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DIET DURING PREGNANCY

*DIETARY PATTERNS AND WEIGHT GAIN RATE
AMONG FINNISH PREGNANT WOMEN*

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TUULA ARKKOLA

DIET DURING PREGNANCY

Dietary patterns and weight gain rate among Finnish pregnant women

Academic dissertation to be presented with the assent of the Faculty of Medicine of the University of Oulu for public defence in Auditorium 12 of the Department of Paediatrics, on 8 January 2010, at 12 noon

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Abstract

Proper nutrition and optimal weight status in pregnancy are important for both the mother and her child. The present study was aimed at assessment of maternal food and nutrient intake, dietary supplement use, dietary patterns, and weight during pregnancy. Additionally, associations between maternal weight, socio-demographic and perinatal factors and advanced beta cell autoimmunity in the offspring were examined.

The results from a one-year cohort of mothers entering the ongoing Type 1 Diabetes Prediction and Prevention (DIPP) study in 1998–99 ($n = 797$) suggested that healthy food choices were positively correlated with maternal age and education. Dietary supplements were used by 85% of the women. However, the intake of vitamin D did not meet the recommendation and folic acid intake was inadequate in 44% of the pregnant women when both food and supplementation intakes were taken into account.

Seven dietary patterns were identified in 3730 pregnant women who entered the DIPP study between 1997 and 2002. The ‘healthy’, the ‘low-fat foods’ and the ‘alcohol and butter’ dietary patterns were positively associated with maternal age and education. The ‘fast food’ dietary pattern was positively associated and the ‘alcohol and butter’ pattern was inversely associated with the rate of maternal weight gain during pregnancy.

Altogether, 4093 children and their mothers comprised the study population in which the relationships between maternal initial body mass index, weight gain rate, and the development of beta cell autoimmunity in the offspring were examined. Maternal weight status during pregnancy was not related to the risk of advanced beta cell autoimmunity. A higher level of maternal education was significantly associated with a decreased risk of advanced beta cell autoimmunity in children.

More attention should be paid to nutritional guidance among Finnish pregnant women, especially as regards young and less well educated women. Dietary patterns may be useful for risk group identification and they may offer a framework for further research concerning diet and health outcomes among mothers and their children.

Keywords: diet, dietary patterns, dietary supplements, eating, energy intake, food frequency questionnaire, pregnancy, socioeconomic factors, type 1 diabetes, weight gain

To my family

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Oulu, October 2009

Tuula Arkkola

Abbreviations

BMI	body mass index
DIPP	Type 1 Diabetes Prediction and Prevention study
FFQ	food frequency questionnaire
GADAs	autoantibodies to the 65-kDa isoform of glutamic acid decarboxylase
GDM	gestational diabetes mellitus
HLA	human leukocyte antigen
IAAs	insulin autoantibodies
IA-2As	autoantibodies to the protein tyrosine phosphatase-related IA-2 molecule
ICAs	islet cell antibodies
IOM	United States Institute of Medicine
JDF	Juvenile Diabetes Foundation
PCA	principal components analysis
RUs	relative units
SAS	Statistical Analysis System
SPSS	Statistical Package for the Social Sciences
T1D	type 1 diabetes
WHO	World Health Organization

List of original articles

This thesis is based on the following articles, which are referred to in the text by their Roman numerals:

- I Arkkola T, Uusitalo U, Pietikäinen M, Metsälä J, Kronberg-Kippilä C, Erkkola M, Veijola R, Knip M & Virtanen SM (2006) Dietary intake and use of dietary supplements in relation to demographic variables among pregnant Finnish women. *Br J Nutr* 96: 913–920.
- II Arkkola T, Uusitalo U, Kronberg-Kippilä C, Männistö S, Virtanen M, Kenward MG, Veijola R, Knip M, Ovaskainen M & Virtanen SM (2008) Seven distinct dietary patterns identified among pregnant Finnish women – associations with nutrient intake and sociodemographic factors. *Pub Health Nutr* 11: 176–182.
- III Uusitalo U, Arkkola T, Ovaskainen M, Kronberg-Kippilä C, Kenward MG, Veijola R, Simell OG, Knip M & Virtanen SM (2009) Unhealthy dietary patterns are associated with weight gain during pregnancy among Finnish women. *Pub Health Nutr* 12: 2392–2399.
- IV Arkkola T, Kautiainen S, Takkinen H, Kenward MG, Nevalainen J, Uusitalo U, Simell O, Ilonen J, Knip M, Veijola R & Virtanen SM (2009) The relationship of maternal weight status in pregnancy to the development of advanced beta-cell autoimmunity in the offspring: a prospective birth cohort study. Manuscript.

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1 Introduction

Proper nutrition during pregnancy is considered important for the wellbeing of both mother and foetus. A balanced diet supports maternal health during pregnancy, delivery and breastfeeding. Maternal nutrition affects the growth and development of the foetus, and also later health outcomes in the offspring. Maternal weight status influences both the mother and her child throughout the entire reproductive cycle, beginning before conception and continuing through lactation. There is a relative paucity of data on maternal diet in pregnancy and the association between diet and gestational weight gain. In addition, little is known about the associations between obesity, excessive weight gain in pregnancy and type 1 diabetes (T1D) in children. According to earlier findings among Finnish girls and women, intakes of vitamin D, folic acid and iron are below the recommended levels (Erkkola *et al.* 1998, Lyytikäinen *et al.* 2005, Paturi *et al.* 2008).

Nutrient requirements increase during periods of growth and development such as pregnancy. An adequate amount of nutrients is needed to support fetal and infant growth and development along with alterations in maternal tissues and metabolism (Picciano 2003). It is estimated that recommended intakes of 14 of the 21 essential micronutrients increase during pregnancy (Allen 2006). Interest in nutrition during pregnancy has been generated by the fetal origins theory of adult disease (Barker 1992). This hypothesis suggests that adult cardiovascular and metabolic disease originate through developmental plasticity and foetal adaptations arising from failure of the materno-placental supply of nutrients to match foetal requirements (Godfrey 2002). Maternal nutrition is thought to be able to programme long-term effects on the offspring without necessarily affecting the infant's size at birth. Experimental data suggest that the period in which these early life events influence lifelong consequences can extend from conception to infancy, depending on the organ system involved (Gluckman *et al.* 2005)

The traditional way to assess diet is to examine the consumption of certain food items or the intake of energy and nutrients. The complexities of diet make it difficult to consider the role of individual foods or nutrients in isolation as nutrients may interact with each other and influence each other's bioavailability and absorption (Michels & Schulze 2005). Dietary pattern analysis is a method that aims to describe the whole diet. The use of dietary patterns might help us to capture some of the complexity of diet that may be lost in nutrient-based analyses

(Jacques & Tucker 2001), and provide additional information when exploring the relationship between nutrition and disease.

As the prevalence of obesity is increasing, overweight conditions and obesity have also become common in pregnant women. Obesity in pregnancy is linked to maternal complications ranging from effects on fertility to effects on delivery and in the postpartum period, as well as many complications affecting the foetus and newborn (Arendas *et al.* 2008). Obese pregnant women are at a higher risk of gestational diabetes (Chu *et al.* 2007, Ogonowski *et al.* 2009). Incidences of pre-eclampsia (O'Brien *et al.* 2003, Frederick *et al.* 2006, Leddy *et al.* 2008) and Caesarean section (Callaway *et al.* 2006, Vehkaoja *et al.* 2006, Poobalan *et al.* 2009) increase with maternal overweight and obesity. Complications due to excessive gestational weight gain also include foetal macrosomia, resulting in the delivery of a large-for-gestational-age infants (Abrams *et al.* 2000, Stotland *et al.* 2004, Helms *et al.* 2006). In the long run, excessive weight gain during pregnancy may increase the risk of weight retention and obesity after pregnancy (Gunderson *et al.* 2000, Rooney & Schauburger 2002), which process may be further increased by relatively early termination of breastfeeding among those who gain excess weight during pregnancy (Hilson *et al.* 2006, Rasmussen 2007). Obesity has increased significantly among children and adolescents (Lobstein *et al.* 2004). Maternal excessive weight gain during pregnancy is associated with an elevated risk of the offspring being overweight (Moreira *et al.* 2007, Oken *et al.* 2007, Wrotniak *et al.* 2008, Mamun *et al.* 2009).

Type 1 diabetes is an autoimmune disease in which the body attacks its pancreatic beta cells. The clinical presentation of T1D is preceded by an asymptomatic period of beta cell autoimmunity varying from a few months to over 10 years (Knip 2002b). Environmental factors appear to play an important role in the pathogenesis of T1D. Maternal obesity before pregnancy (Rasmussen *et al.* 2007) and excessive gestational weight gain (McKinney *et al.* 1997) have been found to predict an increased risk of T1D in children. Other perinatal factors such as pre-eclampsia and Caesarean section are also associated with an increased risk of T1D in the offspring (Dahlquist & Källen 1992, Cardwell *et al.* 2008). The mechanisms of action of different nutritional constituents that may play a role in the development of beta cell autoimmunity are largely unknown. The effects of nutritional risk predictors may be different in the foetal period, in early infancy, and later in childhood (Virtanen & Knip 2003). Finland has the highest incidence of T1D worldwide (Harjutsalo *et al.* 2008).

In the present study we studied maternal dietary intake, supplement use, and dietary patterns during pregnancy. We examined associations between diet, socio-demographic factors and maternal weight gain during pregnancy. Furthermore, we studied associations between maternal initial body mass index (BMI), weight gain during pregnancy and advanced beta cell autoimmunity in Finnish children.

2 Review of the literature

2.1 Maternal diet during pregnancy

2.1.1 Recommendations on dietary intake and supplement use

The latest national nutrition recommendations for pregnant women in Finland are from 2004 (Hasunen *et al.* 2004). The dietary guidelines are based on the Finnish Nutrition Recommendations issued by the National Nutrition Council in 1998, and the latest research. The present Finnish Nutrition Recommendations were published in 2005 (National Nutrition Council 2005). They are based on Nordic Nutrition Recommendations (Becker *et al.* 2006) which were approved in 2004 by the Nordic Council of Ministers.

A proper diet during pregnancy contains sufficient amounts of vegetables, fruit, berries, wholegrain products, vegetable oil, vegetable oil-based margarine, fish, low-fat meat, and fat-free milk products (Table 1). All pregnant women in Finland are recommended to use 10 µg of supplementary vitamin D from October to March. The requirement of supplementary calcium, iron and folic acid are estimated individually (Table 2). Vitamin B₁₂ is an additionally required supplement for vegan pregnant women. A vegan diet is not recommended for pregnant women in Finland because there is not enough evidence concerning its nutritional sufficiency. Vitamin A-containing supplements, liver, and liver products are not recommended because a high retinol intake may increase the risk of malformation and miscarriage. Beta-carotene does not have this effect and may be consumed during pregnancy. There are specially planned multivitamin supplements for pregnant women available in Finland. Alcohol use is not recommended during pregnancy because consumption has been linked to poor birth outcomes and long-term developmental problems in the offspring. Even low levels of alcohol prenatally can have adverse consequences (Bailey & Sokol 2008). The Finnish dietary recommendations for pregnant women are in line with the Nordic recommendations, the only difference being that the recommended intake of folic acid is slightly higher, 500 µg, in the Nordic recommendations (Becker *et al.* 2006) than in the Finnish recommendations (400 µg). According to the recommendations of the World Health Organization (WHO 2004) and in the United States pregnant women should have daily consumption of 600 µg of synthetic folic acid from fortified foods or supplements (Vogelzang 2005). The

influence of food fortification on nutrient intake is poorly examined in Finland, although a growing selection of fortified products is available. In a small study among Finnish pregnant women, fortified mineral water improved folate status and reduced plasma homocysteine concentrations (Järvenpää *et al.* 2007).

It is agreed that the preconception period and pregnancy could be life events leading to increased general nutritional awareness that might influence women's future nutrition-related behaviour (Piirainen *et al.* 2004, Sz wajcer *et al.* 2006). Piirainen *et al.* evaluated the status of dietary and health counselling in prenatal and antenatal clinics in Finland and found that the dietary recommendations were not fully adhered to. For example, only 60% of the nurses in prenatal clinics had advised the use of vitamin D supplements. However, 90% of the subjects in prenatal clinics considered dietary counselling to be adequate (Piirainen *et al.* 2004).

Table 1. Recommendations on food choices during pregnancy in Finland (Hasunen *et al.* 2004).

Food	Recommendation	Main benefit or unfavourable effect
Dairy products	Skimmed milk products 8 dl/day No un-pasteurized milk products or fresh cheeses	Calcium, vitamin D <i>Listeria monocytogenes</i> infection
Fish	Weekly 2–3 times No pike Baltic sea herring (>17 cm) and salmon 1–2 times/month No vacuum-packed fish	Vitamin D, unsaturated fatty acids Contains methylmercury Contain dioxin and PCB-compounds ¹ <i>Listeria monocytogenes</i> infection
Vegetables, fruits, and berries	Daily 5–6 servings (≥ 500 g)	Folic acid, fibre
Vegetable oil-based margarine and vegetable oil	Daily	Essential fatty acids, vitamin D, unsaturated fatty acids
Wholegrain products	Daily	Iron, fibre
Alcohol	Not recommended	Teratogenic effect
Artificial sweeteners	No saccharin and cyclamate	Possible carcinogenic effect
Coffee and other caffeine-containing drinks	< 300 mg caffeine (about 4.5 dl coffee)	Possible risk of preterm delivery, blood pressure ↑
Herbal products	Not recommended	Contents and effects not known
Licorice and salmiak	Continuous use or great amounts (over 50 g) are not recommended	High glycyrrhizin content (risk of preterm delivery)
Liver and liver products	Not recommended	Possible teratogenic effect (retinol)
Raw sprouts	Not recommended	Risk of salmonella infection
Salt	Recommended to reduce	Blood pressure ↑, swelling

¹ Poly Chlorinated Biphenyl compounds

Table 2. Recommended dietary supplementation during pregnancy in Finland (Hasunen *et al.* 2004).

Nutrient	Dose	Target group
Folic acid	400 µg	Women with an unbalanced diet, users of certain forms of medication, women with coeliac disease
	4 mg	If the foetus is at high risk of a neural tube defect, under doctor's supervision
Vitamin D	10 µg	All women, October–March
Calcium, Ca ²⁺	500–1000 mg	Women whose diet does not include enough milk products or other calcium-containing foods
Iron, Fe ²⁺	50 mg ¹	Women with Hb < 110 g/l during the first trimester, or Hb < 100 g/l during a later phase of pregnancy

¹ a store of 500 mg iron is required at the beginning of pregnancy to maintain iron balance throughout the pregnancy period

2.1.2 Food consumption and nutrient intake

Only a few studies have involved examination of food choices during pregnancy. In an earlier Finnish study it was reported that the main sources of energy in the diet during pregnancy were cereal and milk products (Erkkola *et al.* 1998). The consumption of fish and poultry was low. In the United States pregnant and lactating women were more likely to use milk products and to consume larger amounts of these products than were other women (Borrued *et al.* 1993). In a recent Belgian study differences in dietary behaviour between pregnant and non-pregnant women were reported. Pregnant women reported higher consumption of fruit, which resulted in higher fibre intake. They also reported higher consumption of beef and milk products, as well as higher fat intake. No difference in fish consumption between pregnant and non-pregnant women was seen (Verbeke & De Bourdeaudhuij 2007).

According to results reported by Erkkola *et al.*, pregnant women in Finland have an adequate nutrient intake from their diet with the exception of vitamin D, folic acid and iron (Erkkola *et al.* 1998). The levels of these nutrients were also below those recommended in Finnish girls aged 10 to 12 years (Lyytikäinen *et al.* 2005) and in women aged 25 to 64 years (Paturi *et al.* 2008). In Finnish studies, the intake of dietary fibre has been below that recommended (Erkkola *et al.* 1998, Lyytikäinen *et al.* 2005, Järvenpää *et al.* 2007) and the intake of saturated fatty acids above the recommendation (Erkkola *et al.* 1998, Lyytikäinen *et al.* 2005, Järvenpää *et al.* 2007, Paturi *et al.* 2008). In pregnant women, the intake of

sucrose was also above that recommended (Erkkola *et al.* 1998). Studies in other countries have revealed low intakes of vitamin D (Ortega *et al.* 1994, Mathews *et al.* 2000, Giddens *et al.* 2000), folic acid (Ortega *et al.* 1994, Mikode & White 1994, Antal *et al.* 1997, Rogers & Emmett 1998, Mathews *et al.* 2000, Giddens *et al.* 2000, Berg *et al.* 2001, Mouratidou *et al.* 2006, Sherwood *et al.* 2006) and iron (Ortega *et al.* 1994, Mikode & White 1994, Antal *et al.* 1997, Rogers & Emmett 1998, Mathews *et al.* 2000, Giddens *et al.* 2000, Mouratidou *et al.* 2006) during pregnancy.

2.1.3 Dietary supplement use during pregnancy

Although recommendations exist concerning the requirements for some dietary supplements during pregnancy, little is known about how these recommendations are used in practice. The recommendation regarding vitamin D supplementation, at least, is considered to be poorly fulfilled in Finnish pregnant women. There is some evidence however, that during pregnancy a larger proportion of women (70–91%) use dietary supplements (Suitor & Gardner 1990, Erkkola *et al.* 1998, Ervin *et al.* 1999) than during other phases of life (36–52%) (Kaarinen *et al.* 1997, Helakorpi *et al.* 2007, Paturi *et al.* 2008). In women in the US, the use of dietary supplements in general is reported to be slightly greater than elsewhere, 56–57% (Yu *et al.* 2003, Murphy *et al.* 2007). The most used supplemental nutrient during pregnancy is iron (Timbo *et al.* 1994, Erkkola *et al.* 1998, Rogers & Emmett 1998, Ervin *et al.* 1999), followed by folic acid and vitamin D (Rogers & Emmett 1998, Mathews *et al.* 2000). In Norwegian pregnant women, the most commonly used category of supplements was cod liver or fish oil supplements, followed by folic acid and multivitamin supplements (Haugen *et al.* 2008). In several studies among pregnant women, the total intake of vitamin A (Ortega *et al.* 1994, Voyles *et al.* 2000), folic acid, zinc and vitamin B₁₂ (Berg *et al.* 2001) has exceeded the dietary recommendations as a result of the use of supplements.

2.1.4 The roles of socio-demographic factors

Earlier Finnish findings suggest that maternal age and education are associated with the composition of diet during pregnancy. Older women had a higher intake of dietary fibre than younger women and more educated women consumed more vegetables and fruit than less educated ones during pregnancy (Erkkola *et al.* 1998). Young pregnant women, especially smokers, are considered to be a group

at particular risk of low micronutrient intake (Mathews *et al.* 2000, Baker *et al.* 2009).

Many socio-demographic and lifestyle factors have been associated with the use of dietary supplements in general. The most typical female supplement user seems to be a well-educated woman whose diet is already close to the nutrition recommendations without supplement use (Kartinen *et al.* 1997, Ervin *et al.* 1999, Kirk *et al.* 1999, Yu *et al.* 2003, Paturi *et al.* 2008). Greater age has also been associated with higher supplement use (Timbo *et al.* 1994, Yu *et al.* 2003). There is limited and contradictory information concerning supplement use during pregnancy in association with socio-demographic factors. Age and education did not differentiate supplement users and non-users during pregnancy in Finnish women (Erkkola *et al.* 1998), whereas in Norwegian pregnant women a higher level of education (Nilsen *et al.* 2006c) and among British women higher age were associated positively with supplement use during pregnancy (Mathews *et al.* 2000).

2.1.5 Associations with later diseases in the offspring

Placental and foetal growth have been suggested to be particularly vulnerable to problems associated with maternal nutrition during the peri-implantation period and during the first trimester of gestation (Wu *et al.* 2004). Small body size at birth in pre-term and term infants and accelerated weight gain and increase in BMI later in childhood have been associated with increased risks of coronary heart disease and type 2 diabetes later in life (Eriksson 2007). Both maternal under-nutrition and over-nutrition during pregnancy can impair foetal growth. Promoting an optimal intrauterine environment will not only ensure optimal foetal development, but will also reduce the risk of chronic diseases in adulthood. According to the Barker's hypothesis, the human foetus adapts to under-nutrition by means of metabolic changes in the production of foetal and placental hormones which control growth (Barker 1998). These adaptations are presented in Figure 1. Reduced pre- and postnatal growth has been associated with a number of chronic conditions, such as coronary heart disease, stroke, hypertension and type 2 diabetes later in life (Barker *et al.* 2009). In contrast, results from a relatively small UK cohort do not suggest that higher maternal circulating concentrations of nutrients improve fetal and placental growth among the relatively well nourished women of industrialized countries (Mathews *et al.* 2004).

There is contradictory evidence about the association between maternal nutrition during pregnancy and cardiovascular heart disease risk in the offspring. The findings of Huxley and Neil do not support the hypothesis that low birth weight or poor maternal nutrition in pregnancy is associated with cardiovascular heart disease risk factors such as glucose tolerance, blood pressure and components of the lipid profile in adult life (Huxley & Neil 2004). Other findings suggest that low maternal energy intake in pregnancy may increase susceptibility to atherogenesis in the child (Gale *et al.* 2006). In a review study concerning maternal diet and blood pressure of the offspring however, no strong evidence was found that any component of maternal diet during pregnancy (protein, energy, calcium and various other nutrients) influences blood pressure in the offspring (Brion *et al.* 2008).

Foetal and newborn nutrient status regarding vitamin D, and n-3, and n-6 fatty acids, has been shown to be dependent on maternal diet during pregnancy (Connor *et al.* 1996, Zeghoud *et al.* 1997). The offspring of mothers who report high meat or fish and low green vegetable intakes in late pregnancy tend to have increased adult fasting plasma cortisol concentrations in response to psychological stress (Herrick *et al.* 2003). The vitamin D status of mothers in late pregnancy predicted the bone mass of their offspring measured 9 years later (Javaid *et al.* 2006). An increased maternal intake of vitamin D during pregnancy is also reported to decrease the risk of wheeze symptoms and asthma in early childhood (Camargo, Jr. *et al.* 2007, Devereux *et al.* 2007, Erkkola *et al.* 2009). Kovacs concluded in a review that vitamin D deficiency during pregnancy and lactation can lead to hypocalcaemia and rickets in neonates and, especially, infants, but that animal data and limited human data suggest that foetuses are protected from the adverse skeletal effects of vitamin D deficiency. Adaptations in maternal calcium and bone metabolism appear to occur independently of vitamin D status (Kovacs 2008). The risk of childhood asthma and allergic disease have been found to be inversely associated with consumption of apples and fish during pregnancy (Willers *et al.* 2007) and maternal adherence to a Mediterranean diet during pregnancy is reported to have a protective effect against asthma-like symptoms and atopy in childhood (Chatzi *et al.* 2008). In contrast, others have found that maternal dietary patterns do not predict asthma and related outcomes in the offspring after controlling for confounders (Shaheen *et al.* 2009). Additionally, recent study findings suggest that maternal seafood consumption during pregnancy is inversely associated with suboptimal neurodevelopmental outcomes in children (Hibbeln *et al.* 2007). Reported associations between maternal

nutrition during pregnancy and type 1 diabetes in the offspring are reviewed in section 2.5.

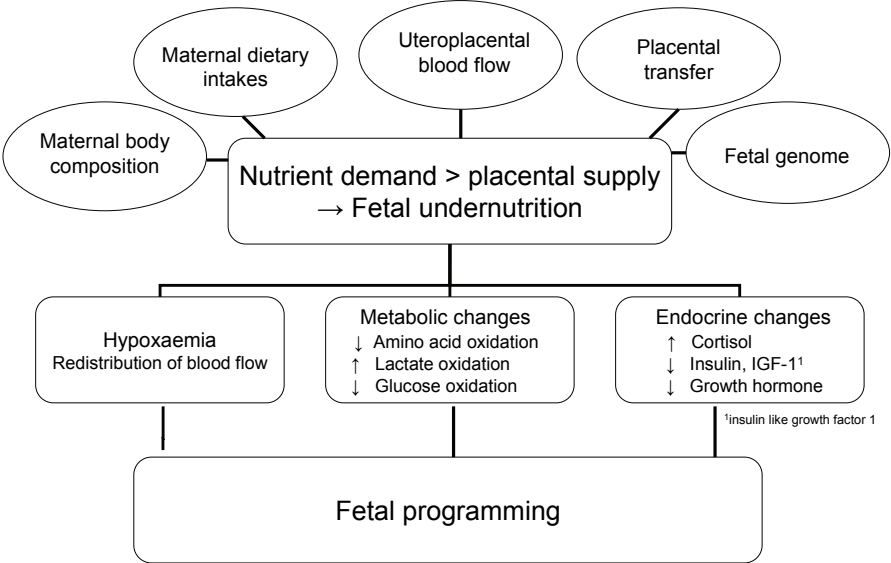


Fig. 1. Foetal adaptations to under-nutrition: a framework (adapted from Barker 1998).

2.2 Dietary pattern analysis

Since the 1980's, statistical methods have been used to generate patterns from collected dietary data (Newby & Tucker 2004). In most studies concerning dietary patterns, food frequency questionnaires (FFQs) or food records are used in primary dietary assessment (Newby & Tucker 2004). Factor and cluster analysis are two commonly used methods to derive eating patterns. Factor analysis reduces data into patterns based upon intercorrelations between dietary items, whereas cluster analysis reduces data into patterns based upon individual differences in mean intakes. No one method of dietary pattern analysis is regarded as better than the others; there is little consensus on which approach should be applied for any given purpose (Moeller *et al.* 2007).

Factor analysis can be used to identify two or more uncorrelated dietary patterns based on foods that tend to be used (or avoided) by the same persons (Jacobson 1986). A factor is formed by food items which correlate strongly with each other but not with other food items. Analysis gives factor loadings between -1 and 1 for each food item depending how much the factor explains the variability of the food item. Negative loading means inverse association between factor and food item. For the purpose of extracting dietary patterns, factor analysis usually starts with a principal components solution (Schulze & Hu 2002). In principal components analysis (PCA), in contrast to other forms of factor analysis its unique variance is also analysed thus its communality is set at 1 (Bryman & Cramer 1999). The pattern variables, called factor scores, are therefore optimized linear combinations of standardized food variables and are constructed to account for as much of the total variance of the food variables as possible (Schulze & Hu 2002).

There are as many factors as variables, although the degree of variance which is explained by successive factors becomes smaller and smaller (Bryman & Cramer 1999). Consequently, the first few factors are the most important. The next step is to decide how many factors should be kept. Two main criteria are used for deciding which factors to exclude: Kaiser's criterion and graphical the scree test. The first involves selection of factors which have an eigenvalue of greater than one. In the scree test, a graph is drawn of the descending variance accounted for by the factors initially extracted. The plot typically shows a break between the steep slope of the initial factors and the gentle one of the later factors. Rotation of the selected factors is aimed at making analysis of the results easier. Rotation does not change the results. Orthogonal rotation (e.g. varimax) produces factors that do not correlate with each other.

2.2.1 Describing dietary composition

Dietary pattern analysis is an approach aimed at describing the whole diet in combination. All foods contribute to nutritional status and it is not the presence or absence of a single food but the appropriate selection of foods in suitable quantities and combinations that is important to health (North & Emmett 2000). The use of dietary patterns might help to capture some of the complexity that may be lost in nutrient-based analyses (Jacques & Tucker 2001), and provide additional information in exploring the relationship between nutrition and health.

Only a few studies in Finland have involved the use of dietary pattern analysis. In cohort studies among male smokers (Balder *et al.* 2003), among women and men (Montonen *et al.* 2005), and among children and adults in a 21-year follow up (Mikkilä *et al.* 2005), two important dietary patterns emerged: healthy and traditional. Dietary patterns have not been analysed earlier among Finnish pregnant women, but there are some studies from other countries (Table 3). The sizes of the subject samples vary considerably (from 80 to 44 612), but there are only a few differences in the methods used. In almost all of the studies, a dietary pattern consistent with current advice for healthy eating was described. This ‘health conscious’ dietary pattern in pregnancy was positively associated with child’s birth weight (Wolff & Wolff 1995), higher maternal age and educational level (Northstone *et al.* 2007), and greater bone size and bone mineral density in the offspring (Cole *et al.* 2008). An opposite pattern, characterized by unhealthy eating choices, was also described in most of the studies. Unhealthy dietary patterns during pregnancy were associated with smoking and less physical activity (Cuco *et al.* 2006) and an increased risk of having a small-for-gestational-age infant (Knudsen *et al.* 2007). No earlier studies concerning dietary patterns and maternal weight gain during pregnancy are available.

2.2.2 Detecting diet-disease associations

Two review articles about dietary patterns in relation to nutrient adequacy, lifestyle and demographic variables, and health outcomes were published in 2004 (Newby & Tucker 2004, Kant 2004). Patterns characterized by increased consumption of fruit, vegetables, whole grain, fish and poultry have generally been reported to be related to micronutrient intake, and to selected biomarkers of dietary exposure and disease risk in the expected direction (Kant 2004). Many variations of a “healthy” or “prudent” pattern have been seen in different populations, which, although having somewhat different food and nutrient compositions, have been associated with less disease, smaller BMI, less mortality, and fewer cases of cancer (Newby & Tucker 2004). Greater age and income and higher level of education have been reported to be among the positive predictors of the so-called healthy dietary patterns (Kant 2004).

In Finnish studies among women and men, prudent dietary patterns have been found to be associated with increased risk of type 2 diabetes (Montonen *et al.* 2005) and cardiovascular disease risk factors such as total and LDL cholesterol concentrations, apolipoprotein B and C-reactive protein concentrations, systolic

blood pressure, insulin levels and concentration of homocysteine (Mikkilä *et al.* 2007). In the first study, two major dietary patterns were analysed by PCA and labeled as ‘prudent’ characterized by greater consumption of fruit and vegetables and ‘conservative’ characterized by greater consumption of potatoes, butter and whole milk (Montonen *et al.* 2005). The second study reported on a ‘traditional pattern’ (high consumption of rye, potatoes, butter, sausage, milk and coffee) and a ‘health-conscious pattern’ (high consumption of vegetables, legumes and nuts, tea, rye, cheese and other dairy products, and alcoholic beverages), analysed by PCA at three time points (Mikkilä *et al.* 2005).

Table 3. Studies of dietary patterns in pregnant women Maternal obesity and weight gain in pregnancy.

Authors (year of publication)	Number of pregnant women	Country	Data collection method	Statistical method	Number of dietary patterns	Main results
Wolff & Wolff (1995)	549	United States	FFQ ¹	PCA ²	7	The nutrient-dense and protein-rich dietary patterns associated positively with increased birth weight.
Cucó <i>et al.</i> (2005)	80	Spain	Dietary record	PCA ²	2	Two stable dietary patterns from preconception to postpartum. Sugar-containing pattern associated with smoking and lower physical activity.
Knudsen <i>et al.</i> (2007)	44 612	Denmark	FFQ ¹	PCA ²	2	Unhealthy dietary pattern associated with increased risk of having a small-for-gestational age infant.
Northstone <i>et al.</i> (2007, 2008)	12 053	United Kingdom	FFQ ¹	PCA ²	5	Health-conscious diet was positively associated with increasing education and age and non-white women.
Crozier <i>et al.</i> (2008)	585	United Kingdom	FFQ ¹ and Food record	PCA ²	2	Dietary patterns appeared to be defined similarly by both FFQ and food record data.
Cole <i>et al.</i> (2008)	198	United Kingdom	FFQ ¹	PCA ²	1	Healthy dietary pattern associated with greater bone size and bone mineral density in the offspring at age of 9.

¹ Food frequency questionnaire, ² Principal component analysis

2.3 Maternal obesity and weight gain in pregnancy

Obesity has become a worldwide epidemic and a critical public health issue. As the prevalence of obesity is increasing, overweight conditions and obesity have also become common in pregnant women. In Finnish pregnant women, a significant increase in average maternal BMI was noticed between 1987 and 2002, the proportion of overweight and obese pregnant women ($\text{BMI} \geq 25 \text{ kg/m}^2$) increased from 22% to 35% and a new BMI category was defined ($\text{BMI} > 40 \text{ kg/m}^2$) during that time period (Vehkajoki *et al.* 2006). In some parts of the US, the prevalence of pre-pregnancy obesity increased by more than 69% from 1993 to 2003 (Kim *et al.* 2007).

Mean pregnancy weight gain has also increased over the past few decades in developed countries (Abrams *et al.* 2000, Kinnunen *et al.* 2003, Rhodes *et al.* 2003). In Finland the increase has been observed in all BMI categories (Kinnunen *et al.* 2003). In response to the increasing trend in maternal weight gain, the US Institute of Medicine has developed guidelines for maternal weight gain based on pre-pregnancy BMI. According to the guidelines three categories of gestational weight gain can be examined: 1) total weight gain, which is the difference between weight before conception and weight just before the delivery, 2) net weight gain, which is total maternal weight gain minus the birth weight of the infant, and 3) rate per week, which is the weight gained over a specified period divided by the duration of the corresponding period in weeks (Institute of Medicine (IOM) 1990). Re-examined guidelines were released recently (Institute of Medicine (IOM) 2009). European recommendations are similar to the IOM's recommendations (Scientific Committee for Food 1993). Consequently, Finnish pregnant women are recommended to gain 7–18 kg depending on maternal BMI at the beginning of pregnancy (Table 4).

Table 4. Recommended gestational weight gain by maternal body mass index¹.

BMI ² before pregnancy	Definition	Recommended weight gain (kg)
18.5–19.9	underweight	12.5–18
20–25 .9	normal weight	11.5–16
≥ 26	overweight	7–11.5

¹Scientific Committee for Food, 1993 / Ministry of Social Affairs and Health, Finland (Hasunen *et al.* 2004)

²BMI= body mass index = kg/m^2

2.3.1 Causes of excessive gestational weight gain

Lifestyle factors such as an inappropriate diet may play a major role in excessive weight gain during pregnancy (Lagiou *et al.* 2004, Olafsdottir *et al.* 2005, Olafsdottir *et al.* 2006). Smoking (Rössner & Öhlin 1995, Gunderson *et al.* 2004) and misperceived pre-pregnancy body weight status (Herring *et al.* 2008) are also associated with excessive gestational weight gain. A recent study from the US indicated that an organized, consistent programme of dietary and lifestyle counselling did reduce weight gain in pregnant women (Asbee *et al.* 2009). There is no information about the role of dietary patterns in maternal weight gain during pregnancy. In general, a Western dietary pattern (characterized by high intakes of red and processed meat, refined grains, sweets, desserts and potatoes), has been shown to be associated with greater weight gain in women (Schulze *et al.* 2006).

2.3.2 Consequences of obesity and excessive gestational weight gain

Obesity in pregnancy is linked to maternal complications ranging from effects on fertility to effects on delivery and in the postpartum period, as well as many complications affecting the foetus and newborn (Arendas *et al.* 2008). Obese pregnant women are at an increased risk of gestational diabetes (Chu *et al.* 2007, Ogonowski *et al.* 2009). Elevated gestational weight gain has been shown to predict impaired glucose tolerance (Herring *et al.* 2009). Women with gestational diabetes mellitus have an increased risk of later development of type 2 diabetes; 15% to 60% will develop type 2 diabetes within 5 to 15 years after delivery (Kim *et al.* 2002). Incidences of pre-eclampsia (O'Brien *et al.* 2003, Dietl 2005, Frederick *et al.* 2006, Leddy *et al.* 2008) and Caesarean section (Dietl 2005, Callaway *et al.* 2006, Vehkaoja *et al.* 2006, Poobalan *et al.* 2009) increase with maternal overweight and obesity during pregnancy. Complications due to excessive gestational weight gain also include Caesarean deliveries and foetal macrosomia resulting in the delivery of a large-for-gestational-age infant (Abrams *et al.* 2000, Stotland *et al.* 2004, Helms *et al.* 2006).

In the long run, excessive weight gain during pregnancy also contributes to the obesity epidemic through larger rates of postpartum weight retention (Gunderson *et al.* 2000, Rooney & Schauburger 2002), which process may be further increased by early termination of breastfeeding (Hilson *et al.* 2006, Rasmussen 2007). Breastfeeding is estimated to increase daily energy expenditure

by approximately 500 kcal and thus helps the mother to recover from gained weight. Maternal excessive weight gain during pregnancy is associated with an increased risk of the offspring being overweight (Moreira *et al.* 2007, Oken *et al.* 2007, Wrotniak *et al.* 2008, Mamun *et al.* 2009).

2.4 Type 1 diabetes

Type 1 diabetes is an autoimmune disease in which the body attacks its insulin-producing beta cells of the pancreas. Lack of insulin causes an increase of fasting blood glucose that begins to appear in the urine above the renal threshold. The condition is lethal unless treated with exogenous insulin.

2.4.1 Epidemiology and genetic susceptibility

The incidence of T1D is continuously increasing in most Western countries (Gale 2002, Patterson *et al.* 2009). Finland has the highest incidence of T1D worldwide, over 64 per 100 000 people per year in 2005. During the years 1980–2005 the incidence of T1D increased most in children aged 0–4 years, the annual increase being almost 5%. The number of new cases diagnosed in Finland at or before 14 years of age is predicted to double in the next 15 years and the age of onset will be younger (Harjutsalo *et al.* 2008).

Genes connected to T1D involve both susceptibility towards, and protection from, the disease (Atkinson & Eisenbarth 2001). The most important genes contributing to T1D susceptibility are located at the human leukocyte antigen (HLA) DQ locus on chromosome 6 (Ilonen *et al.* 1996). The genes encode glycoproteins that are found on the surfaces of most cells and help the immune system to distinguish between self and non-self. More than 90% of patients with T1D carry the predisposing DQ8 (DQA1*0301/DQA1*0302) and/or DQ2 (DQA1*0501/DQB1*0201) alleles. However, only a minority of genetically susceptible individuals progress to the state of clinical disease.

2.4.2 The development of beta-cell autoimmunity

The clinical presentation of T1D is preceded by an asymptomatic period varying from a few months to over 10 years (Knip 2002b). At the time of diagnosis, only 10–20% of the insulin-producing beta cells are estimated to be still functioning.

The appearance of T1D-associated autoantibodies is the first detectable sign of emerging beta-cell autoimmunity. There are four disease-related autoantibodies that have been shown to predict clinical T1D (Knip 2002a). These are classic islet cell antibodies (ICAs), insulin autoantibodies (IAAs), autoantibodies to the 65-kDa isoform of glutamic acid decarboxylase (GADAs), and autoantibodies to the tyrosine phosphatase-related IA-2 molecule (IA-2As). The number of detectable autoantibodies is related to the risk of progression to overt T1D. Most individuals progressing to overt T1D express multiple anti-islet autoantibodies by the time of diabetes onset.

The first autoantibody as regards infants is usually, but not exclusively, IAA, with GADA being the second most frequent (Atkinson & Eisenbarth 2001). In the DIPP study, IAA was shown to emerge as the first detectable antibody more commonly than any other antibody type (Kimpimäki *et al.* 2001).

2.5 The role of environmental factors in the development of T1D

Environmental factors appear to play an important role in the pathogenesis of T1D. Progression to clinical T1D typically requires the unfortunate combination of genetic disease susceptibility, a diabetogenic trigger, and a high degree of exposure to a driving antigen (Knip *et al.* 2005). It is difficult to identify the clear role of any single environmental factor as triggering or modulating the pathogenesis of T1D based on the current body of studies (Peng & Hagopian 2006). The identity of particular environmental factors remains unknown mainly because of the difficulty of linking past exposure with later disease development. The most important factors are thought to be infectious, dietary, perinatal and psychosocial. The most studied environmental factors are nutrition and viruses (Lefebvre *et al.* 2006).

Nutrition

Dietary factors could initiate T1D pathogenesis and accelerate or inhibit its progression (Peng & Hagopian 2006). The mechanisms are not known, but could involve specific food antigens or non-antigenic aspects of diet. Specific exposures and mechanisms may differ at different times of life (e.g. intrauterine, newborn, toddler, older child).

There are only a few findings concerning associations between maternal nutrition and increased risk of T1D in the offspring. Maternal nitrite intake has

been positively associated with the risk for T1D independently of the child's own intake, when adjusted for several socio-demographic factors (Virtanen *et al.* 1994a). There was no association between maternal coffee or tea consumption during pregnancy and T1D in children (Virtanen *et al.* 1994b). Vitamin D supplementation during pregnancy (Brekke & Ludvigsson 2007), as well as the total intake of vitamin D from food (Fronczak *et al.* 2003) have been found to be associated with reduced T1D risk in the child. In contrast, in Norwegian pregnant women, use of cod-liver oil or other vitamin D supplements was not associated with T1D in children (Stene & Joner 2003). In a more recent study an association between more frequent consumption of potatoes during pregnancy and delayed time to the onset of islet-cell autoimmunity onset in children was found (Lamb *et al.* 2008). There were no associations between maternal intake of antioxidant vitamins, or minerals (retinol, β -carotene, vitamin C, vitamin E, selenium, zinc, manganese) during pregnancy and the development of advanced beta cell autoimmunity in the offspring among the DIPP study subjects (Uusitalo *et al.* 2008).

Only a few studies have involved examination of associations between maternal obesity and gestational weight gain and the pathogenesis of T1D in the offspring. In case-control settings, maternal obesity (BMI > 30 kg/m²) before pregnancy predicted a higher risk of islet autoimmunity in children (Rasmussen *et al.* 2009), while maternal weight gains during pregnancy were not significantly different in cases and controls (Dahlquist & Källen 1992, Rasmussen *et al.* 2009). On the other hand, researchers in the UK found that maternal excessive gestational weight gain was a risk factor of T1D in children (McKinney *et al.* 1997). According to some reports, perinatal events such as pre-eclampsia and Caesarean section are associated with an increased risk of T1D in the offspring (Dahlquist & Källen 1992, Cardwell *et al.* 2008). However, in a study by Stene *et al.*, no associations were found between maternal pre-eclampsia, Caesarean section or other perinatal factors and the incidence of T1D in children (Stene *et al.* 2003). In a Finnish study, the size of the mother or the newborn, placental weight and gestational age at delivery were not associated with later onset of T1D (Lammi *et al.* 2009).

Numerous studies have been performed to investigate the role of childhood diet in T1D. The results have been contradictory. Breastfeeding, nicotinamide (vitamin B₃), zinc and vitamins C, D and E have been reported as possibly protecting against T1D, whereas N-nitroso compounds, early exposure to cows' milk and wheat, increased weight gain and obesity may increase the risk

(Virtanen & Knip 2003). However, high serum concentrations of vitamin E did not protect against advanced beta cell autoimmunity in the DIPP study children (Uusitalo *et al.* 2008). Results from the DIPP study also suggest that an early age at introduction of fruit, berries and roots, including potato, associated independently with advanced beta-cell autoimmunity in children (Virtanen *et al.* 2006). Consumption of cod-liver oil (Stene & Joner 2003) and intake of total omega-3 fatty acids (Norris *et al.* 2007) have been associated with a reduced risk of islet cell autoimmunity and T1D in children. Thus far, only infant feeding, cows' milk and vitamin D have been studied in both case-control and cohort settings. It has been suggested that dietary protein sources other than milk (wheat, soy) may also affect the pathogenesis of T1D in susceptible individuals (Lefebvre *et al.* 2006).

Viruses

Viruses have long been regarded as being important environmental factors in the aetiology of T1D. Enteroviruses and several other viruses have been considered to be potential causal agents of human T1D, but their roles are still not clear. Enterovirus infection accompanies or precedes the onset of T1D in many children and enterovirus infection in pregnancy has also been suggested to cause diabetes in children (Hyöty & Taylor 2002).

3 Aims of the study

The aims of this study were:

1. To analyse dietary intake and use of dietary supplements among Finnish pregnant women in relation to socio-demographic factors.
2. To analyse dietary patterns in pregnancy and examine their associations with nutrient intake and socio-demographic factors.
3. To evaluate associations between dietary patterns and weight gain during pregnancy.
4. To study maternal weight during pregnancy and socio-demographic and perinatal factors in association with advanced beta cell autoimmunity in offspring.

4 Subjects and methods

4.1 Study design

This study was performed as a part of the ongoing DIPP study, a prospective, population-based birth cohort study in Finland, started in 1994 (Kupila *et al.* 2001). The DIPP study was established to predict the development of T1D and to search for means to prevent or delay progression to clinical T1D. All the parents of infants delivered at the University Hospitals of Turku, Oulu and Tampere are offered the possibility of screening for the infant's genetic susceptibility in regard to T1D. About 15% of the total population carry an increased genetic risk and are invited to take part in the DIPP study. The participating children are followed as regards diet, growth, viral infections and T1D-associated autoantibodies at the ages of 3, 6, 12, 18 and 24 months, and once a year thereafter. If a child tests repeatedly positive for at least two autoantibodies, the possibility to take part in a randomised double-blind intervention trial with intra-nasal insulin is offered.

The nutrition part of the DIPP study, carried out in Oulu (started in 1996) and Tampere (started in 1997), is aimed at investigating maternal nutrition during pregnancy and lactation as well as the child's nutrition in relation to the natural progression from increased genetic susceptibility to the development of beta cell autoimmunity and eventually clinical T1D. The present study is focused on maternal nutrition and weight status during pregnancy.

4.2 Study subjects

Study I was carried out among a one-year cohort of 797 DIPP mothers (74% of those invited) whose children were born in 1998–99. Altogether, 1075 families with infants at an increased genetic risk of T1D were invited to take part, but 271 refused to participate and seven women had failed to complete the FFQ adequately and were therefore excluded from the analysis.

Studies II and III included mothers who gave birth between October 1997 and December 2002 ($n = 5362$, Figure 2). Complete nutrition information was received from 3730 mothers (70% of those invited), who formed the final study population for Study II. For analysis of Study III ($n=3360$), mothers with twin or triple pregnancies ($n = 98$), and incomplete weight gain information ($n = 272$) were excluded.

Analysis of Study IV was carried out in the same cohort as in Studies II and III. T1D-associated autoantibodies were monitored in 4256 children. When twins and triplets ($n = 163$) were excluded, the final study population consisted of 4093 mother-child pairs (Figure 2). Characteristics of the pregnant women are shown in Table 5 and those of the infants in Table 6.

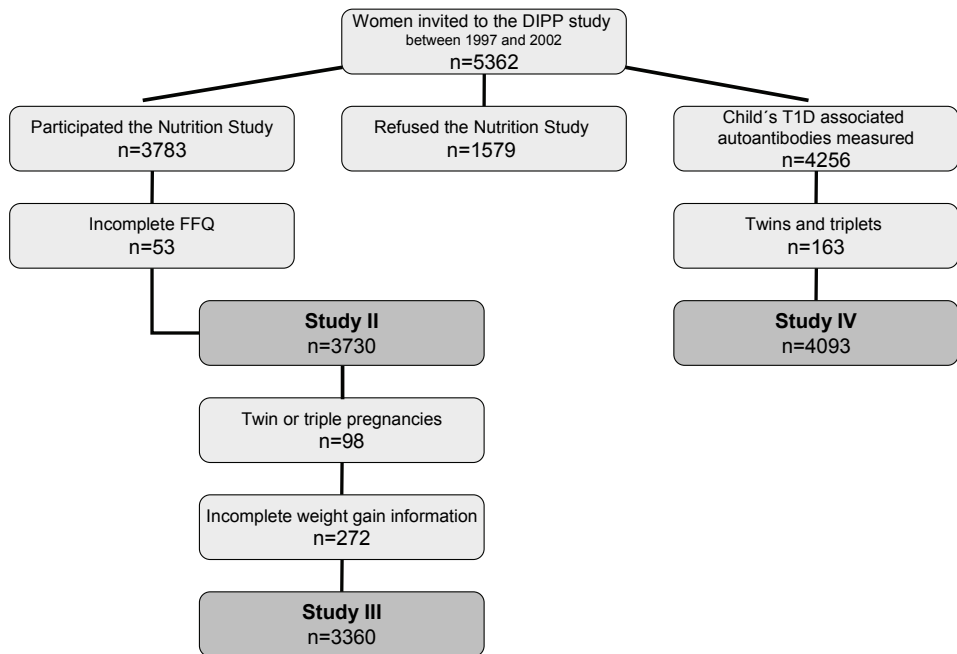


Fig. 2. Study subjects – pregnant women (II, III) and children (IV).

Table 5. Characteristics of the pregnant women (III, n = 3360).

Variable	N	%	Mean (SD)
Age at delivery, years			29.2 (5.2)
< 25	645	19	
25–29	1171	35	
30–34	978	29	
≥ 35	566	17	
Basic education			
no high school certificate	1511	45	
high school certificate	1701	51	
missing data	148	4	
Vocational education			
none	204	6	
vocational school or course	961	28	
upper secondary vocational	1377	41	
academic	730	22	
missing data	88	3	
Smoking during pregnancy			
no	2950	88	
quit smoking ¹	43	1	
yes	282	8	
missing data	85	3	
City			
Tampere	1922	57	
Oulu	1438	43	
Type of living area			
urban	2899	86	
rural	436	13	
missing data	25	1	
BMI (initial), kg/m ²			24.4 (4.3)
< 19.9	121	4	
20–24.9	2095	62	
25–29.9	719	21	
≥ 30	422	13	
Missing data	3	0	
Parity			0.95 (1.4)
0	1545	46	
1	1048	31	
2	461	14	
≥3	281	8	
missing data	25	1	

¹quit smoking during the first trimester of pregnancy

Table 6. Characteristics of infants with HLA-conferred susceptibility to type 1 diabetes.

Characteristics	n	%	Mean	Minimum	Maximum
Sex					
Boy	2162	53			
Girl	1931	47			
HLA-DQB1-conferred risk group					
Moderate risk (DQB1*0302/x)	3303	81			
High risk (DQB1*02/*0302)	790	19			
Familial diabetes ¹					
No	3663	90			
Yes	250	6			
Missing information	180	4			
Gestational age (weeks)					
1 st quarter: <39.0	923	23	39.8	25.0	43.1
2 nd quarter: 39.0–39.9	1000	24			
3 rd quarter: 40.0–40.8	1150	28			
4 th quarter: >40.8	985	24			
Missing information	35	1			
Birth weight (grams)					
1 st quarter: < 3215	905	22	3577	680	5890
2 nd quarter: 3215–3579	1027	25			
3 rd quarter: 3580–3899	1049	26			
4 th quarter: >3899	1084	26			
Missing information	28	1			
Route of delivery					
Caesarean section	507	12			
Vaginal delivery	3558	87			
Missing information	28	1			
Total	4093				

¹ type 1 and type 2 diabetes

4.3 Methods

4.3.1 Dietary data collection

The diet during pregnancy was assessed retrospectively after delivery by means of a self-administered, semi-quantitative 181-item FFQ. The questionnaire was developed especially for the Nutrition Study within the DIPP and it was validated against two 5-day food records in Finnish pregnant women (Erkkola *et al.* 2001). The design of the validation study was identical to that of the study probe. In the validation study, the correlation coefficients between the data in the second questionnaire, completed a month after delivery, and the food records were similar to those obtained between the data in the first questionnaire completed during the period of interest (eighth month of pregnancy), and the food records. The FFQ was focused on the diet during the eighth month of pregnancy, i.e. the month preceding maternity leave in Finland, aiming to obtain information concerning the ordinary diet during pregnancy. Mothers received the questionnaire after delivery and it was strongly emphasized that they were expected to report their food habits during the eighth month of pregnancy. The FFQ was checked by a trained study doctor or nurse at the infant's 3-month visit to the study centre. If required, the FFQ was completed in collaboration with the mother. All the returned questionnaires were then checked by a trained nutritionist. If there were over ten missing answers in a FFQ, it was rejected (53 out of 3783, 1.4%).

The FFQ comprised a list of 181 food items and mixed dishes, grouped under subheadings: 1) milk products, 2) potato, rice and pasta as side dishes, 3) cereals, 4) fat and spreads on bread, 5) fruit and berries, 6) vegetables, 7) salad dressings, 8) warm main courses, 9) fish and egg, 10) beverages, and 11) desserts, sweets and snacks. Open-frequency categories were used in increasing order: not at all, less than once per month and how many times per month, week, or day. The serving sizes were based on commonly used portions identified during earlier Finnish dietary studies, and for some foods (e.g. eggs and beverages), natural units were used. There were additional empty lines for each food group to record foods not listed in the questionnaire. The FFQ included additional questions about special diets, eating places, and about the use of convenience, fried, vacuum-packed, and organic foods. Further information was requested concerning the use and type of dietary fats and oils used in cooking, baking, and salad dressings.

Information about supplement use was collected, covering the whole pregnancy. The mothers received written instructions to record the dietary supplements with brand names, manufacturers of the supplements, amounts of supplements per day, week or month and the month of pregnancy during which the supplements were used. All kinds of dietary supplements which were used as sources of vitamins and minerals, including multivitamins and herbal products, were taken into account. Fortified foodstuffs or drinks were not included. The FFQ is available from the DIPP nutrition study researchers in the National Institute of Health and Welfare, Helsinki.

4.3.2 Assessment of dietary intake

All frequencies from the FFQ data were computed into times per day. To estimate the intake of each food item in grams, standard portion sizes were multiplied by the daily frequencies. The data were analysed by using the in-house software programme of the National Public Health Institute, Helsinki, Finland. The national food composition database Fineli (KTL 2005) was used to calculate daily nutrient intakes. Fineli is continuously updated and is the most comprehensive food composition database in Finland. Nutrient values in the food composition database are derived mainly from chemical analyses of Finnish foods. In addition, complementary data is obtained from the Finnish food industry and international food composition tables. The database currently includes over 3000 individual food items and mixed dishes and more than 290 nutrients and other dietary factors. In the present study, intakes of energy, protein, carbohydrates, sugar, dietary fibre, total fat, saturated fatty acids, monounsaturated fatty acids, polyunsaturated fatty acids, n-3 fatty acids, n-6 fatty acids, essential fatty acids (linoleic and α -linolenic acids), alcohol, vitamins A, D, E and C, folic acid, iron, magnesium, zinc, calcium, nitrate and nitrite were assessed.

The dietary supplement database was based on the database of the National Public Health Institute (Reinivuo et al. 2008). Nutritional information concerning new dietary supplements was added to the database. The information on these new products was obtained from the Finnish pharmacopoeia. Information on dietary supplements other than drugs was obtained from the National Food Administration and from the manufacturers. From the supplements, the intakes of vitamins A, D, E and C, folic acid, calcium, iron and zinc were calculated. In the present study, a supplement user was a mother who had taken at least one of these nutrients as a dietary supplement during pregnancy. Mean daily intake of a

nutrient from a dietary supplement was calculated by multiplying the amount of the nutrient in a supplement on a consumption frequency basis over the whole of the period of pregnancy and dividing the product by the estimated number of days of pregnancy (280). Daily intakes of the nutrients from all supplements used were then summed.

4.3.3 Socio-demographic and anthropometric characteristics

Information on maternal age and education, and child's sex was collected by means of structured questionnaires in the delivery clinics. Information on living area, parity, duration of gestation, child's birth weight and maternal smoking during pregnancy was received from the Finnish Birth Registry.

Weight and height were requested on the same form as food consumption frequencies. Mothers recorded the results of the weight measurements during their first and last antenatal visits. Gestational weeks at the time of the weight measurements were also recorded as well as the mother's height. The first weight measurement was on average obtained during the 10th gestational week (SD 2.3 weeks, variation 3–33 weeks, median 9.4 weeks). The last measurement was carried out during the 39th gestational week on average (SD 2.1 weeks, variation 9–43 weeks, median 39.0 weeks). The mean follow-up time was 29 weeks (SD 3.0 weeks, variation 6–37 weeks, median 29.7 weeks).

The initial BMI was calculated for each woman by dividing her weight (kg) at the first antenatal visit by the square of her height (m²). Weight gain rate was calculated by dividing the weight gain in kilograms by the number of weeks between the first and the last antenatal visits.

4.3.4 Genetics

Umbilical cord blood samples were obtained from all newborn infants at Oulu and Tampere University Hospitals, and the families were offered the possibility of screening for HLA-defined genetic risks of T1D after delivery. The parents received both oral and written information about the DIPP study, and they gave written informed consent for genetic screening at maternity ward.

Umbilical cord blood samples were analysed using a large-scale assay procedure that was developed for rapid screening purposes (Ilonen *et al.* 1996). The method involves time-resolved fluorometry to detect the hybridization of lanthanide-labelled allele-specific oligonucleotide probes to amplified gene

products. Families with an infant carrying high or moderate genetic susceptibility to type 1 diabetes (HLA DQB1*02/*0302 or HLA DQB1*0302/x; x≠*0301 or *0602) were invited to take part in the observational phase of the study.

4.3.5 Immunological methods

The children participating in the DIPP study were monitored for T1D-associated autoantibodies at the ages of 3, 6, 12, 18 and 24 months, and thereafter once a year. The cord blood sample was also analysed. Classic islet cell antibodies (ICAs) were used as a primary screening tool for beta cell autoimmunity. If a child tested positive for ICAs, then insulin autoantibodies (IAAs), autoantibodies to the 65-kDa isoform of glutamic acid decarboxylase (GADAs), and autoantibodies to the protein tyrosine phosphatase-related IA-2 molecule (IA-2As) were also analysed. Positive samples in the cord blood and a decreasing trend after that suggested that these antibodies had been transferred transplacentally from the mother. Such antibodies were excluded from the analysis, because they usually disappeared by the age of 1 year and are not associated with the risk of T1D in offspring (Hämäläinen *et al.* 2000).

Type 1 diabetes-associated autoantibodies were quantified in the Research Laboratory of the Department of Pediatrics, University of Oulu. Islet cell antibodies were quantified by a standard indirect immunofluorescence method on sections of frozen human pancreas from a blood group O donor (Bottazzo *et al.* 1974). The results were expressed in Juvenile Diabetes Foundation (JDF) units. The lowest positive level was 3 JDF units. Serum levels of IAAs were measured with a microassay modified from that described by Williams *et al.* (Williams *et al.* 1997). The IAA levels were expressed in relative units (RUs), and a subject was considered positive when the specific binding exceeded 3.48 RU (1% of healthy Finnish children have a test result over the cut-off limit). GADAs and IA-2As were quantified by means of radiobinding assays as previously described (Savola *et al.* 1998a, Savola *et al.* 1998b). GADA and IA-2A results were also expressed in RUs. The limits for antibody positivity were set at 5.36 RU and 0.43 RU respectively.

4.3.6 Statistical analyses

Study I

The chi square-test was used to evaluate the relationships between age, education, BMI, smoking status and earlier pregnancies, versus supplement use and food consumption habits. Analysis of variance was used to evaluate the relationships between energy and nutrient intake and maternal education level. Differences were considered significant at $p < 0.05$ (two-sided). Statistical analyses were performed by using the Statistical Package for the Social Sciences program (Version 12.0 SPSS Inc., Chicago, IL, U.S.A.).

Study II

For statistical analysis of dietary patterns 181 food items were aggregated into 52 separate food groups. The grouping scheme was based on culinary use and nutrient profiles. Principal components analysis with varimax rotation was used to identify patterns among the food groups. A plot of eigenvalues (i.e. the scree test) indicated a break between the seventh and eighth factors that could be used as a separate criterion to the solution of seven factors that were retained for further analyses. After varimax rotation of the factors, food groups with absolute factor loading ≤ -0.2 or ≥ 0.2 were considered as significantly contributing to a pattern. Factor scores were calculated for each person in each pattern in terms of how closely they fit to the pattern. Factor scores were computed by weighting each factor loading by the factor's eigenvalue, multiplying these weights by the subject's corresponding food-group intake, and summing these products. Factor scores were used to rank individuals. Pearson's correlation coefficients were calculated between dietary patterns and energy and nutrient intake. Multiple linear regression analysis was used to test how age, educational level, smoking, living area and the number of earlier deliveries explained the variance in pattern scores. The Statistical Package for the Social Sciences program (Version 14.0 SPSS Inc., Chicago, IL, U.S.A.) was used in analysing the dietary patterns.

Study III

The general linear models procedure (PROC GLM) was used to test the trends in weight gain rates between quarters of participants determined by quartiles of

dietary pattern scores, and energy and macronutrient intakes. The association between dietary patterns and maternal weight gain rates was assessed using multiple linear regression (PROC REG) analysis. Weight gain rate changes slightly after the 10th week of pregnancy and therefore we added a respective dummy variable into the regression models (initial measurement in ≤ 10 th week: 1, otherwise 0). Analyses were performed with the Statistical Analysis System (SAS) software package version 8.2 (SAS Institute, Inc., Cary, NC, USA).

Study IV

The endpoint of advanced beta cell autoimmunity was interval-censored. To accommodate this structure, a piecewise exponential survival model was used with constant hazard in the intervals 0–0.99, 1–1.99, 2–2.99 and ≥ 3 years. The models were fitted using maximum likelihood in SAS PROC NLMIXED, with standard errors of estimates derived from the observed information matrix. The proportionality of the hazards was tested by adding linear interaction terms of the exposure variables with time to the models. Differences between means by background characteristics were tested with the independent samples *t*-test (for two groups of cases) or ANOVA (for more than two groups of cases). Possible confounding by background characteristics was controlled by adding background variables as covariates in the statistical models. The first set of covariates included genetic risk group and diabetes in a first-degree relative, and the other also included sex, maternal age, gestational age, maternal education, maternal smoking during pregnancy, maternal parity, mode of delivery, birth weight and region of birth (Oulu or Tampere). Both models also included a variable indicating whether the weight was measured for the first time before or after the 10th gestational week. Interaction of weight gain rate and initial BMI with each other or with time as regards the development of advanced beta cell autoimmunity was tested. All the variables were used as categorical items in statistical models. Categorical variables were aggregated into quarters. SAS version 9.1.3 (SAS Institute, Cary, NC) was used in the analyses.

4.3.7 Ethical considerations

The DIPP study was found to be acceptable by the Ethics Committees of the Northern Ostrobothnia and Pirkanmaa Hospital Districts. Written informed consent from the parents was received.

5 Results

5.1 Food choices during pregnancy (I)

The proportions of women daily or weekly consuming selected food items and food groups is shown by age, education and dietary supplement use in Table 7. About 30% of the women over 30 y or with a high school certificate consumed recommended portions (≥ 5) of vegetables, fruit and berries daily, whereas the respective proportions was 16% among both the youngest women and among the women with a lower level of education. The consumption of fish and poultry was more common among older and more educated women than other women. Daily consumption of fruit and berries and weekly consumption of fish were more common among those women who used dietary supplements than those who did not use dietary supplements during pregnancy. Daily consumption of low-fat milk products was more common among women with high school education and among non-supplement users than among women without a high school certificate and supplement users (Table 7).

5.2 Energy and nutrient intake during pregnancy (I and III)

On average, protein provided 16%, carbohydrate 47% and fat 36% of the total energy intake in the diet of Finnish pregnant women. Saturated fatty acids provided 15%, monounsaturated fatty acids 11%, polyunsaturated fatty acids 4% and triglycerides 6% of the total energy intake. The mean intake of dietary fibre was 27.4 g per day. Women under 25 y received less energy ($p = 0.032$), and their energy-adjusted intakes of protein ($p = 0.004$) and dietary fibre ($p < 0.001$) were smaller and the intake of sugar higher ($p = 0.019$) compared with older women. A higher level of basic education was associated with higher energy-adjusted intake of carbohydrates, dietary fibre and n-6 fatty acids and lower intakes of total fat and saturated fatty acids.

There was a positive and consistent association between energy intake and maternal weight gain rate among the pregnant mothers when maternal weight gain rate was studied in quarters of energy intake. Similarly, sucrose intake (percent of energy) was positively and in a dose-response manner associated with the weight gain rate. The percent of energy from protein was inversely associated with maternal weight gain.

On average, women received adequate amounts of the examined vitamins and minerals from food, with the exception of vitamin D. Even the total intake of vitamin D (intake from food and supplements) in the supplement users did not meet the recommendation (Figure 3). Women under 25 years of age had lower intakes of vitamin D, vitamin E, folate, iron, magnesium (for all nutrients $p < 0.001$) and zinc ($p = 0.004$) compared with older women. A higher level of basic education was associated with higher intake of vitamin D, vitamin E (both $p < 0.001$) and iron ($p = 0.041$) from food.

Table 7. Food choices among Finnish pregnant women: proportion (%) consuming at least one serving of selected foods daily or weekly by age, education and the use of supplements.

Food or food group	All women (n=797)			p(χ^2 test)		Basic education		p(χ^2 test)		Supplement use		p(χ^2 test)
	<25 (n=138)	25–29 (n=276)	≥30 (n=366)	Less than high school (n=373)	High school cert (n=424)	Yes (n=679)	No (n=118)					
Daily consumers (%)												
Low-fat milk products ¹	54	58	55	49	59	53	64	<0.01	53	64	0.021	
Skimmed milk	39	39	40	33	45	37	52	<0.01	37	52	<0.01	
Rye bread	76	74	78	74	78	77	71	NS	77	71	NS	
Vegetables, fruit and berries	24	20	29	16	30	24	19	<0.01 ^a	24	19	NS	
(at least five servings)												
Vegetables	88	88	90	83	93	87	85	<0.01	87	85	NS	
Fruit and berries ²	76	77	80	69	82	78	64	<0.01	78	64	<0.01	
Fat spreads	77	83	74	80	76	77	84	0.036	77	84	NS	
Butter	23	25	20	21	23	25	22	NS	25	22	NS	
Soft margarine (> 60% fat)	43	46	39	47	39	41	53	NS	41	53	0.014	
Soft margarine (≤ 60% fat)	22	19	23	19	25	22	20	NS	22	20	NS	
Soft drinks (sugary)	4	5	4	4	5	5	1	NS	5	1	0.041	
Sweets	18	16	18	18	18	14	19	NS	14	19	NS	
Weekly consumers (%)												
Fish	48	49	54	35	60	50	37	<0.01 ^b	50	37	0.011	
Poultry	68	67	75	58	78	68	68	<0.01 ^b	68	68	NS	
Sausage	78	76	80	82	75	78	80	NS	78	80	NS	

¹ skimmed milk and low-fat milk products (≤1% fat), ² including fruit and berry juices.

^a p=0.004 in logistic regression analysis, ^b Same p value in logistic regression analysis. Apart from those marked, p>0.05 in logistic regression analysis.

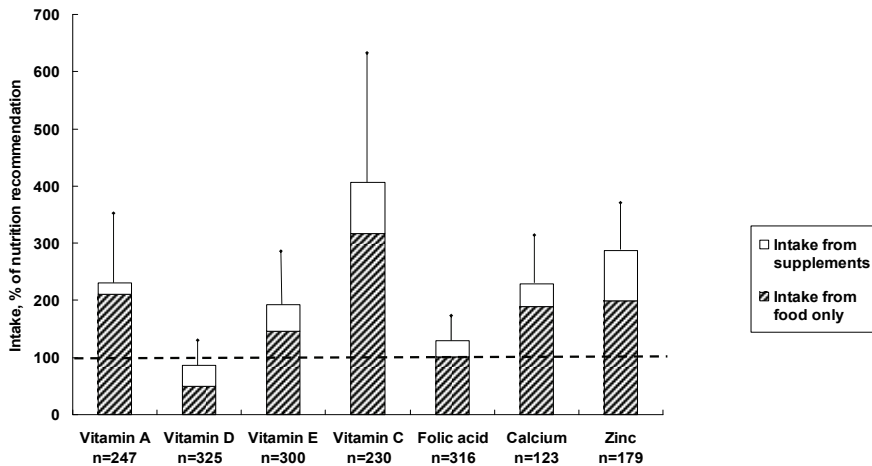


Fig. 3. Intake of vitamins and minerals by supplement users from food only and from supplements, compared with the recommendation (-----). Values are means, with their standard errors represented by vertical bars.

5.3 Dietary supplement use during pregnancy (I)

Most of the women (85%) complemented their diet with at least one nutrient supplement during pregnancy. The most common supplemental nutrient was iron (78%), followed by vitamin D (40%) and folic acid (39%). Of the women, 31% had vitamin A (retinol) supplement, but only two women had vitamin A as a single nutrient supplement. Thus vitamin A was mainly taken as a part of a multivitamin supplement. Iron and calcium were most commonly used as a single nutrient supplements. Intake of vitamins and minerals in supplement users and non-users is seen in Table 8. The upper limit of safe intake was exceeded only as regards supplemental iron. The upper safety limit of iron intake (60 mg daily) was exceeded in 286 women, of whom 16 took more than 250 mg per day. Eighty-five per cent of all women had a total vitamin D intake below the recommended level. The total folic acid intake was below the recommended level in 44% of the women (Table 8).

5.4 Maternal dietary patterns during pregnancy (II and III)

Seven factors were identified to describe the dietary patterns of the Finnish pregnant women (Table 9). Collectively these factors explained 29.5% of the

variability within the sample. The food items with loadings of ≥ 0.2 on a factor were considered to have a strong association with that factor. Negative loading (≤ -0.2) represents an inverse association between the food item and the factor. The seven factors were named ‘Healthy’, ‘Fast foods’, ‘Traditional bread’, ‘Traditional meat’, ‘Low-fat foods’, ‘Coffee’ and ‘Alcohol and butter’ (Table 9).

5.4.1 Patterns and dietary intake (II and III)

Pattern scores were differently associated with energy and nutrient intake. Energy intake correlated positively with ‘Healthy’, ‘Fast foods’, ‘Traditional bread’ and ‘Traditional meat’ patterns and inversely with the ‘Alcohol and butter’ pattern. Intake of dietary fibre correlated positively with ‘Healthy’, ‘Traditional bread’ and ‘Low-fat foods’ patterns and inversely with the ‘Alcohol and butter’ pattern.

Intake of protein, dietary fibre and most of the assessed vitamins correlated with the ‘Healthy’ dietary pattern score. Intake of carbohydrates, sucrose, total fat, saturated fatty acids and vitamin E correlated with the ‘Fast foods’ dietary pattern. The seven dietary patterns seemed to account for relatively large proportions (over 50%) of the variance in energy and nutrient intake except for the intakes of vitamin D (35.3%), vitamin C (38.2%), carotenoids (46.9%) and calcium (39.9) (II, Table 4).

Table 8. Daily intake of vitamins and minerals during pregnancy by the use of dietary supplements, and proportion (%) of the women receiving nutrients below the recommended level.

	Intake							
	Supplement users (n=679)		Supplement non-users (n=118)		p*	Recommended daily intake ¹	Intake below recommendation:	% all women (n=797)
	Mean	SD	Mean	SD				
Vitamin A (µg)	1793	1038	1785	1556	0.942	800	74	9
Vitamin D (µg)	6.7	3.9	4.8	2.6	<0.01	10	676	85
Vitamin E (mg)	16.5	7.6	14.3	5.2	<0.01	10	110	14
Vitamin C (mg)	238	137	235	160	0.815	70	20	3
Folic acid (µg)	454	164	398	136	<0.01	400	349	44
Iron (mg)	72	62	17	5.9	<0.01	- ^a	- ^a	- ^a
Calcium (mg)	1939	717	1960	784	0.780	900	29	4

*By *t*-test, comparison of the total nutrient intake between supplement users and non-users, ¹ Nordic nutrition recommendations (Nordic Working Group on Diet and Nutrition, 1996), ^a No recommendation; approximately 500 mg stored Fe is required during pregnancy.

Table 9. Factor loadings ≤ -0.2 or ≥ 0.2 of different food items in the seven dietary factor categories identified by principal components analysis with varimax rotation among Finnish pregnant women.

Food item	Factor (dietary pattern)						
	Healthy	Fast foods	Traditional bread	Traditional meat	Low-fat foods	Coffee	Alcohol and butter
Leafy vegetables	0.577						
Cabbage	0.537						
Vegetables	0.523						
Fish	0.519						
Vegetarian dishes	0.461						
Legumes, mushrooms	0.447						
Roots	0.421						
Berries	0.408		0.204				
Salad dressing	0.398						0.302
Poultry	0.367						
Fruit	0.361						-0.276
Rice, pasta	0.301						
Egg	0.300	0.212					
Sweets		0.595					
Fast food		0.575					
Snacks		0.537					
Chocolate		0.509					
Fried potatoes		0.493					
Soft drinks		0.444					0.225
Cream	0.232	0.370					
Fruit juices		0.346					-0.214
White bread		0.330					
Processed vegetables	0.206	0.321		0.226			
Light soft drinks		0.307			0.205		
Savouries		0.251	0.214				
Low-fat pastry			0.525			0.246	
Whole-grain bread		-0.252	0.502		0.285		
High-fat pastry		0.420	0.451				
High-fat cheese			0.359				
Sugar, jam			0.358				
Berry juices			0.332				
Meat				0.553			
Nuts, seeds	0.320		0.207	-0.539			
Breakfast cereals	0.389		0.288	-0.470			-0.239

Food item	Factor (dietary pattern)						
	Healthy	Fast foods	Traditional bread	Traditional meat	Low-fat foods	Coffee	Alcohol and butter
Meat dishes	0.257		0.205	0.442			
Sausage		0.222		0.405		0.202	
Potatoes		-0.252	0.310	0.365			
Processed meat		0.225	0.225	0.336	0.321		
Organ meat				0.280			
Spread 40–60%					0.577		
Low-fat cheese	0.283				0.485		
High-fat milk					-0.461	0.281	-0.203
Low-fat milk					0.450		
Butter			0.256		-0.354		0.327
Low-fat sour milk	0.280				0.282		
High-fat sour milk			0.204		-0.250		
Coffee						0.803	
Milk in coffee						0.639	
Tea			0.387			-0.463	
Beer							0.493
Wine, liquor							0.486
Soft margarine 80%				0.307	-0.215		-0.371

5.4.2 The roles of socio-demographic factors (II)

Dietary pattern scores were differently associated with age, educational level, smoking during pregnancy, living area and the number of earlier deliveries. Positive associations were observed as regards age and ‘Healthy’ and ‘Alcohol and butter’ patterns, while ‘Fast foods’ and ‘Traditional meat’ patterns showed inverse associations with age. Positive associations were seen between educational level and ‘Healthy’, ‘Low-fat foods’ and ‘Alcohol and butter’ patterns. Smoking during pregnancy was associated with ‘Fast foods’, ‘Traditional meat’ and with the ‘Coffee’ pattern, in particular. The number of earlier deliveries was positively associated with ‘Traditional bread’, ‘Traditional meat’ and ‘Coffee’ patterns, while inverse associations were observed as regards ‘Fast foods’ and ‘Low-fat foods’ patterns. The results from regression models with socio-demographic factors and the dietary pattern scores of the ‘Healthy’ and ‘Fast foods’ categories are seen in table 10.

Table 10. Socio-demographic factors explaining the variance in dietary pattern scores among pregnant women; regression parameters (with 95% confidence intervals) in multiple linear regression analysis^a.

Socio-demographic factor	Dietary pattern	
	Healthy Model 1	Fast foods Model 2
Age		
25–29 years vs. < 25 years	0.16* (0.06, 0.25)	-0.08 (-0.18, 0.01)
30–34 years vs. < 25 years	0.37* (0.27, 0.47)	-0.18* (-0.28, -0.08)
≥ 35 years vs. < 25 years	0.58* (0.46, 0.70)	-0.34* (-0.46, -0.23)
Basic education		
high school graduates vs. no high school certificate	0.19* (0.12, 0.26)	-0.09* (-0.16, -0.02)
Smoking during pregnancy		
smokers vs. non-smokers	-0.27* (-0.38, -0.16)	0.28* (0.18, 0.39)
Area of living		
Oulu vs. Tampere	-0.19* (-0.26, -0.13)	-0.22* (-0.28, -0.15)
Number of earlier deliveries		
one vs. none	-0.12* (-0.19, -0.04)	-0.05 (-0.13, 0.02)
two or more vs. none	-0.10* (-0.19, - 0.003)	-0.30* (-0.39, -0.21)
	R ² =0.078	R ² =0.064
	F=36.2	F=29.1
	p<0.01	p<0.01

^a Pattern score as a dependent variable and the socio-demographic factors as independent variables,

* Significant (p<0.05)

5.4.3 Dietary patterns and weight gain during pregnancy (III)

The mean gestational weight gain in the present study population was 12.4 kg (SD 4.6) and the mean weight gain rate 0.43 kg/week (SD 0.15). When the maternal weight gain rate was examined in quarters of dietary pattern scores, positive trends were observed between the rate and ‘Fast foods’ and ‘Traditional bread’ dietary pattern scores and inverse trends between the rate and ‘Traditional meat’, ‘Coffee’ and ‘Alcohol and butter’ pattern scores (Table 11).

‘Fast food’ and ‘Traditional bread’ dietary patterns were positively associated, and ‘Traditional meat’, ‘Coffee’ and ‘Alcohol and butter’ dietary patterns inversely associated with maternal weight gain rate in bivariate analyses. When the models were adjusted for maternal age, initial BMI, parity, vocational

education, smoking, living area, birth weight of the infant and gestational week of first weight measurement (before 10th week vs. 10th week or after), only three patterns remained significant in relation to weight gain rate: ‘Fast foods’, ‘Traditional bread’ and ‘Alcohol and butter’.

The ‘Fast foods’ dietary pattern was positively associated with maternal weight gain rate even after including energy, percentage of energy from protein, saturated fatty acids and sucrose into the model. In a similar manner the ‘Alcohol and butter’ pattern was inversely associated with the weight gain rate.

Table 11. Mean (SE) maternal weight gain rate of four subpopulations determined by quartiles of dietary pattern scores.

Dietary pattern	Mean weight gain rate, kg/week ^a				p for trend
	Lowest		Highest		
	1 st quarter	2 nd quarter	3 rd quarter	4 th quarter	
Healthy	0.43 (0.01)	0.44 (0.01)	0.44 (0.01)	0.42 (0.01)	0.109
Fast foods	0.41 (0.01)	0.43 (0.01)	0.44 (0.01)	0.46 (0.01)	<0.0001
Traditional meat	0.43 (0.01)	0.43 (0.01)	0.44 (0.01)	0.43 (0.01)	0.262
Traditional bread	0.41 (0.01)	0.44 (0.01)	0.43 (0.01)	0.44 (0.01)	0.0002
Low-fat foods	0.44 (0.01)	0.43 (0.01)	0.44 (0.01)	0.44 (0.01)	0.252
Coffee	0.43 (0.01)	0.44 (0.01)	0.44 (0.01)	0.43 (0.01)	0.443
Alcohol and butter	0.44 (0.01)	0.44 (0.01)	0.43 (0.01)	0.42 (0.01)	0.014

^a Adjusted for maternal age, initial body mass index, parity, vocational education, smoking, living area, birth weight of the infant, and gestational week of the first weight measurement

5.4.4 Maternal weight status during pregnancy and beta cell autoimmunity in the offspring (IV)

The mean initial BMI was 24.4 kg/m² and the mean weight gain rate was 0.42 kg/week among these pregnant women.

Women in the 4th quartile of initial BMI (> 26 kg/m²) showed a significantly lower weight gain rate during pregnancy than women with a lower initial BMI. Newborns belonging to the 1st quartile of birth weight (< 3215 g) were born to mothers with significantly lower gestational weight gain and initial BMI than infants with higher birth weight. Women with three or more previous deliveries before the present study showed a significantly lower weight gain rate during pregnancy but a higher initial BMI than women with less than three previous pregnancies. Well educated women had a significantly lower initial BMI than less well educated women. Women who underwent Caesarean section delivery had a

significantly higher initial BMI than women experiencing vaginal delivery (IV, Table 1).

Maternal gestational weight gain rate and maternal initial BMI were not associated with the risk of advanced beta cell autoimmunity in children ($p = 0.189$ and $p = 0.476$ respectively). Hazard ratios (95% CI) as regards advanced beta cell autoimmunity in maternal gestational weight gain rate quarters were 0.76 (0.46–1.27), 1.12 (0.71–1.76) and 0.70 (0.41–1.18) for the second, third and fourth quarters compared with the first one, respectively. Concerning maternal initial BMI quarters, HRs (95% CI) as regards the second, third and fourth quarter compared with the first one were 1.21 (0.76–1.91), 0.93 (0.56–1.53) and 0.82 (0.48–1.39), respectively. Among the baseline characteristics examined, HLA-DQB1-positivity and familial diabetes were related to a greater risk and a higher level of maternal education to a smaller risk of advanced beta cell autoimmunity (IV, Table 1). Hazard ratios as regards advanced beta cell autoimmunity in quarters of maternal gestational weight gain, initial BMI and vocational education are shown in figure 4. Statistical model includes factors: gestational weight gain, initial BMI, maternal age, number of previous deliveries, smoking during pregnancy, infant's sex, genetic risk, familial diabetes, gestational age, birth weight, mode of delivery and region of birth.

Analyses concerning initial maternal BMI were performed in two settings. First we used a dataset that included all the mothers in the analyses and secondly we used a dataset that included only mothers whose weight was measured for first time during the first trimester (between 0–13 gestational weeks). These results did not differ (data not shown).

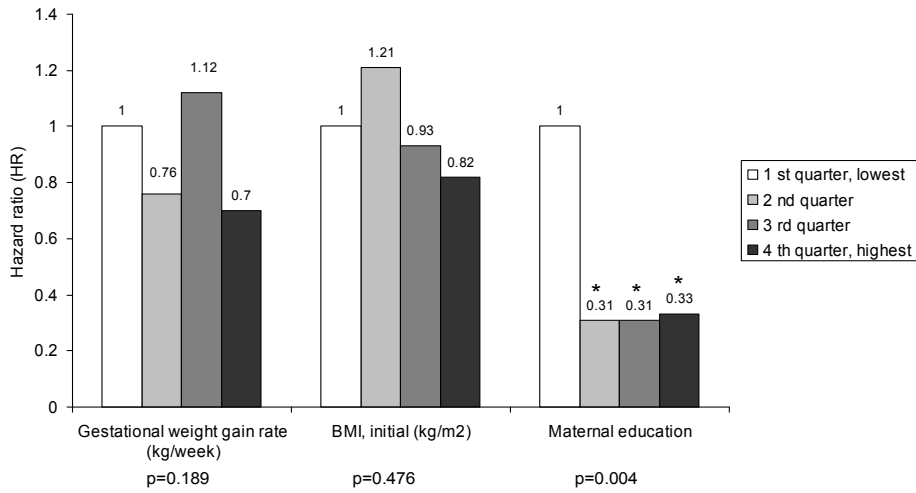


Fig. 4. Hazard ratios as regards advanced beta cell autoimmunity in children by quarters of maternal gestational weight gain, initial BMI, and vocational education. Adjusted for genetic risk and other background and perinatal factors. HRs as regards second, third and fourth quarters compared with the first one.

6 Discussion

6.1 Methodological issues

The present study was carried out as a part of the DIPP Nutrition study, aimed at investigating maternal nutrition during pregnancy and lactation as well as the child's nutrition in relation to the natural progression from increased genetic susceptibility to the development of beta cell autoimmunity and eventually to clinical T1D. The study was not therefore designed only for investigating nutrition during pregnancy. The main methodological disadvantage was that we collected the dietary information retrospectively concerning maternal diet during the eighth month of pregnancy and the women completed the questionnaire 1–3 months after the period of interest. However, earlier findings suggest that diet during a past pregnancy is recalled relatively well even after several years (Bunin *et al.* 2001). The questionnaire covered a limited time period, and important exposures occurring outside this time period could have been missed out. For example, diet during the early stages of pregnancy is perceived to be more important as regards foetal growth and development. It was considered, however, that recording dietary habits during the eighth month of pregnancy would depict many important aspects of a woman's general dietary habits. Earlier findings in a small population of pregnant women suggest that the dietary patterns do not change significantly from preconception to 6 months postpartum (Cuco *et al.* 2006). About 30% (n = 1579) of the invited women refused to take part in the nutrition study. The participation rate is still high, but there may be some differences in the dietary habits of the women who refused compared with our study subjects. Nevertheless, the extensive DIPP birth cohort provided an excellent opportunity to examine the diet and weight status of Finnish pregnant women, an area in which only limited information is currently available.

The food frequency method typically leads to overestimation of food consumption and nutrient intake, particularly of vegetables, but also the intake of energy and energy-yielding nutrients when compared with food records (Nelson & Bingham 1997). Although the energy-adjusted nutrient intakes would be more reliable with this method, we presented absolute intakes of vitamins and minerals (I). This was because of comparison of dietary intake with recommended levels, which are given in absolute values. Subjects may distort their reported diet for several reasons, which can only be revealed by careful validation of the method

(Nelson & Bingham 1997). The FFQ used in the present study was validated in a study similar in design as that of the study probe (Erkkola *et al.* 2001). The intake of foods and nutrients was higher as determined by means of the FFQ than that assessed by using food records. Pearson correlation coefficients for energy-adjusted nutrients ranged from 0.19 to 0.70 and, for foods, from 0.03 to 0.84. On average, 70% of the foods and 69% of the nutrients fell into the same or adjacent quintiles, according to the FFQ and the food record data. The results of the validation study suggests that the FFQ represents a useful tool for categorising pregnant women according to their dietary intake (Erkkola *et al.* 2001). The results of other FFQ validation studies have shown similar results in pregnant women (Greeley *et al.* 1992, Forsythe & Gage 1994, Robinson *et al.* 1996). One advantage in the present study was that FFQ was checked by a trained study nurse during a visit to the study centre. Thus immediate checking for missing answers and errors was possible.

Dietary pattern analysis is used increasingly in nutrition research but it still has weaknesses. The use of dietary patterns may help to capture some of the complexity of diet that is often lost in nutrient-based analyses (Jacques & Tucker 2001). However, the complexity also makes it more prone to subjective interpretations (Martinez *et al.* 1998). Dietary pattern analysis requires many decisions to be made by the investigators that have an impact on the number and type of patterns that are derived, reported and analysed (Newby & Tucker 2004). Another concern to do with dietary pattern analysis is that the patterns extracted in one population may not be reproducible in other populations with different dietary habits (Jacques & Tucker 2001). On the other hand, Balder *et al.* have suggested that some important eating patterns may be shared by various populations (Balder *et al.* 2003).

We used an endpoint reflecting advanced beta cell autoimmunity, which is one of the strengths of this study. Most of the previous studies have involved use of positivity for a single autoantibody as an endpoint, which represents in most cases harmless non-progressive beta cell autoimmunity (Knip 2002b). Previous studies on maternal weight status and the risk of T1D in children have been performed in smaller subject samples and in case-control settings.

6.2 Maternal age, educational level and diet

Age and education were positively associated with daily consumption of vegetables, fruit and berries in the present study. The same association was found

earlier in pregnant women in the US (Bodnar & Siega-Riz 2002). Nevertheless, Finnish pregnant women consumed fewer servings of vegetables, fruit, berries and fish than recommended. The consumption of these foods was also low in another study among pregnant women in the US (Borrud *et al.* 1993). The healthier food choices of the women with a higher level of education were reflected in their higher intakes of dietary fibre and some vitamins. The type of fat in the diet was also closer to recommendations among the more educated women. Food intake in women using supplements has been characterized by ample use of vegetables and fruit (Elmståhl *et al.* 1996, Kaartinen *et al.* 1997, Lyle *et al.* 1998, Kirk *et al.* 1999), as also seen in our study among Finnish pregnant women.

Nutrient supplements are supposed to complement the diet. However, our results revealed that the use of nutrient supplements did not always improve nutrient intake. Some nutrients were received cumulatively and in large amounts from different supplements and at the same time some relevant supplementation was missing. In this study, 85% of the women used at least one dietary supplement. This proportion parallels the results in an earlier study among Finnish pregnant women where 70% of them reported use of at least one dietary supplement (Erkkola *et al.* 1998). The prevalence is higher than the 36% found in non-pregnant Finnish women (Kaartinen *et al.* 1997). In Belgium, 62% of studied pregnant women had used vitamin supplements (Verbeke & De Bourdeaudhuij 2007) and in Norway the proportion of the supplement users was comparable with our results, 81% (Haugen *et al.* 2008). Thirty-five per cent of the women in our study had used single iron supplementation, whereas iron together with some other supplement was used by 49% of the women. Vitamin D and folic acid were the next most common nutrients obtained from dietary supplements. Iron has also been the most common nutrient gained from supplements in previous studies (Erkkola *et al.* 1998, Rogers & Emmett 1998, Mathews *et al.* 2000), followed by folic acid and vitamin D (Rogers & Emmett 1998, Mathews *et al.* 2000). Folic acid supplementation is not generally recommended for pregnant women in Finland and only 5% of the present study population used it as a single nutrient supplement, whereas most of the folic acid users (34% of the women) received nutrients in a multivitamin supplement. In countries where the risk of neural tube defects is higher, folic acid supplementation is recommended before and during pregnancy, and in higher doses than in Finland.

The use of nutrient supplements was associated with age, education and BMI. Supplements were used particularly by the oldest age group, by the most educated women and by those women who were of normal weight before pregnancy. In

Britain also, an association between maternal age and supplement use during pregnancy has been observed (Mathews *et al.* 2000, Nilsen *et al.* 2006b). In Norway, folic acid supplement use has been found to be more common among more educated, older and non-smoking pregnant women than others (Nilsen *et al.* 2006a).

Although vitamin D supplementation is recommended to all pregnant women during wintertime, only 40% of the women studied had used vitamin D supplements during pregnancy and only 15% of all women had a daily intake of 10 µg, as recommended. This is surprising because the data covered the whole calendar year. One reason for the low compliance with vitamin D supplementation might be inadequate counselling. In an earlier study related to dietary and health counselling in well-women clinics in Finland, only 60% of the nurses had given advice to use vitamin D supplements (Piiirainen *et al.* 2004). Results from the US suggest that black and white pregnant women and neonates in the northern US are at a high risk of vitamin D insufficiency, even when mothers are compliant as regards prenatal vitamins (Bodnar *et al.* 2007). The sufficiency of vitamin D intake in general has been a topic recently in Finland. There may be changes in the food fortification policy and the recommended amount may also be somewhat increased in the future. Since 2003, milk has been fortified with vitamin D (0.5 µg/dl) in Finland, but the fortification seems to have had little influence on vitamin D intake among Finnish people. The mothers in this study delivered before 2003.

The use of vitamin A-containing supplements was surprisingly common in our study. Intake of vitamin A was mostly via multivitamin supplementation; only two mothers used it as a single nutrient supplement. Thirty-one per cent of all women received vitamin A from supplements, although vitamin A supplementation is not recommended during pregnancy because of possible teratogenic effect (Hasunen *et al.* 2004). However, the highest level of vitamin A intake from supplements was clearly lower than the highest acceptable daily intake during pregnancy. Beta-carotene was not included in the supplemental vitamin A intake in this study.

6.3 Dietary patterns during pregnancy

We identified and described seven dietary patterns by means of principal components analysis among Finnish pregnant women. The patterns were differently related to energy and nutrient intake, and to the socio-demographic

factors related to the women. Dietary patterns have not been reported earlier in Finnish pregnant women. In two Finnish cohort studies among middle-aged women and men, two important dietary patterns emerged: healthy and traditional (Balder *et al.* 2003, Montonen *et al.* 2005). The dietary data in these studies were collected in the 1960's (Montonen *et al.* 2005) and 1980's (Balder *et al.* 2003). In the light of our results revealing seven dietary patterns, it is presumable that today there is more variation in peoples' eating habits than before. This is partly due to the wider selection of food products available and the presence of different eating styles, even during pregnancy.

According to our results, it seems that age and education are positively correlated with 'Healthy' and 'Alcohol and butter' dietary patterns, whereas 'Fast foods' shows an inverse association. Healthy eating patterns have previously been related to older age (Slattery *et al.* 1998, Williams *et al.* 2000, Terry *et al.* 2001, Costacou *et al.* 2003) and higher educational levels (Williams *et al.* 2000, Terry *et al.* 2001) in women and men. However, in a study by Sánchez-Villegas *et al.*, a higher educational level among women was associated with greater adherence to a 'Western' dietary pattern (similarities in comparison with our 'Fast foods' pattern) (Sanchez-Villegas *et al.* 2003). Smoking was strongly associated with the 'Coffee' and 'Fast foods' dietary patterns. The consumption of coffee has also been strongly correlated with smoking in Mexican American pregnant women (Wolff & Wolff 1995), although coffee was omitted from the dietary pattern analysis. Social, demographic and lifestyle factors related to the mother have also been suggested to have an influence on the early eating patterns of the offspring (North & Emmett 2000). This emphasises the importance of identifying risk groups for targeted dietary guidance during pregnancy.

In our study, energy and nutrient intakes in pregnant women varied among the dietary patterns, in a manner similar to that reported by Schulze *et al.* (Schulze *et al.* 2001). Findings that a 'prudent' dietary pattern (Hu *et al.* 1999) correlated positively with intakes of fibre, folic acid, carotenes and magnesium and inversely with total and saturated fat were consistent with the present results.

6.4 Fast foods and snacking in association with weight gain rate

In the present study, we identified two dietary patterns that were associated with weight gain rate during pregnancy after adjusting for other potential weight gain-related factors. The 'Fast food' pattern characterized by a high rate of consumption of snacks, sweets, soft drinks, hamburgers and other fast foods, was

positively associated and the ‘Alcohol and butter’ –pattern characterized by high alcoholic drink and butter consumption, was inversely associated with maternal weight gain rate. Both of them also demonstrated dose-dependency.

There are many definitions of gestational weight gain. In Finland mothers are recommended to gain 7–18 kg depending on their BMI before pregnancy. We used assessment of weight gain rate because in our study maternal weight gain monitoring started at different points of time, depending on when the mother started visiting the antenatal clinic, and also because the timing of the final measurement varied between the mothers. Estimates of total weight gain as well as of the net weight gain would thus not have been accurate. Weight gain rate changes slightly after the 10th week of pregnancy (U.S. Institute of Medicine, 1990), but we took this into account in regression models by adding a respective dummy variable into the model.

The results of several studies have suggested that snack consumption and/or a high frequency of food consumption is related to higher energy intake (Berteus et al., 2005, Ovaskainen et al., 2005, Kerver et al., 2006). French *et al.* (2002) reported that the frequency of eating at fast food restaurants is associated with higher energy intake and higher body weight. Our results support these findings although we specifically studied weight gain in pregnancy, not in the general population. Our earlier analysis indicated that younger mothers adhered to the fast food dietary pattern most frequently (II), making them vulnerable to elevated weight gain during pregnancy.

Alcohol consumption during pregnancy was observed to be rare (28% of all the mothers) and the amounts consumed were small among our study population. Therefore, even low-frequency maternal alcohol intake turned out to determine a dietary habit that was distinct enough to form an independent dietary pattern in our analyses. In general, people tend to under-report their alcohol consumption, as well as smoking, and reliable assessment is thus difficult. This may especially concern pregnant women. Our study provides limited information for explaining why the ‘Alcohol and butter’ pattern was related to lower weight gain rate. Literature on maternal alcohol intake and gestational weight gain is also scarce. Mothers with high scores in this dietary pattern seemed to be older, had more previous deliveries and they had a higher level of education (II), all factors independently associated with less maternal weight gain compared with others. It is also possible that this group of mothers felt subjectively very healthy and had records of uncomplicated previous pregnancies and were thus less strict with dietary guidelines concerning alcohol use.

Potential limitations of the present study are that physical activity and psychosocial factors were not examined. These factors may affect the weight gain of pregnant women. According to results of a recent review (Schlussel *et al.* 2008), however, only a few studies have revealed an association between physical activity and gestational weight gain. In a Canadian study (Fell *et al.* 2008) it was suggested that pregnancy is an event that leads to a decrease in physical activity. Exercise may not therefore be as important a factor in weight gain control during pregnancy as it is during other phases of life. On the other hand, Olson *et al.* identified physical activity as one of three behavioural determinants of gestational weight gain (Olson & Strawderman 2003). The other two determinants were change in food intake and smoking. There is increasing evidence that psychosocial factors may also affect dietary intake. Findings by Hurley *et al.* suggest that pregnant women who were more fatigued, stressed and anxious consumed more food (Hurley *et al.* 2005).

The overall problem in studies related to gestational weight gain is that they are observational in design, and accordingly they cannot prove causation. However, repeated studies with consistent results can provide compelling evidence for associations. In this study we could not prove causality between diet and weight gain rate, but the results still clearly support the assumption that frequent consumption of fast foods and snacks is a risk predictor of excess maternal weight gain.

6.5 Maternal weight status during pregnancy and advanced beta cell autoimmunity in children

The present cohort study revealed no relationship between maternal BMI and weight gain rate during pregnancy and the risk of advanced beta cell autoimmunity in children. Expected effects of increased HLA-conferred susceptibility and familial diabetes on beta cell autoimmunity risk were seen. In addition, a higher maternal vocational education level was found to be related to a smaller risk of advanced beta cell autoimmunity in the offspring. This association is difficult to explain and possible dietary and lifestyle factors behind the association should be studied further.

A cohort setting and use of an endpoint reflecting advanced beta cell autoimmunity are the major strengths of this study. Previous studies on maternal weight status and the risk of type 1 diabetes in children have been carried out among smaller subject samples and in case-control settings (Dahlquist & Källen

1992, McKinney *et al.* 1997, Rasmussen *et al.* 2009). Most previous studies have involved the use of positivity for a single autoantibody as an endpoint, which represents in most cases harmless non-progressive beta cell autoimmunity (Knip 2002b). Caesarean section delivery has been shown to alter an infant's microbiota and immune function in the gut (Grönlund *et al.* 1999, Salminen *et al.* 2004, Penders *et al.* 2006), which could increase the risk of autoimmune diseases such as T1D in early childhood. A meta-analysis carried out by Cardwell *et al.* revealed a 20% increase in the risk of type 1 diabetes in children after Caesarean section delivery (Cardwell *et al.* 2008). The present results do not support these observations, since Caesarean section seemed to be associated with a smaller risk of advanced beta cell autoimmunity. These opposing results may be due to the small number of children (n = 17) with a positive endpoint who were born by Caesarean section.

Birth weight was not related to the risk of type 1 diabetes in the present study, although in a recent meta-analysis, high birth weight (>4000 g) was considered to be a risk factor of T1D (Harder *et al.* 2009). According to the present results, children belonging to the 4th quarter of birth weight were born to mothers with significantly higher initial BMI than children with lower birth weights.

At the same time as the incidence of T1D has increased rapidly (Harjutsalo *et al.* 2008), obesity has become a worldwide epidemic and a serious public health issue. As the prevalence of obesity is increasing, overweight conditions and obesity have also become common in pregnant women. The present cohort study among children at an increased genetic risk of T1D revealed no associations between maternal BMI or gestational weight gain and advanced beta cell autoimmunity in the offspring.

There is no precise information about the incidence of gestational diabetes mellitus (GDM) in the present study subjects. Data from Western countries suggest that the incidence of GDM is increasing along the global obesity epidemic and approximately 10% of pregnant women are affected (Kaaja & Rönnemaa 2008). GDM reflects a metabolically altered fetal environment associated with infant's high birth weight and increased risk of overweight later in life (Gillman *et al.* 2003).

7 Conclusions and implications for future studies

The findings of the present study suggest that healthy food choices are relatively common among Finnish pregnant women and that the increased nutrient requirements during pregnancy are mostly covered by a balanced diet. The use of nutrient supplements does not support the diet in every respect. In this study we discovered both unnecessary nutrient supplementation and lack of relevant supplementation. Seven dietary patterns were identified for the first time in Finnish pregnant women providing a meaningful interpretation of their dietary habits. The present results strengthen the assumption that young and less well educated women are at risk of having an unbalanced or inadequate diet. A strong association was found between the fast food type of dietary pattern and greater weight gain rate during pregnancy. Thus, young and less well educated women in particular should be a special target group as regards nutrition education, with emphasis on well-planned balanced meals and more precise advice on supplement use in antenatal clinics. This is important for optimal pregnancy outcome, successful breastfeeding, and for the prevention of obesity in later life, among both mothers and children. Nutrition education in antenatal clinics should be more effectively taken into account in nutrition policy planning and implementation.

The rising incidence of T1D, especially in young children, is alarming. Type 1 diabetes has already become an important public health concern among Finnish children. On the basis of current knowledge it is difficult to assess the roles of maternal nutrition and weight status during pregnancy as regards the risk of T1D in children. Associations between maternal BMI and weight gain rate during pregnancy and advanced beta cell autoimmunity in children were not found in the present study. Whether there is some dietary or lifestyle factor behind the association between maternal education and a child's risk of developing beta cell autoimmunity, should be studied further. More studies and new innovative methods are required to provide answers to the question of the role of diet in the development of T1D. Dietary patterns may be a useful tool for risk group identification and they offer a framework for further research concerning diet and health outcomes among mothers and their children.

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Original articles

- I Arkkola T, Uusitalo U, Pietikäinen M, Metsälä J, Kronberg-Kippilä C, Erkkola M, Veijola R, Knip M & Virtanen SM (2006) Dietary intake and use of dietary supplements in relation to demographic variables among pregnant Finnish women. *Br J Nutr* 96: 913–920.
- II Arkkola T, Uusitalo U, Kronberg-Kippilä C, Männistö S, Virtanen M, Kenward MG, Veijola R, Knip M, Ovaskainen M & Virtanen SM (2008) Seven distinct dietary patterns identified among pregnant Finnish women – associations with nutrient intake and sociodemographic factors. *Pub Health Nutr* 11: 176–182.
- III Uusitalo U, Arkkola T, Ovaskainen M, Kronberg-Kippilä C, Kenward MG, Veijola R, Simell OG, Knip M & Virtanen SM (2009) Unhealthy dietary patterns are associated with weight gain during pregnancy among Finnish women. *Pub Health Nutr* 12: 2392–2399.
- IV Arkkola T, Kautiainen S, Takkinen H, Kenward MG, Nevalainen J, Uusitalo U, Simell O, Ilonen J, Knip M, Veijola R & Virtanen SM (2009) The relationship of maternal weight status in pregnancy to the development of advanced beta-cell autoimmunity in the offspring: a prospective birth cohort study. Manuscript.

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