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ASSOCIATION OF BIRTH WEIGHT WITH BODY SIZE AND DIETARY FACTORS AMONG ADOLESCENTS

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SYNTYMÄPAINON YHTEYS NUOREN KEHON KOKOON JA RAVITSEMUKSEEN

Aiemmat tutkimukset ovat osoittaneet, että sekä pienempi että suurempi syntymäpaino on yhteydessä epäterveellisempiin ruokailutottumuksiin nuoruudessa ja kroonisten sairauksien, kuten tyypin 2 diabeteksen ja sydän- ja verisuonitautien, kasvavaan riskiin myöhemmin aikuisiässä. Niillä, joilla on suurempi syntymäpaino, on myös suurempi riski ylipainon ja lihavuuden kehittymiseen sekä suurempaan painonnousuun jo nuoruudessa. Mielenkiintoista on, että syntymäpaino on suoraan yhteydessä rasvattoman massan määrään nuoruudessa sukupuolesta riippumatta ja tytöillä myös rasvamassan määrään. Myös syntymäpainon ja vyötärön ympärysmitan sekä sisäelinten rasvan välillä näyttää olevan käänteinen yhteys. Lisäksi on todettu, että suurempi syntymäpaino on yhteydessä heikompaan ruokavalion laatuun 6–8-vuotiailla lapsilla. Aiempien tutkimusten mukaan voi olla mahdollista, että pienen tai suuren syntymäpainon ja aikuisten kroonisten sairauksien välinen yhteys voitaisiin selittää syntymäpainon ja ruokavalion laadun yhteydellä myöhemmässä elämässä. Tämän tutkielman tavoitteena oli selvittää syntymäpainon yhteyttä kehon kokoon sekä ruokavalioon liittyviin tekijöihin nuoruudessa.

Tämä tutkimus perustui Lasten liikunta ja ravitsemus –tutkimukseen. Tässä tutkielmassa käytettiin kahdeksan vuoden seurantamittaustietoja, kun tutkimushenkilöt olivat 15–17-vuotiaita. Elintarvikkeiden kulutusta arvioitiin neljän päivän ruokapäiväkirjoista ja lisäksi frekvenssikyselyillä. Ruokavalion laadun arvioimiseen käytettiin ruokavalion laatua mittaavia indeksejä, kuten Ruokavalion laatuindeksi (Index of Diet Quality, IDQ) ja Itämeren ruokavalio -indeksi (Baltic Sea Diet Score, BSDS). Syntymäpainon tiedot kerättiin takautuvasti Syntymärekisteristä.

Tämän tutkielman tulosten mukaan syntymäpaino ei ollut yhteydessä nuorten ruokavalion laatuun eikä kehonpainoon nuoruudessa. Syntymäpainon ja vyötärön ympärysmitan välillä oli kuitenkin käänteinen yhteys. Suurempi syntymäpaino oli yhteydessä vähäisempään kasviöljypohjaisten margariinien (rasva 60–80 %) ja käyttöön sekä runsaampaan voin ja voi-kasviöljyseoksien käyttöön nuoruudessa.

Näyttää siltä, että syntymäpaino saattaa olla yhteydessä ruoan kulutukseen ja vyötärön ympärykseen nuoruudessa. Pitkittäistutkimuksia aiheesta tarvitaan lisää, jotta syntymäpainon yhteyttä myöhemmän elämän ruoan kulutukseen ja muihin ravintotekijöihin voidaan selvittää.

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JAKUPOVIĆ, SABINA: Association of birth weight with body size and dietary factors among adolescents

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ASSOCIATION OF BIRTH WEIGHT WITH BODY SIZE AND DIETARY FACTORS AMONG ADOLESCENTS

Previous studies have suggested that both lower and higher birth weight are associated with unhealthier eating habits in adolescence and with a growing risk of chronic diseases, such as type 2 diabetes and cardiovascular diseases, later in adulthood. Those with higher birth weight are also in greater risk to have higher weight and greater weight gain already in adolescence. Moreover, there seems to be an inverse association between birth weight and waist circumference and visceral fat. In addition, it has been established that a higher birth weight is associated with a lower overall diet quality in children. According to previous studies it might be possible that the link between lower or higher birth weight and chronic diseases in adulthood could be explained through the linkage between birth weight and diet quality later in life. The aim of this master's thesis was to investigate the associations of birth weight with body size in adolescence and dietary factors, such as food consumption and diet quality indexes.

This study was based on the Physical Activity and Nutrition in Children (PANIC) Study. The present thesis used the data of the 8-year follow-up measurements when the study subjects were 15-17 years old. Food consumption was assessed by 4-day food records and a food frequency questionnaire. The overall diet quality was defined by dietary quality indexes, such as the Index of Diet Quality (IDQ) and Baltic Sea Diet Score (BSDS). The data for birth weight was gathered retrospectively from the Finnish birth register.

The results of the present thesis showed that birth weight was not associated with adolescents' overall diet quality when using IDQ and BSDS indexes, nor with the weight in adolescence. However, there was an inverse association between birth weight and waist circumference. In addition, higher birth weight was associated with lower consumption of vegetable-oil based margarines (fat 60-80%) in adolescence. Birth weight was directly associated with consumption of butter and butter-based spreads. Based on the current study, it seems that birth weight may be associated with food consumption and waist circumference in adolescence. More longitudinal studies are needed to further establish the association of birth weight with food consumption and other dietary factors later in life.

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Opinnäytetyön yhteenveto suomeksi: SYNTYMÄPAINON YHTEYS NUOREN KEHON KOKOON JA RAVITSEMUKSEEN

JOHDANTO

Syntymäpainoa voidaan käyttää raskausajan indikaattorina mittaamaan sikiön kasvua, joka samalla kertoo myös imeväisen eloonjäämisen mahdollisuuksista (Barker ym. 1993). Syntymäpainoon vaikuttavat olennaisesti sekä sikiön ominaisuudet että äitiin liittyvät tekijät (kohdunsisäinen ympäristö), joihin taas vaikuttavat sekä geneettiset että ympäristötekijät (Hattersley ja Tooke 1999). Äidin ja sikiön hormonaaliset tekijät, kuten insuliiniin ja glukoosiin liittyvät tekijät (Hattersley ja Tooke 1999), istukan toimintahäiriöt tai äidin sairaudet, kuten raskausdiabetes (Gillman ym. 2003), ja ravitsemustila raskauden aikana vaikuttavat syntymäpainoon (Mäkikallio 2019). Nämä tekijät voivat johtaa sikiön kasvun nopeutumiseen tai hidastumiseen raskauden aikana ja siten lisätä riskiä syntyä suurella tai pienellä syntymäpainolla. Suuremman syntymäpainon on osoitettu olevan yhteydessä myöhempään ylipainoon ja lihavuuteen (Gillman ym. 2013, Evensen ym. 2017, Boone-Heinonen et al. 2018). Lisäksi on havaittu, että syntymäpaino saattaa altistaa elintapasairauksille, kuten tyypin 2 diabetekselle ja sepelvaltimotaudille (Boone-Heinonen ym. 2018, Knop ym. 2018, Zanetti ym. 2018).

On oletettu, että jotkut näistä yhteyksistä voidaan selittää sikiön ohjelmoitumisella raskausaikana (Barker 2007, Vickers 2014) tai ravintotekijöillä (Bamfo ja Odibo 2011, Mäkikallio 2019, Sharma ym. 2016, WHO 1995). Terveyden ja sairauksien kehittymisen alkuperän hypoteesin (Developmental origins of health and disease - DOHaD) mukaan kehittyvä sikiö mukautuu kohdunsisäiseen ympäristöön ja voi mukautua myös häiriintyneeseen tai haitalliseen kohdunsisäiseen ympäristöön (Gillman 2005). Tämän hypoteesin mukaan mukautuminen heijastuu suoraan syntymäpainoon. Koska insuliini- ja glukoosiaineenvaihdunnalla on tärkeä rooli sikiön kasvussa ja kehityksessä, raskauden aikaisen sikiön kehittymisen häiriöitä voidaan osittain mitata arvioimalla syntymäpainoa (Barker 1990, Barker ym. 1993, Hattersslay ja Tooke 1999).

Syntymäpainon ja myöhemmän kehonpainon välinen yhteys näyttäytyy jo ennen kouluikää ja kouluikäisillä lapsilla (Apfelbacher ym. 2008, Kitsantas ja Gaffney 2010, Janjua ym. 2012, Parker ym. 2012, Heppe ym. 2013). Erityisesti lapsilla, joilla on suuri syntymäpaino, on suurempi riski ylipainon ja lihavuuden kehittymiseen lapsuudessaan, verrattuna lapsiin, joiden syntymäpaino on pieni tai normaali (Eriksson ym. 2003, Reilly ym. 2005, Li ym. 2007, Apfelbacher ym. 2008, Janjua ym. 2012 Parker ym. 2012, Heppe ym. 2013). Aiemmat tutkimukset viittaavat siihen, että tämä yhteys pysyy koko elinkaaren ajan niin, että syntymäpainoltaan suuripainoiset ylittävät normaalipainon lapsena ja nuorena sekä ovat painoindeksiltään ylipainoisia ja lihavia myös aikuisena (Field ym. 2005, Simmonds ym. 2016). Mielenkiintoista on, että aiemmissa tutkimuksissa on löydetty myös vahva yhteys varhaisen, lapsuudenaikaisen kiihtyneen kasvun ja ylipainon, lihavuuden ja kroonisten sairauksien välillä (Eriksson ym. 2003, Monteiro ym. 2003, Oddy ym. 2004, Toschke ym. 2004, Barker ym. 2005, Reilly ym. 2005, Birbilis ym. 2012, Heppe ym. 2013, Sacco ym. 2013). Kiihtynyttä lapsuudenaikaista kasvua on havaittu erityisesti pienipainoisina syntyneillä tai raskausviikkoihin nähden pienikokoisina syntyneillä (Karlberg ja Albertsson-Wikland 1995).

Ylipainoon ja lihavuuteen liittyvien kroonisten sairauksien kehittymistä arvioitaessa on tärkeää ottaa huomioon ruokavaliotekijät (Ignarro ym. 2007). Syntymäpainon yhteyttä ravintotekijöihin on tutkittu hyvin vähäisesti. Nämä aiemmat tutkimukset ovat antaneet joitain viitteitä siitä, että syntymäpaipainolla voisi olla yhteys ravitsemustekijöihin. Pieni syntymäpaino näyttää liittyvän suurempaan rasvan saantiin (Perälä ym. 2012). Tämä yhteys on löydetty myös aikuisilta, jotka sikiöaikanaan altistuivat nälänhädälle raskauden alkuvaiheessa (Lussana ym. 2008). Samanlaisia tuloksia on raportoitu lasten rasvan saannissa (Stafford ja Lucas 1998). On myös viitteitä siitä, että pienipainoisena syntyneillä lapsilla saattaa olla suuremman kokonaisrasvan saannin lisäksi suurempi tyydyttyneiden rasvahappojen saanti (Shultis ym. 2005, Doornweerd ym. 2017). Lisäksi aiemmat tutkimukset ovat yhdistäneet suuremman syntymäpainon isompaan hiilihydraattien saantiin aikuisilla (Perälä ym. 2012). Suurempi syntymäpaino on myös yhdistetty pienempään marjojen ja hedelmien kulutukseen ja vähäisempään kuidun saantiin sekä suurempaan sakkaroosin ja energian kokonaissaantiin lapsuudessa (Eloranta et al. 2018).

On ehdotettu, että sikiön ohjelmoituminen voi vaikuttaa ruokahaluun ja makumieltymyksiin, ja siksi vaikuttaa myöhempiin ruokavalintoihin (Stein ym. 2006, Ayres ym. 2012). Syntymäpainon,

myöhemmän kehonpainon ja yleisen ruokavalion laadun välisiä yhteyksiä nuoruudessa ei kuitenkaan ole vielä tutkittu riittävästi, jotta niiden suhde ymmärrettäisiin täysin. Kaiken kaikkiaan, aiemmat tutkimukset viittaavat siihen, että varhainen elämä on mahdollisesti yksi tärkeimmistä ajanjaksoista, jotka muokkaavat myöhempiä ruokailutottumuksia, kehonpainon kehityskulkua ja vaikuttavat myöhemmässä elämässä kehittyviin terveysriskeihin.

Tämän opinnäytetyön tavoitteena oli tutkia 15–17-vuotiaiden suomalaisten nuorten syntymäpainon ja kehon koon ja ravintotekijöiden välisiä yhteyksiä. Tutkimuksessa selvitimme syntymäpainon yhteyttä myöhempiin paino- ja ravintotekijöihin, kuten elintarvikkeiden kulutukseen ja ruokavalion laatuindekseihin. Tämä tutkimus perustui Lasten liikunta ja ravitsemus -tutkimuksen (the PANIC Study) kahdeksan vuoden seurantatietoihin.

KIRJALLISUUS

Ylipaino ja lihavuus (painoindeksi > 25 kg/m^2) yleistyvät maailmanlaajuisesti ja niiden tiedetään myös lisäävän riskiä kroonisille elintapasairauksille (Must ym. 1999, Atella ym. 2015, THL 2016). Ylipaino, lihavuus ja krooniset elintapasairaudet ottavat myös suuren osan terveydenhuollon kustannuksista. Esimerkiksi Suomessa 18,9 % 8–9 luokkalaisista, 15,6 % lukiolaisista ja 26,2 % ammattiopistojen opiskelijoista olivat Suomen kouluterveyskyselyn mukaan ylipainoisia tai lihavia (THL 2017). Lisäksi on todettu, että ylipainoinen tai lihava lapsi on herkemmin normaalipainon yläpuolella myös nuoruudessa ja aikuisuudessa (Field ym. 2005, Simmonds ym. 2016). On tärkeä tutkia mekanismeja riskitekijöiden taustalla, jotta voimme paremmin ymmärtää elintapasairauksiin johtavia riskejä. Ymmärtämällä elintapasairauksiin johtavia tekijöitä ja riskejä paremmin voidaan kohdentaa terveydenhuollon resurssit paremmin niille, jotka hyötyvät interventiosta eniten. Tiedetään myös, että interventiot toimivat parhaiten lapsilla ja nuorilla (Magnussen ym. 2010, Viitasalo ym. 2016), minkä takia aikainen riskiryhmien havaitseminen on erityisen tärkeää.

Painonkehitykseen vaikuttavat monet tekijät, esimerkiksi sosioekonominen tausta, geneettiset tekijät ja ympäristötekijät (Kitsantas ja Gaffney 2010, Birbilis ym. 2012, Janjua ym. 2012, Van den Berg ym. 2013, Seyednasrollah ym. 2017, Woo Baidal ym. 2017). Lisäksi syntymäpainon on huomattu vaikuttavan itsenäisesti painonkehitykseen sekä riskiin sairastua elintapasairauksiin (Law ym. 1992,

Must ym. 1999, Eriksson ym. 2003, Monteiro ym. 2003, Barker ym. 2005, Andersen ym. 2010, Birbilis ym. 2012, Janjua ym. 2012, Heppe ym. 2013, Boone-Heinonen ym. 2018), mutta tutkimukset tästä aiheesta ovat osittain erimielisiä, miten paljon ja millä mekanismeilla syntymäpaino vaikuttaa. Näyttäisi kuitenkin siltä, että sekä pieni että suuri syntymäpaino ovat riskitekijöitä myöhemmille elintapasairauksille (Andersen ym. 2010, Boone-Heinonen ym. 2018, Knop ym. 2018).

Aiemmissa tutkimuksissa on havaittu, että syntymäpaino voi vaikuttaa kehonkoostumukseen, mutta myös makumieltymyksiin ja sitä kautta mahdollisesti ruokavalintoihin (Loos ym. 2001, Rasmussen ym. 2005, Stein ym. 2006, De Luca Rolfe ym. 2010, Biosca ym. 2011, Ayres ym. 2012, Liu ym. 2019). Nämä vaikutukset makumieltymyksiin ja kehonkoostumukseen ovat mahdollisesti sikiöaikaisen epigeneettisen ohjelmoitumisen tulosta (Vickers 2014, Barker 2007).

Syntymäpaino

Normaali raskaus kestää 37–41 viikkoa (Ekholm 2019, Timonen 2019). Ennen viikkoa 37 syntyneet luokitellaan ennenaikaisesti syntyneiksi, kun taas 41+6 raskausviikon jälkeen syntyneet luokitellaan yliaikaisiksi. Lisäksi vastasyntynyt voidaan luokitella syntymäpainonsa perusteella pienipainoisena (< 2500 g) tai suuripainoisena (≥ 4000 g) syntyneeksi (Laatio ja Nuutila 2019, Delpapa ym. 1991). Lisäksi vauva voi olla pieni tai suuri raskausviikkoihin nähden, jolloin hänen kokoaan verrataan samalla raskausviikolla syntyneisiin (Mäkikallio 2019, Birbilis ym. 2012). Pienikokoinen raskausviikkoihin nähden tarkoittaa vastasyntynyttä, joka painaa < 10 % vastaavalla viikolla syntyneistä ja vastaavasti suurikokoinen raskausviikkoihin nähden painaa > 10 % vastaavalla viikolla syntyneistä.

Syntymäpainoon vaikuttavat raskausajan pituus ja monet geneettiset tekijät sekä kohdunsisäinen ympäristö (Dunkel 2010, Timonen 2019). Lisäksi äidin raskauden aikainen ruokavalio ja painonnousu ovat tärkeitä tekijöitä syntymäpainon kehityksessä (Bamfo ja Odibo 2011, Erkkola 2011, Sharma ym. 2016, Mäkikallio 2019). Vanhempien sosioekonominen asema, kuten tulot ja koulutus, voivat myös välillisesti vaikuttaa syntymäpainoon. Matalampi sosioekonominen asema on esimerkiksi yhteydessä äidin raskaudenaikaiseen tupakointiin, mikä puolestaan voi vaikuttaa sikiön kasvua hidastavasti (Lawlor ym. 2008, Davies ym. 2018).

Sikiöaikana istukalla on yksi tärkeimmistä rooleista ravintoaineiden ja hapen kuljettamisessa sikiölle sekä kuona-aineiden poistamisessa sikiöstä (Mäkikallio 2019). Istukan häiriöt ovat monisyisiä, mutta niitä voi esiintyä muun muassa silloin, kun istukka on kehittyessään saanut syystä tai toisesta liian vähän ravinteita (Duttaroy ja Basak 2016). Tällöin istukka voi kehittyä normaalista poikkeavaksi muun muassa kokonsa ja muotonsa suhteen, joka taas on yhdistetty muutoksiin sikiön kehityksessä (Eriksson ym. 2000, Harding ym. 2001, Barker ym. 2010, Kajantie ym. 2010, Eriksson ym. 2011). Istukan häiriintyneen toiminnan kautta voi esiintyä sikiön kasvun hidastumista (Bomfo ja Odibo 2011, Sharma ym. 2016). Istukan kehitykseen= vaikuttavia tekijöitä voivat olla esimerkiksi äidin päihteiden käyttö, raskaudenaikaiset tai muut sairaudet (mm. diabetes, anemia, ateroskleroosi) tai äidin ali- tai yliravitsemus raskauden aikana (Duttaroy ja Basak 2016, Mäkikallio 2019). Lisäksi istukan verenvuodot tai kiinnittymiseen liittyvät häiriöt sekä sikiön kromosomaaliset häiriöt tai sikiön infektiot voivat vaikuttaa sikiön normaaliin kasvuun ja kehittymiseen. Myös äidin insuliini- ja glukoositasot ovat keskeisiä, koska ne säätelevät voimakkaasti sikiön kasvua (Vääräsmäki ja Kaaja 2019, Metzger ym. 2008, Landon ym. 2011). Tämän takia muun muassa raskaudenaikaiset glukoosiaineenvaihdunnan häiriöt ja raskausajan diabetes vaikuttavat olennaisesti sikiön syntymäpainoon.

Syntymäpaino ja myöhempi terveys

Sekä suurempi että pienempi syntymäpaino on aiemmissa tutkimuksissa yhdistetty terveyshaittoihin myöhemmässä elämässä (Barker ym. 2005, Jaquet ym. 2000, Barker 2007, Vickers 2014). Erityisesti pienempi syntymäpaino ja pienikokoisuus syntymäviikkoihin nähden on yhdistetty suurempaan riskiin sairastua metaboliseen syndroomaan ja sydän- ja verisuonitauteihin aikuisuudessa (Barker ym. 2005, Jaquet ym. 2000, Andersen ym. 2010). Lisäksi näillä pienikokoisena ja pienipainoisena syntyneillä lapsilla näyttää esiintyvän insuliiniresistenssiä ja keskivartalolihavuutta useammin kuin normaalipainoisina syntyneillä. Toisessa ääripäässä ovat suuripainoisena syntyneet, joilla on aikuisena pienipainoisena ja normaalipainoisena syntyneitä useammin ylipainoa, mutta ovat siitä huolimatta pienemmässä riskissä sairastua sydän- ja verisuonitauteihin tai tyypin 2 diabetekseen kuin pienipainoisena syntyneet (Vohr ym. 1980, Barker ym. 1989, Boney ym. 2005, Schaefer-Graf ym. 2005, Eriksson 2006, Ornoy 2011). Tulokset aiemmista tutkimuksista, jotka ovat selvittäneet suuripainoisena syntyneiden riskiä sairastua myöhempiin elintapasairauksiin ovat kuitenkin ristiriitaisia. Osa tutkimuksista on havainnut syntymäpainon ja myöhempien elintapasairauksien riskin U-muotoisen

riskin, jossa pieni- ja suuripainoisilla on samansuuntaiset riskit (Boone-Heinonen ym. 2018), kun taas osa on havainnut J-muotoisen riskin, jossa suuripainoisilla oli suurempi taipumus elintapasairauksille (Knop ym. 2018).

Syntymäpaino ja myöhempi kehonpaino

Syntymäpainolla ja myöhemmällä painolla näyttää aiempien tutkimusten valossa olevan suora yhteys (Eriksson ym. 2003, Monteiro ym. 2003, Reilly ym. 2005, Li ym. 2007, Apfelbacher ym. 2008, Araujo ym. 2009, Kleiser ym. 2009, Kitsantas ja Gaffney 2010, Janjua ym. 2012, Parker ym. 2012, Gillman ym. 2013, Heppe ym. 2013, Evensen ym. 2017, Boone-Heinonen ym. 2018). Yhteys näyttää olevan kuitenkin selkeämpi lapsuudessa kuin nuoruudessa. Eräässä tutkimuksessa syntymäpainon ja nuoruusiän painon välinen yhteys raportoitiin mutta se oli heikko (Evensen ym. 2017), kun taas toisessa syntymäpainon havaittiin olevan yhteydessä ylipainoon, mutta ei enää lihavuuteen (Birbilis ym. 2012). Tämäkään tulos ei ollut tilastollisesti merkitsevä enää siinä vaiheessa, kun tutkimuksessa huomioitiin ravinnon energian saanti.

Pienipainoisena syntyneillä painonkehitys on monimutkaisempaa. Pienipainoisena syntyneillä ei aiempien tutkimusten mukaan ole riskiä ylipainoon tai lihavuuteen lapsuudessa tai nuoruudessa (O'Callaghan ym. 1997, Monteiro ym. 2003, Li ym. 2007, Apfelbacher ym. 2008, Araujo ym. 2009, Parker ym. 2012, Sacco ym. 2013). Siitä huolimatta pienipainoisena syntyneet kasvavat imeväisiässä ja varhaislapsuudessa nopeammin ja kokevat niin kutsutta kiihtynyttä kasvua (Dos Santos Silva ym. 2002, Hack ym. 2003). Kiihtynyt kasvu imeväiässä sekä varhaislapsuudessa on taas yhdistetty itsenäisesti ja yhdessä pienen syntymäpainon kanssa ylipainoon ja lihavuuteen lapsuudessa ja nuoruudessa (Eriksson ym. 2003, Monteiro ym. 2003, Oddy ym. 2004, Toschke ym. 2004, Reilly ym. 2005, Birbilis ym. 2012, Heppe ym. 2013, Taal ym. 2013).

Syntymäpaino ja myöhempi kehonkoostumus

Aiemmissa tutkimuksissa on vahva näyttö siitä, että syntymäpaino on suoraan yhteydessä pituuteen lapsuudessa ja nuoruudessa (Gail ym. 2001, Loos ym. 2001, Loos ym. 2002, Pietiläinen ym. 2002, Labayen ym. 2006, Adair 2007, Elia ym. 2007, Chomtho ym. 2008, Jelenković ym. 2018). Toisaalta on

näyttöä myös siitä, että pienipainoisena syntyvät, jotka käyvät läpi kiihtyneen kasvun varhaislapsuudessaan saattavat saavuttaa saman pituuden suuripainoisena syntyneiden kanssa tai jopa kiriä pituuskasvussa suuripainoisena syntyneiden ohi (Dos Santos Silva et al. 2002, Hack et al. 2003). Lisäksi on osoitettu, että tyttöjen ja poikien pituuskasvu kehittyy jotakuinkin eri tavalla nuoruudessa. Suuripainoisena syntyneet tytöt usein kasvavat pituutta nopeammin kuin muut aina kuukautisten alkamiseen asti ja saavuttavatkin mahdollisesti suuremman pituuden kuin pienipainoisena syntyneet tytöt (Gale ym. 2001, Loos ym. 2002, Sachdev ym. 2005, Labayen ym. 2006, Adair 2007, Workman & Kelly 2017). Toisaalta osassa aiemmista tutkimuksista on näyttänyt siltä, että syntymäpaino vaikuttaa tyttöjen pituuteen vain varhaislapsuuteen asti ja olisi tämän jälkeen riippumaton syntymäpainosta (Casey ym. 1991, Knops ym. 2005).

Kehonkoostumusta selvittäneissä tutkimuksissa havaittiin, että kehonkoostumus oli suuripainoisena syntyneillä terveyttä edistävämpi kuin pienipainoisena syntyneillä (Loos ym. 2001, Rasmussen ym. 2005, De luca Rolfe ym. 2010, Biosca ym. 2011). Pienipainoisena syntyneillä kehonkoostumus näyttäisi erityisesti suosivat rasvamassaa ja viskeraalisen rasvan kehittymistä, joka on havaittu jo lapsuudessa ja nuoruudessa ja näyttäisi vaikuttavan myös aikuisuudessa (Loos ym. 2001, Rasmussen ym. 2005, De Luca Rolfe ym. 2010). Lisäksi pieni syntymäpaino on yhdistetty suurempaan ihonalaisrasvan määrään ja suurempaan vyötärö-lantio suhteeseen aikuisilla naisilla ja miehillä (Law ym. 1992, Te Velde ym. 2003, Berbieri ym. 2009) ja suurempaan vyötärönympärykseen naisilla ja joissain tutkimuksissa myös miehillä (Te Velde ym. 2003, Barbieri ym. 2009, Pereira-Freire ym. 2015). Toisaalta myös suuri syntymäpaino on yhdistetty suurempaan vyötärönympärykseen lapsuudessa (Sacco ym. 2013, Pereira-Freire ym. 2015), mutta suuripainoisilla kehon koostumus näyttää suosivan rasvattoman massan kertymistä rasvamassaa enemmän (Evensen ym. 2018, Chomtho ym. 2008).

Syntymäpaino ja myöhempi ravitsemus

Ravitsemuksella on tärkeä rooli ylipainon ja lihavuuden sekä elintapasairauksien kehittymisessä (Ignarro ym. 2007). Aiemmissa tutkimuksissa on pohdittu, että syntymäpaino saattaa vaikuttaa myöhempään sairastumisriskiin nimenomaan sikiöaikaisen ohjelmoitumisen kautta niin, että sikiöaikainen ympäristö vaikuttaa ruokamieltymyksiimme ja valintoihimme (Stein ym. 2006, Ayres ym. 2012). Tiedetäänkin, että pieni syntymäpaino lisää suolaisen mieltymystä sekä mieltymystä

hiilihydraattipitoiseen ruokavalioon (Breen ym. 2006, Stein ym. 2006, Escobar ym. 2014, Tam ym. 2015). Toisaalta pieni syntymäpaino on yhdistetty pienempään kasvisten, hedelmien ja marjojen käyttöön varhaisaikuisuudessa (Kaseva ym. 2013). Lisäksi suomalaisia aikuisia tutkivassa tutkimuksessa pienipainoisena syntyneet käyttivät vähemmän hiilihydraatteja ja kuituja (Perälä ym. 2012). Vastaavasti suuripainoisena syntyneet saivat aikuisuudessa enemmän hiilihydraatteja (Perälä ym. 2012). Toisessa suomalaisessa tutkimuksessa suuripainoisena syntyneet saivat lapsuudessa enemmän sakkaroosia (Eloranta ym. 2018). Toisaalta lapsilla ei havaittu suurempaa kokonaishiilihydraattien saantia (Eloranta ym. 2018). Lapsilla suuri syntymäpaino on myös yhdistetty pienempään marjojen ja hedelmien käyttöön (Eloranta ym. 2018), kun taas aikuisilla suuripainoisena syntyminen on yhdistetty vastaavasti suurempaan hedelmien ja marjojen käyttöön (Perälä ym. 2012).

Suurempi syntymäpaino on yhdistetty suurempaan energiansaantiin niin lapsuudessa, nuoruudessa kuin aikuisuudessakin (Doornweerd ym. 2017, Bischoff ym. 2018, Eloranta ym. 2018). Lisäksi suuripainoisena syntyneillä oli erään tutkimuksen mukaan heikompi ruokavalion kokonaislaatu 6–8-vuotiaana, kun ruokavalion laadun arviointiin käytettiin Suomalaisten lasten terveyttä edistävän ruokavalion mittaria (Finnish Children Healthy Eating Index, FCHEI).

TUTKIMUKSEN TAVOITTTEET

Tutkimuksen tavoitteena oli tutkia syntymäpainon yhteyksiä kehon kokoon ja ruokavalioon liittyviin tekijöihin nuorilla. Tutkimuskysymyksiä oli kolme:

1. Onko syntymäpaino yhteydessä kehon kokoon, kuten kehonpainoon, pituuteen ja painoindeksiin, nuoruudessa?
2. Onko syntymäpaino yhteydessä kehonkoostumukseen, kuten kehon rasvamassan ja rasvattoman massa määrään, nuoruudessa?
3. Onko syntymäpaino yhteydessä ruokavalion laatuun, ruoan kulutukseen ja ravintoaineiden saantiin nuoruudessa?

Aiempien tutkimusten pohjalta tässä tutkielmassa asetettiin kolme hypoteesia:

H1: Syntymäpaino on suoraan yhteydessä painoon, pituuteen ja painoindeksiin sekä käänteisesti yhteydessä vyötärönympärykseen nuoruudessa.
H2: Syntymäpaino on käänteisesti yhteydessä kehon rasvamassan määrään ja suoraan yhteydessä kehon rasvattoman massan määrään nuoruudessa.
H3: Syntymäpaino on käänteisesti yhteydessä ruokavalion laatuun ja runsasrasvaiseen ruokavalioon sekä suoraan yhteydessä runsashiilihydraattiseen ruokavalioon sekä energian saantiin nuoruudessa.

AINEISTO JA MENETELMÄT

Tässä pro gradu –tutkielmassa käytetiin Itä-Suomen yliopiston Lasten liikunta ja ravitsemus –tutkimuksen aineistoa. Lasten liikunta ja ravitsemus -tutkimus on vuonna 2007 alkanut pitkäkestoinen liikunta- ja ravitsemusinterventiotutkimus. Vuonna 2007–2009 tutkimuksessa aloitti 512 6–8-vuotiasta lasta, joista on kerätty tietoja takautuvasti. Heitä on seurattu nuoruuteen asti. Seurantamittauksiin osallistui 277 nuorta, joista 126 oli tyttöjä ja 151 poikia. Seurantamittaukset alkoivat tammikuussa 2016 ja päättyivät vuoden 2018 alussa. Syntymäpainotiedot kerättiin takautuvasti Terveyden ja hyvinvoinnin laitoksen ylläpitämästä syntymärekisteristä.

Nykypaino ja –pituus mitattiin kahdeksan vuoden seurantamittauksissa, kun tutkittavat olivat 15–17-vuotiaita. Pituus mitattiin kahteen kertaan ja analyyseissä käytettiin näiden mittausten keskiarvoa. Mikäli kahden mittauksen välinen ero oli yli 0,5 cm, tehtiin vielä kolmas mittaus. Tällöin keskiarvo laskettiin kahden toisiaan lähimpänä olevan mittaustuloksen perusteella. Mittaus tehtiin seinään kiinnitetyllä mittanauhalla. Tutkittavat olivat ilman kenkiä ja pää Frankfortin asennossa. Paino mitattiin kahteen kertaan ja analyyseissä käytetiin näiden keskiarvoa. Painon mittaus tehtiin Inbody 720 -bioimpedanssilaitteeseen kuuluvalla vaa'alla aamulla paastossa, kevyessä vaatetuksessa, virtsarakko tyhjänä. Pituudesta ja painosta laskettiin painoindeksi sekä suomalaisia kasvukäyriä käyttäen iänmukainen painoindeksin keskihajontapistemäärä (body mass index standard deviation score, BMI-SDS). Kehonkoostumuksen rasvan määrä mitattiin kaksienergiaisella röntgenabsorptiometrialla (dual-energy X-ray absorptiometry, DXA).

Seurantamittauksissa selvitettiin ruokavalio 15–17 vuoden iässä. Ruokavalion laatua arvioitiin käyttämällä mittareina Ruokavalion laatuindeksiä (IDQ) sekä Itämeren ruokavalioindeksiä (BSDS). Molemmat mittarit kuvaavat terveyttä edistävän ruokavalion toteutumista suhteessa pohjoismaisiin ja suomalaisiin ravitsemussuosituksiin (Leppälä ym. 2010, Kanerva ym. 2013). IDQ on laskettu ruokavaliota mittaavista frekvenssikyselyistä ja BSDS on laskettu 4-päivän ruokapäiväkirjoista.

Tässä tutkielmassa aineisto analysoitiin ohjelmalla IBS SPSS versio 25.0. Syntymäpainon ja myöhemmän kehonpainon ja kehonkoostumuksen sekä ruokavalion yhteyksien selvittämiseen käytettiin lineaarista regressioanalyysia. Tyttöjen ja poikien eroja aineistossa analysoitiin Studentin T-testillä sekä X^2-testillä. Vakioinnit tehtiin kahteen otteeseen. Mallissa 1 vakioitiin tutkimusryhmä, ikä, sukupuoli ja tarvittaessa myös energiansaanti. Mallissa 2 vakioitiin aiempien lisäksi raskausaika (viikot), äidin ikä synnyttäessä, aikaisempien synnytysten määrä, tupakointi raskauden aikana, painoindeksi ennen raskautta, raskausajan diabetes ja kotitalouden kokonaistulot. Mallissa 1 oli tutkittavia 277 ja Mallissa 2 137.

TULOKSET

Tytöt ja pojat erosivat toisistaan tilastollisesti merkitsevästi syntymäpituudeltaan (cm) (P=0,002*),* sekä seurantatutkimuksien aikana painoltaan (kg) (P < 0,001) ja pituudeltaan (cm) (P< 0,001). Pojat olivat pitempiä syntyessään sekä painavampia ja pitempiä 15–17-vuotiaana. Syntymäpaino ei olut tilastollisesti merkitsevästi yhteydessä painon (kg, BMI, BMI-SDS), vyötärönympäryksen (cm) eikä DXA rasvamassan mittauksissa mallissa 1 (n 277). Syntymäpaino oli suoraan yhteydessä pituuteen (cm ja SDS) mallissa 1, mutta tulos ei ollut merkitsevä mallin 2 vakiointien jälkeen. Mallissa 2 (n 137) syntymäpaino oli käänteisesti yhteydessä vyötärönympärykseen (ß = - 0,117, P = 0,025).

Syntymäpainolla ja ruokavalion kokonaislaadulla ei ollut yhteyttä kummassakaan mallissa, kun mittareina käytettiin IDQ- ja BSDS-indeksejä. Myöskään syntymäpainon ja ravintoaineiden saannissa ei ollut tilastollisesti merkitseviä yhteyksiä. Syntymäpainon ja eri ruokien käytön välillä oli merkitseviä yhteyksiä. Mallissa 1 oli käänteinen yhteys syntymäpainon ja perunan (standardoitu regressiokerroin ß = -0,133, P = 0,038) ja kasviöljypohjaisten margariinien (60–80 %) käytön välillä (ß = -0,196, P = 0,001). Suora yhteys oli syntymäpainon ja voin sekä voi-kasviöljyseosten välillä (ß = 0,171, P = 0,009). Mallissa

2 tulokset olivat samanlaisia, mutta syntymäpainon ja perunan käytön yhteys ei ollut enää merkitsevä. Lisäksi tilastollisesti merkitseviä eroja ilmeni syntymäpainon ja rasvaisen (> 17 %) juuston (ß = 0,307, P = 0,002), punaisen lihan (ß = -0,192, P = 0,047), makkaroiden (ß = -0,287, P = 0,004), kananmunien (ß = -0,230, P = 0,03) ja suolan (ß = -0,236, P = 0,014) käytön välillä.

POHDINTA JA JOHTOPÄÄTÖKSET

Tutkielman tavoitteena oli tutkia syntymäpainon yhteyttä kehonpainoon, pituuteen ja kehonkoostumukseen sekä ruoan kulutukseen, ravintoaineiden saantiin ja ravitsemuksen laatuun. Aiempien tutkimusten perusteella luotiin hypoteesit syntymäpainon ja kehonpainon sekä pituuden suorasta yhteydestä sekä syntymäpainon ja vyötärönympäryksen käänteisestä yhteydestä. Lisäksi syntymäpainon ja ruokavalion laadun välillä oletettiin suoraa yhteyttä, joka näkyisi myös suuripainoisena syntyneiden suurempana energiansaantina ja hiilihydraattipitoisten ruokien suosimisena.

Tässä tutkimuksessa oli merkittäviä heikkouksia, kuten vakiointien jälkeen tapahtunut tutkittavien määrän lasku. Lisäksi erittäin pienipainoisena ja suuripainoisena syntyneiden määrät aineistossa olivat melko pienet, joten tutkimuksessa havainnoitiin lähinnä normaalipainoisena syntyneiden välillä esiintyviä eroja. Vahvuuksina tässä tutkimuksessa oli luotettavista kansallisista arkistoista saatu tieto koskien syntymäpainoa, raskausaikaa ja äidin painoa ennen raskautta. Lisäksi ruuankäyttötiedot oli kerätty sekä 4-päivän ruokapäiväkirjojen sekä ruuan käytön frekvenssikyselyiden pohjalta. Nämä oli yksilöllisesti ohjattu ja tarkistettu jokaisen tutkittavan kanssa. Myös seurantamittaukset pituuden ja painon suhteen kerättiin useampaan kertaan, joista käytettiin mittausten keskiarvoa. DXA-mittauksilla saatiin myös luotettavaa tietoa kehonkoostumuksesta.

Tämän tutkielman heikkoudet tulee ottaa huomioon tulosten tulkinnassa. Tulokset kuitenkin pysyivät tilastollisesti merkitsevinä myös mallin 2 lisävakiointien jälkeen. Aiempi tutkimusnäyttö tukee tuloksia syntymäpainon ja vyötärönympäryksen käänteisestä yhteydestä, mikä osaltaan lisää tuloksen luotettavuutta (Loos ym. 2001, Te Velde ym. 2003, Barbieri ym. 2009, Pereira-Freire ym. 2015).

Tämän tutkielman tulosten mukaan syntymäpaino ei ole yhteydessä painoon, painoindeksiin tai pituuteen nuoruudessa. Tulokset kuitenkin vahvistavat aiempaa näyttöä siitä, että pienipainoisuus syntymässä on yhteydessä suurempaan vyötärönympärykseen, mikä näkyy jo nuoruudessa (Loos ym. 2001, Te Velde ym. 2003, Barbieri ym. 2009, Pereira-Freire ym. 2015). Lisäksi syntymäpaino näyttäisi vaikuttavan ruokailutottumuksiin niin, että pienipainoisena syntyneet käyttävät enemmän runsasrasvaisia margariineja, punaista lihaa, makkaroita, kananmunia ja suolaa, kun taas suuripainoisena syntyneet käyttävät ruokavalioissaan enemmän voita ja voi-kasviöljyseoksia sekä runsasrasvaisia juustoja. Erot eivät kuitenkaan näy ravintoainetasolla tai ruokavalion kokonaislaadussa.

ASSOCIATION OF BIRTH WEIGHT WITH BODY SIZE AND DIETARY FACTORS AMONG ADOLESCENTS

1 INTRODUCTION

Birth weight is an important predictor of infant survival and a key indicator of pregnancy outcomes (Barker et al. 1993). Birth weight is influenced by both fetal characteristics and maternal factors (mediated by the intrauterine environment) where genetic and environmental factors play an important role (Hattersley & Tooke 1999). Maternal and fetal hormonal factors, such as those related to insulin and glucose homeostasis (Hattersley & Tooke 1999), placental dysfunction or maternal diseases, such as gestational diabetes mellitus (Gillman et al. 2003), and nutritional status during pregnancy have an impact on birth weight (Mäkikallio 2019). These factors might lead to accelerated or decelerated fetal growth during pregnancy and thus increase the risk to be born with high or low birth weight. Differences in birth weight have been found to be associated with later overweight and obesity (Gillman et al. 2013, Evensen et al. 2017, Boone-Heinonen et al. 2018), and with higher susceptibility to lifestyle diseases, such as type 2 diabetes and coronary artery disease in later life (Boone-Heinonen et al. 2018, Knop et al. 2018, Zanetti et al. 2018).

It is hypothesized that some of these associations might be explained by fetal programming (Barker 2007, Vickers 2014) or dietary factors (Bamfo & Odibo 2011, Mäkikallio 2019, Sharma et al. 2016, WHO 1995). According to the developmental origins of health and disease (DOHaD) hypothesis (Gillman 2005), the possible adaptations in the response to a disturbed or adverse intrauterine environment made by a developing fetus, are reflected directly to birth weight. Since insulin and glucose metabolism have an important prenatal role in fetal growth and development, the disturbances during this developmental period in the womb can be partly measured by assessing birth weight (Barker 1990, Barker et al. 1993, Hattersslay & Tooke 1999).

The association between birth weight and later body weight seems to be visible as early as in preschool and school aged children (Apfelbacher et al. 2008, Kitsantas & Gaffney 2010, Janjua et al.

2012, Parker et al. 2012, Heppe et al. 2013). Especially children born with high birth weight tend to have higher risk of overweight and obesity during their childhood when compared to children born with low or normal birth weight (Eriksson et al. 2003, Reilly et al. 2005, Li et al. 2007, Apfelbacher et al. 2008, Janjua et al 2012 Parker et al. 2012, Heppe et al. 2013). Previous studies suggest that this association remains across the life span and the risk of being overweight or obese in adulthood seems to follow children and adolescents born with higher birth weight in later life (Field et al. 2005, Simmonds et al. 2016). Interestingly, earlier studies have found a strong association of early growth rebound or rapid growth with overweight, obesity and chronic diseases (Eriksson et al. 2003, Monteiro et al. 2003, Oddy et al. 2004, Toschke et al. 2004, Barker et al. 2005, Reilly et al. 2005, Birbilis et al. 2012, Heppe et al. 2013, Sacco et al. 2013). This early growth rebound has been seen especially among infants born with low birth weight or as small for gestational age (Karlberg & Albertsson-Wikland 1995, Taal et al. 2013).

When assessing the development of overweight and obesity related chronic diseases, it is important to take dietary factors into account (Ignarro et al.2007). The association of birth weight with dietary factors has not been largely studied, but the existing studies do point out some dietary differences depending on birth weight category. Low birth weight seems to be associated with higher fat intake (Perälä et al. 2012). Interestingly, this association has also been found among adults that were exposed to famine in early stages of gestation (Lussana et al. 2008). Similar results have been reported for higher fat intake among young children (Stafford & Lucas 1998, Bischoff et al. 2018). Moreover, some previous studies have suggested that birth weight might predict the intake of saturated fats (Shultis et al. 2005, Doornweerd et al. 2017). However, studies concentrating on the associations of birth weight and dietary factors still remain scarce and inconsistent in their results. Furthermore, there are indications that high birth weight might associate with higher carbohydrate intake among adults (Perälä et al. 2012), yet severe fetal growth restriction seems to have a similar outcome on young women (Barbieri et al. 2009). Higher birth weight has also been linked to lower berry and fruit consumption and lower fiber intake among children while, in contrast, the consumption of sucrose and overall energy intake was higher (Eloranta et al. 2018). It has been suggested that fetal programming can influence appetite and taste preferences, and therefore have an impact on later dietary preferences (Stein et al. 2006, Ayres et al. 2012). However, the associations between birth weight, later body weight and overall diet quality in adolescence have yet to be studied more

intensively to fully understand their relationship. All in all, previous studies suggest that early life might be one of the key periods involved in priming the later dietary habits, body weight trajectories and health risks associated with them.

To address this hypothesis, the aim of the present thesis was to study the associations between birth weight and later body size and dietary factors among 15 to 17-year-old Finnish adolescents. Therefore, we investigated the association of birth weight with later body weight, height and body composition and dietary factors, such as overall diet quality, food consumption and nutrients. The present study was based on the 8-year follow-up data from the Physical Activity and Nutrition in Children (PANIC) Study.

2 LITERATURE REVIEW

2.1 Public health point of view of overweight and obesity

Normal weight is associated with a healthy cardiometabolic risk profile and a low risk of type 2 diabetes and cardiovascular disease (Must et al. 1999). However, overweight (body mass index (BMI ≥25 – <30 kg/m^2) and obesity (BMI ≥ 30 kg/m^2) are increasing worldwide, and act as substantial risk factor for chronic health conditions and contribute to the burden of higher health care costs (Must et al. 1999, Atella et al. 2015, THL 2016). Based on the Finnish School Health Survey (2017) 18.9 % of 8th and 9th graders, 15.6 % of high school students and 26.2 % of vocational school students were overweight or obese in Finland (THL 2017). In addition, it has been suggested that overweight in childhood or adolescence increase the risk of overweight or obesity in adulthood (Field et al. 2005, Simmonds et al. 2016). In fact, risk of obesity in adulthood increases 5-folds among obese children and adolescents compared to those with normal weight (Simmonds et al. 2016).

Currently, public health strategies that aim to prevent obesity and metabolic complications, such as type 2 diabetes, focus on promoting healthy lifestyle and weight management (WHO 2016b). However, the effects of lifestyle behavior and weight loss on type 2 diabetes risk may vary between individuals depending on genetic variation (Tuomilehto et al. 2001, Knlower et al. 2002). Moreover, it has been demonstrated that having normal body weight is crucial in the prevention of type 2 diabetes, regardless of genetic predisposition (Schnurr et al. 2020), underlining the importance of healthy weight management by lifestyle interventions across the lifespan. To plan and implement effective lifestyle interventions for obese children and adolescents, there is a need to understand the mechanisms behind the pathophysiology that seems to be affected by many different lifestyle factors, such as diet and physical activity (Lin & Morrison 2002, Birbilis et al. 2012).

Various socioeconomical, genetic and environmental factors are known to have an effect on weight development (Kitsantas & Gaffney 2010, Birbilis et al. 2012, Janjua et al. 2012, Seyednasrollah et al. 2017, Woo Baidal et al. 2017). As far as socioeconomical status is concerned, low level of parental education (for less than 12 years) seems to be inversely associated with both birth weight (Janjua et al. 2012, Van den Berg et al. 2013) and childhood body weight (Birbilis et al. 2012). Socioeconomic status,

where especially the level of parental education, has been reported to be inversely associated with consumption of energy-dense foods (Birbilis et al. 2012). Parents who have a low socioeconomic status are also more likely to smoke and less likely to breastfeed, which are also associated with higher weight gain in children (Van den Berg et al. 2013).

2.2 Factors impacting weight development and body size

Previous studies have reported an association between birth weight and body weight later in life (Law et al. 1992, Eriksson et al. 2003, Monteiro et al. 2003, Barker et al. 2005, Birbilis et al. 2012, Janjua et al. 2012, Heppe et al. 2013), however, not all results have been consistent (Evensen et al. 2018). Birth weight has been determined as an independent risk factor for development of chronic diseases, such as type 2 diabetes mellitus and coronary heart disease later in life (Must et al. 1999, Andersen et al. 2010, Boone-Heinonen et al. 2018, Knop et al. 2018). Interestingly, both higher and lower birth weight seem to be a risk of developing chronic diseases (Andersen et al. 2010, Boone-Heinonen et al. 2018, Knop et al. 2018). Recently, a Mendelian Randomization study showed that birth weight has also an effect on body composition by associating positively with muscle mass and body fat (Liu et al. 2019). Here, a higher birth weight increased both fat-free mass and fat mass, and it was also indicated that a low fat-free mass might explain why lower birth weight is increasing the type 2 diabetes risk.

Identifying children who have increased risk of being overweight or obese and are in an increased risk of developing lifestyle-related diseases is essential (Oken & Gillman 2003, Magnussen et al. 2010, Viitasalo et al. 2016). Early prediction of individual susceptibility to lifestyle-associated diseases is crucial to reduce health care costs and prevent later disease burden (THL 2016). Noteworthy, it is well established that lifestyle interventions aiming to reduce lifestyle-related diseases have the most beneficial impact when implemented in childhood or adolescence compared to implementations only in adulthood (Magnussen et al. 2010, Viitasalo et al. 2016). Furthermore, obesity and unfavourable lifestyle have been shown to be associated with increased risk of type 2 diabetes regardless of genetic predisposition. Interestingly, even among individuals with low genetic risk for type 2 diabetes and who has a favourable lifestyle, obesity was associated with a >8-fold risk of type 2 diabetes compared with normal-weight individuals in the same genetic risk and lifestyle (Schnurr et al. 2020). However, further

studies on identifying the individuals with higher risk for developing other chronic diseases, such as cardiovascular disease are highly required to design proper prevention strategies.

Puberty is an important factor that needs to be considered when assessing body size, including body weight, height, BMI and body composition, in adolescence. It is known that the onset of puberty differs between boys and girls (Siervogel et al. 2000). In addition, puberty has a differential effect on the body composition depending on the gender. The overall fat mass increases in adolescence in both genders, but among girls the fat mass seems to increase at earlier age compared to boys. In boys, the onset of puberty increases fat mass and fat-free mass simultaneously, and it grows steadily between the ages from 8 to18 approximately, with a more rapid growth around 12–15 years of age. However, in girls the overall growth of fat-free mass during puberty is not as big as in boys. In addition, the increase in fat-free mass lasts approximately only until the age of 15 in girls. Age at menarche (the first occurrence of menstruation) should also be considered when assessing body composition in girls. This is due to repeatedly reported inverse association between the age at menarche and BMI and adiposity (Van Lenthe et al. 1996, Labayen et al. 2009a). Moreover, it is important to recognize that in both genders, children with higher prepubertal BMI seem to reach puberty in earlier stage than normal weight children (De Leonibus et al. 2014), and early onset of menarche seems to be associated with an unfavorable body composition (Labayen et al. 2009a). It has been hypothesized that this association might be explained due to a fetal programming effect.

2.3 Birth weight

Duration of a normal pregnancy is approximately 40 weeks (Ekholm 2019). Pregnancies and infants are defined preterm if the birth occurs before the week 37, whereas infants born after 41+6 weeks of gestation are defined as post-term (Timonen 2019). The birth weight classifications are presented in detail in Table 1.

Table 1. Classifications for birth weight. (Delpapa *et al.* 1991, Sharma *et al.* 2016, Laatio & Nuutila 2019)

Definition	Birth weight (g) or (%)
Low birth weight	< 2500 g
Normal birth weight	2500–3999 g
High birth weight	≥ 4000 g
Large for gestational age	> 10 %*
Small for gestational age	< 10 %*
Slow fetal growth	- 2 SD
Fast fetal growth	+ 2 SD

*compared with infants born in the same week of gestation.

An infant is considered as low birth weight when birth weight is below 2500 grams (Laatio & Nuutila 2019), whereas if birth weight is over 4000 grams, it is classified as high birth weight (Delpapa *et al.* 1991). Thus, a normal birth weight ranges from 2500 g to <4000 g in full term pregnancy, defined as 40 weeks of gestation. As seen in Table 1 weight standards are also set according to gestational age. This means that the birth weight is compared with the birth weight of infants born in the same week of gestation. Therefore, preterm infants born with low birth weight might still have an appropriate birth weight according to gestational age (Sharma *et al.* 2016). A definition of small for gestational age is used for infants 10 % of lighter weight (Mäkikallio 2019) and a definition large for gestational age when the infant is 10 % heavier than others born during the same week of gestation (Birbilis *et al.* 2012). Furthermore, growing curves are used largely to measure children's normal growth based on weight and height development of the age group. Same definitions are used for newborns, where a value less than two from the standard deviation score (-2 SD) is defined as slow fetal growth and may lead to small gestational age and low birth weight (Erkkola 2011). Value two or more above standard deviation (-2 SD) is therefore defined as faster fetal growth and may lead to large for gestational age or high birth weight.

Gestational age plays a crucial role in determination of final birth weight. The most important period for fetal growth, and thus development of height and body mass starts from 29th week of gestation (Sankilampi *et al*. 2013). From the 29th week onwards, the infant grows rapidly in size (both fetal

height and body mass), slowing down slightly towards the end of gestation. Therefore, being born preterm increases the risk for low birth weight (Laatio & Nuutila 2019), while post-term infants tend to be heavier compared to infants born between the 37 and 40 weeks of gestation (Timonen 2019).

In addition to the duration of gestation, there are many genetic and prenatal factors that play an important role in development of birth weight. Genetic factors can explain as much as 50 % of the infant's birth weight (Dunkel 2010). In addition, it is hard to distinguish between fetal and maternal effects on birth weight, due to the correlation between fetal and maternal genotypes and confounding by environmental factors or maternal socioeconomic status, where unmeasured lifestyle and health-related factors have an important role (Lawlor *et al.* 2008, Davies *et al.* 2018). In addition, parental body weight and body composition as well as dietary factors of the mother (Erkkola 2011, Mäkikallio 2019) and maternal weight gain during pregnancy have an impact on birth weight (Bamfo & Odibo 2011, Sharma *et al.* 2016, WHO 1995). Furthermore, offspring birth weight has been found to be inversely related to maternal insulin resistance in late adulthood, regardless of the association of glucose intolerance during pregnancy with heavier offspring birth weight (Lawlor *et al.* 2002).

Malnutrition and lower than recommended weight gain during pregnancy can cause intrauterine growth restriction, and lead to low birth weight (Bomfo & Odibo 2011). World Health Organization (WHO) (2016a) recommendations for maternal weight gain during pregnancy is set between 5.0 and 18.0 kg, depending on the starting weight prior to pregnancy. The previous studies emphasize that higher than recommended weight gain during pregnancy may lead to higher birth weight (Bamfo & Odibo 2011, Sharma *et al.* 2016, WHO 1995). Based on the previous studies, prepregnancy weight should always be considered when investigating the associations of weight gain during pregnancy with birth weight (Bamfo & Odibo 2011, Sharma *et al.* 2016, WHO 1995). Moreover, in mothers with prepregnancy body weight below BMI of 40 kg/m^2, losing weight during pregnancy is increasing the risk of being born as small for gestational age, whereas in mothers with BMI > 40 kg/m^2 this risk has not been observed (Beyerlein *et al.* 2010). In addition, the risk of preterm birth is increased in overweight or obese mothers that either lost weight or gained less weight than is recommended. Similar outcomes were reported when weight gain recommendations were not met among mothers with prepregnancy BMI below 25 kg/m^2 (classified as normal weight or underweight).

During pregnancy, the placental functioning and maternal hormonal factors are influencing fetal growth throughout the gestation (Dunkel 2010, Mäkikallio 2019). The main physiological functions of the placenta are the transfer of nutrients and oxygen to the developing fetus and the removal of waste products from the fetus (Mäkikallio 2019). In other words, the fetal development is affected by the adequate quantity and quality of nutritional supply as well as by the ability of placenta to transport these substances to the fetus (Duttaroy & Basak 2016). Causes of insufficient functionality of placenta are diverse but some maternal diseases are known to have an impact on placenta (Mäkikallio 2019). The development of the placenta is influenced by the supply of nutrients (Duttaroy & Basak 2016) and different sizes and shapes of placenta are associated with different health outcomes (Eriksson *et al.* 2000, Harding *et al.* 2001, Barker *et al.* 2010, Kajantie *et al.* 2010, Eriksson *et al.* 2011). Poorly managed diseases, such as diabetes mellitus, high blood pressure or existing deformities of the womb can cause fetal growth restriction, which should not be confused with intrauterine growth restriction (Bomfo & Odibo 2011, Sharma *et al.* 2016). However, both intrauterine growth restriction and fetal growth restriction can lead to low birth weight and can be caused by similar risk factors. Risk factors for lower birth weight are presented in detail in Table 2.

Table 2. Risk factors for low birth weight (Duttaroy & Basak 2016, Mäkikallio 2019).

Risk factors for low birth weight	
Related to mother:	**Risk factors**
Exposure to toxic substances	Smoking of cigarettes, alcohol, drugs.
Mother's diseases	Diabetes, atherosclerosis, anaemia, hypertension.
Other maternal factors influencing pregnancy	Age, overweight and obesity, multiple pregnancy, pre-eclampsia, malnutrition, very excessive physical activity.
Related to placenta	Detached placenta, placental haemorrhage.
Related to fetus	Chromosomal abnormalities, syndromes, metabolic disorders, infections.

As shown in Table 2, active or passive smoking, alcohol consumption or misusage of drugs are found to increase the risk of fetal growth restriction and therefore lead to low birth weight (Bamfo & Odibo 2011, Sharma *et al.* 2016). In Europe, roughly 10 % of pregnant mothers smoke during pregnancy

(Lange *et al.* 2018). Some components of tobacco, such as nicotine and some heavy metals (cadmium, lead, methylmercury), are known to pass through placenta to the fetus (Barr *et al* 2007, Griffiths & Campbell 2014), and to cause intrauterine growth restriction leading to decrease in birth weight (Duttaroy & Basak 2016).

Previously, a causal association between maternal higher gestational glucose levels and higher offspring birth weight has been reported (Tyrrell *et al.* 2016). One possible explanation to this is that higher maternal gestational glucose levels are a result of the insufficient response to gestational insulin resistance by beta cells (Freathy *et al.* 2010, Hayes *et al.* 2013). This leads eventually to increased trans-placental perfusion, which then in response stimulates fetal insulin secretion. Because insulin acts as the most important growth promoting factor during the gestation, it also leads to higher birth weight as has been also suggested by the Pedersen hypothesis (Pedersen 1968). In contract, a reduced fetal insulin secretion follows also a higher fetal insulin resistance, which leads to lower impact of the insulin on the fetus and thus lower birth weight, as suggested by fetal insulin hypothesis (Hattersley & Tooke 1999). In addition, fetal genetic effects link lower birth weight with reduced insulin secretion, and eventually with higher risk of type 2 diabetes in adulthood. Furthermore, fetal growth problems may trigger an abnormal fetal secretion of a range of hormones, such as leptin, insulin growth factor-1, and glucocorticoids that may influence overall development and predispose to later disease (Sharma *et al.* 2016).

Glucose acts as one of the main energy sources for a growing fetus (Vääräsmäki & Kaaja 2019). Normally, glucose levels are only ~0.5–1.0 mmol/l lower in the fetus than in mother, and therefore maternal hyperglycaemia causes hyperglycaemia also in the fetus and might in the end result in fetal macrosomia (high birth weight). However, unlike glucose, insulin is not transported through the placenta, and thus fetus must produce insulin by itself. Lower production levels of insulin can cause growth restriction in the fetus and lead to low birth weight (Metzger *et al.* 2008, Landon *et al.* 2011).

Maternal factors, such as age, prepregnancy BMI and weight gain during pregnancy, as well as maternal diseases and substance abuse are all influencing birth weight. Some studies have also suggested that maternal age during pregnancy might affect offspring health (Fall *et al.* 2015). It has been well reported that advanced maternal age is associated with fetal macrosomia and with being

born as large for gestational age (Koo *et al.* 2012, Kenny *et al.* 2013, Fall *et al.* 2015). Morevore, a prospective study by Fall *et al.* (2015) reported an association between young maternal age (≤19 years old) and the increased risk of preterm birth and being born with low birth weight.

2.4 Birth weight and later health

Several studies have linked low birth weight with increased risk of insulin resistance, trunk accumulation of fat, metabolic syndrome, and cardiovascular diseases in adulthood, and of these metabolic syndrome and insulin resistance have also been observed in offspring born small for gestational age throughout childhood and later life (Barker *et al.* 2005, Jaquet *et al.* 2000). Low birth weight has also been linked to impaired glucose tolerance, and individuals with both low birth weight and obesity later in life seem to have the most disadvantageous glucose tolerance of all (Jones & Ozanne 2009, Ornoy 2011).

At the opposite extreme, high birth weight and its effect on later insulin resistance and cardiovascular diseases is more arguable. Some studies have linked high birth weight with obesity yet lower risk of coronary heart disease and type 2 diabetes, while others have found an association with increased risk for developing metabolic syndrome in offspring of mothers with gestational diabetes (Vohr *et al.* 1980, Barker *et al.* 1989, Boney *et al.* 2005, Schaefer-Graf *et al.* 2005, Eriksson 2006, Ornoy 2011). Offspring of obese mothers have also been shown to be at greater risk of developing metabolic syndrome, suggesting that fetuses of obese mothers, who do not fulfill the clinical criteria for gestational diabetes, may still be exposed to intrauterine factors that lead to impaired fetal metabolic programming and thus, affect fetal growth and postnatal outcomes (Boney *et al.* 2005).

Both low and high birth weight are associated with several health-related issues later in life, which might be explained by epigenetic fetal programming (Barker 2007, Vickers 2014). According to epigenetic programming theory, the environment of the growing fetus is giving clues of the outside world and therefore the epigenetics are modified. These changes can be long lasting and explain some of the associations between birth weight and later health outcomes.

Exposure to low or high nutrition levels during fetal life is associated with increased risk of obesity, insulin resistance and type 2 diabetes later in life (Parsons *et al.* 2001, Armitage *et al.* 2004). As mentioned in chapter 2.1, there are many factors affecting the placenta and its' ability to transport essential substances ensuring normal growth of the fetus. It is hypothesized that the placenta can adapt to changing environment and thus promote fetal survival when needed (Duttaroy & Basak 2016). However, it seems that the adaptation might indeed promote the offspring survival and yet increase the risk of developing metabolic syndrome later in life.

When investigating the risk of developing diseases, the association of birth weight seems to follow U-shape (Boone-Heinonen *et al.* 2018). However, there is some controversy around the effects of birth weight. Knop *et al.* (2018) found a J-shaped association, where high birth weight seemed to be a stronger indicator of developing diseases than low birth weight. In contrary to this, Andersen *et al.* (2010) studied Danish and Finnish populations and found that birth weight below 3400 g was associated with increased risk of chronic diseases, whereas infants born with over 4000 g had no risk of developing diseases in adult life. Boone-Heinonen *et al.* (2018) showed an BMI-independent pathway, where higher birth weight was associated with higher odds of prediabetes in women, but not in men. In addition, higher birth weight predicted faster increase in BMI in adolescence and having higher BMI in general. Based on these findings, it was suggested that especially in girls, slowing BMI gain is critical for diabetes prevention (Boone-Heinonen *et al.* 2018). In addition, offspring of both younger and advanced age mothers seem to have a higher adult fasting glucose concentration (Fall *et al.* 2015).

There is a strong evidence supporting the association between low birth weight and diseases later in life (Andersen *et al.* 2010, Boone-Heinonen *et al.* 2018, Knop *et al.* 2018). One hypothesis explaining this association is that low energy intake during pregnancy might affect development of fetal fat cells in order to favor more essential organs (Padoan *et al.* 2004, McMillen & Robinson 2005). When the child is born to an environment where energy supplies are no longer scarce, the fat deposition ensues in the visceral adipose tissue (Crescenzo *et al.* 2003, Ibanez *et al.* 2006). In other words, the body starts to compensate by storing more visceral body fat, which again is known to increase the risk of lifestyle related diseases. The accumulation of visceral body fat might lead to insulin resistance and therefore to development of type 2 diabetes (Jaquet *et al.* 2000). One study also suggests a possibility that high

birth weight together with accelerated weight gain in the first 2 years of life could program insulin sensitivity and adipose tissue metabolism in a way that children and adolescents could be obese but metabolically healthy (Bouhours-Nouet *et al.* 2008). These findings can explain why low birth weight together with early rapid weight gain or weight rebound in childhood has been associated with increased risk of metabolic and cardiovascular diseases later in life (Barker *et al.* 2005, Andersen *et al.* 2010, Knop *et al.* 2018).

2.5 Association of birth weight with body weight later in life

When observing preschool children or children starting school, the association between birth weight and childhood body weight has been shown (Apfelbacher *et al.* 2008, Kitsantas & Gaffney 2010, Janjua *et al.* 2012, Parker *et al.* 2012, Heppe *et al.* 2013). This means that overweight or obese children are more likely to have been born with higher than normal birth weight (Eriksson *et al.* 2003, Reilly *et al.* 2005, Li *et al.* 2007, Apfelbacher *et al.* 2008, Janjua *et al* 2012 Parker *et al.* 2012, Heppe *et al.* 2013). More specifically, birth weight over ≥ 3500 grams (Apfelbacher *et al.* 2008) or ≥ 4000 grams is increasing the risk of overweight and obesity in childhood (Li *et al.* 2007, Apfelbacher *et al.* 2008, Kitsantas & Gaffney 2010).

In adolescence, the association between birth weight and body weight seems to follow similar pattern as that observed in childhood. Most studies have found an association between birth weight and body weight in adolescence (Eriksson *et al.* 2003, Monteiro *et al.* 2003, Araujo *et al.* 2009, Kleiser *et al.* 2009, Gillman *et al.* 2013, Evensen *et al.* 2017, Boone-Heinonen *et al.* 2018), although some have found the association to be rather modest (Evensen *et al.* 2017). In addition, birth weight seems not to affect only body weight but also weight gain in adolescence, which means that those with higher birth weight seem to have accelerated weight gain also in their youth (Boone-Heinonen *et al.* 2018)**.** One study also found that large for gestational age infants were more likely to become obese in adolescence, but not overweight (Birbilis *et al.* 2012). However, this association disappeared when adjusted for dietary energy intake, which suggests that dietary factors might have a bigger role in adolescent obesity over birth weight.

While some studies have indicated that both low and high birth weight are linked to obesity, individuals with low birth weight seem more susceptible to the metabolic complications of obesity than those with high birth weight (Jones & Ozanne 2009, Ornoy 2011, Sharma *et al.* 2016). Even though the overall risk of developing diseases seems to follow U-shape pattern in birth weight, there is no association between low birth weight and higher BMI in childhood (O'Callaghan *et al.* 1997, Apfelbacher *et al.* 2008, Li *et al.* 2007, Parker *et al.* 2012, Sacco *et al.* 2013) nor in adolescence (Monteiro *et al.* 2003, Araujo *et al.* 2009). Although, most of the studies have had a very small sample size of low birth weight infants which makes it difficult to set reliable conclusions. However, some prior studies have reported that infants with intrauterine growth problems, especially the ones born as small for gestational age, are prone to early adiposity rebound and later obesity (Ornoy 2011, Galjaard *et al.* 2013).

Current studies, focusing mostly on postnatal growth factors, state that postnatal growth patterns and timing of the adiposity rebound during childhood are linked to obesity in adulthood (Araujo *et al.* 2016, Bouhours-Nouet *et al.* 2008). Previous studies have demonstrated that children with low birth weight, who undergo more rapid growth in early childhood or infancy, might experience catch-up growth or even pass those born heavier (Dos Santos Silva *et al.* 2002, Hack *et al.* 2003). Rapid growth or weight rebound in early childhood or infancy seems to increase the risk of overweight and obesity in adolescence (Monteiro *et al.* 2003, Birbilis *et al.* 2012). Interesting is that infants small for gestational age seem to have more accelerated growth, reported as rebound or catch-up growth, during first two years of life while infants large for gestational age are more likely to experience decelerated growth (Taal *et al.* 2013). This might explain why low birth weight alone does not lead to overweight or obesity in all cases, but together with rapid growth the outcome is very different. While early rapid growth seems to have a great impact on later health outcomes, it is still unknown in which time period during childhood rapid growth increases the risk of overweight and obesity the most.

One study showed that the period of rapid growth occurring between 20 months and 43 months of age was associated with overweight, whereas accelerated weight gain before 20 months of age was associated with both overweight and obesity (Monteiro *et al.* 2003), suggesting that the risk was higher the earlier the period of rapid growth occurred. Other studies found that rapid growth during first 6 months of life was associated with both overweight and obesity (Birbilis *et al.* 2012) and higher

adiposity risk in adolescence (Oddy *et al.* 2004). Similarly, rapid growth during the first 24 months (Toschke *et al.* 2004) and in the first 12 months of life (Reilly *et al.* 2005, Heppe *et al.* 2013) have been associated with overweight or obesity already at the age of school entry.

As mentioned before, even though low birth weight was not associated with body weight in adolescence in all cases, growth rebound in low birth weight infants has been reported to increase the risk for higher than normal weight in adolescence (Monteiro *et al.* 2003). Many studies also linked rapid growth during infancy and early childhood independently to higher weight in adolescence (Eriksson *et al.* 2003, Monteiro *et al.* 2003, Oddy *et al.* 2004).

Only some differences between genders have been demonstrated regarding the association between birth weight and later body weight. Monteiro *et al.* (2003) found that boys with birth weight of ≥ 4000 g had a greater risk of overweight and obesity in adolescence, while girls appeared to have only increased risk for overweight.

To conclude, birth weight seems to be associated with body weight in childhood and adolescence, and this association of birth weight with body weight seems to differ between the genders. Rapid growth and growth rebound during early childhood are increasing the risk of overweight and obesity among individuals born with either with high or low birth weight. It is still unknown at which time period the more intense rapid growth increases the risk of overweight and obesity the most. However, it is important to notice that these studies did not investigate the differences in body composition, but only body weight or BMI as such.

2.6 Associations of birth weight with body height and body composition later in life

Birth weight has been directly associated with height in both genders (Pietiläinen *et al.* 2002, Chomtho *et al.* 2008, Jelenković *et al.* 2018). This association can already be seen in young, preschool aged children (Elia *et al.* 2007, Chomtho 2008) and in later childhood and adolescence (Jelenković *et al.* 2018). In men, a twin study reported that height increased 3.3 cm per one kilogram increase in birth weight (Loos *et al.* 2001). In adolescence, it has been reported that girls with higher birth weight grew faster before menarche and tend to be taller upon adulthood compared to girls born with lower birth

weight (Gale *et al.* 2001, Loos *et al.* 2002, Sachdev *et al.* 2005, Labayen *et al.* 2006, Adair 2007, Workman & Kelly 2017). Previous studies have demonstrated that children with low birth weight, who undergo more rapid growth in early childhood or infancy might experience catch-up-growth or even pass those born heavier (Dos Santos Silva *et al.* 2002, Hack *et al.* 2003). However, the association of birth weight with height in girls seems to be visible only until early childhood and thereafter the catch-up growth in height among girls is regardless of birth weight category (Casey *et al.* 1991, Knops *et al.* 2005).

Children born small or large for gestational age seem to be associated with fat-free mass in childhood (Biosca *et al.* 2011). Moreover, small for gestational age seems to be associated with higher fat mass compared to appropriate and large for gestational age, whereas no significant association was reported in fat mass in children born large for gestational age (Biosca *et al.* 2011). However, study group of Pereira-Freire *et al.* (2015) did not find any such association in birth weight with fat mass or fat-free mass. In addition, having higher fat mass, low birth weight seems to be associated with visceral fat, specifically (Loos *et al.* 2001, Rasmussen *et al.* 2005, De Luca Rolfe *et al.* 2010). This distribution of fat favoring visceral adiposity has been reported in both adults and adolescents. In addition, those born with low birth weight seem to have a higher waist circumference (Pereira-Freire *et al.* 2015). Low birth weight has also been associated with higher waist-to-hip ratio and higher subcutaneous fat mass in adult men and women (Law *et al.* 1992, Te Velde *et al.* 2003, Berbieri *et al.* 2009) and higher waist circumference in adult women (Te Velde *et al.* 2003, Barbieri *et al.* 2009).

Interestingly, also high birth weight seems to be associated with an increased risk for higher waist circumference as early as in 5–8-year-old children and therefore increase the risk for obesity and overweight later in life (Sacco *et al.* 2013, Pereira-Freire *et al.* 2015). When assessing body composition in adolescence, some have found high birth weight to be directly associated with higher fat-free mass in both genders (Evensen *et al.* 2018) but some reported the association only in late childhood, among mid-adolescence-aged boys (Chomtho *et al.* 2008). There seemed to be no associations in fat mass or truncal fat mass in either sex (Chomtho *et al.* 2008). Some have found an association between high birth weight and fat mass to be visible only in girls (Evensen *et al.* 2018). In addition, the study group of Boone-Heinonen *et al.* (2018) reported that girls born with high birth weight had a higher risk for higher waist circumference (> 80 cm) in adolescence, but the same outcome was not identified

in boys (Boone-Heinonen *et al.* 2018). One study researched twin men between 18–34 years of age and found that those born with higher birth weight than their twins were heavier as adults but had lower waist-to-hip ratio and less subcutaneous fat and more fat-free mass than the lighter twin (Loos *et al.* 2001). However, not all have managed to find differences in body composition based on gender (Sacco *et al.* 2013, Pereira-Freire *et al.* 2015).

To conclude, birth weight is associated with height in both genders, although in girls, the onset of menarche seems to slow and eventually stunt the growth in height. Low birth weight seems to increase the risk for higher fat mass and lower fat-free mass. In addition, those with lower birth weight seem to have bigger visceral and subcutaneous fat mass, and in females, also higher waist circumference. Waist circumference seems to be higher also in high birth weight children, compared to those born with normal birth weight. However, offspring born with high birth weight seem to have a healthier waist-to-hip ratio, less subcutaneous and visceral fat mass and a higher fat-free mass than those born with low birth weight.

2.7 Association of birth weight with dietary factors later in life

Dietary factors have a role in developing overweight and obesity related chronic diseases, such as type 2 diabetes and cardiovascular diseases (Ignarro *et al.* 2007). Because birth weight seems also to be associated with later disease outcomes (Andersen *et al.* 2010, Boone-Heinonen *et al.* 2018, Knop *et al.* 2018) it has been hypothesized that fetal environment might affect dietary choices also later in life (Stein *et al.* 2006, Ayres *et al.* 2012). However, research on the associations of birth weight with dietary factors are limited and somewhat contradicting. There is some evidence suggesting that birth weight could be giving some reference to the future dietary preferences (Kaseva *et al.* 2013, Doornweerd *et al.* 2017, Eloranta *et al.* 2018). In fact, prior studies implement that both low and high birth weight might be associated with unhealthier dietary choices, but with some contradicting results (Lussana *et al.* 2008, Perälä *et al.* 2012, Kaseva *et al.* 2013, Doornweerd *et al.* 2017, Eloranta *et al.* 2018). Also, there are some possible differences between the genders. In late adolescence and young adulthood, daily energy intake is reported to be higher in males than females (Oluwagbemigun *et al.* 2019) and in 3-year-olds, girls have shown higher ability to delay a response to an eating impulse, than boys (Silveira *et al.* 2012).

2.7.1 Birth weight and nutrient intake

Starting with energy intake, those born with low birth weight seem to have increased overall energy intake in adolescence and young adulthood (Doornweerd et al. 2017, Bischoff et al. 2018). Also, high birth weight infants seem to have a greater energy intake in childhood (Eloranta et al. 2018). Offspring of mothers exposed to famine in early gestation, are more likely to consume a higher-fat diet as adults (Lussana *et al.* 2008). It seems that low birth weight leads to increased overall fat intake in children (Stafford & Lucas 1998, Bischoff *et al.* 2018). Same outcome has also been reported in adults (Perälä *et al.* 2012). This association, however, seems to be reported more among boys (Bischoff *et al.* 2018). In girls, this association seems to follow an opposite pattern, with association between birth weight and fat intake.

Only few studies have investigated the association of birth weight and saturated fat intake and have indicated that low birth weight infants seem to have especially higher saturated fat intake (Shultis *et al.* 2005, Doornweerd *et al.* 2017). Perälä *et al.* (2012) was unable to find the association between birth weight and later intake of saturated fats in Finnish adults, between ages 56–70 years old. However, Shultis *et al.* (2005) noticed that the association of birth weight and saturated fat intake was visible only in early childhood and the association seemed to disappear at the age of seven. Although there is some contradicting result, where low birth weight infants had a higher saturated fat intake still as young adults, aged from 13 to 22 years (Doornweerd *et al.* 2017).

When investigating protein and carbohydrates, the results seem controversy. In boys, birth weight has not been reported as a predictor of protein and carbohydrate intake (Bischoff *et al.* 2018), and yet in some studies, low birth weight has been associated with lower carbohydrate and fiber intake (Perälä *et al.* 2012, Doornweerd *et al.* 2017). In study by Lussana *et al.* (2008), there was no significant difference in the association between birth weight and carbohydrate intake between genders, when studying those exposed to famine. At the same time, there are several other studies reporting that low birth weight girls and women seem to have increased preferences for carbohydrates (Breen *et al.* 2006, Escobar *et al.* 2014, Tam *et al.* 2015). Also, young girls and women born with intrauterine growth restriction seem to have increased impulsivity towards sweet food rewards compared to normal

weight counterparts without intrauterine growth restriction (Barbieri *et al.* 2009, Silveira *et al.* 2012). In contrary, lower birth weight has also been associated with preferences to salty taste (Stein *et al.* 2006).

High birth weight has been mostly associated with higher intake of carbohydrates (Perälä *et al.* 2012) and sucrose intake (Eloranta *et al.* 2018). Perälä *et al.* (2012) reported that high birth weight infants were more likely to have a higher carbohydrate, sucrose, fructose and fiber consumption in adulthood. Study group of Eloranta *et al.* (2018) also reported that high birth weight was associated with higher intake of sucrose in children 6–8 years old, but lower fiber intake.

To conclude, birth weight seems to be associated with nutrient intake in a gender-specific manner, although not all studies have focused on nor reported any gender-based differences. When born to non-food-restricted environment, low birth weight infants have probably a higher energy intake during adolescence and early adulthood, where increased percentage of energy intake comes from fat or carbohydrate sources. So far, it seems that in boys low birth weight increases higher fat intake, and some have reported an opposite association in girls. In girls, fat intake seems to be increasing with increasing birth weight, whereas low birth weight girls seem to have a higher palate for carbohydrates. In higher birth weight group, it is suggested that high birth weight increases carbohydrate intake in adulthood and sucrose in mid and late childhood. However, fiber intake has been shown to be higher in adults and lower in childhood, compared to low- or normal birth weight groups. Also, both higher and lower birth weight have been associated with higher consumption of foods containing higher levels of fiber, for example, fruits and berries, depending on age.

2.7.2 Birth weight, food consumption and overall diet quality

Previous studies have highlighted the possible associations between birth weight and dietary choices. Based on these studies low birth weight has been associated with lower consumption of vegetables, fruits and berries in early adulthood (Kaseva *et al*. 2013). Low birth weight has also been associated with lower consumption of carbohydrate- and fiber-rich foods, such as berries, fruits and rye in adult population (Perälä *et al.* 2012). However, Eloranta *et al.* (2018) reported an association of high birth weight with a lower berry and fruit consumption in children between ages 6–8 years. In adult population, a contradicting result was reported, where higher birth weight seemed to increase the

intake of fruits and berries (Perälä *et al.* 2012). Studies that investigate overall diet quality rather than specific intake of nutrients or foods are scarce. However, study group of Eloranta *et al.* (2018) reported as part of the PANIC Study that there was an association between high birth weight and poorer overall diet quality in 6–8-year-old children, using Finnish Children Healthy Eating Index. This association was found in boys but not in girls.

2.8 Summary of the literature

The conclusions of how prenatal environment impacts birth weight, later dietary preferences and body composition and therefore increases the risk of chronic diseases are presented below in Figure 1.

Based on the previous literature and as pictured in figure 1, prenatal environment, including nutrition, maternal factors and function of placenta lead to fetal programming. Furthermore, fetal programming influences the birth outcome, that is term at birth and body size at birth. All the factors together influence the birth weight and thereafter also the dietary factors and development of body weight and composition later in life. Being born with low birth weight increases the preference to both salty and sweet tase, consumptions of foods high in fat when compared to those born with high birth weight. In addition those with low birth weight have increased overall energy intake, when compared to normal birth weight counterparts. Furthermore, low birth weight increases the risk of early catch-up growth and affects the development of body composition by favoring the accumulation of visceral fat and fat mass. However, the BMI of low birth weight infants seems to be lower in later life compared to those born with high birth weight. On the other hand, high birth weight infants prefer energy rich food choices in their diet, consume foods rich in carbohydrates and similarly to low birth weight counterparts, have increased energy intake compared to normal birth weight infants. Those born with high birth weight have increased BMI throughout the life span, but lower visceral and subcutaneous fat mass than those born with low birth weight. In addition, high birth weight infants seem to develop healthier body composition, favoring fat-free mass.

To conclude, both low and high birth weight increase the risk of developing lifestyle related diseases, such as type 2 diabetes and cardiovascular disease.

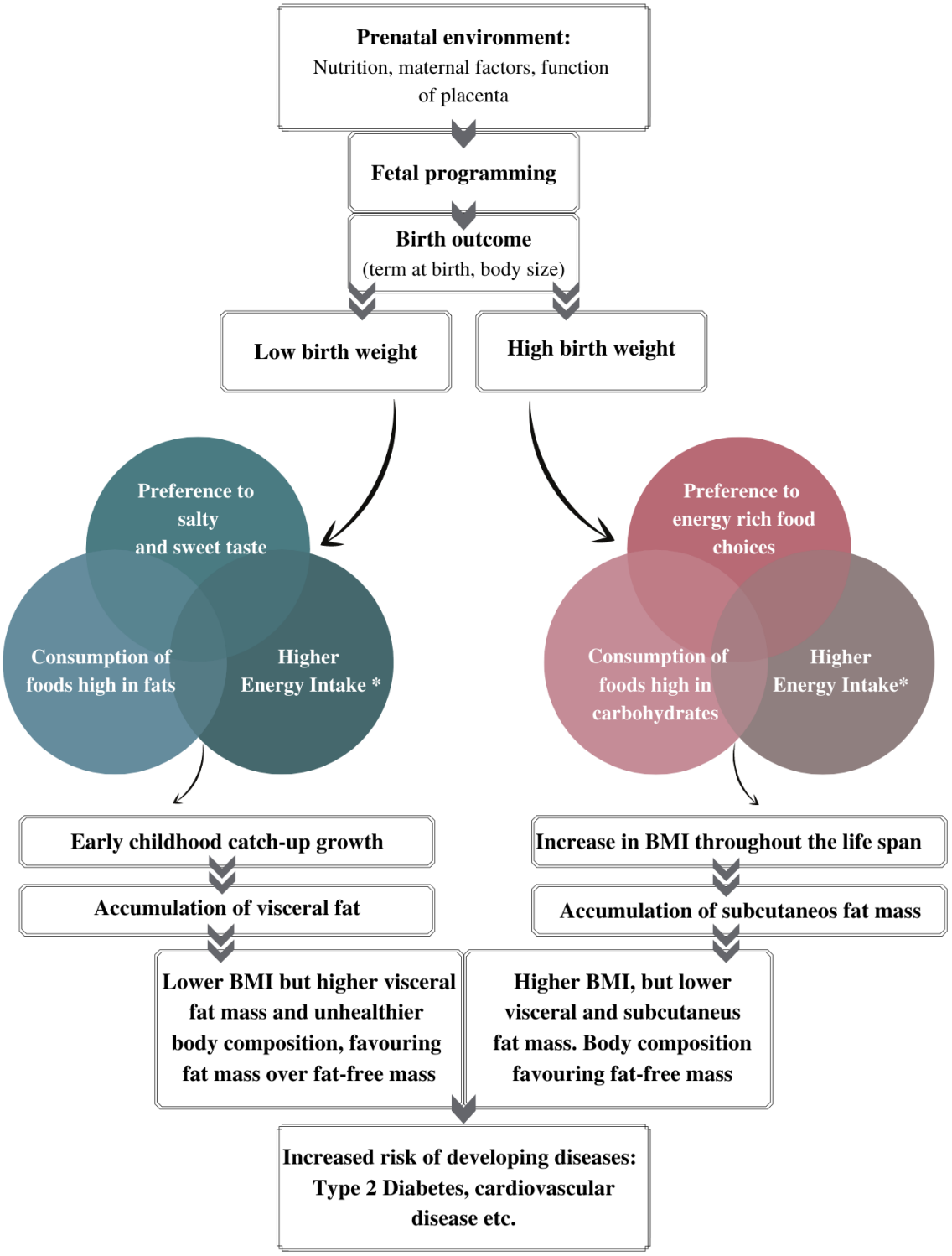

Figure 1. The role of prenatal environment, later dietary choices and future risk of developing diseases.

BMI, body mass index. * Higher energy intake compared with normal birth weight

3 OBJECTIVES

The overall aim of this study was to investigate the associations of birth weight with body size, body composition and dietary factors, including overall diet quality, among adolescents. To accomplish the overall aim, following specific key questions needed to be studied:

1. Is birth weight associated with body size, such as body weight, height and BMI in adolescence?
2. Is birth weight associated with body composition, such as body fat mass and body fat percentage in adolescence?
3. Is birth weight associated with overall diet quality, food consumption, and nutrient intake in adolescence?

Overall, the hypotheses in the present study are:

H1. There is a direct association between birth weight and weight and height and indirect association between birth weight and waist circumference in adolescence.
H2: There is an indirect association between birth weight and body fat mass and a direct association berween birth weight and fat free mass in adolescence.
H3. There is an indirect association of birth weight with diet quality and high fat diet and a direct association of birth weight with high carbohydrate diet and higher energy intake in adolescence.

4 MATERIALS AND METHODS

4.1 Study design and study population

The present study population consisted of 277 adolescents aged 15–17 years from the PANIC –study, that is a physical activity and dietary intervention study with an ongoing follow-up. The baseline measurements were conducted in 2007–2009, when the children were 6–8 years old. Initially, 736 children and their parents were invited by a letter to participate in the study. Altogether 512 children of the invited 736 children, took part in the PANIC study. The 8-year follow up measurements were conducted in 2016–2018 for 277 adolescents (126 girls, 151 boys) 15–17 years of age.

The present study used retrospectively collected data on birth weight and pregnancy as well as the data from 8-year follow up measurements for the analysis. Adolescents with inaccurate data on dietary factors and those who did not have valid data on birth weight in the birth register of the National Institute for Health and Welfare were excluded from the analysis. After the exclusions, 227 adolescents were included in the present study.

The PANIC study has been issued with a favorable statement regarding the research plan by the Research Ethics Committee of the Northern Savo Hospital District in 2006 and 2015. All participants were given personal identification number which had been used to store and process the collected data in respect of the Personal Data act. Taking part in the study has been voluntary and all individuals have been able to quit the study at any moment without explanations. All participants gave written informed consent at inclusion.

4.2 Assessment of body size and composition

The data on gestational age and birth weight and length were collected retrospectively from the birth register provided by the National Institute for Health and Welfare. In addition, the data on maternal body weight and weight before pregnancy were collected from the birth register of Kuopio University Hospital. Maternal BMI was calculated from weight and height by dividing body weight in kg by height in meters squared. We defined individuals as normal weight, overweight and obese if they had a BMI <25 kg/m^2, ≥25–<30 kg/m^2 and ≥ 30 kg/m^2, respectively.

At adolescence, body height was measured three times using a wall-mounted stadiometer in the Frankfurt position and the mean of two closest values were used for the analyses. Body weight was measured two times using the InBody 720 device (Biospace, Seoul, Korea) after overnight fasting, empty bladder and standing in light clothing. BMI was calculated from the participants using the measured weight and height similarly to the calculations of maternal BMI. BMI-SDS was calculated based of Finnish growth references (Saari et al. 2011). Body fat mass was measured using dual energy X-ray absorptiometry (DXA).

4.3 Assessment of diet

Food consumption and energy and nutrient intake were assessed during the 8-year follow-up using 4-day food records. The food records were analysed using Micro Nutrica dietary analysis software, version 2.5 (The Social Insurance Institution of Finland). Furthermore, separate foods were combined more descriptive groups with IBM SPSS version 25, for the further analyses. For example, all breads, cereal, flours and other grain products were categorized based on their fiber content to high-fiber and low-fiber grain products. Categorized food groups are presented below in Table 3.
Moreover, the participants filled a food consumption questionnaire at a study visit. Based on this questionnaire the Index of Diet Quality (IDQ) was assessed. Both IDQ and Baltic sea Diet Score (BSDS) were chosen to assess overall diet quality of the adolescent. BSDS was calculated from the 4-day food records. The food was categorized into larger food groups using the variable computing tool on IBM SPSS software as shown below in Table 3.

Table 3. Food groups by category.

Food groups	Description
High-fiber grain products	Grain products > 5 % fiber Bread, Other fiber rich grain products incl. Flour, bran, pasta, groat, cereals.
Low-fiber grain products	Low fiber products < 5 % fiber Bread, other grain products incl. Flour, bran, pasta, groat, cereals, rice, couscous, salty grain products incl. Karelian pasty.
Vegetables	Vegetables, roots, mushrooms, legumes, nuts, tofu, tomato sauce.
Potatoes	Potato and potato containing products.
Fruits and berries	Fruits, berries and products made out of fruits and berries.
Butter & butter-based spreads	Butter & butter-based spreads.
Low-fat margarines	Margarines containing < 60 % fat.
High fat margarines	Margarines containing fat 60–80 %, liquid margarines.
Oils	Oils incl. oil-based salad dressing.
Skimmed milk & low-fat sour milk	Dairy < 1 % Fat. Incl. milk, sour milk, yoghurt, quark.
High-Fat milk & sour milk	Dairy > 1 % Fat. Incl. milk, sour milk, yoghurt, quark.
Cheese > 17 %	All cheese products > 17 % of fat.
Cheese < 17 %	All cheese products < 17 % of fat.
Red meat	Beef, pork, lamb, reindeer, horse.
Sausages	All sausages and frankfurters.
Poultry	Chicken, turkey.
Fish	Fish, fish products incl. fish paste, shellfish.
Eggs	Eggs.
Sugar-sweetened beverages	All sugar-sweetened beverages, carbonated and non-carbonated
Sugar free and fruit juices	Juices with no added sugar.
Sweets	Sugar, sweets, chocolate.
Ready meals	Ready cooked meals, ready salty pastries, ready salads, fast food
Salt	Salt.

Instead of assessing the amount of specific nutrients in the diet, the IDQ assesses how healthy the overall diet is in respect of the Nordic Nutrition Recommendations and the Finnish National Nutrition Recommendations (Leppälä *et al*. 2010, Mäkelä & Laitinen 2012). IDQ is a validated tool that consists of 18 questions where answers are scored between 0–15 points of which 10–15 points are considered as an overall healthy diet. It has been reported that IDQ is a reliable tool to assess protein, sucrose, fiber, calcium, iron and vitamin C intakes as well as the quality of fatty acids in a diet (Mäkelä & Laitinen 2012). However, it does not assess the absolute amount of nutrients and should not be used for those purposes. BSDS however, is a tool that has been formed specifically to describe the relationship between diet and health in the Nordic countries (Kanerva *et al.* 2013). BSDS as a tool can provide associations with higher intakes of carbohydrates (E%), fiber, vitamins and minerals and lower intakes of saturated fatty acids (SAFA) (E%) and alcohol intake (E%) in a way that higher score indicates healthier choices in respect of the National Finnish nutrition guidelines. However, BSDS might associate poorly with some nutrients, for example sucrose intake which must be considered when interpreting the results. The utilization of both tools together can provide a more extensive view on the overall diet and help diminish the weaknesses that might occur if only one of these tools is utilized. Therefore, in this thesis we chose to use both IDQ and BSDS for the valuation of overall diet quality.

4.4 Other assessments

A questionnaire was administered to the parents where the information about their chronic diseases and conditions, parental education and annual household income were established. Parental education was defined as highest completed degree or an ongoing degree whereas annual household income was reported to accuracy of 10 000 € and was categorized as ≤ 30 000€/year, 30 001–60 000 €/year or >60 000 €/year.

In addition, maternal age at child's birth, information about possible multiple pregnancies and number of previous births (0 or ≥1) and previous pregnancies were collected retrospectively from the National Institute for Health and Welfare. Also, the data on gestational diabetes mellitus was collected from the birth register of Kuopio University Hospital.

4.5 Statistical methods

The data for this study was analyzed using IBM SPSS Statistics software version 25.0 for Windows. The level of significance was set at $P < 0.05$. The association of birth weight with dietary factors, including diet quality indexes, food consumption and nutrient intake, as well as body weight, height and composition, were analyzed using the linear regression analysis. Linear regression analysis was compatible with assessing the associations between linear variables that were all normally distributed according to the histograms provided by IBM SPSS software.

Linear regression models 1 and 2 were formed to investigate the association of birth weight with weight and dietary factors in adolescents. Model 1 was adjusted for age, gender and study group. In addition, all variables excluding total energy intake, nutrient intake, body composition measurements and weight were adjusted with total energy intake. These analyses were made for a study sample of 227 children. In model 2, additional adjustment for gestational age, maternal age at birth, number of previous births, maternal BMI before pregnancy, maternal gestational diabetes, parental education and household income, and BMI-SDS in adolescence was made. In these analyses we excluded the adjustment of BMI-SDS when analyzing weight, height, BMI or BMI-SDS. In Model 2, the study population dropped to 137.

5 RESULTS

5.1 Characteristics

As seen in Table 4, there were no significant differences between boys and girls in regard of birth weight (g) or gestational age (weeks). However, boys were longer at birth (P-value =0.002). Most of the study population were born with normal birth weight and in appropriate term of gestation. However, boys were significantly taller and heavier at the time of 8-year follow-up than girls. Even so, there were no significant differences regarding BMI-SDS. Girls had significantly more fat mass (kg and %) than boys. However, waist circumference (cm) was bigger in boys than in girls.

Table 4. Characteristic of study group and their parents

	All children (n 277)		**Girls (n 112)**		**Boys (n 115)**		
	Mean or %	**SD or n**	**Mean or %**	**SD or n**	**Mean or %**	**SD or n**	**P value***
Characteristics of children at birth							
Gestational age (weeks) mean and SD [1]	39.3	2.1	39.1	0.2	39.4	0.2	0.387
Birth weight (g) mean and SD	3539	542	3477	587	3600	488	0.860
Birth length (cm) mean and SD [2]	49.99	2.1	49.5	0.2	50.5	0.2	**0.002**
Characteristics of adolescents at the age of 15–17 years							
Age (years), mean and SD	15.8	0.4	15.7	0.0	15.8	0.0	0.110
Weight (kg), mean and SD [3]	61.86	13.4	57,8	0.8	65.9	1,5	**<0.001**
Height (cm), mean and SD [3]	171.17	8.4	165.9	0.5	176.2	0.7	**<0.001**
Height, SDS, mean and SD [9]	0.07	1.0	0.9	0.9	0.1	1.0	0.551
BMI-SDS, mean and SD [3]	-0.039	0.9	0.04	0.1	-0.1	0.1	0.224
BMI, mean and SD[9]	21.02	229	20.9	114	21.04	115	0.907
Fat mass (kg), mean and n ∫	14.5	228	16.9	115	12.0	113	**<0.001**
Fat percentage, mean and n ∫	22.9	228	28.7	115	17.0	113	**<0.001**
Waist circumference (cm), mean and n [9]	73.0	229	70.0	114	75.9	115	**<0.001**
Parental characteristics							
Maternal age at birth (years), mean and SD [1]	30.44	5.2	29.9	0.5	30.9	0.6	0.185
Maternal number or previous births, % and n [4]		192	51.6	99	48.4	93	0.856
0	30.7	59	31.3	31	30.1	28	
>1	69.3	133	68.7	68	69.9	65	

Maternal smoking during pregnancy [5]		177	0.10	87	0.06	90	0.247
No smoking	71.3	164	89.8	79	94.4	85	
Smoked	6.1	14	10.2	9	5.6	5	
Maternal BMI before pregnancy (kg/m2), mean and sd n [1]	22.7	4.2	22.6	0.4	22.8	0.5	0.797
Maternal gestational diabetes, % and n [6]		226		114		114	0.207
No	92.5	211	94.7	108	90.4	103	
Yes	7.5	17	5.3	6	9.6	11	
Household income, € per year, % and n [7]		213	50.2	107	49.8	106	0.102
< 30 000	8.9	19	6.5	7	11.3	12	
30 001 – 60 000	22.5	48	28.0	30	17.0	18	
>60 000	68.5	146	65.4	70	71.7	76	
Parental education, % and n [8]		216	50.9	110	49.1	106	0.140
Vocational school or less	13.4	29	13.6	15	13.2	14	
Polytechnic	42.1	91	48.2	53	35.8	38	
University	44.4	96	38.2	42	50.9	54	

SDS, Standard Deviation Score. * Differences between girls and boys assessed using Student's t-test and Pearson's X^2 test. [1] = n 183 (n 91 in girls, n 92 in boys). [2] = n 178 (n 88 in girls, n 90 in boys). [3] = n 225 (n 111 in girls, 114 in boys). [4] = n 192 (n 99 in girls, n 93 in boys). [5] = n 178 (n 88 in girls, n 90 in boys). [6] = n 228 (n 114 in girls, n 114 in boys). [7] = n 213 (n 107 in girls, n 106 in boys). [8] = n 216 (n 110 in girls, n 106 in boys). [9] = n 229 (n 114 in girls, 115 in boys). ∫ = n 228 (n 115 in girls, n 113 in boys).

Dietary factors and differences between girls and boys are presented below in table 5. Girls and boys varied in diet quality measures when BSDS was used as a measure of diet quality but not when measured with IDQ. There were differences in food consumptions in boys and girls regarding potato consumption, fruits and berries, butter and butter based spreads, skimmed milk and low-fat sour milk, red meat, sausages, sugar-sweetened beverages, ready meals and salt consumption. In addition, total energy intake and macronutrient intake, that is protein intake, fat intake, carbohydrate intake were different in girls and boys.

Table 5. Dietary factors of study group at age of 15–17 years.

	All children (n 230)		**Girls (n 115)**		**Boys (n 115)**		
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**P value***
Diet quality indexes and food consumption (g)							
IDQ*	9.2	2.6	9.6	2.54	8.9	2.63	0.05
BSDS	11.8	4.1	12.5	4.36	11.1	3.73	**0.008**

High-fiber grain products	85.7	63.1	76.6	4.6	94.9	6.8	0.28
Low-fiber grain products	126.0	71.6	118.1	7.0	133.9	66.7	0.094
Vegetables, roots and mushrooms	124.3	75.3	133.7	7.2	114.9	72.1	0.059
Potatoes	83.9	62.5	70.8	5.5	96.9	62.9	**0.001**
Fruits and berries	102.3	109.7	129.5	113.8	75.2	9.2	**<0.001**
Butter & butter-based spreads	9.3	10.0	7.6	8.07	11.0	11.4	**0.012**
Low fat margarines	1.0	5.4	0.6	2.2	1.4	7.3	0.222
High fat margarines	10.6	12.5	9.2	8.8	12.0	15.2	0.089
Oils	5.6	5.2	5.1	4.0	6.1	6.1	0.122
Skimmed milk & low-fat sour milk	362.7	339.4	274.5	276.8	450.8	373.0	**<0.001**
High fat milk & sour milk	142.8	177.5	127.0	154.8	158.6	197.0	0.178
Cheese < 17 % of fat	12.8	20.5	13.3	19.5	12.3	21.5	0.721
Cheese > 17 % of fat	15.9	15.6	15.4	13.1	16.4	17.8	0.624
Red meat	62.9	50.6	43.5	31.3	82.3	58.4	**<0.001**
Sausages	25.3	39.1	14.0	26.1	36.7	46.1	**<0.001**
Poultry	38.5	40.6	35.3	37.1	41.7	43.8	0.228
Fish	20.0	25.2	17.5	23.1	22.4	27.0	0.135
Eggs	18.0	19.6	16.5	18.1	19.5	21.0	0.241
Sugar-sweetened beverages	147.1	186.7	101.8	148.6	192.3	209.4	**<0.001**
Sugar free and fruit juices	121.8	160.6	118.8	141.0	124.7	178.6	0.781
Sweets	39.6	37.1	39.5	31.0	39.7	42.4	0.955
Ready meals	21,4	48.6	13.8	30.1	29.1	60.9	**0.017**
Salt	2.2	1.1	1.9	0.9	2.6	1.2	**<0.001**
Macronutrient intake (E%) and energy intake (kcal)							
Total energy intake	1841.5	544.7	1632.7	437.9	2050.3	562.5	**<0.001**
Protein intake	80.3	29.3	68.1	22.6	92.6	30.2	**<0.001**
Fat intake (total)	70.1	25.2	61.8	21.7	78.4	25.8	**<0.001**
MUFA	24.4	10.1	21.4	8.2	27.4	10.9	
PUFA	13.0	5.6	11.6	4.8	14.4	5.9	
SAFA	25.8	9.5	22.6	8.6	9.3	9.3	
Carbohydrate intake	216.0	71.8	195.4	57.2	236.5	78.9	**<0.001**

IDQ, Index of Diet Quality. BSDS, Baltic Sea Diet Score. MUFA, monounsaturated fatty acids. PUFA, Polyunsaturated fatty acids. SAFA, Saturated fatty acids. Differences between girls and boys assessed using Student's t-test. * = n 228 (n in girls 113, n in boys 115).

5.2 The association of birth weight with body size at age of 15–17 years

Birth weight (g) was not associated with weight (kg) or BMI (kg/m_2 and SDS) when adjusted for study group, age and gender, as seen in Table 6. In addition, waist circumference and body composition measurements were adjusted for energy intake. However, in model 1 birth weight was directly associated with height (cm and SDS).

Table 6. Association of birth weight with body size measurements at age 15–17, model 1.

	Birth weight (g)	
Body size and body composition in 15–17-year old (n=226)	**ß**	**P-value**
Weight, height and body mass measures		
Weight (kg)	0.103	0.107
Height (cm)	0.148	**0.005**
Height SDS	0.188	**0.005**
BMI (kg/m^2)	0.053	0.424
BMI-SDS	0.086	0.203
DXA measures and body composition		
Fat mass (kg)*	0.055	0.387
Fat percentage %*	0.021	0.701
Waist circumference (cm)	0.003	0.968

BMI, body mass index. SDS, standard deviation score. DXA, dual-energy x-ray absorptiometry.
* n = 225. Weight, BMI, BMI-SDS adjusted with gender, age and study group. Height, waist circumference and DXA measurements adjusted additionally with energy intake.

Further adjustments were made, as shown in Table 7, for gestational age, maternal age at birth, number of previous births, smoking during pregnancy, BMI before pregnancy, gestational diabetes and household income. In addition, body composition measurements were adjusted for BMI-SDS of the adolescent. There was a significant association between birth weight and waist circumference suggesting inverse association in adolescence. No other significant associations were reported.

Table 7. Association of birth weight with body size measurements at age 15–17, model 2.

	Birth weight (g)	
Body size and body composition in 15–17-year old (n=137)	**ß**	**P-value**
Weight, height and body mass measurements		
Weight (kg)	0.070	0.450
Height (cm)	0.113	0.154
Height SDS	0.161	0.126

BMI (kg/m^2)	0.053	0.596
BMI-SDS	0.107	0.287
DXA measurements and body composition		
Fat mass (kg)*	0.134	0.165
Fat percentage %*	0.079	0.333
Waist circumference (cm)	**-0.117**	***0.025***

BMI, body mass index. SDS, standard deviation score. DXA, dual-energy x-ray absorptiometry.
* n = 135. Weight, BMI, BMI-SDS, height and waist circumference adjusted for gender, age, study group, gestational age, maternal age at birth, smoking during pregnancy, BMI before pregnancy, gestational diabetes and household income. DXA measurements and waist circumference additionally adjusted with BMI-SDS and energy intake.

5.3 The association of birth weight with dietary factors

As presented below in Table 8, no significant associations were reported in overall diet quality, when adjusted for gender, study group, age and energy intake using IDQ and BSDS as predictors of overall diet quality. With these adjustments, significant associations of birth weight were reported for the consumption of potatoes, butter and butter-based spreads, high fat (60-80 %) margarines, but with no other food items. Our results suggest inverse association of birth weight with consumption of potatoes, high fat margarines and a direct association of birth weight with butter and butter-based spreads. There were also no significant associations of birth weight with the intake of nutrients nor total energy when adjusted for study group, age and gender.

Table 8. The association of birth weight with dietary factors of adolescents at age 15–17 years, model 1.

Dietary factors of adolescents at age 15–17 (n=227)	**ß**	**P-value**
Diet quality		
Index of Diet Quality	-0.073	0.270
Baltic Sea Diet Score	0.031	0.630
Food consumption (g)		
High-fibre grain products (g/MJ)	0.054	0.393
Low-fiber grain products (g/MJ)	-0.093	0.131
Vegetables, roots and mushrooms	0.020	0.760
Potatoes	**-0.133**	**0.038**
Fruits and berries	0.082	0.192
Butter & butter-based spreads	**0.171**	**0.009**
Low fat margarines	-0.002	0.976
High fat margarines	**-0.196**	**0.001**
Oils	0.041	0.523

Skimmed milk & low-fat sour milk	-0.051	0.406
High fat milk & sour milk	0.019	0.770
Cheese < 17 % of fat	0.039	0.537
Cheese > 17 % of fat	0.097	0.134
Red meat	-0.050	0.409
Sausages	-0.041	0.522
Poultry	0.038	0.564
Fish	-0.040	0.549
Eggs	-0.011	0.866
Sugar-sweetened beverages	-0.053	0.411
Sugar free and fruit juices	-0.061	0.352
Sweets	0.110	0.081
Ready meals	-0.067	0.311
Salt	-0.087	0.145
Macronutrient intake (E%) and energy intake (kcal)		
Total energy intake	0.003	0.967
Protein intake	-0.068	0.304
Fat intake (total)	0.038	0.578
MUFA	0.015	0.825
PUFA	-0.011	0.868
SAFA	0.023	0.737
Carbohydrate intake	0.003	0.969

IDQ, Index of Diet Quality, BSDS, Baltic Sea Diet Score. Diet quality and food consumption were adjusted for study group, age, gender and energy intake. Macronutrient intake and Energy intake were adjusted for study group, age and gender.

Further adjustments were made in model 2 for gestational age, maternal age at delivery number of previous births, smoking during pregnancy, BMI before pregnancy, gestational diabetes and household income and BMI-SDS in adolescence, which dopped the study population to 137 and 132. As seen in Table 9, with further adjustments, birth weight was associated with the consumption of butter and butter-based spreads, high fat margarines, cheese containing > 17 % of fat, red meat, sausages, eggs and salt. Our results suggest inverse association of birth weight with the consumption of high fat margarines, red meat, sausages, eggs and salt. In addition, there was a direct association of birth weight with the consumption of butter and butter-based spreads and high fat cheese products. The association of birth weight with consumption of potatoes was not significant after further adjustments.

Table 9. The association of birth weight with dietary factors of adolescents at age 15–17 years, model 2.

Dietary factors of adolescents at age 15–17. (n=137)	ß	P-value
Diet quality		
Index of Diet Quality	-0.130	0.207
Baltic Sea Diet Score	0.180	0.080
Food consumption (g)*		
High-fibre grain products (g/MJ)	0.840	0.427
Low-fiber grain products (g/MJ)	-0.020	0.823
Vegetables, roots and mushrooms	0.114	0.301
Potatoes	-0.136	0.179
Fruits and berries	0.035	0.741
Butter & butter-based spreads	**0.231**	**0.028**
Low fat margarines	0.087	0.427
High fat margarines	**-0.265**	**0.008**
Oils	0.045	0.655
Skimmed milk & low fat sour milk	-0.054	0.586
High fat milk & sour milk	0.066	0.664
Cheese < 17 %	0.037	0.729
Cheese > 17 %	**0.307**	**0.002**
Red meat	**-0.192**	**0.047**
Sausages	**-0.287**	**0.004**
Poultry	0.143	**0.171**
Fish	0.067	0.535
Eggs	**-0.230**	**0.030**
Sugar-sweetened beverages	-0.079	0.446
Sugar free and fruit juices	-0.046	0.672
Sweets	0.093	0.336
Ready meals	-0.014	0.894
Salt	**-0.236**	**0.014**
Macronutrient intake (E%) and energy intake		
Total energy intake	-0.058	0.557
Prot intake	-0.074	0.426
Fat intake (total)	-0.015	0.880
MUFA	0.021	0.834
PUFA	-0.046	0.650
SAFA	-0.060	0.560
Carbohydrate intake	0.003	0.969

IDQ, Index of Diet Quality. BSDS, Baltic Sea Diet Score. * n = 132.

Adjusted for study group, age, gender, energy intake, maternal age at birth, smoking during pregnancy, BMI before pregnancy, gestational diabetes and household income, excluding adjusting for energy intake in Macronutrient intake and Energy intake measurements.

6 DISCUSSION

6.1 Birth weight and body size

In the current study, the association of birth weight with waist circumference was not significant when adjusted for gender, study group, age and energy intake. However, the results of the current study reported an inverse association, when adjusted for gender, age, study group, gestational age, maternal age at birth, smoking during pregnancy, BMI before pregnancy, gestational diabetes and household income. The results indicate that those born lighter have a higher waist circumference, while those born heavier had a smaller waist circumference. Our results were in line with previous studies, suggesting lower birth weight to increase waist circumference (Loos *et al.* 2001, Te Velde *et al.* 2003, Barbieri *et al.* 2009, Pereira-Freire *et al.*2015). Also, previous studies have reported an association of birth weight with higher waist-to-hip ratio and increase in abdominal fat mass (Law *et al.* 1992, Loos *et al.* 2001, Te Velde *et al.* 2003, Berbieri *et al.* 2009). All these variables measure the accumulation of excess fat in the abdominal region. However, some studies reported the association of birth weight with higher waist circumference only in females (Te Velde *et al.* 2003, Barbieri *et al.* 2009) and not in both genders. In our study, gender-based differences were not analyzed, but we did adjust all analyses for gender and therefore gender differences should not be a confounding factor in the analyses.

Other studies have reported an association of birth weight with body size and body composition, including body weight, height, fat mass and fat-free mass . Previous studies have indicated that birth weight is directly associated with weight and BMI in childhood (Eriksson *et al.* 2003, Reilly *et al.* 2005, Li *et al.* 2007, Apfelbacher *et al.* 2008, Janjua *et al* 2012 Parker *et al.* 2012, Heppe *et al.* 2013) and in adolescence (Eriksson *et al.* 2003, Monteiro *et al.* 2003, Araujo *et al.* 2009, Kleiser *et al.* 2009, Gillman *et al.* 2013, Evensen *et al.* 2017, Boone-Heinonen *et al.* 2018). However, some have reported a rather modest association among adolescents (Evensen *et al.* 2017) and even suggested that dietary factors may have a bigger role in adolescent obesity, over birth weight (Birbilis *et al.* 2012). Also, birth weight has been inversely associated with early catch-up growth, suggesting that those born lighter have increased early growth rebound in infancy or early childhood (Karlberg & Albertsson-Wikland 1995, Ornoy 2011, Galjaard *et al.* 2013), which again has been associated with unfavorable body

composition in regard of risk factors of chronic diseases (Crescenzo *et al.* 2003, Barker *et al.* 2005, Ibanez *et al.* 2006, Andersen *et al.* 2010, Knop *et al.* 2018). In addition, several previous studies have reported that in girls, the impact of birth weight on height can be seen only until early childhood and, thereafter seems to be no association of birth weight and height (Casey *et al.* 1991, Knops *et al.* 2005). On the other hand, several other studies suggested that even though girls with higher birth weight grew faster only until menarche, they tended to be taller upon adulthood compared to girls with lower birth weight (Adair 2007, Gale *et al.* 2001, Labayen *et al.* 2006, Loos *et al.* 2002, Sachdev *et al.* 2005, Workman & Kelly 2017). We were unable to confirm the association of birth weight with body weight or body composition among adolescents. However, there was a direct association between birth weight and height (cm and SDS) in model 1 adjustments, which then disappeared after model 2 adjustments. In our study, most of the study population was born with a normal birth weight and we had a very small sample size of both low and high birth weight infants which might explain the inability to report these associations.

6.2 Birth weight and dietary factors

In previous studies, the associations of birth weight with dietary factors have been rather inconsistent and still insufficiently studied. However, there is some evidence suggesting that both low birth weight (Doorweerd *et al.* 2015, Bischoff *et al.* 2018) and high birth weight (Eloranta *et al.* 2018) seem the increase the overall energy intake in childhood or adolescence. There was only one study investigating the associations between birth weight and overall diet quality, implementing healthy eating indices as measures of diet quality. In the study of Eloranta *et al.* (2018), they found significant associations of a higher birth weight with lower diet quality in children at the age of 6–8 years, while using data from the PANIC Study and Finnish Children Healthy Eating Index (FCHEI) as an index for diet quality. In the current study, we chose to use BSDS and IDQ indexes for measuring overall diet quality and were unable to find significant associations between birth weight and diet quality. We were also unable to confirm the association of birth weight with energy intake.

Most previous studies have reported a greater fat intake in infants with low birth weight (Stafford & Lucas 1998, Lussana *et al.* 2008, Perälä *et al.*2012, Bischoff *et al.* 2018). Some have suggested a direct

association among girls, indicating that high birth weight would lead to higher fat intake when compared to normal birth weight (Bischoff *et al.* 2018). In our study, birth weight was not associated with fat intake nor with saturated fat intake. Some other studies made in predominantly Finnish population have also not found the associations with birth weight and fat intake or saturated fat intake (Perälä *et al.* 2012, Eloranta *et al.* 2018). However, the studies that have suggested low birth weight to increase the saturated fat intake (Shultis *et al.* 2005, Doornweerd *et al.* 2017) are rather inconsistent. Shultis *et al. (*2005) claimed the association to be visible only until early childhood, while Doornweerd *et al.* (2017) found these outcomes in young adults, 13–22 years old. It is possible that differences in these studies are due to national dietary differences but also, it is impossible to make conclusions with still so little evidence on the topic.

When investigating consumption of foods containing high or low amounts of fat, or foods high in saturated fats, our results might explain the inconsistence in studies assessing overall fat intake. Based on the current study, there was an inverse association of birth weight with some foods containing high amount of unsaturated fats, such as high fat margarines (Fat > 60 %). At the same time there was an inverse association with foods containing higher amount of saturated fats, such as red meat and sausages. Based on our study there was a direct association of birth weight with consumption of butter and butter-based spreads and high-fat cheese (fat > 17%). It could be hypothesized, that both lower and higher birth weight groups prefer different foods high or low in fat in their diet. This might explain the difficulty to observe significant associations in overall nutrient intake.

Previous studies have suggested that low birth weight infants have preference for both salty and sweet taste (Stein *et al.* 2006, Barbieri *et al.* 2009, Silveira *et al.* 2012), even though the association between low birth weight and higher carbohydrate intake has not been reported (Lussana *et al.* 2008, Perälä *et al.* 2012, Doornweerd *et al.* 2017, Eloranta *et al.* 2018). Some have even found a direct association of birth weight with sucrose intake (E%) (Eloranta *et al.* 2018). In our study, sucrose intake was not assessed as such, but we did analyse consumption of sugar-sweetened beverages and sweets and did not find any significant association with birth weight. However, also the previous research is inconsistent, while most of the studies suggesting low birth weight to increase the preference for carbohydrates or sweet taste have reported it only among females and not males (Breen *et al.* 2006, Barbieri *et al.* 2009, Silveira *et al.* 2012, Escobar *et al.* 2014, Tam *et al.* 2015). It is possible, that a

difference exists among genders and therefore the association was not detected in the current study. However, the current study does confirm inverse association of birth weight with salt consumption, suggesting that those lighter at birth have greater salt consumption in adolescence, and vice versa.

6.3 Strengths and limitations

The strengths of the present study are that the data on gestational age and birth weight as well as maternal body weight and weight before pregnancy were obtained from reliable national records instead of self-reporting. In addition, our follow-up data on body size of the adolescents were collected by 2-time measurements, minimizing the possibility of error. We did not have to use self-reported data on body size measures. Furthermore, being able to use DXA-measurements for body composition gives more reliable information on each subject.

Another strength of this study was a reliable and individually instructed and reviewed data on food consumption and nutrient intake. In addition, food consumption and nutrient intake was calculated from 4-day food records and food consumption questionnaires, giving specific information of the diet. Furthermore, there was a strength in using both IDQ and BSDS for the valuation of overall diet quality. First, both tools assess overall diet quality in respect of Nordic and Finnish nutrition recommendations. Our study group consisted of Finnish adolescents and therefore national and regional nutrition recommendations are an essential tool to assess diet in the region. Second, utilizing both IDQ and BSDS, we diminished the weaknesses that might have occurred if using only one of these tools. For example, BSDS associates poorly with some nutrients whereas IDQ is seen as a reliable tool for nutrient intake.

The current study had also some major limitations. One of the main limitations was the relatively small population after our model 2 adjustments. This limitation occurred mainly because of the lack of data on maternal factors during pregnancy. These maternal factors were important confounding factors of the observed associations and therefore were still chosen to be preserved in the analysis. Furthermore, we did not analyse whether there were gender specific differences in the associations of birth weight with dietary factors or body size in adolescence but rather concentrated in overall associations. It is

also important to notify that our study group consisted of induviduals? adolescents? mostly born with normal birth weight and on appropriate term, in full weeks of gestation. Therefore, the current study is not reliable when investigating outcomes of very low and high extremes of birth weight, but rather tendencies that might occur in normal birth weight range. It can also explain why our results were somewhat inconsistent with previous research on dietary factors and body size.

6.4 Implications and future perspectives

Chronic diseases and diseases classified as lifestyle-related diseases bring substantial health care costs (Must et al. 1999, Atella et al. 2015, THL 2016). Public health strategies are currently focusing to prevent obesity and metabolic complications through promoting healthy lifestyle and weight management (WHO 2016b). Understanding the development of chronic diseases helps us to implement effective interventions to those that might benefit from it the most, while at the same time focusing health care costs efficiently. For this, we need to understand the pathways from which chronic diseases develop. Only through understanding which factors are of importance depending on birth weight, can we start planning effective interventions. Being able to predict future risk factors of developing chronic diseases in the future, we can better identify those that will need early guidance and intervention. Moreover, these findings could be of high importance for counselling and managing pregnancies to avoid adverse birth weight related outcomes.

Studies focusing on the associations between birth weight and dietary factors are yet scarce. Only one study taking into account overall diet quality by using diet quality indexes was found. Furthermore, most of the studies concentrated on nutrient intake rather than food consumption age groups varied largely, making it impossible to make reliable conclusions of the associations between birth weight and dietary factors. More studies are needed on these topics to fully understand the associations. Based on the possible gender differences, it would be important to study girls and boys separately, especially during and after onset of menarche. In addition, when studying the associations of birth weight with body composition, the differences between girls and boys after menarche, should be taken into account. Furthermore, for all these analyses would be important to take into account mother’s diet during pregnancy and also parent’s current diets when analysing children still living with their parents.

7 CONCLUSIONS

In the present study, the aim was to identify the associations of birth weight with body size and composition and dietary factors, such as diet quality, food consumption and nutrient intake in adolescence. Based on the previous research, direct association was hypothesized between birth weight and body weight and height in adolescence. In addition, an indirect association was hypothesized between birth weight and waist circumference in adolescence. Indirect associations were hypothesized regarding birth weight and diet quality and high fat diet while in contrast, a direct association was assumed with carbohydrate intake and energy intake in adolescence.

In recent years, a lot of effort has been put to study factors modulating birth weight and related effects on body size and later health issues. However, these associations are still not fully clear and remain to be understood in detail. To conclude, the present findings suggest that birth weight does not associate with weight or BMI in adolescence. In addition, it was left unclear whether birth weight was associated with height in adolescence, while the association was significant only in model 1 adjustments. However, these results do suggest that lower birth weight might associate with higher waist circumference already in adolescence. In addition, there might be some differences in dietary preferences between lower and higher birth weight groups, both balancing between unhealthier and healthier food choices. That is, higher birth weight was associated with higher consumption of butter and high fat cheese whereas lower birth weight was associated with higher consumption of high fat margarines, red meat, sausages, eggs and salt. Therefore, there might not be significant differences regarding overall diet quality or macronutrient intake.

We had major limitations in the current study, regarding the notable loss in our study population after further adjustments and our small sample size on very low and high birth weight infants. Hence, this should be taken into account when making conclusions about low and high birth weight individuals based on these results. More longitudinal and prospective studies are needed to truly understand the effects of birth weight on later risk factors of chronic diseases.

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