year z-score	6.4	10.0	10.0	29.8	35.1	*100.0*	*8,155*	
				Class at birth (%)				
I&II	20.4	23.2	20.6	17.0	13.3	*17.2*	*1354*	p<0.001
IIINM	9.6	10.1	8.6	10.3	8.9	*9.4*	*742*	
IIIM	49.9	45.3	48.6	46.4	51.2	*48.6*	*3827*	
IV&V&S	20.2	21.4	22.2	26.3	26.6	*24.7*	*1947*	
				Rutter score 16 years (%)				
Normal	66.2	65.6	59.5	53.7	51.6	*56.4*	*3189*	P<0.001
Borderline	29.5	29.2	32.5	32.2	34.1	*32.4*	*1830*	
Case	4.3	5.2	8.0	14.1	14.4	*11.3*	*636*	
				Class at 33 years (%)				
I&II	38.9	38.8	34.9	27.8	22.1	*29.1*	*1966*	p<0.001
IIINM	36.3	37.3	37.6	37.5	41.5	*38.8*	*2628*	
IIIM	7.4	5.3	6.1	8.7	9.6	*8.1*	*546*	
IV&V	17.4	18.6	21.3	26.1	26.8	*24.1*	*1628*	
				Qualifications at 33 years (%)				
None	0.7	4.3	9.4	14.7	11.5	*10.4*	*584*	p<0.001
< O level	13.5	13.9	16.3	15.6	19.7	*16.8*	*941*	
O level	37.4	33.8	30.6	36.3	40.0	*36.4*	*2035*	
A level	14.2	11.2	11.0	9.8	9.5	*10.4*	*583*	
Higher	34.2	36.7	32.7	23.6	19.3	*26.0*	*1456*	

[a] Tests for linear trend use 7-year z-score as a continuous variable

Appendix 4.4: Associations between 7-year reading z-score and 7-16 year change in z-score with adult smoking and drinking at 23-42 years

Table A4.4.1a. Association between childhood reading trajectories and adult smoking [OR (95% CI)]

	Adjusted[d]	Adjusted + childhood social class[e]	Adjusted + behavioural problems[f]	Adjusted + adult social class[g]	Adjusted + adult qualifications[h]	Adjusted +all[i]
Reading z-score[a]			***Men***			
			23 year Current smoking [bc]			
7 years	1.24 (1.15, 1.34)	1.22 (1.13, 1.32)	1.09 (1.00, 1.18)	1.08 (0.99, 1.17)	1.01 (0.93, 1.11)	0.91 (0.82,1.00)
Change 7-16 years	1.14 (1.07, 1.22)	1.14 (1.07, 1.21)	1.10 (1.03, 1.18)	1.08 (1.01, 1.16)	1.06 (0.99, 1.13)	1.02 (0.96, 1.10)
Reading z-score[a]			*33 year Current smoking* [bc]			
7 years	1.30 (1.21, 1.4)	1.26 (1.17, 1.36)	1.13 (1.04, 1.22)	1.11 (1.02, 1.21)	1.02 (0.93, 1.11)	0.91 (0.83, 1.00)
Change 7-16 years	1.20 (1.13, 1.28)	1.19 (1.12, 1.27)	1.15 (1.08, 1.23)	1.13 (1.06, 1.21)	1.09 (1.02, 1.17)	1.06 (0.99, 1.13)
Reading z-score[a]			*42 year Current smoking* [bc]			
7 years	1.43 (1.31, 1.56)	1.36 (1.24, 1.49)	1.22 (1.11, 1.34)	1.19 (1.08, 1.31)	1.11 (1.00, 1.24)	1.00 (0.89, 1.11)
Change 7-16 years	1.27 (1.17, 1.37)	1.25 (1.16, 1.34)	1.21 (1.12, 1.31)	1.18 (1.09, 1.27)	1.15 (1.06, 1.25)	1.11 (1.02, 1.20)
Reading z-score[a]			***Women***			
			23 year Current smoking [bc]			
7 years	1.37 (1.28, 1.48)	1.31 (1.22, 1.42)	1.15 (1.06, 1.25)	1.21 (1.12, 1.32)	1.02 (0.93, 1.12)	0.94 (0.85, 1.03)
Change 7-16 years	1.32 (1.24, 1.41)	1.30 (1.22, 1.38)	1.24 (1.16, 1.32)	1.26 (1.18, 1.34)	1.18 (1.11, 1.27)	1.15 (1.07, 1.23)
Reading z-score[a]			*33 year Current smoking* [bc]			
7 years	1.65 (1.53, 1.78)	1.58 (1.46, 1.70)	1.38 (1.27, 1.49)	1.47 (1.35, 1.59)	1.22 (1.11, 1.34)	1.13 (1.03, 1.25)
Change 7-16 years	1.34 (1.26, 1.43)	1.32 (1.23, 1.41)	1.24 (1.16, 1.33)	1.28 (1.20, 1.37)	1.20 (1.12, 1.28)	1.16 (1.08, 1.24)
Reading z-score[a]			*42 year Current smoking* [bc]			
7 years	1.69 (1.55, 1.84)	1.59 (1.45, 1.74)	1.40 (1.28, 1.54)	1.48 (1.35, 1.63)	1.25 (1.12, 1.39)	1.17 (1.04, 1.30)
Change 7-16 years	1.36 (1.27, 1.46)	1.33 (1.23, 1.43)	1.25 (1.16, 1.35)	1.29 (1.20, 1.39)	1.21 (1.12, 1.31)	1.17 (1.08, 1.27)

[a] z-scores (from models of trajectories 7-16 y) are reversed; increase in score represents decline in ability rank.
[b] sample with data on drinking, reading and all covariates; 3265 men and 3584 women at 23 years; 3700 men and 3939 women at 33 years; 3206 men and 3552 women at 42 years
[c] current smokers compared to non-smokers (including ex-smokers)
[d] model 1= 7 years reading score + change in reading 7-16 years
[e] model 2 = model 1 + social class of origin
[f] model 3 = model 2 + behavioural problems (16 years, Rutter score)
[g] model 4 = model 2 + adult social class
[h] model 5 = model 2 + adult qualifications
[i] model 6 = model 2 + behavioural problems (16 years, Rutter score) + adult qualifications + adult social class

Table A4.4.1b Association between childhood reading trajectories and adult non-drinking (vs drinking) [OR (95% CI)]

	Adjusted[d]	Adjusted + childhood social class[e]	Adjusted + behavioural problems[f]	Adjusted + adult social class[g]	Adjusted + adult qualifications[h]	Adjusted +all[i]
Reading z-score[a]			***Men***			
			23 year Non-drinking[bc]			
7 years	1.39 (1.22, 1.58)	1.40 (1.23, 1.61)	1.40 (1.22, 1.61)	1.46 (1.26, 1.70)	1.37 (1.17, 1.60)	1.41 (1.20, 1.66)
Change 7-16 years	1.01 (0.90, 1.13)	1.02 (0.91, 1.14)	1.02 (0.91, 1.14)	1.03 (0.92, 1.16)	1.00 (0.89, 1.13)	1.02 (0.90, 1.15)
Reading z-score[a]			*33 year Non-drinking*[bc]			
7 years	1.41 (1.27, 1.56)	1.40 (1.26, 1.56)	1.34 (1.19, 1.49)	1.32 (1.17, 1.48)	1.31 (1.16, 1.48)	1.25 (1.10, 1.42)
Change 7-16 years	1.28 (1.17, 1.40)	1.28 (1.17, 1.40)	1.26 (1.15, 1.38)	1.25 (1.14, 1.37)	1.24 (1.13, 1.36)	1.23 (1.12, 1.35)
Reading z-score[a]			*42 year Non-drinking*[bc]			
7 years	1.43 (1.27, 1.61)	1.39 (1.23, 1.57)	1.30 (1.15, 1.48)	1.27 (1.11, 1.45)	1.30 (1.13, 1.49)	1.22 (1.05, 1.41)
Change 7-16 years	1.18 (1.07, 1.31)	1.17 (1.06, 1.30)	1.15 (1.04, 1.28)	1.13 (1.02, 1.26)	1.14 (1.02, 1.27)	1.12 (1.01, 1.25)
Reading z-score[a]			***Women***			
			23 year Non-drinking[bc]			
7 years	1.53 (1.42, 1.66)	1.47 (1.35, 1.60)	1.42 (1.30, 1.56)	1.37 (1.25, 1.49)	1.34 (1.21, 1.48)	1.28 (1.16, 1.42)
Change 7-16 years	1.16 (1.08, 1.24)	1.14 (1.06, 1.22)	1.12 (1.05, 1.21)	1.10 (1.03, 1.18)	1.10 (1.02, 1.18)	1.08 (1.00, 1.16)
Reading z-score[a]			*33 year Non-drinking*[bc]			
7 years	1.45 (1.35, 1.56)	1.42 (1.31, 1.53)	1.39 (1.28, 1.51)	1.36 (1.25, 1.47)	1.36 (1.24, 1.49)	1.33 (1.21, 1.46)
Change 7-16 years	1.06 (1.00, 1.13)	1.05 (0.98, 1.12)	1.04 (0.97, 1.11)	1.03 (0.97, 1.10)	1.03 (0.97, 1.11)	1.03 (0.96, 1.10)
Reading z-score[a]			*42 year Non-drinking*[bc]			
7 years	1.56 (1.43, 1.69)	1.52 (1.39, 1.67)	1.42 (1.30, 1.56)	1.42 (1.29, 1.56)	1.35 (1.21, 1.50)	1.28 (1.15, 1.43)
Change 7-16 years	1.11 (1.04, 1.20)	1.11 (1.03, 1.19)	1.07 (1.00, 1.15)	1.07 (0.99, 1.16)	1.05 (0.97, 1.14)	1.03 (0.95, 1.11)

[a] z-scores (from models of trajectories 7-16 y) are reversed; increase in score represents decline in ability rank.
[b] sample with data on drinking, reading and all covariates; 3275 men and 3597 women at 23 years; 3752 men and 3990 women at 33 years; 3205 men and 3552 women at 42 years.
[c] non-drinkers compared to those drinking more often than on special occasions
[d] model 1= 7 years reading score + change in reading 7-16 years
[e] model 2 = model 1 + social class of origin
[f] model 3 = model 2 + behavioural problems (16 years, Rutter score)
[g] model 4 = model 2 + adult social class
[h] model 5 = model 2 + adult qualifications
[i] model 6 = model 2 + behavioural problems (16 years, Rutter score) + adult qualifications + adult social class

Table A4.4.1c. Association between childhood reading trajectories and adult binge drinking (vs non and light drinking) [OR (95% CI)]

	Adjusted[d]	Adjusted + childhood social class[e]	Adjusted + behavioural problems[f]	Adjusted + adult social class[g]	Adjusted + adult qualifications[h]	Adjusted +all[i]
			Men			
Reading z-score[a]			*23 year Binge-drinking*[bc]			
7 years	1.14 (1.05, 1.22)	1.11 (1.03, 1.20)	1.06 (0.98, 1.15)	1.04 (0.95, 1.13)	1.02 (0.93, 1.11)	0.97 (0.89, 1.07)
Change 7-16 years	1.13 (1.06, 1.21)	1.13 (1.06, 1.20)	1.11 (1.04, 1.19)	1.10 (1.03, 1.17)	1.09 (1.02, 1.16)	1.07 (1.00, 1.15)
Reading z-score[a]			*33 year Binge-drinking*[bc]			
7 years	1.07 (1.00, 1.16)	1.03 (0.95, 1.11)	1.00 (0.92, 1.09)	0.95 (0.88, 1.04)	0.91 (0.84, 1.00)	0.88 (0.80, 0.97)
Change 7-16 years	1.10 (1.03, 1.17)	1.08 (1.01, 1.15)	1.07 (1.01, 1.14)	1.05 (0.98, 1.12)	1.03 (0.96, 1.10)	1.02 (0.95, 1.09)
Reading z-score[a]			*42 year Binge-drinking*[bc]			
7 years	1.16 (1.07, 1.25)	1.10 (1.01, 1.20)	1.04 (0.96, 1.14)	1.05 (0.96, 1.15)	1.03 (0.94, 1.13)	0.98 (0.89, 1.08)
Change 7-16 years	1.13 (1.05, 1.21)	1.11 (1.04, 1.19)	1.09 (1.02, 1.17)	1.09 (1.01, 1.17)	1.08 (1.01, 1.16)	1.06 (0.99, 1.14)
			Women			
Reading z-score[a]			*23 year Binge-drinking*[bc]			
7 years	0.86 (0.79, 0.94)	0.86 (0.78, 0.94)	0.86 (0.78, 0.95)	0.89 (0.80, 0.98)	0.91 (0.81, 1.02)	0.92 (0.82, 1.03)
Change 7-16 years	0.97 (0.90, 1.05)	0.97 (0.90, 1.05)	0.98 (0.90, 1.06)	0.99 (0.91, 1.07)	0.99 (0.92, 1.08)	1.00 (0.92, 1.08)
Reading z-score[a]			*33 year Binge-drinking*[bc]			
7 years	1.06 (0.96, 1.16)	1.07 (0.96, 1.18)	1.05 (0.95, 1.17)	1.01 (0.91, 1.13)	0.99 (0.87, 1.12)	0.96 (0.85, 1.09)
Change 7-16 years	1.12 (1.03, 1.22)	1.13 (1.04, 1.23)	1.12 (1.03, 1.22)	1.10 (1.01, 1.20)	1.09 (1.00, 1.19)	1.08 (0.99, 1.18)
Reading z-score[a]			*42 year Binge-drinking*[bc]			
7 years	1.35 (1.22, 1.49)	1.29 (1.16, 1.43)	1.25 (1.12, 1.40)	1.24 (1.10, 1.38)	1.14 (1.00, 1.29)	1.11 (0.98, 1.27)
Change 7-16 years	1.15 (1.05, 1.25)	1.13 (1.03, 1.23)	1.11 (1.02, 1.22)	1.10 (1.01, 1.21)	1.07 (0.98, 1.18)	1.06 (0.97, 1.17)

[a] z-scores (from models of trajectories 7-16 y) are reversed; increase in score represents decline in ability rank.
[b] sample with data on drinking, reading and all covariates; 3275 men and 3597 women at 23 years; 3752 men and 3990 women at 33 years; 3205 men and 3552 women at 42 years
[c] binge drinkers compared to light drinkers plus non-drinkers
[d] model 1= 7 years reading score + change in reading 7-16 years
[e] model 2 = model 1 + social class of origin
[f] model 3 = model 2 + behavioural problems (16 years, Rutter score)
[g] model 4 = model 2 + adult social class
[h] model 5 = model 2 + adult qualifications
[i] model 6 = model 2 + behavioural problems (16 years, Rutter score) + adult qualifications + adult social class

Table A4.4.1d. Odds ratio (95% CI) for heavy drinking by childhood reading trajectories, adult qualifications and social position.

	Adjusted[d]	Adjusted + childhood social class[e]	Adjusted + behavioural problems[f]	Adjusted + adult social class[g]	Adjusted + adult qualifications[h]	Adjusted +all[i]
			Men			
Reading z-score[a]			*23 year Heavy-drinking* [bc]			
7 years	1.13 (1.04, 1.23)	1.14 (1.04, 1.24)	1.09 (1.00, 1.20)	1.07 (0.97, 1.17)	1.08 (0.97, 1.19)	1.03 (0.93, 1.14)
Change 7-16 years	1.04 (0.97, 1.12)	1.04 (0.97, 1.12)	1.03 (0.96, 1.11)	1.02 (0.94, 1.10)	1.02 (0.94, 1.10)	1.00 (0.93, 1.08)
Reading z-score[a]			*33 year Heavy-drinking* [bc]			
7 years	1.03 (0.94, 1.14)	0.99 (0.89, 1.10)	0.93 (0.84, 1.04)	0.92 (0.83, 1.03)	0.87 (0.77, 0.98)	0.83 (0.73, 0.94)
Change 7-16 years	1.08 (0.99, 1.17)	1.06 (0.98, 1.15)	1.04 (0.96, 1.13)	1.03 (0.95, 1.12)	1.00 (0.92, 1.09)	0.99 (0.90, 1.08)
Reading z-score[a]			*42 year Heavy-drinking* [bc]			
7 years	1.05 (0.96, 1.15)	1.01 (0.93, 1.11)	0.98 (0.89, 1.08)	0.99 (0.89, 1.09)	0.92 (0.83, 1.02)	0.90 (0.81, 1.00)
Change 7-16 years	1.06 (0.98, 1.14)	1.05 (0.97, 1.13)	1.03 (0.96, 1.11)	1.03 (0.95, 1.11)	1.00 (0.93, 1.08)	0.99 (0.92, 1.07)
			Women			
Reading z-score[a]			*23 year Heavy-drinking* [bc]			
7 years	0.84 (0.73, 0.98)	0.86 (0.73, 1.01)	0.84 (0.71, 0.99)	0.87 (0.74, 1.03)	0.85 (0.70, 1.03)	0.84 (0.69, 1.02)
Change 7-16 years	1.00 (0.88, 1.13)	1.01 (0.89, 1.14)	1.00 (0.88, 1.14)	1.01 (0.89, 1.15)	1.00 (0.88, 1.14)	1.00 (0.87, 1.14)
Reading z-score[a]			*33 year Heavy-drinking* [bc]			
7 years	0.82 (0.67, 1.00)	0.90 (0.73, 1.11)	0.82 (0.66, 1.02)	0.90 (0.72, 1.12)	0.83 (0.64, 1.06)	0.80 (0.62, 1.03)
Change 7-16 years	1.03 (0.88, 1.22)	1.08 (0.91, 1.28)	1.04 (0.87, 1.23)	1.09 (0.91, 1.29)	1.05 (0.88, 1.25)	1.04 (0.87, 1.24)
Reading z-score[a]			*42 year Heavy-drinking* [bc]			
7 years	1.05 (0.91, 1.20)	1.09 (0.95, 1.26)	1.05 (0.91, 1.22)	1.09 (0.94, 1.27)	1.04 (0.88, 1.24)	1.03 (0.86, 1.22)
Change 7-16 years	0.97 (0.86, 1.09)	0.99 (0.88, 1.12)	0.97 (0.86, 1.10)	1.00 (0.88, 1.13)	0.97 (0.86, 1.10)	0.97 (0.86, 1.10)

[a] z-scores (from models of trajectories 7-16 y) are reversed; increase in score represents decline in ability rank.
[b] sample with data on drinking, reading and all covariates; 3295 men and 3597 women at 23 years; 3752 men and 3990 women at 33 years; 3205 men and 3552 women at 42 years
[c] heavy drinkers compared to light drinkers plus non-drinkers
[d] model 1= 7-year reading z-score + change in reading z-score 7-16 years
[e] model 2 = model 1 + social class of origin
[f] model 3 = model 2 + behavioural problems (16 years, Rutter score)
[g] model 4 = model 2 + adult social class
[h] model 5 = model 2 + adult qualifications
[i] model 6 = model 2 + behavioural problems (16 years, Rutter score) + adult qualifications + adult social class

Table A4.4.1e RRR of drinking frequency (baseline is daily drinking) per SD decrease in reading 7-year z-score and 7-16 year z-score, mena

Drinking frequency	*Adjusted reading z-score*[b]	*+ childhood social class*[c]	*+ behavioural problems*[e]	*+ adult qualifications*[f]	*+ adult social class*[g]	*+all*[h]
23 years			7-year z-score			
Daily	1	1	1	1	1	1
Weekly	1.11 (1.02, 1.20)	1.08 (0.99, 1.17)	1.09 (1.00, 1.19)	1.10 (1.00, 1.21)	1.07 (0.98, 1.17)	1.09 (0.99, 1.21)
Monthly	1.23 (1.07, 1.42)	1.21 (1.04, 1.40)	1.22 (1.05, 1.42)	1.18 (1.00, 1.39)	1.19 (1.02, 1.40)	1.18 (1.00, 1.40)
Infrequent/ Never	1.49 (1.29, 1.73)	1.49 (1.28, 1.73)	1.50 (1.28, 1.75)	1.45 (1.22, 1.73)	1.54 (1.3, 1.82)	1.50 (1.25, 1.79)
			7-16 year change in z-score			
Daily	1	1	1	1	1	1
Weekly	1.08 (1.01, 1.15)	1.07 (1.00, 1.15)	1.07 (1.00, 1.15)	1.08 (1.00, 1.16)	1.07 (0.99, 1.14)	1.08 (1.00, 1.16)
Monthly	1.08 (0.95, 1.22)	1.07 (0.95, 1.21)	1.08 (0.95, 1.22)	1.06 (0.94, 1.20)	1.07 (0.94, 1.21)	1.06 (0.94, 1.20)
Infrequent/ Never	1.06 (0.95, 1.19)	1.06 (0.95, 1.19)	1.06 (0.95, 1.20)	1.05 (0.93, 1.19)	1.07 (0.95, 1.21)	1.06 (0.94, 1.20)
33 years			7-year z-score			
Daily	1	1	1	1	1	1
Weekly	1.30 (1.18, 1.43)	1.28 (1.16, 1.42)	1.31 (1.19, 1.45)	1.34 (1.20, 1.49)	1.18 (1.06, 1.31)	1.27 (1.14, 1.42)
Monthly	1.35 (1.20, 1.53)	1.33 (1.17, 1.51)	1.36 (1.19, 1.55)	1.34 (1.16, 1.55)	1.23 (1.07, 1.41)	1.29 (1.11, 1.49)
Infrequent/ Never	1.75 (1.53, 2.00)	1.72 (1.50, 1.98)	1.67 (1.45, 1.92)	1.66 (1.42, 1.93)	1.51 (1.30, 1.75)	1.51 (1.29, 1.77)
			7-16 year change in z-score			
Daily	1	1	1	1	1	1
Weekly	1.11 (1.03, 1.20)	1.11 (1.03, 1.20)	1.12 (1.03, 1.21)	1.13 (1.04, 1.22)	1.07 (0.99, 1.16)	1.10 (1.02, 1.19)
Monthly	1.07 (0.97, 1.18)	1.07 (0.97, 1.18)	1.07 (0.97, 1.19)	1.07 (0.97, 1.19)	1.03 (0.93, 1.14)	1.05 (0.95, 1.16)
Infrequent/ Never	1.38 (1.25, 1.54)	1.38 (1.24, 1.53)	1.37 (1.23, 1.52)	1.35 (1.21, 1.51)	1.31 (1.17, 1.46)	1.31 (1.17, 1.46)

[a] z-scores are estimated from models of reading trajectories 7-16y. Z-scores are reversed, ie an increase represents a decline in SDS (rank) for ability.
[b] sample with information on drinking, reading score and all covariates; 3295 men at 23 years; 3752 men at 33 years
[c] model 1= 7 years reading z-score + change in reading z-score 7-16 years
[d] model 2 = model 1 + social class of origin
[e] model 3 = model 2 + behavioural problems (16 years, Rutter score)
[f] model 4 = model 2 + adult qualifications
[g] model 5 = model 2 + adult social class
[h] model 6 = model 2 + behavioural problems (16 years, Rutter score) + adult qualifications + adult social class

Drinking frequency	*Adjusted reading z-score*[b]	*+ childhood social class*[c]	*+ behavioural problems*[e]	*+ adult qualifications*[f]	*+ adult social class*[g]	*+all*[h]
42 years			7-year z-score			
Daily	1	1	1	1	1	1
Weekly	1.21 (1.11, 1.32)	1.16 (1.06, 1.27)	1.15 (1.05, 1.26)	1.16 (1.05, 1.28)	1.09 (0.99, 1.21)	1.11 (1.00, 1.23)
Monthly	1.39 (1.20, 1.62)	1.33 (1.13, 1.55)	1.26 (1.07, 1.49)	1.29 (1.08, 1.53)	1.26 (1.06, 1.49)	1.22 (1.01, 1.46)
Infrequent/ Never	1.66 (1.45, 1.90)	1.57 (1.36, 1.80)	1.45 (1.26, 1.68)	1.45 (1.24, 1.70)	1.37 (1.17, 1.59)	1.29 (1.09, 1.52)
			7-16 year change in z-score			
Daily	1	1	1	1	1	1
Weekly	1.08 (1.01, 1.16)	1.07 (0.99, 1.15)	1.07 (0.99, 1.15)	1.07 (0.99, 1.15)	1.04 (0.97, 1.12)	1.05 (0.97, 1.13)
Monthly	1.18 (1.05, 1.33)	1.16 (1.03, 1.31)	1.15 (1.01, 1.29)	1.15 (1.01, 1.30)	1.14 (1.00, 1.29)	1.13 (0.99, 1.28)
Infrequent/ Never	1.26 (1.13, 1.41)	1.24 (1.11, 1.39)	1.21 (1.08, 1.36)	1.20 (1.07, 1.34)	1.17 (1.04, 1.31)	1.15 (1.02, 1.29)

[a] z-scores are estimated from models of reading trajectories 7-16y. Z-scores are reversed, ie an increase represents a decline in SDS (rank) for ability.
[b] sample with information on drinking, reading score, and all covariates; 3205 men at 42 years
[c] model 1= 7 years reading z-score + change in reading z-score 7-16 years
[d] model 2 = model 1 + social class of origin
[e] model 3 = model 2 + behavioural problems (16 years, Rutter score)
[f] model 4 = model 2 + adult qualifications
[g] model 5 = model 2 + adult social class
[h] model 6 = model 2 + behavioural problems (16 years, Rutter score) + adult qualifications + adult social class

Table A4.4.1f RRR of drinking frequency (baseline is daily drinking) per SD decrease in reading 7-year z-score and 7-16 year z-score, women[a]

Drinking frequency	*Adjusted reading z-score*[b]	*+ childhood social class*[c]	*+ behavioural problems*[e]	*+ adult qualifications*[f]	*+ adult social class*[g]	*+all*[h]
23 years			7-year z-score			
Daily	1	1	1	1	1	1
Weekly	1.47 (1.28, 1.69)	1.37 (1.19, 1.59)	1.38 (1.19, 1.60)	1.33 (1.13, 1.57)	1.38 (1.19, 1.60)	1.35 (1.14, 1.59)
Monthly	1.68 (1.45, 1.96)	1.50 (1.27, 1.76)	1.46 (1.24, 1.71)	1.37 (1.14, 1.65)	1.46 (1.23, 1.72)	1.35 (1.12, 1.63)
Infrequent/ Never	2.22 (1.92, 2.57)	1.99 (1.71, 2.32)	1.92 (1.64, 2.24)	1.77 (1.48, 2.10)	1.84 (1.57, 2.16)	1.70 (1.42, 2.02)
			7-16 year change in z-score			
Daily	1	1	1	1	1	1
Weekly	1.15 (1.04, 1.26)	1.12 (1.01, 1.23)	1.12 (1.01, 1.23)	1.10 (1.00, 1.22)	1.12 (1.01, 1.24)	1.11 (1.00, 1.23)
Monthly	1.20 (1.08, 1.34)	1.15 (1.02, 1.29)	1.14 (1.01, 1.27)	1.11 (0.98, 1.25)	1.13 (1.01, 1.27)	1.10 (0.98, 1.24)
Infrequent/ Never	1.32 (1.19, 1.47)	1.26 (1.13, 1.41)	1.24 (1.11, 1.39)	1.2 (1.07, 1.35)	1.22 (1.09, 1.36)	1.18 (1.05, 1.33)

Drinking frequency	*Adjusted reading z-score*[b]	*+ childhood social class*[c]	*+ behavioural problems*[e]	*+ adult qualifications*[f]	*+ adult social class*[g]	*+all*[h]
33 years			7-year z-score			
Daily	1	1	1	1	1	1
Weekly	1.53 (1.31, 1.80)	1.43 (1.22, 1.68)	1.49 (1.26, 1.76)	1.40 (1.17, 1.66)	1.34 (1.13, 1.58)	1.39 (1.17, 1.66)
Monthly	1.77 (1.51, 2.09)	1.60 (1.35, 1.89)	1.69 (1.42, 2.00)	1.53 (1.27, 1.84)	1.53 (1.28, 1.82)	1.56 (1.29, 1.88)
Infrequent/ Never	2.25 (1.91, 2.65)	2.04 (1.73, 2.42)	2.08 (1.76, 2.47)	1.91 (1.59, 2.3)	1.85 (1.56, 2.20)	1.87 (1.56, 2.25)
			7-16 year change in z-score			
Daily	1	1	1	1	1	1
Weekly	1.11 (0.99, 1.23)	1.08 (0.97, 1.2)	1.10 (0.98, 1.23)	1.07 (0.96, 1.19)	1.05 (0.94, 1.17)	1.07 (0.95, 1.19)
Monthly	1.18 (1.05, 1.32)	1.13 (1.01, 1.27)	1.16 (1.03, 1.30)	1.11 (0.99, 1.25)	1.11 (0.98, 1.25)	1.12 (0.99, 1.26)
Infrequent/ Never	1.19 (1.06, 1.33)	1.14 (1.02, 1.28)	1.15 (1.02, 1.30)	1.11 (0.99, 1.25)	1.09 (0.97, 1.23)	1.10 (0.98, 1.24)

Drinking frequency	*Adjusted reading z-score*[b]	*+ childhood social class*[c]	*+ behavioural problems*[e]	*+ adult qualifications*[f]	*+ adult social class*[g]	*+all*[h]
42 years			7-year z-score			
Daily	1	1	1	1	1	1
Weekly	1.27 (1.14, 1.42)	1.18 (1.05, 1.33)	1.21 (1.08, 1.36)	1.16 (1.01, 1.32)	1.13 (1, 1.28)	1.15 (1.01, 1.32)
Monthly	1.58 (1.38, 1.82)	1.42 (1.23, 1.65)	1.46 (1.25, 1.7)	1.34 (1.13, 1.59)	1.35 (1.16, 1.57)	1.34 (1.13, 1.59)
Infrequent/ Never	1.96 (1.73, 2.22)	1.8 (1.58, 2.05)	1.72 (1.5, 1.96)	1.56 (1.35, 1.82)	1.61 (1.41, 1.85)	1.48 (1.27, 1.72)
			7-16 year change in z-score			
Daily	1	1	1	1	1	1
Weekly	1.17 (1.07, 1.27)	1.14 (1.04, 1.24)	1.15 (1.05, 1.26)	1.13 (1.03, 1.24)	1.12 (1.02, 1.22)	1.15 (1.01, 1.32)
Monthly	1.29 (1.15, 1.45)	1.24 (1.11, 1.39)	1.26 (1.12, 1.41)	1.21 (1.07, 1.37)	1.21 (1.08, 1.36)	1.34 (1.13, 1.59)
Infrequent/ Never	1.29 (1.16, 1.42)	1.25 (1.12, 1.38)	1.22 (1.10, 1.35)	1.18 (1.06, 1.31)	1.19 (1.07, 1.32)	1.48 (1.27, 1.72)

[a] z-scores are estimated from models of reading trajectories 7-16y. Z-scores are reversed, ie an increase represents a decline in SDS (rank) for ability.
[b] sample with information on drinking, reading score, social class at birth, Rutter score at 16 years, highest qualifications and social class. 3597 women at 23 years; 3990 women at 33 years; 3552 women at 42 years
[c] model 1= 7 years reading score + change in reading 7-16 years
[d] model 2 = model 1 + social class of origin
[e] model 3 = model 2 + behavioural problems (16 years, Rutter score)
[f] model 4 = model 2 + adult qualifications
[g] model 5 = model 2 + adult social class
[h] model 6 = model 2 + behavioural problems (16 years, Rutter score) + adult qualifications + adult social class

Chapter 5, Health behaviours and midlife glucose homeostasis

Introduction

This chapter examines associations between lifecourse cigarette smoking and alcohol consumption and midlife glucose homeostasis, as highlighted in the conceptual framework (Figure 5.1). Chapter 1 indicated that there is a growing literature demonstrating that tobacco and alcohol use are associated with type 2 (non insulin dependent) diabetes onset. Increasing risks accrue from more cigarette pack-years and non-drinking or heavy drinking. Three outcomes relating to glucose homeostasis will be studied: (i) HbA_{1c} in the whole sample, (ii) a group with elevated HbA_{1c}, who may have undiagnosed type 2 diabetes, plus known type 2 diabetes cases and (iii) a group with metabolic syndrome. As illustrated in Figure 5.1, associations between lifecourse cigarette or alcohol use and diabetes risk may operate via their effects on adiposity, so this pathway will be investigated. Confounding by other health behaviours including diet and physical activity, although for simplicity not illustrated in Figure 5.1, will be considered because these behaviours are associated both with smoking and drinking (Chapter 3) and also with adiposity and diabetes risk.

Mechanisms underlying associations between alcohol and tobacco and glucose regulation

Smoking and diabetes risk

An association between smoking and diabetes onset is biologically plausible. Cigarette smoking may impair insulin sensitivity directly or via increased oxidative stress. Experimental studies report that smoking increases blood glucose level after an oral glucose challenge, acutely impairing insulin sensitivity as well as increasing serum total cholesterol, triglycerides, LDL cholesterol, blood pressure and heart rate (Frati et al. 1996). Smoking is also reported to impair the insulin-stimulated transport of glucose in skeletal muscle. Dose-response associations have been reported between increasing number of pack-years of cigarettes or amount smoked and raised diabetes risk or HbA_{1c} levels (Manson et al. 2000; Sargeant et al. 2001a; Will et al. 2001) and also between time since quitting and reducing diabetes risk (Sargeant et al 2001a), which strengthen the case for a causal effect of cigarette smoking. Additionally, in diabetic patients, smoking worsens symptoms including nephropathy (Mehler et al. 1998). Associations between smoking and insulin sensitivity may be due to altered fat deposition: whilst smokers are on average leaner than non-smokers, they are more likely to be centrally obese (have larger waist circumference or waist:hip ratios) than non-smokers which is particularly associated with diabetic risk (Barrett-Connor & Khaw 1989). Whilst the mechanism through which central adiposity increases diabetic risk remains uncertain, it is thought that central adiposity indicates greater intra-abdominal fat stores which might induce hyperinsulinemia and insulin resistance by releasing free fatty acids which reduce hepatic insulin clearance. Epidemiologic studies

provide support for increased risk of poor glucose control associated with central obesity and also support the possibility that tobacco (and alcohol) may raise diabetes risk through their associations with central obesity (discussed below).

Alcohol and diabetes risk

When alcohol is consumed it is not stored in the body, but is metabolized as the preferred energy source over carbohydrates and other sources, resulting in reduced glucose disposal and hyperinsulinemia. However, alcohol also inhibits gluconeogenesis and may result in better maintenance of normal blood sugar levels if consumed in moderation(Van De Wiel 2004). The action of alcohol on insulin levels varies; in a fasting state high alcohol intake can result in hypoglycemia because of reduced gluconeogenesis combined with impaired glycogenolysis when glycogen stores are low, preventing maintenance of normal blood sugar levels. For example, after consumption of 48 grams alcohol (~6 units) gluconeogenesis reduced by about 45% and there was a 12% reduction in hepatic glucose output (Siler et al. 1998). However in a non-fasting state when glycogen stores are adequate, alcohol may reduce glucose disposal, resulting in hyperinsulinemia and resistance to insulin.

Alcohol intake is also associated with increased HDL cholesterol levels and fibrinolytic activity and reduced clotting (Agarwal 2002). A meta-analysis of experimental studies reported beneficial effects of 30g /day ethanol consumption in raising HDL cholesterol by 3.99 mg/dl (95%CI 3.25 to 4.73), and triglyceride levels by 5.69 mg/dl (95%CI 2.49, 8.89), as well as modestly improving haemostatic factors (Rimm et al. 1999); factors which are important in development of metabolic syndrome and cardiovascular disease. A daily dose of 30 g ethanol (3 British units) was estimated to reduce coronary heart disease risk by 25% (Rimm et al 1999). As with smoking, some of the effect of alcohol use on diabetes risk or glucose homeostasis may be attributable to increased body mass index and in particular to central adiposity.

Types of alcohol use and diabetes risk

The mechanisms for cardiovascular health benefits of wine consumption are often attributed to the presence of antioxidant and antithrombotic constituents in wine as oxidation of LDL cholesterol is involved in atherosclerotic plaque formation. However, to date clinical trials of anti-oxidant substances are not conclusive (Warnholtz & Munzel 2000). There is evidence that wine consumption (rather than other types of alcohol) is also associated with lower diabetes risk (Djousse et al. 2004).

Evidence from Epidemiologic studies

Diabetes risk

Prospective studies indicate that smokers are at up to twice the risk of developing diabetes as non-smokers (Manson et al 2000; Sairenchi et al. 2004; Will et al 2001). In ex-smokers, diabetes risk returns to the level in non-smokers after 5 years (women) and 10 years (men)(Will et al 2001). Many studies report non-linear associations between alcohol use and subsequent onset of diabetes with higher risk in non-drinkers and heavy drinkers compared to moderate drinkers (Conigrave et al. 2001; Perry et al. 1995; Rimm et al. 1995; Wannamethee et al. 2002). A recent systematic review estimated that consumption of 1-3 drinks per day was associated with a reduction in risk of diabetes incidence between 33 and 55% compared to non-drinkers; heavy drinking was associated with up to 43% increase in incidence. It was also concluded that moderate alcohol consumption does not acutely impair glycemic control in diabetic patients (Howard et al. 2004).

Associations between alcohol or tobacco use and diabetes risk may operate through increased BMI and waist circumference (central obesity), if heavy drinkers, non-drinkers and smokers have higher levels of adiposity (Figure 5.1). Smokers are on average leaner than non-smokers, although they are more likely to be centrally obese than non-smokers (Barrett-Connor & Khaw 1989). In middle-aged British men, consistently heavy drinkers or men who became heavy drinkers over a five year follow-up were more likely to gain weight or be obese compared to stable non-occasional drinkers; whereas the BMI of stable light drinkers did not differ significantly from the stable non-occasional drinkers (Wannamethee & Shaper 2003). Heavy drinking is also associated with larger waist circumference; a cohort study of 35-79 year olds reported that drinking frequency was inversely associated with central adiposity whilst drinking intensity (drinks/ day) was positively related to central adiposity even controlling for potential confounders (Dorn et al. 2003). Studies have reported that the association between heavy alcohol use and diabetes onset is in part mediated by body weight (Perry et al 1995; Wannamethee et al 2002).

To date, associations between tobacco or alcohol use and diabetes risk have been documented in several large studies, mostly of men and located in the USA. These studies commonly use retrospectively collected information on tobacco and alcohol use, sometimes with a long time period before onset of disease, during which it is assumed that behaviour does not change. This assumption is challenged by the high levels of behaviour change, particularly for heavy drinkers observed at least in recent generations in the UK as discussed in Chapter 3. There are several weaknesses which have not been consistently investigated in existing literature. First, lifecourse measures of exposure to health behaviours are lacking. Secondly, co-occurrence of smoking and drinking habits have not been accounted for although their effects on diabetes risk may act in opposing directions. Confounding factors, such as physical activity, diet and other risk factors

which may also be related to tobacco or alcohol use have not been consistently controlled for. Further, the pathways through which alcohol and tobacco may act on diabetes risk notably body size (as BMI or waist circumference) have not been systematically included in existing studies. Finally, a recent review of diabetes risk also highlighted that whilst heaviness of drinking has been studied, the associations between frequency of drinking consumed is poorly characterized (Howard et al 2004).

Glycosylated Haemoglobin

Few studies have investigated associations between health behaviours and glucose homeostasis, prior to diabetes onset. Clinical trials of lifestyle interventions focus on weight loss, dietary changes and exercise programs in high risk population groups, but there is less evidence of how other lifestyle habits influence the population distribution of glucose regulation. Chapter 1 discussed the accumulating evidence that risks associated with increasing levels of glucose dysregulation start at lower levels than seen in diabetic subjects. The main modifiable influences on glucose regulation which have been repeatedly studied are firstly body size, indexed by BMI; secondly measures of central adiposity including waist circumference; and thirdly, measures of type and quantity of diet, physical activity and cardiorespiratory fitness (Bassuk & Manson 2005). The associations between alcohol and tobacco with glucose regulation in general population samples are less studied, but there is some evidence suggesting their importance. Smokers have higher HbA_{1c} than non-smokers (Gulliford & Ukoumunne 2001; Simon et al. 1989); in one cross-sectional study, a dose-response relationship between HbA_{1c} and number of cigarettes smoked among current smokers, and pack-years among ex-smokers was identified (Sargeant et al 2001a). Cross-sectional studies have reported associations between elevated HbA_{1c} levels and heavier alcohol intake, although frequency of drinking has not been investigated (Boeing et al. 2000; Gulliford & Ukoumunne 2001; Harding et al. 2002). No studies investigate associations between lifecourse exposure to alcohol and tobacco use and HbA_{1c}.

Metabolic syndrome

Few studies of associations between alcohol and tobacco use and metabolic syndrome exist, although associations are in the same direction as with diabetes (Freiberg et al. 2004; Park et al. 2003). There is sparse evidence about associations of trajectories of alcohol and tobacco with metabolic syndrome; a study of adults in their thirties reported that consistently lower alcohol consumption was associated with metabolic syndrome, but did not find an association with cigarette smoking (Ferreira et al. 2005). A second study reported that smoking, drinking >4 units/ day, not eating fruit and vegetables and not exercising at more time points over a 14-year follow-up increased risk of metabolic syndrome (Chandola et al. 2006a).

Aims

The association between lifecourse health behaviours, as opposed to single cross-sectional measures, with glucose homeostasis is not clear. Analyzing trajectories of tobacco and alcohol use is important firstly because current behaviour fails to capture behaviour change over time (described in chapter 3) and secondly, alcohol or tobacco exposure may have cumulative effects. Chapter 3 also showed that smoking and drinking co-occur. Because the effects of some combinations of smoking and drinking on glucose regulation are hypothesized to act in opposite directions, it is important to assess the associations between smoking or drinking with glucose homeostasis whilst taking the other into account.

This chapter will investigate associations between lifecourse alcohol and tobacco use and three outcomes describing glucose homeostasis (i) HbA_{1c} (ii) elevated HbA_{1c} / diabetes risk (iii) metabolic syndrome. The main objectives are to establish whether:

1. there are cross sectional associations between (i) tobacco and (ii) alcohol use at 23, 33, 42 and 45 years and glucose homeostasis;
2. *trajectories* or *change* in health behaviours through the lifecourse affect mid-life glucose homeostasis;
3. the associations between measures of alcohol or tobacco and glucose homeostasis are confounded by each other or by diet and physical activity;
4. associations between health behaviours and glucose homeostasis operate through the pathway of adiposity.

Specifically, the frequency and amount of alcohol use, as well as never, ex, current and heaviness of smoking will be investigated in relation to glucose homeostasis. Additionally, the joint effects of tobacco and alcohol use will be investigated; to see if there are any modifying effects of tobacco use on glucose homeostasis by alcohol use (or vice versa). From a public health perspective, the magnitude and in etiological fraction of the effects of alcohol and tobacco use on disease burden will be compared.

Methods

As discussed in Chapter 2 sample representativeness was examined by comparing the distribution of social class at birth in the original birth sample with the distribution in the analysis sample with valid HbA_{1c} (n=7799). There was some under-representation of participants with manual social origins (Appendix 5.1).

For aim one, geometric means (95% CI) of HbA_{1c} are presented for the groups of smokers and differences in HbA_{1c} by smoking status were tested using linear regression models with robust standard errors. The same approach was taken for groups of drinking frequency and amount.

Associations between HbA_{1c} levels and drinking frequency were tested using linear regression analyses, with the mid-point of each drinking frequency category treated as a continuous variable (for example, 45-year drinking frequency was coded as; almost daily, 1-3 times/ week, 1-2 times/ month, less often, never, so median weekly frequencies were coded as 5.5, 2.5, 0.75, 0.1875 and 0 times per week). Similarly, trends in prevalence of elevated HbA_{1c} / diabetes and metabolic syndrome by drinking frequency were tested using logistic regression analyses. J or U shaped associations were expected for amount of alcohol consumed so linear and quadratic contrasts were tested using median units/week as a continuous measure in regression analyses. To illustrate, weekly alcohol consumption for men was grouped as 0, 1-10, 11-21, 22-35, 36-50 and >50 units; these groups were then assigned median values for testing trends (for the heaviest consumption category it was assumed that the class size was the same as the previous class, as in other similar analyses).

For aim 2 the associations between change in drinking and smoking habits between 23 and 42 (or 45) years and 45-year glucose homeostasis was investigated. The association between the measure of glucose homeostasis and the duration of exposure to a behaviour and was investigated using the count variables as predictors in regression models. The count variables summarize the number of time-points that a person was a particular type of drinker. Smoking history was summarized between 23 and 42 years (see Chapter 3). Participants with data at 23, 33, 42 and 45 years were classified into daily drinkers or non-drinkers at 0, 1, 2, 3 or 4 occasions, participants with data at 23, 33 and 42 years were classified into heavy or binge drinkers on 0-3 occasions. Models were run first for those with complete data on all the adult time points and then for those with incomplete data.

Next, associations between changes in health behaviours 23-42 years and diabetes risk were tested in repeated measures multilevel models (in MLwiN 2.0). These models investigate if there were stronger associations with glucose homeostasis for recent (42-year) compared to earlier (23-year) adult smoking or drinking patterns. The outcome variable of the repeated measures model must be a measure taken on more than one occasion. Therefore to assess whether the trajectories of, eg drinking frequency at 23, 33 and 42 years, differed according to diabetes status, models were set up as follows. The outcome of the model was drinking frequency at 23, 33 and 42 years. The predictor variables were dummy variables of time point contrasting (i) 33 years with 23 years and (ii) 42 years with 23 years. The dummy variables indicate whether drinking frequency differs between 33 years and 23 years and also between 42 years and 23 years. A binary variable "diabetes risk" indicates whether the diabetic group have a different trajectory of drinking outcome 23-42 years to the non-diabetic group. Finally interactions between time-point with diabetes risk were included, to indicate whether the association between drinking frequency and diabetes risk is different for drinking frequency at

33 years compared to 23 years and also at 42 years compared to 23 years. If recent drinking patterns are important in establishing diabetes risk, drinking frequency at 42 years would be expected to be more strongly associated with diabetes risk than drinking frequency at 23 years. Several sets of models were run; contrasting (i) non-drinkers with other drinkers (ii) daily drinkers against all other drinkers plus non-drinkers (iii) current smokers against non-smokers and (iv) ex-smokers against current smokers.

For aim 3, the regression models used for aim 2 were adjusted for *a priori* confounders; leisure time physical activity, inactivity and diet. Attenuation of the coefficients for alcohol or tobacco were interpreted as evidence for confounding.

For aim 4, the mediating roles of BMI and waist circumference were evaluated in the regression models. Attenuation of the coefficient estimates for smoking or drinking in the adjusted models were interpreted as mediation through the pathway of adiposity.

Results

Outcomes

HbA_{1c}

Valid HbA_{1c} was available for 7799 participants (excluding type 1 diabetes), of which 7754 were not taking drugs which would alter HbA_{1c} levels. As expected, geometric mean HbA_{1c} was higher for men than for women; 5.26% (95% CI 5.25, 5.28) compared to 5.15% (95% CI 5.13, 5.16). HbA_{1c} was higher (indicting poorer glucose regulation) in cohort members with higher body mass index and waist circumference (Table 5.1). Current smokers had higher HbA_{1c} levels than non-smokers and less frequent drinkers had higher HbA_{1c} levels than more frequent drinkers. HbA_{1c} was higher in the most and least physically active groups. Participants may have taken up frequent exercise in response to poor health status. The units of HbA_{1c} levels are percentage of total haemoglobin that is glycated, so when differences in mean levels between groups are reported in this chapter, these are absolute differences in HbA_{1c} level (which is measured in percentage points), rather than proportionate, ie percentage change in the HbA_{1c} level.

High HbA_{1c} / type 2 diabetes

Prevalence of type 2 diabetes in the analysis sample (n=7799) by 45 years was 1.6% in men (n=64) and 1.2% in women (n=47). Participants with diabetes had markedly higher HbA_{1c} levels than those without: 7.97% vs 5.20% in men and 7.19% vs 5.12% in women. For analyses of elevated HbA_{1c} / diabetes risk, the diabetics (n=111) were grouped with HbA_{1c} $\geq$6% (total

n=319). Analyses were repeated using a cut point of HbA_{1c} ≥7%, ie 49 participants at high risk of developing diabetes were analysed with the 111 diabetics.

Metabolic syndrome

Chapter 2 (Table 2.6) presented the prevalence of the constituent parts of the metabolic syndrome of which large waist circumference and elevated triglycerides were the most common. Nearly one third of men and one half of the women did not have any of the risk factors. Prevalence of metabolic syndrome (≥3 risk factors) was 13% in men (n=490) and 10% in women (n=385). HbA_{1c} level was 0.5% higher in men and women with metabolic syndrome than those without. Analyses were repeated using a cut-point of HbA_{1c} ≥6% and ≥7% in the definition of metabolic syndrome.

Results for selected analyses are presented for a definition of (i) elevated HbA_{1c} /diabetes and (ii) metabolic syndrome using HbA_{1c} cut points of both ≥6% and ≥7%.

Frequency of drinking alcohol:

- **Is less frequent alcohol use associated with (i) higher HbA_{1c} levels (ii) increased risk of diabetes and (iii) increased risk of metabolic syndrome?**

Cross-sectional trends in HbA_{1c} by frequency of drinking alcohol (Aim 1)

Geometric mean 45-year HbA_{1c} increased with less frequent alcohol consumption at each adult age; in men who drank daily at age 23, mean HbA_{1c} was 5.22% (95%CI 5.19, 5.24) compared to 5.38% (95%CI 5.26, 5.50) for "never" drinkers; at age 45 equivalent means were 5.18% (95%CI 5.16, 5.20) compared to 5.40% (95%CI 5.30, 5.50) (Table 5.2). In both sexes, the special occasion and non-drinkers had consistently higher HbA_{1c} than more frequent drinkers at each age. To summarise trends in HbA_{1c} by drinking frequency, linear regression models with first linear and then quadratic terms for median values of weekly drinking frequency were run separately for each adult age. Where quadratic trends were significant, the linear trends are no longer interpreted. There was evidence for significant linear trends at each adult age except for 23 years among men. Quadratic trends were significant in men and women at 42 and 45 years. At the later ages the special occasion and never-drinkers have higher HbA_{1c} levels compared to more frequent drinkers.

Interactions between drinking frequency and gender on HbA_{1c} were tested. At 42 years, women who drank less frequently had higher HbA_{1c} relative to drinkers on most days, compared to men.

Cross-sectional trends in (i) high HbA1c and (ii) metabolic syndrome by frequency of drinking alcohol (Aim 1)

Prevalence of elevated HbA_{1c} /diabetes and metabolic syndrome is higher in less frequent drinkers. There was evidence for linear trends of increasing prevalence with decreasing drinking frequency from 33 years onwards in men and from 23 years onwards in women (Table 5.3). However there were quadratic trends in prevalence of metabolic syndrome and elevated HbA_{1c} or diabetes at 45 years (as seen with HbA_{1c}). There were no interactions between drinking frequency and gender on elevated HbA_{1c}. Interactions between gender and drinking frequency on metabolic syndrome were seen at 42 and at 45 years (in the same direction as with HbA_{1c}); odds of metabolic syndrome in 45-year daily drinkers compared to non-drinkers were 3.03 (95%CI 2.10, 4.37) in women and 1.59 (95%CI 1.18, 2.13) in men.

Never and special occasion drinkers

Geometric mean HbA_{1c} and prevalence of elevated HbA_{1c} / diabetes or of metabolic syndrome did not differ between "never" drinkers and "special occasion" drinkers among men or women. It could be argued that alcohol exposure of "special occasion" drinkers is very low, so it is unlikely that differences in any health effects between "special occasion" and "never" drinkers are due to alcohol exposure. Therefore "special occasion" and "never" drinkers are grouped together for the next analyses and referred to as "non-drinkers" (as in Chapter 3).

Lifecourse drinking frequency and HbA_{1c} (Aim 2)

β coefficients estimate change in mean HbA_{1c} per time-point (0, 1, 2, 3, 4 adult surveys) that a participant was (i) a daily drinker or (ii) a non-drinker (Table 5.4). Results suggest that the association between drinking frequency and HbA_{1c} is cumulative; participants who were daily drinkers at more surveys had lower mean HbA_{1c} levels (confirmed with significant linear trends in HbA_{1c}). To illustrate, mean HbA_{1c} of women who were daily drinkers at all four surveys was 0.19% lower than women who never reported daily drinking. The more often that a participant was a non-drinker, the higher their mean HbA_{1c} eg women who were non-drinkers at all four adult surveys had HbA_{1c} 0.18% higher than women who never reported non-drinking.

To investigate whether recent drinking status was more closely associated with HbA_{1c} than past drinking, the number of time points 23-42 years that a person was (i) a daily drinker or (ii) a non-drinker was stratified by 45-year drinking status. Mean HbA_{1c} was greater in groups who were non-drinkers on more occasions 23-42 years in both the 45-year drinkers and the non-drinkers. Among men who were drinkers at 45 years, mean HbA_{1c} for drinkers on three previous occasions was 5.24 (95% CI 5.22, 5.27) and 5.44 (95%CI 5.94, 6.00) for non-drinkers on three previous occasions. Equivalent values among the 45-year non-drinkers were 5.40 (95%CI 5.31, 5.93) compared to 5.57 (95%CI 5.34, 5.82). Significant trends in mean HbA_{1c} by

prior drinking frequency, when stratified by current drinking frequency confirms that both past and current drinking frequency are associated with HbA_{1c} levels.

Multilevel models of drinking frequency and HbA_{1c}

Drinking on most days

The associations between drinking frequency across adulthood and glucose regulation were tested in multilevel repeated measures models with outcomes (i) daily drinker and (ii) non-drinking at 23, 33 and 42 years. Predictors were survey time (33 and 42 years) and a dummy variable for elevated HbA_{1c} and, in separate models, metabolic syndrome (Table 5.7a and b). Among women, a significant main effect of elevated HbA_{1c} /diabetes risk status (0.39, $p<0.001$) indicated that diabetics had less than half the odds of being daily-drinkers 23-42 than the non-diabetic group. The association with metabolic syndrome was in the same direction (0.50, $p<0.001$); daily drinking throughout adulthood was also protective against metabolic syndrome. Among men, there were interactions between elevated HbA_{1c} and time point; the protective effect of daily drinking on high HbA_{1c} was greater at 33 years than at 23 years. Men who were daily drinkers at 33 years were half as likely to have high HbA_{1c} as daily drinkers at 23 years. These effect estimates were larger for the group with $HbA_{1c} \geq 7\%$. There was not a significant protective effect of daily drinking 23-42 years on metabolic syndrome for men.

Non-drinking

Non-drinking 23-42 years was associated with higher risks of elevated HbA_{1c} /diabetes and metabolic syndrome. Men had twice the odds of having elevated HbA_{1c} if they were non-drinkers 23-42 years compared to drinkers (Table 5.7a). In women the odds of being in the elevated HbA_{1c} group were more than doubled for 42-year non-drinkers compared to 23-year non-drinkers (Table 5.7b). Overall men and women with metabolic syndrome had a 30-40% increase in the odds of being non-drinkers 23-42 than the group without metabolic syndrome.

In summary, cross sectional analyses showed that more frequent drinkers had lower (i) mean HbA_{1c} (ii) lower risk of being in the elevated HbA_{1c} group and (iii) lower risk of having metabolic syndrome. Frequent drinking on more occasions was associated with lower HbA_{1c} and lower risks of elevated HbA_{1c} / diabetes or metabolic syndrome. Current and past drinking frequency were associated with mean HbA_{1c} levels. Multilevel models indicated that daily drinking through adulthood is associated with reduced risk of elevated HbA_{1c} /diabetes in men and women and metabolic syndrome in women. Conversely never drinking was associated with higher risks of both outcomes in men and women.

Associations between non-drinking and diabetes risk have been investigated in the literature and it is hypothesised that raised risks found in non-drinkers relative to more moderate drinkers may

be due to heavier drinkers quitting drinking because of ill health and creating a spurious association. There was not evidence to support this hypothesis in relation to diabetes risk in the cohort (see Appendix 5.2)

Amount of alcohol consumed and HbA_{1c}:

- **Is there is any evidence that the amount of alcohol consumed is associated with (i)HbA_{1c} and also (ii) increased risk of diabetes and (iii) increased risk of metabolic syndrome?**

Cross sectional analyses of amount of alcohol consumed and HbA_{1c} (Aim 1)
Amount of alcohol consumed in the past week was not strongly associated with HbA_{1c} (Table 5.5). J-shaped associations in risk of diabetes with alcohol consumption were expected, so linear and quadratic trends in HbA_{1c} were tested in drinkers (ie excluding non-drinkers). There were no significant trends in men. In women, HbA_{1c} declined in a linear fashion with heavier drinking at 23 and 33 years, and there was a quadratic trend at 42 years where the heaviest drinkers had a slightly elevated mean HbA_{1c} level compared to lighter drinkers: 5.02 (95%CI 4.98, 5.07) for ≥22 units/week compared to 5.00 (95%CI 4.96, 5.04) for 15-21 units/week. There was not evidence of associations between prevalence of (i) metabolic syndrome and (ii) elevated HbA_{1c} /diabetes with heaviness of drinking (Table 5.6). However numbers were small, particularly in the heavier drinking categories for women, which could obscure associations.

Lifecourse heaviness of drinking (Aim 2)
Mean HbA_{1c} was not associated with repeated heavy drinking over the 23-42 year period. Likewise prevalence of elevated HbA_{1c} /diabetes and metabolic syndrome were not associated with cumulative heaviness of drinking, as expected from the cross sectional analyses (data not presented). Multilevel models confirmed these results.

In summary there was not consistent evidence that heaviness of drinking was associated with HbA_{1c} levels or elevated HbA_{1c} / diabetes or metabolic syndrome, either from cross sectional or longitudinal analyses.

Cumulative binge drinking (Aim 2)
At each age, the lighter (ie non-binge drinkers) had similar HbA_{1c} to binge drinkers; in men, mean HbA_{1c} in 42-year binge drinkers was 5.26 (95%CI 5.23, 5.28) compared to 5.24 (95%CI 5.22, 5.26) in the lighter drinkers and 5.42 (95%CI 5.35, 5.50) in the non-drinkers. Equivalent values for women were 5.10 (95%CI 5.09, 5.12) in light drinkers 5.13 (95%CI 5.08, 5.17) in binge drinkers and 5.28 (95%CI 5.24, 5.31) in non-drinkers. The same patterns are seen at earlier ages (data not presented). At 45 years, more data about heaviness of drinking on

occasions was collected. HbA_{1c} level varied slightly by the usual number of units consumed per drinking occasion, but differences were not statistically significant; mean HbA_{1c} was slightly higher in men and women consuming fewer units per occasion compared to those consuming up to 7 units and the few drinkers of more than 10 units per occasion had highest HbA_{1c}. The frequency of drinking ≥6 units /occasion was not significantly associated with HbA_{1c} levels in men, but there were differences for women. Mean HbA_{1c} for women drinking ≥6 units /occasion at least weekly was 5.01 (4.98, 5.04) compared to 5.12 (5.09, 5.15) for monthly or less. In both sexes, consistent binge drinkers 23-42 years had similar HbA_{1c} to the consistent non-binge (lighter) drinkers and both groups had lower HbA_{1c} than consistent non-drinkers and similar patterns were seen with metabolic syndrome in (data not presented). Multilevel models of binge drinking at 23-42 years did not find associations with elevated HbA_{1c} /diabetes (using ≥6% or ≥7%), or metabolic syndrome.

Cross-sectional associations between drinking frequency and amount of alcohol consumed (Aim 1)

Frequency and heaviness of drinking are positively associated; more frequent drinkers consume more alcohol in a week (Chapter 3, Table 3.9). Among habitual drinkers (daily, weekly and monthly drinkers), the separate effects of frequency of drinking alcohol were compared to the effects of amount of alcohol consumed on (i) HbA_{1c} (ii) elevated HbA_{1c} (reported diabetes and HbA_{1c} ≥6%) and (iii) metabolic syndrome. Interactions between frequency and amount of alcohol were tested and no interactions were seen for any of the three measures of glucose homeostasis. There was not consistent evidence to suggest that the effects of drinking frequency differed by amount of alcohol consumed.

In summary there was not evidence that within different frequencies of drinking, the heaviness of drinking was associated with poorer glucose regulation.

Cigarette smoking status:

- **Is smoking status (current, ex and never) associated with (i) higher HbA_{1c} levels, (ii) increased risk of diabetes and (iii) increased risk of metabolic syndrome?**

Cross sectional analyses: smoking status (Aim 1)

Current smokers had higher mean HbA_{1c} on average than ex or never smokers: 5.41% (95% CI 5.37, 5.45) compared to 5.25% (95% CI 5.22, 5.28) and 5.20% (95% CI 5.17, 5.22) for men's classified by 42-year smoking (Table 5.8). The main difference was between current and never smokers, eg at 42 years -0.21 % for men and -0.13% for women. Smoking status at 23 and 33 years was similarly associated with HbA_{1c}, although differences were slightly smaller.
Diabetes prevalence is highest in the current smokers at each adult age, and patterns are similar

across the ages. Whilst numbers are small, elevated HbA_{1c} /diabetes prevalence is also greater in the current than never smokers (Table 5.9).

Cross sectional analyses: number of cigarettes smoked (Aim 1)

- **Is there a dose-response association with number of cigarettes smoked?**

Amount smoked is associated with HbA_{1c}: at each age there was a dose response relationship with the heaviest smokers (≥20 cigarettes/day) having higher levels of HbA_{1c} than the lighter smokers (1-19 /day) and the non-smokers (Table 5.8). In men mean HbA_{1c} was 0.17% lower in non-smokers compared to smokers of 1-10 cigarettes /day and 0.23% lower compared to smokers of ≥20 cigarettes/day at 42 years. In women equivalent differences were 0.08% and 0.12%, (both $p<0.005$). These results were confirmed in linear regression analyses of HbA_{1c} and smoking (Table 5.11a, column 1).

Prevalence of elevated HbA_{1c} /diabetes and metabolic syndrome increased with increasing amount smoked at each age (Table 5.9). Table 5.11b (column 1) confirmed that smoking was associated with higher odds of elevated HbA_{1c}/ diabetes; ORs were raised in lighter and heavier current smokers compared to the never smokers; at 42 years, OR 2.06 (95%CI 1.27, 3.35) in smokers of 1-19 cigarettes/ day and 2.39 (95%CI 1.56, 3.69) in smokers of ≥20 cigarettes/ day. Among women the odds of elevated HbA_{1c}/ diabetes were significantly different from the odds in non-smokers only in smokers of ≥20 cigarettes/ day at 33 years. For metabolic syndrome, those smoking ≥20 cigarettes/ day at any one survey were between 1.7 and 2.5 times more likely than never smokers to have metabolic syndrome, Table 5.11c.

Lifecourse associations with ex-smoking (Aim 2)

- **Are ex-smokers who quit more recently at higher risk of poorer glucose control than those who quit earlier?**

Ex-smokers were classified by recency of quitting: before 23 years, between 23 and 33 years and between 33 and 42 years. Mean HbA_{1c} levels of quitters prior to 23 years were not significantly different from levels for those who quit between 23 and 33 years. Men who quit later (between 33 and 42 years) had higher HbA_{1c} levels than men who quit earlier (between 23 and 33 years) (Table 5.8). Additionally the prevalence of metabolic syndrome and elevated HbA_{1c} / type 2 diabetes decreased with time since quitting (Table 5.9), suggesting that risk of poor glucose control decreases with time elapsed since quitting smoking.

Lifecourse smoking status and HbA_{1c} (Aim 2)

Table 5.10 presents mean HbA_{1c} associated with adult smoking history. Men who were heavy smokers at 42-years had mean HbA_{1c} 5.43% (95% CI 5.38, 5.48), compared to 5.19% (95% CI 5.17 5.22) in never smokers 23-42 years. For women the equivalent means were 5.28% (95% CI

5.23, 5.33) and 5.12% (95% CI 5.10, 5.14). Prevalence of diabetes and metabolic syndrome are also higher in heavier smokers than never smokers.

The association between smoking status 23-42 years and HbA_{1c} was tested in repeated measures multilevel models. Men with elevated HbA_{1c} /diabetes had 1.8 times greater odds of having ever smoked than never smoked compared to those with HbA_{1c} <6%; among women the estimate was 1.4 (Table 5.7a). In neither men nor women were there significant interactions between smoking status and occasion; there was not evidence that the association between smoking status and diabetes risk was different for smoking at 23 compared to smoking at 33 or smoking at 23 compared to smoking at 42 years. Diabetes risk was not associated with ex-smoking compared to current smoking. However, men and women with metabolic syndrome had higher odds of being current smokers 23-42 and reduced odds of being ex-smokers 23-42 years. There was no evidence of interactions between smoking status and occasion for metabolic syndrome.

In summary, cross-sectional analyses provided consistent evidence that smokers had higher mean HbA_{1c} levels and heavier smoking was associated with higher mean HbA_{1c}, elevated HbA_{1c} / type 2 diabetes or metabolic syndrome, particularly in men. Multilevel models confirmed that current smoking trajectories 23-42 years were associated with higher risk of having elevated HbA_{1c} / type 2 diabetes or metabolic syndrome. Ex-smoking 23-42 years was associated with lower risks in women.

Alcohol and tobacco use

- **Are the associations between alcohol and diabetes risk robust to adjustment for smoking and vice versa?**

Cross sectional multivariate analyses (Aims 3 and 4)

In Tables 5.11a-c the associations between (i)smoking and (ii)drinking frequency and diabetes risk described above are summarised as β coefficients for associations with HbA_{1c} and ORs for elevated HbA_{1c} /diabetes and for metabolic syndrome. Column 1 (unadjusted) presents estimates of the association between smoking and drinking frequency separately with HbA_{1c}. Column 2 presents estimates from multivariate models mutually adjusted for smoking and drinking frequency. Interestingly, adjusting smoking for drinking frequency and also drinking for smoking status little changed the associations with HbA_{1c} (Table 5.11a). Waist circumference and BMI are major determinants of glucose homeostasis; larger waist circumference is associated with poorer glucose homeostasis (Appendix 5.3). In Table 5.11a column 3, multivariate models were further adjusted for waist circumference and BMI. Adjustment very slightly reduced the estimates for drinking, particularly never and infrequent drinking and also for heavier smoking, indicating that adiposity may be on the pathway between heavy smoking and non-drinking and adult glucose homeostasis. The estimates of effect size of

smoking and drinking were greater at later ages than earlier ages, even when adjusted for body size measured at 45 years. Similar patterns of results were seen for elevated HbA_{1c} / diabetes or metabolic syndrome (Tables 5.11b and c).

The next models were adjusted for diet and inactivity (column 4). Effect estimates for drinking or smoking on HbA_{1c} were little changed on adjustment, associations between drinking or smoking and HbA_{1c} were largely independent of diet and physical activity. For the most part, similar patterns of results were seen for elevated HbA_{1c} / diabetes or metabolic syndrome (Tables 5.11b and c). For elevated HbA_{1c} / diabetes the estimates for smoking and drinking remained significant in men but in contrast, were completely attenuated in women, providing evidence of confounding. There were no significant associations between 23-year drinking frequency and elevated HbA_{1c} / diabetes. Odds of elevated HbA_{1c} / diabetes increased with lower drinking frequency drinking at later ages and were mostly still significant on adjustment in non-drinkers. For example, adjusted OR for high HbA_{1c} / diabetes was 2.07 (95%CI 1.07, 3.96) in women non-drinkers at 45 years compared to daily drinkers. Among men the OR remained raised for monthly, infrequent and never drinkers after adjustment. The excess in odds of metabolic syndrome in heavier smokers was robust to adjustment for drinking frequency, activity, diet and adiposity in men, whilst the estimates of the effect of heavy smoking in women appeared to be more attenuated than in men.

- *Are there interactions between tobacco and alcohol use on diabetes risk?*

Associations between alcohol or tobacco with HbA_{1c} level, diabetes risk or metabolic syndrome act in opposite directions and potentially through different pathways. Therefore interactions between tobacco and alcohol use were tested; no evidence for interactions between alcohol and tobacco use on the outcomes studied was found.

Adjusted analyses (Aims 3 and 4)

The association between the number of occasions that a participant was a non-drinker and also a daily drinker reported earlier, was little changed after adjustment for waist circumference, body mass index, diet, inactivity and smoking status (Table 5.4). The association between adult daily or non-drinking 23-42 years and diabetes risk or metabolic syndrome tested in the multilevel models was robust and little attenuated on adjustment for waist circumference, body mass index, diet, inactivity and smoking status.

For adult smoking status 23-42 years, the association with diabetes risk or metabolic syndrome tested in the multilevel models was robust and little attenuated on adjustment for adiposity, diet and physical activity among the men. However among the women, the association between current smoking compared to non-smoking 23-42 years and elevated HbA_{1c} ≥6%/ diabetes was

attenuated and no-longer significant on adjustment for all of these factors, indicating that the association between smoking and elevated HbA_{1c} was explained by the *a priori* confounders. Associations between current smoking compared to non-smoking 23-42 years and metabolic syndrome was not robust to adjustment for drinking, diet and physical activity.

These patterns are confirmed by the adjusted cross-sectional analyses in Table 11a-c; physical activity and diet weakly mediated associations but adiposity is a stronger mediator although adiposity did not completely mediate between smoking and drinking and any outcome at any age.

In summary the effects of smoking and drinking frequency on glucose regulation are similar when adjusted for each other. However adjustment for adiposity reduces the association indicating that this may be on the pathway to poor glucose regulation. Additional adjustment for other lifestyle factors attenuated the associations, particularly among women, both in the cross sectional and in the longitudinal analyses.

Smoking and drinking public health impact on glucose regulation

- *How do the effects of alcohol and tobacco use compare in magnitude and in etiological fraction for disease burden?*

The most beneficial patterns of smoking and drinking with respect to HbA_{1c} levels were to be a frequent drinker (drinking on most days of the week) and never smoke. Combined these behaviours are associated with 0.43% lower HbA_{1c} than is seen among the non-drinker group who are smokers. The prevalence of frequent drinkers who never smoked in the cohort is 13.2% men and 8.4% women; 1.7% men and 2.5% women were non-drinkers who smoked at 42 years. The most common constellation of drinking and smoking was being a non-smoker and drinking 1-3 times per week at 42 years, and this group had mean HbA_{1c} of 5.16 (95% CI 5.14, 5.18). Based on the mean HbA_{1c} levels in the cohort of smokers at 42 years, if the current smokers in the sample became ex-smokers their mean HbA_{1c} would reduce by 0.14%. In public health terms whilst it is universally advocated that smokers should try to quit smoking, taking up drinking on health grounds is not advised.

In summary the most beneficial habits were frequent drinking and never smoking; they were associated with 0.43% lower HbA_{1c} than among the non-drinker group who are smokers

Discussion

Main findings

The analyses presented here provide evidence that in a population-based sample of mainly white Caucasian adults, increasing HbA_{1c} levels are associated with less frequent consumption of alcohol and heavier cigarette smoking across adulthood. Cross sectional analyses showed that

more frequent drinkers had lower (i) mean HbA_{1c} (ii) risk of being in the elevated HbA_{1c} group and (iii) risk of having metabolic syndrome. There were consistent associations between drinking frequency in twenties, thirties and forties and metabolic profile in mid-life, because drinking frequency changes across the lifecourse, if only the proximal drinking patterns were relevant to the outcomes, consistent associations at each of the earlier life-stages would not be expected. Lifecourse analyses confirmed that daily drinking on more occasions was associated with lower HbA_{1c} and lower risk of elevated HbA_{1c}/diabetes or metabolic syndrome in mid-life. Current as well as past drinking frequency were associated with mean HbA_{1c} levels and repeated measures analyses indicated that frequency of drinking through adulthood was associated with diabetes and metabolic syndrome risk (although daily drinking trajectories were not associated with reduced risks of metabolic syndrome in men). There was not however, consistent evidence that heaviness of drinking was associated with HbA_{1c} levels or elevated HbA_{1c} / diabetes or metabolic syndrome, either from cross-sectional or lifecourse analyses. Additionally, there was not evidence that at different drinking frequencies, amount of alcohol consumed was associated with glucose regulation. Wine consumption was consistently associated with lower HbA_{1c} levels and lower risk of elevated HbA_{1c} / type 2 diabetes or metabolic syndrome. Less frequent drinking and greater adiposity are separately associated with poorer glucose regulation, but there was not consistent evidence for interactions between body size and alcohol use on glucose regulation. Cross-sectional analyses provided consistent evidence that smokers had higher mean HbA_{1c} levels and heavier smoking was associated with higher mean HbA_{1c} or elevated HbA_{1c} / type 2 diabetes, particularly among men. Multilevel models confirmed that current smoking trajectories 23-42 years were associated with higher risk of having elevated HbA_{1c} / type 2 diabetes.

The effects of smoking and drinking frequency on glucose regulation are similar when adjusted for each other. However adjustment for adiposity reduces associations indicating that it mediates between smoking and dinking and poor glucose regulation. Additional adjustment for other lifestyle factors (diet and physical activity) slightly attenuated the associations, particularly among women, both in the cross sectional and in the lifecourse analyses.

Strengths and weaknesses

The general strengths of the prospective study design with a population based sample of men and women and the repeated measures of health behaviours were addressed in chapter 3. The particular benefits of this study relevant to addressing the questions set out in this chapter are firstly that the 1958 cohort is unique in having long term prospective ascertainment of health behaviours along side a measure of HbA_{1c} in a population sample. This gives stronger evidence of causality of associations between health behaviours and health outcomes than cross-sectional studies, because the temporal sequence of events is clear. Most existing longitudinal studies of

smoking or drinking and development of diabetes largely rely on single measures of smoking or drinking and unlike this study, do not take account of changes in behaviour over time. Weaknesses are that at present the prevalence of diabetes or elevated HbA_{1c} in the cohort is low which may limit the power to detect associations between diabetes risk and exposures. Chapter 2 reported details of measurement of HbA_{1c} and calibration and reliability as well as discussions about the two outcomes metabolic syndrome and elevated HbA_{1c} levels/ diabetes. The ten year age gaps between surveys mean that although change in behaviour is documented, it is possible that behaviour change between the surveys was concealed.

Effect size

The size of the differences in HbA_{1c} levels between groups with different smoking and drinking habits reported in this study look small. However the standard deviation of HbA_{1c} in the analysis sample (excluding those on oral anti-diabetics and steroids), is 0.528 in men and 0.428 in women. The adjusted effect sizes associated with differences between the smoking and drinking groups (up to 0.3%) correspond to half a standard deviation in the population HbA_{1c} level. Differences in mean HbA_{1c} levels between groups are of the same order of magnitude as found in other studies. The size of the differences in HbA_{1c} levels seen between the different groups can be compared to the effects of pharmaceutical drugs on HbA_{1c} levels as tested in clinical trials. Whereas the adjusted difference in HbA_{1c} by smoking and drinking groups is about 0.2%, in trial settings anti-diabetic drugs can achieve between 0.5 and 1.5% reduction in HbA_{1c} over a time period. Reductions of 0.5% HbA_{1c} are reported to be clinically significant in the trial literature. For example, the DIGEM trial in type 2 diabetic patients with HbA_{1c} >6.2% aimed to find a reduction of HbA_{1c} of 0.5% on the basis that this is "associated with clinically important reductions in diabetic complications." Whether similar reductions in HbA_{1c} level would be associated with lower risk of adverse consequences in the non-diabetic population whose HbA_{1c} level is lower to start with was unclear until recently. However evidence is accumulating of associations between HbA_{1c} and mortality across the spectrum of HbA_{1c} levels (de Vegt et al. 1999; Khaw et al. 2001; Khaw et al. 2004). To put into perspective the importance of health behaviours for diabetes onset, the effect size of smoking on risk of onset of diabetes was estimated to be similar to mild overweight or hypertension in a study 21,000 US male physicians (Manson et al 2000).

The associations of heavy smoking and infrequent drinking at 45 years and metabolic syndrome remained elevated after adjustment; ORs around 1.5 to 2. These represent moderate strength associations which will confer non-trivial extra risks of morbidity and mortality, particularly as they apply to large sections of the population. Smoking and less frequent drinking were also significantly associated with elevated HbA_{1c} / diabetes risks particularly in men, although in women the effects were reduced on adjustment for adiposity, diet and activity.

Changing exposure to alcohol

Drinking and smoking patterns change over age in the cohort. If only the most recent behaviours were associated with the health outcomes, then consistent associations between eg drinking frequency at each age and the diabetes risk outcomes would not be expected. The consistency of the associations was confirmed in repeated measures analysis. To address the concern that diagnosis of disease may be associated with behavioural change; that sick people would quit drinking and then move into the non-drinking group at later ages and artificially inflate the disease risks in this group additional analyses were run (Appendix 5.2). The risk of each of the outcomes did not differ between the non-drinkers at 45 years who had never drunk compared to those who had stopped drinking. Adjusted analyses of drinking and smoking were re-run excluding the known diabetic group who might have changed their behaviour. The patterns of HbA_{1c} and elevated HbA_{1c} were similar to the original analysis which included known diabetics. Behavioural change after diagnosis of diabetes is therefore unlikely to account for higher risks in non-drinkers. Additionally, as discussed in chapter 3, the stability of the non-drinker group is relatively high and greater than the heavy drinker group.

Greater instability among heavy drinkers, instead suggests that risks associated with heavy drinking rather than non-drinking may be biased. For example, among men 44% of non-drinkers in their 20s were still non-drinkers in their 40s, 50% had taken up moderate drinking and 6% were heavy-drinkers. 38% of heavy drinkers at 23 years were still heavy drinkers at 42 years, 55% cut down to moderate drinking and only 7% became non-drinkers. Given that the majority of men change drinking habits over twenty years (and there is even more change among women heavy drinkers), this suggests that estimates of associations between diabetes risks and alcohol or tobacco use categorized solely on baseline exposure may need to be re-evaluated as there may be substantial misclassification. Using a measure of exposure at a single time-point may give biased estimates of risk attributable to either heaviness or frequency of alcohol use. Despite this, most literature about alcohol and diabetes or cardiovascular disease risk does not take account of changes in behaviour over time. Changes in smoking habits over time have often been characterized better than alcohol, by using pack-years of exposure. In Britain and most western societies, the prevalence of smoking declines with increasing age and the prevalence of both heavy drinking and of abstaining declines with age, (up to the age range studied here). It is likely that the direction of bias would be towards weakening the reported associations rather than strengthening them (Emberson et al. 2005b). Longer follow-ups are reported to be associated with weaker effect estimates (Gmel et al. 2003). A Danish study investigated duration of follow-up and size of risk estimates for several outcomes related to alcohol consumption (Nielsen et al. 2005); the apparent protective effect of moderate alcohol

consumption on all cause mortality and CHD was attenuated with longer follow-up, whereas the increased risk associated with high consumption of alcohol became more pronounced with longer follow-up time. Changes in risk estimates over time of the effect of alcohol may be due to changes in drinking pattern over the follow up, changes in other risk factors over the follow up, healthy survivors or sick quitters, or there may be an age effect where the protective effects are confined to older age groups or it could be due to chance. Most of these issues can be addressed with a prospective cohort study design although using only one age cohort it is not possible to untangle age and period effects.

Analyses presented here which take account of changing exposure to tobacco and alcohol over two decades add to the literature because changing exposure is currently recognised in few papers. One such uses the British Doctors Study to investigate associations between alcohol use using averaged exposures over time and mortality (Doll et al. 2005). A second study investigated cardiovascular diseases and mortality in the British Regional Heart Study; using baseline measures there were u-shaped associations with major CHD, stroke and all-cause mortality. Adjusting for average alcohol intake during the twenty year follow-up period indicated that the risks of non-drinking had been over-estimated and the risks for moderate and heavy drinking were underestimated (Emberson et al. 2005a). The only study taking account of changing alcohol use in relation to diabetes risk is in the Dutch prospective EPIC study which uses a calculation of alcohol–years on the basis of retrospectively reported alcohol consumption when participants were aged 20 and 40 years(Beulens et al. 2005).

Non-drinkers

There has been much discussion of the importance of the baseline group in estimating the risks of non-drinking compared to moderate or heavy drinking on mortality or other outcomes. Since Shaper's suggestion in 1988 that the non-drinkers may include sick quitters who artificially raise the disease risk in this group, studies have tried to take account of this by excluding ex-drinkers (Shaper et al. 1988). The non-drinkers are a heterogenous group: there are some lifetime abstainers as well as recovered alcoholics and people who are ill. If ex-alcoholics are at higher risk of developing diabetes, putting them in the null group (no alcohol) may reduce the estimates of the association between alcohol use and diabetes risk. However as Doll et al explain in relation to their analyses of alcohol in relation to mortality, the inclusion of ex-heavy drinkers would not explain the results because the increase in risk in the heavy drinkers is not large enough to account for the inflation of risk in the non-drinkers by some ex-heavy drinkers(Doll & Peto 1995). In order for non-drinkers to elevate risks because they include ex-drinkers, the effects of alcohol on glucose regulation would have to be large and long-lasting. This would imply that there were large differences between the magnitude of association

between non-drinking and heavy drinking, which has not been confirmed by meta-analyses of drinking and diabetes risk.

Most "never-drinkers" have consumed some alcohol in the past (Appendix 5.2). It is therefore it is questionable whether it is useful to try to identify them as the baseline group. Studies using reported "lifetime abstainers" as a baseline group are likely to include some past drinkers: analysis of the 1958 cohort indicated that most people reporting non-drinking in midlife were in fact drinkers at previous ages. "Never" drinkers may have similar exposure to alcohol as "special occasion" drinkers; some exposure to alcohol mostly at a low level or in the past. The possibility of residual confounding in this group cannot be entirely ruled out. Never-drinkers could be excluded from analyses, or special occasion or light drinkers used as baseline (some studies repeat analyses with both non-drinkers and light drinkers as baseline groups). Shaper argues that the ideal reference group for studies on alcohol and health is the light / special occasion drinkers of up to 15g alcohol / day (1.88 UK units), because they are "norm" and they do not have spuriously elevated disease risk, presumably also because they are at the nadir of the risk curve(Shaper et al 1988). In the 1958 cohort there is not evidence that the disease risks differ between special occasion and "never" drinkers. Depending on biological mechanisms proposed to explain the disease risk, low exposure in "special occasion" drinkers may be equivalent to those who do not habitually drink at all. It is difficult to see how low level exposures would translate into meaningful changes in haemostatic variables. A recent meta-analysis of the association between alcohol use and type 2 diabetes risk reports that investigations of the sick quitter hypothesis have not shown it to be problematic(Koppes et al. 2005). Likewise the sick quitter hypothesis is not supported by 1958 cohort data. A study which separated ex- and never drinkers found that odds of metabolic syndrome did not differ between the two groups, neither did the odds of having any separate component of metabolic syndrome (Djousse et al 2004)

Alcohol use and HbA_{1c}

More frequent drinking was associated with lower HbA_{1c}, lower odds of having elevated HbA_{1c} /diabetes, or metabolic syndrome, but there was little evidence for associations with heaviness of drinking. There was not evidence for different effects of drinking heaviness in the drinking frequency strata; for example, frequent consumption of one or two units of alcohol per day did not have different consequences to frequent consumption of more than seven or 10 units of alcohol per day. Binge drinking was also not associated with poor glucose regulation.
From existing literature, lighter drinkers were expected to have lower HbA_{1c} in mid-life than non- or heavy drinkers and higher drinking frequency was expected to associated with HbA_{1c}, similarly to diabetes risk. In the 1958 cohort, associations between frequency of dinking and HbA_{1c} conformed to expectations more than with amount consumed. However relatively few

studies of HbA_{1c} and alcohol exist to compare 1958 cohort results with and few other studies examine drinking frequency. The 1958 cohort is younger and has better glucose regulation than many other samples studied.

Associations between HbA_{1c} levels and drinking frequency in 1958 cohort are of the same order of magnitude as other studies; differences of 0.1% to 0.2% HbA_{1c} between drinkers on<1 day/ week and drinkers on 3-7 days/week are reported (Mukamal et al. 2005). A study of 459 normal weight and overweight women (from the Nurses Health Study) reported lower HbA_{1c} among more frequent drinkers. They also reported that simultaneous adjustment for frequency and amount of alcohol intake did not change the associations between amount of alcohol and HbA_{1c} levels. Whilst the results for frequency of drinking fit with the results seen in the 1958 cohort, the results for mutual adjustment are in contrast to the results from 1958 cohort data where stratifying the amount of alcohol intake by frequency of drinking resulted in non-significant associations with frequency (Kroenke et al. 2003). In a small cross-sectional sample of the Health Professionals Follow-up Study, drinking frequency was categorized at higher levels; 1-3, 4-5 or 6-7 drinking days per week and associations with HbA_{1c} were not seen, but frequent drinkers had lower c-peptide and insulin levels, adjusted for average daily consumption, age, BMI, smoking physical activity, hypertension and diet (Meyer et al. 2003). The study did not provide evidence for interactions between frequency of consumption and amount of alcohol consumed daily on HbA_{1c} c-peptide or insulin levels, which mirrors the findings from the 1958 cohort data.

In relation to amount of alcohol consumed, a British regional study (EPIC Norfolk) reported that increasing weekly alcohol intake were broadly inversely related to HbA_{1c} levels. Heavier weekly drinking was associated with lower HbA_{1c} than lighter drinking; mean HbA_{1c} in women drinking >0 to ≤0.75 units/week was 5.39 compared to 5.15 in women drinking >7.25 units/ week. Associations were robust to adjustment for total energy intake, age, further education dietary measures, smoking, family history of diabetes, physical activity, waist:hip ratio and body mass index (Harding et al 2002). The EPIC Norfolk sample is older, has poorer glycemic regulation and much lower levels of alcohol consumption than the 1958 cohort. The Potsdam EPIC cohort of 1773 middle-aged men and women reported that mean HbA_{1c} decreased across quintiles of increasing alcohol consumption, from 4.99% to 4.67%. However this study suffers from low participation rate (~35%)(Boeing et al 2000). The 1994 Health Survey for England (a large sample of non-diabetic white Europeans) reported that HbA_{1c} decreased with increasing weekly alcohol intake. There were gender differences in the association between HbA_{1c} and alcohol consumption: in models adjusted for age, BMI, WHR, physical activity, educational attainment and smoking, there was a significant association between alcohol consumption and HbA_{1c} in men. Men drinking 0-6 units in the past week had -0.12% lower HbA_{1c} than non-

drinkers. Men drinking 7-20 units/ week did not have significantly different HbA_{1c} to non-drinkers whilst the heavier drinkers 21-42 and >42 units/week had lower HbA_{1c} eg -0.244 (95%CI -0.371, -0.117) for ≥42 units/week, compared to non-drinkers. On the other hand, there was there was weak evidence for a similar trend in declining HbA_{1c} with increasing alcohol use in a week in women. Among women the lowest HbA_{1c} values were instead associated with the group consuming 21-41 units/ week the heavy drinkers had HbA_{1c} lower than non-drinkers; -0.147% (95%CI -0.223, -0.071)(Gulliford & Ukoumunne 2001). The Nurses Health study reported trends in increasing HbA_{1c} with increasing average alcohol intake per day. Mean HbA_{1c} was 5.29% and was 0.05% lower in women consuming 0.1-15g alcohol / day, 0.11% lower for 15-<35g/day and 0.06 lower for ≥35 g/day (Kroenke et al 2003). A cross-sectional study of 462 men aged 48-82 years from the Health Professionals Follow-up Study reported that mean HbA_{1c} levels did not differ linearly with increasing categories of daily alcohol intake (Meyer et al 2003). Compared to abstainers, consumers of 1-1.9 drinks/ day had 0.21% lower HbA_{1c} whereas consumers of ≥3 drinks/day had 0.10% lower HbA_{1c} levels in multivariate adjusted models.

Alcohol use and Diabetes risk

Associations between lower drinking frequency and higher diabetes risk were seen in both cross-sectional and lifecourse analyses. Daily drinking on more occasions was associated with lower risk of being in the elevated HbA_{1c}/diabetes group in men whilst non-drinking on more occasions was associated with higher risk. There were not clear associations between diabetes risk and amount of alcohol consumed or binge drinking. In contrast to existing evidence (which mostly fails to take account of behavioural change over time), associations between heaviness of alcohol use and diabetes onset was not seen in the 1958 cohort. A recent meta-analysis reported a reduction in risk of around 30% among moderate drinkers (5-30g alcohol per day, equivalent to 0.6-3.8 British units/day) compared to low consumption or abstaining (<5g alcohol per day). However it was concluded that evidence about risk at ≥30 g of alcohol per day is inconsistent. Most studies report that heavy drinkers were at increased risk of type 2 diabetes compared to moderate drinkers, however whether high consumers are also at increased risk compared to low consumers or abstainers is less clear (Carlsson et al. 2005). The 1958 cohort data did find that the non-drinkers were at higher risk than any of the drinking groups but didn't find systematically raised risks of diabetes in the heavier drinkers. However, the J-shaped curve is reported to vary with context: societies with high average intake are supposedly those who drink with meals rather than binge and have nadir of risk at higher levels. Also, the older the sample at baseline the more pronounced the protective effect and the longer the follow-up the less pronounced the effects (Gmel et al 2003). Most studies of alcohol use and diabetes risk measure alcohol use in average grams /day of alcohol, however two studies report drinks/ week (a similar format to the 1958 cohort). In the ARIC study which followed-up middle aged men and women over 3-6 years, heavy drinking (>21 drinks/ week) compared to ≤1 drink/week was

associated with excess risk of diabetes onset in men but not in women (Kao et al. 2001). The British Regional Heart Study found a non-linear association between alcohol use and diabetes onset over 12.8 years of follow-up. The nadir of the risk was in men consuming 16-42 units/week relative to occasional drinkers (RR 0.6, 95%CI 0.4-1.0) (Perry et al 1995). It is at these levels of consumption that the nadir of the prevalence of diabetes risk appears in the 1958 cohort although the trends were not very consistent.

One of the meta-analyses of diabetes risk and heaviness of drinking highlighted that frequency of drinking, type of drink, gender and ethnic differences all need to be investigated. These points are confirmed by another meta-analyses of heaviness of drinking and diabetes risk which also reports that the pattern of drinking and specifically frequency of drinking was not investigated in enough studies to be looked at in the meta-analysis and that drinking frequency needs further investigation (Koppes et al 2005). Drinking frequency was investigated in a study of men aged 48-82 years from the American Health Professionals Follow-up Study; within strata of drinking frequency, risk of diabetes onset was relatively constant over categories of drinks consumed per drinking day. Diabetes risk was lower in more frequent drinkers (≥5 days/ week) than less frequent drinkers (1-2 days/ week); RR 0.60 (95% CI 0.43, 0.84) over 12 years of follow up (Conigrave et al 2001).

Very few studies of alcohol use and diabetes risk have taken account of changing alcohol use across the lifecourse. A study which reports that it is the first to look at lifetime alcohol consumption and diabetes risk is the Dutch Prospect EPIC study of diabetes risk in older women (Beulens et al 2005). Alcohol–years were calculated from the retrospectively reported number of standard alcoholic drinks (10 g alcohol) consumed daily at age 20 and 40. The amount of alcohol consumed was multiplied by the number of years in an age bracket, from 20-30 years and from 30 until inclusion in the study, the association between diabetes onset and heaviness of drinking in the women based on lifetime alcohol use was linear until adjusted for baseline alcohol intake when it became u-shaped. The association between diabetes onset and heaviness of drinking in the women based on current alcohol use was linear. The authors report that the reliability of their method of assessing lifetime alcohol intake is reasonable however, data was gathered retrospectively. Unlike the 1958 data, in the Dutch study an association between heaviness of drinking and diabetes onset was seen. In contrast, the 1958 data pointed towards associations between repeated measures of frequency of drinking alcohol with more occasions of being a daily drinker associated with lower risk of being in the elevated HbA_{1c} or diabetes group. The studies discussed so far mainly report information about the amount of alcohol consumed rather than the frequency of drinking. In alcohol epidemiology it is increasingly recognized that the frequency as well as the amount consumed may have important implications for health risks.

Alcohol use and Metabolic syndrome

Drinking frequency was associated with metabolic syndrome, both in cross-sectional and lifecourse analyses; trajectories of more frequent drinking were associated with reduced odds of metabolic syndrome. Other studies about number of drinking days and metabolic syndrome are rare. In contrast, heaviness of drinking was not clearly associated with metabolic syndrome and nor was binge drinking in the 1958 cohort. This was not in line with expectations from results of previous studies; associations between light to moderate alcohol use and lower risk of cardiovascular disease and elements of the metabolic syndrome are repeatedly reported. Cross-sectional analysis of 8125 men and women from American NHANES III data revealed that increasing number of drinks/ month were associated with reduced odds of metabolic syndrome; OR 0.65(95%CI 0.54, 0.79) for 1-19 drinks/ month and OR 0.34 (95%CI 0.26, 0.47) ≥20 drinks/month (Freiberg et al 2004). Most of the separate constituent parts of the metabolic syndrome were associated with the drinks/month; elevated HDL, triglycerides, waist circumference and fasting insulin. There were non-significant trends in elevated fasting blood glucose and elevated blood pressure with increasing drinking quantity, after adjustment for age, sex, race, physical activity, education, income, smoking and diet. However "drinks per month" does not indicate the frequency of drinking days, so results are hard to compare with 1958 results. Increasing average daily alcohol consumption is associated with decrease odds of metabolic syndrome (Djousse et al 2004). A u-shaped association was seen in men with the lowest adjusted OR of metabolic syndrome in the 12-24g/d group OR 0.66 (95%CI 0.44, 0.99) compared to abstainers. There was a dose-response association in women, with the lowest OR in the heaviest consumers ≥24 g/day OR 0.39 (95%CI 0.21, 0.74) compared to 0.80 (95%CI 0.43, 1.34) in lighter consumers of 0.1-2.5 g/day. Differences between the results from 1958 study may be in part due to different categorisation of metabolic syndrome as well as different categorsiation of alcohol use. Existing studies of metabolic syndrome and alcohol trajectories have not investigated drinking frequency but have examined heaviness of drinking and reported that trajectories of heavier drinking were at greater risk of metabolic syndrome(Chandola et al 2006a; Ferreira et al 2005).

Alcohol and adiposity

Associations between alcohol use and diabetes risk may be mediated by associations between increased drinking frequency with lower BMI and smaller waist circumference, so analyses were adjusted for BMI and waist circumference. Associations between drinking frequency and HbA_{1c} and also high HbA_{1c} were attenuated but still significant on adjustment for BMI. Other studies have investigated whether adiposity mediates the association between heaviness of drinking and diabetes risk and there is some evidence that this is the case. However in the 1958 cohort there was not evidence of associations between heaviness of drinking and diabetes risk so this was not examined. Interactions between the amount of alcohol consumed and body mass

index were investigated and none were found in the present data. Although some other studies have reported interactions, the meta analysis of alcohol use and diabetes risk that considered adiposity did not find any significant interactions between alcohol use and adiposity (Koppes et al 2005).

Smoking and HbA_{1c}

Cross-sectional analysis of the 1958 cohort fit with reports from previous studies that HbA_{1c} is higher in smokers than in non-smokers(Boeing et al 2000; Gulliford & Ukoumunne 2001; Simon et al 1989). A cross sectional study of Health Survey for England data reported effect sizes of similar magnitude to those in 1958 cohort (Gulliford & Ukoumunne 2001). Mean HbA_{1c} of smokers of ≥20 cigarettes/ day was an average 0.21% (men) and 0.18% (women) higher than of never-smokers in 1958 cohort data, in comparison with 0.277% (95%CI 0.218, 0.336) in Health Survey for England. Gulliford et al also found that ex-smokers had similar HbA_{1c} levels to never smokers. In the EPIC Potsdam study of middle aged men and women, cross sectional analysis revealed that current smokers had HbA_{1c} levels 0.02% lower than non-smokers in men whilst the mean HbA_{1c} levels in women smokers did not differ from non-smokers. In univariate analyses smokers (compared to never smokers) were at increased the odds of being in the top tertile of HbA_{1c}, but this was fully mediated by anthropometrical and lifestyle variables. In contrast, among women ex-smoking was associated with reduced risks of elevated HbA_{1c} levels; OR 0.56 (95% CI 0.37, 0.85)(Boeing et al 2000). Data from the EPIC Norfolk study indicated a dose-response relationship between HbA_{1c} level and firstly number of cigarettes smoked among current smokers and secondly with the number of pack-years among ex-smokers (Sargeant et al 2001a). The studies mentioned above use information about pack-years of smoking in order to characterize exposure to cigarettes (Boeing et al 2000; Sargeant et al 2001a), but lack prospective information which would minimize misclassification due to recall bias.

Smoking and diabetes risk

Smoking was associated with increased risk of elevated HbA_{1c} or diabetes and ORs for smoking 1-19 or ≥20 cigarettes/day compared to never smoking were little changed and remained around 2 after adjustment for important confounding factors in men. However the associations between 42-year smoking and raised HbA_{1c} or diabetes in women were not significant. Data about the association between smoking and increased risk of diabetes is becoming more conclusive (Perry 2001). In the last decade, large scale prospective follow-up studies have reported that smoking is associated with up to double the risk of diabetes onset, similar to risks reported in men in the 1958 cohort (Manson et al 2000; Sairenchi et al 2004; Will et al 2001). A longitudinal study of 40-59 year old men recruited from General Practitioner registers in the UK, followed up on

average 12.8 years reported elevated odds diabetes in smokers compared to non-smokers, although amount smoked was not associated with risk (Perry et al 1995). The Male Health Professionals Follow-up Study in USA followed 41,810 men aged 40-75 years and reported increased relative risk of diabetes onset in the smokers of >25 cigarettes/day compared to non-smokers; 1.94 (95%CI 1.25, 2.03)(Rimm et al 1995). Similarly increased risks were reported in the male Physicians Health Study; there were significantly raised risks of developing diabetes in the smokers of both 1-19 and >20 cigarettes/ day compared to non-smokers, which persisted after adjustment for risk factors including BMI and physical activity. Ex-smokers were also at slightly higher risk than non-smokers. The number of pack-years of smoking was significantly linearly associated with diabetes onset. The multivariate fully adjusted risk for the smokers of >40 pack-years compared to never smokers was 1.6 (95%CI 1.3, 2.1)(Manson et al 2000). Similar patterns of increased risks are also reported among women using data from the large Nurses Health Study based in the USA. In the 11,247 women who participated, the fully adjusted relative risk of diabetes in the smokers >25 cigarettes/day compared to non-smokers was 1.4 (95%CI 1.2, 1.7). There was also a significant dose-response with the number of cigarettes smoked (Rimm et al. 1993). There is also evidence from the very large scale Cancer Prevention Study in USA that among ex-smokers the risk of diabetes returns to that of non-smokers after 5 years (women) and 10 years (men)(Will et al 2001). This evidence of a dose-response in risk complements the dose-response association seen between pack years smoked in ex-smokers and levels of HbA_{1c} investigated as a continuous variable. The evidence about increased risks of diabetes in female smokers from other studies is in contrast to the findings from the 1958 cohort on elevated HbA_{1c} / diabetes however, they do fit with the direction and magnitude of estimates for metabolic syndrome.

Smoking and metabolic syndrome

Smokers were at higher risk of metabolic syndrome that the non-smokers in the 1958 cohort and the effect sizes were similar to other studies. Among the men in the 1958 cohort the OR of metabolic syndrome in the smokers of >20 cigarettes /day at 42 years compared to never smokers was 1.70 (95% CI 1.29, 2.26), and this was almost unchanged in a fully adjusted model. Among women the equivalent OR for metabolic syndrome in heavy smokers was 2.56 which reduced to 2.20 (95% CI 1.45, 3.35) on adjustment. In NHANES III male current smokers had OR of metabolic syndrome (defined by ATP III criteria) of 1.5 (95%CI 1.1, 2.2) compared to never smokers, whilst ex-smoking was not associated with metabolic syndrome (Park et al 2003). Among women the equivalent ORs were 1.8 (95%CI 1.2, 2.6) for current smokers and 1.5 (95%CI 1.2, 2.0) for ex-smokers. Two recent studies have examined development of trajectories of tobacco use on the development of the metabolic syndrome, one examining onset by mid-thirties found no association whilst the other, studying older adults

reported that smokers were at greater risk of metabolic syndrome, as was seen in the 1958 data (Chandola et al 2006a; Ferreira et al 2005).

Gender

Studies of the effects of alcohol use on cardiovascular outcomes have reported that there are different associations between alcohol use and cardiovascular risk for men and for women (Tolstrup et al. 2006), the meta analysis of diabetes risk and alcohol use does not find significant gender differences (Koppes et al 2005). However many published studies focus on one gender. In this thesis, data analyses were carried out separately by gender on the basis that there may be different patterns of associations between patterns of alcohol intake and disrupted glycemic control. The patterns of smoking and drinking differ according to gender (Chapter 3) and there may be gender differences in alcohol metabolism. Also all three indicators of glucose regulation were worse in men than in women. In this dataset daily drinking was compared to less frequent drinkers was associated with lower HbA_{1c} in women than in men. There were also greater odds of developing metabolic syndrome in women who were daily drinkers compared to never drinkers (OR=3) compared to men (OR=1.7). If the effects of alcohol or tobacco are mediated by body size and in particular by central adiposity, any gender differences in the patterns of central adiposity may be important. Indeed adjusted results of regression analyses suggested that the associations between smoking and alcohol use and metabolic syndrome or diabetes risk were more attenuated for women than men.

Conclusions

Associations between HbA_{1c} levels and lifetime smoking and drinking frequency are already apparent in midlife in a sample of this large population based cohort of men and women. Whilst the effect size is small, it applies to a large proportion of the cohort. Investigation of repeated measures of alcohol use and HbA_{1c} is novel and the finding that past drinking in addition to current drinking status was associated with to HbA_{1c} levels adds importantly to the literature. Moderate associations between the risk of metabolic syndrome or elevated HbA_{1c} levels with drinking frequency were evident in men although they were explained by other health behaviours and adiposity in women. The cohort are entering the age bracket where there is rapid increase in the incidence of diabetes, so increases in HbA_{1c} levels associated with lifestyle in mid-forties and at earlier life stages may become increasingly important in determining disease risk.

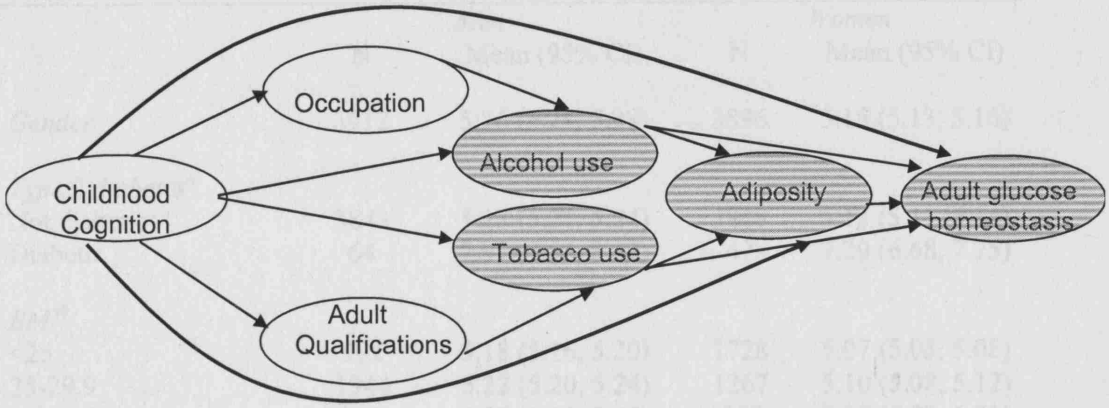


Figure 5.1 Conceptual Framework

Table 5.1. Geometric mean 45-year HbA_{1c} by co-variates, measured cross sectionally

	Men		*Women*	
	N	Mean (95% CI)	N	Mean (95% CI)
Gender	3912	5.26 (5.25, 5.28)	3896	5.15 (5.13, 5.16)
Type 2 diabetes[a]				
Not diabetic	3843	5.23 (5.21, 5.24)	3845	5.13 (5.11, 5.14)
Diabetic	64	7.97 (7.54, 8.42)	47	7.20 (6.68, 7.75)
BMI[b]				
<25	992	5.18 (5.16, 5.20)	1728	5.07 (5.05, 5.08)
25-29.9	1944	5.22 (5.20, 5.24)	1267	5.10 (5.08, 5.12)
30-34.9	763	5.37 (5.32, 5.42)	556	5.27 (5.22, 5.31)
>35	203	5.68 (5.55, 5.82)	338	5.54 (5.45, 5.63)
Waist circumference[b]				
<0.94 men and <0.88 women	1435	5.18 (5.16, 5.20)	1522	5.06 (5.04, 5.07)
0.94-1.02 men and 0.80-0.88 women	1216	5.22 (5.20, 5.24)	949	5.08 (5.06, 5.10)
>1.02 men and >0.88 women	1243	5.41 (5.37, 5.45)	1401	5.28 (5.25, 5.31)
Diet score[a]				
Unhealthy quartile	663	5.29 (5.23, 5.34)	639	5.20 (5.16, 5.24)
Quartile 2	697	5.27 (5.23, 5.31)	1058	5.18 (5.15, 5.21)
Quartile 3	1245	5.26 (5.23, 5.29)	789	5.15 (5.11, 5.18)
Healthy quartile	1191	5.25 (5.22, 5.28)	1321	5.09 (5.07, 5.11)
Physical activity[a]				
4-7 times / week	921	5.26 (5.22, 5.29)	1048	5.16 (5.13, 5.18)
2-3 times /week	826	5.21 (5.17, 5.24)	817	5.09 (5.06, 5.12)
1 time /week	791	5.25 (5.21, 5.29)	645	5.13 (5.09, 5.16)
≤2-3 times/ month	1244	5.32 (5.28, 5.35)	1272	5.19 (5.16, 5.21)
Smoking[a]				
Never	1781	5.20 (5.17, 5.22)	1850	5.12 (5.10, 5.14)
Ex	1115	5.25 (5.22, 5.28)	1034	5.11 (5.09, 5.14)
Current	904	5.41 (5.37, 5.45)	924	5.23 (5.25, 5.26)
Drinking[b]				
Most days	1234	5.20 (5.17, 5.22)	803	5.02 (5.00, 5.05)
2/3 times per week	1318	5.24 (5.21, 5.26)	1163	5.08 (5.06, 5.10)
2-4 times per month	789	5.30 (5.26, 5.34)	870	5.17 (5.14, 5.20)
Rarely	368	5.41 (5.34, 5.48)	731	5.29 (5.25, 5.33)
Not in past 12 months	180	5.50 (5.37, 5.63)	317	5.34 (5.27, 5.41)

[a] reported at 42-year interview
[b] reported at 45-year interview

Table 5.2 Mean HbA_{1c} (at 45 years) by frequency of drinking through adulthood[a]

	23 years		33 years		42 years		45 years	
Usual frequency of alcohol consumption	% (n)	Geometric Mean (95% CI)	N (%)	Geometric Mean (95% CI)	N (%)	Geometric Mean (95% CI)	N (%)	Geometric Mean (95% CI)
Men								
Most days	32.5 (1060)	5.22 (5.19, 5.24)	18.0 (605)	5.17 (5.14, 5.20)	25.2 (941)	5.19 (5.16, 5.22)	32.1 (1223)	5.18 (5.16, 5.20)
Weekly	50.5 (1646)	5.22 (5.20, 5.24)	55.3 (1862)	5.22 (5.20, 5.24)	54.9 (2045)	5.22 (5.20, 5.23)	34.1 (1299)	5.22 (5.19, 5.24)
2-3 times/ month	9.1 (297)	5.25 (5.19, 5.31)	15.3 (515)	5.25 (5.22, 5.28)	8.9 (330)	5.26 (5.21, 5.32)	20.0 (762)	5.23 (5.21, 5.26)
Special Occasion	5.3 (175)	5.25 (5.18, 5.30)	8.8 (295)	5.28 (5.21, 5.35)	7.7 (288)	5.35 (5.28, 5.41)	9.4 (358)	5.36 (5.30, 5.42)
Never drinker	2.6 (83)	5.38 (5.26, 5.50)	2.7 (92)	5.34 (5.23, 5.46)	3.3 (124)	5.35 (5.23, 5.45)	4.5 (172)	5.40 (5.30, 5.50)
Total	100 (3261)		100 (3369)		100 (3728)		100 (3814)	
Linear trend	p=0.105		P<0.001		p<0.001		p<0.001	
Quadratic trend	p=0.103		P=0.349		p=0.001		P=0.005	
Women								
Most days	10.7 (358)	5.05 (5.02, 5.09)	7.3 (254)	5.01 (4.97, 5.05)	15.4 (576)	4.99 (4.96, 5.01)	20.9 (358)	5.02 (4.99, 5.05)
Weekly	46.5 (1559)	5.11 (5.09, 5.13)	41.4 (1450)	5.08 (5.06, 5.11)	50.3 (1887)	5.10 (5.08, 5.12)	30.2 (1153)	5.07 (5.05, 5.09)
2-3 times/ month	16.5 (554)	5.13 (5.10, 5.16)	24.3 (850)	5.16 (5.13, 5.18)	12.2 (459)	5.21 (5.16, 5.25)	22.6 (862)	5.16 (5.14, 5.19)
Special Occasion	21.6 (723)	5.17 (5.15, 5.20)	22.4 (779)	5.19 (5.16, 5.21)	16.3 (610)	5.24 (5.21, 5.27)	18.6 (709)	5.24 (5.21, 5.27)
Never drinker	4.8 (160)	5.18 (5.12, 5.24)	4.8 (169)	5.24 (5.17, 5.31)	5.8 (218)	5.24 (5.18, 5.30)	7.9 (300)	5.26 (5.21, 5.31)
Total	100 (3354)		100 (3502)		100 (3750)		100 (3822)	
Linear trend	p<0.001		P<0.001		p<0.001		p<0.001	
Quadratic trend	p=0.927		P=0.067		p=0.022		p<0.001	

[a]Sample includes type 2 diabetics, but excludes type 1diabetes and those on oral antidiabetics or steroids; n=7663

[b] linear and quadratic trends in hba1c tested using linear regression with linear and quadratic terms of median drinking frequency

Table 5.3 Prevalence [% (n)] of metabolic syndrome and type 2 diabetes at 45 years by frequency of drinking through adulthood[a]

Usual frequency of alcohol consumption	Metabolic syndrome				High HbA_{1c} (≥6% & Type 2 Diabetes)			
	23 years	33 years	42 years	45 years	23 years	33 years	42 years	45 years
Men								
Most days	11.6 (121)	10.6 (62)	12.1 (110)	11.6 (139)	4.1 (44)	2.3 (14)	3.5 (33)	3.0 (37)
1-3 times/ week	12.4 (199)	11.7 (213)	11.8 (236)	11.5 (145)	4.7 (79)	4.5 (85)	4.6 (96)	4.1 (54)
1-3 times/ month	12.9 (37)	13.8 (69)	13.8 (45)	12.4 (94)	3.0 (9)	4.4 (23)	5.7 (19)	5.5 (43)
Special Occasion	14.3 (25)	18.2 (54)	16.7 (47)	17.7 (62)	7.2 (13)	9.5 (29)	6.7 (20)	8.5 (31)
Never drinker	15.0 (12)	12.4 (11)	19.1 (23)	17.9 (30)	4.7 (4)	8.4 (8)	10.9 (14)	12.3 (22)
Total	12.4 (394)	12.4 (409)	12.7 (463)	12.6 (470)	4.5 (149)	4.7 (159)	4.8 (183)	4.8 (187)
Linear trend	P=0.249	P=0.009	P=0.067	P=0.023	P=0.438	P<0.001	p<0.001	P<0.001
Quadratic trend	P=0.667	P=0.157	P=0.016	P=0.023	P=0.978	P=0.728	P=0.272	P=0.029
Women								
Most days	5.8 (20)	4.9 (12)	5.8 (32)	5.3 (41)	1.9 (7)	0.8 (2)	1.4 (8)	1.8 (14)
1-3 times/ week	10.2 (154)	9.1 (128)	8.4 (154)	7.2 (81)	3.2 (50)	3.4 (50)	2.2 (42)	1.6 (19)
1-3 times/ month	11.5 (62)	11.1 (92)	14.8 (66)	10.9 (91)	3.8 (21)	3.0 (26)	4.5 (21)	3.0 (26)
Special Occasion	10.7 (76)	10.9 (82)	12.1 (72)	16.4 (113)	3.3 (24)	3.8 (30)	6.3 (39)	6.1 (44)
Never drinker	13.8 (22)	13.4 (22)	16.2 (34)	14.5 (43)	5.5 (9)	6.4 (11)	6.7 (15)	7.7 (24)
Total	10.2 (334)	9.9 (336)	9.9 (359)	9.9 (369)	3.3 (111)	3.4 (119)	3.3 (125)	3.3 (127)
Linear trend	P=0.004	P<0.001	P<0.001	P<0.001	P=0.091	P=0.025	P<0.001	P<0.001
Quadratic trend	P=0.181	P=0.392	P=0.323	P=0.012	P=0.627	P=0.205	P=0.080	P<0.001

[a]Sample includes type 2 diabetics, but excludes type 1diabetes; n=7799

[b] Difference in metabolic syndrome or elevated HbA_{1c} by median frequency of drinks/week tested by logistic regression with linear and quadratic terms for median drinking frequency

Table 5.4 β coefficients from regression analyses of 45-year HbA_{1c} on lifecourse frequency of drinking at 23, 33, 42 and 45 years [a]

	Daily drinkers			Non-drinkers		
	% (n)	β (95%CI)[b]	Adjusted β (95%CI)[c]	% (n)	β (95%CI)[b]	Adjusted β (95%CI)[c]
Men (n=2777)						
Never	46.1 (1280)	Reference group[d]	Reference group[d]	77.0 (2137)	Reference group[e]	Reference group[e]
1 occasion	23.4 (649)	-0.031 (-0.074, 0.012)	-0.046 (-0.087, -0.004)	11.6 (323)	0.064 (0.020, 0.108)	0.042 (0.001, 0.084)
2 occasions	13.7 (379)	-0.030 (-0.090, 0.030)	-0.038 (-0.095, 0.019)	5.5 (152)	0.131 (0.007, 0.255)	0.096 (-0.021, 0.213)
3 occasions	10.7 (297)	-0.061 (-0.138, 0.017)	-0.064 (-0.139, 0.011)	4.0 (112)	0.111 (-0.014, 0.236)	0.110 (-0.014, 0.235)
4 occasions	6.2 (172)	-0.104 (-0.158, -0.049)	-0.120 (-0.174, -0.064)	1.8 (50)	0.154 (0.069, 0.238)	0.152 (0.059, 0.245)
Linear trend test		P=0.006	P<0.001		P<0.001	P<0.001
Women (n=2969)						
Never	69.1 (2050)	Reference group[d]	Reference group[d]	52.0 (1519)	Reference group[e]	Reference group[e]
1 occasion	15.6 (462)	-0.079 (-0.127, -0.031)	-0.053 (-0.100, -0.007)	20.7 (603)	0.060 (0.018, 0.102)	0.037 (-0.004, 0.079)
2 occasions	9.4 (278)	-0.159 (-0.203, -0.116)	-0.123 (-0.166, -0.081)	11.4 (333)	0.124 (0.078, 0.170)	0.084 (0.040, 0.128)
3 occasions	4.2 (125)	-0.191 (-0.255, -0.127)	-0.156 (-0.213, -0.075)	8.5 (248)	0.146 (0.096, 0.196)	0.098 (0.050, 0.146)
4 occasions	1.8 (54)	-0.192 (-0.261, -0.123)	-0.144 (-0.213, -0.075)	7.3 (214)	0.180 (0.126, 0.234)	0.139 (0.086, 0.193)
Linear trend test		P<0.001	P<0.001		P<0.001	P<0.001

[a] Sample excludes type 1 diabetics and those taking medications which might alter HbA_{1c} levels (including oral anti-diabetics and steroids); n=7754

[b] estimated β coefficient from linear regression model.

[b] estimated β coefficient from linear regression model adjusted for smoking between 23 and 42 years, diet at 42 years, physical activity at 42 years , waist circumference and BMI at 45 years

[d] The reference group for the daily drinker models are the participants who never reported daily drinking between 23 and 45 years., ie they were less frequent or non-drinkers

[e] The reference group for the non-drinker models are the group who did not report non-drinking between 23 and 45 years ie they were always more frequent drinkers.

Table 5.5 Geometric mean HbA_{1c} and 95% confidence intervals (measured at 45 years) by heaviness of drinking through adulthood[a]

	23 years		33 years		42 years	
Past week alcohol consumption (units)	% (N)	Geometric Mean (95% CI)	% (N)	Geometric Mean (95% CI)	% (N)	Geometric Mean (95% CI)
Men						
Non drinker	2.6 (83)	5.39 (5.26, 5.50)	2.7 (92)	5.34 (5.23, 5.46)	3.3 (124)	5.34 (5.23, 5.45)
Special Occasion	5.4(175)	5.24 (5.18, 5.30)	8.8 (295)	5.28 (5.21, 5.35)	7.7 (288)	5.34 (5.28, 5.41)
Not in past week (0)	4.6 (151)	5.21 (5.12, 5.29)	6.0 (202)	5.26 (5.20, 5.31)	5.0 (185)	5.26 (5.19, 5.34)
Light (1-10)	24.6 (802)	5.22 (5.19, 5.25)	31.2 (1050)	5.22 (5.19, 5.24)	25.5 (949)	5.22 (5.20, 5.25)
Moderate (11-21)	24.1 (785)	5.23 (5.19, 5.26)	23.5 (793)	5.21 (5.18, 5.24)	21.3 (791)	5.24 (5.20, 5.29)
Heavy (22-35)	17.5 (570)	5.21 (5.18, 5.24)	15.7 (528)	5.20 (5.17, 5.23)	16.2 (603)	5.23 (5.19, 5.27)
Very heavy (36-50)	10.5 (343)	5.22 (5.18, 5.26)	7.0 (234)	5.22 (5.17, 5.28)	10.0 (371)	5.21 (5.17, 5.25)
Extremely heavy (>50)	10.8 (352)	5.22 (5.18, 5.26)	5.2 (175)	5.17 (5.11, 5.22)	11.0 (409)	5.26 (5.21, 5.31)
Total N	3261		3369		3720	
In habitual drinkers:						
linear trend[b]		P=0.701		P=0.210		P=0.802
quadratic trend[b]		P=0.745		P=0.730		P=0.323
Women						
Non drinker	4.8 (160)	5.18 (5.12, 5.24)	4.8 (169)	5.24 (5.17, 5.31)	5.8 (218)	5.24 (5.18, 5.30)
Special Occasion	21.6 (723)	5.17 (5.15, 5.20)	22.2 (779)	5.19 (5.16, 5.21)	16.3 (610)	5.24 (5.21, 5.27)
Not in past week (0)	8.5 (284)	5.15 (5.11, 5.19)	10.2 (356)	5.15 (5.11, 5.18)	6.2 (231)	5.17 (5.12, 5.23)
Light (1-7)	34.4 (1155)	5.12 (5.10, 5.15)	38.0 (1332)	5.11 (5.09, 5.13)	35.9 (1345)	5.13 (5.11, 5.15)
Moderate (8-14)	18.2 (611)	5.09 (5.06, 5.12)	16.2 (568)	5.07 (5.04, 5.11)	21.0 (787)	5.08 (5.05, 5.10)
Heavy (15-21)	6.6 (220)	5.06 (5.01, 5.12)	5.2 (181)	5.04 (5.00, 5.09)	8.5 (317)	5.00 (4.96, 5.04)
Very heavy (>22)	6.0 (201)	5.07 (5.02, 5.11)	3.3 (117)	5.06 (4.99, 5.13)	6.4 (240)	5.02 (4.98, 5.07)
Total N	3354		3502		3748	
In habitual drinkers:						
linear trend[b]		P=0.007		P=0.017		P<0.001
quadratic trend[b]		P=0.377		P=0.307		P=0.028

[a]Sample includes type 2 diabetics, but excludes type 1diabetes and those on oral antidiabetics and steroid medication; n=7663

[b] linear and quadratic trends in HbA_{1c} tested using linear regression with median weekly alcohol units. Tested in habitual drinkers: 0 units - extremely heavy.

Table 5.6 Prevalence of metabolic syndrome and type 2 diabetes (at 45 years) by heaviness of drinking through adulthood[a]

	Metabolic syndrome % (n)			High HbA_{1c} (≥6% & Type 2 Diabetes) % (n)		
Past week alcohol consumption (units)	*23 years*	*33 years*	*42 years*	*23 years*	*33 years*	*42 years*
Men						
Non-drinker	14.5 (37)	16.8 (64)	17.4 (70)	6.4 (17)	9.2 (37)	8.0 (34)
Not in the past week (0)	14.4 (21)	13.4 (27)	13.7 (25)	2.6 (4)	7.2 (15)	6.8 (13)
Light (1-10)	12.5 (98)	12.0 (122)	11.4 (105)	4.2 (34)	4.2 (44)	5.3 (51)
Moderate (11-21)	12.4 (95)	10.1 (79)	10.4 (80)	5.4 (43)	3.2 (26)	4.0 (32)
Heavy (22-34)	11.2 (62)	11.6 (59)	10.7 (64)	3.5 (20)	3.9 (21)	3.8 (23)
Very heavy (35-50)	11.7 (39)	14.3 (33)	13.7 (50)	5.4 (19)	4.2 (10)	3.2 (12)
Extremely heavy (>51)	12.1 (42)	14.0 (24)	16.8 (67)	3.3 (12)	3.4 (6)	4.1 (17)
Total N	12.4 (394)	12.4 (409)	12.7 (461)	4.5 (149)	4.7 (159)	4.8 (182)
Linear trend	P=0.676	P=0.294	P=0.003	P=0.566	P=0.799	P=0.160
Quadratic trend	P=0.629	P=0.246	P=0.747	P=0.450	P=0.740	P=0.179
Women						
Non-drinker	11.3 (98)	11.3 (104)	13.2 (106)	3.7 (33)	4.3 (41)	6.4 (54)
Not in the past week (0)	13.0 (36)	10.5 (36)	11.7 (26)	3.9 (11)	2.5 (9)	1.7 (4)
Light (1-7)	9.2 (103)	8.8 (115)	9.1 (119)	2.7 (32)	3.2 (43)	2.8 (38)
Moderate (8-14)	9.9 (59)	10.1 (56)	7.6 (58)	3.4 (21)	3.7 (21)	2.0 (16)
Heavy (15-21)	9.5 (20)	10.3 (18)	7.8 (24)	3.6 (8)	1.1 (2)	2.8 (9)
Very heavy (>22)	9.6 (18)	6.4 (7)	10.8 (25)	3.0 (6)	2.6 (3)	1.7 (4)
Total N	10.2 (334)	9.9 (336)	9.8 (358)	3.3 (111)	3.4 (119)	3.3 (125)
Linear trend	P=0.806	P=0.911	P=0.747	P=0.629	P=0.403	P=0.340
Quadratic trend	P=0.747	P=0.157	P=0.093	P=0.422	P=0.869	P=0.887

[a] Sample includes type 2 diabetics, but excludes type 1 diabetes and steroid medications

[b] linear and quadratic trends using logistic regression with median weekly alcohol units. Tested in habitual drinkers: 0 units - extremely heavy.

Table 5.7a. Multilevel repeated measures models testing the differences between smoking trajectories by diabetes risk and metabolic syndrome status (Men).

	HbA_{1c}≥ 6% /diabetes		HbA_{1c}≥ 7% /diabetes		Metabolic syndrome (6% HbA_{1c})		Metabolic syndrome (7% HbA_{1c})	
Smoking	unadjusted	adjusted[a]	Unadjusted	adjusted[a]	Unadjusted	adjusted[b]	unadjusted	adjusted[b]
Current vs non								
Main effect	1.82	1.65	1.33	1.71	1.41	1.41	1.30	1.30
	P<0.0001	p<0.0001	P=0.1157	P=0.009	P=0.0002	P=0.004	P=0.007	P=0.010
Interaction 1*2	No		No		No		No	
Interaction 1*3	No		No		No		No	
Ex vs current								
Main effect	0.77	0.64	0.91	0.68	0.71	0.74	0.78	0.81
	P=0.089	P=0.008	P=0.6504	P=0.99	P=0.003	P=0.010	P=0.031	P=0.079
Interaction 1*2	No		No		No		No	
Interaction 1*3	No		No		No		No	
Drinking								
Daily								
Main effect	0.88	0.98	0.69	0.75	0.90	0.91	0.91	0.93
	P=0.507	P=0.899	P=0.200	P=0.328	P=0.210	P=0.278	P=0.282	P=0.409
Interaction 1*2	0.50	0.47	0.26	0.27	No		No	
	P=0.039	P=0.033	P=0.040	P=0.046				
Interaction 1*3	0.73	0.695	0.88	0.83	No		No	
	P=0.242	P=0.190	P=0.740	P=0.638				
Non-drinker								
Main effect	1.97	1.86	2.47	2.36	1.47	1.39	1.43	1.37
	P<0.001	P=0.0006	P<0.0001	p<0.0001	P=0.001	P=0.006	P=0.0034	P=0.011
Interaction 1*2	No		No		No		No	
Interaction 1*3	No		No		No		No	

[a]Adjusted for television watching, diet at 42 years, waist circumference at 45 years and BMI at 45 years. Smoking models are also adjusted for daily drinking and drinking models are also adjusted for current smoking.

[b]Adjusted for television watching, diet at 42 years. Smoking models are also adjusted for daily drinking and drinking models are also adjusted for current smoking. NB in models with interactions, the main effect is from the model with the interaction term and represents the effect of risk6 or risk7 at occasion 1.

Table 5.7b. Multilevel repeated measures models testing the differences between drinking and smoking trajectories by diabetes risk metabolic syndrome status (women).

	HbA_{1c}≥ 6% /diabetes		HbA_{1c}≥ 7% /diabetes		Metabolic syndrome (6% HbA_{1c})		Metabolic syndrome (7% HbA_{1c})	
Smoking	unadjusted	adjusted[a]	unadjusted	adjusted[a]	unadjusted	adjusted[b]	unadjusted	adjusted[b]
Current vs non								
Main effect	1.39	1.21	1.21	0.85	1.63	1.49	1.58	1.46
	P=0.0084	P=0.171	p>0.05	P=0.454	P<0.001	P<0.001	P<0.001	P<0.001
Interaction 1*2	No		No		No		No	
Interaction 1*3	No		No		No		No	
Ex vs current								
Main effect	0.82	0.84	0.91	1.16	0.779	0.84	0.81	0.85
	P=0.188	P=0.328	P=0.650	P=0.585	P=0.014	P=0.061	P=0.022	P=0.087
Interaction 1*2	No		No		No		No	
Interaction 1*3	No		No		No		No	
Drinking								
Daily								
Main effect	0.39	0.58	0.44	0.68	0.50	0.51	0.49	0.49
	P=0.0002	P=0.036	P=0.797	P=0.317	P<0.001	P<0.001	P<0.001	P<0.001
Interaction 1*2	No		No		No		No	
Interaction 1*3	No		No		No		No	
Non-drinker								
Main effect	1.22	0.887	1.82	1.23	1.31	1.27	1.27	1.23
	P=0.350	P=0.598	P=0.006	P=0.281	P<0.001	P=0.003	P=0.001	P=0.012
Interaction 1*2	1.18	1.20	No		1.06		No	
	P=0.556	P=0.556			P=0.755			
Interaction 1*3	2.27	2.38	No		1.37		No	
	P=0.003	P=0.003			P=0.08			

[a]Adjusted for television watching, diet at 42 years, waist circumference at 45 years and BMI at 45 years. Smoking models are also adjusted for daily drinking and drinking models are also adjusted for current smoking.

[b]Adjusted for television watching, diet at 42 years. Smoking models are also adjusted for daily drinking and drinking models are also adjusted for current smoking.

Table 5.8 Geometric mean 45 year HbA_{1c} by smoking at each adult survey[a].

	Men			Women		
	%	N	Mean	%	N	Mean
Smoking			*23 years*			*23 years*
Never	52.3	1701	5.170 (5.159, 5.191)	54.0	1806	5.112 (5.094, 5.131)
Ex	10.7	348	5.214 (5.166, 5.263)	10.3	345	5.105 (5.067, 5.143)
Current (all)	37.0	1204	5.309 (5.286, 5.332)	35.7	1193	5.150 (5.129, 5.171)
Total	100.0	3253		100.0	3344	
Difference[b]			P<0.001			P<0.001
Cigarettes/day						
1-19	19.1	621	5.353 (5.315, 5.391)	21.9	733	5.118 (5.091, 5.145)
≥20	17.9	583	5.251 (5.211, 5.292)	13.8	460	5.201 (5.167, 5.234)
Difference[c]			P<0.001			P<0.001
			33 years			*33 years*
Never	48.7	1614	5.168 (5.146, 5.190)	49.5	1712	5.104 (5.086, 5.124)
Ex	22.5	745	5.184 (5.156, 5.213)	21.5	742	5.090 (5.064, 5.116)
Current (all)	28.8	955	5.275 (5.228, 5.323)	29.1	1006	5.186 (5.162, 5.210)
Total	100.0	3314		100.0	3460	
Difference[b]			P<0.001			P<0.001
Cigarettes/day						
1-19	13.0	429	5.306 (5.270, 5.342)	16.2	559	5.131 (5.102, 5.161)
≥20	15.9	526	5.378 (5.342, 5.415)	12.9	447	5.256 (5.218, 5.294)
Difference[c]			P<0.001			P<0.001
			42 years			*42 years*
Never	47.1	1753	5.169 (5.148, 5.191)	48.9	1831	5.111 (5.093, 5.130)
Ex	29.2	1085	5.209 (5.185, 5.234)	27.0	1010	5.082 (5.060, 5.105)
Current (all)	23.7	883	5.371 (5.343, 5.399)	24.2	906	5.207 (5.183, 5.232)
Total	100.0	3721		100.0	3747	
Difference[b]			P<0.001			P<0.001
Cigarettes/day						
1-19	10.5	389	5.340 (5.305, 5.375)	13.7	514	5.192 (5.156, 5.227)
≥20	13.3	494	5.396 (5.353, 5.439)	10.5	392	5.228 (5.196, 5.261)
Difference[c]			P<0.001			P<0.001
Age quit smoking						
Ex <23 years	4.2	158	5.196 (5.131, 5.267)	4.4	163	5.106 (5.051, 5.161)
Ex 23-33 years	12.7	472	5.162 (5.124, 5.199)	12.6	452	5.073 (5.041, 5.107)
Ex 33-42 years	12.2	455	5.264 (5.226, 5.301)	10.5	395	5.083 (5.045, 5.120)

[a] Sample (n=7663) excludes (i) type 1 diabetes and (ii) participants on medication likely to alter HbA_{1c}.
[b] difference in ln (HbA_{1c}) based on anova of current, ex never smokers
[c] difference in ln (HbA_{1c}) based on anova of non-smokers, 1-19 and ≥20 cigarette/ day smokers.

Table 5.9 Prevalence of Metabolic syndrome and type 2 diabetes in men and women at 45 years according to smoking at each adult survey[a]

Smoking	Metabolic syndrome				High HbA_{1c} (≥6% & Type 2 Diabetes)			
	Men		Women		Men		Women	
	23 years				*23 years*			
	%	N	%	N	%	N	%	N
Never	11.1	184	3.0	54	8.1	141	3.2	55
Ex	9.9	33	3.2	11	12.1	41	4.5	16
Current (all)	14.9	177	3.7	45	12.8	149	6.4	79
Total Difference[b]	P=0.003		P=0.510		p<0.001		P<0.001	
Cigarettes/day								
1-19	12.5	76	3.1	23	11.8	84	5.1	32
≥20	17.5	101	4.7	22	14.6	65	7.9	47
Difference[c]	p<0.001		P=0.158		p<0.001		p<0.001	
	33 years				*33 years*			
Never	11.3	177	2.7	47	7.5	125	3.4	56
Ex	10.8	79	3.2	24	10.2	74	4.5	34
Current (all)	15.8	148	4.6	47	13.8	135	6.9	67
Total Difference[b]	P=0.001		P=0.115		p<0.001		P<0.001	
Cigarettes/day								
1-19	12.8	54	3.4	19	10.7	58	5.9	26
≥20	18.2	94	6.2	28	17.8	77	7.7	41
Difference[c]	P<0.001		P=0.002		p<0.001		P<0.001	
	42 years				*42 years*			
Never	11.5	197	2.8	51	7.7	137	3.4	60
Ex	12.4	133	3.8	39	10.7	106	5.3	59
Current (all)	15.2	131	3.8	35	13.2	116	6.9	62
Total Difference[b]	P=0.031		P=0.201		p<0.001		P<0.001	
Cigarettes/day								
1-19	12.3	47	3.5	18	9.5	47	6.6	26
≥20	17.5	84	4.3	17	17.9	69	7.2	36
Difference[c]	P=0.003		P=0.482		p<0.001		P=0.003	
Age quit smoking								
Ex <23 years	3.5	13	3.3	3	6.0	20	4.8	6
Ex 23-33 years	9.4	40	9.8	9	10.3	34	10.3	13
Ex 33-42 years	16.0	68	12.0	11	11.5	46	14.3	18

[a] Sample (n=7663) excludes (i) type 1 diabetes and (ii) participants on medication likely to alter HbA_{1c}.
[b]Differences in proportions based on chi squared test of current, ex and never smokers
[c] Differences in proportions based on chi squared test of non-smokers, 1-19 and ≥20 cigarette/ day smokers.

Table 5.10 Mean 45-year HbA_{1c} prevalence of metabolic syndrome and type 2 diabetes by lifecourse smoking history[a]

Smoking at 23, 33 & 42 years		HbA_{1c}	Metabolic syndrome		High HbA_{1c} (≥6% & Type 2 Diabetes)	
	N	Mean (95%CI)[b]	%	N	%	N
Men						
Never	1771	5.197 (5.172, 5.222)	11.5	197	3.4	60
Quit <33 years	642	5.202 (5.165, 5.241)	9.7	60	4.8	31
Quit 33-42 years	465	5.315 (5.265, 5.365)	16.2	73	6.0	28
1-19 cigarettes/day 42 years	397	5.389 (5.337, 5.442)	12.3	47	6.5	26
≥ 20 cigarettes/day 42 years	501	5.426 (5.378, 5.475)	17.5	84	7.2	36
Total	3776		12.7	461	4.8	181
Linear trend[c]		P<0.001	P<0.001		P=0.001	
Women						
Never	1840	5.119 (5.100, 5.138)	7.8	137	2.8	51
Quit <33 years	625	5.115 (5.079, 5.152)	10.2	62	3.4	21
Quit 33-42 years	402	5.115 (5.067, 5.163)	11.6	44	4.5	18
1-19 cigarettes/day 42 years	516	5.196 (5.161, 5.231)	9.5	47	3.5	18
≥ 20 cigarettes/day 42 years	398	5.279 (5.226, 5.333)	17.9	69	4.3	17
Total	3832		9.9	359	3.3	125
Linear trend[c]		P<0.001	p<0.001		P=0.332	

[a] Sample (n=7663) excludes (i) type 1 diabetes and (ii) participants on medication likely to alter HbA_{1c}.
[b] Geometric mean
[c] tested with linear regression model for HbA_{1c} and logistic model for HbA_{1c} ≥6% and metabolic syndrome.

Table 5.11a. β coefficients for 45-year HbA_{1c} by drinking frequency and smoking habit at each survey.

	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]
23 years	Men				Women			
Smoking:	(n=3084)				(n=3183)			
Never	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Ex	0.06	0.06	0.06	0.06	-0.02	-0.02	-0.03	-0.03
	(-0.01, 0.12)	(-0.00, 0.13)	(-0.00, 0.13)	(-0.00, 0.13)	(-0.07, 0.03)	(-0.07, 0.02)	(-0.07, 0.02)	(-0.07, 0.02)
1-19/ day	0.09	0.09	0.10	0.10	0.00	0.01	0.01	0.01
	(0.05, 0.13)	(0.06, 0.13)	(0.06, 0.14)	(0.06, 0.13)	(-0.03, 0.04)	(-0.03, 0.04)	(-0.03, 0.04)	(-0.03, 0.04)
≥20/day	0.20	0.20	0.19	0.19	0.08	0.09	0.07	0.06
	(0.14, 0.25)	(0.14, 0.25)	(0.13, 0.24)	(0.13, 0.24)	(0.04, 0.12)	(0.05, 0.13)	(0.03, 0.11)	(0.02, 0.10)
Drinking								
frequency	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Daily								
≥2/week	0.00	0.01	0.01	0.01	0.07	0.08	0.06	0.06
	(-0.04, 0.04)	(-0.03, 0.05)	(-0.03, 0.05)	(-0.03, 0.05)	(0.03, 0.12)	(0.04, 0.13)	(0.02, 0.11)	(0.02, 0.10)
≥ 1/ month	0.04	0.06	0.05	0.05	0.09	0.10	0.07	0.06
	(-0.04, 0.13)	(-0.03, 0.14)	(-0.03, 0.13)	(-0.03, 0.13)	(0.04, 0.14)	(0.05, 0.15)	(0.02, 0.12)	(0.02, 0.11)
Non-drinker	0.04	0.05	0.05	0.05	0.13	0.14	0.11	0.10
	(-0.02, 0.09)	(-0.00, 0.11)	(-0.01, 0.10)	(-0.01, 0.10)	(0.09, 0.17)	(0.10, 0.18)	(0.07, 0.15)	(0.06, 0.15)

[a] model 1= smoking; model 2=drinking frequency
[b] model 3= smoking + drinking frequency
[c] model 4= model 3 + waist circumference and BMI at 45 years
[d] model 5= model 4 + diet at 42 years, inactivity (TV watching) at 45 years

Table 5.11a. continued

33 years	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]
	Men				*Women*			
Smoking:	*(n=3130)*				*(n=3293)*			
never	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Ex	0.02	0.02	0.02	0.02	-0.02	-0.01	-0.02	-0.02
	(-0.03, 0.06)	(-0.02, 0.07)	(-0.02, 0.07)	(-0.02, 0.06)	(-0.06, 0.01)	(-0.05, 0.02)	(-0.06, 0.01)	(-0.06, 0.01)
1-19/ day	0.13	0.14	0.14	0.14	0.02	0.02	0.02	0.02
	(0.08, 0.18)	(0.09, 0.18)	(0.09, 0.19)	(0.09, 0.19)	(-0.02, 0.06)	(-0.01, 0.06)	(-0.01, 0.06)	(-0.01, 0.06)
≥20/day	0.21	0.21	0.20	0.21	0.15	0.15	0.13	0.13
	(0.16, 0.26)	(0.15, 0.26)	(0.15, 0.25)	(0.15, 0.25)	(0.10, 0.20)	(0.10, 0.20)	(0.09, 0.19)	(0.08, 0.18)
Drinking								
frequency	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Daily								
≥2/week	0.05	0.06	0.06	0.07	0.07	0.08	0.06	0.05
	(0.01, 0.09)	(0.02, 0.10)	(0.02, 0.11)	(0.02, 0.11)	(0.03, 0.12)	(0.03, 0.13)	(0.01, 0.11)	(0.00, 0.10)
≥ 1/ month	0.07	0.09	0.08	0.08	0.15	0.15	0.12	0.11
	(0.03, 0.12)	(0.04, 0.13)	(0.03, 0.12)	(0.03, 0.12)	(0.09, 0.21)	(0.10, 0.21)	(0.07, 0.18)	(0.06, 0.17)
Non-drinker	0.15	0.14	0.14	0.14	0.19	0.17	0.14	0.13
	(0.06, 0.23)	(0.06, 0.22)	(0.06, 0.22)	(0.06, 0.23)	(0.13, 0.24)	(0.12, 0.22)	(0.09, 0.19)	(0.08, 0.18)

[a] model 1= smoking; model 2=drinking frequency
[b] model 3= smoking + drinking frequency
[c] model 4= model 3 + waist circumference and BMI at 45 years
[d] model 5= model 4 + diet at 42 years, inactivity (TV watching) at 45 years

Table 5.11a continued

	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]
42 years	Men N=3616				Women N=3642			
Smoking:								
Never	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Ex	0.04	0.04	0.04	0.04	-0.03	-0.02	-0.03	-0.03
	(0.00, 0.08)	(0.01, 0.08)	(-0.00, 0.07)	(-0.00, 0.07)	(-0.07, -0.00)	(-0.05, 0.01)	(-0.06, 0.00)	(-0.06, 0.00)
1-19/ day	0.16	0.15	0.17	0.17	0.08	0.08	0.08	0.08
	(0.12, 0.20)	(0.11, 0.20)	(0.13, 1.21)	(0.13,0.21)	(0.03, 0.12)	(0.03, 0.12)	(0.04, 0.13)	(0.04, 0.12)
≥20/day	0.23	0.23	0.22	0.23	0.11	0.10	0.09	0.08
	(0.17, 0.29)	(0.17, 0.29)	(0.17, 0.28)	(0.17, 0.29)	(0.07, 0.15)	(0.06, 0.14)	(0.05, 0.13)	(0.04, 0.12)
Drinking frequency	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Daily								
≥2/week	0.02	0.03	0.02	0.02	0.11	0.11	0.10	0.09
	(-0.02, 0.06)	(-0.01, 0.07)	(-0.02, 0.06)	(-0.01, 0.06)	(0.08, 0.15)	(0.08, 0.15)	(0.07, 0.13)	(0.06, 0.13)
≥ 1/ month	0.07	0.07	0.05	0.05	0.24	0.24	0.18	0.18
	(-0.00, 0.15)	(-0.01, 0.14)	(-0.02, 0.12)	(-0.02, 0.12)	(0.17, 0.30)	(0.17, 0.30)	(0.12, 0.24)	(0.12, 0.24)
Non-drinker	0.17	0.16	0.14	0.15	0.26	0.25	0.20	0.20
	(0.09, 0.25)	(0.08, 0.24)	(0.06, 0.22)	(0.07, 0.22)	(0.22, 0.30)	(0.21, 0.29)	(0.16, 0.24)	(0.16, 0.24)

[a] model 1= smoking; model 2=drinking frequency
[b] model 3= smoking + drinking frequency
[c] model 4= model 3 + waist circumference and BMI at 45 years
[d] model 5= model 4 + diet at 42 years, inactivity (TV watching) at 45 years

Table 5.11a continued

	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]
45 years	Men N=3605				Women N= 3634			
Smoking:[e]								
Never	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Ex	0.04	0.05	0.04	0.04	-0.03	-0.01	-0.03	-0.03
	(0.00, 0.08)	(0.01, 0.09)	(0.00, 0.08)	(0.00, 0.08)	(-0.07, -0.00)	(-0.05, 0.02)	(-0.06, 0.00)	(-0.06, 0.01)
1-19/ day	0.16	0.15	0.17	0.17	0.08	0.09	0.09	0.09
	(0.12, 0.20)	(0.11, 0.20)	(0.13, 0.21)	(0.13, 0.21)	(0.03, 0.12)	(0.04, 0.13)	(0.05, 0.13)	(0.04, 0.13)
≥20/day	0.23	0.23	0.22	0.23	0.11	0.10	0.09	0.08
	(0.17, 0.29)	(0.17, 0.29)	(0.16, 0.28)	(0.17, 0.29)	(0.07, 0.15)	(0.07, 0.14)	(0.05, 0.13)	(0.04, 0.13)
Drinking frequency	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Daily								
≥2/week	0.04	0.05	0.04	0.04	0.04	0.04	0.03	0.03
	(0.00, 0.08)	(0.01, 0.09)	(0.00, 0.08)	(0.00, 0.08)	(0.00, 0.08)	(0.01, 0.08)	(-0.01, 0.06)	(-0.01, 0.06)
≥ 1/ month	0.06	0.06	0.05	0.05	0.15	0.15	0.12	0.12
	(0.02, 0.10)	(0.02, 0.10)	(0.01, 0.09)	(0.01, 0.09)	(0.10, 0.19)	(0.11, 0.20)	(0.08, 0.17)	(0.08, 0.16)
Non-Drinker	0.22 (0.15, 0.29)	0.21 (0.14, 0.30)	0.20 (0.13, 0.26)	0.20 (0.13, 0.27)	0.23 (0.19, 0.27)	0.22 (0.18, 0.27)	0.17 (0.15, 0.22)	0.17 (0.13, 0.21)

[a] model 1= smoking; model 2=drinking frequency
[b] model 3= smoking + drinking frequency
[c] model 4= model 3 + waist circumference and BMI at 45 years
[d] model 5= model 4 + diet at 42 years, inactivity (TV watching) at 45 years
[e] 42-year smoking.

Table 5.11b ORs for 45-year elevated HbA_{1c} (≥6%) and type 2 diabetes by drinking frequency and smoking habit at each survey.

	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]
23 years	*Men* N=3128				*Women* N=3209			
Smoking:								
Never	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Ex	1.53	1.56	1.58	1.60	1.00	0.99	0.97	0.96
	(0.85, 2.76)	(0.87, 2.84)	(0.85, 2.94)	(0.86, 2.99)	(0.50, 1.98)	(0.50, 1.96)	(0.46, 2.07)	(0.46, 2.02)
1-19/ day	1.71	1.74	1.76	1.76	0.93	0.98	1.06	1.03
	(1.08, 2.72)	(1.09, 2.78)	(1.08, 2.89)	(1.08, 2.88)	(0.55, 1.57)	(0.57, 1.62)	(0.61, 1.84)	(0.59, 1.80)
≥20/day	2.87	2.93	2.64	2.65	1.45	1.50	1.16	1.09
	(1.89, 4.34)	(1.94, 4.42)	(1.71, 4.06)	(1.71, 4.06)	(0.85, 2.47)	(0.88, 2.57)	(0.66, 2.03)	(0.62, 1.93)
Drinking frequency	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Daily								
≥2/week	1.13	1.22	1.13	1.13	1.55	1.59	1.25	1.26
	(0.77, 1.66)	(0.83, 1.80)	(0.76, 1.69)	(0.76, 1.70)	(0.69, 3.46)	(0.71, 3.55)	(0.55, 2.86)	(0.54, 2.92)
≥ 1/ month	0.76	0.82	0.65	0.66	1.92	1.99	1.49	1.50
	(0.36, 1.58)	(0.39, 1.71)	(0.30, 1.40)	(0.31, 1.39)	(0.80, 4.59)	(0.84, 4.76)	(0.60, 3.73)	(0.59, 3.80)
Non-drinker	1.47	1.59	1.37	1.36	1.72	1.79	1.23	1.21
	(0.79, 2.66)	(0.87, 2.92)	(0.74, 2.53)	(0.73, 2.53)	(0.75, 3.98)	(0.77, 4.13)	(0.51, 2.97)	(0.50, 2.96)

[a] model 1= smoking; model 2=drinking frequency
[b] model 3= smoking + drinking frequency
[c] model 4= model 3 + waist circumference and BMI at 45 years
[d] model 5= model 4 + diet at 42 years, inactivity (TV watching) at 45 years

Table 5.11b continued

	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]
33 years	N=3178				N= 3293			
Smoking:								
never	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Ex	1.37	1.44	1.42	1.39	1.15	1.18	1.03	1.03
	(0.88, 2.13)	(0.92, 2.25)	(0.90, 2.25)	(0.88, 2.20)	(0.69, 1.92)	(0.71, 1.97)	(0.60, 1.76)	(0.60, 1.75)
1-19/ day	1.90	1.93	1.94	1.94	1.01	1.03	1.14	1.12
	(1.17, 3.08)	(1.19, 3.14)	(1.17, 3.20)	(1.16, 3.25)	(0.56, 1.83)	(0.57, 1.86)	(0.61, 2.15)	(0.60, 2.10)
≥20/day	2.45	2.42	2.21	2.22	2.11	2.13	1.82	1.68
	(1.60, 3.75)	(1.57, 3.73)	(1.41, 3.46)	(1.40, 3.50)	(1.27, 3.50)	(1.28, 3.53)	(1.04, 3.19)	(0.94, 3.01)
Drinking frequency	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Daily								
≥2/week	2.00	2.13	2.20	2.23	4.19	4.29	3.73	3.83
	(1.11, 3.63)	(1.18, 3.83)	(1.19, 4.05)	(1.20, 4.11)	(1.01, 17.36)	(1.04, 17.70)	(0.82, 17.07)	(0.81, 17.99)
≥ 1/ month	1.95	2.10	1.85	1.92	3.46	3.60	2.99	2.95
	(0.97, 3.92)	(1.05, 4.21)	(0.90, 3.78)	(0.94, 3.95)	(0.81, 14.80)	(0.85, 15.26)	(0.67, 14.07)	(0.61, 14.31)
Non-drinker	4.37	4.41	4.06	4.12	4.90	5.07	3.12	3.08
	(2.29, 8.36)	(2.30, 8.46)	(2.04, 8.07)	(2.06, 8.28)	(1.19, 20.88)	(1.22, 21.11)	(0.68, 14.39)	(0.65, 14.66)

[a] model 1= smoking; model 2=drinking frequency
[b] model 3= smoking + drinking frequency
[c] model 4= model 3 + waist circumference and BMI at 45 years
[d] model 5= model 4 + diet at 42 years, inactivity (TV watching) at 45 years

Table 5.11b continued

	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]
42 years	Men N=3671				Women N=3669			
Smoking:								
Never	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Ex	1.70	1.77	1.74	1.71	1.30	1.44	1.28	1.29
	(1.17, 2.47)	(1.22, 2.58)	(1.18, 2.56)	(1.16, 2.52)	(0.84, 2.01)	(0.93, 2.22)	(0.80, 2.05)	(0.81, 2.05)
1-19/ day	2.06	2.02	2.44	2.40	1.23	1.20	1.38	1.31
	(1.27, 3.35)	(1.23, 3.30)	(1.47, 4.05)	(1.45, 4.04)	(0.70, 2.16)	(0.69, 2.10)	(0.73, 2.60)	(0.70, 2.46)
≥20/day	2.39	2.35	2.30	2.29	1.32	1.21	1.01	0.91
	(1.56, 3.69)	(1.51, 3.63)	(1.44, 3.60)	(1.42, 3.68)	(0.72, 2.41)	(0.65, 2.24)	(0.51, 1.99)	(0.45, 1.86)
Drinking frequency	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Daily								
≥2/week	1.45	1.56	1.45	1.45	1.82	1.86	1.71	1.77
	(0.96, 2.21)	(1.03, 2.37)	(0.94, 2.24)	(0.94, 2.24)	(0.81, 4.08)	(0.83, 4.17)	(0.77, 3.76)	(0.80, 3.93)
≥ 1/ month	1.73	1.74	1.37	1.37	2.53	3.65	1.87	1.85
	(0.95, 3.14)	(0.95, 3.17)	(0.75, 2.49)	(0.75, 2.50)	(1.47, 8.47)	(1.52, 8.76)	(0.77, 4.58)	(0.75, 4.57)
Non-drinker	2.58	2.56	2.08	2.05	5.25	5.46	3.61	3.53
	(1.55, 4.30)	(1.53, 4.28)	(1.21, 3.57)	(1.18, 3.55)	(2.32, 11.87)	(2.47, 12.08)	(1.61, 8.09)	(1.56, 8.01)

[a] model 1= smoking; model 2=drinking frequency
[b] model 3= smoking + drinking frequency
[c] model 4= model 3 + waist circumference and BMI at 45 years
[d] model 5= model 4 + diet at 42 years, inactivity (TV watching) at 45 years
v

Table 5.11b continued

	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]	Unadjusted [a]	+Smoking/ drinking [b]	+ BMI/ WC [c]	+ activity & diet [d]
45 years	N= 3659				N= 3661			
Smoking:[e]								
never	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Ex	1.70	1.83	1.73	1.73	1.30	1.44	1.24	1.22
	(1.17, 2.47)	(1.25, 2.66)	(1.18, 2.55)	(1.18, 2.55)	(0.84, 2.01)	(0.92, 1.93)	(0.77, 1.94)	(0.77, 1.94)
1-19/ day	1.99	1.89	2.27	2.27	1.24	1.25	1.36	1.28
	(1.22, 3.26)	(1.14, 3.12)	(1.34, 3.83)	(1.34, 3.83)	(0.71, 2.17)	(0.71, 2.19)	(0.72, 2.56)	(0.68, 2.42)
≥20/day	2.40	2.27	2.22	2.22	1.32	1.21	1.03	0.93,
	(1.56, 3.69)	(1.46, 3.53)	(1.38, 3.59)	(1.38, 3.59)	(0.72, 2.41)	(0.66, 2.25)	(0.53,2.01)	(0.46,1.88)
Drinking frequency	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
Daily								
≥2/week	1.39	1.47	1.40	1.38	0.94	0.97	0:90	0.93
	(0.89, 2.17)	(0.94, 2.31)	(0.88, 2.21)	(0.87, 2.20)	(0.46, 1.93)	(0.47, 2.00)	(0.43, 1.89)	(0.44, 1.94)
≥ 1/month	1.99	2.10	1.79	1.81	1.80	1.89	1.29	1.32
	(1.25, 3.18)	(1.31, 3.36)	(1.10, 2.91)	(1.11, 2.97)	(0.92, 3.55)	(0.95, 3.73)	(0.64, 2.59)	(0.65, 2.67)
Non-drinker	3.74	3.75	3.22	2.26	3.84	3.99	2.11	2.07
	(2.38, 5.87)	(2.38, 5.91)	(1.99, 5.20)	(1.40, 3.63)	(2.09, 7.04)	(2.17, 7.34)	(1.11, 4.02)	(1.07, 3.96)

[a] model 1= smoking; model 2=drinking frequency
[b] model 3= smoking + drinking frequency
[c] model 4= model 3 + waist circumference and BMI at 45 years
[d] model 5= model 4 + diet at 42 years, inactivity (TV watching) at 45 years
[e] 42-year smoking

Table 5.11c ORs for 45-year metabolic syndrome by drinking frequency and smoking habit at each survey.

	Unadjusted[a]	+Smoking/ drinking[b]	+ activity & diet[c]	Unadjusted[a]	+Smoking/ drinking[b]	+ activity & diet[c]
23 years	Men N=3024			Women N=3107		
Smoking:						
Never	Reference	Reference	Reference	Reference	Reference	Reference
Ex	0.93 (0.62, 1.38)	0.95 (0.63, 1.41)	0.93 (0.63, 1.39)	1.45 (0.99, 2.13)	1.42 (0.97, 2.10)	1.41 (0.95, 2.08)
1-19/ day	1.18 (0.88, 1.58)	1.20 (0.89, 1.61)	1.13 (0.84, 1.52)	1.46 (1.09, 1.95)	1.50 (1.12, 2.01)	1.45 (1.08, 1.94)
≥20/day	1.76 (1.34, 2.30)	1.78 (1.36, 2.33)	1.66 (1.26, 2.19)	1.81 (1.30, 2.50)	1.90 (1.37, 2.63)	1.75 (1.26,2.44)
Drinking frequency	Reference	Reference	Reference	Reference	Reference	Reference
Daily						
≥2/week	1.06 (0.83, 1.36)	1.10 (0.86, 1.41)	1.10 (0.85, 1.41)	1.71 (1.05, 2.77)	1.81 (1.11, 2.94)	1.77 (1.09, 2.87)
≥ 1/ month	1.16 (0.77, 1.73)	1.18 (0.79, 1.77)	1.17 (0.78, 1.76)	1.99 (1.17, 3.37)	2.15 (1.27, 3.65)	2.07 (1.22, 3.51)
Non-drinker	1.27 (0.84, 1.91)	1.30 (0.86, 1.95)	1.27 (0.85, 1.92)	1.97 (1.19, 3.25)	2.12 (1.28, 3.50)	2.01 (1.21, 3.33)
33 years	N=3071			N= 3215		
Smoking:						
never	Reference	Reference	Reference	Reference	Reference	Reference
Ex	1.02 (0.76, 1.35)	1.03 (0.78, 1.38)	1.01 (0.76, 1.34)	1.33 (0.98, 1.81)	1.37 (1.00, 1.86)	1.35 (0.99, 1.84)
1-19/ day	1.21 (0.87, 1.69)	1.23 (0.88, 1.71)	1.19 (0.85, 1.66)	1.39 (0.99, 1.95)	1.40 (1.00, 1.97)	1.34 (0.95, 1.88)
≥20/day	1.88 (1.42, 2.48)	1.86 (1.40, 2.47)	1.73 (1.29, 2.31)	2.55 (1.86, 3.51)	2.61 (1.90, 3.58)	2.38 (1.72, 3.30)
Drinking frequency	Reference	Reference	Reference	Reference	Reference	Reference
Daily						
≥2/week	1.09 (0.80, 1.48)	1.12 (0.82, 1.53)	1.11 (0.81, 1.52)	1.77 (0.96, 3.27)	1.84 (1.00, 3.40)	1.79 (0.97, 3.31)
≥ 1/ month	1.27 (0.87, 1.85)	1.31 (0.89, 1.92)	1.32 (0.90, 1.94)	2.28 (1.22, 4.25)	2.41 (1.29, 4.51)	2.33 (1.25, 4.36)
Non-drinker	1.65 (1.12, 2.42)	1.62 (1.10, 2.38)	1.60 (1.08, 2.36)	2.33 (1.26, 4.33)	2.43 (1.31, 4.51)	2.32 (1.25, 4.31)

[a] model 1= smoking; model 2=drinking frequency
[b] model 3= smoking + drinking frequency
[c] model 4= model 3 + diet at 42 years, inactivity (TV watching) at 45 years

Table 5.11c continued

	Unadjusted[a]	Adjusted[b]	Adjusted[c]	Unadjusted[a]	Adjusted[b]	Adjusted[c]
42 years	Men N=3550			Women N=3552		
Smoking:						
Never	Reference	Reference	Reference	Reference	Reference	Reference
Ex	1.12 (0.88, 1.42)	1.12 (0.88, 1.43)	1.10 (0.86, 1.40)	1.40 (1.06, 1.83)	1.48 (1.13, 1.94)	1.46 (1.11, 1.92)
1-19/ day	1.11 (0.79, 1.57)	1.07 (0.76, 1.52)	1.03 (0.73, 1.46)	1.26 (0.89, 1.79)	1.26 (0.88, 1.79)	1.19 (0.84, 1.70)
≥20/day	1.73 (1.31, 2.29)	1.68 (1.26, 2.22)	1.52 (1.13, 2.04)	2.51 (1.82, 3.45)	2.49 (1.80, 3.45)	2.24 (1.60, 3.14)
Drinking frequency	Reference	Reference	Reference	Reference	Reference	Reference
Daily						
≥2/week	0.97 (0.76, 1.23)	0.99 (0.77, 1.27)	0.97 (0.75, 1.24)	1.55 (1.04, 2.31)	1.61 (1.08, 2.40)	1.58 (1.06, 2.35)
≥ 1/ month	1.20 (0.82, 1.74)	1.20 (0.82, 1.74)	1.17 (0.80, 1.72)	2.83 (1.80, 4.44)	2.98 (1.90, 4.68)	2.83 (1.80, 4.44)
Non-Drinker	1.49 (1.07, 2.07)	1.46 (1.04, 2.03)	1.39 (0.99, 1.95)	2.53 (1.66, 3.84)	2.55 (1.68, 3.88)	2.42 (1.59, 3.68)
45 years	N=3539			N= 3545		
Smoking:[d]						
never	Reference	Reference	Reference	Reference	Reference	Reference
Ex	1.10 (0.87, 1.41)	0.97 (0.75, 1.25)	0.95 (0.73, 1.23)	1.39 (1.06, 1.83)	1.47 (0.99, 2.20)	1.46 (0.98, 2.17)
1-19/ day	1.07 (0.75, 1.51)	1.08 (0.81, 1.44)	1.06 (0.79, 1.41)	1.26 (0.89, 1.80)	2.39 (1.60, 3.55)	2.36 (1.59, 3.51)
≥20/day	1.71 (1.29, 2.27)	1.58 (1.18, 2.13)	1.52 (1.13, 2.04)	2.50 (1.82, 3.44)	3.52 (2.43, 5.12)	3.39 (2.34, 4.92)
Drinking frequency	Reference	Reference	Reference	Reference	Reference	Reference
Daily						
≥2/week	0.95 (0.74, 1.23)	1.12 (0.88, 1.43)	1.10 (0.86, 1.40)	1.41 (0.94, 2.10)	1.53 (1.17, 2.01)	1.51 (1.15, 1.99)
≥ 1/ month	1.08 (0.81, 1.43)	1.03 (0.72, 1.46)	0.99 (0.69, 1.41)	2.23 (1.50, 3.31)	1.30 (0.91, 1.85)	1.24 (0.87, 1.77)
Non-Drinker	1.60 (1.19, 2.15)	1.66 (1.25, 2.21)	1.52 (1.13, 2.03)	3.44 (2.37, 4.98)	2.46 (1.77, 3.41)	2.25 (1.60, 3.15)

[a] model 1= smoking; model 2=drinking frequency
[b] model 3= smoking + drinking frequency
[c] model 4= model 3 + diet at 42 years, inactivity (TV watching) at 45 years
[d] 42-year smoking.

Appendix Chapter 5 health behaviours and health outcomes

Appendix 5.1

Table A.5.1.1 Sample representativeness; distribution [n,%] of social class at birth in the original birth sample compared with the distribution in the sample with valid HbA_{1c}

	Birth sample		Analysis sample[a]	
	N	% (95%CI)	N	% (95%CI)
Total N	16,966		7214	
Men				
Class I&II professional	1488	17.0 (16.2,17.8)	698	19.3 (18.0,20.6)
Class IV&V & no head of household	2096	23.9 (23.0,24.8)	778	21.5 (20.2,22.9)
Women				
Class I&II professional	1391	16.9 (16.1,17.8)	652	18.1 (16.9,19.4)
Class IV&V & no head of household	2025	24.7 (23.7,25.6)	800	22.2 (20.9,23.6)

[a]sample at 45 years=7799. The total N with data on social class at birth is 7214/7799

There is some evidence that the analysis sample under-represents those in more manual social classes.

Appendix 5.2 The sick quitter hypothesis

Investigating the sick quitter hypothesis is not a primary research aim in this thesis, but is relevant to the results. The J-shaped curve of the association between alcohol intake and disease risk with higher risk to non-drinkers and heavier drinkers has been questioned on several grounds. A recent review reported that the effect is due to errors in classifying ex-drinkers with non-drinkers and classifying special occasion drinkers with non-drinkers (Fillmore 2006). It is increasingly suggested that the elevated risk in non-drinkers is due to residual confounding and that the non-drinker effect is not a real effect (Shaper 1995). Non-drinkers are reported to have poorer mental (Caldwell et al. 2002) and physical health (Doll et al 2005), and may have poorer profiles of mid-life glucose regulation. However, uncertainties remain about the direction of the association between non-drinking and health, which may be confounded to some degree by past drinking history (Shaper et al 1988) and social disadvantage (Van Oers et al. 1999). Non-drinkers are repeatedly reported to be more from manual social groups at different stages of the lifecourse and also to be of lower educational level (Rodgers et al. 2000).

In contrast, it has been argued that confounding is unlikely as the two groups would have to be exceedingly different. Doll also argues that the increased risk due to inclusion of ex-heavy drinkers would not explain the results because the increase in risk in the heavy drinkers is not large enough to account for the inflation of risk in the non-drinkers by some ex-heavy drinkers (Doll & Peto 1995).

In the data in order to test the hypothesis that the non-drinkers were at higher risk because they include a group of individuals who have quit drinking because of health problems, the mean HbA_{1c} in the true "never" drinkers was compared to the mean HbA_{1c} of never drinkers at 45 years who reported drinking more often than on special occasions at 23, 33 or 42 .

Table A5.2.1 Drinking history (at 23, 33 and 42 years) of cohort members who reported that they had never drunk alcohol at 45 years

Ever drunk alcohol? (45y)	Number of surveys (23, 33 or 42 years) drinking more than on special occasions is reported				
	0	1	2	3	Total
Yes	28	72	120	112	332
No	2	4	15	87	108
Total	30	76	135	199	440

87/108 who reported that they had "never drunk alcohol" at the 45-year survey also never reported drinking more often than on special occasions 23-42 years. The remaining 21/108 reported drinking more frequently than on special occasions on at least one adult survey, they are therefore classified here as ex-drinkers.

Table A5.2.2 Mean HbA_{1c} and the frequency of elevated HbA_{1c} or metabolic syndrome in the 332+21 "ex-drinkers" compared to the 87 "true" never drinkers

Non-drinkers at 45 years	HbA_{1c} Geometric mean (95%CI) (n)	HbA_{1c} ≥6% (%, n)	Metabolic syndrome (%, n)
All non-drinkers	5.424 (5.344, 5.505) (n=351)	9.5% (33/348)	16.1% (53/330)
Non-drinkers who drank at ≥1 previous survey	5.438 (5.347, 5.531) (n=285)	10.3% (29/283)	16.1% (43/267)
Non-drinkers, did not drink at any previous survey	5.363 (5.198, 5.533) (n=66)	6.2% (4/65)	15.9% (10/63)
Difference[a]		P=0.394	P=0.964

[a]Difference tested with chi squared test

Whilst the number of the true non-drinkers is small, the data do not lend support to the "sick quitter hypothesis", that the non-drinkers who were ex-drinkers are at greater risk than the other non-drinkers who did not drink in the past. There were not significant differences between the two non-drinker groups for any of the three outcome measures.

Analyses presented in the chapter are also re-run excluding the known or treated diabetics and results are not much changed; there are still main effects of drinking frequency and smoking on HbA_{1c} risk. Together these results suggest that raised risks in non-drinkers are not due to the sick quitter effect.

Analyses excluding the known or treated diabetics

Table A5.2.3 Association between smoking and drinking history and high HbA_{1c}(>=6%), OR (95%CI) excluding known and treated diabetics, men (n=3078)

	Unadjusted	+ drinking and smoking	+ BMI and waist circumference	+ diet and physical activity
		23 years		
Non-smoker	Reference	Reference	Reference	Reference
Ex-smoker	1.61 (0.78, 3.32)	1.62 (0.78, 3.34)	1.70 (0.79, 3.63)	1.65 (0.76, 3.58)
1-19/day	1.80 (1.02, 3.19)	1.81 (1.02, 3.19)	1.93 (1.07, 3.48)	1.82 (1.00, 3.30)
>20/day	2.86 (1.71, 4.79)	2.90 (1.74, 4.84)	2.73 (1.60, 4.65)	2.61 (1.52, 4.47)
Daily drinker	Reference	Reference	Reference	Reference
>2/week	1.10 (0.68, 1.76)	1.19 (0.74, 1.90)	1.08 (0.66, 1.77)	1.09 (0.67, 1.79)
>2/month	0.89 (0.38, 2.05)	0.96 (0.42, 2.22)	0.80 (0.34, 1.91)	0.83 (0.34, 2.00)
Non-drinker	1.52 (0.65, 3.54)	1.11 (0.48, 2.56)	1.00 (0.44, 2.27)	0.97 (0.43, 2.22)
		33 years		
Non-smoker	Reference	Reference	Reference	Reference
Ex-smoker	1.16 (0.66, 2.03)	1.21 (0.69, 2.12)	1.20 (0.67, 2.13)	1.19 (0.67, 2.11)
1-19/day	1.61 (0.87, 2.98)	1.63 (0.88, 3.00)	1.59 (0.83, 3.04)	1.59 (0.83, 3.03)
>20/day	2.68 (1.62, 4.41)	2.64 (1.6, 4.35)	2.45 (1.46, 4.09)	2.43 (1.43, 4.12)
Daily drinker	Reference	Reference	Reference	Reference
>2/week	1.57 (0.81, 3.02)	1.67 (0.87, 3.20)	1.74 (0.90, 3.39)	1.76 (0.90, 3.46)
>2/month	1.47 (0.66, 3.26)	1.57 (0.71, 3.49)	1.40 (0.62, 3.16)	1.45 (0.64, 3.30)
Non-drinker	3.01 (1.43, 6.33)	2.95 (1.41, 6.20)	2.77 (1.28, 6.01)	2.84 (1.29, 6.27)
		42 years		
Non-smoker	Reference	Reference	Reference	Reference
Ex-smoker	1.55 (0.97, 2.48)	1.60 (1.00, 2.55)	1.53 (0.95, 2.48)	1.50 (0.93, 2.43)
1-19/day	2.00 (1.10, 3.63)	1.97 (1.08, 3.58)	2.34 (1.27, 4.31)	2.29 (1.23, 4.23)
>20/day	2.62 (1.57, 4.37)	2.59 (1.54, 4.34)	2.59 (1.49, 4.50)	2.48 (1.40, 4.38)
Daily drinker	Reference	Reference	Reference	Reference
>2/week	1.23 (0.76, 2.00)	1.32 (0.81, 2.14)	1.20 (0.73, 1.97)	1.20 (0.73, 1.99)
>2/month	1.50 (0.74, 3.06)	1.49 (0.73, 3.03)	1.21 (0.60, 2.46)	1.21 (0.60, 2.45)
Non-drinker	1.84 (0.98, 3.45)	1.78 (0.94, 3.35)	1.42 (0.73, 2.79)	1.35 (0.68, 2.68)
		44 years		
Non-smoker	Reference	Reference	Reference	Reference
Ex-smoker	1.55 (0.97, 2.48)	1.63 (1.02, 2.61)	1.56 (0.97, 2.51)	1.54 (0.96, 2.48)
1-19/day	2.01 (1.11, 3.66)	1.88 (1.02, 3.47)	2.21 (1.18, 4.15)	2.18 (1.16, 4.09)
>20/day	2.62 (1.57, 4.38)	2.52 (1.50, 4.26)	2.51 (1.43, 4.41)	2.44 (1.37, 4.35)
Daily drinker	Reference	Reference	Reference	Reference
>2/week	1.50 (0.89, 2.55)	1.59 (0.94, 2.70)	1.51 (0.88, 2.59)	1.50 (0.87, 2.58)
>2/month	1.33 (0.72, 2.45)	1.37 (0.74, 2.55)	1.19 (0.63, 2.25)	1.20 (0.63, 2.29)
Non-drinker	3.68 (2.15, 6.30)	3.63 (2.11, 6.22)	3.13 (1.77, 5.54)	3.06 (1.72, 5.44)

Table A5.2.4 Association between smoking and drinking history and high HbA_{1c}(>=6%), OR (95%CI) excluding known and treated diabetics, women (n=3174)

	Unadjusted	+ drinking and smoking	+ BMI and waist circumference	+ diet and physical activity
		23 years		
Non-smoker	Reference	Reference	Reference	Reference
Ex-smoker	1.09 (0.48, 2.48)	1.08 (0.47, 2.45)	1.12 (0.46, 2.73)	1.11 (0.46, 2.71)
1-19/day	1.02 (0.54, 1.91)	1.05 (0.56, 1.97)	1.14 (0.6, 2.19)	1.13 (0.59, 2.17)
>20/day	1.42 (0.73, 2.77)	1.48 (0.76, 2.88)	1.21 (0.61, 2.37)	1.17 (0.59, 2.35)
Daily drinkers	Reference	Reference	Reference	Reference
>2/week	1.94 (0.68, 5.52)	2.00 (0.70, 5.67)	1.75 (0.63, 4.83)	1.80 (0.64, 5.07)
>2/month	2.18 (0.71, 6.75)	2.27 (0.74, 7.00)	1.75 (0.58, 5.34)	1.81 (0.58, 5.66)
Non-drinker	1.77 (0.59, 5.30)	1.83 (0.61, 5.52)	1.33 (0.44, 4.03)	1.35 (0.44, 4.16)
		33 years		
Non-smoker	Reference	Reference	Reference	Reference
Ex-smoker	0.94 (0.49, 1.80)	0.96 (0.50, 1.83)	0.83 (0.42, 1.63)	0.83 (0.43, 1.63)
1-19/day	1.07 (0.53, 2.13)	1.08 (0.54, 2.15)	1.23 (0.60, 2.54)	1.21 (0.59, 2.49)
>20/day	2.15 (1.18, 3.91)	2.18 (1.2, 3.97)	1.88 (0.98, 3.63)	1.82 (0.92, 3.59)
Daily drinkers	Reference	Reference	Reference	Reference
>2/week	5.88 (0.80, 43.21)	6.01 (0.83, 43.76)	5.21 (0.68, 39.98)	5.35 (0.68, 41.89)
>2/month	5.12 (0.68, 38.68)	5.27 (0.71, 39.4)	4.2 (0.53, 33.47)	4.15 (0.51, 33.56)
Non-drinker	6.10 (0.82, 45.49)	6.12 (0.83, 45.42)	3.62 (0.46, 28.3)	3.64 (0.46, 28.88)
		42 years		
Non-smoker	Reference	Reference	Reference	Reference
ex smoker	1.05 (0.61, 1.82)	1.16 (0.67, 1.99)	1.05 (0.60, 1.86)	1.07 (0.61, 1.88)
1-19/day	1.21 (0.62, 2.34)	1.18 (0.61, 2.29)	1.33 (0.64, 2.75)	1.29 (0.63, 2.64)
>20/day	1.18 (0.56, 2.47)	1.09 (0.51, 2.31)	0.96 (0.43, 2.15)	0.89 (0.38, 2.12)
Daily drinkers	Reference	Reference	Reference	Reference
>2/week	1.74 (0.67, 4.53)	1.76 (0.68, 4.57)	1.59 (0.63, 4.00)	1.66 (0.66, 4.16)
>2/month	3.38 (1.20, 9.55)	3.43 (1.22, 9.66)	1.81 (0.64, 5.15)	1.83 (0.64, 5.18)
Non-drinker	4.72 (1.83, 12.2)	4.78 (1.87, 12.24)	2.89 (1.13, 7.39)	2.88 (1.13, 7.38)
		44 years		
Non-smoker	Reference	Reference	Reference	Reference
Ex-smoker	1.05 (0.61, 1.81)	1.15 (0.67, 1.98)	1.01 (0.57, 1.80)	1.03 (0.58, 1.82)
1-19/day	1.21 (0.63, 2.35)	1.23 (0.63, 2.38)	1.33 (0.64, 2.74)	1.28 (0.63, 2.63)
>20/day	1.18 (0.56, 2.46)	1.10 (0.52, 2.33)	0.97 (0.43, 2.15)	0.91 (0.38, 2.14)
Daily drinkers	Reference	Reference	Reference	Reference
>2/week	0.81 (0.35, 1.89)	0.83 (0.35, 1.92)	0.78 (0.33, 1.84)	0.81 (0.34, 1.88)
>2/month	1.78 (0.82, 3.86)	1.82 (0.84, 3.95)	1.25 (0.57, 2.74)	1.29 (0.59, 2.83)
Non-drinker	3.03 (1.49, 6.12)	3.07 (1.52, 6.21)	1.63 (0.78, 3.40)	1.62 (0.77, 3.39)

Appendix 5.3 Adiposity and HbA_{1c}

Adiposity is strongly predictive of diabetes, high HbA_{1c} and metabolic syndrome. Many epidemiologic studies have shown that larger BMI and more specifically higher waist circumference is strongly associated with diabetes risk. Because adiposity is believed to be on the pathway to diabetes, it is investigated in this chapter as a potential mediating factor between health behaviours and diabetes risk.

The associations between concurrent BMI and waist circumference with the diabetes risk/ high HbA_{1c} measure are summarized below.

Table A5.3.1 Association between BMI or Waist circumference and HbA_{1c} or elevated HbA_{1c}.

Adiposity measured at 45 years	HbA_{1c}	HbA_{1c} ≥6%[a]	HbA_{1c} ≥7%[a]
Men (n=3872)			
BMI (Kg/m^2)	0.023	1.20	1.21
	(0.017, 0.029)	(1.16, 1.24)	(1.17, 1.26
Waist circumference	0.097	2.05	2.25
(per 10cm increase)	(0.073, 0.121)	(1.82, 2.31)	(1.95, 2.61)
Women (n=3841)			
BMI (Kg/m^2)	0.021	1.20	1.18
	(0.018, 0.025)	(1.17, 1.23)	(1.15 1.22)
Waist circumference	0.096	2.60	2.69
(per 10cm increase)	(0.079, 0.112)	(2.29, 2.95)	(2.26, 3.21)

[a] includes the known diabetics

Men and women with higher BMI had progressively higher HbA_{1c} and higher risk of elevated HbA_{1c} or diabetes. The risk was similar in men and women. For example each unit increase in BMI was associated with 0.02% increase in HbA_{1c} or 1.2 times the odds of high HbA_{1c}. So $5kg/m^2$ higher BMI would be associated with 1.2^5=2.3 times the odds of elevated HbA_{1c} /diabetes.

Larger waist circumference at 45 years was associated with higher HbA_{1c}; each 10cm increase in waist circumference was associated with 0.1% higher HbA_{1c}. Higher waist circumference was also associated with higher risk of elevated HbA_{1c} /diabetes. Each increase of 10cm in waist circumference approximately doubled the odds of elevated HbA_{1c} /diabetes. The association between waist circumference and high HbA_{1c} is stronger in women than in men in this dataset: there is a statistically significant interaction between high HbA_{1c} (>6%, plus known diabetics) and waist circumference on gender.

Appendix 5.4 Adult social class and HbA_{1c}

Associations between HbA_{1c} and childhood and adult social position were investigated. HbA_{1c} was higher in women from more manual social origins, but not in men. Prevalence of elevated HbA_{1c} and metabolic syndrome was higher in men and in women from manual social origins.

Adult social position was not significantly associated with mean HbA_{1c} elevated HbA_{1c} or metabolic syndrome in men. Among women, mean HbA_{1c} and prevalence of metabolic syndrome were higher in women with more manual jobs than women with professional jobs. Because adult social class was not related to diabetes/ high HbA_{1c}, adult class was not considered as a confounder of the association between lifestyle behaviours and elevated HbA_{1c} in men or in women. However there is some evidence of association between adult class and mean HbA_{1c} or metabolic syndrome in the women. Therefore among women, social class in adulthood should be considered as a confounder of the association between adult health behaviours and metabolic syndrome. For consistency this will be dealt with in the chapter on cognition, health behaviours and health outcomes where more complex models are presented.

Table A5.4.1 Association between child and adult social class and HbA_{1c} and high HbA_{1c} [a].

RG social class	I&II	IIINM	IIIM	IV & V & single	p (trend)
Men (n=3596)		*Childhood social class [b]*			
HbA_{1c}	5.25 (5.20, 5.29)	5.18 (5.14 5.21)	5.22 (5.20, 5.24)	5.26 (5.22, 5.29)	0.187
$HbA_{1c} \geq 6\%$ / diabetes	2.6 (18)	2.8 (10)	4.9 (86)	6.6 (51)	<0.001
Metabolic syndrome	9.8 (65)	9.4 (33)	12.8 (217)	15.9 (118)	<0.001
Women (n=3580)					
HbA_{1c}	5.08 (5.05, 5.10)	5.12 (5.08, 5.15)	5.13 (5.11, 5.15)	5.17 (5.12, 5.22)	<0.001
$HbA_{1c} \geq 6\%$ / diabetes	1.9 (12)	1.4 (5)	3.7 (66)	3.9 (31)	0.016
Metabolic syndrome	4.9 (31)	6.6 (23)	10.7(181)	13.8 (106)	<0.001
Men (n=3656)		*Adult social class [c]*			
HbA_{1c}	5.20 (5.17, 5.22)	5.15 (5.11, 5.19)	5.27 (5.24, 5.29)	5.29 (5.24, 5.34)	0.080
$HbA_{1c} \geq 6\%$ / diabetes	3.8 (65)	4.3 (14)	4.9 (55)	5.5 (21)	0.372
Metabolic syndrome	11.4 (185)	11.4 (36)	14.1 (152)	12.5 (46)	0.176
Women (n=3727)					
HbA_{1c}	5.11 (5.09, 5.13)	5.11 (5.08, 5.13)	5.16 (5.10, 5.18)	5.15 (5.12, 5.17)	<0.001
$HbA_{1c} \geq 6\%$ / diabetes	3.2 (40)	2.4 (25)	2.7 (6)	3.2 (19)	0.676
Metabolic syndrome	8.0 (94)	8.6 (86)	13.2 (28)	11.7 (67)	<0.01

[a] includes known type 2 diabetes, but excludes known type 1diabetes and participants taking steroids.
[b] social class of father at birth
[c] own social class at 33 years or 23 years if missing

Chapter 6, Childhood Cognitive Development and Mid-life Glucose Homeostasis

Introduction

An emerging research literature (discussed in Chapter 1) indicates that poorer childhood cognitive ability is associated with elevated morbidity (Martin et al. 2004) and mortality risks in adulthood (Hart et al. 2003b; Hart et al. 2004; Kuh et al. 2004; Osler et al. 2003; Pearce et al. 2006; Whalley & Deary 2001). These remarkable findings pertain to early adult illness (including cardiovascular diseases, stroke, cancer and serious illness and psychiatric conditions) and all cause mortality (Batty et al. 2005b; Batty et al. 2006a; Shipley et al. 2006). This chapter first evaluates whether childhood cognition is associated with adult glucose homeostasis. Chapter 1 discussed several possible pathways underlying these associations including through attained adult social position and qualifications (arrows from childhood cognitive ability to adult glucose homeostasis in Figure 6.1) and these are examined in this chapter. Chapter 7 will investigate other pathways, particularly through lifecourse health behaviours, building on associations between cognition and health behaviours reported in Chapter 4.

It is expected that poorer 7-year cognitive ability will be associated with poorer mid-life glucose regulation, in line with evidence from two studies published to date (Martin et al 2004; Starr et al. 2000). It is also expected that change (decline) in cognitive ability rank across childhood will be associated with poorer mid-life glucose regulation. Change in ability rank reflects cognitive growth or decline, and change in school engagement. These may in turn influence the risks of diabetes, either directly, or through intermediary pathways including attainment of adult educational qualifications, and occupational group. Adult social status is associated with material circumstances, access to resources, expectation about health behaviours (Wardle & Steptoe 2003), patterns of health behaviours through adult life, and growth in adiposity which is expected to be a key pathway to diabetes risk (illustrated in Figure 1 and discussed in detail in Chapter 1). Indeed, other prospective studies report associations between childhood ability and adult BMI and obesity (Lawlor et al. 2006a).

The rationale for examining associations between childhood cognition and diabetes risk is based on firstly, the little published evidence about cognitive ability and diabetes risk which suggests associations (Martin et al 2004; Starr et al 2000). Secondly, the associations between cognitive ability and other health outcomes, including cardiovascular outcomes (which are more common in diabetic patients) (Batty et al. 2005a; Hart et al 2004; Lawlor et al. 2005a) and obesity (Lawlor et al 2006a). Thirdly, studies have reported associations between early life factors, in particular birthweight and early social position, which are associated with both adult glucose regulation (Lawlor et al. 2002; Newsome et al. 2003) and cognitive ability (Jefferis et al. 2002; Lawlor et al. 2005b; Richards et al. 2001). Fourthly, individuals with diabetes have poorer adult

cognitive functioning, decline in cognitive ability over time and higher risks of dementia at older ages compared to those with normal glucose control (Allen et al. 2004; Kanaya et al. 2004).

Very little evidence exists about the associations between childhood cognition and glucose homeostasis. Long-term prospective cohorts or retrospectively linked data with the required information needed are rare. One such study is the Providence Rhode Island study, a prospective birth cohort covering 6 cities. Higher 7-year cognitive ability was inversely associated with self-reported diabetes by mid-thirties: OR 0.31 per SD increase in full-scale IQ, $p<0.05$, however the number of cases of diabetes was low (n=14). Higher 7-year IQ was also associated with lower odds of having any serious illness (including cancer, diabetes, heart disease and others); OR 0.65 (95%CI 0.47, 0.89). The association was little changed after adjustment for adult educational level, indicating separate effects of childhood ability (Martin et al 2004). Further evidence comes from retrospective data-linkage of health or mortality data of samples of survivors of a national ability test that was performed in schools by 11 year olds in Scotland in 1932 (Hart et al. 2003a). One such study linked data about health status at in men aged 77 years to their ability tests taken in 1932 and found that men with diabetes had lower mean 11-year test scores compared to men without diabetes (Starr et al 2000). However there were only 10 cases of diabetes and differential loss to follow up may have resulted in bias. Following up a different group of survivors of working age who took the same 11-year ability test, blood sugar levels, cholesterol and BMI were not associated with 11-year IQ (although height and blood pressure were)(Hart et al 2004). A further study based on a regional Scottish cohort born in the 1950s did not find significant associations between diabetes and 11-year IQ tests, although the prevalence of diabetes was low (89/5340= 1.7%) as the cohort are relatively young (aged 44-52 years). The study did however report inverse associations between 11-year IQ and obesity which were somewhat mediated by adult educational level (Batty et al. 2007a). Hence, to date evidence relating childhood ability to adult glucose regulation is sparse and inconsistent, based either on cohorts with low diabetes prevalence, or small numbers of traced adults at older ages.

Mechanisms underlying the associations

Prior studies of childhood cognitive ability and mortality have proposed (Whalley & Deary 2001) and tested (Kuh et al 2004) a series of explanations for the associations. Aside from the pathway between childhood cognition and adult health behaviours (Chapter 4), the following mechanisms (explored in more detail in Chapter 1) may be important. Firstly, childhood cognition may mediate between social and physical conditions in early life which are in turn associated with adult disease risk, although little evidence to date supports this pathway (Kuh et al 2004; Osler et al 2003). Secondly, cognitive ability may be on the pathway to adult social

trajectories, because it predicts adult educational level and occupational position, which are in turn associated with adult health. Evidence from studies of childhood cognition and adult mortality suggests that this is an important pathway (Hart et al 2003b; Kuh et al 2004). Thirdly, childhood cognition may reflect general body integrity; it is possible that associations between childhood ability and poor adult health are driven by the group with lowest cognitive ability scores. There was some evidence to support this in studies of mortality risk (Kuh et al 2004).

This chapter investigates the three main pathways between childhood ability and adult glucose homeostasis listed above. Firstly, childhood social background may be a common cause of the associations between cognitive ability and adult health status. Secondly, (illustrated in Figure 6.1) there may be pathways from childhood cognitive ability to adult social position and educational level then on to glucose homeostasis. Thirdly, cognitive ability may be directly associated with glucose homeostasis and the association may be strongest in lower ability groups.

Childhood social origins as a potential confounder

Childhood social background correlates strongly with cognitive ability in the 1958 cohort and other studies (Hart et al 2003a; Jefferis et al 2002; Lawlor et al 2005b) and is also associated with HbA_{1c}, diabetic risk and metabolic syndrome (Langenberg et al. 2006; Lawlor et al. 2006c; Power et al. 2007). Adults from manual childhood origins have elevated risk of having higher HbA_{1c}, being insulin resistant or having poorer metabolic control. There is little evidence specifically relating to social gradients in HbA_{1c} by child and adult social position, but in the 1946 British Birth cohort, manual childhood social class was independently and significantly associated with being in the top quartile of HbA_{1c} (>5.8%) in men; OR 1.6 (95%CI 1.0, 2.5), however the association was accounted for by adult social position and educational qualifications. The association between social origins and elevated HbA_{1c} was not significant in women; OR 1.2 (95%CI 0.8, 2.0).

Previous analyses of the 1958 cohort indicate that both child and adult social position were associated with HbA_{1c} levels: each change in childhood social position over a six-point social class scale, from professional towards manual groups, was associated with an increase of 0.034 (0.022, 0.047) % HbA_{1c} level, ie a difference of 0.17% HbA_{1c} level across the scale. Adjustment for adult social position association only partially attenuated the association; 0.026 (0.013, 0.039). There was little evidence of confounding of the association between adult social position and HbA_{1c} by childhood social class; adjusted coefficient 0.031 (0.017, 0.044)(Power et al 2007). Cross sectional analysis of 60-79 year olds in the British Women's Heart and Health Study reported that the odds of insulin resistance in women of professional social class of origin was 1.45 (95%CI 1.27, 1.62) and increased to 1.75(95%CI 1.64, 1.87) in women from manual

unskilled class of origin, adjusted for adult social position (Lawlor et al 2002). The detrimental effect of manual social position in childhood was stronger than that in adulthood and appeared to accumulate through life. A record linkage study of mortality records of more than 1,800,000 Swedish men and women indicated that manual compared to non-manual childhood social origins were associated with an elevated hazard ratio of diabetes mortality of 1.41 (95%CI 1.21, 1.62) after adjustment for parental age, educational attainment and marital status plus own adult social class (Lawlor et al 2006c). The 1946 birth cohort found evidence of a significantly increased risk of metabolic syndrome associated with manual social origins in women, adjusted for adult class and education, but the association was not significant in men (Langenberg et al 2006).

At present it is not clear what aspects of childhood social circumstances are on the pathway to development of diabetes. Associations between childhood cognitive ability and diabetes risk may work through social background and highest educational achievements. Childhood social position may reflect the importance of own educational abilities in shaping subsequent life trajectories. Because child ability and adult socio-economic position are strongly positively correlated, associations between adult socio-economic position and diabetes risk may be confounded by childhood ability.

Adult social position and highest educational qualifications

Adult social position and highest educational qualifications are associated with both childhood ability and adult diabetes risk, and are hence a plausible pathway between cognition and diabetes risk. Socially disadvantaged adults have higher risks of developing metabolic syndrome, even taking into account behavioural risk factors (Brunner et al. 1997; Wamala et al. 1999). To illustrate, in the Whitehall study men in the lowest occupational grade had 2.2 (95%CI 1.6-2.9) times greater odds of having metabolic syndrome than men in the highest occupational grade, the equivalent estimate for women was 2.8 (95%CI 1.6-4.9) (Brunner et al 1997). In German adults, men in unskilled manual classes had 3.79 (95% CI 1.96, 7.35) times odds of having diabetes compared to men from professional occupation. Diabetes risk increased non-linearly with highest qualifications achieved; men with up to 10 years education but no apprenticeship had 8.54 (95% CI 2.74, 26.25) times the odds of developing diabetes compared to men with a university degree (Geyer et al. 2006). Similarly, studies of men and women in Europe and Australia have found that less educated men and women were at higher risks of diabetes (Dalstra et al. 2005; Rodgers et al. 2005). Evidence from the 1946 British birth cohort also indicates that men and women with lower levels of education were at increased risk of having elevated HbA_{1c} after taking account of child and adult social position; OR 1.7 (95%CI 1.0, 3.2) for men. Educational gradients in metabolic syndrome were seen in men and women, but after taking into account child and adult social position only persisted in men; OR 2.5

(95%CI 1.3, 4.5) (Langenberg et al 2006). Additionally a Finnish study reported educational gradients in fasting plasma insulin and glucose and WHO or NCEP defined metabolic syndrome (Silventoinen et al. 2005)

Adult adiposity

Associations between cognitive ability, social position and diabetes risk may operate through associations between social background and obesity, as adult obesity and weight gain strongly predict diabetes (Colditz et al. 1990; Wannamethee et al. 2005). Poorer childhood ability is associated with greater adult weight and weight gain across adulthood (Chandola et al. 2006b), and cognition through childhood into adult life is associated with growth; both with height and with weight at different adult life stages (Richards et al. 2002). Poor childhood social position is associated with increased adiposity in adulthood (Parsons et al. 1999). In the 1958 cohort social gradients in obesity change over the lifecourse; childhood social class is not associated with childhood obesity but is associated with adult obesity, and adult class is also associated with adult obesity (Power et al. 2003a). Manual social class is associated with higher risks of obesity and this is confirmed in studies of other cohorts (Power et al. 2004). Central adiposity which is strongly associated with diabetes risk is also associated with social position. Manual social origins were associated with higher waist hip ratios – a difference of ~2.5% across the spectrum of social groups in the 1946 British birth cohort (Langenberg et al. 2003). Despite social gradients in total and central obesity, many studies examining associations between social position and diabetes or diabetes risk do not adjust for obesity, to establish whether effects of social position on diabetes risk are separate from effects on obesity. In this study adiposity is included as a mediating factor between cognitive ability, social position and diabetes risk, illustrated in Figure 6.1. However, in analyses of metabolic syndrome it is not appropriate to adjust for obesity as it is part of the outcome variable.

Early influences on type 2 diabetes

A large body of evidence documents early life influences on development of type 2 diabetes. Smaller size at birth (reflecting poor growth *in utero*), particularly in combination with increased BMI in later life, raises adult disease risk (Newsome et al 2003). Although not a main focus of analyses in this thesis, the potential confounding effect of birthweight is investigated in the analyses of cognition and diabetes risk. Birthweight is associated with childhood cognitive ability (Shenkin et al. 2004). Specifically in the 1958 cohort, higher birthweight was associated with higher 7-year maths and reading ability rank, although birthweight was not associated with change in maths and reading rank 7-16 years (Jefferis et al 2002). Birthweight is also associated with diabetes risk, in particular lower birthweight infants grow up to have higher insulin resistance, although the associations with insulin secretion are not clear (Newsome et al 2003). The associations between birthweight and diabetes risk may be U and J shaped. Low

birthweight infants who gain weight in adulthood are at higher risk than normal birthweight infants as are high birthweight infants who may be the result of pregnancies with gestational diabetes (Harder et al. 2007). Whilst the main effects of birthweight on diabetes risk are not of primary interest, birthweight is included in analyses of associations between cognition and diabetes risk.

Aims

The main aims of this chapter are:

1. To examine the associations between maths or reading ability (at separate ages and trajectories 7-16 years) and adult glucose homeostasis; specifically (i) HbA_{1c} levels, (ii) prevalence of high HbA_{1c} /diabetes and (iii) metabolic syndrome. Further, to investigate linearity of associations between cognitive ability and adult glucose homeostasis.

2. To examine whether there are independent effects of childhood cognitive ability on glucose homeostasis, taking into account birthweight and childhood social class.

3. To examine the mediating roles of adult occupational class and educational qualifications as pathways between childhood cognitive ability and adult glucose homeostasis.

4. To examine the mediating role of BMI and central adiposity in the association between childhood ability and adult glucose homeostasis.

Methods

Measures

Maths and reading z-scores and trajectories, highest educational qualifications, social position, birthweight adjusted for gestational age and three adult measures of glucose homeostasis from the 45-year survey and are all described in detail in Chapter 2.

Sample

The analysis sample includes men and women with estimated maths or reading test trajectories and information on childhood and adult social position, highest educational achievement and the adult health outcome of interest. Exclusions were described in Chapter 2. The sample varied for the three measures of glucose homeostasis and was smallest for metabolic syndrome (n=6259). To investigate sample representativeness in the 45-year analysis sample compared to the birth sample, the distribution of social class at birth in the original sample (n=16,966) was compared to the sample with information on HbA_{1c} at 45 years (n=7214) in Appendix 6.1, Table 6.1.1. Manual social groups were somewhat under-represented in analyses.

Statistical analyses

The distributions of the glucose homeostasis measures were examined and summarized in Table 2.6 Chapter 2. For the first aim, the associations between maths z-scores and glucose homeostasis were assessed using a series of linear or logistic regression models as appropriate. First the associations between cognitive ability at separate ages (7, 11 and 16 years) and HbA_{1c}, diabetes risk and metabolic syndrome were established. Next, the associations between estimates of the trajectories of reading and maths z-score between 7 and 16 years (7-year z-score (intercept) and 7-16 year change in z-score (slope)) and the 3 measures of 45-year glucose homeostasis were modeled in linear or logistic regression models. Linearity of associations between cognition and each outcome was tested by including quadratic terms for the z-scores.

For the next aims, regression models were built up in stages according to chronology of exposures across the lifecourse. First the 7-year z-score and 7-16 year change in z-score of were entered and the following variables were individually added in separate models;

- Social position of origin and birthweight, to see if associations between maths and adult glucose homeostasis were confounded by (i) childhood social position or (ii) birthweight (aim 2).
- Adult social position; to test if associations between childhood maths and adult glucose metabolism operate through adult social position (aim 3).
- Highest educational qualifications achieved (as a pathway) (aim 3).
- Adult BMI and waist circumference at 45 years (as a pathway) (aim 4).
- All exposures; to see if associations between childhood maths and adult glucose homeostasis operate through the multiple pathways, or whether there are direct effects.

Coefficients for the 7-year maths z-score and the 7-16 year maths z-score are presented. These are mutually adjusted coefficients, representing effects not mediated by the pathway variables included in that model. To understand the pathways, the associations between the pathway variables (eg adult social class) and the outcome variables are also presented in the adjusted models, these coefficients are the effects conditional on background variables in the model. Analyses for maths were repeated for reading scores.

Results

Associations between cognitive ability measured at 7, 11 and 16 years and (i) HbA_{1c} levels, (ii) prevalence of high HbA_{1c}/diabetes and (iii) metabolic syndrome - Aim 1

Descriptive data and correlations between maths and reading tests are in Chapter 2, Appendix 2.2. As in previous chapters, maths and reading z-scores are coded inversely so higher z-score represents lower ability level. Figures 6.2-4 display the associations between cognitive ability at the separate ages and HbA_{1c}, diabetes risk and metabolic syndrome. Lower maths and reading ability (higher z-scores) from all three stages in childhood were consistently associated with higher risks of poorer adult glucose homeostasis. 1 SD increase in 7-year maths z-score was associated with 0.02% higher 45-year HbA_{1c} and 1 SD higher 16-year maths z-score was associated with 0.02% higher HbA_{1c} in men and 0.03% in women (Figures 6.2a and 6.2b). 1 SD increase in 7-year reading z-score was associated with 0.03% higher HbA_{1c} and 0.05% for 16-year z-score. Testing interactions between maths or reading z-score by gender on HbA_{1c} did not reveal significant gender differences. The OR for elevated HbA_{1c} / type 2 diabetes was significantly greater than one for maths and reading at all ages except 7-year maths in women (Figure 6.3 and 6.3b). 1 SD higher maths and reading z-score were associated with higher risk of elevated HbA_{1c} / type 2 diabetes eg OR 1.25 (95% CI 1.06, 1.47) for 7-year maths z-score in men. ORs for metabolic syndrome were significantly elevated for each SD higher reading or maths z-score at 7, 11 and 16 years (Figure 6.4a and 6.4b).

Univariate associations between quintiles of estimated maths and reading trajectories (7-year z-score and change 7-16 years) and each measure of glucose homeostasis are summarised in gender-specific tables (Appendix 6.2). Lower 7-year ability was consistently associated with poorer outcomes for each measure of glucose homeostasis, whereas associations with the slope (ie 7-16 year change in rank) were less consistent. In regression models with linear and quadratic terms for 7-year z-score and also for 7-16-year change in z-score, linear associations between 7-year maths (and reading) and each measure of glucose homeostasis were observed. Significant linear associations between 7-16 year change in maths and reading were only observed for continuous HbA_{1c} among men. There was not evidence for non-linear associations between the 7-year maths (or reading) z-scores and adult glucose homeostasis, or with the 7-16 year change in maths (or reading) z-scores.

Tables in Appendix 6.2 also report univariate associations between each of the pathway factors which will be used in the multivariate models and quintiles of maths and reading intercept and slope. The pathway factors were consistently associated with both maths and reading. These associations are summarised in column 2 of Tables 6.1- 6.3 as coefficients from unadjusted models of the associations between each pathway variable listed in column 1 and the outcome measure.

HbA_{1c}

HbA_{1c} level is measured as a percentage of haemoglobin bound to glucose so the coefficients from linear regression analyses refer to an additive increase level of HbA_{1c} (measured in percent) rather than a multiplicative percentage change in HbA_{1c} level (described in Chapter 2). The distribution of HbA_{1c} is narrow (SD 0.62), so the coefficients in the linear regression models are small numbers. Poorer 7-year ability was associated with an increase in mean percentage HbA_{1c}: 0.03 (95%CI 0.01, 0.05) in men and 0.02 (95%CI 0.01, 0.04) in women per SD increase in maths z-score. There was not evidence of a significant association between the 7-16 year change in maths z-score and HbA_{1c} level in either men or women (Table 6.1). Similarly, 1 SD increase in reading z-score at 7 years was associated with increases of 0.04% in HbA_{1c} level in men and 0.027% in women, but 7-16 year change in reading z-score was not associated with HbA_{1c} in men or women (Appendix 6.3, Table 6.3.1).

Elevated HbA_{1c} / type 2 diabetes

Poorer 7-year maths ability was associated with increased odds of elevated HbA_{1c} / type 2 diabetes; 36% (men) and 34% (women) per SD increase in 7-year maths z-score (Table 6.2, Column 2). There was no evidence of an association with change in maths score rank. Similar associations were seen for reading scores (Appendix 6.3, Table 6.3.2, Column 2).

Metabolic syndrome

Poorer 7-year maths ability was associated with increased odds of metabolic syndrome; 23% (men) and 34% (women) per SD increase in 7-year maths z-score (Table 6.3). There was no evidence of an association of metabolic syndrome with 7-16 years change in maths z-score. Again, similar associations were seen for reading scores (Appendix 6.3,Table 6.3.3).

In summary, poorer 7-year maths or reading ability was consistently associated with poorer glucose regulation; across the population distribution of HbA_{1c}, for the elevated HbA_{1c} / diabetes group and for metabolic syndrome. Change maths or reading rank 7-16 years was consistently not associated with any outcome.

Columns 4-8 of tables 6.1-6.3 contain coefficients from a series of regression models, entering the pathway variables separately in chronological order. The coefficients are associations between maths (or reading) 7-year z-score and 7-16-year change in z-score with the outcome measure, sequentially adjusted for the pathway variables indicated in column 1.

The confounding roles of childhood social position and birthweight in the association between childhood cognitive ability and adult glucose homeostasis - Aim 2

The roles of (i) social position of origin and (ii) birthweight as confounders of the association between maths and reading z-scores and adult glucose homeostasis were investigated. Manual

social class at birth and lower birthweight were associated with lower 7-year maths and reading rank and manual social class at birth was also associated with poorer 7-16 year maths and reading trajectories (Appendix 6.2).

Social class at birth

In column 2, row 3 of Tables 6.1-6.3 the unadjusted associations between social class at birth and the three measures of glucose homeostasis in turn is presented. Social position at birth was significantly associated with each measure of glucose homeostasis (except for continuous HbA_{1c} in men). Column 3 of Tables 6.1-6.3 contain the adjusted coefficients of 7-year maths z-score and 7-16 year change in z-score. In women, adjustment for class at birth, attenuated associations; social position of origin in part confounds the association between 7-year maths and diabetes risk. On adjustment, the association between a 1 SD increase in 7-year maths z-score and HbA_{1c} was reduced from a rise of 0.02% (95%CI 0.01, 0.04) to 0.02% (95%CI -0.00, 0.03) (Table 6.1). In men there was no main effect of social position at birth on HbA_{1c} and the association between cognition and HbA_{1c} was unchanged. On adjustment the association between 7-year maths z-score and HbA_{1c} / type 2 diabetes was reduced from OR 1.36 (95%CI 1.14, 1.63) per SD decrease in maths z-score, to OR 1.29 (95%CI 1.08, 1.56) in men and from OR 1.34 (95%CI 1.08, 1.65) to 1.26 (95%CI 1.01, 1.57) in women (Table 6.2). Similarly, reductions in the OR for metabolic syndrome on adjustment for social class at birth were seen in men and women (Table 6.3). The patterns of results from reading scores mirrored those for maths scores (Appendix 6.3, Tables 6.3.1, 6.3.2, 6.3.3).

Additionally, in the final column of Tables 6.1-6.3 the fully adjusted models indicate that for women social position of origin had lasting effects on metabolic syndrome which are only partly mediated through childhood cognition and later social position. For men there are not lasting effects of early social position on glucose homeostasis.

Birthweight

In a series of regression models for each of the three measures of glucose homeostasis as the dependent variable, with birthweight and gestational age as independent variables, birthweight was only associated with high HbA_{1c} /diabetes in men (OR 0.64; 95%CI 0.43, 0.96 per Kg increase in birthweight). Appendix 6.4 presents analyses of high HbA_{1c} /type 2 diabetes in men including birthweight (adjusted for gestational age). Tables A6.4.1-3 indicate that higher birthweight was associated with lower odds of elevated HbA_{1c}. Birthweight with or without adjustment for gestational age was not a strong or consistent confounder of the association between maths or reading and glucose homeostasis. Therefore the main models were presented without adjustment for these birthweight and gestational age.

In summary, social position at birth explained part of the associations between 7-year maths or reading and adult HbA_{1c} level in women and also diabetes risk and metabolic syndrome in both sexes. Birthweight was not a strong or consistent confounder of the association between maths or reading and glucose homeostasis.

Occupation and educational qualifications as pathways between childhood cognitive ability and glucose homeostasis - Aim 3

Social position in adulthood

Tables 6.1-6.3 column 2, contain unadjusted coefficients for the associations between 33-year social class or educational qualifications with each glucose homeostasis outcome. Manual adult social position was associated with higher HbA_{1c} in both sexes, with higher odds of elevated HbA_{1c} in men and metabolic syndrome in women. Adjustment for adult social class attenuated the association between glucose homeostasis and 7-year maths z-score. Adult class was a pathway between cognition and HbA_{1c} in both sexes; for example coefficients were attenuated from 0.03% (95%CI 0.02, 0.05) per SD increase in 7-year maths z-score to 0.02% (95%CI 0.00, 0.04) in men (Table 6.1, column 5). There was only a small attenuation of the association with elevated HbA_{1c} /diabetes risk in men, for example, from OR 1.36 to 1.32 for 7-year maths z-score (Table 6.2). Adult class mediated between 7-year maths z-score and metabolic syndrome risk in women; estimates were attenuated from 1.39 to 1.26 per SD decrease in 7-year maths z-score (Table 6.3).

Educational Qualifications

Tables 6.1-6.3 column 2 indicate that having fewer compared to more educational qualifications by 33 years was associated with higher risks of poor glucose homeostasis. Level of qualifications mediated between 7-year maths (or reading) z-score and HbA_{1c} level in both men and women. For example, the association between 7-year maths z-score and HbA_{1c} was reduced from 0.03% (95%CI 0.02, 0.05) per SD increase in z-score (lower ability) to 0.02% (95%CI 0.00, 0.04) in men (Table 6.1, column 6), and completely mediated in women. Educational qualifications substantially mediated the association between 7-year maths z-score and elevated HbA_{1c} /diabetes risk in men and women. The OR of elevated HbA_{1c} /diabetes associated with 1 SD increase in z-score reduced from 1.36 (95%CI 1.14, 1.63) to 1.15 (95%CI 0.93, 1.42) in men and from 1.34 (95%CI 1.08, 1.65) to 1.20 (95%CI 0.93, 1.55) in women (Table 6.2). Highest qualifications also mediated between 7-year maths z-score and metabolic syndrome. The OR for metabolic syndrome was reduced from 1.24 (95%CI 1.11, 1.39) to 1.14 (95%CI 1.01, 1.30) in men and from 1.39 (95%CI 1.22, 1.58) to 1.14 (95%CI 0.98, 1.33) in women (Table 6.3).

In summary, the association between 7-year ability and 45-year HbA_{1c} operated in part through

adult social position, as did the association with metabolic syndrome in women. However the association between 7-year ability and 45-year elevated HbA_{1c} /diabetes risk did not operate through social position in men. In contrast, highest qualifications were a more consistent pathway than adult social position; the association between 7-year ability and later HbA_{1c}, elevated HbA_{1c} /type 2 diabetes risk or metabolic syndrome were all mediated in large part through educational qualifications.

Central and total obesity as pathways between childhood cognitive ability and glucose metabolism - Aim 4

BMI and Waist Circumference

There were main effects of both 45-year BMI and waist circumference on HbA_{1c} levels: 1 kg/m^2 increase in BMI was associated with an increase of 0.02% in HbA_{1c} level whilst 1cm increase in waist circumference was associated with 0.01% increase in HbA_{1c} level (Table 6.1, column 2). One SD increase in 45-year BMI (4.36 Kg/m^2 in men), was associated with 0.09% increase in HbA_{1c} level and 1 SD increase in waist circumference (11.23 cm in men), was associated with 0.11% higher HbA_{1c} level. Models of glucose regulation and 7-year maths z-score and 7-16 year change in z-score were separately adjusted for BMI and waist circumference (Table 6.1, columns 7 and 8). In men the association between 7-year maths and HbA_{1c} level was reduced to 0.02% on adjustment for either BMI or for waist circumference. However the association between HbA_{1c} and 7-16 year change in maths z-score was entirely mediated by BMI and waist circumference. For women, adjustments for BMI and waist circumference both completely mediated associations with 7-year maths z-score and similar patterns were seen with reading scores (Table 6.1).

Associations between adult adiposity and elevated HbA_{1c} /diabetes risk were seen. Each Kg/m^2 increase in BMI at 45 years was associated with an OR of 1.21 (95%CI 1.17, 1.25) for elevated HbA_{1c} /diabetes and each centimetre increase in waist circumference was associated with 1.08 (95%CI 1.06, 1.09) increase in odds of elevated HbA_{1c} / diabetes in men and similar associations were seen in women (Table 6.2, column 2). As with HbA_{1c} level, when separate adjustments for BMI and waist circumference were made to the models of 7-year maths z-score and 7-16 year change in z-score, in men the association between initial level of maths ability and elevated HbA_{1c} /diabetes was partly mediated with either adjustment, but still significant. For women, the adjustments fully mediated the association between 7-year maths z-score and elevated HbA_{1c} /diabetes. Again, similar patterns were seen with reading scores (Table 6.2).

Models of metabolic syndrome were not adjusted for total and central adiposity because central adiposity is part of the definition of the metabolic syndrome.

In men, adjustment for BMI or waist circumference partly mediated the associations between childhood ability and adult HbA_{1c} level or elevated HbA_{1c} /diabetes risk. In women the associations were completely mediated on adjustment.

Full models

The final column of Tables 6.1-6.3 presents fully adjusted models for each outcome which indicate how the associations of childhood maths (and reading) trajectories were mediated by all the factors together. None of the associations between 7-year ability and each outcome were robust to concurrent adjustment for all the pathways. Adult social position, educational level and adiposity together entirely mediated associations between 7-year ability and later glucose homeostasis, indicating that associations between 7-year level and 7-16 year change in maths (or reading ability) and adult glucose homeostasis appear to be indirect. The only exception to this was the association between initial reading level at 7 years and HbA_{1c} level in men (Table 6.2).

In summary, the associations between childhood cognitive ability and adult glucose homeostasis operated through attained adult social position, educational level and adiposity.

Pathways from cognitive ability to central and total adiposity

Because adiposity was a major pathway between childhood ability and adult HbA_{1c} and high HbA_{1c} /diabetes, analyses were repeated with adiposity as the outcome, to better understand pathways from childhood ability to adiposity (Appendix 6.4). Poorer 7-year maths (and reading) rank were consistently associated with higher risks of adult obesity (BMI >30kg/m^2) and with central obesity (large waist circumference). 7-16 year change in maths or reading z-scores were not associated with 45-year total or central obesity. Associations between 7-year maths (or reading) z-scores and total or central obesity were little confounded by birthweight and somewhat attenuated on adjustment for social position of origin, although significant associations remained. Associations between 7-year maths (or reading) z-scores and total or central obesity were mainly mediated through qualification level. Attenuation on adjustment for adult social position was weaker (and similar in magnitude to adjustment for childhood social position). When all the variables were added to the model together, the association between 7-year maths (or reading) z-scores and total obesity remained significant in both men and women, indicating long-lasting effects of 7-year maths (or reading) z-scores on total obesity. In contrast, in the fully adjusted models, the association between 7-year maths z-scores and central obesity remained significant in women and in men for reading ability but was entirely mediated (attenuated to null) in the other two models.

In summary there was more consistent evidence for independent effects of cognition on adiposity than on diabetes risk itself.

Discussion

Summary of results

Consistent associations were seen between childhood cognitive ability with adult HbA_{1c}, elevated HbA_{1c} /type 2 diabetes and metabolic syndrome (indicated by direct arrows between cognitive ability and glucose homeostasis in Figure 6.1). Poorer 7-year maths or reading ability was consistently associated with higher risks of poor adult glucose regulation, both across the population distribution of HbA_{1c} and in the high risk group (participants with HbA_{1c} ≥6% or type 2 diabetes) and higher risks of metabolic syndrome. For the most part associations were not seen between 7-16 year change in maths (or reading) and adult glucose homeostasis. The size of effect associated with one SD increase in 7-year maths z-score (lower ability) was an increase of 0.02-0.03% in HbA_{1c} level, for example from 5.0 to 5.2%, and the odds of elevated HbA_{1c} /diabetes or of metabolic syndrome were around 1.3.

There was not evidence to suggest that the associations between either maths or reading trajectories with any of the three glucose regulation outcomes were non-linear. An alternative explanation for the association between cognitive ability and adult glucose homeostasis, might be that they share a common cause, for example lower birthweight has been associated with higher risks of diabetes and higher risks of poorer cognitive development, but this was not supported by the data, with the exception of a weak association between birthweight and continuous HbA_{1c} level in men. In contrast, there was some evidence that social position of origin was a common cause of both childhood cognitive development and adult glucose regulation; social class of origin attenuated the cognition-glucose homeostasis association to a similar degree to adjustment for social position in adulthood.

Turning to other pathways illustrated in Figure 6.1, there was evidence that adult social position and, more consistently, adult educational level mediated between childhood cognition and adult glucose homeostasis. As expected, the pathways from childhood cognitive ability to adiposity and then on to adult glucose dysregulation were important. Figure 6.1 indicates several potential pathways between childhood cognition and adult adiposity. There was evidence that pathways between childhood cognition and adult BMI and waist circumference were mainly mediated through highest qualifications attained and adult social position. There was not evidence that birthweight was a common cause of childhood cognition and adult adiposity, although childhood social position did partly confound the association. However associations between 7-year ability and adult obesity remained significant on adjustment for the other pathways. In

summary, the findings imply that poorer early childhood cognition has modestly influences glucose regulation in men and women three decades later; raising HbA_{1c} levels 0.02% and increasing odds of diabetes or metabolic syndrome risk by around 1.3 times, per standard deviation increase in 7-year ability. To some extent this is confounded by social position of origin but the remaining association between cognitive ability and adult glucose regulation appears to operate through adult educational qualifications, social position and adiposity.

Strengths and weaknesses

In addition to the general strengths and weaknesses identified in previous chapters in relation to study design (Chapter 3) and the cognitive ability tests (Chapter 4), further strengths and weaknesses relate to the analyses and the approach taken here. The strengths of the study include the objective measures of glucose regulation and adiposity measured by the nurse at 45 years (discussed in Chapter 2). The study benefits from the measure of HbA_{1c} which, as discussed in Chapter 2, indicates long-term glucose regulation (the amount of circulating blood in the previous glucose 4-6 weeks). HbA_{1c} level was analysed using a standardized laboratory procedure and standardized to Diabetes Control and Complication Trial values. Availability of HbA_{1c} in a sample who were mostly not diagnosed with type 2 diabetes permitted investigation of population-level associations between cognition and glucose regulation, giving insight into the mechanisms that might link cognitive development to glucose regulation. The results suggested that the associations hold across the range of HbA_{1c} levels and were not confined to the most at-risk group ≥6% or ≥7% HbA_{1c}. Whilst the self-reporting of type 2 diabetes was at 42 years and nearly three years may have elapsed between the self-report at 42 and the survey at 45 years, the HbA_{1c} data and information about current medications give a good indication of the group with type 2 diabetes. The substitution of HbA_{1c} for standard blood glucose measures (which are part of the WHO or NCEP standard definitions of the metabolic syndrome) is a draw-back when attempting to compare results from this study with other studies. However other studies have substituted HbA_{1c} for fasting plasma glucose in the definition of metabolic syndrome (discussed in chapter 2). Oral glucose tolerance testing which is the gold standard for assessing glucose regulation is impractical given the time and cost implications in a cohort study of this size. In the same vein, the triglyceride measurement, which is part of the definition of the metabolic syndrome, was based on a non-fasting blood sample. To address the problem, a cut-point for "very high" rather than "high" was used to indicate elevated triglycerides. The benefit of using three related outcomes is that the results for each outcome validate the results for the other outcomes to a degree. By using HbA_{1c} as a continuous outcome, as well as looking at the high risk groups, the population level associations can be investigated and contrasts drawn between the two. Investigating the metabolic syndrome as well as the HbA_{1c}–based outcomes widens the remit of the study to a much larger group of adults who are at risk of serious detrimental health outcomes. In relation to anthropometry, weights and measurements were

taken using standardized protocols and equipment by trained nurses; and then waist circumference and BMI were treated as continuous outcomes as well as being categorized according to conventional public health cut-points. In addition, the 1958 cohort benefits from prospective data on a range of confounder or pathway variables.

How this study adds to the literature

The results presented in this chapter add to the literature on cognition and health outcomes. As discussed in the introduction, at present evidence relating childhood cognitive ability to adult glucose regulation is sparse and not consistent; it is based either on cohorts with low prevalence of diabetes (Batty et al 2007; Martin et al 2004), or studies with very small numbers of cases in older adulthood (Starr et al 2000). Much of the literature on cognition and health outcomes is based on retrospectively linked data (for example the various follow-ups of the 1932 Scottish Mental Survey and the Children of the 1950s cohort) and many studies focus only on men. The 1958 cohort does not suffer from these draw-backs. To date there is some evidence of inverse associations between diabetes risk and (a) childhood cognitive ability and (b) final level of educational qualifications. However separate measures of cognitive ability at different stages of childhood and also *changes* in cognitive ability across childhood have not been investigated in relation to diabetes risk. Therefore this study adds to the literature on childhood cognition and diabetes risk firstly by investigating childhood ability and change in cognitive function between 7 and 16 years. Secondly, by investigating a range of outcomes related to diabetes risk. Thirdly it specifically examines pathways between childhood cognition and glucose homeostasis. Few studies have information on the intermediate pathway variables which may explain the effects of ability on later glucose homeostasis. Those that do have information have tended to focus on factors from early life or later life, but not both. In contrast this study assesses whether there were confounding effects of social background and birthweight and then addresses several pathways; through adult social position, educational qualifications and midlife adiposity. Only one (recently published) study aimed to investigate pathways between childhood cognitive ability and diabetes risk; in a retrospectively linked cohort no association between 11-year ability and diabetes at age 44-52 years was found and hence no insight into mediating pathways was gained (Batty et al 2007). In addition to being able to study pathways through social position and educational level, further pathways between cognition and glucose homeostasis including lifecourse health behaviours will also be evaluated in the next chapter.

Results of each of the aims relating to the associations between cognitive ability and glucose regulation will be discussed in turn.

Unadjusted associations between cognition and glucose homeostasis

As expected from the few prior studies of the associations between cognition and glucose dysregulation (Martin et al 2004; Starr et al 2000) (and the studies on other health outcomes or mortality), there were associations between poorer initial ability and greater risk of all three measures of diabetes risk in both men and women, and were consistently in the same direction. However change in ability between 7 and 16 years was not associated with diabetes risks in mid-life. Whilst this study did not provide evidence that change in ability was related to diabetes onset, it had been expected that measures of change in cognitive ability rank through childhood might reflect a process of cognitive growth and school engagement which would in turn influence the risks of diabetes, either directly, or through other intermediary pathways. There is little direct evidence about the associations between childhood IQ and glucose homeostasis with which to compare the results reported here. The three relevant studies are of different age groups and whilst diabetes prevalence rises with age, the association of diabetes risk with cognitive ability may not necessarily change with age. One relevant study is the Providence Rhode Island study, a regional arm of the National Collaborative Perinatal Project which is a prospective birth cohort covering 6 cities in USA (Martin et al 2004). Diabetes (onset ≥ 18 years old) was self-reported when participants were in their mid-thirties and, like the analyses presented here from the 1958 cohort, the Rhode Island study used a measure of IQ at age 7 years. One standard deviation increase in full scale IQ at age 7 was associated with OR of 0.31 for self reported diabetes in the Rhode Island study, $p<0.05$, however there were only 14 cases of diabetes so it is reasonable to expect that the point estimate may be unstable (Martin et al 2004). To compare, in the 1958 cohort equivalent estimates of the ORs for elevated HbA_{1c} /type 2 diabetes per standard deviation lower reading and maths ability were between 0.69 and 0.77. For metabolic syndrome the ORs were between 0.75 to 0.81 (these estimates are ORs in Tables 6.2 and 6.3 reversed to relate to increase rather than a decrease in ability rank). The 1958 cohort effect estimates appear to be weaker than those with full scale IQ from Rhode Island, but given that there are fewer cases in the RI study (which did not present confidence intervals), it is difficult to establish whether the estimates differ. Another relevant study draws on a cohort of men in Scotland aged 77 years with health data retrospectively linked to their ability tests taken at age 11 years, in 1932. Respondents at age 77 with type 2 diabetes had lower ability scores than men who were traced and did not have diabetes: 10 men with diabetes had a mean 11-year test score of 32.4 (SD 17.1) and 201 men without diabetes had a mean test score of 40.1 (SD 13.2) (Starr et al 2000). Again, the numbers were low and the presentation of the data makes direct comparisons of the effect size between the Scottish study and the 1958 cohort study difficult. In contrast, in another Scottish study which has linked the same 11-year ability test taken in 1932 to outcomes in a different group of survivors of working age, there was no evidence that blood sugar levels, cholesterol and BMI were associated with 11 year IQ, although height and blood pressure were (Hart et al 2004). Whereas in analyses of the 1958

cohort, 7-year maths or reading ability were consistently associated with 45-year BMI. The final study is a retrospectively linked cohort of Scottish children born between 1950 and 1956 who took part in a school-based survey in 1962. 11-year IQ was not significantly associated with diabetes at age 44-52 years OR 0.93 (95%CI 0.73, 1.18) (Batty et al 2007) however this was based on 89 cases of diabetes, perhaps with a higher prevalence of diabetes an association might have been seen, like in the 1958 cohort where the larger study size increases power to detect moderate effects.

Unadjusted associations between cognition and adult adiposity

Obesity is an important mediator of the association between childhood cognition and diabetes risk, therefore in order to further understand the pathways from cognition to adiposity, additional analyses were conducted with high waist circumference and obesity as outcomes. After taking account of the confounding effect of social class of origin, there was some evidence of independent effects of initial maths or reading ability on obesity that were not entirely mediated by adult social class or educational qualifications.

Several sources report associations between childhood obesity and childhood ability(Li 1995), adult educational level or IQ with adult obesity and finally, childhood cognitive ability with adult obesity (Halkjaer et al. 2003; Lawlor et al 2006a). The first group of studies indicated that childhood obesity was associated with poorer school performance. There is a large literature about adult educational level and adult obesity: the findings mirror those reported above with adult social position and obesity, less educated adults are at higher risk of total and central adiposity. The studies of childhood ability and later body mass index have shown that children who scored less well on tests of ability are at greater risks of having larger BMI in adult life. A study based on the childhood ability tests from the Scottish Mental Survey in 1932 linked with information about adult survivors in the occupation-based Midspan studies reported an inverse association between childhood IQ and adult BMI. However the mediating role of adult factors were not considered (Hart et al 2004). A recent study using data from 1958 cohort up to the age of 42 years reported that performance on the 11-year general ability test was associated with both BMI at 42 years and growth in BMI from 16 to 42 years (Chandola et al 2006b).

Next the pathways between cognition and each of the measures of glucose homeostasis will be reviewed in turn indicating how the results from 1958 data fit with other studies. However, given the sparse literature about cognition and diabetes risk or metabolic syndrome, the associations between cognition and other health outcomes will also be discussed. In fact, there is very little literature about childhood cognition and other single disease endpoints; other studies have mostly looked at the associations between childhood ability and groups of diseases or causes of mortality (often grouped as all cause or CHD related mortality). However, a note of

caution is necessary because drawing direct comparisons of effect between this study and other literature about such diverse end-points must be tentative, as it is likely that different pathways will be important for different types of diseases, because of varying disease mechanisms.

Non linearity

It is relevant to examine whether the association between childhood cognition and the risk of adult glucose regulation is linear. If the association is confined to the group with the lowest cognitive scores, this offers an insight into the pathway from cognition to health, indicating that only individuals in the lowest ability group are at high risk and potentially a target group for intervention. For example, preterm or low birthweight babies are at higher risk of neurodevelopmental delays and poorer cognitive development through childhood as well as being at risk of other health sequelae (Shenkin et al 2004). If there was a non-linear association between cognition and adult glucose regulation this would imply that associations summarized across the spectrum of cognitive ability were not very accurate representations of the true associations. In the 1958 cohort, there was not evidence for non-linear associations between cognitive ability and glucose regulation; ie associations between cognitive ability and glucose regulation were not stronger at the lower end of the spectrum of cognitive ability than at the higher end. Although (age-appropriate) tests of maths and reading rather than standardized IQ tests were used to measure cognitive ability in the 1958 cohort, it is unlikely that other tests of cognitive ability would point to different conclusions, given the strong inter-correlation between results of cognitive tests in different domains of cognitive ability (Neisser et al. 1996). There is not much evidence of non-linearity in associations between cognition and other health outcomes. In the existing literature, the evidence of non-linearity between cognitive ability and adult health is limited to mortality; mid-life mortality risks were higher in the quartile with lowest cognitive ability compared to other quartiles of ability in the 1946 birth cohort and also in the Danish Metropolit Cohort based on record linkage of data about men born in 1953(Kuh et al 2004; Osler et al 2003). There was not evidence for non-linearity in the association between childhood cognitive ability and obesity in a Scottish prospective birth cohort (Lawlor et al 2006a).

Early life factors: birthweight

The results from analyses presented here indicate that associations between childhood ability and adult diabetes risk are independent of birthweight and birthweight for gestational age. Thus there was no evidence that intra-uterine growth was a common cause of the cognitive trajectories and diabetes risk. Other studies have not investigated this. However, a recently published study using the Children of the 1950s retrospective cohort did not find any association between cognitive ability and diabetes risk and analysis with birthweight as a mediator was presented even though there was no association between cognitive abilty and

diabetes to be mediated (Batty et al 2007). In the same study, associations were however found between cognitive ability with overweight (BMI ≥ 25 Kg/m^2) and obesity (BMI ≥ 30 Kg/m^2) at age 44-52 years which were hardly changed on adjustment for birthweight. However gestational age was not recorded and birthweight was analysed as three categories. Not many other datasets have the information available to look at how birthweight may alter any association between cognition and later health outcomes. An exception is the revitalized Danish Metropolit cohort comprising men and women born in 1953. This cohort is of a similar age to the 1958 cohort so comparisons are pertinent. An investigation into coronary heart disease and stroke found significant associations between age 12-year IQ and adult coronary heart disease which were little changed on adjustment for birthweight, however social class of father at birth explained part of the association between cognitive ability and coronary heart disease. There was no evidence that stroke was associated with cognitive ability (Batty et al 2005a). Additionally, although not of central interest to the pathways studied in this analysis, but of interest to the large literature about the association between intra-uterine growth retardation and adult diabetes risk, there was no evidence that childhood cognition mediated associations between lower birthweight and later increased diabetes risk in adulthood. This suggests that the associations between (i) lower birthweight or poorer intra-uterine growth and (ii) cognition and later diabetes risk operate separately.

Early life factors: social position in childhood

Adult glucose homeostasis and social position in childhood

In contrast to birthweight, there was evidence that childhood cognitive ability and adult glucose regulation share a common cause in social position of origin. Hence childhood cognition mediates between early life social position and adult glucose regulation. As discussed in the introduction, there is evidence from other studies that early life social position is associated with poor glucose regulation (Lawlor et al 2002; Lawlor et al. 2003a; Newsome et al 2003). However there is little other evidence about the inter-relationships between childhood social class, childhood IQ and later diabetes risk.

Adult adiposity and social position in childhood

In the 1958 cohort, there was evidence that childhood ability and adult adiposity shared a common cause in childhood social position, indicated by partial confounding of the association between childhood cognitive ability and obesity (or high waist circumference). The pathways reported between childhood ability and adiposity via early social position are congruent with other research on social gradients in obesity. Early life disadvantage is also associated with adult obesity(Power et al 2004). In the prospective 1946 British birth cohort; manual childhood social origins were associated with higher risks of central and total obesity in adulthood, even after taking into account adult social position. (Langenberg et al 2003).

As a related, but separate point, there were also main effects of social class of origin (and in adulthood) on adult adiposity which were separate to the effects of cognitive ability, so whilst social position explained part of the effect of cognition on obesity there were additional, separate, effects of social class in both child and adulthood. This fits with other evidence that associations between childhood social position and adult overweight are in part mediated by childhood cognitive ability; OR for overweight in manual vs non-manual social group of origin was 1.33 (95% CI 1.17, 1.49), attenuated to 1.17 (95% CI 1.03, 1.32) on adjustment for 11 year IQ (Lawlor et al 2005a).

Other health outcomes and social position in childhood

Whilst not directly comparable, for further context, and looking more broadly at literature relating to other disease outcomes, a small study investigating a group of morbidity outcomes did not find effects of broad indicators of early social position (overcrowding, demi-span and number of teeth participants still had aged 77 years) on health status indexed by "any disease" age 77 years. However the grouping of "any disease" is rather problematic and the social measures were varied and non-standard (Starr et al 2000). Three studies of IQ and mortality have incorporated early social position. The first modeled survival up to age 76 years from another subsample of Scottish men and women who took the 1932 Moray House Test aged 11 years. Structural equation models indicated that the association between IQ and survival was best conceptualized with IQ as a mediating factor between childhood social position (indexed by overcrowding from area-based census data and father's occupational position from death certificates) and age at death (Whalley & Deary 2001). This also fits with conclusions of an investigation into all cause mortality aged 15-49 years in participants of the Danish Metropolit cohort. Lower 11-year IQ was associated with higher risks of mortality when adjusted for just father's social class and also when additionally adjusted for birthweight (Osler 2003). Only the lowest IQ quartile had significantly different mortality risks to the highest quartile in both models; hazard ratio (HR) 1.53 (95%CI 1.19, 1.57) adjusted for social class and birthweight. The Newcastle thousand families study which prospectively followed births from 1947 also reported associations between cognitive ability and mortality in men; HR 0.57 (95% CI 0.37, 0.86) per SD increase in 11-year IQ. This association was little changed on adjustment for early life social position; HR 0.60 (95% CI 0.39, 0.92) (Pearce et al 2006). However, similar comparisons based on analyses of English and maths ability indicated that the HRs for mortality associated with the 11-year scores were attenuated to levels near non-significance, suggesting that early social position explained the associations between English or maths ability and later mortality more completely than the associations with a general IQ measure. At present, there are only a few studies of IQ, early social position and later health or mortality outcomes. However given the wider literature about poorer early life social position being associated with

many other poorer health outcomes (Blane et al. 1996; Brunner et al. 1999; Wadsworth & Kuh 1997; Wannamethee et al. 1996), the results discussed here raise the question of whether the associations between social origins and health might operate in part through the effects of social background on childhood ability.

Social origins may be reflecting a broad constellation of factors in the prenatal and early home or school environment. Indeed, prior work on cognitive trajectories in the 1958 cohort examined what factors from the home environment (such as parents' reading to the child, whether the parents took an interest in the child's progress at school) and school environment (for example, whether there was a parent teacher association or if there were social events at the school) accounted for the association between social class at birth and the 7-year reading and maths ability and the change in ability rank between 7 and 16 years. Factors from the home and school environment which were found to be important in explaining the social gradient in initial maths ability were mother reading to the child and father's interest in the child's schooling. However the home and school factors did little to explain the association between birthweight and the cognitive trajectories to age 16 years (Power et al. 2006). Some of these early life factors associated with cognitive ability may be important in setting up trajectories into adulthood that influence later social status, health behaviours, coping strategies and employment prospects that may in turn influence trajectories of child and adult height and weight and thereby risks of developing poor glucose regulation in midlife. If this is the case, then investigating these factors may help to clarify the pathways between childhood ability and later glucose regulation.

Adult factors: social position in adulthood and educational qualifications

Adult glucose homeostasis and adult socioeconomic position

Ability in childhood predicts educational achievements and adult social position (Fergusson & Horwood 1995; Hart et al 2003a; Neisser et al 1996), both of which are important determinants of many adult health outcomes including diabetes. Indeed, here as in other studies, manual adult occupational position was associated with poorer glucose metabolism (Kumari et al. 2004). Few other studies look at HbA_{1c} in relation to social position (Power et al 2007; Thomas et al. 2007b). The models of HbA_{1c}, diabetes risk and metabolic syndrome were consistent in that social position in adulthood moderately attenuated the association between initial ability and diabetes outcomes, more so in men than in women, indicating that adult social position is a pathway between childhood cognition and adult glucose regulation.

Obesity and adult socioeconomic position

Pathways from childhood cognition via adult social position to adult total or central obesity mirrored pathways seen for diabetes risk; adult class attenuated the associations with initial ability. In the UK (and other developed countries), social inequalities in obesity have been

repeatedly demonstrated; manual groups are more likely to be obese than non-manual groups (Power et al. 2003b; Power et al 2004). In the 1946 British birth cohort, adult social position was associated with adult obesity in women but not in men, after adjusting for childhood social position (Langenberg et al 2003).

In addition to social gradients in total obesity, central obesity is socially graded with higher risks in more manual groups(Brunner et al 1997). However, there is less evidence about the mediating role of adult social position between childhood cognitive ability and adult obesity. A comparable study with relevant information is the retrospective children of the 1950s cohort which reported inverse associations between 11-year IQ and overweight and obesity at 44-52 years. Associations were weakly attenuated by social position in adulthood (indexed by housing tenure, car ownership, occupational class and income). For example the OR of BMI $\geq 30 Kg/m^2$ associated with 1 SD change 11-year IQ was 0.78 (95%CI 0.72, 0.83) and 0.80 (95%CI 0.74, 0.86) on adjustment for adult social position. Like the 1958 cohort, even after adjustment for adult social position, there remained significant associations between childhood ability and adult obesity.

Other health outcomes and adult socioeconomic position

Studies of early cognition and other health outcomes which adjust for adult social position have reported, for example, that the association between 11-year Scottish Mental Survey test score and early onset (<65 years) cardio-vascular disease was only slightly attenuated but not entirely mediated by adult social class and area deprivation measures, for example, the Rate Ratio (RR) for cardio-vascular disease reduced from 1.22 (95%CI 1.06, 1.39) to 1.19 (95%CI 1.03, 1.38). In contrast, the RR for coronary heart disease was unchanged by adjustment for adult social position (Hart et al 2004). There is also support for a pathway between childhood ability and later mortality risks via adult social position. Associations between childhood ability and later mortality risks were substantially attenuated by adjustment for own adult socioeconomic position in the 1946 British birth cohort, particularly in men (Kuh et al 2004), and also in Scottish cohorts (Hart et al 2003b). Additionally, in the West of Scotland study both adult occupational position and area-based deprivation mediated between childhood ability and adult self-rated health and mortality (Batty et al. 2006b).

Adult glucose homeostasis and adult educational qualifications

In the 1958 cohort there were consistent associations between lower levels of educational qualifications and each measure of poorer glucose regulation, as seen in other studies (Silventoinen et al 2005; Wamala et al 1999). Associations between 7-year maths or reading ability and adult glucose regulation were strongly attenuated by adult educational qualifications, particularly among men, suggesting that childhood cognitive ability may be more strongly associated with adult qualifications in men. Indeed, in the 1958 cohort the men gained higher

adult qualifications than the women. Other studies of childhood ability and diabetes risk have not investigated the mediating role of adult educational qualifications. However, to give some context to the results, the mediating role of adult qualifications for other health outcomes is discussed. Other studies which investigating adult education as mediator between cognition and morbidity report varied results. In the Providence Rhode Island study the mediating role of education was not studied for diabetes as a single endpoint, but the odds of having any serious illness (including cancer, diabetes, heart disease and others) decreased with increasing 7-year IQ; Odds Ratio (OR) 0.65 (95%CI 0.47, 0.89) and the association hardly changed on adjustment for adult educational level; OR 0.67 (95%CI 0.48, 0.95) (Martin et al 2004). However in analyses of all cause mortality age 26-54 years in the 1946 British birth cohort, adjustment for adult educational status substantially attenuated mortality risks in men (from a Hazard Ratio of 2.0 (95%CI 1.2, 3.4) to HR of 1.5 (95%CI 0.9, 2.7)), but not for women (unadjusted HR of 1.1(95%CI 0.7, 2.1) and adjusted HR of 1.1 (95%CI 0.6, 2.1)).

Adult adiposity and adult educational qualifications

In line with findings presented here based on the 45-year obesity data from the 1958 cohort, a previous study of the cohort looking at growth in BMI between age 16 and 42 years reported that associations between cognition and later obesity were mediated by attained adult educational qualifications (by 23 years) and summary measures of diet indicated by consumption of fresh fruit, fried food and chips (Chandola et al 2006b). A study of men entering the Danish Military draft board (median age 19 years) reported inverse associations between cognitive ability scores measured at that time and concurrent BMI, and also inverse associations with change in BMI at a later survey (Halkjaer et al 2003). The study also had information about the men's highest educational level and demonstrated inverse associations between BMI and educational level. However the associations between cognitive ability and obesity were all attenuated to null on adjustment for educational level. The authors concluded that educational attainment may act as a mediator between cognitive ability and later BMI, or that the IQ test may be a marker of educational attainment (the timing of the test being after most men gained their qualifications). The greater importance of adult qualifications in contrast to childhood ability was also seen in a study using the children of the 1950s cohort (Lawlor et al 2006a). The cohort includes children born in Scotland between 1950 and 1956, the sex and age adjusted mean change in adult BMI (within the range of ages 45-42 years) for each standard deviation increase in the 7-year intelligence test was -0.35 kg/m^2. The association between 7-year ability and adult BMI was entirely mediated by adult educational level. This was a sibling pair study which allowed a comparison of the associations between educational level and adult BMI within and between sibling pairs; the within-sibling pair effect of adult qualifications on BMI was greater than that between sibling pairs which gives further insight into the association between education and BMI. The authors did not conclude that low childhood IQ resulted in

low adult educational level and in turn that raised the risk of adult obesity. However the absence of association between educational level and adult BMI within sibling pairs was interpreted as evidence that the educational level-BMI association was due to factors shared by siblings from the same family such as social position, parental intelligence, school and neighbourhood characteristics. Other data from the 1946 study also indicates that weight and weight gain were associated with cognitive ability in early adulthood and educational achievements, whilst there was some association between cognitive ability and adult height (Richards et al 2002).

Adult qualifications and occupational position are sometimes used interchangeably in epidemiological studies, however they may tap into different aspects of accumulated life experience. Indeed when associations between the disease outcomes with these two measures are compared, they do not show identical results. For example analysis of German data indicated that there were gradients in diabetes by income, adult social class and also non-linear associations with highest qualifications, and that these were independent effects, representing separate dimensions (Geyer et al 2006). Analysis of British mortality data also found that there were varying effects of social position and education on the different mortality endpoints (Davey Smith et al. 1998). Occupational social position is often used as an indicator of income and available material resources and hence opportunities to take healthy life choices. Occupational social position reflects the type of employment and the prestige associated with a certain job, it may indicate whether a person is likely to be in a physically risky job, or have low job security and poor working conditions. The importance of education as opposed to occupational measures of class in explaining health differentials may be ascribed to its strong correlation with knowledge and how to use knowledge to adapt to new or challenging situations. Educational level may also reflect more of a cultural than a material heritage, and because education is started in childhood, is correlated with childhood social origins. Education may also influence self esteem and self confidence which are known to be associated with behavioural choices (Leganger & Kraft 2003) (discussed in Chapter 4 on cognition and health behaviours). Given the complex nature of diabetes, there may be pathways from cognitive ability to poorer health operating via level of self-care and care-seeking in patients with diabetes. There is a literature about the associations between type 2 diabetes and educational achievements discussing the importance of education in influencing decisions about care seeking, service use and self-monitoring of diabetes but this will be discussed in chapter 7.

Associations between childhood IQ and adult health may be due to childhood IQ representing the effects of adult IQ level which is more critical than childhood IQ in shaping adult occupational and domestic circumstances and expectations and attitudes towards health behaviours. If childhood ability indeed reflects later adult IQ then studies with both childhood and adult IQ should show that the effects of childhood ability are mediated by adult ability. It is not possible to test this hypothesis in this dataset due to the lack of IQ data in adulthood. Whilst

final educational qualifications are strongly correlated with IQ they offer an incomplete measure of the construct.

Adult factors: adiposity in adulthood as a mediator between cognition and diabetes

Associations between cognition and diabetes may operate through adult obesity. It is well established that obesity (Colditz et al 1990), and in particular central obesity (large waist circumference or high ratio of waist :hip circumference) (Chan et al. 1994), are important risk factors for diabetes onset. In line with current knowledge, analyses presented here indicated that both BMI and waist circumference were important mediators on the pathway to diabetes risk; the analyses of HbA_{1c} and high HbA_{1c}/diabetes indicate that part of the effect of cognition acts through both total and central adiposity. The associations between childhood cognition and adult adiposity have been discussed above and there was evidence that highest educational level strongly mediates between 7-year cognitive ability and adult obesity and large waist circumference.

Adult ability and diabetes risk

The literature about childhood IQ and adult disease fits with well known associations between disease and cognition at older ages; there is evidence that presence of diabetes and metabolic syndrome are associated with cognitive decline in adult life (Allen et al 2004; Elias et al. 2005; Messier 2005)(Yaffe 2004). Adult vascular diseases are associated with decline in adult cognitive functioning. It is thought that in late adulthood, poorer circulation seen in vascular disease affects other organs and systems also affects brain functioning and cognitive ability. There is little literature about HbA_{1c} levels, but a small study reports that HbA_{1c} levels in healthy non-diabetic men aged 65-70 years were associated with verbal memory; subjects with higher HbA_{1c} had lower scores on memory tests. However, whilst HbA_{1c} was correlated with plasma glucose, plasma glucose itself was not correlated with memory test scores (MacLullich et al. 2004). A longitudinal study reported inverse associations between HbA_{1c} levels and verbal fluency tests in women aged 42-89 years (Kanaya et al 2004). Other research exists showing that adults with diabetes have poorer cognitive functioning and greater decline in cognitive functioning (Allen et al 2004; Kumari & Marmot 2005). However the results presented here and elsewhere (Martin et al 2004) indicate that people with poorer midlife glucose regulation were more likely to have poorer cognitive ability already in childhood. Taking this information together with the demonstrated continuities in cognition from childhood to adulthood cognitive functioning and decline (Richards et al. 2004), raises the possibility that the reported deficits in cognitive ability among diabetics may be due in part to selection processes. If there is indeed selection, and individuals with lower childhood cognitive ability are at greater risk of diabetes and of cognitive decline in adulthood, then the literature about mid-life cognitive ability and diabetic status may need to be re-evaluated. Whilst there are quite plausible mechanisms for cognitive impairment arising from poor metabolic control, studies which do not take

account of pre-morbid cognitive functioning may overestimate the effects of poor metabolic control on adult cognition. The slow and silent onset of poor metabolic control also means that it may be difficult to conduct such studies as many people with poor control will not know their status and long-term follow up studies would be required to achieve a full evaluation of the true strength of association between poor glycaemic control and later cognitive decline.

Summary and next stages

This chapter has focused on the importance of childhood ability and later diabetic risks. The evidence discussed here points to the importance of childhood cognitive ability and social background setting up pathways into adult life, which then shape diabetes risk. These pathways may operate through attained socio economic status and educational level. This may be via accumulation of risk factors through exposure to different social situations, relating for example to employment and also through attitudes to health behaviours, particularly if they impact on adiposity. Putting this into context, other research relating factors from childhood to adult diabetic risk has been focused on the importance of growth *in utero* and subsequent growth trajectories through childhood. Adults who were small at birth and exhibit catch up growth in later life are at higher risk of developing diabetes than those who were larger infants (Newsome et al 2003). Adiposity through the life course has been investigated as a risk factor for diabetes whilst proximate, adult obesity and in particular central obesity (waist circumference and waist-hip ratio) confer increasing risks for developing diabetes (Chan et al 1994; Colditz et al. 1995; Jeffreys et al. 2005; Wannamethee et al 2005). There is also some evidence that there are associations between diabetes risk and childhood anthropometry (Lawlor et al. 2006b). A large amount of literature about diabetes risks is related to diet and physical activity. Firstly there are the studies which have followed up non-diabetic population samples and report that groups with higher fat, lower fibre diets or more sedentary lifestyles are at higher risks of developing disrupted glucose metabolism or even diabetes (Bassuk & Manson 2005; Hu et al. 2001; Manson et al. 1992). Secondly there are many large-scale intervention trials among sufferers of diabetes involving improvements in diet and activity with the aim of improving blood sugar control (Davies et al. 2004; Orchard et al. 2005). The theme of health behaviours will be taken up further in the next chapter with the intention of further unpacking the associations between childhood ability and later risk of poor glucose regulation. The analyses presented so far have helped to start setting up models for pathways to disease risk but the next chapter will build on and extend the results presented so far.

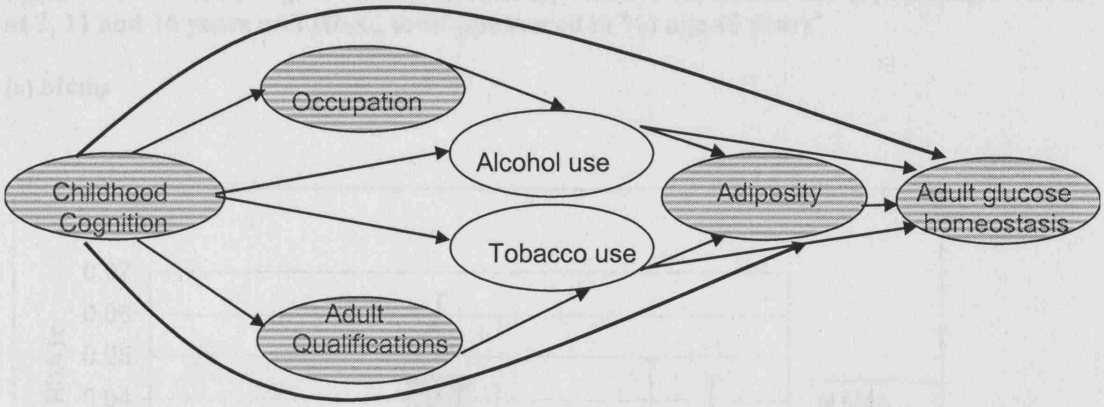
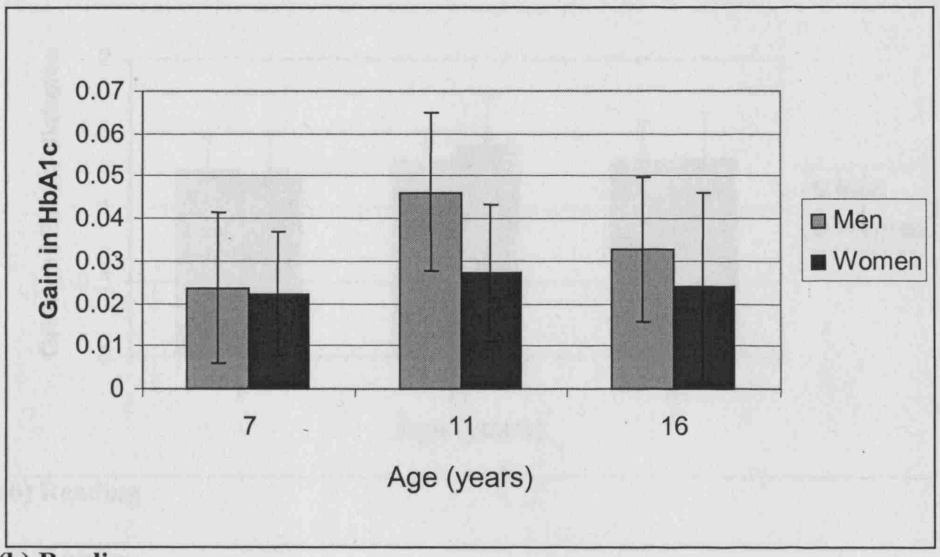


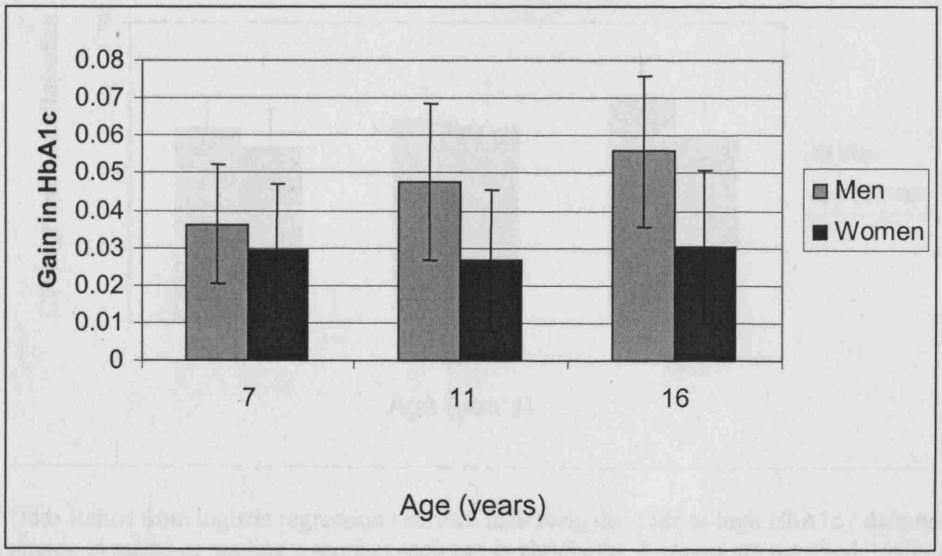
Figure 6.1 Conceptual framework, outlining main relationships to be examined

Figure 6.2 Association [β coefficient (95%CI)] between (a) maths and (b) reading z-scores at 7, 11 and 16 years and HbA_{1c} level (measured in %) age 45 years[a]

(a) Maths



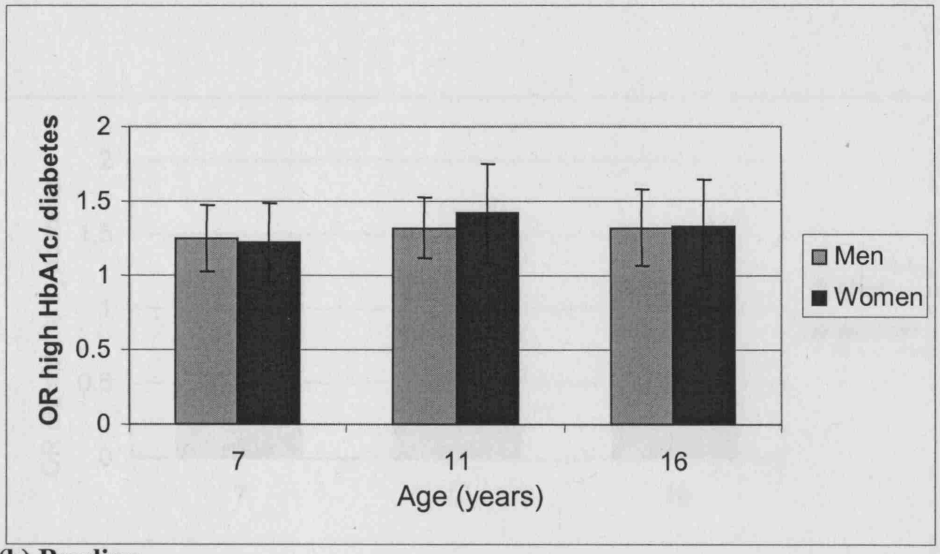
(b) Reading



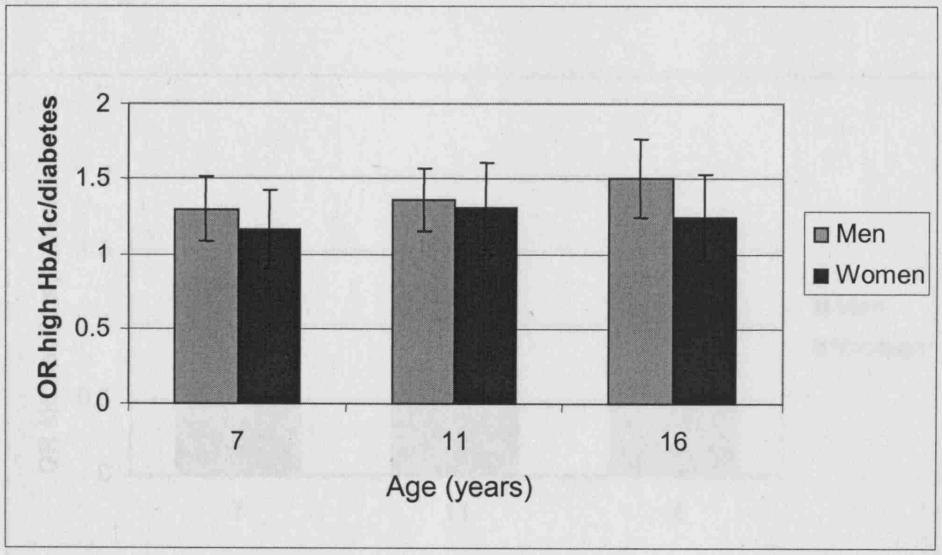
[a] b coefficients from linear regression analyses indicating the change in HbA_{1c} level per SD increase in maths or reading z-score at each age in childhood. Z-scores are reversed; increase in z-score represents decline in ability rank.

Figure 6.3 Association [OR (95%CI)] between (a) maths and (b) reading z-scores at 7, 11 and 16 years and presence of elevated HbA1c / diabetes age 45 years[a]

(a) Maths



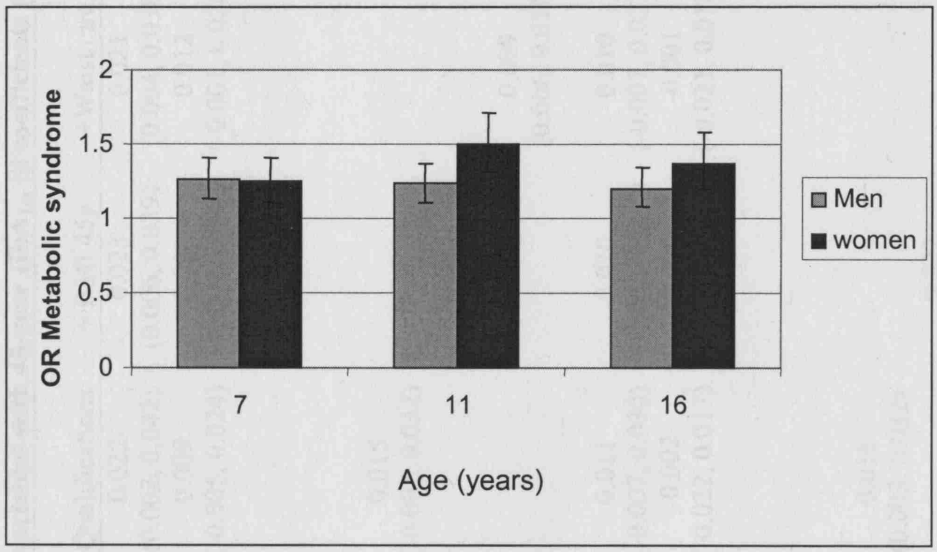
(b) Reading



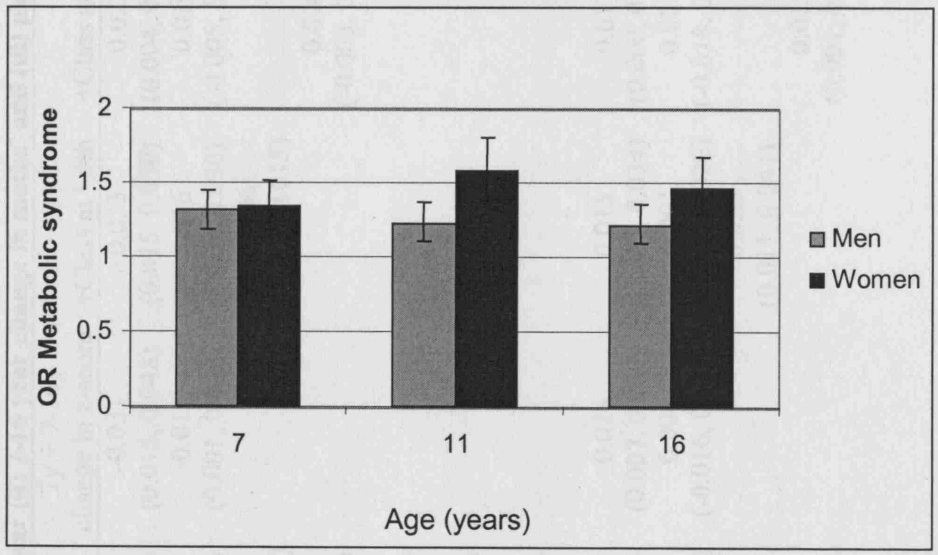
[a] Odds Ratios from logistic regression analyses indicating the odds of high HbA1c / diabetes per SD increase in maths or reading z-score at each age in childhood. Z-scores are reversed; increase in z-score represents decline in ability rank.

Figure 6.4 Association [OR (95%CI)] between (a) maths and (b) reading z-scores at 7, 11 and 16 years and presence of metabolic syndrome age 45 years[a]

(a) Maths



(b) reading



[a] Odds Ratios from logistic regression analyses indicating the odds of metabolic syndrome per SD increase in maths or reading z-score at each age in childhood. Z-scores are reversed; increase in z-score represents decline in ability rank.

Table 6.1 Associations between (i) 7-year (ii) 7-16 year change in maths[a] and (iii) pathways variables with 45-year HbA_{1c}, [β coefficients (95% CI)]

Men	N=3107 Unadjusted	7y + 7-16y change in z-score	+Class at birth	+Class at 33 y	+Qualifications	+ BMI 45y	+Waist circ.	+ All
7-year maths z-score	0.031 (0.014, 0.047)	0.031 (0.015, 0.048)	0.033 (0.015, 0.050)	0.023 (0.004, 0.043)	0.022 (0.002, 0.042)	0.023 (0.006, 0.039)	0.021 (0.004, 0.038)	0.015 (-0.006, 0.036)
7-16y change in maths z-score	0.014 (0.001, 0.028)	0.015 (0.001, 0.028)	0.016 (0.002, 0.030)	0.010 (-0.005, 0.025)	0.009 (-0.005, 0.024)	0.011 (-0.002, 0.025)	0.012 (-0.001, 0.026)	0.008 (-0.007, 0.023)
Class at birth	0.006 (-0.013, 0.025)		-0.006 (-0.027, 0.015)					-0.018 (-0.040, 0.004)
Class at 33y	0.028 (0.012, 0.044)			0.016 (-0.003, 0.036)				0.015 (-0.004, 0.035)
Qualifications (33y)	0.027 (0.013, 0.040)				0.015 (-0.002, 0.032)			0.007 (-0.011, 0.024)
BMI (45y)	0.022 (0.015, 0.029)					0.021 (0.014, 0.029)		0.006 (-0.002, 0.014)
Waist circ (45y)	0.009 (0.007, 0.012)						0.009 (0.006, 0.012)	0.007 (0.004, 0.010)
Women	N=3260							
7-year maths z-score	0.023 (0.007, 0.038)	0.023 (0.007, 0.040)	0.015 (-0.003, 0.034)	0.017 (0.000, 0.034)	0.011 (-0.007, 0.030)	0.010 (-0.006, 0.027)	0.010 (-0.007, 0.027)	0.000 (-0.019, 0.020)
7-16y change in maths z-score	0.000 (-0.019, 0.019)	0.004 (-0.016, 0.024)	-0.001 (-0.022, 0.020)	0.001 (-0.018, 0.021)	-0.002 (-0.022, 0.017)	0.000 (-0.020, 0.020)	-0.001 (-0.021, 0.018)	-0.006 (-0.026, 0.013)
Class at birth	0.028 (0.016, 0.041)		0.026 (0.011, 0.041)					0.012 (-0.003, 0.026)
Class at 33y	0.020 (0.005, 0.034)			0.015 (0.001, 0.029)				0.004 (-0.009, 0.017)
Qualifications (33y)	0.021 (0.007, 0.035)				0.018 (0.003, 0.032)			0.006 (0.008, 0.020)
BMI (45y)	0.021 (0.018, 0.025)					0.022 (0.017, 0.026)		0.009 (0.002, 0.015)
Waist circ (45y)	0.010 (0.008, 0.011)						0.010 (0.008, 0.011)	0.006 (0.003, 0.009)

[a] z-scores (from models of trajectories 7-16 y) are reversed; increase in score represents decline in ability rank.

Table 6.2 Associations between level and change in childhood maths[a] with 45-year elevated Hba1c/ type 2 diabetes, [OR (95% CI)]

Men	n=3147							
	Unadjusted	7-year + 7-16 year change in z-score	+Class at birth	+Class at 33 y	+Qualifications	+ BMI 45y	+Waist circ. 45y	+ All
7y maths z-score	1.36 (1.14, 1.62)	1.36 (1.14, 1.63)	1.29 (1.08, 1.56)	1.32 (1.08, 1.60)	1.15 (0.93, 1.42)	1.25 (1.04, 1.50)	1.24 (1.03, 1.49)	1.11 (0.89, 1.39)
7-16y change in maths z-score	1.06 (0.90, 1.25)	1.08 (0.91, 1.27)	1.04 (0.87, 1.23)	1.05 (0.88, 1.25)	0.97 (0.80, 1.16)	1.06 (0.90, 1.26)	1.06 (0.89, 1.25)	0.99 (0.82, 1.19)
Class at birth	1.34 (1.12, 1.61)		1.24 (1.02, 1.50)					1.08 (0.88, 1.31)
Class at 33y	1.20 (1.04, 1.40)			1.08 (0.91, 1.28)				0.94 (0.78, 1.13)
Qualifications	1.36 (1.19, 1.55)				1.30 (1.11, 1.54)			1.21 (1.01, 1.45)
BMI (45y)	1.21 (1.17, 1.25)					1.21 (1.16, 1.25)		1.13 (1.04, 1.22)
Waist circ (45y)	1.08 (1.06, 1.09)						1.07 (1.06, 1.09)	1.03 (1.00, 1.06)
Women	n=3288							
7y maths z-score	1.32 (1.07, 1.62)	1.34 (1.08, 1.65)	1.26 (1.01, 1.57)	1.33 (1.06, 1.67)	1.20 (0.93, 1.55)	1.16 (0.92, 1.46)	1.13 (0.90, 1.42)	1.14 (0.86, 1.52)
7-16y change in maths z-score	0.99 (0.82, 1.19)	1.05 (0.86, 1.28)	1.01 (0.83, 1.24)	1.05 (0.86, 1.28)	1.00 (0.81, 1.23)	1.02 (0.83, 1.26)	0.99 (0.81, 1.22)	0.99 (0.79, 1.25)
Class at birth	1.31 (1.06, 1.62)		1.23 (0.98, 1.54)					1.08 (0.84, 1.39)
Class at 33y	1.10 (0.93, 1.30)			1.01 (0.84, 1.21)				0.88 (0.71, 1.10)
Qualifications	1.23 (1.06, 1.44)				1.16 (0.95, 1.40)			1.04 (0.83, 1.29)
BMI (45y)	1.20 (1.17, 1.23)					1.20 (1.17, 1.24)		1.01 (0.95, 1.08)
Waist circ (45y)	1.10 (1.09, 1.12)						1.10 (1.09, 1.12)	1.10 (1.06, 1.13)

[a] z-scores (from models of trajectories 7-16 y) are reversed; increase in score represents decline in ability rank.

Table 6.3. Associations between level and change in childhood maths[a] with 45-year metabolic syndrome, [OR (95% CI)]

Men	N=3057					
	Unadjusted	7-year + 7-16 year change in z-score	+Class at birth	+Class at 33 y	+Qualifications	+ All
7y maths z-score	1.23 (1.09, 1.37)	1.23 (1.10, 1.37)	1.19 (1.06, 1.34)	1.21 (1.07, 1.37)	1.13 (0.99, 1.29)	1.12 (0.98, 1.29)
7-16y change in maths z-score	1.01 (0.91, 1.13)	1.02 (0.92, 1.13)	1.00 (0.90, 1.11)	1.01 (0.91, 1.13)	0.97 (0.86, 1.09)	0.96 (0.86, 1.08)
Class at birth	1.16 (1.04, 1.30)		1.12 (0.99, 1.26)			1.10 (0.98, 1.24)
Class at 33y	1.09 (0.99, 1.20)			1.02 (0.92, 1.14)		0.97 (0.87, 1.09)
Qualifications	1.18 (1.08, 1.29)				1.14 (1.02, 1.27)	1.13 (1.01, 1.27)
Women	n=3202					
7-year maths z-score	1.38 (1.22, 1.56)	1.42 (1.25, 1.61)	1.32 (1.16, 1.51)	1.29 (1.12, 1.48)	1.17 (1.00, 1.36)	1.10 (0.94, 1.28)
7-16y change in maths z-score	1.03 (0.92, 1.15)	1.11 (0.98, 1.24)	1.06 (0.94, 1.19)	1.06 (0.94, 1.19)	1.00 (0.88, 1.14)	0.97 (0.85, 1.10)
Class at birth	1.39 (1.22, 1.58)		1.29 (1.13, 1.48)			1.23 (1.07, 1.41)
Class at 33y	1.33 (1.20, 1.47)			1.23 (1.10, 1.37)		1.13 (1.01, 1.27)
Qualifications	1.38 (1.26, 1.52)				1.31 (1.16, 1.46)	1.21 (1.07, 1.37)

[a] z-scores (from models of trajectories 7-16 y) are reversed; increase in score represents decline in ability rank.

Chapter 6 Childhood cognitive development and mid-life glucose homeostasis

Appendix 6.1	**Sample representativeness**
Appendix 6.2	**Associations between maths and reading trajectories and pathway variables**
Appendix 6.3	**Associations between reading trajectories and HbA_{1c}, elevated HbA_{1c} /type 2 diabetes and metabolic syndrome**
Appendix 6.4	**Associations between maths or reading trajectories and HbA_{1c}, elevated HbA_{1c} /type 2 diabetes and metabolic syndrome, including birthweight and gestational age**
Appendix 6.5	**Associations between maths or reading trajectories and total and central obesity**

Table A.6.1 Sample representativeness; distribution [%(n)] of social class at birth in the original birth sample compared with the distribution in the sample with valid HbA_{1c} and the analysis sample

	Birth sample		45-year sample with HbA_{1c} [a]		Analysis sample for HbA_{1c} models[b]	
	N	% (95%CI)	N	% (95%CI)	N	% (95%CI)
Total N	16,966		7214		6109	
Men						
Class I&II professional	1488	17.0 (16.2,17.8)	698	19.3 (18.0,20.6)	606	20.2 (18.9,21.8)
Class IV&V & no head of household	2096	23.9 (23.0,24.8)	778	21.5 (20.2,22.9)	608	20.3 (18.9,21.8)
Women						
Class I&II professional	1391	16.9 (16.1,17.8)	652	18.1 (16.9,19.4)	565	18.1 (16.8,19.5)
Class IV&V & no head of household	2025	24.7 (23.7,25.6)	800	22.2 (20.9,23.6)	678	21.7 (20.3,23.2)

[a]sample at 45 years=7799. The total N with data on social class at birth is 7214/7799

[b]Analysis sample at 45 years for HbA_{1c} models=6109. The total N with data on social class at birth is 6109.

There is some evidence that the 45 year sample under-represents those in more manual social classes. Further there is evidence that the analysis sample for the HbA_{1c} models (with full data on all the pathway factors presented in the regression analyses) is more biased towards the professional classes and less representative of those with manual origins, particularly among men.

Appendix 6.2

Table A.6.2.1a Distribution (%) of maths7-year z-score by the pathway variables (men)

	Quintiles of maths7-year z-score					*Total*		
	Highest ability	2	3	4	Lowest Ability	*%*	*n*	Linear trend[a]
Intercept	21.0	20.4	20.0	19.7	18.9	*100*	*8643*	
			Birthweight (Kg)					
<2.5	3.2	3.5	4.5	6.2	7.8	*5.0*	*388*	P<0.001
2.5-3.0	11.6	14.6	16.7	17.5	20.3	*16.0*	*1250*	
3.0-3.5	33.6	37.0	34.6	36.4	34.1	*35.2*	*2743*	
3.5-4.0	38.2	31.6	33.0	30.2	27.8	*32.3*	*2516*	
4.0-max	13.5	13.3	11.2	9.8	9.9	*11.6*	*904*	
			45-year BMI (Kg/m^2)					
Min- 25	28.0	26.4	25.0	22.3	21.4	*25.1*	*1151*	P<0.001
25- 30	52.5	49.8	48.9	48.2	47.0	*49.5*	*2269*	
30- 35	14.2	20.0	19.8	22.2	23.3	*19.5*	*891*	
35-max	5.0	3.9	6.0	7.3	8.3	*5.9*	*269*	
			45-year waist circumference					
Low	39.0	38.0	37.0	32.6	36.1	*31.7*	*1644*	P<0.001
Medium	32.7	31.0	33.3	29.9	31.2	*27.5*	*1419*	
High	28.6	31.0	29.5	37.6	32.8	*40.8*	*1492*	
HbA_{1c} [a]	5.236	5.241	5.265	5.341	5.382	*5.283*	*3921*	P<0.001
			HbA_{1c} >6% /diabetes					
No	95.8	96.7	94.4	92.7	91.9	*94.6*	*3664*	P<0.001
Yes	4.2	3.3	5.6	7.3	8.1	*5.5*	*211*	
			Metabolic syndrome					
No	89.5	90.4	87.8	83.9	82.9	*82.9*	*3244*	P<0.001
Yes	10.5	9.6	12.2	16.1	17.2	*12.6*	*470*	

[a] Tests for linear trend use intercept as a continuous variable and BMI, waist circumference & HbA_{1c} as continuous variables

Table A.6.2.b Distribution (%) of maths7-year z-score by pathway variables (women)

	Quintiles of maths7-year z-score					*Total*		
	Highest ability	2	3	4	Lowest Ability	*%*	*n*	Linear trend[a]
Intercept	19.0	19.5	19.5	20.3	21.2	*100.0*	*8643*	
			Birthweight (Kg)					
<2.5	2.9	5.5	6.0	8.5	10.5	*6.8*	*388*	P<0.001
2.5-3.0	18.8	21.4	20.4	22.7	25.3	*21.8*	*1250*	
3.0-3.5	40.8	39.0	39.6	40.4	39.3	*39.8*	*2743*	
3.5-4.0	29.2	26.7	26.9	22.6	18.9	*24.8*	*2516*	
4.0-max	8.3	7.3	7.2	5.8	6.0	*6.9*	*904*	
			45-year BMI (Kg/m^2)					
Min- 25	48.6	45.9	41.4	41.7	38.4	*43.5*	*1151*	P<0.001
25- 30	32.2	33.4	33.4	31.4	33.7	*32.8*	*2269*	
30- 35	12.8	13.6	14.5	17.0	15.2	*14.6*	*891*	
35-max	6.4	7.1	10.7	9.9	12.7	*9.2*	*269*	
			45-year waist circumference					
Low	44.4	41.6	36.8	35.7	38.6	*33.0*	*1644*	P<0.001
Medium	23.9	23.2	25.2	26.1	24.4	*23.9*	*1419*	
High	31.8	35.3	38.1	38.3	37.0	*43.1*	*1492*	
HbA_{1c} [a]	5.236	5.241	5.265	5.341	5.382	*5.283*	*3921*	P<0.001
			HbA_{1c} >6% /diabetes					
No	97.4	96.7	97.0	96.0	94.4	*96.3*	*3664*	P<0.001
Yes	2.6	3.3	3.0	4.4	5.7	*3.7*	*211*	
			Metabolic syndrome					
No	94.5	89.8	90.1	89.3	84.5	*89.9*	*3244*	P<0.001
Yes	5.5	10.2	9.9	10.7	15.5	*10.1*	*470*	

[a] Tests for linear trend use intercept as a continuous variable and BMI, waist circumference & HbA_{1c} as continuous variables

Table A.6.2.2a Distribution (%) of 7-16 year change in maths z-score by pathway variables (men)

	Quintiles of 7-16 year change in maths z-score					*Total*		
	Highest ability	2	3	4	Lowest Ability	*%*	*n*	Linear trend[a]
Slope	23.2	21.0	19.8	19.3	16.8	*100.0*	*8643*	
			Birthweight (Kg)					
<2.5	4.3	5.6	5.1	4.6	5.5	*5.0*	*388*	P=0.005
2.5-3.0	14.0	16.8	16.1	16.5	17.0	*16.0*	*1250*	
3.0-3.5	35.2	33.7	35.6	35.5	36.0	*35.2*	*2743*	
3.5-4.0	34.5	33.2	29.8	32.6	30.5	*32.3*	*2516*	
4.0-max	12.0	10.8	13.5	10.8	11.0	*11.6*	*904*	
			45-year BMI (Kg/m^2)					
Min- 25	27.5	24.1	25.1	24.3	23.3	*25.1*	*1151*	p=0.033
25- 30	48.7	51.8	48.7	47.7	51.3	*49.5*	*2269*	
30- 35	18.5	18.4	19.7	21.1	20.5	*19.5*	*891*	
35-max	5.3	5.8	6.6	6.9	5.0	*5.9*	*269*	
			45-year waist circumference					
Low	36.5	36.5	36.8	33.9	36.1	*36.5*	*1644*	p=0.425
Medium	31.2	31.3	30.5	31.1	31.0	*31.7*	*1419*	
High	32.3	32.2	32.7	35.0	32.8	*31.7*	*1492*	
			HbA_{1c}					
Mean	5.236	5.241	5.265	5.341	5.382	*5.283*	*3921*	p=0.006
			HbA_{1c} >6% /diabetes					
No	96.1	94.2	93.4	93.1	95.5	*94.6*	*3664*	p=0.197
Yes	3.9	5.8	6.7	6.9	4.6	*5.5*	*211*	
			Metabolic syndrome					
No	88.0	88.6	87.6	86.0	88.5	*87.4*	*3244*	
Yes	12.0	11.4	12.5	14.1	11.5	*12.7*	*470*	P=0.005

[a] Tests for linear trend use intercept as a continuous variable and BMI, waist circumference & HbA_{1c} as continuous variables

Table A.6.2.2b Distribution (%) of 7-16 year change in maths z-score by pathway variables (women)

	Quintiles of 7-16 year change in maths z-score					*Total*		
	Highest ability	2	3	4	Lowest Ability	*%*		Linear Trend[a]
Slope	16.6	16.6	20.3	20.8	23.4	*100.0*	*1908*	
			Birthweight (Kg)					
<2.5	6.6	6.7	6.7	7.2	6.6	*6.8*	*503*	P<0.001
2.5-3.0	21.1	23.0	24.1	20.8	20.1	*21.8*	*1620*	
3.0-3.5	39.1	40.5	39.3	41.2	38.9	*39.8*	*2963*	
3.5-4.0	25.9	23.8	23.4	23.6	26.9	*24.8*	*1843*	
4.0-max	7.2	5.9	6.5	7.1	7.6	*6.9*	*513*	
			45-year BMI (Kg/m^2)					
Min- 25	47.1	42.8	45.5	40.7	41.9	*43.5*	*2015*	p=0.019
25- 30	29.9	36.0	32.3	33.7	32.3	*32.8*	*1521*	
30- 35	14.4	13.2	12.8	16.1	15.9	*14.6*	*675*	
35-max	8.6	8.0	9.5	9.6	10.0	*9.2*	*426*	
			45-year waist circumference					
Low	44.4	38.0	39.4	36.2	38.6	*36.0*	*1778*	p=0.002
Medium	21.2	25.7	26.7	25.0	24.4	*23.7*	*1125*	
High	34.4	36.3	33.8	38.9	37.0	*40.3*	*1703*	
			HbA_{1c}					
Mean	5.148	5.131	5.179	5.162	5.176	*5.160*	*3899*	p=0.249
			HbA_{1c} >6% /diabetes					
No	96.2	97.0	96.9	95.9	95.7	*96.3*	*3717*	p=0.713
Yes	3.8	3.0	3.1	4.2	4.3	*3.7*	*143*	
			Metabolic syndrome					
No	90.8	89.7	90.2	90.3	88.8	*89.9*	*3326*	p=0.038
Yes	9.2	10.3	9.8	9.7	11.2	*10.1*	*374*	

[a] Tests for linear trend use intercept as a continuous variable and BMI, waist circumference & HbA_{1c} as continuous variables

Table A.6.2.3a Distribution (%) of 7-year reading z-score by pathway variables (men)

	Quintiles of 7-year reading z-score					*Total*		
	Highest ability	2	3	4	Lowest Ability	*%*	*N*	Linear trend[a]
Intercept	15.5	18.6	20.3	21.4	24.1	*100.0*	*8644*	
				Birthweight (Kg)				
<2.5	2.8	3.3	3.8	6.2	7.7	*5.0*	*388*	P<0.001
2.5-3.0	12.3	14.8	15.7	16.0	19.9	*16.0*	*1250*	
3.0-3.5	35.6	34.5	34.1	36.8	34.8	*35.2*	*2744*	
3.5-4.0	35.6	33.9	34.6	30.7	28.2	*32.3*	*2517*	
4.0-max	13.7	13.6	11.8	10.3	9.5	*11.6*	*903*	
				45-year BMI (Kg/m^2)				
Min- 25	32.7	24.6	23.7	22.8	22.7	*25.1*	*1151*	P<0.001
25- 30	48.1	54.2	49.5	49.6	45.9	*49.5*	*2268*	
30- 35	14.1	16.8	21.9	21.0	23.0	*19.5*	*891*	
35-max	5.1	4.4	4.9	6.6	8.4	*5.9*	*270*	
				45-year waist circumference				
Low	40.1	36.8	36.3	33.6	34.1	*36.1*	*1644*	P<0.001
Med	31.6	33.9	32.0	31.8	26.2	*31.2*	*1419*	
High	28.3	29.3	31.7	34.6	39.7	*32.8*	*1492*	
				HbA_{1c}				
Mean	5.203	5.236	5.248	5.39	5.338	*5.283*	*3921*	P<0.001
				HbA_{1c} >6% /diabetes				
No	96.4	96.4	95.6	93.6	90.9	*94.6*	*3,664*	P<0.001
Yes	3.6	3.6	4.4	6.5	9.1	*5.5*	*211*	
				Metabolic syndrome				
No	90.7	91.3	85.5	86.7	82.9	*87.4*	*3244*	P<0.001
Yes	9.3	8.7	14.5	13.3	17.1	*12.7*	*470*	

[a] Tests for linear trend use intercept as a continuous variable and BMI, waist circumference & HbA_{1c} as continuous variables

Table A.6.2.3b Distribution (%) of 7-year reading z-score by the pathway variables (women)

	Quintiles of 7-year reading z-score					*Total*		
	Highest ability	2	3	4	Lowest ability	*%*	*N*	linear trend[a]
Intercept	24.8	21.5	21.5	18.5	15.6	*100.0*	*8,155*	
				Birthweight (Kg)				
<2.5	3.7	5.3	7.3	8.5	11.4	*6.8*	*504*	P<0.001
2.5-3.0	19.8	19.7	22.4	22.5	26.3	*21.8*	*1620*	
3.0-3.5	40.0	41.6	39.4	40.0	37.2	*39.8*	*2961*	
3.5-4.0	28.6	26.6	24.3	22.1	19.6	*24.8*	*1842*	
4.0-max	8.1	6.9	6.7	6.9	5.5	*6.9*	*515*	
				45-year BMI (Kg/m^2)				
Min- 25	48.5	46.4	41.8	38.8	35.5	*43.5*	*2015*	P<0.001
25- 30	33.1	31.9	33.0	33.1	33.3	*32.8*	*1522*	
30- 35	12.9	14.0	15.2	15.6	16.9	*14.5*	*674*	
35-max	5.6	7.8	10.0	12.6	14.2	*9.2*	*426*	
				45-year waist circumference				
Low	44.2	40.2	39.3	33.8	27.9	*38.6*	*1778*	P<0.001
Med	25.1	24.5	21.8	24.8	26.5	*24.4*	*1125*	
High	30.6	35.3	38.9	41.4	45.6	*37.0*	*1703*	
				HbA_{1c}[a]				
Mean	5.113	5.128	5.176	5.192	5.263	*5.160*	*3899*	P<0.001
				HbA_{1c} >6% /diabetes				
No	97.7	96.7	95.5	95.4	94.9	*96.3*	*3,717*	P=0.001
Yes	2.3	3.3	4.5	4.6	5.2	*3.7*	*143*	
				Metabolic Syndrome				
No	93.8	91.2	88.7	87.7	83.1	*89.9*	*3326*	P<0.001
yes	6.2	8.8	11.3	12.3	16.9	*10.1*	*374*	

[a]Tests for linear trend use intercept as a continuous variable and BMI, waist circumference & HbA_{1c} as continuous variables

Table A.6.2.4a Distribution (%) of 7-16 year change in reading z-score by the pathway variables (men)

	Quintiles of 7-16 year change in reading z-score					*Total*		
	Highest ability	2	3	4	Lowest ability	*%*	*n*	linear trend[a]
Slope	32.8	29.7	20.9	10.8	5.8	*100.0*	*8644*	
				Birthweight (Kg)				
<2.5	4.1	4.8	6.2	7.2	2.3	*5.0*	*388*	P=0.008
2.5-3.0	14.2	15.5	18.6	17.9	16.4	*16.0*	*1250*	
3.0-3.5	36.7	34.6	34.0	33.9	36.3	*35.2*	*2744*	
3.5-4.0	33.8	33.0	29.9	29.0	34.4	*32.3*	*2517*	
4.0-max	11.2	12.2	11.3	12.1	10.7	*11.6*	*903*	
				45-year BMI (Kg/m^2)				
Min- 25	26.3	25.1	24.7	22.8	23.8	*25.1*	*1151*	p=0.351
25- 30	50.2	48.3	48.7	50.8	51.3	*49.5*	*2268*	
30- 35	18.1	20.2	20.0	21.3	19.2	*19.5*	*891*	
35-max	5.4	6.4	6.7	5.2	5.8	*5.9*	*270*	
				45-year waist circumference				
Low	35.0	36.2	36.4	35.8	36.1	*42.7*	*1644*	p=0.224
Medium	32.9	29.2	30.8	32.1	31.2	*28.5*	*1419*	
High	32.1	34.6	32.8	32.1	32.8	*28.9*	*1492*	
				HbA_{1c}				
Mean	5.237	5.301	5.330	5.301	5.304	*5.283*	*3921*	p=0.006
				HbA_{1c} >6% /diabetes				
No	95.5	94.1	93.9	94.1	93.6	*94.6*	*3664*	p=0.083
Yes	4.5	5.9	6.1	5.9	6.4	*5.5*	*211*	
				Metabolic syndrome				
No	86.8	86.2	88.2	89.6	89.8	*87.4*	*3244*	p=0.155
Yes	13.2	13.8	11.8	10.4	10.2	*12.7*	*470*	

[a] Tests for linear trend use intercept as a continuous variable and BMI, waist circumference & HbA_{1c} as continuous variables

Table A.6.2.4b Distribution (%) of 7-16 year change in reading z-score by the pathway variables (women)

	Quintiles of 7-16 year change in reading z-score					*Total*		
	Highest ability	2	3	4	Lowest ability	*%*	*n*	linear trend[a]
Slope	6.4	10.0	10.0	29.8	35.1	*100.0*	*8,155*	
				Birthweight (Kg)				
<2.5	5.8	6.5	6.5	7.6	6.5	*6.8*	*504*	p=0.692
2.5-3.0	20.7	23.2	22.1	21.2	21.8	*21.8*	*1620*	
3.0-3.5	40.4	38.5	39.0	40.4	39.9	*39.8*	*2961*	
3.5-4.0	26.7	24.7	26.1	24.1	24.2	*24.8*	*1842*	
4.0-max	6.4	7.1	6.2	6.7	7.6	*6.9*	*515*	
Higher	34.2	36.7	32.7	23.6	19.3	*26.0*	*1456*	
				45-year BMI (Kg/m^2)				
Min- 25	39.3	45.8	45.1	43.0	43.0	*43.5*	*2015*	p=0.511
25- 30	33.1	30.5	33.4	33.1	33.0	*32.8*	*1522*	
30- 35	16.7	15.3	12.4	14.7	14.9	*14.5*	*674*	
35-max	11.0	8.4	9.1	9.2	9.1	*9.2*	*426*	
				45-year waist circumference				
Low	33.8	41.3	40.4	38.1	38.6	*38.1*	*1778*	p=0.722
Medium	24.8	25.6	23.8	25.0	24.4	*23.8*	*1125*	
High	41.4	33.1	35.8	36.8	37.0	*38.0*	*1703*	
				HbA_{1c}				
Mean	5.219	5.145	5.151	5.151	5.165	*5.160*	*3899*	p=0.475
				HbA_{1c} >6% /diabetes				
No	94.5	96.4	97.0	96.5	96.1	*96.3*	*3717*	p=0.831
Yes	5.5	3.6	3.0	3.5	3.9	*3.7*	*143*	
				Metabolic syndrome				
No	89.7	91.3	91.6	89.9	88.6	*89.9*	*3326*	p=0.097
Yes	10.3	8.7	8.5	10.1	11.4	*10.1*	*374*	

[a] Tests for linear trend use intercept as a continuous variable and BMI, waist circumference & HbA_{1c} as continuous variables

Appendix 6.3:

Table A6.3.1 Associations between 7-year and 7-16 year change in reading z-score[a] with 45-year HbA_{1c}, and univariate associations between each variable and HbA_{1c}, [β coefficients (95% CI)]

Men	n=3107 Unadjusted	7-year + 7-16 y change z-score	+Class at birth	+Class at 33 y	+Qualifications	+ BMI 45y	+Waist circumference	+ All
7-year reading z-score	0.039 (0.020, 0.057)	0.038 (0.019, 0.057)	0.040 (0.019, 0.060)	0.031 (0.008, 0.054)	0.030 (0.009, 0.051)	0.028 (0.009, 0.047)	0.028 (0.009, 0.047)	0.024 (0.001, 0.048)
7-16 year change in reading z-score	0.012 (-0.003, 0.026)	0.009 (-0.005, 0.023)	0.009 (-0.004, 0.023)	0.006 (-0.009, 0.020)	0.006 (-0.008, 0.020)	0.009 (-0.004, 0.023)	0.012 (-0.001, 0.026)	0.009 (-0.005, 0.024)
Class at birth	0.006 (-0.013, 0.025)		-0.007 (-0.028, 0.014)					-0.019 (-0.040, 0.003)
Class at 33y	0.028 (0.012, 0.044)			0.014 (-0.006, 0.035)				0.013 (-0.008, 0.033)
Qualifications (33y)	0.027 (0.013, 0.040)				0.013 (-0.002, 0.028)			0.005 (-0.012, 0.021)
BMI (45y)	0.022 (0.015, 0.029)					0.021 (0.014, 0.028)		0.005 (-0.003, 0.013)
Waist circumference (45y)	0.009 (0.007, 0.012)						0.009 (0.006, 0.012)	0.007 (0.004, 0.010)
Women	n=3260							
7-year reading z-score	0.027 (0.010, 0.044)	0.027 (0.009, 0.044)	0.019 (-0.001, 0.038)	0.020 (0.003, 0.037)	0.014 (-0.004, 0.033)	0.011 (-0.007, 0.028)	0.012 (-0.006, 0.029)	0.001 (-0.017, 0.020)
7-16 year change in reading z-score	-0.004 (-0.020, 0.012)	-0.001 (-0.018, 0.016)	-0.005 (-0.022, 0.013)	-0.004 (-0.020, 0.012)	-0.006 (-0.023, 0.010)	0.000 (-0.016, 0.015)	-0.002 (-0.018, 0.014)	-0.006 (-0.021, 0.010)
Class at birth	0.028 (0.016, 0.041)		0.025 (0.011, 0.039)					0.011 (-0.003, 0.025)
Class at 33y	0.020 (0.005, 0.034)			0.015 (0.001, 0.028)				0.004 (-0.009, 0.017)
Qualifications (33y)	0.021 (0.007, 0.035)				0.017 (0.002, 0.032)			0.005 (-0.009, 0.020)
BMI (45y)	0.021 (0.018, 0.025)					0.021 (0.017, 0.025)		0.009 (0.002, 0.015)
Waist circumference (45y)	0.010 (0.008, 0.011)						0.010 (0.008, 0.011)	0.006 (0.003, 0.009)

[a]Reading scores are derived from multilevel models of initial level and change in reading ability between 7 and 16 years. The reading intercept is the predicted value for maths ability rank at 7 years and reading slope is the change in reading ability rank between 7 and 16 years. The scores are transformed to standard deviation scores and coded inversely (higher scores correspond to lower ability in the reading tests).

Table A6.3.2. Associations between level and change in childhood reading[a] with 45-year elevated HbA_{1c} / type 2 diabetes, [OR (95% CI)]

Men	n=3147 Unadjusted	7-year + 7-16 year change in reading z-score	+Class at birth	+Class at 33 y	+Qualifications	+ BMI 45y	+Waist circumference	+ All
7-year reading z-score	1.44 (1.20, 1.73)	1.44 (1.20, 1.73)	1.37 (1.13, 1.65)	1.40 (1.15, 1.72)	1.24 (1.01, 1.53)	1.31 (1.09, 1.58)	1.31 (1.09, 1.58)	1.21 (0.97, 1.52)
7-16 year change in reading z-score	1.07 (0.91, 1.26)	1.05 (0.89, 1.24)	1.03 (0.87, 1.22)	1.04 (0.87, 1.23)	0.99 (0.84, 1.18)	1.05 (0.89, 1.25)	1.08 (0.91, 1.28)	1.04 (0.87, 1.24)
Class at birth	1.34 (1.12, 1.61)		1.22 (1.01, 1.47)					1.06 (0.87, 1.30)
Class at 33y	1.20 (1.04, 1.40)			1.05 (0.88, 1.25)				0.92 (0.76, 1.11)
Qualifications	1.36 (1.19, 1.55)				1.25 (1.07, 1.47)			1.18 (0.99, 1.40)
BMI (45y)	1.21 (1.17, 1.25)					1.20 (1.16, 1.25)		1.12 (1.04, 1.22)
Waist circ (45y)	1.08 (1.06, 1.09)						1.07 (1.06, 1.09)	1.03 (1.00, 1.06)
Women	n=3288							
7-year reading z-score	1.30 (1.06, 1.59)	1.29 (1.05, 1.58)	1.21 (0.97, 1.50)	1.27 (1.02, 1.59)	1.13 (0.88, 1.45)	1.10 (0.88, 1.38)	1.09 (0.87, 1.36)	1.07 (0.81, 1.42)
7-16 year change in reading z-score	0.93 (0.77, 1.12)	0.95 (0.79, 1.15)	0.93 (0.77, 1.12)	0.95 (0.78, 1.15)	0.90 (0.74, 1.10)	0.98 (0.81, 1.19)	0.93 (0.76, 1.13)	0.93 (0.75, 1.15)
Class at birth	1.31 (1.06, 1.62)		1.25 (1.00, 1.56)					1.10 (0.86, 1.41)
Class at 33y	1.10 (0.93, 1.30)			1.03 (0.86, 1.24)				0.89 (0.72, 1.11)
Qualifications	1.23 (1.06, 1.44)				1.20 (0.99, 1.46)			1.06 (0.86, 1.32)
BMI (45y)	1.20 (1.17, 1.23)					1.20 (1.17, 1.24)		1.01 (0.95, 1.08)
Waist circ (45y)	1.10 (1.09, 1.12)						1.10 (1.09, 1.12)	1.10 (1.06, 1.13)

[a]Reading scores are derived from multilevel models of initial level and change in reading ability between 7 and 16 years. The reading intercept is the predicted value for maths ability rank at 7 years and reading slope is the change in reading ability rank between 7 and 16 years. The scores are transformed to standard deviation scores and coded inversely (higher scores correspond to lower ability in the reading tests).

Table A6.3.3. Associations between level and change in childhood reading[a] with 45-year metabolic syndrome, [OR (95% CI)]

Men	n=3057 Unadjusted	7-year + 7-16 year change in reading z-score	+Class at birth	+Class at 33 y	+Qualifications	+ All
7-year reading z-score	1.24 (1.10, 1.39)	1.25 (1.12, 1.40)	1.21 (1.08, 1.36)	1.22 (1.08, 1.39)	1.14 (1.00, 1.30)	1.13 (0.98, 1.29)
7-16 year change in reading z-score	0.89 (0.80, 0.98)	0.87 (0.79, 0.97)	0.87 (0.78, 0.96)	0.86 (0.78, 0.96)	0.84 (0.76, 0.94)	0.84 (0.76, 0.94)
Class at birth	1.16 (1.04, 1.30)		1.13 (1.00, 1.26)			1.10 (0.97, 1.24)
Class at 33y	1.09 (0.99, 1.20)			1.05 (0.94, 1.17)		0.99 (0.88, 1.11)
Qualifications	1.18 (1.08, 1.29)				1.16 (1.05, 1.29)	1.15 (1.03, 1.28)
Women	n=3202					
7-year reading z-score	1.45 (1.28, 1.64)	1.48 (1.31, 1.68)	1.39 (1.22, 1.58)	1.36 (1.19, 1.56)	1.25 (1.08, 1.46)	1.18 (1.01, 1.38)
7-16 year change in reading z-score	1.07 (0.95, 1.19)	1.12 (1.00, 1.26)	1.09 (0.97, 1.22)	1.08 (0.96, 1.21)	1.04 (0.92, 1.17)	1.01 (0.90, 1.14)
Class at birth	1.39 (1.22, 1.58)		1.26 (1.10, 1.45)			1.21 (1.05, 1.39)
Class at 33y	1.33 (1.20, 1.47)			1.21 (1.08, 1.34)		1.13 (1.00, 1.27)
Qualifications	1.38 (1.26, 1.52)				1.36 (1.12, 1.41)	1.18 (1.04, 1.33)

[a]Reading scores are derived from multilevel models of initial level and change in reading ability between 7 and 16 years. The reading intercept is the predicted value for maths ability rank at 7 years and reading slope is the change in reading ability rank between 7 and 16 years. The scores are transformed to standard deviation scores and coded inversely (higher scores correspond to lower ability in the reading tests).

Appendix 6.4 Models of associations between childhood maths and reading z-scores with diabetes risk, including birthweight and gestational age

Table A.6.4.1a. β coefficients for the associations between childhood maths z-scores 7-16 years with 45-year HbA_{1c}

Men	n=2683 Unadjusted	7-year + 7-16 year change in maths z-score	+Class at birth	+ Birth weight	+Class at 33 y	+ Qualifications	+ All
7-year maths z-score	0.02 (0.00, 0.04)	0.02 (0.00, 0.04)	0.02 (0.01, 0.04)	0.02 (0.00, 0.04)	0.01 (-0.01, 0.03)	0.01 (-0.01, 0.03)	0.00 (-0.02, 0.03)
7-16 year change in maths z-score	0.01 (0.00, 0.03)	0.01 (0.00, 0.03)	0.01 (0.00, 0.03)	0.01 (0.00, 0.03)	0.01 (-0.01, 0.02)	0.00 (-0.01, 0.02)	0.00 (-0.01, 0.02)
Class at birth	0.00 (-0.02, 0.02)		-0.01 (-0.04, 0.01				-0.02 (-0.04, 0.00)
Birthweight	-0.04 (-0.08, 0.00)			-0.03 (-0.08, 0.01)			-0.03 (-0.08, 0.01)
Class at 33y	0.03 (0.01, 0.05)				0.02 (0.00, 0.04)		0.02 (0.00, 0.04)
Qualifications	-0.03 (-0.04, -0.01)					-0.02 (-0.04, -0.01)	-0.02 (-0.04, 0.00)
Women	n=2803						
7-year maths z-score	0.02 (0.00, 0.03)	0.02 (0.00, 0.04)	0.01 (-0.01, 0.03)	0.02 (0.00, 0.03)	0.01 (0.00, 0.03)	0.01 (-0.01, 0.03)	0.00 (-0.02, 0.02)
7-16 year change in maths z-score	0.00 (-0.02, 0.02)	0.00 (-0.02, 0.02)	-0.01 (-0.03, 0.02	0.00 (-0.02, 0.02)	0.00 (-0.02, 0.02)	0.00 (-0.03, 0.02)	-0.01 (-0.03, 0.01)
Class at birth	0.03 (0.02, 0.05)		0.03 (0.01, 0.05)				0.03 (0.01, 0.05)
Birthweight	-0.04 (-0.08, 0.01)			-0.03 (-0.07, 0.01)			-0.03 (-0.07, 0.01)
Class at 33y	0.02 (0.00, 0.03)				0.01 (0.00, 0.03)		0.01 (-0.01, 0.02)
Qualifications	-0.02 (-0.03, 0.00)					-0.01 (-0.03, 0.00)	0.00 (-0.02, 0.01)

Table A.6.4.1b β coefficients for the associations between childhood reading z-scores 7-16 years with 45-year HbA_{1c}

Men	n=2683 Unadjusted	7-year + 7-16 year change in reading z-score	+Class at birth	+ Birth weight	+Class at 33 y	+ Qualifications	+ All
7-year reading z-score	0.03 (0.01, 0.05)	0.03 (0.01, 0.05)	0.03 (0.01, 0.05)	0.03 (0.01, 0.05)	0.02 (-0.01, 0.04)	0.02 (-0.01, 0.04)	0.01 (-0.01, 0.04)
7-16 year change in reading z-score	0.01 (-0.01, 0.02)	0.01 (-0.01, 0.02)	0.01 (-0.01, 0.02)	0.01 (-0.01, 0.02)	0.00 (-0.01, 0.02)	0.00 (-0.01, 0.02)	0.00 (-0.01, 0.02)
Class at birth	0.00 (-0.02, 0.02)		-0.01 (-0.04, 0.01				-0.02 (-0.04, 0.00)
Birthweight	-0.04 (-0.08, 0.00)			-0.03 (-0.08, 0.01)			-0.03 (-0.08, 0.01)
Class at 33y	0.03 (0.01, 0.05)				0.02 (0.00, 0.04)		0.02 (-0.01, 0.04)
Qualifications	-0.03 (-0.04, -0.01)					-0.02 (-0.04, 0.00)	-0.02 (-0.03, 0.00)
Women	n=2803						
7-year reading z-score	0.02 (0.00, 0.04)	0.02 (0.00, 0.04)	0.01 (-0.01, 0.03)	0.02 (0.00, 0.04)	0.01 (0.00, 0.03)	0.01 (-0.01, 0.03)	0.00 (-0.02, 0.02)
7-16 year change in reading z-score	0.00 (-0.02, 0.01)	0.00 (-0.02, 0.02)	-0.01 (-0.03, 0.01	0.00 (-0.02, 0.02)	-0.01 (-0.02, 0.01)	-0.01 (-0.03, 0.01)	-0.01 (-0.03, 0.01)
Class at birth	0.03 (0.02, 0.05)		0.03 (0.02, 0.05)				0.03 (0.01, 0.04)
Birthweight	-0.04 (-0.08, 0.01)			-0.03 (-0.07, 0.01)			-0.03 (-0.07, 0.01)
Class at 33y	0.02 (0.00, 0.03)				0.01 (0.00, 0.03)		0.01 (-0.01, 0.02)
Qualifications	-0.02 (-0.03, 0.00)					-0.01 (-0.03, 0.00)	0.00 (-0.02, 0.01)

Table A.6.4.2a. ORs for the associations between childhood maths z-scores 7-16 years with 45-year elevated HbA_{1c} / type 2 diabetes

Men	n=2715 Unadjusted	7-year + 7-16 year change in maths z-score	+Class at birth	+ Birth weight	+Class at 33 y	+ Qualifications	+ All
7-year maths z-score	1.30 (1.07, 1.58)	1.30 (1.07, 1.58)	1.25 (1.02, 1.53)	1.27 (1.04, 1.55)	1.26 (1.01, 1.56)	1.08 (0.86, 1.36)	1.05 (0.83, 1.33)
7-16 year change in maths z-score	1.00 (0.83, 1.19)	1.00 (0.84, 1.21)	0.98 (0.81, 1.18)	0.99 (0.83, 1.20)	0.98 (0.81, 1.19)	0.90 (0.73, 1.09)	0.88 (0.72, 1.08)
Class at birth	1.24 (1.02, 1.50)		1.16 (0.94, 1.42)				1.11 (0.90, 1.37)
Birthweight	0.64 (0.43, 0.96)			0.67 (0.45, 1.01)			0.68 (0.45, 1.02)
Class at 33y	1.16 (0.98, 1.36)				1.07 (0.88, 1.29)		0.97 (0.80, 1.19)
Qualifications	0.75 (0.65, 0.87)					0.75 (0.63, 0.90)	0.76 (0.63, 0.92)
Women	n=2832						
7-year maths z-score	1.30 (1.05, 1.62)	1.31 (1.05, 1.64)	1.21 (0.96, 1.53)	1.29 (1.03, 1.61)	1.32 (1.04, 1.69)	1.22 (0.93, 1.59)	1.16 (0.88, 1.53)
7-16 year change in maths z-score	0.97 (0.80, 1.18)	1.03 (0.83, 1.26)	0.98 (0.79, 1.21)	1.02 (0.83, 1.26)	1.03 (0.83, 1.27)	0.99 (0.79, 1.23)	0.96 (0.77, 1.20)
Class at birth	1.39 (1.10, 1.75)		1.33 (1.04, 1.70)				1.31 (1.02, 1.68)
Birthweight	0.68 (0.43, 1.07)			0.73 (0.46, 1.16)			0.75 (0.47, 1.17)
Class at 33y	1.07 (0.89, 1.28)				0.98 (0.80, 1.20)		0.93 (0.74, 1.15)
Qualifications	0.84 (0.71, 1.00)					0.90 (0.74, 1.11)	0.92 (0.74, 1.14)

Table A.6.4.2b. ORs for the associations between childhood reading z-scores 7-16 years with 45-year elevated HbA_{1c} / type 2 diabetes

Men	n=2715 Unadjusted	7-year + 7-16 year change in reading z-score	+Class at birth	+ Birth weight	+Class at 33 y	+ Qualifications	+ All
7-year reading z-score	1.40 (1.15, 1.71)	1.40 (1.15, 1.71)	1.36 (1.10, 1.67)	1.37 (1.12, 1.67)	1.39 (1.11, 1.73)	1.22 (0.97, 1.53)	1.20 (0.95, 1.53)
7-16 year change in reading z-score	1.04 (0.87, 1.24)	1.01 (0.85, 1.22)	1.01 (0.84, 1.21)	1.02 (0.85, 1.22)	1.01 (0.84, 1.22)	0.97 (0.80, 1.16)	0.98 (0.81, 1.18)
Class at birth	1.24 (1.02, 1.50)		1.12 (0.92, 1.38)				1.08 (0.88, 1.33)
Birthweight	0.64 (0.43, 0.96)			0.69 (0.46, 1.03)			0.69 (0.46, 1.05)
Class at 33y	1.16 (0.98, 1.36)				1.02 (0.84, 1.23)		0.94 (0.77, 1.14)
Qualifications	0.75 (0.65, 0.87)					0.80 (0.67, 0.96)	0.80 (0.67, 0.96)
Women	n=2832						
7-year reading z-score	1.27 (1.02, 1.58)	1.25 (1.01, 1.56)	1.15 (0.91, 1.45)	1.23 (0.99, 1.54)	1.25 (0.98, 1.58)	1.12 (0.86, 1.46)	1.07(0.81, 1.40)
7-16 year change in reading z-score	0.89 (0.72, 1.08)	0.91 (0.74, 1.11)	0.87 (0.71, 1.07)	0.91 (0.74, 1.11)	0.91 (0.74, 1.12)	0.87 (0.70, 1.07)	0.85 (0.69, 1.05)
Class at birth	1.39 (1.10, 1.75)		1.36 (1.07, 1.73)				1.33 (1.04, 1.70)
Birthweight	0.68 (0.43, 1.07)			0.71 (0.45, 1.13)			0.74 (0.47, 1.16)
Class at 33y	1.07 (0.89, 1.28)				1.01 (0.83, 1.24)		0.94 (0.76, 1.17)
Qualifications	0.84 (0.71, 1.00)					0.86 (0.70, 1.06)	0.88 (0.70, 1.10)

Table A.6.4.3a. ORs for the associations between childhood maths z-scores 7-16 years with 45-year metabolic sydrome

Men	n=2611 Unadjusted	7-year + 7-16 year change in maths z-score	+Class at birth	+ Birth weight	+Class at 33 y	+ Qualifications	+ All
7-year maths z-score	1.25 (1.10, 1.42)	1.25 (1.10, 1.41)	1.21 (1.06, 1.37)	1.24 (1.09, 1.40)	1.22 (1.07, 1.40)	1.13 (0.98, 1.31)	1.11 (0.95, 1.29)
7-16 year change in maths z-score	0.97 (0.87, 1.09)	0.98 (0.87, 1.10)	0.95 (0.85, 1.07)	0.97 (0.87, 1.10)	0.96 (0.85, 1.09)	0.92 (0.81, 1.04)	0.90 (0.79, 1.03)
Class at birth	1.18 (1.05, 1.33)		1.14 (1.00, 1.29)				1.11 (0.98, 1.27)
Birthweight	0.96 (0.75, 1.24)			0.97 (0.75, 1.25)			0.98 (0.76, 1.27)
Class at 33y	1.11 (1.00, 1.23)				1.05 (0.93, 1.18)		0.99 (0.87, 1.12)
Qualifications	0.83 (0.75, 0.91)					0.85 (0.76, 0.96)	0.86 (0.76, 0.98)
Women	n=2725						
7-year maths z-score	1.34 (1.17, 1.53)	1.37 (1.19, 1.57)	1.26 (1.09, 1.45)	1.36 (1.18, 1.56)	1.29 (1.11, 1.50)	1.15 (0.97, 1.36)	1.09 (0.92, 1.30)
7-16 year change in maths z-score	1.01 (0.90, 1.14)	1.08 (0.95, 1.23)	1.02 (0.90, 1.17)	1.08 (0.95, 1.22)	1.05 (0.92, 1.20)	0.99 (0.86, 1.13)	0.96 (0.83, 1.10)
Class at birth	1.44 (1.25, 1.66)		1.36 (1.17, 1.58)				1.30 (1.12, 1.52)
Birthweight	0.84 (0.63, 1.11)			0.91 (0.69, 1.20)			0.92 (0.70, 1.22)
Class at 33y	1.22 (1.10, 1.37)				1.13 (1.00, 1.28)		1.04 (0.91, 1.19)
Qualifications	0.75 (0.68, 0.84)					0.79 (0.70, 0.90)	0.84 (0.73, 0.96)

Table A.6.4.3b. ORs for the associations between childhood reading z-scores 7-16 years with 45-year metabolic syndrome

Men	n=2611 Unadjusted	7-year + 7-16 year change in reading z-score	+Class at birth	+ Birth weight	+Class at 33 y	+ Qualifications	+ All
7-year reading z-score	1.26 (1.11, 1.43)	1.27 (1.12, 1.45)	1.23 (1.08, 1.40)	1.26 (1.11, 1.43)	1.23 (1.07, 1.42)	1.15 (1.00, 1.33)	1.12 (0.97, 1.31)
7-16 year change in reading z-score	0.88 (0.78, 0.98)	0.86 (0.77, 0.97)	0.86 (0.76, 0.96)	0.87 (0.77, 0.97)	0.85 (0.76, 0.96)	0.83 (0.74, 0.94)	0.83 (0.74, 0.94)
Class at birth	1.18 (1.05, 1.33)		1.14 (1.00, 1.29)				1.10 (0.97, 1.26)
Birthweight	0.96 (0.75, 1.24)				0.98 (0.76, 1.26)		1.00 (0.77, 1.29)
Class at 33y	1.11 (1.00, 1.23)				1.06 (0.94, 1.20)		1.00 (0.88, 1.13)
Qualifications	0.83 (0.75, 0.91)					0.85 (0.76, 0.95)	0.86 (0.76, 0.97)
Women	n=2725						
7-year reading z-score	1.39 (1.21, 1.59)	1.40 (1.22, 1.61)	1.29 (1.12, 1.49)	1.40 (1.21, 1.60)	1.33 (1.15, 1.55)	1.20 (1.01, 1.42)	1.14 (0.96, 1.35)
7-16 year change in reading z-score	1.03 (0.91, 1.17)	1.07 (0.95, 1.22)	1.03 (0.91, 1.17)	1.07 (0.95, 1.22)	1.05 (0.92, 1.19)	1.00 (0.88, 1.15)	0.98 (0.86, 1.12)
Class at birth	1.44 (1.25, 1.66)		1.34 (1.16, 1.56)				1.29 (1.11, 1.51)
Birthweight	0.84 (0.63, 1.11)			0.90 (0.68, 1.18)			0.92 (0.70, 1.21)
Class at 33y	1.22 (1.10, 1.37)				1.12 (0.99, 1.27)		1.04 (0.91, 1.18)
Qualifications	0.75 (0.68, 0.84)					0.81 (0.71, 0.92)	0.85 (0.74, 0.98)

Appendix 6.5 Models of 45 year obesity (BMI≥30 Kg/m^2) and central obesity (waist circumference≥1.02m (men) and 0.88m (women)).

Table A.6.5.1 Association between childhood maths z-scores 7-16 years with total obesity at 45-years (OR, 95%CI)

Men	n=2916	7-year + 7-16 year change in maths z-score	+Class at birth	+Birthweight	+Class at 33y	+Qualifications	+All
	Unadjusted						
7-year maths z-score	1.29 (1.18, 1.41)	1.29 (1.18, 1.41)	1.23 (1.12, 1.35)	1.30 (1.19, 1.43)	1.22 (1.11, 1.34)	1.18 (1.06, 1.30)	1.14 (1.02, 1.27)
7-16 year change in maths z-score	1.05 (0.97, 1.14)	1.06 (0.98, 1.15)	1.02 (0.94, 1.11)	1.07 (0.98, 1.16)	1.02 (0.94, 1.11)	1.00 (0.92, 1.09)	0.97 (0.88, 1.06)
Class at birth			1.21 (1.10, 1.33)				1.18 (1.08, 1.30)
Birthweight				1.18 (1.00, 1.40)			1.19 (1.01, 1.41)
Class at 33y					1.13 (1.03, 1.23)		1.06 (0.97, 1.16)
Qualifications						0.86 (0.79, 0.93)	0.89 (0.82, 0.97)

Women	n=3048	7-year + 7-16 year change in maths z-score	+Class at birth	+Birthweight	+Class at 33y	+Qualifications	+All
	Unadjusted						
7-year maths z-score	1.24 (1.14, 1.36)	1.26 (1.15, 1.38)	1.19 (1.08, 1.31)	1.27 (1.16, 1.40)	1.20 (1.09, 1.32)	1.02 (0.93, 1.11)	1.12 (1.00, 1.24)
7-16 year change in maths z-score	1.02 (0.94, 1.10)	1.07 (0.98, 1.16)	1.03 (0.94, 1.12)	1.07 (0.98, 1.16)	1.04 (0.96, 1.13)	0.89 (0.82, 0.96)	0.99 (0.91, 1.08)
Class at birth			1.23 (1.12, 1.35)				1.21 (1.10, 1.33)
Birthweight				1.17 (0.98, 1.38)			1.18 (0.99, 1.40)
Class at 33y					1.12 (1.03, 1.21)		1.07 (0.98, 1.17)
Qualifications						0.89 (0.82, 0.96)	0.93 (0.85, 1.02)

Table A.6.5.2 Association between childhood maths z-scores 7-16 years with central obesity at 45-years (OR, 95%CI)

Men	n=2804	7-year + 7-16 year change in maths z-score	+Class at birth	+Birthweight	+Class at 33y	+Qualifications	+All
	Unadjusted						
7-year maths z-score	1.22 (1.13, 1.33)	1.22 (1.13, 1.33)	1.19 (1.09, 1.30)	1.24 (1.13, 1.35)	1.18 (1.08, 1.29)	1.14 (1.03, 1.25)	1.14 (1.03, 1.26)
7-16 year change in maths z-score	0.99 (0.92, 1.07)	1.00 (0.92, 1.08)	0.98 (0.90, 1.06)	1.00 (0.92, 1.08)	0.98 (0.90, 1.06)	0.95 (0.88, 1.04)	0.94 (0.87, 1.03)
Class at birth	1.15 (1.06, 1.25)		1.11 (1.02, 1.21)				1.10 (1.01, 1.20)
Birthweight	1.28 (1.08, 1.52)			1.33 (1.11, 1.58)			1.34 (1.12, 1.60)
Class at 33y	1.13 (1.05, 1.21)				1.08 (0.99, 1.17)		1.92 (0.84, 1.00)
Qualifications	0.85 (0.80, 0.91)					0.89 (0.82, 0.96)	0.91 (0.84, 0.99)
Women	n=2839						
7-year maths z-score	1.17 (1.08, 1.27)	1.19 (1.10, 1.29)	1.12 (1.03, 1.22)	1.21 (1.12, 1.32)	1.16 (1.07, 1.27)	1.10 (1.00, 1.21)	1.08 (0.98,1.20)
7-16 year change in maths z-score	1.04 (0.97, 1.12)	1.08 (1.00, 1.16)	1.04 (0.96, 1.12)	1.07 (0.99, 1.16)	1.07 (0.99, 1.15)	1.03 (0.96, 1.12)	1.00(0.92, 1.09)
Class at birth	1.27 (1.18, 1.38)		1.22 (1.13, 1.33)				1.21 (1.11, 1.32)
Birthweight	1.19 (1.01, 1.41)			1.27 (1.07, 1.50)			1.29 (1.09, 1.52)
Class at 33y	1.12 (1.04, 1.20)				1.06 (0.98, 1.14)		1.01 (0.93, 1.09)
Qualifications	0.85 (0.80, 0.90)					0.89 (0.82, 0.96)	0.93 (0.85, 1.01)

Chapter 7, Cognition, health behaviours and mid-life glucose homeostasis.

Introduction

Previous chapters have separately explored associations between childhood cognitive development and health behaviours; health behaviours and glucose homeostasis; childhood cognitive development and diabetes risk, pathways illustrated by arrows in Figure 7.1. Poorer childhood ability was associated with raised HbA_{1c} levels and with higher risks of elevated HbA_{1c} /diabetes or metabolic syndrome in mid-life. In models investigating trajectories of cognitive ability, 7-year maths or reading ability was more consistently associated with poorer glucose regulation outcomes than change in ability rank between 7 and 16 years (Chapter 6). A series of explanations for these associations with a summary of supporting evidence were discussed in Chapter 1, and explored in more depth in Chapter 6. In Chapter 6 associations between childhood cognitive ability and adult glucose homeostasis were not abolished by confounding by birthweight for gestational age or social position of origin (in line with other research, see Chapter 1). In contrast, adult educational qualifications years and social position were important pathways between childhood cognitive ability and mid-life glucose homeostasis. Again this was in line with evidence from other studies reviewed in chapter 1. The benefits of greater cognitive test results at 7 years for better glucose regulation were seen across the spectrum of cognitive ability, and were not confined to lower cognitive abilities. This finding was in contrast to the 1946 birth cohort which found some evidence for non-linear associations between mortality rates and childhood cognitive ability (Kuh et al. 2004).

This chapter extends analyses in Chapter 6 by exploring whether childhood cognitive ability influences mid-life glucose homeostasis through its association with lifecourse smoking and drinking. This pathway is illustrated in Figure 7.1 by arrows from cognition to smoking and drinking and onwards to adult social position and adiposity and finally to glucose homeostasis.

Chapter 4 reported associations between childhood cognitive ability and uptake and persistence of smoking and drinking through adult life. Poorer 7-year maths or reading tests were consistently associated with raised odds of non-drinking at separate adult surveys and also with reporting non-drinking at more surveys. Poorer 7-year ability was associated with cigarette smoking and smoking more heavily at each adult age, and reporting smoking at more surveys. The change in relative rank of maths or reading ability between ages seven and sixteen years was associated with smoking, and being a heavier smoker ($\geq$20 cigarettes/day). Binge drinking at age 42 was associated with lower 7-year ability and with a decline in ability rank between 7 and 16 years. The literature on educational differences in the uptake and persistence of smoking

and of drinking was described in Chapter 4 and indicates widespread support from other studies of the finding that initiation of smoking and drinking is more common in individuals with poorer school achievements or cognitive ability. Whilst there was less evidence about the associations between cognitive ability and adult cigarette smoking and alcohol consumption, existing evidence points in the direction of persistence of unhealthy behaviours being associated with poorer ability.

The reason for investigating the role of smoking and drinking as pathways between cognitive ability and glucose homeostasis is that cognitive ability is associated with smoking and drinking patterns (Chapter 4) and these in turn are also associated with glucose homeostasis (Chapter 5). Cognitive ability is also associated with glucose homeostasis. It is therefore expected that lifecourse measures of (i) cigarette smoking or (ii) alcohol drinking status will be on the pathway between childhood ability and adult glucose regulation. Specifically, heavy smoking, persistent smoking and non-drinking are expected to mediate between lower cognitive ability and higher risks of central obesity and poor glucose regulation. The lifecourse smoking and drinking history measures investigated in this chapter are selected based on their associations with firstly, cognition and secondly, glucose homeostasis (reported in chapters 4 and 5). Studying pathways between cognition and glucose metabolism should give insights into accumulation of health risks through life. Some pathways to diabetes risk are better studied, including the role of contemporary body size and diet or physical activity, and from a life-course perspective, weight change and socio-economic position at different life stages have been investigated (Lawlor et al. 2002; Lidfeldt et al. 2007; Parker et al. 2003). Smoking and drinking are much less studied than these other pathways in relation to diabetes risk. It is of particular interest to understand pathways involving modifiable behaviours as they are amenable to policy intervention.

Educational gradients, or inequalities, in adult health are the focus of a wide literature and the role of health behaviours in explaining educational gradients in health has been much studied. However given that childhood ability is strongly associated with uptake and (as seen in the 1958 cohort, also with persistence) of health behaviours, health behaviours may be particularly important pathways from childhood ability to adult health, rather than from final qualifications to adult health. To date, most studies looking to the underlying causes of health inequalities use single measures of health behaviours and assume no changes in behaviours over time. As yet only few studies have begun to challenge this perspective and include multiple measures of health behaviours (Emberson et al. 2005a; Emberson et al. 2005b). Use of baseline measures only was found to underestimate the associations between exposure and health outcome (Emberson et al 2005b).

The focus in this chapter on health behaviours as a pathway to later poor glucose regulation does not mean that social factors are seen as unimportant, but rather that the importance of material factors in generating health inequalities is well established while health behaviours across the lifecourse have been less rigorously studied. Confounders of the association between cognition and mid-life glucose homeostasis need to be account for as well as proposed mediators. A wider range of confounders are investigated here than in Chapter 6, where birthweight for gestational age was not found to be a common cause of the associations, and there was evidence for partial confounding by social position of origin. In addition a range of pathways between childhood cognition and mid-life glucose homeostasis will be considered, with a particular focus on the role of health behaviours relative to other pathways. The rationale for including variables as pathways between childhood cognitive ability and adult glucose homeostasis was that they were expected to be associated with both childhood cognitive development and diabetes risk (or obesity, given its importance as a risk factor). The pathway factors were those which were temporally between the exposure of interest, childhood cognitive ability and the outcome, 45-year glucose regulation. The evidence about the associations between the confounding factors and also the pathway factors to be considered in this chapter with (a) childhood cognitive ability and (b) obesity and diabetes risk is now summarised.

Social position of origin

The rationale for including social position of origin as a confounding factor during childhood was examined in Chapters 1 and 6.

Birthweight or intrauterine growth

Chapter 1 reviewed evidence about associations between birthweight and (i) cognition and (ii) glucose homeostasis. Although birthweight was expected to act as a common cause of childhood cognitive ability and adult diabetes risk, there was little evidence for this in analyses in Chapter 6. Birthweight was not associated with adult glucose homeostasis outcomes, with the exception of elevated HbA_{1c} / diabetes in men and birthweight did not substantially confound associations between reading and elevated HbA_{1c} / diabetes.

Maternal smoking during pregnancy

Maternal smoking during pregnancy was considered as a potential confounder because it is associated with poorer cognitive development in childhood and into early adulthood (Butler & Goldstein 1973; Fogelman & Manor 1988; Lassen & Oei 1998; Lawlor et al. 2006b; Rantakallio 1983). Although a recent study suggested that the associations were due to confounding by factors in the home (Batty et al. 2006b). Maternal smoking is also associated with subsequent raised risks of obesity in childhood and adulthood, in this cohort and other studies (Huang et al. 2006; Power & Jefferis 2002). Additionally, maternal smoking was associated with elevated 45-

year HbA_{1c} in the 1958 cohort (OR 1.33, 95%CI 1.04, 1.71), an association that was mediated primarily through adult BMI and waist circumference (Thomas et al. 2007b). Since the majority of studies suggest an effect of maternal smoking on cognitive development, maternal smoking is considered as a confounder.

Infant feeding

Many studies report associations between mode of infant feeding and childhood cognitive ability. One systematic review concluded that breast feeding compared to bottle feeding was beneficial to cognitive ability in childhood, even taking into account social factors. There were greater benefits to low birthweight than normal birthweight infants (Anderson et al. 1999). However a more recent systematic review with the addition of one very large study estimated that the beneficial effects of breast feeding (of short duration in non-low birthweight infants) was largely due to the confounding effects of maternal cognitive ability and other home factors including level of cognitive stimulation in the home, age of mother at birth, birth order and family financial hardship. However a weakness of the most recent study was that although it included a large variety of home factors, data on gestational age was not available (Der et al. 2006).

Recent systematic reviews report protective effects of breast feeding on subsequent obesity (Harder et al. 2005; Owen et al. 2005). Studies which adjusted for confounding factors (including parents' BMI, maternal smoking in pregnancy and in early life) reported smaller but still significant associations between breast feeding and subsequent overweight; the odds ratio of subsequent obesity among breast fed compared to not breast fed was 0.93 (95% CI 0.88, 0.99). A systematic review of breastfeeding and diabetes risk indicated that breast feeding compared to bottle feeding was associated with decreased risk of diabetes in adulthood OR 0.61 (95%CI 0.44, 0.85), marginally lower insulin concentrations but not serum glucose concentrations in later life (Owen et al. 2006). Infant feeding is considered here as a confounder of the cognition–glucose homeostasis associations.

Childhood height

Two recent prospective cohort studies provide evidence that height growth is associated with cognitive ability in childhood (Pearce et al. 2005; Richards et al. 2002). Evidence from the 1946 British birth cohort study indicated that even adjusting for parent socioeconomic position, education and age, the cross sectional associations between greater height and higher cognitive ability at 8 and 15 years persist (Richards et al 2002). The Newcastle Thousand Families study also report that greater height at 9 and 13 years as well as increased growth between 9 and 13 years is associated with cognitive ability, even taking into account social background (Pearce et al 2005). However it is unlikely that growth in height causes increases in cognitive ability, rather height and cognitive ability may have common causes in social background, childhood

nutrition and genetic influences. Indeed in many epidemiologic studies childhood height is used as a sensitive indicator of social background. Intervention studies using growth hormone to supplement height growth do not find associations with increasing cognitive ability (Gale 2005). Therefore childhood height is not considered as a potential mediator between cognitive development and adult obesity or diabetes risk.

Childhood Behavioural Problems

A further factor which is investigated is the role of behavioural maladjustment at 7 and 11 years; internalising or externalising behaviours may mediate between cognitive development and uptake and then persistence of smoking and drinking. There is much evidence that poorer behavioural adjustment in childhood is associated with poorer cognitive development (Hinshaw 1992; Plomin et al. 2002). The associations between low cognitive ability and behavioural problems are evident from early childhood, for example, at age 8 and persist into later childhood when cognitive delay is associated with conduct and social problems (Fergusson & Horwood 1995). The direction of causality between cognitive ability and disruptive behavioural patterns has proved difficult to disentangle, nevertheless disruptive behaviour is associated with poorer cognitive achievements in childhood, so is included as a potential pathway to or from cognitive abilities to later uptake of health behaviours and subsequent diabetes risk. Poor behaviour ratings from parents and teachers are also associated with uptake of cigarette smoking and alcohol use.

There is little evidence about childhood behavioural problems in relation to diabetes risk, but associations between obesity and behavioural problems have been reported (Lumeng et al. 2003). Given the importance of obesity as a mediating factor between cognition and diabetes risk, the role of behavioural problems is therefore of interest. Childhood behavioural problems are also associated with higher risk of initiation of smoking and drinking in adolescence and early adulthood (Donovan 2004; Tyas & Pederson 1998). Behavioural maladjustment has also been reported to explain part of the associations between childhood cognitive ability and adult substance misuse (Fergusson et al. 2005), which is a further reason to consider behavioural problems as potential mediators between cognitive ability and later diabetes risk.

Adolescent smoking and drinking

As discussed in Chapter 4, poorer childhood cognitive development, and lower educational ability or aspirations are associated with higher risk of initiation of smoking and drinking (Donovan 2004; Tyas & Pederson 1998). Adolescent smoking is strongly associated with adult smoking (Chassin et al. 1990) and adolescent drinking is moderately associated with adult drinking habits (Jefferis et al. 2005). Additionally adolescent smoking and drinking habits are associated with subsequent adult educational attainment or adult social position (King et al.

2000; King et al. 2006; Koivusilta et al. 2003). The detrimental role of smoking and drinking on glucose homeostasis and increasing risk of type 2 diabetes was discussed in Chapter 6. Therefore adolescent drinking and smoking habits were considered as mediators of the association between childhood cognitive ability and mid-life glucose homeostasis.

Diet and physical activity in adulthood

Literature about associations between cognitive ability in childhood and adult diet or physical activity is sparse. A recent study of the 1970 British birth cohort reported that higher 10-year cognitive ability was associated with more intense physical activity and healthier diet at age 30 years (Batty et al. 2007b). This fits with other, more abundant evidence of gradients in these health behaviours using measures of social position or educational achievement (which in turn are correlated with cognitive ability)(Dowler 2001; Schoon & Parsons 2003). There is extensive evidence for associations between low levels of physical activity or poor diet in adulthood and diabetes risk (Hu et al. 2001; Weinstein et al. 2004). Undiagnosed diabetics (with high HbA_{1c} levels) are reported to have poorer diet than diagnosed diabetics (Bates et al. 2004). Diet and activity are the major targets for behavioural change in diabetes management (Klein et al. 2004) and successful intervention studies based on diet and activity have shown improved blood-glucose regulation or delayed diabetes onset (Diabetes Prevention Program Research Group 2002). Because both diet and physical activity were expected to be associated with both cognitive ability and diabetes and obesity risk, they were considered as mediators between cognitive ability in childhood and mid-life glucose homeostasis.

Adult social class or educational qualifications

Childhood cognitive ability is strongly associated with subsequent educational qualifications and adult occupational position (Fergusson et al 2005; Nettle 2003). Social or educational gradients in HbA_{1c}, diabetes or metabolic syndrome are also reported (Dalstra et al. 2005; Geyer et al. 2006; Langenberg et al. 2006; Wamala et al. 1999). Hence social class in adulthood or adult educational qualifications are considered as mediators between childhood cognitive ability and adult glucose regulation.

Adult adiposity

In Chapter 6 adult adiposity was reported to mediate between childhood cognition and adult glucose regulation. Adult adiposity will be investigated in this chapter because of associations between childhood cognitive ability and adult obesity (Hart et al. 2004; Lawlor et al. 2006a), and the well-established links between increasing levels of both BMI and in particular waist circumference with higher HbA_{1c} level (Gulliford & Ukoumunne 2001) and poorer metabolic functioning (Colditz et al. 1995; Kahn et al. 2006; Koh-Banerjee et al. 2004; Perry et al. 1995). Adult weight, BMI and central adiposity are also associated with social position in child and

adulthood (Brunner et al. 1999; Langenberg et al. 2003; Power et al. 2003) as well as educational qualifications (Halkjaer et al. 2003) (discussed in Chapter 6). Many studies report associations between cigarette smoking and patterns of alcohol consumption and increasing adiposity (Dorn et al. 2003; Istvan et al. 1995). Therefore the pathway through obesity to glucose homeostasis will be studied.

Weight gain in adulthood

Cognitive ability in early adulthood is associated with subsequent weight gain; as seen in the 1946 British birth cohort. Cross-sectional associations between cognitive ability and weight at 8 and 16 years were accounted for by social background, but at later ages, associations between cognitive test scores and weight became apparent (Richards et al 2002). In addition weight gain between ages 16 and 26 years was associated with cognition at 26 years, independent of social background (Richards et al 2002). The associations between weight gain at later ages and later adult cognitive test scores were not investigated. Analyses of the 1958 cohort data indicate that 11-year cognitive ability was associated with weight gain between 16 and 42 years, although the associations were mediated by educational level and dietary habits (Chandola et al. 2006b). In addition to evidence that concurrent weight is associated with diabetes risk, weight gain through the lifecourse is associated with increased risks of diabetes (Colditz et al 1995) and metabolic syndrome (Hillier et al. 2006). Therefore analyses in this chapter will include weight gain across adulthood as a pathway from cognitive ability to adult glucose homeostasis.

Aims

The aims are to investigate pathways across the life course to three measures of glucose homeostasis; HbA_{1c}, elevated HbA_{1c} /diabetes and metabolic syndrome. Although components of the proposed pathways from cognition to glucose homeostasis (illustrated in Figure 7.1) have been addressed in Chapter 6, the specific objectives listed below will be addressed here in combined analyses. This chapter investigates

1. whether and to what extent degree associations between cognitive ability and glucose regulation are confounded by common causes in childhood.
2. the mediating role of lifecourse health behaviours (i) persistent and heavy smoking and (ii) consistent non or infrequent drinking in associations between cognitive ability and glucose regulation.
3. the degree to which associations between cognitive ability and glucose regulation are mediated by social trajectories ie social position and qualifications attained in adult life.
4. the degree to which associations between cognitive ability and glucose regulation are mediated by adiposity in adulthood.

5. the degree to which associations between cognitive ability and adiposity in adulthood are mediated by lifecourse pathways, in particular health behaviours.

Methods

Sample

The analysis samples in this chapter differ by outcome variable. Participants with type 1 diabetes and medications (listed in Chapter 2) that might alter their HbA_{1c} level (n=45) were excluded from analyses of HbA_{1c}. Analyses were re-run excluding a further 345 participants taking steroid medication which may also alter HbA_{1c} level (Appendix 2.3). Main effects were slightly smaller, but patterns of results were the same so data are not presented.
Table A.7.1 (Appendix 7.1) indicates differences between the target sample at 45 years and the analysis sample, the less advantaged groups are under-represented. Analyses in this chapter include variables from across the lifecourse so the number of cases with complete data reduces substantially, more than in previous chapters which used fewer variables. Therefore multiple imputation using the *ice* procedure (multiple imputation by chained equations) in Stata version 9.2 (Royston 2004) was used. Under the assumption that data was missing at random (MAR), imputations were performed for each separate outcome under investigation. The covariates for the lifecourse models were imputed, but not the outcomes themselves. First, imputation models including variables predicting drop-out identified from previous analyses were run to create imputed datsets (Hawkes & Plewis 2006). Next, substantive models were run using imputed datasets. 20 cycles and 5 datasets were used for imputation models, for comparison some models were also run with 20 cycles and 10 datasets and the results of the substantive models were not materially changed; only the second decimal place of the regression coefficients differed. Selected complete case analyses are in Appendix 7.3 (Tables A7.3.1 to A7.3.5) for comparison with imputed data. Results from complete case analyses are consistent with results using imputed datasets, but point estimates were less stable and confidence intervals wider.

Analysis

HbA_{1c} was treated as in previous chapters; for descriptive analyses geometric means of HbA_{1c} were computed for the categorical pathway variables. HbA_{1c} was not transformed and regression models used robust standard errors. Regression models were built up according to the temporal sequence of the independent variables, to account for accumulation of effects over the lifecourse.

The first step in analysis was selection of variables. To address Aim 1, on the basis of *a priori* expectations from literature about cognitive ability and glucose homeostasis, potential common causes of the association between cognitive ability and glucose homeostasis were identified for

inclusion in analysis. These exposures occurred prior to the 7-year cognitive test measures. To address aims 2-4, a second set of pathway variables that occurred at the same time or after the 7-year cognitive test measures were identified for inclusion if they were associated with both cognitive test scores and glucose regulation or adult adiposity and were likely pathways through which cognitive ability in childhood might act on glucose regulation or adiposity in midlife. Linear regression models summarised univariate associations between each of the confounder variables and (i) the maths tests scores (intercept and then slope) and then (ii) HbA_{1c}. Variables which were significantly associated with both HbA_{1c} and the maths test scores were retained for the multivariable analysis as confounders. For the sake of model simplicity other variables were not retained. The same selection process was applied to the mediating factors; hence a subset of confounders and mediators were retained for analyses.

Coefficients from regression models for the association between maths z-scores and glucose regulation from the following three stages of analyses are presented in tables. The second stage of analysis was to assess to what degree adjustments for the selected confounding and mediating factors changed the associations between (i) 7-year z-score and (ii) 7-16 year change in maths z-score and HbA_{1c}. Adjustments were made for each confounding (or mediating) factor in turn. The percentage change in the adjusted β coefficient for maths z-score compared to unadjusted was calculated; [(adjusted coefficient/ unadjusted coefficient *100)-100].

The third stage of analysis used a series of multivariable linear regression models each containing all predictors from a single block listed in the table ie confounders from birth, pathway factors from childhood; adult diet and activity; adult smoking and drinking and so forth. The percentage change in the adjusted coefficient for (i) 7-year maths z-score (ii) 7-16 year change in maths z-score, was calculated for each multivariate model.

The fourth stage of analysis was to build up regression models of HbA_{1c} and maths ability, adding in each block of exposures from across the lifecourse in temporal sequence. Coefficients for the association between adult outcome and maths z-score are presented first adjusted for the childhood block (the common causes or confounders) and then for pathway variables occurring later in childhood or in adulthood (including social and lifestyle factors). Analyses described above for maths scores were run with reading scores, conclusions are similar, so results for reading scores are in Appendix 7.2.

The same process of variable selection and building up univariate and multivariate models in temporal sequence of the confounders and pathways was repeated for (i) elevated HbA_{1c} (>6%) or diabetes and (ii) metabolic syndrome using logistic regression models. The percentage

change in the Odds Ratio (OR) for elevated HbA_{1c} level per SD decrease in maths intercept (and slope) was calculated as $[(OR_{adjusted} - OR_{unadjusted})/ (OR_{unadjusted} -1)]*100$.

As all adult factors act contemporaneously, the final models were built up entering adult variables in different order to see if conclusions were affected.

Because adult adiposity is such an important pathway to glucose homeostasis, (Chapter 6), and potentially a pathway between health behaviours and glucose homeostasis, analyses were repeated using 45-year body mass index and waist circumference as outcomes.

Results

The complete case sample had higher 7-year maths ability (lower z-score) and change in z-score between 7 and 16 years than the target sample (cases with valid 45-year HbA_{1c} data). To illustrate, among men mean 7 year maths z-score was -0.279, SD 0.955 (n=1580) in the complete case sample and -0.165, SD 0.975 (n=3852) in the target sample. The mean in the target sample is less than zero because of sample attrition between 7 years and 45 years. Table A7.1 (Appendix 7.1) presents the distributions of key pathway variables in the 45-year target sample with valid HbA_{1c} data compared to the smallest of the complete case analysis samples 1607 (men) and 1652 (women); there are higher proportions from professional and managerial social class at birth in the complete case analysis sample compared to the target sample (21% compared to 19% in men) and the unskilled manual and no male head of household group is less represented (20% compared to 22% in men). There are more never smokers and less heavy smokers, and among women, there are more frequent drinkers in the complete case analysis sample.

Table 7.1 presents the distribution of the lifecourse variables which were considered as (i) confounding factors (ie those occurring before age 7 years when the first cognitive test was taken) and (ii) pathway factors occurring after the cognitive test and which are proposed to be mediators of the association between childhood maths or reading rank (z-scores at 7 years and the change to 16 years). Based on analyses in previous chapters indicating that drinking frequency rather than quantity was most consistently associated with the three glucose homeostasis measures, drinking history between 23 and 42 years was summarised as the number of occasions a participant was a non-drinker as non-drinkers had highest risk of poor glucose regulation. The baseline group were those who were drinkers at each adult survey. A summary variable indicating smoking history and amount smoked from age 23 to 42 years was used in the models.

Only variables in Table 7.1 which were associated with both the glucose regulation outcome measure and either intercept or slope were used in regression analyses in subsequent tables (7.2-7.7). Tables 7.2-7.7 focus on the associations between HbA_{1c} and (i) 7-year maths z-score (in column 1) and (ii) 7-16 year change in maths z-score (in column 3). The effect of adjustment for each of the pathway factors sequentially was summarised as the percentage change in the coefficient in columns 2 and 4. Tables 7.2-7.7 use datasets with multiple imputation of covariates.

Maths and HbA_{1c}

Tables 7.2a and b present β coefficients from linear regression models of HbA_{1c} with independent variables (i) 7-year maths z-score and (ii) 7-16 year change in maths z-score, in men and women respectively. Section 1 presents unadjusted estimates. In men poorer 7-year maths ability and decline in ability rank 7-16 years were associated with increased HbA_{1c} ; 0.04% HbA_{1c} per SD increase in 7-year z-score and 0.02% HbA_{1c} per SD increase in 7-16 year change in maths z-score.

Section 2 presents coefficients for the same associations, adjusted for each confounding factor from birth in turn (social class of origin, birthweight for gestational age and family history) and then the pathway factors in childhood (externalising behaviour problems, adolescent smoking and drinking). Adjustments little changed the association between 7-year maths z-score and HbA_{1c}. However adjustments for adult social class and for educational qualifications, reduced the associations between 7-year maths z-score and HbA_{1c} by 13% and 26% respectively. The association between 7-16 year change in maths z-score and HbA_{1c} was entirely mediated by adolescent smoking, adult class or qualifications. Adult lifestyle factors modestly mediated the association between 7-year maths z-score and HbA_{1c}, most notably physical inactivity at 45 years. Smoking history between 23 and 42 years mediated the association to a greater extent, accounting for 31% of the effect. Smoking entirely mediated the association between 7-16 year change in maths z-score and HbA_{1c}. Non-drinking mediated the association between 7-year maths and HbA_{1c} by 23% and between 7-16 year change in maths and HbA_{1c} by 12%; to a lesser extent than smoking history. 45-year BMI and waist circumference were stronger mediators of the associations between 7-year and 7-16 year change in maths and HbA_{1c} than adult weight gain.

Section 3 presents multivariate models adjusting for variables listed in section 2 in blocks (groups). The first model includes confounders from birth; social class of origin, birthweight and family history of diabetes, and the childhood model includes externalising behaviour problems, adolescent smoking and drinking. As expected from the small effects of separately adjusting for the confounding variables from birth, simultaneous adjustment for the birth

confounders barely changed the estimate for 7-year z-score (3%) or 7-16 year z-score. The childhood and adult pathway models substantially mediated association between 7-year maths z-score (or 7-16 year z-score) and HbA_{1c}. Smoking and drinking together accounted for more of the association between 7-year maths and HbA_{1c} (51%), than adiposity (26%), social factors (23%) or activity and diet (36%).

Section 4 presents cumulative models, adding blocks of pathway factors in temporal sequence across the lifecourse; each row contains all the variables from the row above. After adjusting for confounders from birth, the child factors did not entirely mediate associations between 7-year maths and HbA_{1c} although they mediated the association with 7-16 year z-score. However, adjustment for adult qualifications and social position, fully mediated the association between 7-year maths and HbA_{1c}. Addition of other lifestyle and adiposity variables did not offer additional explanations.

Because the adult factors were contemporaneous, models in section 4 were built up entering adult variables in a different order (data not presented). Adding any adult block to a model with the childhood block abolished the effect of cognition on HbA_{1c} and subsequent additions of other adult blocks offered no further explanation.

Table 7.2b uses the same structure to present results for women. Poorer 7-year maths ability was associated with increased HbA_{1c}; 0.03% per SD increase z-score. Change in 7-16 year maths z-score was not significantly associated with HbA_{1c} levels: 0.01 (95% CI -0.01, 0.02), so percentage change in the coefficients was not calculated.

Section 2 contains estimates of the association between 7-year maths z-scores and HbA_{1c} level, adjusted for each of the confounding factors from birth in turn. The association was partly attenuated (by 31%) on adjustment for social class of origin. When the pathway or mediating factors were examined separately, childhood externalising behavioural problems and drinking frequency at 16 years partly mediated the association, accounting for 19% and 12% respectively. Adult social class attenuated the association between 7-year maths z-scores and HbA_{1c} to a similar to degree to that seen in men (19%). Adult educational qualifications entirely mediated the association between 7-year maths and HbA_{1c} level. Physical activity and diet were partial mediators, accounting for between 8 and 23% of the association. As for men, 45-year inactivity was a strong mediator (23% reduction in 7-year maths coefficient on adjustment for computer use). Smoking and drinking were stronger mediating pathways accounting for 27% and 54% respectively of the association between 7-year maths z-score and HbA_{1c} level. Drinking history, BMI or waist circumference on their own each entirely mediated the association between 7-year maths and HbA_{1c} level.

The third section presents multivariate models and the pattern of results is similar to that seen in men. Childhood externalising problems and 16-year drinking partly mediate between 7-year maths and HbA_{1c}. However, the association was entirely mediated by each of the separate adult blocks; social class and qualifications; activity and diet; smoking and drinking; and adult adiposity. The bottom section in the table presents results of cumulative models. Once the childhood factors were taken into account, the pathways between 7-year maths and HbA_{1c} are accounted for and the adult factors offer little additional explanations.

In summary cognitive ability appears to be associated with later HbA_{1c} through pathways including childhood social position, externalising behaviour, adult drinking and smoking histories and social position and education and adiposity. Adult smoking and drinking, social position and adiposity blocks were particularly important pathways.

Maths and elevated HbA1c / type 2 diabetes

Tables 7.3a and 7.3b present Odds Ratios for the associations between maths level and change and elevated HbA_{1c} / type 2 diabetes at 45 years for men and women respectively. Lower 7-year maths ability rank (higher z-score) was associated with elevated HbA_{1c} /diabetes; OR 1.31 (95%CI 1.13, 1.53) in men and 1.32 (1.09, 1.59) in women. 7-16 year maths z-score change was not associated with elevated HbA_{1c} /type 2 diabetes. Only the percentage change in coefficients for 7-year maths z-score were calculated. In section 2, adjustment for social class at birth partly mediated the association between 7-year maths and elevated HbA_{1c} /diabetes in men and women by 26% and 19% respectively. Among men, childhood behavioural problems, adolescent drinking and adult social position were weak pathways between 7-year maths and high HbA_{1c} / type 2 diabetes. In women, childhood behavioural problems partly mediated the association (25%) and in both sexes adult qualifications completely mediated the association. The lifestyle factors diet and activity accounted for between 6 and 27% of the association; in both sexes the largest mediating factor was inactivity (indexed by 45-year television watching). Smoking history mediated the association, by 11% in men and 6% in women. Non-drinking histories were stronger mediators; 27 % in men and 31% in women. As expected, 45-year BMI and waist circumference were strong mediators between 7-year maths and elevated HbA_{1c}/ type 2 diabetes; accounting for most of the association in men and all of the association in women, whilst weight gain was weaker (as with continuous HbA_{1c}).

Section 3 presents multivariable models. Birth factors did not entirely confound the association between 7-year maths z-score and elevated HbA_{1c}, nor did childhood factors entirely mediate the association. However, in both sexes, when social class and educational qualifications were adjusted together they entirely mediated the association. Additionally, among women, when

smoking and drinking were included in a model together, they entirely mediated the association, as did 45-year BMI and weight change between 23 and 45 years.

In section 4, in cumulative models indicate the association between 7-year maths z-scores and high HbA_{1c} /diabetes was robust to adjustment for confounding factors from birth. In men externalising behaviour and adolescent drinking were not strong pathways whereas in women, externalising behaviours entirely mediated the association. In men, adjustment for adult class and qualifications entirely mediated the association. Adding other health behaviours or adiposity gave no additional explanatory power. For men, additional analyses (not presented) varied the order adult pathways were entered into the model, the addition of any adult block to the childhood model entirely mediated the association between 7-year maths and high HbA_{1c}.

In summary the association between 7-year maths ability and high HbA_{1c} /type 2 diabetes is robust to adjustment for social position at birth. Pathways between childhood maths rank and later elevated HbA_{1c} operated through externalising behaviour in women and, in men, adult educational qualifications were important mediators of the association. A history of non/infrequent drinking, 45-year physical inactivity and 45-year BMI were important mediators between childhood ability at 7 years and elevated HbA_{1c} levels at 45 years.

Maths and metabolic syndrome

Tables 7.4a and 7.4b present ORs for the associations between 7-year maths z-score or 7-16 year change in z-score and presence of metabolic syndrome in men and women respectively. Higher 7-year maths z-score (ie lower maths ability rank) was associated with metabolic syndrome; OR 1.24 (95%CI 1.12, 1.38) in men and 1.40 (1.24, 1.58) in women. The association between the change in maths z-score 7-16 years and metabolic syndrome was not significant in men and was confounded by early social position in women. Therefore percentage changes in the coefficients of 7-16 year change in maths z-score are not presented. In section 2, adjustment for social class of origin partly attenuated the association between 7-year maths and metabolic syndrome in both sexes (by 17% and 25% respectively). In both sexes adult educational qualifications were the main pathway between 7-year maths and metabolic syndrome. Diet and activity were not dominant pathways. However 45-year physical inactivity (television viewing) accounted for 17% of the association in men and 15% in women. Smoking and non-drinking history each mediated the association, by 8% in men and 15% in women. Change in body weight during adulthood did not mediate between 7-year maths z-score and 45-year metabolic syndrome.

In section 3, birth factors only partly confounded the association between 7-year maths z-score and metabolic syndrome and childhood factors partly mediated the association. None of the

adult blocks entirely mediated the association between 7-year maths and metabolic syndrome, with the exception of social class and educational qualifications which entirely mediated the association in women.

In section 4 associations between 7-year maths and metabolic syndrome were not confounded by birth factors and externalising behaviour was a stronger mediator in women than in men. However addition of class and qualifications entirely mediated the association. Addition of other health behaviours or measures of adiposity gave no additional explanatory power. Varying the order of the adult blocks were added to models of the childhood block, indicated that only class and qualifications entirely mediated the association with metabolic syndrome. Other variables were partial mediators, although smoking and drinking were complete mediators in women.

In summary 7-year maths z-score was inversely associated with metabolic syndrome at age 45 years. The association was partly mediated by early social position and childhood behavioural problems. Adult educational level and physical inactivity were important pathways. Smoking and drinking histories were mediators particularly in women.

Maths and 45-year BMI

Adult smoking and drinking were dominant mediators of the associations between childhood cognitive ability and the glucose homeostasis outcomes, as were BMI and waist circumference. Chapter 3 investigated the pathways between cognitive ability and adult health behaviours. Acknowledging the role of obesity as a mediator between 7-year maths z-score and 7-16 year change in maths z-score with HbA_{1c} level and elevated HbA_{1c} /type 2 diabetes (Tables 7.2 and 7.3) similar analyses are presented in order to understand how health behaviours contribute to the associations between childhood cognition and adiposity as adiposity is a major mediating pathway to diabetic risk.

Poorer 7-year maths ability was significantly associated with higher 45-year BMI; 0.39 Kg/m^2 (95%CI 0.26, 0.52) in men and 0.59 (0.39, 0.79) in women per SD increase in maths z-score. Associations were partly confounded by social class at birth, and less so by maternal smoking during pregnancy. Externalising problems in childhood mediated the association between 7-year maths and 45-year BMI to a similar degree in men and women (13% and 12%). Adult social class and qualifications were strong mediators of the associations. Educational qualifications substantially attenuated the association between 7-year maths and 45-year BMI: by 39% and 50% in men and women. Of the diet and activity measures studied, 45-year physical inactivity, indexed by TV watching was the strongest mediator, accounting for 18 and 22% of the associations in men and women respectively. Adjusting for smoking history increased the coefficient for the association between 7-year maths and 45-year BMI; ex smokers have higher

BMI than non or current smokers. Non-drinking history mediated the association between 7-year maths and 45-year BMI in men (7%), and to a larger degree in women (30%).

The childhood block and the adult social block accounted for most of the maths-BMI association, partly attenuating the association with 7-year z-score in section 3. In section 4, the association between 7-year maths and 45-year BMI was fully mediated after addition of adult class and qualifications. However, including the behavioural factors before adult social factors only partly mediated the associations (data not presented).

Decline in maths ability rank between 7 and 16 years was significantly associated with increased adult BMI: each SD increase in maths z-score rank was associated with 0.13 (95%CI 0.01, 0.25) kg/m^2 increase in 45 year BMI in men and 0.29 (95%CI 0.13, 0.44) kg/m^2 in women. However adjustment for confounders from birth, attenuated associations to null.

Maths and 45-year waist circumference

Tables 7.6a and 7.6b show that poorer 7-year maths ability was significantly associated with larger 45-year waist circumference; 0.97 cm (95%CI 0.62, 1.31) increase in men and 1.36 cm (0.98, 1.73) in women per SD increase in 7-year maths z-score. The associations were partly confounded by social class at birth, and to lesser extent by other birth factors. Externalising problems in childhood mediated the association between 7-year maths and 45-year waist circumference similarly in men and women (14% and 15%). Adult social class and qualifications strongly mediated the associations between 7-year maths and 45-year waist circumference. Educational qualifications attenuated the association by 43% in men and 52% in women. Of the diet and activity measures studied, physical inactivity at 45 years, (TV watching) was the strongest mediator, attenuating the association by 21% in men and 23% in women. Smoking history did not mediate the association whilst non-drinking history did mediate the association between 7-year maths and 45-year waist circumference to a small amount in men (5%), and a larger degree in women (23%).

In the multivariate models, confounders from birth attenuated the associations. The adult social block was the strongest mediator of the association between 7-year maths and waist circumference, however even taking into account adult social measures, an inverse association between childhood maths scores and waist circumference remained. When the blocks were added together in the cumulative life course model, the combination of child and adult social position completely mediated the associations between 7-year maths and waist circumference. Hence, the association between maths ability and 45-year waist circumference was fully mediated.

There were significant associations between change in maths rank from 7 to 16 years and adult waist circumference in women. Decline in ability rank (1 SD increase in maths z-score 7-16 years) was associated with 0.74 cm (95%CI 0.38, 1.10). This association was robust to adjustment for the group of confounding factors from birth. However adult social position entirely mediated the association. However, including the behavioural factors before adult social factors only partly mediated the associations (data not presented).

In summary maths ability was associated with adiposity in part through the effects on childhood factors and notably adult achieved qualifications and social position.

Health behaviours and glucose homeostasis

As part of Aim 2 assessing the mediating role of health behaviours between cognition and glucose homeostasis, the coefficients for the summary measures of smoking and non-drinking in models presented in tables 7.2-7.6 were examined. In a univariate model heavy smoking was associated with 0.23% higher HbA_{1c} in men (0.11% in women). Adding cognitive ability, and all adult exposures partly attenuated associations (smoking coefficients reduced between 1% and 35%), although they remained significant. Similarly on adjustment for all variables percentage change for lifecourse non-drinking was up to 36%. In the final model with all lifecourse predictors, smoking and non-drinking were the only variables still significantly associated with HbA_{1c} level. Associations between smoking and elevated HbA_{1c} /diabetes were mediated by cognition and other lifestyle variables. About half of the associations with non-drinking were mediated, but some association remained in the final model. The associations between smoking or non-drinking with metabolic syndrome were mediated in the final model, although metabolic syndrome was still associated with heavy smoking; for example OR 2.07 (95%CI 1.38 ,3.10) associated with smoking >20/day at 42 years in women and OR 1.43 (1.04, 1.97) for men.

Discussion

Summary of findings

Associations between childhood cognitive ability and the three measures of adult glucose homeostasis were partly confounded by childhood factors, but associations remained after adjustment. The associations between childhood cognitive ability and glucose homeostasis were mediated by factors from across the lifecourse, notably tobacco and alcohol use throughout adulthood, own attained social position and educational qualifications as well as adiposity and physical inactivity in mid-adult life and poor behavioural adjustment in childhood. There was no evidence of direct effects of cognitive ability on mid-life glucose homeostasis (illustrated in Figure 7.1 with a direct arrow from cognitive ability to glucose regulation). Rather, data

suggested that cognition exerted an influence on glucose homeostasis indirectly through pathway factors. Smoking history and a lifecourse indicator of infrequent drinking were both important pathways, more so for HbA_{1c} as a continuous outcome, compared to elevated HbA_{1c} or metabolic syndrome. Other dominant pathways between cognition and glucose homeostasis were adult educational qualifications and adult adiposity. In this thesis, the role of health behaviours in mediating between cognition and adult glucose regulation is a particular interest. There were significant associations between 7-year maths ability with BMI and waist circumference which were in part confounded by birth factors, although they were still robust to adjustment for confounders. As expected, adult educational level was a strong mediator of the association between 7-year maths and BMI or waist circumference. However there was less evidence for the importance of smoking and drinking histories as mediators of associations between cognitive ability and adiposity.

Strengths and weaknesses

General strengths and weaknesses about the high quality of the study design and measurement of exposures and outcomes were discussed in previous chapters. Further, the prospective data on a wide range of pathways are a key strength. In existing literature about childhood cognition and adult health or mortality, very few studies have investigated intermediary pathways in any detail. Many studies have very limited data on intermediary pathway factors which is mostly limited to factors contemporary to the childhood mental testing and secondly, to data collected at a single adult follow-up (Deary et al. 2004; Lawlor et al. 2005a). The 1958 cohort is one of few data sets with potential to investigate lifecourse pathways from childhood ability to later health outcomes with good quality prospective data. The only previous study of cognitive ability and diabetes risk was in a younger population and suffered from very low numbers of cases and could not look at diabetes in isolation (Martin et al. 2004). Analyses presented here are the first large scale study of childhood cognitive development and diabetes risk and also more generally, one of the first studies of childhood cognitive ability and adult health or mortality to model the intermediary pathways fully. This study demonstrates associations across the whole spectrum of cognitive ability with adult health outcomes, implying that associations between cognition and adult health are not just driven by excessive disease burden in lower scoring groups. The 1958 cohort is not limited to a sub-population, eg of gifted individuals. Further, the 1958 cohort benefits from a large population-based sample including both sexes; to date much work on childhood cognitive ability and health outcomes has focused on follow-up studies based on occupational groups which are predominantly male (Batty et al. 2006a).

The methodology used to study the lifecourse pathways between cognitive ability and midlife glucose homeostasis has strengths and weaknesses: cumulative lifecourse models were built up

based on the temporal sequence of the variables entered into the models and was structured around the framework in Figure 7.1. This method of analysis benefits from simplicity and repeated measures were taken into account by summary statistics. For the maths and reading trajectories repeated measures methodology was used and for the health behaviours, a simpler strategy based on counts was used. The count variables were chosen on the basis of associations observed between cognition and health behaviours (Chapter 4) and also health behaviours and glucose regulation (Chapter 5). The lifecourse models of the mediating pathways between cognitive ability in childhood and adult glucose homeostasis used the smoking history and the count variable summarising the number of adult surveys that a participant was a non-drinker. Although these models do not use specific multilevel or repeated measures methodology, by using summary measures of behaviour, a simpler modelling strategy could be undertaken which is easier to present and explain. A weakness of the cumulative lifecourse modelling strategy based on the temporal ordering of the variables is that the effects of variables that occur simultaneously in time are not separated out. Also, the ordering of the variables in the models, particularly in the final multivariate blocks will affect the interpretation of the results. The study suffers from weaknesses inherent to the study design, namely loss to follow-up resulting in bias. In this chapter where many variables from across the lifecourse are incorporated in models, this issue has been addressed by using multiple imputation of covariates, including variables predictive of drop-out in the imputation models for efficient estimation of missing covariates. Multiple imputation enables efficient analysis of data with missing information, but requires assumptions about patterns of missingness. It is not possible to know whether the missing at random assumption holds, but imputation should reduce bias compared to analyses based on complete cases. Analyses based on multiple imputation with varying numbers of cycles were compared complete case analysis. The latter showed a similar direction of results to the multiple imputations, although the coefficient estimates were smaller because of the lower numbers in the sample, the similarity lent strength to the interpretation of the effects. The strengths and weaknesses of the reading and maths scores were discussed in Chapter 4. Whilst the repeated measures are beneficial, the modelling strategy of predicting individual trajectories of change deals with missing data but has the draw back of only allowing for linear change as there are only three time points. An outstanding issue in the study of cognition and adult health is residual confounding. For example, because health behaviours tend to cluster into healthy and unhealthy groups and the self-reported measures of diet and physical activity simplify patterns of complex behaviours, it may be that the particular effects of one type of behaviour are not completely accounted for. However the wide range of behavioural and social pathways investigated in this study should minimise the possibility of residual confounding.

Investigating the degree to which associations between cognitive ability and glucose regulation are confounded by common causes in childhood- Aim 1.

One potential explanation for the associations of childhood cognition with later adult health outcomes may be through confounding. Several potential common causes were considered in this chapter and the rationale for choosing the variables that were used was presented in Chapter 1. The results indicated that associations between childhood cognitive ability and the three measures of adult glucose dysregulation and also central and total adiposity were all somewhat attenuated but robust to adjustment for confounding factors from childhood. A range of confounders was considered; only those which were associated with both the cognitive test score and the outcome were entered in the model. In each of the analyses, social position of origin was the most dominant of the childhood confounders. The importance of early social background on development of cognitive trajectories has been demonstrated in this cohort (Fogelman et al. 1978; Jefferis et al. 2002) and in other contexts(Lawlor et al. 2005b; Lawlor et al 2006b). Additionally, social background is likely affect adult health through a variety of pathways; through differential exposures to significant health risks in childhood, tracking of social position, initiation of health behaviours. Thus childhood cognitive ability may mediate between childhood physical and social disadvantage and adult health status. The hypothesis that associations between childhood cognition and adult disease my be due to the fact that childhood cognition reflects poorer growth and development *in utero*, poor nutrition and physical illnesses accumulated prior to cognitive testing was not fully tested in this chapter, but social position which is associated with these factors was a partial confounder. The hypothesis was not supported in analyses of the 1946 British birth cohort (where the effect of cognitive ability was independent of childhood socioeconomic position and illness), or a Danish cohort where mortality risk associated with cognitive ability remained elevated after adjustment for birthweight and early socio-economic position (Kuh et al 2004; Osler et al. 2003). In the Aberdeen cohort (born in 1921), 11-year cognitive ability measured in the 1932 Scottish Mental Survey was associated with mortality risk up to age 76 years. The best fitting models had cognitive ability as a mediating variable between early social and material disadvantage (Whalley & Deary 2001). Analyses of a more recent cohort, born 1950-1956, reported that the effects of early socioeconomic position on adult health behaviours (binge drinking, smoking and obesity) measured in midlife were mediated via childhood cognitive ability (Lawlor et al 2005a). These studies suggest that cognitive ability is an important factor on the pathway from early disadvantage to health behaviours and also to mortality risks.

Investigating the mediating roles of lifecourse smoking and non-drinking in associations between cognitive ability and glucose regulation- Aim 2

Chapter 5 discussed biological mechanisms underlying the associations between smoking or alcohol use with glucose homeostasis and associations between (i) smoking history and (ii)

consistent non or infrequent drinking with adult glucose dysregulation were observed. Compared to non-smokers, and ex-smokers current smokers and especially heavier smokers had higher mean HbA_{1c} and raised risks of elevated HbA_{1c} / type 2 diabetes or metabolic syndrome. Non- or infrequent drinking both cross sectionally and longitudinally across adulthood were associated with poorer glucose homeostasis. Chapter 5 reviewed the evidence that smoking and drinking were associated with diabetes risk through their influence on adiposity.

In a multivariate model of HbA_{1c} and cognition scores including both smoking and drinking, the association between cognition and HbA_{1c} level was entirely mediated. Smoking and drinking were stronger mediators than adult adiposity, activity and diet and adult social class and educational level. It is notable that smoking and drinking play such a large part in the association between 7-year cognitive ability and HbA_{1c} level across the whole range of HbA_{1c}, not just in the high risk groups. This finding fits with (i) the strong associations reported between childhood cognitive ability and the smoking and drinking measures (Chapter 4) and (ii) the associations between increased tobacco use and non-drinking and diabetes risk (Chapter 5). In multivariate models, smoking and drinking together partly mediated associations between childhood cognitive ability and elevated HbA_{1c} / type 2 diabetes, to a similar degree to the mediating role of adult social position. Whilst smoking and drinking together in the multivariate model mediated (but again, not entirely) the associations between childhood cognitive ability and metabolic syndrome, adult educational level or social position were stronger mediators.

In addition to cigarette smoking and alcohol use, other health behaviours must be considered in understanding pathways from cognitive ability to diabetes risk, because of the way in which health behaviours tend to cluster. There is evidence that smokers are more likely to engage in unhealthy alcohol drinking patterns and also have poorer diets for example, with higher saturated fat content, less dietary fibre and vitamin C (Sargeant et al. 2001a) and adults with less frequent alcohol consumption (for example, less often than monthly, compared to most days of the week) are more sedentary, have less fruit and vegetable intake (Tolstrup et al. 2005). Dietary fat , fruit and vegetable intake, fish consumption and vitamin C levels have been reported to be associated with HbA_{1c} levels (Harding et al. 2001; Harding et al. 2004; Sargeant et al. 2000; Sargeant et al. 2001b). Additionally lower levels of physical activity are associated with HbA_{1c} levels (Harding et al 2001) and risk of diabetes (Bassuk & Manson 2005) or metabolic syndrome (Bertrais et al. 2005; Ekelund et al. 2005; Farrell et al. 2004). For example a recent review reported that physically active individuals have 30-50% lower risk of diabetes than inactive individuals (Bassuk & Manson 2005). Exercise, specifically aerobic resistance training is a core part of the treatment recommended for patients with type 2 diabetes. A prospective Dutch cohort study following adults to age 36 years reported that there was greater

central fat deposition, decreased cardio pulmonary fitness levels and decreased levels of intense physical activity in men and women who developed metabolic syndrome(Ferreira et al. 2005).

The main effects of smoking and drinking on HbA_{1c} or glucose homeostasis were independent of each other and of measures of physical activity and diet (Chapter 5). The physical activity and diet measures which are presented in each results table were those which were significantly associated with the glucose homeostasis outcome. There is much literature about the associations between diet or activity and diabetes risk. However, at present there are no other studies of associations between cognitive development in childhood and diabetes risk in mid-life, or of the role of mediators of the associations with which to compare these findings directly. The results of analyses of physical activity and diet, indicated that the most consistent mediator of associations between childhood cognition and adult glucose homeostasis were inactivity in adulthood, in particular television viewing. Although simple measures of leisure time physical activity based on frequency of exercise were used in analyses presented here, even using these simple measures, physical inactivity was consistently associated with poorer glucose regulation in adulthood. In the 1958 cohort physical activity at 23, 33 and 42 years as well as inactivity at 45 years were associated with trajectories of childhood cognitive development; lower test scores were associated with less frequent physical activity and more inactivity (data not presented). Lower levels of physical activity and poor diet may be initiated in adolescence when smoking and alcohol use patterns are also initiated. The role of the different health behaviours varied somewhat depending on the particular measure of glucose homeostasis. Whilst the diet and physical activity entirely mediated the association between cognition and HbA_{1c} level in women but not in men, they partially mediated between either elevated HbA_{1c} or metabolic syndrome. Hence health behaviours are part of a pathway to mid-life health outcomes. The mediating roles fit with literature documenting the associations between both cognitive ability and health behaviours and also health behaviours and glucose homeostasis.

There is a substantial literature examining social and educational inequalities in mortality and morbidity which has attempted to quantify the relative importance of material, behavioural and psychosocial exposures on the educational differences in mortality outcomes (Kilander et al. 2001; Lantz et al. 2001; Lynch et al. 1996; van Lenthe et al. 2002; van Oort et al. 2005). Whilst the other studies are not directly comparable to the aim of studying the pathways between early childhood ability and later glucose regulation, they highlight relevant issues. The studies mostly found that there were modest effects of behavioural factors (variously including current drinking, smoking history, BMI and current physical activity) on the different mortality risks studied and that there were important effects of material factors such as housing tenure, employment status and income on mortality risks. The relative effect sizes differed in the studies as would be expected in different cultural contexts and different disease end points. One

study specifically examines pathways between educational gradients in metabolic syndrome (and also CHD). The study, set in Finland, reported educational gradients in metabolic syndrome across three categories of final educational qualifications: university education, middle education and basic education (lasting 9 years). In this case, the estimates of the educational gradients were little changed on taking account of adult smoking, drinking, fresh fruit and vegetable consumption and leisure time physical activity (Silventoinen et al. 2005).

In addition to any direct effect of smoking or drinking on glucose regulation, there are also other reasons to expect that smoking may be associated with diabetes risk. Associations between glucose homeostasis and unhealthy behaviour patterns may operate through residual confounding with other social factors or other unhealthy behaviours, notably diet and physical activity, with poor mental health which may promote smoking habits or even through avenues such as job stress and strain which have also been hypothesised to be associated with metabolic syndrome onset (Chandola et al. 2006a). One strand of social epidemiology has concentrated on the importance of material factors in shaping disease risks. For example that increased income levels allow access to certain goods and services which make healthy choices easier or more accessible. Also, education may shape social norms about behaviours as well as influencing occupational trajectories. Social class based on occupational groups may influence health through the workplace environment, not only through exposure to risky or hazardous exposures in the workplace, but there is also a strand of social epidemiology which emphasises the importance of psychosocial exposures linked to control over work environment, and work stress. Health behaviours may be related to both social factors (and indeed may represent a rational response to disadvantaged material circumstances (Lawlor et al. 2003b)) and also to poorer psychosocial well being as smoking and drinking are used as coping mechanisms in response to stress(Graham et al. 2006).

Investigating the degree to which associations between cognitive ability and glucose regulation are mediated by social trajectories; social position and qualifications attained in adult life- Aim 3

Associations between childhood cognition and each measure of glucose regulation operated through adult social position and educational qualifications. Educational level in particular mediated between childhood ability and subsequent glucose regulation (or BMI and waist circumference). Educational level completely mediated associations between cognitive ability and HbA_{1c} level in women and also elevated HbA_{1c} /type 2 diabetes in both sexes. The role of education in mediating the associations with metabolic syndrome was pronounced, although it was a partial mediator. Chapter 6 investigated the mediating role of educational level and social class and discussed how findings about the mediating role of adult social position fit with existing literature. The current chapter builds on Chapter 6 because the magnitude of the

mediating role of education is compared to the magnitude of role of other health behaviours. For HbA_{1c} level, the mediating role of education is smaller than that of smoking and drinking but was similar in magnitude to the role of adult adiposity, which was surprising. The mediating role of highest educational level was expected to be very strong given that educational level is strongly predicted by childhood cognitive trajectories and it was not expected that smoking and drinking histories would be mediators of similar magnitude. In the lifecourse models, building up the explanatory variables in temporal sequence, once adult social factors were added to the confounders from birth and the childhood pathway factors the associations between childhood ability and later glucose regulation were entirely mediated. Hence educational level is a key part of the pathway between childhood cognitive development and adult diabetes risk.

The finding that adult educational level mediates between childhood cognition and diabetes risk fits with the limited current knowledge about the pathways between cognition and diabetes (Martin et al 2004; Starr et al. 2000). The mediating roles of education or adult social position are also consistent with previous findings about the associations between achieved social position and educational qualifications gained by mid-life and glucose regulation. Diabetes risk has been repeatedly shown to be greater in less educated and manual social groups (Brunner et al. 1997; Dalstra et al 2005; Langenberg et al 2006; Silventoinen et al. 2005).

There is little other literature with which to make direct comparisons of the mediating roles of lifecourse variables in the associations between childhood ability and later diabetes risk because the field of cognitive epidemiology is still emerging. However, given the educational gradients seen in measures of glucose regulation including HbA_{1c}, and in prevalence of metabolic syndrome, diabetes and related mortality, (Chaturvedi et al. 1998; Lidfeldt et al. 2003; Mokdad et al. 2003; Wamala et al 1999) the underlying reasons for educational gradients have been investigated. For example, a study of socioeconomic difference in type 2 diabetes in Swedish men and women reported that established risk factors, BMI, physical activity and cigarette smoking (as well as family history of diabetes) explained nearly half of the social gradients in diabetes risk, without further attenuation adding in psychosocial characteristics (Agardh et al. 2004). The existence of educational and social gradients in diabetes has mostly been couched in terms of arguments about behavioural responses to complex messages about medication, self monitoring and self care (Gottfredson 2004). The large UK Prospective Diabetes Study has demonstrated the benefit of good glycaemic control in preventing complications in type 2 diabetes(UK Prospective Diabetes Study (UKPDS) 1998). However, management of diabetes with good glycaemic control can be complex and challenging, including regular monitoring of HbA_{1c} as well as nephropathy and eye and foot examinations. Treatment for blood pressure and lipid control also needs to be monitored because of the greater risks of cardiovascular

complications in diabetic subjects. An investigation of treatment adherence among diabetic patients stratified by their level of schooling indicated that less educated diabetic patients were more likely to switch treatments leading to poorer health status. Further, in a randomised controlled trial setting, an intensive treatment regime had beneficial results for the glycaemic control of less educated patients (Goldman & Smith 2002). Likewise more educated individuals may be more likely to attend screening or identify problems earlier than those with less education. Functional health literacy which involves reading and understanding appointment forms and prescriptions may be another pathway to worse diabetic risk in individuals with lower cognitive ability(Brown et al. 2004). There is a literature documenting that the process of care diabetic for diabetic patients is differentiated by educational level for example, diabetic patients with less education are reported to have lower rates of lipid measurements, opthalmologic visits as well as receiving fewer foot and dilated eye examinations and having less understanding of HbA_{1c} monitoring (Brown et al 2004). A study of diabetic patients recruited from primary care clinics in a public hospital in USA reported that glycemic contol was associated with educational level. Compared to having less than a high school education, graduating from high school and having some college education were associated with lower HbA_{1c} levels: -0.45 % and -0.22 % HbA_{1c} respectively (Schillinger et al. 2006). Analysis of this sample indicated that after taking into account socio-demographic characteristics of the sample, health literacy was associated with lower HbA_{1c} levels (Schillinger et al. 2002). In the same low-income sample, health literacy mediated between educational level and glycemic control indicated by HbA_{1c} level; pathway analysis indicated that the inclusion of health literacy accounted for the associations between education and HbA_{1c} levels (Schillinger et al 2006). In the same population better health literacy was associated with diabetes management and care.

In addition self-efficacy has been proposed as a pathway underlying the educational gradients in health outcomes: self-efficacy refers to patients' confidence in their own ability to carry out certain behaviours, greater self-efficacy in relation to self-care may increase the chances that a person takes the appropriate steps to self-care. In the same study of diabetic patients mentioned above, diabetes self-efficacy was associated with self-care: good diet, exercise, self-monitoring of blood glucose and foot care. However, adherence to medication was not associated with self-efficacy (Sarkar et al. 2006).

The studies discussed above provide some explanations for associations between the lower levels of cognitive ability or educational qualfications and diabetes risk. However if the main means through which education affects progression of diabetes risk is through limited understanding of medication, necessity of visiting health care provider and negotiating the difficulties of self glucose monitoring, the continuous association between sub-clinical HbA_{1c} levels and education is not satisfactorily explained. The association between childhood

cognitive ability, mediated by educational level with the whole spectrum of HbA_{1c}, not just the diabetic patients suggests that there are other pathways that operate. It suggests that educational level is a marker for other behaviours which influence HbA_{1c} level. These may include health behaviours (smoking, drinking and physical activity) which are influenced by cognitive ability and are in turn associated with poorer metabolic control and adiposity.

More general and pervasive social determinants of health may also be important in explaining the educational gradient in diabetes risk. Health varies according to neighbourhood type: affluent or deprived (availability of fresh cheap foods, transport, housing). Type of job and the associated job control or job strain have been investigated as potential underlying causes of social or educational gradients in cardiovascular health outcomes in the UK. The pathways mentioned above may also apply to development of higher HbA_{1c} levels and metabolic syndrome, not just diagnosed diabetes. Because of the importance of obesity and central obesity in particular in diabetes risk, the importance of the pathways between educational ability and diabetes should also be considered. The higher rates of obesity in groups with poorer educational status may involve access to cheap unhealthy foods, less opportunities for physical activity (be it living in areas with fewer recreational open spaces or inability to afford costs of participating in sports or gyms), poorer transport links and also higher rates of smoking and poorer mental health.

Investigating the degree to which associations between cognitive ability and glucose regulation are mediated by adiposity in adulthood- Aim 4

The results presented in this chapter fit with results from chapter 6 which showed that adult adiposity was an important mediator between childhood cognitive ability and HbA_{1c} levels; both across the spectrum of HbA_{1c} and in the "high risk" group. This chapter includes an additional measure which is weight change over adulthood. As mentioned in the introduction there is evidence that weight change during adulthood is associated with childhood cognitive ability (Chandola et al 2006b) and with adult glucose regulation (Ferreira et al 2005; Hillier et al 2006). Weight gain is also associated with adult educational level (Halkjaer et al 2003; Lahmann et al. 2000; Wagner et al. 2001). In men, weight gain made modest contribution to HbA_{1c} level in men, compared to the effects of BMI and waist circumference at age 45 years, although it made a more substantial contribution to HbA_{1c} levels in women. A similar pattern was seen for high HbA_{1c}. The reasons for any gender difference in the effect of weight gain as a mediator between cognitive ability and adult HbA_{1c} may be due to gender-differences in the associations between childhood cognitive development and weight gain although the basis for this is not clear.

Investigating the degree to which associations between cognitive ability and adiposity in adulthood are mediated by lifecourse pathways, in particular health behaviours- Aim 5

7-year ability, rather than the change in ability to 16 years, was the aspect of cognitive development which was most consistently associated with mid-life BMI in men and women. The association between cognitive ability and adiposity operated most strongly through social class of origin, maternal smoking during pregnancy, behavioural maladjustment (women). However, attained qualifications and social position in adulthood were important mediating pathways; each mediating a substantial part (but not all) of the association between cognition and BMI. Hence although higher levels of childhood cognition are associated with superior adult education and more professional social position which each in turn influence risks of adiposity, there is some evidence that cognition has a separate and additional association with mid-life BMI. A study of Danish men attending military draft board reported that the association between IQ at draft age and adult obesity or weight change at a subsequent follow-up operated entirely through adult qualifications (Halkjaer et al 2003). This is in line with other work based on the 1958 cohort which examined BMI at 42 years and change in BMI between 16 and 42 years (Chandola et al 2006b). An association between 11-year general ability (verbal and non-verbal tests), and 42-year BMI was entirely mediated by qualifications achieved by 23 years and also by an index of healthy diet. However the dietary score used (frequency of consuming chips, other fried food and fresh fruit at 33 years) (Chandola et al 2006b) was more limited than the 33 and 42 year scores used in the analyses presented in this chapter. The study found that there was no direct association between 11-year ability and change in BMI from 16 to 42 years, whereas there were indirect associations operating through educational qualifications and diet. In the analysis presented here for cognition and 45-year BMI, out of the behavioural measures studied, it was physical inactivity indexed by television viewing at 45 years which was the strongest pathway. When examined separately the pathway factors did not fully mediate the cognition-adiposity associations reported in the 1958 cohort data, however when modelled jointly in cumulative models, the association between cognitive ability and 45-year BMI was fully mediated by the pathway factors. One study investigated pathways underlying the educational gradients in obesity at age 30 years in men and women in Northern Sweden and reported that there were gender differences in the pathways (Novak et al. 2005). For men, low parental support of education at 16 years, lack of physical activity and alcohol consumption at 30 years as well as not participating in associations for social activities were important pathways. Whereas for women there were several factors in adolescence which were important pathways: age at menarche, physical activity, parental divorce, popularity in school and control in school. Additionally having restricted financial resources were important in adult life.

Conclusions

The analyses of the 1958 cohort data indicate that associations between childhood cognitive ability and the three measures of adult glucose dysregulation were all robust to adjustment for confounding factors from childhood. Indeed childhood cognition may act in part to explain the link between early social position and later HbA_{1c}. Childhood cognitive ability influenced glucose dysregulation in adult life through a variety of mediating factors from across the lifecourse. Poor behavioural adjustment in childhood, tobacco and alcohol use throughout adulthood, own attained social position and educational qualifications as well as adiposity and physical inactivity in mid-adult life were the most consistent pathways between childhood cognition and subsequent diabetes risk. Hence there was not evidence of direct effects of cognitive ability on glucose dysregulation in mid-life. Smoking history and a lifecourse indicator of drinking frequency, focusing on infrequent drinking, were both substantial pathways between childhood ability rankings at 7 years and later measures of HbA_{1c} and to a lesser extent also for elevated HbA_{1c} or metabolic syndrome. The dominant mediating pathways between cognition and glucose dysregulation were attainment of adult educational qualifications and adult adiposity. Adult educational level also mediated the association between 7-year maths and BMI or waist circumference. However there was less evidence for the importance of lifecourse smoking and drinking histories as mediators of associations between cognitive ability and adiposity. Therefore studies of the underlying causes of inequalities in health behaviours and adiposity according to final educational qualifications may give further insights into the pathways from childhood cognitive development to adult diabetes risk.

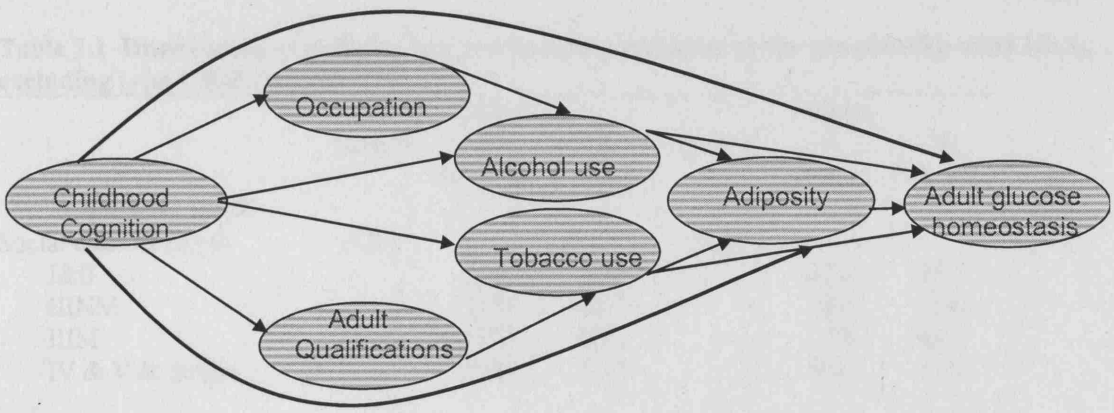


Figure 7.1 Conceptual framework, outlining main relationships to be examined

Table 7.1 Distribution of pathway and confounding variables in the sample with valid HbA_{1c}, excluding type 1 diabetics, n=7799

		Male			Female	
	Total N	N or mean	% or SD	Total N	N or mean	% Or SD
Childhood block						
Social class of origin	3614			3600		
I&II		698	19.3		652	18.1
IIINM		361	10.0		359	10.0
IIIM		1777	49.2		1789	49.7
IV & V & Single		778	21.5		800	22.2
Birthweight (Kg)	3186	3.419	0.515	3576	3.264	0.499
Maternal smoking in pregnancy (>4th month)	3663			3636		
Non smoker		2483	67.8		2447	67.3
Smoker		1180	32.2		1189	32.7
Infant feeding	3409			3441		
Not breast fed		1033	30.3		1012	29.4
Breast fed < 1 month		791	23.2		830	24.1
Breast fed > 1 month		1558	45.7		1578	45.6
Don't know		27	0.8		21	0.6
Family history diabetes	3401			3430		
Yes		3288	96.7		3314	96.6
No		77	2.3		89	2.6
Don't know		36	1.1		27	0.8
7 year maths z-score	3852	-0.121	0.714	3845	-0.052	0.694
Change in maths z-score 7-16 years	3852	-0.056	0.400	3844	0.054	0.328
General ability (11 years)	2383	44.5	15.5	3380	46.5	14.9
Externalising behaviour	3750			3758		
At 7 or 11 years		21.4	803		12.9	484
Neither		78.6	2947		87.1	3274
Smokes (16 years)	3003			3034		
Non smoker, <1/day		2046	68.1		2136	70.4
1-19 /week		242	8.1		333	11.0
>20 / week		715	23.8		565	18.6
Drinks alcohol (16 years)	3016			3033		
Past week		1634	54.2		1256	41.4
Past month		553	18.3		596	19.7
Infrequent		693	23.0		1002	33.0
Never		136	4.5		179	5.9

Table 7.1 continued

	Total N	Male N or mean	% or SD	Total N	Female N or mean	% Or SD
Adult social block						
Social class (33 years)	3264			3308		
I&II		1382	42.3		1132	34.2
IIINM		349	10.7		1204	36.4
IIIM		1068	32.7		245	7.4
IV & V		465	14.3		77	20.0
Qualifications (33 years)	3354			3492		
None		214	6.4		280	8.0
< O level		406	12.1		561	16.1
O level		800	23.9		1299	37.2
A level		878	26.2		371	10.6
Higher		1056	31.5		981	28.1
Adult behavioural block						
Activity (23 years)	3323			3405		
<1 / month		1274	38.3		2101	61.7
1-3 / month		605	18.2		497	14.6
1-2 / week		744	22.4		542	15.9
≥ 3 / week		700	21.1		265	7.8
Activity (33 years)	3428			3549		
<2-3 / month		1031	30.1		1047	29.5
1 / week		761	22.2		818	23.1
2-3 / week		844	24.6		734	20.7
4 -7 / week		792	23.1		950	26.8
Activity (42 years)	3801			3806		
<2-3 / month		1255	33.0		1285	33.8
1 / week		791	20.8		650	17.1
2-3 / week		830	21.8		818	21.5
4 -7 / week		925	24.3		1053	27.7
PC use (45 years)	3725			3712		
None		984	26.4		1252	33.7
< 1 hours / day		1879	50.4		1957	52.7
≥ 1 hours / day		862	23.1		503	13.6
TV viewing (45 years)	3815			3 800		
< 3 hours / day		2925	76.7		2966	78.1
≥ 3 hours / day		890	23.3		834	22.0

Table 7.1 continued

	Total N	Male N or mean	% or SD	Total N	Female N or mean	% Or SD
33 year Diet; quartiles	3428			3548		
Q1 unhealthy		1116	32.6		518	14.6
Q2 less healthy		930	27.1		717	20.2
Q3 more healthy		744	21.7		916	25.8
Q4 healthiest		638	18.6		1397	39.4
42 year Diet; quartiles	3796			3807		
Q1 unhealthy		1191	31.4		639	16.8
Q2 less healthy		1245	32.8		1058	27.8
Q3 more healthy		697	18.4		789	20.7
Q4 healthiest		663	17.5		1321	34.7
42-year smoking history	3795			3804		
Never		1778	46.9		1848	48.6
Quit <33 years		644	17.0		628	16.5
Quit 33-42 years		469	12.4		405	10.7
Smokes 1-19/ day		401	10.6		521	13.7
Smokes ≥20 / day		503	13.3		402	10.6
Frequency of non-drinking 23, 33, 42 or 45 years	3907			3892		
0 occasions		2980	76.3		2012	51.7
1 survey		470	12.0		818	21.0
2 surveys		247	6.3		468	12.0
≥ 3 surveys		210	5.4		594	15.3
Adult adiposity						
Weight change 23-45 years, Kg	3286	13.63	9.57	3364	12.85	10.57
Waist circumference, cm (45 years)	3894	98.2	10.9	3870	85.3	12.7
BMI, kg/m^2 (45 years)	3902	27.7	4.2	3887	26.9	5.5

Table 7.2a Association between HbA_{1c} and (i)7-year maths z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for men [β coefficients (95%CI)].

Univariate Models [a] (n=3831)	7year maths z-score	% change[d]	7-16 year change in maths z-score	% change[d]
1.Unadjusted	0.039 (0.020, 0.058)		0.017 (0.002, 0.031)	
2.Unadjusted +				
Birth (confounders)				
Social class of origin	0.039 (0.018, 0.060)	0	0.017 (0.002, 0.032)	0
Birthweight	0.038 (0.019, 0.057)	-3	0.017 (0.002, 0.031)	0
Family history	0.039 (0.019, 0.058)	0	0.017 (0.002, 0.031)	0
Childhood (pathways)				
Externalising problems	0.036 (0.016, 0.055)	-8	0.015 (0.000, 0.030)	-12
Drinking (16 years)	0.037 (0.017, 0.056)	-5	0.018 (0.003, 0.032)	6
Smoking (16 years)	0.037 (0.018, 0.056)	-5	0.012 (-0.003, 0.026)	-29
Adult Social Factors (33 years)				
Social class	0.034 (0.012, 0.057)	-13	0.014 (-0.001, 0.030)	-18
Qualifications	0.029 (0.005, 0.054)	-26	0.011 (-0.003, 0.026)	-35
Adult Lifestyle Factors				
Activity and diet				
Physical activity (23 years)	0.037 (0.017, 0.056)	-5	0.017 (0.002, 0.031)	0
Physical activity (33 years)	0.038 (0.018, 0.057)	-3	0.016 (0.002, 0.031)	-6
Physical activity (42 years)	0.036 (0.016, 0.056)	-8	0.016 (0.002, 0.031)	-6
PC use (45 years)	0.034 (0.014, 0.053)	-13	0.014 (0.000, 0.028)	-18
TV watching (45 years)	0.034 (0.015, 0.054)	-13	0.014 (0.000, 0.029)	-18
Diet (33 years)	0.037 (0.018, 0.056)	-5	0.016 (0.001, 0.030)	-6
Smoking and Non-Drinking				
Smoking 23-42 years	0.027 (0.007, 0.046)	-31	0.006 (-0.008, 0.020)	-65
Non-drinking 23-44 years	0.030 (0.010, 0.050)	-23	0.015 (0.000, 0.030)	-12
Adult adiposity (45 years)				
Weight change 23-45 years	0.038 (0.018, 0.057)	-3	0.019 (0.005, 0.033)	12
BMI 45 years	0.030 (0.011, 0.049)	-23	0.014 (0.001, 0.028)	-18
Waist circumference 45 years	0.029 (0.010, 0.049)	-26	0.015 (0.001, 0.029)	-12
3.Multivariate models (each block separately)[b]				
Birth	0.038 (0.017, 0.058)	-3	0.017 (0.002, 0.032)	0
Childhood	0.031 (0.011, 0.050)	-21	0.011 (-0.003, 0.025)	-35
Adult Social Factors	0.030 (-0.012, 0.072)	-23	0.010 (-0.005, 0.026)	-41
Activity and diet	0.025 (0.005, 0.045)	-36	0.011 (-0.003, 0.025)	-35
Smoking and drinking	0.019 (-0.002, 0.039)	-51	0.005 (-0.009, 0.019)	-71
Adult adiposity	0.029 (0.009, 0.048)	-26	0.014 (0.001, 0.028)	-18
4.Multivariate models (blocks together)[c]				
Birth block	0.038 (0.017, 0.058)	-3	0.017 (0.002, 0.032)	0
+ childhood	0.029 (0.009, 0.050)	-26	0.011 (-0.003, 0.026)	-35
+ social class & qualifications 33 y	0.022 (-0.004, 0.047)	-44	0.007 (-0.008, 0.022)	-59
+ activity & diet 23-42 years	0.016 (-0.010, 0.042)	-59	0.006 (-0.010, 0.021)	-65
+ smoking & drinking 23-42 years	0.011 (-0.015, 0.037)	-72	0.004 (-0.011, 0.020)	-76
+ All	0.005 (-0.020, 0.030)	-87	0.005 (-0.010, 0.019)	-97

[a] Linear regression models of HbA_{1c} predicted by 7-year and 7-16 year change in maths z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All coefficients are for maths z-scores.
[b] Each model includes 7-year and 7-16 year change in maths z-score and all the variables listed in the block.
[c] Same as [b] but models are cumulative, each containing everything in the previous model.
[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table 7.2b Association between HbA_{1c} and (i)7-year maths z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for women [β coefficients (95%CI)].

Univariate Models [a] (n=3832)	7-year maths z-score	% change[d]	7-16 year change in maths z-score
1.Unadjusted	0.026 (0.011, 0.040)		0.006 (-0.012, 0.023)
2.Unadjusted +			
Birth (confounders)			
Social class of origin	0.018 (0.002, 0.034)	-31	
Family history	0.025 (0.010, 0.039)	-4	
Childhood (pathways)			
Externalising problems	0.021 (0.006, 0.037)	-19	
Drink 16 years	0.023 (0.008, 0.038)	-12	
Adult Social Factors (33 years)			
Social class	0.021 (0.006, 0.036)	-19	
Qualifications	0.014 (-0.002, 0.031)	-46	
Adult Lifestyle Factors			
Activity and diet			
Physical activity 23 years	0.023 (0.008, 0.037)	-12	
Physical activity 42 years	0.024 (0.009, 0.039)	-8	
PC use (45 years)	0.020 (0.004, 0.036)	-23	
TV watching (45 years)	0.022 (0.007, 0.037)	-15	
Diet (33 years)	0.021 (0.006, 0.036)	-19	
Diet (42 years)	0.024 (0.009, 0.039)	-8	
Smoking and Non-Drinking			
Smoking 23-42 years	0.019 (0.004, 0.033)	-27	
Non-drinking 23-44 years	0.012 (-0.002, 0.027)	-54	
Adult adiposity (45 years)			
Weight change 23-45 years	0.021 (0.007, 0.036)	-19	
BMI 45 years	0.013 (-0.002, 0.027)	-50	
Waist circumference 45 years	0.012 (-0.002, 0.027)	-54	
3.Multivariate models (each block separately)[b]			
Birth	0.017 (0.001, 0.034)	-35	
Childhood	0.019 (0.003, 0.035)	-27	
Adult Social Factors	0.013 (-0.004, 0.029)	-50	
Activity and diet	0.014 (-0.002, 0.030)	-46	
Smoking and drinking	0.006 (-0.008, 0.021)	-77	
Adult adiposity	0.012 (-0.003, 0.026)	-54	
4.Multivariate models (blocks together)[c]			
Birth block	0.017 (0.001, 0.034)	-35	
+ childhood	0.011 (-0.007, 0.029)	-58	
+ social class & qualifications 33 y	0.002 (-0.017, 0.021)	-92	
+ activity & diet 23-42 years	-0.001 (-0.020, 0.019)	-104	
+ smoking & drinking 23-42 years	-0.005 (-0.024, 0.014)	-119	
+ All	-0.007 (-0.026, 0.012)	-127	

[a] Linear regression models of HbA_{1c} predicted by 7-year and 7-16 year change in maths z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All coefficients are for maths z-scores.
[b] Each model includes 7-year and 7-16 year change in maths z-score and all the variables listed in the block.
[c] Same as [b] but models are cumulative, each containing everything in the previous model.
[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table 7.3a Association between $HbA_{1c} \geq 6\%$ and (i) 7-year maths z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for men [OR (95%CI)].

Univariate Models [a] (n=3907)	7year maths z-score	% change[d]	7-16 year change in maths z-score
1.Unadjusted	1.31 (1.13, 1.53)		1.09 (0.95, 1.26)
2.Unadjusted +			
Birth (confounders)			
Social class of origin	1.23 (1.05, 1.44)	-26	
Family history	1.30 (1.12, 1.52)	-3	
Childhood (pathways)			
Externalising problems	1.30 (1.12, 1.52)	-2	
Drinking (16 years)	1.29 (1.11, 1.51)	-6	
Adult Social Factors (33 years)			
Social class	1.29 (1.09, 1.54)	-6	
Qualifications	1.18 (0.97, 1.42)	-43	
Adult Lifestyle Factors			
Activity and diet			
Physical activity (33 years)	1.29 (1.11, 1.50)	-6	
Physical activity (42 years)	1.27 (1.09, 1.49)	-11	
PC use (45 years)	1.26 (1.08, 1.47)	-16	
TV watching (45 years)	1.24 (1.06, 1.45)	-23	
Smoking and Non-Drinking			
Smoking 23-42 years	1.27 (1.09, 1.48)	-11	
Non-drinking 23-44 years	1.23 (1.05, 1.43)	-27	
Adult Adiposity (45 years)			
Weight change 23-45 years	1.29 (1.11, 1.50)	-6	
BMI (45 years)	1.20 (1.02, 1.41)	-35	
Waist circumference (45 years)	1.20 (1.02, 1.41)	-35	
3.Multivariate models (each block separately)[b]			
Birth	1.22 (1.04, 1.43)	-28	
Childhood	1.29 (1.10, 1.50)	-6	
Adult Social Factors	1.18 (0.97, 1.43)	-43	
Activity and inactivity	1.18 (1.00, 1.38)	-43	
Smoking and drinking	1.19 (1.02, 1.39)	-39	
Adult adiposity	1.19 (1.02, 1.40)	-39	
4.Multivariate models (each block together)[c]			
Birth block	1.22 (1.04, 1.43)	-28	
+ childhood	1.2 (1.02, 1.42)	-35	
+ social class & qualifications 33 y	1.13 (0.93, 1.37)	-59	
+ activity & diet 23-42 years	1.08 (0.89, 1.32)	-73	
+ smoking & drinking 23-42 years	1.04 (0.85, 1.27)	-86	
+ all	1.05 (0.85, 1.30)	-83	

[a] Logistic regression models of $HbA_{1c} \geq 6$ %, predicted by 7-year and 7-16 year change in maths z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All ORs are for maths z-scores.
[b] Each model includes 7-year and 7-16 year change in maths z-score and all the variables listed in the block.
[c] Same as [b] but models are cumulative, each containing everything in the previous model.
[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table 7.3b Association between $HbA_{1c} \geq 6\%$ and (i) 7-year maths z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for women [OR (95%CI)].

Univariate Models [a] (n=3892)	7-year maths z-score	% change[d]	7-16 year change in maths z-score
1.Unadjusted	1.32 (1.09, 1.59)		1.06 (0.89,1.26)
2.Unadjusted +			
Birth (confounders)			
Social class of origin	1.26 (1.03, 1.53)	-19	
Family history	1.31 (1.09, 1.58)	-3	
Childhood (pathways)			
Externalising problems	1.24 (1.02, 1.50)	-25	
Adult Social Factors (33 years)			
Social class	1.33 (1.08, 1.63)	2	
Qualifications	1.20 (0.96, 1.51)	-37	
Adult Lifestyle Factors			
Activity and diet			
Physical activity (42 years)	1.30 (1.08, 1.57)	-6	
PC use (45 years)	1.34 (1.10, 1.63)	6	
TV watching (45 years)	1.23 (1.02, 1.49)	-27	
Smoking and Non-Drinking			
Smoking 23-42 years	1.30 (1.08, 1.57)	-6	
Non-drinking 23-44 years	1.22 (1.01, 1.48)	-31	
Adult Adiposity (45 years)			
Weight change 23-45 years	1.29 (1.06, 1.56)	-10	
BMI (45 years)	1.14 (0.93, 1.40)	-57	
Waist circumference (45 years)	1.11 (0.91, 1.37)	-66	
3.Multivariate models (each block separately)[b]			
Birth	1.25 (1.02, 1.52)	-23	
Childhood	1.24 (1.02, 1.50)	-25	
Adult Social Factors	1.20 (0.96, 1.51)	-37	
Activity and inactivity	1.25 (1.02, 1.53)	-23	
Smoking and drinking	1.20 (0.99, 1.46)	-37	
Adult adiposity	1.10 (0.89, 1.35)	-69	
4.Multivariate models (each block together)[c]			
Birth block	1.25 (1.02, 1.52)	-23	
+ childhood	1.17 (0.95, 1.43)	-48	
+ social class & qualifications 33 y	1.09 (0.86, 1.38)	-72	
+ activity & diet 23-42 years	1.09 (0.86, 1.39)	-72	
+ smoking & drinking 23-42 years	1.05 (0.82, 1.34)	-86	
+ all	1.00 (0.75, 1.32)	-101	

[a] Logistic regression models of $HbA_{1c} \geq 6$ %, predicted by 7-year and 7-16 year change in maths z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All ORs are for maths z-scores.
[b] Each model includes 7-year and 7-16 year change in maths z-score and all the variables listed in the block.
[c] Same as [b] but models are cumulative, each containing everything in the previous model.
[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table 7.4a Association between metabolic syndrome and (i) 7-year maths z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for men [OR (95%CI)].

Univariate Models [a] (n=3765)	7year maths z-score	% change[d]	7-16 year change in maths z-score
1.Unadjusted	1.24 (1.12, 1.38)		1.04 (0.95, 1.14)
2.Unadjusted +			
Birth (confounders)			
Social class of origin	1.20 (1.08, 1.33)	-17	
Family history	1.24 (1.12, 1.37)	0	
Childhood (pathways)			
Externalising problems	1.23 (1.10, 1.36)	-21	
Adult Social Factors (33 years)			
Social class	1.22 (1.09, 1.37)	-8	
Qualifications	1.14 (1.02, 1.28)	-42	
Adult Lifestyle Factors			
Activity and diet			
Physical activity (23 years)	1.23 (1.11, 1.36)	-4	
Physical activity (33 years)	1.24 (1.12, 1.38)	0	
Physical activity (42 years)	1.22 (1.11, 1.35)	-8	
PC use (45 years)	1.23 (1.11, 1.37)	-4	
TV watching (45 years)	1.20 (1.08, 1.33)	-17	
Smoking and Non-Drinking			
Smoking 23-42 years	1.22 (1.10, 1.35)	-8	
Non-drinking 23-44 years	1.22 (1.10, 1.35)	-8	
Adult Adiposity (45 years)			
Weight change 23-45 years	1.23 (1.11, 1.37)	-4	
3.Multivariate models (each block separately)[b]			
Birth	1.20 (1.08, 1.33)	-17	
Childhood	1.23 (1.10, 1.36)	-4	
Adult Social Factors	1.14 (1.01, 1.29)	-42	
Activity and inactivity	1.18 (1.07, 1.32)	-25	
Smoking and drinking	1.20 (1.08, 1.33)	-17	
Adult adiposity	1.23 (1.11, 1.37)	-4	
4.Multivariate models (each block together)[c]			
Birth block	1.20 (1.08, 1.33)	-17	
+ childhood	1.18 (1.06, 1.32)	-25	
+ social class & qualifications 33 y	1.11 (0.98, 1.26)	-54	
+ activity & diet 23-42 y	1.10 (0.97, 1.24)	-58	
+ smoking & drinking 23-42 y	1.09 (0.96, 1.24)	-63	
+ all	1.08 (0.94, 1.23)	-67	

[a] Logistic regression models of metabolic syndrome, predicted by 7-year and 7-16 year change in maths z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All ORs are for maths z-scores.

[b] Each model includes 7-year and 7-16 year change in maths z-score and all the variables listed in the block.

[c] Same as [b] but models are cumulative, each containing everything in the previous model.

[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table 7.4b Association between metabolic syndrome and (i) 7-year maths z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for women [OR (95%CI)].

Univariate Models [a] (n=3745)	7year maths z-score (intercept)	% change [d]	7-16 year change in maths z-score (slope)
1.Unadjusted	1.40 (1.24, 1.58)		1.13 (1.00, 1.27)
2.Unadjusted +			
Birth (confounders)			
Social class of origin	1.30 (1.15, 1.48)	-25	
Maternal smoking	1.38 (1.22, 1.55)	-5	
Family History	1.38 (1.22, 1.55)	-5	
Childhood (pathways)	1.34 (1.19, 1.52)	-15	
Drinking (16 years)			
Smoking (16 years)	1.34 (1.19, 1.52)	-15	
Externalising problems	1.38 (1.22, 1.55)	-5	
Adult Social Factors (33 years)			
Social class	1.29 (1.13, 1.46)	-28	
Qualifications	1.16 (1.00, 1.35)	-60	
Adult Lifestyle Factors			
Activity and diet			
Diet (33 years)	1.37 (1.21, 1.54)	-7	
Physical activity (23 years)	1.37 (1.22, 1.55)	-7	
Physical activity (33 years)	1.38 (1.23, 1.56)	-5	
Physical activity (42 years)	1.38 (1.23, 1.56)	-5	
PC use (45 years)	1.41 (1.24, 1.59)	3	
TV watching (45 years)	1.34 (1.19, 1.51)	-15	
Smoking and Non-Drinking			
Smoking 23-42 years	1.34 (1.19, 1.52)	-15	
Non-drinking 23-44 years	1.34 (1.19, 1.51)	-15	
Adult Adiposity (45 years)			
Weight change 23-45 years	1.40 (1.23, 1.60)	0	
3.Multivariate models (each block separately)[b]			
Birth	1.28 (1.13, 1.45)	-30	
Childhood	1.31 (1.16, 1.48)	-23	
Adult Social Factors	1.13 (0.97, 1.31)	-68	
Activity and diet	1.32 (1.16, 1.49)	-20	
Smoking and drinking	1.29 (1.14, 1.45)	-28	
Adult adiposity	1.40 (1.23, 1.60)	0	
4.Multivariate models (each block together)[c]			
Birth block	1.28 (1.13, 1.45)	-30	
+ childhood	1.20 (1.06, 1.37)	-50	
+ social class & qualifications 33 y	1.03 (0.88, 1.20)	-93	
+ activity & diet 23-42 y	1.03 (0.88, 1.20)	-93	
+ smoking & drinking 23-42 y	1.01 (0.86, 1.19)	-98	
+ all	1.04 (0.88, 1.23)	-90	

[a] Logistic regression models of metabolic syndrome, predicted by 7-year and 7-16 year change in maths z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All ORs are for maths z-scores.

[b] Each model includes 7-year and 7-16 year change in maths z-score and all the variables listed in the block.

[c] Same as [b] but models are cumulative, each containing everything in the previous model.

[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table 7.5a Association between 45-year BMI and 7-year (i)7-year maths z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for men [β coefficients (95%CI)].

Univariate Models [a] (n=4651)	7-year maths z-score	% change[d]	7-16 year change in maths z-score	% change[d]
1.Unadjusted	0.389 (0.256, 0.521)		0.129 (0.006, 0.252)	
2.Unadjusted +				
Birth (confounders)				
Social class of origin	0.288 (0.154, 0.423)	-26	0.050 (-0.075, 0.176)	-61
Birth weight	0.407 (0.275, 0.540)	4	0.135 (0.011, 0.260)	5
Breast feeding	0.372 (0.239, 0.504)	-4	0.118 (-0.004, 0.241)	-9
Smoking in pregnancy	0.349 (0.218, 0.481)	-10	0.102 (-0.020, 0.225)	-21
Family history	0.381 (0.249, 0.514)	-2	0.127 (0.004, 0.250)	-2
Childhood (pathways)				
Externalising problems	0.337 (0.203, 0.470)	-13	0.102 (-0.023, 0.227)	-21
Adult Social Factors (33 years)				
Social class	0.298 (0.154, 0.443)	-23	0.062 (-0.068, 0.192)	-52
Qualifications	0.236 (0.089, 0.382)	-39	0.017 (-0.123, 0.156)	-87
Adult Lifestyle Factors				
Activity and diet				
Physical activity (33 years)	0.384 (0.251, 0.516)	-1	0.126 (0.002, 0.250)	-2
Physical activity (42 years)	0.375 (0.241, 0.509)	-4	0.124 (0.002, 0.247)	-4
PC use (45 years)	0.426 (0.294, 0.559)	10	0.155 (0.033, 0.277)	20
TV watching (45 years)	0.320 (0.187, 0.454)	-18	0.089 (-0.033, 0.212)	-31
Diet (33 years)	0.399 (0.264, 0.534)	3	0.130 (0.005, 0.255)	1
Smoking and Non-Drinking				
Smoking 23-42 years	0.428 (0.293, 0.564)	10	0.163 (0.037, 0.289)	26
Non-drinking 23-44 years	0.363 (0.227, 0.500)	-7	0.124 (0.001, 0.247)	-4
3.Multivariate models (each block separately)[b]				
Birth	0.254 (0.121, 0.388)	-35	0.031 (-0.094, 0.156)	-76
Childhood	0.337 (0.203, 0.470)	-13	0.102 (-0.023, 0.227)	-21
Adult Social Factors	0.202 (0.051, 0.354)	-49	-0.008 (-0.149, 0.132)	-106
Activity and diet	0.367 (0.232, 0.503)	-5	0.121 (-0.002, 0.245)	-6
Smoking and drinking	0.400 (0.261, 0.540)	3	0.158 (0.032, 0.284)	22
4.Multivariate models (blocks together)[c]				
Birth block	0.254 (0.121, 0.388)	-36	0.031 (-0.094, 0.156)	-76
+ childhood	0.209 (0.075, 0.342)	-46	0.008 (-0.119, 0.135)	-94
+ social class & qualifications 33 years	0.108 (-0.044, 0.259)	-72	-0.069 (-0.209, 0.072)	-105
+ activity & diet 23-42 years	0.103 (-0.043, 0.250)	-74	-0.066 (-0.207, 0.075)	-105
+ smoking & drinking 23-42 years	0.089 (-0.060, 0.239)	-77	-0.046 (-0.185, 0.093)	-104

[a] Linear regression models of 45-year BMI predicted by 7-year and 7-16 year change in maths z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All coefficients are for maths z-scores.

[b] Each model includes 7-year and 7-16 year change in maths z-score and all the variables listed in the block.

[c] Same as [b] but models are cumulative, each containing everything in the previous model.

[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table 7.5b Association between 45-year BMI and (i)7-year maths z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for women [β coefficients (95%CI)].

Univariate Models [a] (n=4697)	7-year maths z-score	% change[d]	7-16 year change in maths z-score	% change[d]
1.Unadjusted	0.594 (0.394, 0.793)		0.285 (0.127, 0.443)	
2.Unadjusted +				
Birth (confounders)				
Social class of origin	0.421 (0.223, 0.619)	-29	0.172 (0.011, 0.333)	-40
Smoking in pregnancy	0.559 (0.362, 0.757)	-6	0.267 (0.108, 0.426)	-6
Family history	0.585 (0.387, 0.783)	-2	0.282 (0.125, 0.440)	-1
Childhood (pathways)				
Externalising problems	0.521 (0.319, 0.722)	-12	0.259 (0.101, 0.418)	-9
Drinking (16 years)	0.580 (0.378, 0.783)	-2	0.291 (0.133, 0.450)	2
Adult Social Factors (33 years)				
Social class	0.473 (0.259, 0.686)	-20	0.221 (0.059, 0.382)	-22
Qualifications	0.298 (0.073, 0.522)	-50	0.137 (-0.031, 0.306)	-52
Adult Lifestyle Factors				
Physical activity (23 years)	0.504 (0.305, 0.703)	-15	0.245 (0.086, 0.403)	-14
Physical activity (33 years)	0.572 (0.373, 0.771)	-4	0.272 (0.113, 0.430)	-5
Physical activity (42 years)	0.567 (0.369, 0.766)	-5	0.255 (0.098, 0.412)	-11
PC use (45 years)	0.583 (0.368, 0.798)	-2	0.270 (0.111, 0.429)	-5
TV watching (45 years)	0.464 (0.263, 0.665)	-22	0.233 (0.077, 0.390)	-18
Smoking and Non-Drinking				
Smoking 23-42 years	0.622 (0.415, 0.829)	5	0.306 (0.145, 0.466)	7
Non-drinking 23-44 years	0.417 (0.227, 0.607)	-30	0.221 (0.065, 0.376)	-22
3.Multivariate models (each block separately)[b]				
Birth	0.389 (0.193, 0.585)	-35	0.157 (-0.003, 0.318)	-45
Childhood	0.506 (0.302, 0.711)	-15	0.266 (0.107, 0.424)	-7
Adult Social Factors	0.255 (0.028, 0.483)	-57	0.110 (-0.058, 0.279)	-61
Activity and diet	0.406 (0.192, 0.619)	-32	0.183 (0.026, 0.341)	-36
Smoking and drinking	0.443 (0.246, 0.641)	-25	0.240 (0.083, 0.398)	-16
4.Multivariate models (blocks together)[c]				
Birth block	0.389 (0.193, 0.585)	-35	0.157 (-0.003, 0.318)	-45
+ childhood	0.306 (0.105, 0.508)	-48	0.139 (-0.022, 0.300)	-51
+ social class & qualifications 33	0.069 (-0.157, 0.294)	-88	0.016 (-0.154, 0.186)	-94
+ activity & diet 23-42 y	0.037 (-0.191, 0.265)	-94	-0.004 (-0.173, 0.166)	-101
+ smoking & drinking 23-42 y	-0.012 (-0.239, 0.215)	-102	0.011 (-0.155, 0.177)	-96

[a] Linear regression models of 45-year BMI predicted by 7-year and 7-16 year change in maths z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All coefficients are for maths z-scores.

[b] Each model includes 7-year and 7-16 year change in maths z-score and all the variables listed in the block.

[c] Same as [b] but models are cumulative, each containing everything in the previous model.

[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table 7.6a Association between 45-year waist circumference and (i)7-year maths z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for men [β coefficients (95%CI)].

Univariate Models [a] (n=4626)	7year maths z-score	% change [d]	7-16 year change in maths z-score
1.Unadjusted	0.966 (0.621, 1.311)		0.126 (-0.194, 0.445)
2.Unadjusted + Birth (confounders)			
Social class of origin	0.784 (0.430, 1.139)	-19	
Birth weight	1.035 (0.692, 1.378)	7	
Smoking in pregnancy	0.877 (0.535, 1.220)	-9	
Breast feeding	0.917 (0.573, 1.262)	-5	
Family history	0.946 (0.601, 1.291)	-2	
Childhood (pathways)			
Externalising problems	0.829 (0.480, 1.178)	-14	
Adult Social Factors			
Social class (33 years)	0.797 (0.429, 1.166)	-17	
Qualifications (33 years)	0.550 (0.118, 0.981)	-43	
Adult Lifestyle Factors			
Physical activity (23 years)	0.888 (0.533, 1.243)	-8	
Physical activity (33 years)	0.932 (0.582, 1.282)	-4	
Physical activity (42 years)	0.902 (0.559, 1.245)	-7	
PC use (45 years)	1.046 (0.695, 1.397)	8	
TV watching (45 years)	0.761 (0.417, 1.104)	-21	
Diet (33 years)	0.950 (0.606, 1.295)	-2	
Diet (42 years)	0.984 (0.636, 1.332)	2	
Smoking and Non-Drinking			
Smoking 23-42 years	1.022 (0.671, 1.373)	6	
Non-drinking 23-44 years	0.913 (0.559, 1.266)	-5	
3.Multivariate models (each block separately)[b]			
Birth	0.704 (0.350, 1.058)	-27	
Childhood	0.829 (0.480, 1.178)	-14	
Adult Social Factors	0.495 (0.059, 0.932)	-49	
Activity and diet	0.794 (0.438, 1.151)	-18	
Smoking and drinking	0.964 (0.604, 1.324)	0	
4.Multivariate models (blocks together)[c]			
Birth block	0.704 (0.350, 1.058)	-27	
+ childhood	0.581 (0.221, 0.941)	-40	
+ social class & qualifications 33 y	0.287 (-0.155, 0.728)	-70	
+ activity & diet 23-42 y	0.230 (-0.199, 0.658)	-76	
+ smoking & drinking 23-42 y	0.227 (-0.208, 0.662)	-77	

[a] Linear regression models of 45-year waist circumference predicted by 7-year and 7-16 year change in maths z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All coefficients are for maths z-scores.

[b] Each model includes 7-year and 7-16 year change in maths z-score and all the variables listed in the block.

[c] Same as [b] but models are cumulative, each containing everything in the previous model.

[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table 7.6b Association between 45-year waist circumference and (i)7-year maths z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for men [β coefficients (95%CI)].

Univariate Models [a] (n=4665)	7-year maths z-score	% change [d]	7-16 year change in maths z-score
1.Unadjusted	1.630 (1.233, 2.027)		0.156 (-0.202, 0.514)
2.Unadjusted +			
Birth (confounders)			
Social class of origin	1.271 (0.860, 1.683)	-22	
Birth weight	1.691 (1.277, 2.106)	4	
Smoking in pregnancy	1.566 (1.168, 1.964)	-4	
Breast feeding	1.594 (1.197, 1.992)	-2	
Family history	1.594 (1.199, 1.988)	-2	
Childhood (pathways)			
Externalising problems	1.440 (1.030, 1.850)	-12	
Adult Social Factors			
Social class (33 years)	1.308 (0.890, 1.726)	-20	
Qualifications (33 years)	0.912 (0.436, 1.388)	-44	
Adult Lifestyle Factors			
Physical activity (23 years)	1.447 (1.048, 1.846)	-11	
Physical activity (33 years)	1.570 (1.174, 1.965)	-4	
Physical activity (42 years)	1.551 (1.157, 1.944)	-5	
PC use (45 years)	1.629 (1.222, 2.035)	0	
TV watching (45 years)	1.326 (0.929, 1.723)	-19	
Diet (33 years)	1.562 (1.162, 1.962)	-4	
Smoking and Drinking			
Smoking 23-42 years	1.559 (1.154, 1.964)	-4	
Non-drinking 23-44 years	1.289 (0.891, 1.687)	-4	
3.Multivariate models (each block separately)[b]			
Birth	1.241 (0.820, 1.662)	-24	
Childhood	1.440 (1.030, 1.850)	-12	
Adult Social Factors	0.788 (0.318, 1.258)	-52	
Activity and diet	1.224 (0.814, 1.634)	-25	
Smoking and drinking	1.218 (0.814, 1.623)	-25	
4.Multivariate models (blocks together)[c]			
Birth block	1.241 (0.820, 1.662)	-24	
+ childhood	1.055 (0.622, 1.488)	-35	
+ social class & qualifications 33 y	0.456 (-0.020, 0.932)	-72	
+ activity & diet 23-42 y	0.396 (-0.075, 0.868)	-76	
+ smoking & drinking 23-42 y	0.260 (-0.210, 0.731)	-84	

[a] Linear regression models of 45-year waist circumference predicted by 7-year and 7-16 year change in maths z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All coefficients are for maths z-scores.

[b] Each model includes 7-year and 7-16 year change in maths z-score and all the variables listed in the block.

[c] Same as [b] but models are cumulative, each containing everything in the previous model.

[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Appendix 7 Lifecourse models of glucose homeostasis

Appendix 7.1 Sample representativeness

Table A7.1.1 Distribution of key variables in the sample with valid HbA_{1c}, excluding type 1 diabetics (n=7799) compared to the complete case analysis samples presented for the lifecourse regression models.

	Male						Female					
	Target sample with valid HbA_{1c}[a]			Complete case analysis sample n=1580[b]			Target sample with valid HbA_{1c}[a]			Analysis sample[b]		
	Total N	N or mean	% or SD	Total N	N or mean	% or SD	Total N	N or mean	% or SD	Total N	N or mean	% or SD
Social class of origin	3786			1580			3783			2007		
I&II Professional		744	19.7		343	21.7		698	18.5		395	19.7
III Non Manual		377	10.0		160	10.1		371	9.8		191	9.5
III Manual		1839	48.6		773	48.9		1859	49.1		1011	50.4
IV & V & Single		826	21.8		304	19.2		855	22.6		410	20.4
7 year maths z-score	3852	-0.165	0.975	1580	-0.279	0.955	3845	-0.074	0.984	2007	-0.159	0.981
Change in maths z-score 7-16 years	3852	-0.144	1.03	1580	-0.262	1.142	3845	0.171	1.04	2007	0.132	1.149
Social class (33 years)	3264			1580			3308			2007		
I&II Professional		1382	42.3		700	44.3		1132	34.2		687	34.2
III Non Manual		349	10.7		180	11.4		1204	36.4		753	37.2
III Manual		1068	32.7		509	32.2		245	7.4		154	7.7
IV & V		465	14.3		191	12.1		77	20.0		413	20.5
Smoking history (42 years)	3795			1580			3804			1575		
Never		1778	46.9		792	50.1		1848	48.6		1001	49.9
Quit <33 years		644	17.0		279	17.7		628	16.5		363	18.1
Quit 33-42 years		469	12.4		189	12.0		405	10.7		206	10.3
Smokes 1-19/ day		401	10.6		156	9.9		521	13.7		260	13.0
Smokes ≥20 / day		503	13.3		164	10.7		402	10.6		177	8.8
Number of occasions Non/ infrequent drinking 23- 44 years	3907			1580			3892			2007		
0		2980	76.3		1240	78.5		2012	51.7		1049	52.3
1		470	12.0		187	11.8		818	21.0		403	20.1
2		247	6.3		72	4.6		468	12.0		236	11.8
≥3		210	5.4		81	5.1		594	15.3		319	15.8
BMI, kg/m^2 (45 years)	3902	27.7	4.2	1580	27.6	3.9	3887	26.9	5.5	1575	27.7	3.9
Waist circumference, cm (45 years)	3894	98.2	10.9	1580	97.8	10.3	3870	85.3	12.7	1575	98.3	10.3

Appendix 7.2 Association between glucose homeostasis and reading trajectories

Table A7.2.1a Association between HbA_{1c} and 7-year reading z-score and change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for men [β coefficients (95%CI)].

Univariate Models [a] (n=3831)	7y Reading z-score	% change[d]	7-16year change in reading z-score	% change[d]
1.Unadjusted	0.044 (0.025, 0.062)		0.018 (0.002, 0.035)	
2.Unadjusted +				
Birth (confounders)				
Social class of origin	0.043 (0.023, 0.064)	-2	0.018 (0.002, 0.035)	0
Birthweight	0.043 (0.024, 0.061)	-2	0.018 (0.002, 0.035)	0
Family history	0.043 (0.025, 0.061)	-2	0.018 (0.002, 0.035)	0
Childhood (pathways)				
Externalising problems	0.040 (0.020, 0.060)	-9	0.018 (0.002, 0.034)	0
Drinking (16 years)	0.042 (0.023, 0.060)	-5	0.017 (0.001, 0.033)	-6
Smoking (16 years)	0.041 (0.023, 0.059)	-7	0.016 (0.000, 0.032)	-11
Adult Social Factors (33 years)				
Social class	0.039 (0.017, 0.062)	-11	0.016 (0.000, 0.033)	-11
Qualifications	0.035 (0.013, 0.058)	-20	0.015 (-0.002, 0.033)	-17
Adult Lifestyle Factors				
Activity and diet				
Physical activity (23 years)	0.042 (0.023, 0.060)	-5	0.018 (0.001, 0.034)	0
Physical activity (33 years)	0.042 (0.024, 0.060)	-5	0.018 (0.001, 0.034)	0
Physical activity (42 years)	0.041 (0.022, 0.060)	-7	0.018 (0.001, 0.034)	0
PC use (45 years)	0.039 (0.020, 0.058)	-11	0.017 (0.001, 0.033)	-6
TV watching (45 years)	0.039 (0.021, 0.058)	-11	0.017 (0.000, 0.033)	-6
Diet (33 years)	0.041 (0.023, 0.060)	-7	0.018 (0.001, 0.034)	0
Smoking and Non-Drinking				
Smoking 23-42 years	0.032 (0.013, 0.050)	-27	0.013 (-0.003, 0.029)	-28
Non-drinking 23-45 years	0.036 (0.016, 0.055)	-18	0.015 (-0.001, 0.031)	-17
Adult adiposity (45 years)				
Weight change 23-45 years	0.043 (0.025, 0.061)	-2	0.020 (0.004, 0.036)	11
BMI 45 years	0.034 (0.016, 0.052)	-23	0.018 (0.002, 0.034)	0
Waist circumference 45 years	0.034 (0.016, 0.052)	-23	0.021 (0.005, 0.037)	17
3.Multivariate models (each block separately)[b]				
Birth	0.042 (0.022, 0.062)	-5	0.018 (0.002, 0.035)	0
Childhood	0.036 (0.016, 0.055)	-18	0.014 (-0.002, 0.029)	-22
Adult Social Factors	0.033 (0.009, 0.058)	-25	0.014 (-0.003, 0.032)	-22
Activity and diet	0.031 (0.012, 0.050)	-30	0.015 (-0.002, 0.031)	-17
Smoking and drinking	0.025 (0.006, 0.044)	-43	0.01 (-0.005, 0.026)	-44
Adult adiposity	0.034 (0.015, 0.052)	-23	0.021 (0.005, 0.036)	17
4.Multivariate models (blocks together)[c]				
Birth block	0.042 (0.022, 0.062)	-5	0.018 (0.002, 0.035)	0
+ childhood	0.035 (0.014, 0.055)	-20	0.014 (-0.001, 0.029)	-35
+ social class & qualifications 33 y	0.029 (0.004, 0.053)	-34	0.012 (-0.005, 0.028)	-59
+ activity & diet 23-42 years	0.024 (-0.001, 0.050)	-45	0.011 (-0.006, 0.028)	-65
+ smoking & drinking 23-42 years	0.020 (-0.005, 0.045)	-55	0.01 (-0.007, 0.027)	-76
+ All	0.015 (-0.009, 0.038)	-66	0.014 (-0.003, 0.03)	-97

[a] Linear regression models of HbA_{1c} predicted by 7-year and 7-16 year change in reading z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All coefficients are for reading z-scores.
[b] Each model includes 7-year and 7-16 year change in reading z-score and all the variables listed in the block.
[c] Same as [b] but models are cumulative, each containing everything in the previous model.

[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table A7.2.1b Association between HbA_{1c} and 7-year reading z-score and change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for women [β coefficients (95%CI)].

Univariate Models [a] (n=3832)	7y Reading z-score	% change [d]	7-16 year change in reading z-score
1.Unadjusted	0.029 (0.014, 0.044)		-0.000 (-0.014, 0.014)
2.Unadjusted +			
Birth (confounders)			
social class of origin	0.021 (0.005, 0.038)	-28	
Family history	0.028 (0.013, 0.043)	-3	
Childhood (pathways)			
Externalising problems	0.024 (0.009, 0.040)	-17	
Drink 16 years	0.026 (0.011, 0.041)	-10	
Adult Social Factors (33 years)			
Social class	0.024 (0.009, 0.039)	-17	
Qualifications	0.016 (0.000, 0.031)	-45	
Adult Lifestyle Factors			
Activity and diet			
Physical activity 23 years	0.026 (0.010, 0.041)	-10	
Physical activity 42 years	0.027 (0.012, 0.042)	-7	
PC use (45 years)	0.023 (0.007, 0.039)	-21	
TV watching (45 years)	0.025 (0.010, 0.041)	-14	
Diet (33 years)	0.024 (0.008, 0.039)	-17	
Diet (42 years)	0.026 (0.011, 0.042)	-10	
Smoking and Non-Drinking			
Smoking 23-42 years	0.021 (0.006, 0.036)	-28	
Non-drinking 23-45 years	0.013 (-0.001, 0.028)	-55	
Adult adiposity (45 years)			
Weight change 23-45 years	0.025 (0.010, 0.039)	-14	
BMI 45 years	0.014 (-0.001, 0.029)	-52	
Waist circumference 45 years	0.015 (0.000, 0.030)	-48	
3.Multivariate models (each block separately)[b]			
Birth	0.021 (0.004, 0.037)	-28	
Childhood	0.022 (0.005, 0.038)	-24	
Adult Social Factors	0.014 (-0.002, 0.029)	-52	
Activity and diet	0.017 (0.000, 0.034)	-41	
Smoking and drinking	0.006 (-0.008, 0.021)	-79	
Adult adiposity	0.014 (-0.001, 0.028)	-52	
4.Multivariate models (blocks together)[c]			
Birth block	0.021 (0.004, 0.037)	-28	
+ childhood	0.014 (-0.005, 0.032)	-52	
+ social class & qualifications 33 y	0.003 (-0.015, 0.02)	-90	
+ activity & diet 23-42 years	0.000 (-0.019, 0.018)	-100	
+ smoking & drinking 23-42 years	-0.007 (-0.026, 0.011)	-124	
+ All	-0.010 (-0.028, 0.007)	-103	

[a] Linear regression models of HbA_{1c} predicted by 7-year and 7-16 year change in reading z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All coefficients are for reading z-scores.
[b] Each model includes 7-year and 7-16 year change in reading z-score and all the variables listed in the block.
[c] Same as [b] but models are cumulative, each containing everything in the previous model.
[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table A7.2.2a Association between $HbA_{1c} \geq 6\%$ and (i) 7-year reading z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for men [OR (95%CI)].

Univariate Models [a] (n=3907)	7-year reading z-score	% change[d]	7-16 year change in reading z-score
1.Unadjusted	1.39 (1.20, 1.61)		1.08 (0.93, 1.26)
2.Unadjusted +			
Birth (confounders)			
Social class of origin	1.31 (1.12, 1.52)	-9	1.06 (0.91, 1.23)
Family history	1.38 (1.19, 1.60)	-1	1.08 (0.93, 1.26)
Childhood (pathways)			
Externalising problems	1.39 (1.19, 1.62)	0	1.08 (0.93, 1.26)
Drinking (16 years)	1.37 (1.18, 1.59)	-2	1.07 (0.92, 1.25)
Adult Social Factors			
Social class (33 years)	1.39 (1.18, 1.63)	0	1.08 (0.92, 1.27)
Qualifications (33 years)	1.27 (1.07, 1.52)	-13	1.05 (0.90, 1.22)
Adult Lifestyle Factors			
Activity and diet			
Physical activity (33 years)	1.37 (1.18, 1.59)	-2	1.07 (0.92, 1.25)
Physical activity (42 years)	1.36 (1.17, 1.58)	-3	1.08 (0.92, 1.25)
PC use (45 years)	1.35 (1.16, 1.57)	-4	1.08 (0.92, 1.26)
TV watching (45 years)	1.32 (1.13, 1.54)	-8	1.06 (0.91, 1.24)
Smoking and Non-Drinking			
Smoking 23-42 years	1.35 (1.16, 1.57)	-4	1.06 (0.91, 1.23)
Non-drinking 23-45 years	1.31 (1.12, 1.52)	-9	1.06 (0.91, 1.23)
Adult Adiposity (45 years)			
Weight change 23-45 years	1.38 (1.19, 1.60)	-1	1.10 (0.94, 1.28)
BMI (45 years)	1.27 (1.09, 1.48)	-13	1.09 (0.93, 1.27)
Waist circumference (45 years)	1.27 (1.09, 1.48)	-13	1.11 (0.95, 1.30)
3.Multivariate models (each block separately)[b]			
Birth	1.30 (1.11, 1.52)	-10	1.06 (0.91, 1.23)
Childhood	1.37 (1.18, 1.60)	-2	1.07 (0.92, 1.25)
Adult Social Factors	1.28 (1.07, 1.54)	-12	1.05 (0.90, 1.23)
Activity and inactivity	1.27 (1.09, 1.49)	-13	1.05 (0.90, 1.23)
Smoking and drinking	1.27 (1.09, 1.48)	-13	1.04 (0.89, 1.21)
Adult adiposity	1.26 (1.08, 1.47)	-14	1.10 (0.94, 1.28)
4.Multivariate models (each block together)[c]			
Birth block	1.30 (1.11, 1.52)	-10	1.06 (0.91, 1.23)
+ childhood	1.28 (1.09, 1.50)	-12	1.05 (0.90, 1.22)
+ social class & qualifications 33 y	1.23 (1.02, 1.47)	-17	1.03 (0.88, 1.21)
+ activity & diet 23-42 years	1.20 (1.00, 1.44)	-20	1.03 (0.88, 1.21)
+ smoking & drinking 23-42 years	1.16 (0.96, 1.40)	-25	1.01 (0.86, 1.19)
+ all	1.16 (0.96, 1.42)	-25	1.05 (0.89, 1.24)

[a] Logistic regression models of $HbA_{1c} \geq 6$ %, predicted by 7-year and 7-16 year change in reading z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All ORs are for reading z-scores.
[b] Each model includes 7-year and 7-16 year change in reading z-score and all the variables listed in the block.
[c] Same as [b] but models are cumulative, each containing everything in the previous model.
[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table A7.2.2b Association between $HbA_{1c} \geq 6\%$ and (i) 7-year reading z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for women [OR (95%CI)]

Univariate Models [a] (n=3892)	7 year reading z-score	% change[d]	7-16 year change in reading z-score
1.Unadjusted	1.27 (1.06, 1.53)		0.98 (0.83,1.16)
2.Unadjusted +			
Birth (confounders)			
Social class of origin	1.20 (0.99, 1.46)	-26	
Family history	1.26 (1.05, 1.51)	-4	
Childhood (pathways)			
Externalising problems	1.19 (0.99, 1.44)	-30	
Adult Social Factors (33 years)			
Social class	1.26 (1.03, 1.53)	-4	
Qualifications	1.11 (0.89, 1.40)	-59	
Adult Lifestyle Factors			
Activity and diet			
Physical activity (42 years)	1.25 (1.04, 1.50)	-7	
PC use (45 years)	1.29 (1.06, 1.56)	7	
TV watching (45 years)	1.19 (0.98, 1.43)	-30	
Smoking and Non-Drinking			
Smoking 23-42 years	1.25 (1.04, 1.51)	-7	
Non-drinking 23-45 years	1.16 (0.96, 1.40)	-41	
Adult Adiposity (45 years)			
Weight change 23-45 years	1.25 (1.04, 1.51)	-7	
BMI (45 years)	1.10 (0.90, 1.35)	-63	
Waist circumference (45 years)	1.09 (0.89, 1.33)	-67	
3.Multivariate models (each block separately)[b]			
Birth	1.19 (0.98, 1.44)	-30	
Childhood	1.19 (0.99, 1.44)	-30	
Adult Social Factors	1.10 (0.88, 1.39)	-63	
Activity and inactivity	1.20 (0.99, 1.46)	-26	
Smoking and drinking	0.94 (0.79, 1.12)	-137	
Adult adiposity	1.07 (0.87, 1.32)	-74	
4.Multivariate models (each block together)[c]			
Birth block	1.19 (0.98, 1.44)	-30	
+ childhood	1.11 (0.91, 1.35)	-59	
+ social class & qualifications 33 y	1.00 (0.79, 1.27)	-100	
+ activity & diet 23-42 years	1.00 (0.79, 1.27)	-100	
+ smoking & drinking 23-42 years	0.94 (0.74, 1.20)	-122	
+ all	0.95 (0.73, 1.24)	-119	

[a] Logistic regression models of $HbA_{1c} \geq 6\%$, predicted by 7-year and 7-16 year change in reading z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All ORs are for reading z-scores.
[b] Each model includes 7-year and 7-16 year change in reading z-score and all the variables listed in the block.
[c] Same as [b] but models are cumulative, each containing everything in the previous model.
[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table A7.2.3a Association between metabolic syndrome and (i) 7-year reading z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for men [OR (95%CI)]

Univariate Models [a] (n=3765)	7 year reading z-score	% change[d]	7-16 year change in reading z-sore
1.Unadjusted	1.29 (1.17, 1.43)		0.92 (0.84, 1.01)
2.Unadjusted +			
Birth (confounders)			
Social class of origin	1.25 (1.12, 1.38)	-15	
Family history	1.29 (1.17, 1.43)	1	
Childhood (pathways)			
Externalising problems	1.28 (1.15, 1.41)	-5	
Adult Social Factors (33 years)			
Social class	1.27 (1.14, 1.42)	-7	
Qualifications	1.19 (1.06, 1.33)	-36	
Adult Lifestyle Factors			
Activity and diet			
Physical activity (23 years)	1.28 (1.16, 1.42)	-2	
Physical activity (33 years)	1.29 (1.17, 1.43)	1	
Physical activity (42 years)	1.28 (1.16, 1.42)	-4	
PC use (45 years)	1.30 (1.17, 1.44)	2	
TV watching (45 years)	1.25 (1.12, 1.38)	-16	
Smoking and Non-Drinking			
Smoking 23-42 years	1.27 (1.15, 1.41)	-6	
Non-drinking 23-45 years	1.27 (1.15, 1.41)	-7	
Adult Adiposity (45 years)			
Weight change 23-45 years	1.30 (1.17, 1.44)	3	
3.Multivariate models (each block separately)[b]			
Birth	1.24 (1.12, 1.38)	-16	
Childhood	1.28 (1.15, 1.41)	-5	
Adult Social Factors	1.18 (1.05, 1.33)	-37	
Activity and inactivity	1.25 (1.12, 1.39)	-15	
Smoking and drinking	1.25 (1.13, 1.39)	-13	
Adult adiposity	1.30 (1.17, 1.44)	-15	
4.Multivariate models (each block together)[c]			
Birth block	1.24 (1.12, 1.38)	0	
+ childhood	1.23 (1.10, 1.37)	-7	
+ social class & qualifications 33 y	1.16 (1.03, 1.30)	-35	
+ activity & diet 23-42 years	1.16 (1.02, 1.31)	-35	
+ smoking & drinking 23-42 years	1.15 (1.02, 1.30)	-39	
+ all	1.15 (1.01, 1.31)	-38	

[a] Logistic regression models of elevated metabolic syndrome predicted by 7-year and 7-16 year change in reading z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All ORs are for reading z-scores.

[b] Each model includes 7-year and 7-16 year change in reading z-score and all the variables listed in the block.

[c] Same as [b] but models are cumulative, each containing everything in the previous model.

[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table A7.2.3b Association between metabolic syndrome and (i) 7-year reading z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for women [OR (95%CI)]

Univariate Models [a] (n=3745)	7 year reading z-score	% change[d]	7-16 y change in reading z-score	% change[d]
1.Unadjusted	1.46 (1.30, 1.65)		1.14 (1.03, 1.27)	
2.Unadjusted +				
Birth (confounders)				
Social class of origin	1.37 (1.21, 1.55)	-20	1.11 (1.00, 1.23)	-21
Maternal smoking	1.44 (1.28, 1.63)	-4	1.14 (1.02, 1.26)	0
Family history	1.45 (1.29, 1.63)	-2	1.13 (1.02, 1.26)	-7
Childhood (pathways)				
Externalising problems	1.41 (1.25, 1.59)	-11	1.13 (1.02, 1.26)	-7
Drink (16 years)	1.44 (1.28, 1.63)	-4	1.13 (1.02, 1.26)	-7
Smoke (16 years)	1.46 (1.29, 1.64)	0	1.13 (1.02, 1.26)	-7
Adult Social Factors (33 years)				
Social class	1.36 (1.20, 1.55)	-22	1.10 (0.99, 1.22)	-29
Qualifications	1.25 (1.07, 1.46)	-46	1.06 (0.95, 1.19)	-57
Adult Lifestyle Factors				
Activity and diet				
Diet (33 years)	1.43 (1.26, 1.62)	-7	1.12 (1.01, 1.25)	-14
Physical activity (23 years)	1.44 (1.28, 1.63)	-4	1.14 (1.02, 1.26)	0
Physical activity (33 years)	1.45 (1.28, 1.63)	-2	1.13 (1.02, 1.26)	-7
Physical activity (42 years)	1.45 (1.29, 1.63)	-2	1.13 (1.02, 1.25)	-7
PC use (45 years)	1.47 (1.30, 1.67)	2	1.14 (1.03, 1.27)	0
TV watching (45 years)	1.41 (1.25, 1.59)	-11	1.12 (1.01, 1.25)	-14
Smoking and Non-Drinking				
Smoking 23-42 years	1.41 (1.25, 1.59)	-11	1.11 (1.00, 1.23)	-21
Non-drinking 23-45 years	1.40 (1.24, 1.58)	-13	1.13 (1.02, 1.25)	-7
Adult Adiposity (45 years)				
Weight change 23-45 years	1.46 (1.27, 1.68)	0	1.19 (1.06, 1.32)	36
3.Multivariate models (each block separately)[b]				
Birth	1.35 (1.19, 1.52)	-24	1.10 (0.99, 1.22)	-29
Childhood	1.38 (1.22, 1.56)	-17	1.12 (1.00, 1.24)	-14
Adult Social Factors	1.21 (1.03, 1.42)	-54	1.05 (0.93, 1.17)	-64
Activity and inactivity	1.39 (1.21, 1.59)	-15	1.11 (0.99, 1.23)	-21
Smoking and drinking	1.35 (1.19, 1.52)	-24	1.09 (0.99, 1.22)	-36
Adult adiposity	1.46 (1.27, 1.68)	0	1.19 (1.06, 1.32)	36
4.Multivariate models (each block together)[c]				
Birth block	1.35 (1.19, 1.52)	-24	1.10 (0.99, 1.22)	-29
+ childhood	1.28 (1.12, 1.45)	-39	1.08 (0.97, 1.20)	-43
+ social class & qualifications 33 y	1.11 (0.94, 1.31)	-76	1.02 (0.91, 1.15)	-86
+ activity & diet 23-42 years	1.11 (0.94, 1.32)	-76	1.02 (0.90, 1.14)	-86
+ smoking & drinking 23-42 years	1.09 (0.92, 1.29)	-80	1.01 (0.89, 1.14)	-93
+ all	1.12 (0.92, 1.36)	-74	1.05 (0.92, 1.19)	-64

[a] Logistic regression models of elevated metabolic syndrome predicted by 7-year and 7-16 year change in reading z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All ORs are for reading z-scores.

[b] Each model includes 7-year and 7-16 year change in reading z-score and all the variables listed in the block.

[c] Same as [b] but models are cumulative, each containing everything in the previous model.

[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table A7.2.4a Association between 45-year BMI and 7-year reading z-score and change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for men [β coefficients (95%CI)]

Univariate Models [a] (n=4620)	7y Reading z-score	% change	7-16year change in reading z-score
1.Unadjusted	0.438 (0.303, 0.572)		0.016 (-0.102, 0.134)
2.Unadjusted +			
Birth			
Social class of origin	0.333 (0.197, 0.469)	-24	
Birthweight	0.453 (0.319, 0.587)	3	
Breast feeding	0.422 (0.288, 0.556)	-4	
Smoking in pregnancy	0.404 (0.270, 0.537)	-8	
Family history	0.430 (0.296, 0.564)	-2	
Childhood			
Externalising problems	0.385 (0.248, 0.522)	-12	
Adult Social Factors (33 years)			
Social class	0.345 (0.196, 0.494)	-21	
Qualifications	0.288 (0.135, 0.440)	-34	
Adult Lifestyle Factors			
Activity and diet			
Physical activity (33 years)	0.435 (0.298, 0.572)	-1	
Physical activity (42 years)	0.431 (0.297, 0.566)	-2	
PC use (45 years)	0.425 (0.291, 0.560)	-3	
TV watching (45 years)	0.491 (0.353, 0.630)	12	
Diet (33 years)	0.368 (0.232, 0.504)	-16	
Diet (42 years)	0.445 (0.307, 0.583)	2	
Smoking and Non-Drinking			
Smoking 23-42 years	0.474 (0.337, 0.612)	8	
Non-drinking 23-45 years	0.414 (0.277, 0.550)	-5	
3.Multivariate models (each block separately)[b]			
Birth	0.315 (0.181, 0.449)	-28	
Childhood	0.385 (0.248, 0.522)	-12	
Adult Social Factors	0.257 (0.099, 0.415)	-41	
Activity and diet	0.442 (0.297, 0.586)	-32	
Smoking and drinking	0.448 (0.309, 0.588)	2	
4.Multivariate models (blocks together)[c]			
Birth block	0.315 (0.181, 0.449)	-28	
+ childhood	0.274 (0.136, 0.411)	-37	
+ social class & qualifications 33 y	0.190 (0.034, 0.346)	-57	
+ activity & diet 23-42 years	0.229 (0.074, 0.384)	-48	
+ smoking & drinking 23-42 years	0.213 (0.058, 0.367)	-51	

[a] Linear regression models of BMI predicted by 7-year and 7-16 year change in reading z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All coefficients are for reading z-scores.
[b] Each model includes 7-year and 7-16 year change in reading z-score and all the variables listed in the block.
[c] Same as [b] but models are cumulative, each containing everything in the previous model.
[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table A7.2.4b Association between 45-year BMI and 7-year reading z-score and change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for women [β coefficients (95%CI)]

Univariate Models [a] (n=4672)	7y Reading z-score	% change	7-16year change in reading z-score
1.Unadjusted	0.703 (0.507, 0.900)		0.005 (-0.165, 0.175)
2.Unadjusted +			
Birth			
Social class of origin	0.531 (0.331, 0.732)	-24	
Smoking in pregnancy	0.672 (0.476, 0.868)	-4	
Family history	0.693 (0.497, 0.889)	-1	
Childhood			
Externalising problems	0.634 (0.436, 0.832)	-10	
Drinking (16 years)	0.693 (0.494, 0.891)	-1	
Adult Social Factors (33 years)			
Social class	0.578 (0.373, 0.782)	-18	
Qualifications	0.402 (0.164, 0.639)	-43	
Adult Lifestyle Factors			
Activity and diet			
Physical activity (23 years)	0.619 (0.423, 0.815)	-12	
Physical activity (33 years)	0.679 (0.483, 0.875)	-3	
Physical activity (42 years)	0.668 (0.473, 0.863)	-5	
PC use (45 years)	0.687 (0.475, 0.900)	-2	
TV watching (45 years)	0.581 (0.381, 0.780)	-17	
Smoking and Non-Drinking			
Smoking 23-42 years	0.729 (0.529, 0.929)	4	
Non-drinking 23-45 years	0.514 (0.327, 0.702)	-27	
3.Multivariate models (each block separately)[b]			
Birth	0.502 (0.303, 0.701)	-29	
Childhood	0.622 (0.421, 0.823)	-12	
Adult Social Factors	0.355 (0.118, 0.593)	-50	
Activity and diet	0.514 (0.304, 0.723)	-27	
Smoking and drinking	0.539 (0.348, 0.730)	-23	
4.Multivariate models (blocks together)[c]			
Birth block	0.502 (0.303, 0.701)	-29	
+ childhood	0.425 (0.221, 0.629)	-40	
+ social class & qualifications 33 y	0.179 (-0.058, 0.417)	-75	
+ activity & diet 23-42 years	0.147 (-0.096, 0.390)	-79	
+ smoking & drinking 23-42 years	0.081 (-0.154, 0.317)	-88	

[a] Linear regression models of BMI predicted by 7-year and 7-16 year change in reading z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All coefficients are for reading z-scores.
[b] Each model includes 7-year and 7-16 year change in reading z-score and all the variables listed in the block.
[c] Same as [b] but models are cumulative, each containing everything in the previous model.
[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table A7.2.5a Association between 45-year waist circumference and 7-year reading z-score and change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for men [β coefficients (95%CI)]

Univariate Models [a] (n=4626)	7 year reading z-score	% change[d]	7-16 year change in reading z-score
1.Unadjusted	1.031 (0.682, 1.380)		-0.291 (-0.590, 0.008)
2.Unadjusted +			
Birth (confounders)			
Social class of origin	0.831 (0.465, 1.197)	-19	
Birth weight	1.100 (0.745, 1.455)	7	
Smoking in pregnancy	0.954 (0.606, 1.302)	-7	
Breast feeding	0.983 (0.634, 1.331)	-5	
Family history	1.010 (0.660, 1.360)	-2	
Childhood (pathways)			
Externalising problems	0.890 (0.537, 1.243)	-14	
Adult Social Factors (33 years)			
Social class	0.827 (0.446, 1.207)	-20	
Qualifications	0.588 (0.167, 1.009)	-43	
Adult Lifestyle Factors			
Physical activity (23 years)	0.970 (0.615, 1.325)	-6	
Physical activity (33 years)	0.989 (0.640, 1.337)	-4	
Physical activity (42 years)	0.976 (0.627, 1.326)	-5	
PC use (45 years)	1.146 (0.785, 1.507)	11	
TV watching (45 years)	0.814 (0.462, 1.166)	-21	
Diet (33 years)	1.012 (0.664, 1.361)	-2	
Diet (42 years)	1.055 (0.703, 1.406)	2	
Smoking and Non-Drinking			
Smoking 23-42 years	1.088 (0.734, 1.442)	6	
Non-drinking 23-45 years	0.976 (0.620, 1.332)	-5	
3.Multivariate models (each block separately)[b]			
Birth	0.810 (0.440, 1.180)	-21	
Childhood	0.890 (0.537, 1.243)	-14	
Adult social factors	0.521 (0.093, 0.949)	-49	
Activity and diet	0.909 (0.545, 1.273)	-12	
Smoking and drinking	1.030 (0.669, 1.391)	0	
4.Multivariate models (blocks together)[c]			
Birth block	0.810 (0.440, 1.180)	-21	
+ childhood	-0.403 (-0.706, -0.099)	-139	
+ social class & qualifications 33 y	0.396 (-0.049, 0.841)	-62	
+ activity & diet 23-42 years	0.431 (-0.014, 0.875)	-58	
+ smoking & drinking 23-42 years	0.427 (-0.023, 0.876)	-59	

[a] Linear regression models of waist circumference predicted by 7-year and 7-16 year change in reading z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All coefficients are for reading z-scores.

[b] Each model includes 7-year and 7-16 year change in reading z-score and all the variables listed in the block.

[c] Same as [b] but models are cumulative, each containing everything in the previous model.

[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table A7.2.5b Association between 45-year waist circumference and 7-year reading z-score and change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for women [β coefficients (95%CI)]

Univariate Models [a] (n=4665)	7 year reading z-score	% change[d]	7-16 year change in reading z-score
1.Unadjusted	1.630 (1.233, 2.027)		0.156 (-0.202, 0.514)
2.Unadjusted +			
Birth (confounders)			
Social class of origin	1.271 (0.860, 1.683)	-22	
birth weight	1.691 (1.277, 2.106)	4	
Smoking in pregnancy	1.566 (1.168, 1.964)	-4	
Breast feeding	1.594 (1.197, 1.992)	-2	
Family history	1.594 (1.199, 1.988)	-2	
Childhood (pathways)			
Externalising problems	1.440 (1.030, 1.850)	-12	
Adult Social Factors (33 years)			
Social class	1.308 (0.890, 1.726)	-20	
Qualifications	0.912 (0.436, 1.388)	-44	
Adult Lifestyle Factors			
Physical activity (23 years)	1.447 (1.048, 1.846)	-11	
Physical activity (33 years)	1.570 (1.174, 1.965)	-4	
Physical activity (42 years)	1.551 (1.157, 1.944)	-5	
PC use (45 years)	1.629 (1.222, 2.035)	0	
TV watching (45 years)	1.326 (0.929, 1.723)	-19	
Diet (33 years)	1.562 (1.162, 1.962)	-4	
Smoking and Non-Drinking			
Smoking 23-42 years	1.559 (1.154, 1.964)	-4	
Non-drinking 23-45 years	1.289 (0.891, 1.687)	-4	
3.Multivariate models (each block separately)[b]			
Birth	1.241 (0.820, 1.662)	-24	
Childhood	1.440 (1.030, 1.850)	-12	
Adult Social Factors	0.788 (0.318, 1.258)	-52	
Activity and diet	1.224 (0.814, 1.634)	-25	
Smoking and drinking	1.218 (0.814, 1.623)	-25	
4.Multivariate models (blocks together)[c]			
Birth block	1.241 (0.820, 1.662)	-24	
+ childhood	1.055 (0.622, 1.488)	-35	
+ social class & qualifications 33 y	0.456 (-0.020, 0.932)	-72	
+ activity & diet 23-42 y	0.396 (-0.075, 0.868)	-76	
+ smoking & drinking 23-42 y	0.260 (-0.210, 0.731)	-84	

[a] Linear regression models of waist circumference predicted by 7-year and 7-16 year change in reading z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All coefficients are for reading z-scores.

[b] Each model includes 7-year and 7-16 year change in reading z-score and all the variables listed in the block.

[c] Same as [b] but models are cumulative, each containing everything in the previous model.

[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Appendix 7.3 Selected complete case analyses (women)

Table A7.3.1 Association between HbA_{1c} and (i)7-year maths z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for women [β coefficients (95%CI)].

Univariate Models[a] (n=2189)	7-year maths z-score	% change[d]	7-16 year change in maths z-score
1.Unadjusted	0.029 (0.004, 0.054)		0.013 (-0.016, 0.041)
2.Unadjusted +			
Birth (confounders)			
Social class of origin	0.021(-0.007,0.048)	-28	
Family history	0.028(0.003,0.053)	-28	
Childhood (pathways)			
Externalising problems	0.020(-0.005,0.045)	-31	
Drink 16 years	0.026(0.000,0.051)	-10	
Adult Social Factors (33 years)			
Social class	0.023(-0.002,0.048)	-31	
Qualifications	0.004(-0.023,0.031)	-10	
Adult Lifestyle Factors			
Activity and diet			
Physical activity 23 years	0.026(0.002,0.050)	-10	
Physical activity 42 years	0.026(0.001,0.050)	-10	
PC use (45 years)	0.026(-0.001,0.052)	-10	
TV watching (45 years)	0.022(-0.003,0.047)	-24	
Diet (33 years)	0.023(-0.003,0.049)	-21	
Diet (42 years)	0.028(0.003,0.053)	-3	
Smoking and Non-Drinking			
Smoking 23-42 years	0.020(-0.005,0.044)	-31	
Non-drinking 23-44 years	0.015(-0.009,0.040)	-48	
Adult adiposity (45 years)			
Weight change 23-45 years	0.024(-0.001,0.049)	-17	
BMI 45 years	0.010(-0.015,0.035)	-66	
Waist circumference 45 years	0.009(-0.016,0.034)	-69	
3.Multivariate models (each block separately)[b]			
Birth	0.019(-0.008,0.047)	-34	
Childhood	0.016(-0.011,0.042)	-45	
Adult Social Factors	0.004(-0.025,0.034)	-86	
Activity and diet	0.015(-0.011,0.041)	-48	
Smoking and drinking	0.006(-0.018,0.03)	-79	
Adult adiposity	0.004(-0.021,0.029)	-86	
4.Multivariate models (blocks together)[c]			
Birth block	0.019(-0.008,0.047)	-34	
+ childhood	0.007(-0.023,0.036)	-76	
+ social class & qualifications 33 y	-0.011(-0.045,0.022)	-62	
+ activity & diet 23-42 years	-0.012(-0.045,0.021)	-59	
+ smoking & drinking 23-42 y	-0.016(-0.048,0.016)	-45	
+ All	-0.018(-0.049,0.014)	-38	

[a] Linear regression models of HbA_{1c} predicted by 7-year and 7-16 year change in maths z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All coefficients are for maths z-scores.
[b] Each model includes 7-year and 7-16 year change in maths z-score and all the variables listed in the block.
[c] Same as [b] but models are cumulative, each containing everything in the previous model.
[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table A7.3.2 Association between $HbA_{1c} \geq 6\%$ and (i) 7-year maths z-score and (ii) change 7 - 16 years, adjusted for lifecourse factors, singly and then in blocks for women [OR (95%CI)].

Univariate Models [a] (n=2726)	7-year maths z-score	% change[d]	7-16 year change in maths z-score
1.Unadjusted	1.23(0.99,1.54)		1.08(0.88,1.32)
2.Unadjusted +			
Birth (confounders)			
Social class of origin	1.15(0.91,1.45)	-35	
Family history	1.22(0.98,1.53)	-4	
Childhood (pathways)			
Externalising problems	1.15(0.91,1.44)	-35	
Adult Social Factors (33 years)			
Social class	1.25(0.98,1.59)	9	
Qualifications	1.16(0.89,1.51)	-30	
Adult Lifestyle Factors			
Activity and diet			
Physical activity (42 years)	1.21(0.97,1.52)	-9	
PC use (45 years)	1.23(0.98,1.56)	0	
TV watching (45 years)	1.14(0.90,1.43)	-39	
Smoking and Non-Drinking			
Smoking 23-42 years	1.21(0.96,1.52)	-9	
Non-drinking 23-44 years	1.15(0.91,1.44)	-35	
Adult Adiposity (45 years)			
Weight change 23-45 years	1.21(0.96,1.53)	-9	
BMI (45 years)	1.07(0.84,1.37)	-70	
Waist circumference (45 years)	1.06(0.83,1.35)	-74	
3.Multivariate models (each block separately)[b]			
Birth	1.14(0.90,1.44)	-39	
Childhood	1.15(0.91,1.44)	-35	
Adult Social Factors	1.15(0.88,1.50)	-35	
Activity and inactivity	1.14(0.90,1.45)	-114	
Smoking and drinking	1.13(0.89,1.42)	-43	
Adult adiposity	1.00(0.78,1.29)	-100	
4.Multivariate models (each block together)[c]			
Birth block	1.14(0.90,1.44)	-39	
+ childhood	1.06(0.84,1.34)	-74	
+ social class & qualifications 33 y	1.02(0.77,1.34)	-91	
+ activity & diet 23-42 years	1.00(0.76,1.32)	-100	
+ smoking & drinking 23-42 years	0.97(0.73,1.29)	-113	
+ all	0.96(0.70,1.32)	-117	

[a] Logistic regression models of $HbA_{1c} \geq 6$ %, predicted by 7-year and 7-16 year change in maths z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All ORs are for maths z-scores.
[b] Each model includes 7-year and 7-16 year change in maths z-score and all the variables listed in the block.
[c] Same as [b] but models are cumulative, each containing everything in the previous model.
[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Table A.7.3.3 Association between metabolic syndrome and (i) 7-year maths z-score and (ii) change 7 -16 years, adjusted for lifecourse factors, singly and then in blocks for women [OR (95%CI)],

Univariate Models [a] (n=2027)	7year maths z-score (intercept)	% change [d]	7-16 year change in maths z-score (slope)
1.Unadjusted	1.52 (1.30, 1.78)		1.13 (0.99, 1.29)
2.Unadjusted +			
Birth (confounders)			
Social class of origin	1.38(1.17,1.63)	-27	
Maternal smoking	1.49(1.27,1.75)	-6	
Family History	1.51(1.29,1.77)	-2	
Childhood (pathways)			
Externalising Problems	1.45(1.23,1.70)	-13	
Drinking (16 years)	1.48(1.26,1.74)	-8	
Smoking (16 years)	1.51(1.28,1.77)	-2	
Adult Social Factors (33 years)			
Social class	1.39(1.17,1.64)	-25	
Qualifications	1.26(1.04,1.53)	-50	
Adult Lifestyle Factors			
Activity and diet			
Diet (33 years)	1.49(1.27,1.75)	-6	
Physical activity (23 years)	1.49(1.27,1.76)	-6	
Physical activity (33 years)	1.50(1.28,1.76)	-4	
Physical activity (42 years)	1.50(1.28,1.76)	-4	
PC use (45 years)	1.54(1.31,1.82)	4	
TV watching (45 years)	1.50(1.27,1.76)	-4	
Smoking and Non-Drinking			
Smoking 23-42 years	1.47(1.25,1.73)	-10	
Non-drinking 23-44 years	1.45(1.23,1.71)	-13	
Adult Adiposity (45 years)			
Weight change 23-45 years	1.54(1.29,1.83)	4	
3.Multivariate models (each block separately)[b]			
Birth	1.35(1.14,1.59)	-33	
Childhood	1.38(1.17,1.63)	-27	
Adult Social Factors	1.21(1.00,1.47)	-60	
Activity and diet	1.47(1.24,1.74)	-10	
Smoking and drinking	1.41(1.19,1.66)	-21	
Adult adiposity	1.54(1.29,1.83)	4	
4.Multivariate models (each block together)[c]			
Birth block	1.35(1.14,1.59)	-33	
+ childhood	1.24(1.04,1.48)	-54	
+ social class & qualifications 33 y	1.07(0.88,1.31)	-87	
+ activity & diet 23-42 y	1.08(0.88,1.33)	-85	
+ smoking & drinking 23-42 y	1.06(0.86,1.31)	-88	
+ all	1.10(0.88,1.38)	-81	

[a] Logistic regression models of metabolic syndrome, predicted by 7-year and 7-16 year change in maths z-score, using imputed data. Univariate models are adjusted for the variable in column 1. All ORs are for maths z-scores.

[b] Each model includes 7-year and 7-16 year change in maths z-score and all the variables listed in the block.

[c] Same as [b] but models are cumulative, each containing everything in the previous model.

[d] % change = [(adjusted coefficient/unadjusted coefficient)*100]-100

Chapter 8, Conclusions

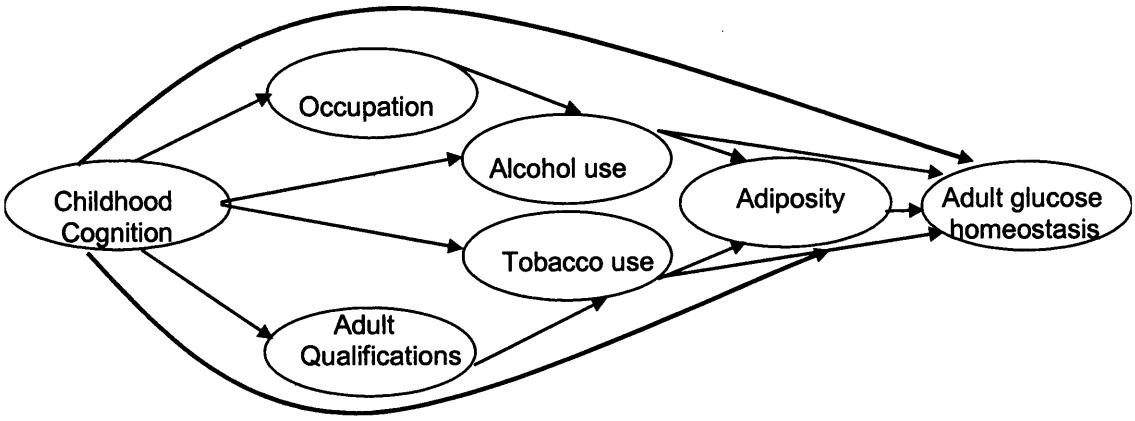


Figure 8.1 Conceptual framework

This thesis aimed to investigate the pathways to adult glucose homeostasis, illustrated in the conceptual framework. The aims were first, to examine the prevalence and co-occurrence of smoking and several dimensions of alcohol use, both cross-sectional associations and also trajectories of behaviours across adulthood. Second, to establish whether childhood cognition was associated with single measurements or trajectories of adult health behaviours. Further, to investigate whether associations between childhood cognitive ability and adult health behaviours were mediated by highest educational achievements and adult occupational position. The third aim was to establish if tobacco and alcohol use at single adult ages and trajectories across adulthood was associated with mid-life glucose regulation. Then, to investigate whether associations were independent of confounding (by diet and physical activity) and if associations operated through adult adiposity. The fourth aim was to establish if childhood cognition was associated with mid-life glucose regulation and if associations were robust to adjustment for confounders, and if associations operate through adult social position, educational level or adiposity. The fifth aim was to establish if associations between cognition and mid-life glucose regulation were robust to adjustment for confounders, and to investigate if associations operated through adult health behaviours. All of these aims were achieved and the main findings, methodological considerations, generalisability of findings to other settings and implications for policy development are now discussed.

Main findings

Prevalence of cigarette smoking and binge or heavy drinking peaked at age 23 years and declined thereafter. Binge drinking and smoking remained prevalent into mid-forties, and many adults reported these behaviours repeatedly, so they are clearly not problems confined to early adult years. Smoking was more stable than drinking patterns. By age 42 years, half of the

cohort had smoked regularly and half of those who smoked had quit, resulting in a substantial proportion likely to bear health consequences. Non-drinking was a relatively stable (minority) behaviour pattern, more stable than the harmful drinking patterns of binge or heavy drinking. Prevalence of heavy drinking was low at later adult ages and a very small minority (mostly men) repeatedly reported drinking heavily. The co-occurrence of smoking and drinking changed over time as drinkers stopped smoking as they grew older. Lower childhood cognitive ability was associated with smoking and with non-drinking and binge drinking at single ages and across adulthood. The associations were not eliminated on adjustment for childhood social class and operated in part through the pathway of childhood behavioural problems and to a greater degree through adult educational qualifications and social position.

Consistent associations between heavier and more persistent smoking trajectories and poorer glucose homeostasis were observed. Unexpectedly, drinking frequency was more consistently associated with glucose regulation than amount (heaviness): infrequent drinking both proximally in time to the outcome and, more distally, over the lifecourse were associated with poorer outcomes, even adjusting for confounders. The effects of tobacco and alcohol operated in small part through adiposity, although independent associations remained after adjustment for other health behaviours and adiposity. Associations between 7-year cognition and glucose regulation were partially but not completely confounded by early life factors. Childhood cognition was associated with mid-life glucose homeostasis through intermediary pathways rather than directly; through attainment of fewer adult educational qualifications, manual occupational position and increased adult adiposity. Smoking and drinking histories were important pathways from cognition to HbA_{1c} levels, and similar in magnitude to the role of adiposity. However smoking and drinking were less important pathways between childhood cognition and metabolic syndrome. Whilst the change in ability rank was to some degree confounded by childhood social position it was, like the initial level of ability, also mediated by highest qualifications achieved in adulthood and by health behaviours.

What this study adds

Each chapter discussed in detail, how the main findings fit with and extend relevant existing literature. Overall, this thesis extends existing literature on cognitive epidemiology in the following ways. Firstly, to date little evidence about cognition and diabetes risk exists. Three related measures of glucose homeostasis were investigated and consistency in findings lends further weight to observed associations. Secondly, associations between level and change in cognitive ability and health behaviours and also health outcomes were studied, whilst existing studies have focused on single measures of cognitive ability. Thirdly, pathways between cognition and adult health behaviours were studied in detail, including repeated measures of trajectories of health behaviours and also investigating different dimensions of alcohol and tobacco use. Fourthly, pathways between cognition and adult health from childhood through to

adulthood were studied with an emphasis on the mediating roles of child and adult exposures. Fifthly, information about confounding factors from childhood was included. Findings about the pathways between cognitive ability and health behaviours have general applicability to existing cognitive epidemiology literature. To date less research exists on drinking frequency in relation to diabetes risk compared to heaviness of drinking, so this study adds to existing literature both by investigating frequency at single and repeated time points.

The study of lifecourse smoking and drinking adds to literature about stability and change in behaviour patterns because of the extended follow-up period. It also poses questions about the validity of using single measures of drinking or smoking behaviours in observational studies of disease risk. Whilst lifestyle factors have been much studied in epidemiology of chronic diseases, most studies investigating the aetiology of chronic disease risk use single measures of adult health behaviours and assume that behaviours do not change over time. To date, few studies have addressed this shortcoming by analyzing repeated measures of health behaviours (Emberson et al. 2005a; Emberson et al. 2005b), so by investigating repeated measures of health behaviours (rather than baseline measures) this study adds to literature about smoking and drinking and diabetes risk. Using only baseline measures of health behaviour underestimates associations between the exposure and health outcome if there is variability in the health behaviour over time (Emberson et al 2005b). Part of the problem is the scarcity of long-term repeated measures data on health behaviours; the 1958 cohort is one of few studies which allows these behaviour trajectories to be investigated. However the instability in behaviour over decades suggests that behavioural change should be considered in design of epidemiologic studies.

The finding that non-drinking was relatively stable over two decades whilst heavy drinking showed little continuity challenges the validity of the j-shaped associations reported between increasing alcohol intake and several disease outcomes. The validity of the elevated disease risks in non-drinkers is debated; it has been hypothesised that higher risks are due to past heavy-drinking history of non-drinkers (Shaper et al. 1988). Results for the 1958 cohort did not suggest that raised risks of diabetes in non-drinkers was due to ex-heavy drinking. Heavy drinking (and to a lesser degree binge drinking) were unstable over two decades. This lack of continuity calls into question risks reported in cohort studies which categorise drinking at baseline and relate baseline exposure to disease risk sometimes many years later, without assessing change over time in behaviour.

Lifecourse epidemiology framework

Analyses of the 1958 cohort using a lifecourse framework provided evidence that health behaviours over decades contributed to accumulation of disease risks. Lifecourse frameworks have been used elsewhere in social epidemiology and cumulative effects of poorer social

circumstances over the lifecourse are reported to elevate risks of chronic diseases including diabetes and cardiovascular disease (Blane et al. 1996; Lawlor et al. 2002; Lawlor et al. 2003a; Lidfeldt et al. 2007). The work presented in this thesis does not repeat other work on behavioural determinants of health, but using a lifecourse framework sought to understand how childhood cognitive development contributes to setting up patterns of behaviours throughout life and how these in turn influence adult diabetes risk. Whilst lifecourse epidemiology and, in particular, research on the early origins of adult disease (including diabetes) (Godfrey & Barker 2000), have challenged the prevailing adult-focused paradigm of chronic disease aetiology, this thesis used both perspectives. The lifecourse framework has the advantage of focusing on understanding causal pathways which may be "upstream" or distal. Yet, studying more classical behavioural risk factors holds the appeal of studying behaviours which are potentially modifiable and could be the focus of powerful population-oriented interventions. Studying the role of behavioural risk factors in chains of risk which may start in childhood affords insight into development of, in this instance, type 2 diabetes risk.

Methodological considerations

The prospectively-gathered repeated measures data about a population-based sample are a major strength of the 1958 cohort, however repeated measures data raise difficulties for analysis because standard techniques assume that data are independent. A two-stage approach was taken in this thesis. First cognitive trajectories for each individual were estimated using a hierarchical model with between person variation for intercept at 7 years and slope between 7 and 16 years. Second, the associations between the estimated cognitive trajectories and continuous, dichotomous or categorical adult outcomes were analysed in fixed effects regression models and repeated outcomes in adulthood were modelled using random effects models, taking account of the data at repeated adult time-points. The two-stage approach has the benefit of taking account of the correlations between the cognitive tests within individuals. The repeated measures models make use of all data and estimate trajectories for individuals with incomplete data. The two-stage approach of estimating the values of a baseline variable using repeated measures models has been used previously and shown to be valid (Morrell et al. 2003).

The lifecourse exposures to smoking and drinking were indicated by count or summary variables in fixed effects regression analyses and the strengths and weaknesses of this approach were discussed in chapter 7. Additional confirmatory analyses used formal repeated measures models. The latter are complex and harder to interpret in the context where the repeated measures are the exposure rather than the outcome. Therefore for simplicity of presentation, summary measures were used, which was particularly appropriate in chapters 6 and 7 where repeated measures logistic models containing many covariates may be unstable.

An alternative approach would have been to use trajectory models and define latent classes of

trajectories, both for cognitive trajectories and for categorical health behaviour trajectories. Both random effects models and trajectory models are simplifications of processes of change over time, the choice to use random effects models in this thesis for the trajectories of cognitive development was based on the specific questions and data properties. Linear and continuous associations between cognitive ability and later smoking or drinking and also diabetes risk were expected. The hypothesis that there would also be associations with change in ability was well summarised by using a continuous intercept and slope rather than specifying specific limits to the distribution of trajectories, ie determining the shape of trajectories. In addition the hypothesis that the associations between childhood cognitive ability and adult outcomes might be non-linear and driven by stronger associations in the lower-scoring groups was tested by modelling quadratic terms in the intercept and slope. Rather than setting a specific cut-point to identify a low ability group, non-linear effects were tested using continuous linear and quadratic terms. Linear associations between childhood cognitive ability and adult outcomes were observed so the method of describing the cognitive trajectories using a group average with individual level deviations was chosen.

Other possibilities would be path analyses or structural equation modelling (SEM) which simultaneously take account of data at each life stage and are effectively a series of simultaneous regression equations. Both give insight into the inter-relation between the pathway variables. However these methods are mostly used for continuous, normally distributed, outcomes whereas in this study the health behaviour trajectories were categorical data, and two of the outcomes were binary. Hence the data did not immediately lend itself to SEM analyses, although generalisations of the methods have now been developed for use with dichotomous outcomes. The advantages of SEM compared to the series of regression analyses building up lifecourse models (conditional models) that was used in Chapters 6 and 7, are that direct and indirect effects are more easily estimated using SEM. Whereas using the approach of building up lifecourse models where variables are added in temporal order, direct or indirect effects are inferred from the changes in regression coefficients on adjustment and these changes are dependent on the order in which variables are entered into the models. However the latter conditional modelling approach has the benefit of simplicity and has been much used in lifecourse research. Comparative analyses indicates that results of joint analyses using path analyses or SEM tend to be similar to the type of conditional modelling approach that was used in this thesis, with the caveat that interpretation of the latter may be harder because it is not so straightforward to estimate direct and indirect pathways (De Stavola et al. 2006).

Inevitably a longitudinal study over many decades suffers from sample attrition. There has been drop-out at each of the surveys since birth and when many covariates from different life stages are used as in analyses presented in Chapter 7, missing data become a serious concern.

Multilevel models were used to take account of missing data in analyses of cognitive trajectories and also for analyses of trajectories of health behaviours and glucose regulation. In the lifecourse models presented in Chapter 7, multiple imputation was used to impute missing data on covariates. A strength of imputation is that models for imputing datasets included variables from the whole lifecourse associated with drop-out (Hawkes & Plewis 2006). The substantive regression analyses using imputed data are expected to give more efficient coefficient estimates and should reduce bias compared to a complete case analysis. Indeed, complete case analyses showed associations in the same direction, but of weaker magnitude and with larger standard errors than analyses using imputed data. The analyses of imputed data were interpreted in detail in Chapter 7. In each chapter biases in the separate analysis samples relative to the birth sample were investigated; more socially deprived groups were consistently under-represented in the analysis samples. This may result in underestimation of the strength of associations if exposure or outcome are associated with social position of origin. As sensitivity tests, main analyses were repeated with both reading and maths tests and also with different cut points for elevated HbA_{1c} and metabolic syndrome. These were expected to give similar patterns of results and the finding that they did lent strength to interpretation of results.

Generalisability of findings

As discussed in earlier chapters, the 1958 cohort is a primarily Caucasian sample representative of births in Great Britain at the time, and it is to this group that the results of this work can be most readily applied. The cohort does not fully represent the ethnic diversity of the current adult population or children currently starting their life trajectories in Great Britain. The participants who were consistently followed up into adulthood were of slightly higher social position and as in any large scale longitudinal survey the most socially excluded groups are most poorly represented. Ethnicity is important because Caucasians are at lower risk of diabetes than other groups and also patterns of smoking and drinking differ between ethnic groups. Nevertheless the sample still includes many participants from across a social spectrum.

Glucose homeostasis

HbA_{1c} measurements were standardized so findings about HbA_{1c} should be generalisable to the wider population born in the UK around 1958. Diabetes plus elevated HbA_{1c} was used as a high risk group, with the aim of identifying a population with diagnosed or undiagnosed diabetes, just as large numbers of undiagnosed diabetics exist in the general population in addition to the diagnosed diabetics. This outcome is relevant to public health and should be reasonably generalisable. Studying metabolic syndrome gives slightly different insights to studying HbA_{1c} because metabolic syndrome comprises several components and increases in adiposity, blood pressure or blood lipids confer risks for cardiovascular disease as well as diabetes. Poor regulation is part of the spectrum of "pre-diabetic" disorders affecting increasing numbers of adults across the UK. Because disrupted glucose homeostasis raises risks of developing

diabetes and, in turn cardiovascular disease, it presents major current and future population health challenges and is an important outcome to study in the whole population (Coutinho et al. 1999; Gerstein 1997; Gerstein 2004; Khaw et al. 2001). A standard metabolic syndrome definition was modified for use with available data, but patterns of associations and pathways observed should give insight into development of an "at risk" group.

Results for total and central obesity should be generalisable as they were defined in standard ways. At 45 years, prevalence of obesity in the cohort was similar to other national surveys (Zaninotto et al. 2006, p.2). Pathways to glucose homeostasis operated partly through adiposity. Whilst the cohort are in their mid forties and prevalence of elevated HbA_{1c} and metabolic abnormalities is relatively low, associations of risk factors with obesity may foreshadow future associations with diabetes and HbA_{1c}. If expected age-related gains in adiposity and decreases in glucose regulation occur, associations between, for example, heaviness and frequency of drinking and HbA_{1c} may become more pronounced.

Childhood cognitive ability

The external validity of the cognitive ability tests was discussed in detail in Chapter 2: the assessments were not standard IQ tests but were age-appropriate and tests of key skills. Cognitive ability was analysed as relative ranks and the benefits of measuring relative rather than absolute change over time in scores is recognised by previous research; it reduces the difficulties of comparing different types of test appropriate for different age groups (Goldstein 1983). Extrapolating associations seen in the 1958 cohort to other settings must be cautious because associations between cognition and either health behaviours or diabetes risk may be specific to locations and times. Changes in social norms, expectations and in the macro-economic environment may all alter associations between cognition and the outcomes. The dynamic nature of the associations is illustrated by the change in the association between cognition and binge drinking in women with increasing age. However, associations between cognition and health behaviours and glucose risk were predominantly in the expected directions and complement the growing literature about the associations between cognitive ability and later health outcomes(Batty et al. 2006a). Whilst change in ability level across the school years was associated with health behaviour trajectories, and with 45-year adiposity, it was not associated with the glucose homeostasis measures. The question of whether change in ability would be associated with other health outcomes remains.

Pathways between cognitive ability and glucose homeostasis

Extrapolating the pathways between cognitive ability and glucose homeostasis must take into consideration first, whether the pathway factors was adequately measured, and secondly, if associations between cognition and the pathway factor and also the pathway and glucose

regulation remain stable over time. It may be reasonable to assume that pathways reflecting biological processes; for example increased body mass index resulting in poorer glucose homeostasis should be valid in other population samples with similar ethnic origins (and genetic predisposition to adiposity and glucose regulation) and of similar age groups (glucose homeostasis declines with age). However, pathways which depend on social context, in particular all the health behaviours may be not be valid in contexts where uptake, initiation and persistence of health behaviours follow different social patterns. The change in smoking and drinking over adulthood in this primarily Caucasian cohort may be specific to the particular geographical and cultural setting and time period. Consumption follows secular trends influenced by availability: the real price of alcohol has reduced several fold since 1970s (The Academy of Medical Sciences 2004) and real price of tobacco has increased. Secular changes in drinking cultures and acceptability of smoking may affect educational gradients in drinking frequency and smoking in other generations and hence associations between cognitive ability and health behaviours seen here may not apply to other settings.

Effect size

Associations between childhood cognition and adult glucose homeostasis (indicated by direct arrows in Figure 8.1), were consistent but weak. Higher 7-year z-scores (lower ability) were consistently associated with lower risks of poor adult glucose regulation, both across the population distribution of HbA_{1c} and in the high risk group (participants with HbA_{1c} ≥6% or type 2 diabetes) and higher risks of metabolic syndrome. For the most part, associations were not observed between 7-16 year change in maths (or reading) and adult glucose homeostasis. One SD increase in 7-year maths z-score was associated with an increase of 0.02-0.03% in HbA_{1c} level (for example from 5.00% to 5.02%) and the ORs for elevated HbA_{1c} /diabetes or metabolic syndrome were around 1.3.

7-16 year change in z-scores (declining ability rank) was consistently associated with higher risks of adult smoking; fully adjusted ORs were between 1.1 and 1.3, for smoking at one adult survey and between 1.5 and 1.9 for heavy persistent smoking. Higher 7-year z-scores (lower ability) were consistently associated with non-drinking; fully adjusted ORs were between 1.2 and 1.4 for non-drinking at any single adult survey and similar for repeated non-drinking. Associations between cognition and binge or heavy drinking were for the most part mediated by adult educational qualifications and social position.

Associations between health behaviours and adult glucose homeostasis were stronger than between childhood cognition and adult glucose homeostasis. Heavy compared to never smoking was associated with a gain of 0.11% HbA_{1c} in women and 0.23% in men. Non-drinking at two or more adult surveys compared to always reporting drinking increased HbA_{1c} by between 0.15% and 0.20%. ORs for elevated HbA_{1c} /diabetes and metabolic syndrome associated with

smoking and drinking histories were around 1.5 to 2. There were independent associations between drinking frequency or smoking with glucose regulation that were not completely mediated by other adult health behaviours or social pathways. In the full longitudinal models presented in Chapter 7, including confounders and pathways from across the whole lifecourse, the only variables predictive of any of the three measure of glucose regulation in the fully-adjusted longitudinal models were the drinking frequency and smoking summary variables.

The sizes of the associations reported between cognitive ability and health behaviours and also between health behaviours and adult glucose regulation were modest; whereas associations between cognitive ability and adult glucose regulation were weak and entirely mediated by the pathways studied. Although effect sizes were modest, it does not mean that they cannot have important affect population outcomes. Large absolute differences in risk can arise from small shifts in risk factors in a whole population (Rose 1992). The whole range of cognitive ability was studied and effects were not concentrated in one sub-group, so the associations between cognition and smoking or drinking and likewise between smoking or drinking with glucose homeostasis should be viewed in the context of risks to the whole population. The standard deviation of the HbA_{1c} distribution is 0.53% in men and 0.43% in women, so adjusted differences in HbA_{1c} levels associated with smoking or drinking of up to 0.3% correspond to over half a SD in HbA_{1c}. Chapter 5 concluded that associations between smoking or drinking and adult HbA_{1c} observed in the 1958 cohort represent non-trivial increases in population risk. Reductions in HbA_{1c} associated with lifecourse non-smoking and frequent drinking were smaller than reductions achieved in patients using oral anti-diabetics. However the reductions apply to the whole spectrum of HbA_{1c} levels and may be important in preventing adults developing poor regulation and entering the high risk group.

The benefits of lower HbA_{1c} levels for preventing onset of irreversible complications in the diabetic population have been demonstrated (Stratton et al. 2000). Recently, evidence has emerged that individuals with already elevated HbA_{1c} levels are not the only group likely to have health benefits from reducing HbA_{1c} levels. Increases in HbA_{1c} below levels associated with metabolic disturbances and diabetes are linearly associated with mortality risks, without evidence of a threshold effect (Khaw et al 2001). However some evidence exists for a threshold in the association between mortality and fasting plasma glucose at lower glucose levels (Brunner et al. 2006).

Policy considerations

Cognition and health behaviours

Associations between cognition and health behaviour trajectories were investigated not because cognition was expected to be the major determinant of these behaviours, but in order to

understand pathways between childhood cognitive ability and subsequent morbidity risk which are repeatedly reported in a rapidly growing literature (Deary & Batty 2006). Encouraging development of cognitive skills of children is a key part of schooling and is very important for social and economic reasons, and needs to be done irrespective of any associations between cognition and subsequent health behaviour trajectories and health outcomes. The pervading importance of childhood cognition on health is seen in the fact that successful economic and educational trajectories were in turn associated with adult health behaviours and health status. The vulnerability of adults who had poorer childhood cognition to more health-harming behaviours operated in major part through the acquisition of educational qualifications and to a slightly lesser degree, through attained social position. Therefore in terms of levelling social inequalities in health, targeting interventions related to health behaviours at less educated groups (with the exception of binge drinking related policies in younger women) may be warranted, in addition to trying to raise educational standards and achievement of children in disadvantaged circumstances.

Factors other than cognitive ability are clearly important for designing policy interventions, these include the legal framework regulating use and access, social norms and expectations about behaviour (for example regulation of smoking in public spaces regulates tobacco use and changes expectations and norms about smoking). Therefore whilst providing simple and clear health promotion messages is desirable, other means of driving behavioural change such as price and access to tobacco and alcohol are stronger policy levers than health education (The Academy of Medical Sciences 2004).

The stability and change in smoking and drinking across two decades of adult life suggest that policies aimed at reducing alcohol-related harm need to consider older adults in addition to adolescents and young adults in whom harmful drinking behaviours are most prevalent. Men were observed to engage in more binge and heavy drinking than women and were hence at increased risks of alcohol-related harm. There is evidence that reductions in average alcohol consumption in a population are associated with reductions in alcohol-related harm (The Academy of Medical Sciences 2004). Therefore population-wide interventions to promote moderate rather than heavy or binge drinking would be appropriate.

Evidence about behavioural change from epidemiologic studies needs to be translated into behavioural advice and change programs which work in practice. Theories of behavioural change can inform development of successful behavioural change programs. For example, knowledge of the health risks associated with a behaviour is a poor predictor of that behaviour, whilst self efficacy in relation to a behaviour is more important, for example knowing that

smoking is bad for your health is a poor predictor of quitting but feeling able to quit is a better predictor.

Diabetes risk

The pathways to glucose homeostasis demonstrated in this thesis contribute to evidence required for evidence-based policies about preventive lifestyle changes in a healthy population. Understanding pathways is important because lowering HbA_{1c} levels and risks of metabolic syndrome in the general population should translate into lower risks of onset of diabetes and cardiovascular disease with attendant mortality risks. The large and increasing population health burden of type 2 diabetes and, becoming increasingly clear, of metabolic syndrome merit public health interventions to treat existing cases and importantly, to aid early detection and prevent onset. Policy responses may be at different levels. Primary prevention targets the whole population at risk, justification for such interventions comes from the increasing mortality risks seen across the whole spectrum of HbA_{1c}, below levels associated with diabetes and also because beta cell dysfunction is present for many years prior to diagnosis (Turner et al. 1995). The need for both upstream and downstream interventions as a response to the global diabetes epidemic has been recognised (Zimmet et al. 2001). Diabetes risks increase with poor quality diet and sedentary lifestyles which are difficult behaviours to change, so in addition to targeted behavioural change programs, action at a societal level to make healthier choices easier and more accessible, is required to alter these determinants of disease. Examples of societal influences were discussed in chapter 7. In contrast secondary prevention focuses on specific at risk groups in a population. Primary and secondary prevention interventions may need to be delivered in separate ways, corresponding to the different target groups; the healthy population and at risk groups.

Primary prevention of diabetes

General policy responses to health behaviours have been discussed and evidence about glucose regulation is discussed now. Consistent associations between infrequent or non-drinking and persistent and heavy smoking were seen for all glucose homeostasis measures. Whilst the possibility of residual confounding cannot be entirely eliminated (discussed in Chapter 7), the association between health behaviours and adult glucose regulation was much stronger than between cognitive ability and glucose regulation. As expected from the relative effect sizes, in the final models in Chapter 7, the confounding effects of cognition on health behaviours and glucose regulation were not strong and independent effects of smoking or drinking on glucose homeostasis remained. These associations were only partly confounded by adult physical activity and dietary patterns, and only partly mediated by adult adiposity. The independent associations observed between smoking and drinking frequency with HbA_{1c} levels in the

"normal" range suggest that healthy living advice for the whole population could usefully include messages about smoking and drinking.

Nevertheless glucose regulation is only one of many alcohol-related outcomes that need to be considered when formulating alcohol-related policies. For example heavy alcohol consumption has many social costs to people around the drinkers as well as physical consequences for themselves. At present, taking up drinking on medical grounds is not recommended because of potential social and health problems associated with alcohol use. Because infrequent alcohol consumption was associated with increased risks it may be more relevant to consider targeting non-drinkers as an "at risk" group for screening and targeting preventive behavioural interventions. However among the population of current drinkers, the relative merit of frequent rather than infrequent drinking patterns could be emphasised. A pragmatic health message encompassing evidence about other health consequences of heaviness of drinking is that heaviness of drinking should be moderated and binge drinking avoided. Whilst heaviness of drinking and episodic (binge) drinking were not consistently associated with HbA_{1c} levels in this cohort, there are sufficient other health and social reasons for discouraging binge drinking and this is recognised in current government policy (Prime Minister's Strategy Unit 2004).

The consistently detrimental role of smoking on HbA_{1c} levels across the population range in addition to its many other negative health consequences clearly indicates that policy messages should continue to emphasise the wide range of negative health consequences, discourage initiation and encourage cessation, as current British smoking policies do. However, policies targeting one behaviour can impact on other behaviours and risk factors. Changing several behaviours at once and maintaining successful change can be difficult to achieve in reality. For example, quitting smoking is often associated with weight gain, which is particularly detrimental to diabetes risk. The literature provides scant evidence in a general rather than a high risk population, of associations between diabetes risk and multiple behaviour changes, which include smoking, as smoking is not currently considered a main risk factor for diabetes. However, existing data from trials of other outcomes have been analysed in relation to diabetes risk. In the MRFIT trial of multiple behaviour changes, middle-aged men were counselled to improve diet, increase physical activity and stop smoking. Among smokers the intervention was associated with an increased risk of onset of diabetes over 6 years of follow-up HR 1.26 (95%CI 1.10, 1.45) compared to HR 0.82 (95%CI 0.68, 0.98) among non-smokers and this was thought to be due to weight gain and antihypertensive drug use among smokers (Davey Smith et al. 2005). The authors interpreted results cautiously because the trial was aimed at lowering cardiovascular risk so analyses of diabetes risk were post hoc. Also the intervention differed between smokers and non-smokers; because smokers were encouraged to quit, they received less dietary advice. Additionally, inclusion criteria for non-smokers was for higher blood

pressure and lipids than for smokers, and non-smokers were heavier and had greater BMI at baseline. The MRFIT data indicated that quitting smoking alone was insufficient to prevent diabetes onset. It highlighted that support may be needed in behavioural change programs which may have adverse consequences and underlines the importance of a holistic approach to all facets of behavioural change and attendant risks. For example because smoking and drinking cluster together and share behavioural cues, interventions aimed at multiple aspects of unhealthy behaviour may be pragmatic in order to achieve maximum health benefits across a range of outcomes, but they need to be carefully designed. Changing multiple behaviours offers potential for gaining from synergistic effects of several behaviours on a health outcomes. However, in this instance there was not evidence that smoking and drinking had synergistic effects on any of the glucose homeostasis outcomes.

Secondary prevention of diabetes

Secondary prevention interventions target specific high risk groups, such as individuals with metabolic syndrome or elevated HbA_{1c} levels. In high risk groups such as those with metabolic syndrome, or older adults, life histories of smoking and alcohol use could be considered as components of diabetes risk scores which can be used to evaluate an individual's risk. Several scores exist, one of which includes smoking history (Griffin et al. 2000). The results presented here could also inform behavioural change programs for at risk groups. Individuals with metabolic syndrome or diabetes have increased risks of cardiovascular disease, so intensive lifestyle changes to modify both glucose homeostasis and cardiovascular risks are merited to prevent disease onset. There is now a sound evidence base from several large-scale trials in Europe, Asia and USA in populations of different ethnicities and in varied cultural settings, indicating the greater benefits of intensive lifestyle change of diet and physical activity compared to pharmacologic interventions for preventing progression to type 2 diabetes in high risk populations (with impaired glucose tolerance, IGT) (Diabetes Prevention Program Research Group 2002; Pan et al. 1997; Tuomilehto et al. 2001). For example, diet and activity interventions reduced progression of IGT to diabetes by 58% over 3 years compared to 31% with metformin (Diabetes Prevention Program Research Group 2002). The lifestyle interventions centred around 30 minutes/day moderate intensity physical activity to sustain 5-7% body weight loss and varied dietary interventions reducing caloric intake from fat. The programmes were well-designed and supported, for example including group or personal training and target-setting. A caveat is that behavioural change may be hard to attain and maintain in practice; it requires input from a variety of sources with expertise in physical activity and nutrition as well as support for smoking cessation. In a context where there is little support for and resources dedicated to behaviour change, it is easy to argue that using drugs to regulate metabolic control may be more effective than lifestyle interventions. Where intensive lifestyle change is unsuccessful, pharmacologic interventions are clearly important. However

behavioural change has potentially long-lasting effects; in the Diabetes Prevention Program trial when the drug treatment was withdrawn the levels of risk returned to the previous untreated levels, but with lifestyle intervention benefits were maintained. Also, it has been argued that lack of data on long-term outcomes of drug interventions and their high cost mean that lifestyle intervention should be the main tool for reducing diabetes onset (Tuomilehto & Wareham 2006). Indeed, the new International Diabetes Federation guidelines for prevention of type 2 diabetes overwhelmingly supports lifestyle over pharmalogic intervention for targeting at risk groups and for prevention in the whole population (Alberti et al. 2007). The multiple health benefits to other non-diabetic disorders which are expected to accrue from moderating alcohol use and quitting smoking are another reason to promote behavioural change interventions.

General policy points

In considering provision of treatments, efficacy, the duration of effects, side effects and costs must be taken into account. Existing evidence about behavioural interventions and diabetes onset does not focus on alcohol and tobacco use, because they have not been considered the main risk behaviours, hence formal evaluations of the economic and health benefits of these behaviour changes are not available. However cost effectiveness of different treatment options for individuals with diabetes in different country and age-group settings have been studied and it was concluded that intensive lifestyle changes (to diet, physical activity and weight loss) as well as metformin and acarbose all stopped or slowed progress to diabetes and were all affordable (Herman et al. 2005).

A question arising from results presented here is whether to add messages about tobacco and alcohol use. The results in this thesis indicate that smoking in particular is a proximal risk factor for diabetes and elevated HbA_{1c}. If screening high risk groups in middle age is viable, then smoking and non-drinking may be considered for identification of high risk groups. In non-diabetic groups, benefits from quitting smoking and amongst drinkers, adopting a frequent rather than infrequent alcohol drinking pattern were suggested by the results in this thesis. In considering overall cost-effectiveness, the location and the risk profile of a population and the costs of intervention are all important. The formulation of any behavioural change program must be culture and location specific and should draw on the literature about theory and practice of behaviour change programs. If multiple behaviours cannot be successfully targeted, pragmatic decisions about the most effective and cost effective interventions based on sequential changes of separate behaviours need to be taken.

Childhood cognition and adult glucose homeostasis

The modest associations between childhood cognitive ability and adult glucose homeostasis were mostly mediated by adult health behaviours, adult qualifications and occupational level

and adult adiposity. Although cognitive ability sets up a trajectory to adult social position and educational qualifications as well as health related behaviours, its weak effects on glucose regulation do not make it an obvious target for intervention to change adult glucose regulation. Policies targeting these upstream pathway factors are more likely to have direct effects on diabetes risk than downstream interventions which although beneficial, may be expected to have multiple and indirect effects. The role of tobacco and alcohol use in regulation of HbA_{1c} in the not at risk population group, indicates that messages about not smoking and moderate drinking are appropriate for this population group.

Future work

This study suggests future directions for epidemiologic and policy-oriented research. These include, for example, the efficacy of interventions aimed at changing multiple behaviours in reducing diabetes risk. Future work could investigate the efficacy of interventions aimed at changing multiple behaviours, in comparison to for example, sequential programs aiming for a series of changes. This study could not test theories of behavioural change. Future studies of behavioural change could investigate cognition and input from health psychology to understand the processes of behavioural changes and hence achieve and maintain healthy behavioural patterns.

In epidemiologic studies, mendelian randomisation could be used to investigate whether associations observed between behaviours and outcomes are not residually confounded, provided that good genetic markers for the behavioural measures are identified. At the 45-year survey cell lines were created for many participants. Once genotyping is completed, it will be possible to investigate candidate genes for diabetes onset and poor glucose regulation and evaluate how they interact with cognitive development, behavioural and social exposures. There may be sub-groups for whom certain behavioural patterns are differentially associated with diabetes risk. Candidate gene studies for type 2 diabetes have reported odds ratios associated with candidate genes between 1.15 and 1.5; relatively modest effect sizes. However they may not be independent and could act in cumulative or multiplicative fashion (Barroso et al. 2003). Common genetic variants associated with cognitive development may also be associated with uptake of addictive behaviours including tobacco and problem alcohol use, or onset of obesity or aspects of glucose dysregulation.

Alcohol use and Cognition in mid-life

The observed association between childhood cognition and adult alcohol use challenges reported beneficial effects of alcohol use on midlife cognitive ability. The 1958 cohort is one of few datasets with information on early life cognitive ability and change in ability, and, in future surveys will have the potential to investigate mid-life cognition. For example, one study of associations between alcohol use and adult ability (aged in their fifties) that did adjust for

childhood ability, reported that associations were explained by childhood ability (Krahn et al. 2003).

Diabetes and Cognition in mid-life

Several studies of diabetes and later cognitive decline exist (Brayne et al. 2005; Messier 2005) as well as a small but growing literature on obesity and adult later cognitive change (Elias et al. 2005). Diabetic and obese individuals are at greater risk of poor cognitive functioning and decline in cognitive functioning including onset of dementia or alzheimers disease. There is evidence both from cross-sectional studies, where the direction of associations is unclear, but also from prospective studies starting in adulthood. However, even in prospective studies the possibility that the obese or diabetic patients started with poorer cognitive abilities in earlier life has not been systematically ruled out; very few data sets are available which have the relevant data to tackle this question.

Childhood behavioural problems and adult mental health

New research reports associations between higher childhood ability and poorer mental health in the fifth decade of life (Hatch et al. 2007). The role of childhood behavioural problems and adult mental health as pathways in future work on cognitive abilities and other health outcomes could be investigated as they have been little studied. In this thesis childhood behavioural problems were included as pathways between cognition and smoking and drinking and also as pathway between cognition and adult glucose homeostasis. As expected, behavioural problems were associated with smoking and drinking and partly mediated associations with childhood cognition.

Conclusion

This thesis investigated pathways across life and provided evidence about chains of risk that accumulate to influence mid-life glucose regulation. The growing population burden of diabetes risks mean that understanding proximal influences on risks is important for the current at risk population and understanding the chains of risks is important to future populations at risk. Cognition in childhood has a long reach on adult outcomes through its role in shaping social trajectories and the uptake and persistence of alcohol and tobacco use which in turn were significantly associated with glucose adult regulation. This study adds further weight to evidence that use of alcohol and tobacco should be considered when identifying groups at risk of diabetes and in maintaining optimal glucose regulation at pre-diabetic ranges. As reviewed above, unanswered questions remain about how chains of risks from cognition operate over the lifecourse. This thesis has provided evidence on which to base future studies and hypotheses as well as informing design of distal and proximal policy interventions.

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