



Cohort Profile

Cohort Profile: The Finnish Health in Teens (Fin-HIT) study: a population-based study

Rejane Augusta de Oliveira Figueiredo,^{1,2*}† Sabina Simola-Ström,^{1†}
 Trine B Rounge,^{1,2,3} Heli Viljakainen,^{1,4} Johan G Eriksson,^{1,5} Eva Roos^{1,6}
 and Elisabete Weiderpass^{1,2,3,7,8}

¹Genetic Epidemiology Group, Folkhälsan Research Center, Helsinki, Finland, ²Faculty of Medicine, University of Helsinki, Helsinki, Finland, ³Department of Research, Cancer Registry of Norway, Institute of Population-Based Cancer Research, Oslo, Norway, ⁴Department of Food and Environmental Sciences, University of Helsinki, Helsinki, Finland, ⁵Department of General Practice and Primary Healthcare, University of Helsinki and Helsinki University Hospital, Helsinki, Finland, ⁶Department of Public Health, University of Helsinki, Helsinki, Finland, ⁷Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden and ⁸Department of Community Medicine, Faculty of Health Sciences, University of Tromsø, Arctic University of Norway, Tromsø, Norway

*Corresponding author. Folkhälsan Research Center, University of Helsinki, Biomedicum 1 - P.O. Box 63, Helsinki 00014, Finland. E-mail: rejane.figueiredo@helsinki.fi

†These authors contributed equally.

Editorial decision 7 August 2018; Accepted 22 August 2018

Why was the cohort set up?

The prevalence of overweight and obesity in children and adolescents is increasing globally. In high-income countries, the prevalence of obesity has plateaued, although the rate is still high.^{1,2} Children with overweight and obesity are likely to stay obese into adulthood and tend to develop certain diseases, such as pulmonary, cardiovascular and metabolic diseases, more frequently and at a younger age.^{3,4} Overweight and obesity develop as a consequence of the imbalance between energy intake and energy expenditure, and they are heavily influenced by poor eating habits, inadequate sleep and low physical activity level.^{5,6} Only about 20% of 13–15-year-old adolescents worldwide achieve the recommended 60 min per day of moderate-to-vigorous physical activity.⁷ At the same time, the number of hours per day that children and adolescents sit in front of a screen, especially in front of a computer screen, is increasing.⁸

The aetiology of overweight and obesity is complex and results from environmental factors, genetic susceptibility and their interaction.⁹ Whereas 70% of obesity has been estimated

to be hereditary, only 1–2% can currently be explained by known genetic risk loci.^{10–12} There is substantial evidence that epigenetic mechanisms have a role in the regulation of adipogenesis and glucose homeostasis.^{13–15} However, there is a need for more in-depth understanding, and the associations between DNA methylation and body size also need to be verified, preferably in an age group in which dieting and medication use are less likely. Studies of animal models and humans suggest that the gut microbiome might also be associated with weight regulation.¹⁶ Less is known about the role of the oral microbiome and its association with overweight and obesity;¹⁷ most studies on the topic are based on animal models.¹⁸ Nonetheless, one study showed that some bacteria, such as *Campylobacter rectus* and *Neisseria*, are present in the oral microbiome in higher amounts among subjects with obesity than among normal-weight subjects.¹⁹ Large studies using independent culturing methods are needed to validate these findings.

Supported by and coordinated at the Folkhälsan Research Center in Helsinki, Finland, the Finnish Health in Teens (Fin-HIT) study was initiated with the aim to follow up and

understand long-term changes in body size from adolescence to adulthood. Within this cohort several risk factors for overweight and obesity, such as lifestyle, mental health, family environment and microbial, genetic and epigenetic markers, as well as the association between these factors, are being studied.

Who is in the cohort?

The Fin-HIT Study cohort, initiated in 2011, comprises adolescents aged around 9–12 years at enrolment, together with one adult responsible for each participant (henceforth referred to as ‘parents’), and is planned to be followed for 25 years. This age range was chosen as it denotes a period during which most participants are about to enter puberty. Moreover, according to our own focus group discussions with adolescents, individuals in this age range are cognitively mature enough to participate. Adolescents are defined as individuals 10–19 years old,²⁰ but for simplicity, we will henceforth use the term ‘adolescents’ for all our study participants, including the 9-year-olds. The Fin-HIT-study includes 11 407 adolescents and 9935 parents of these adolescents (one parent per adolescent), the vast majority of whom are mothers (Figure 1).

Baseline recruitment

Geographically, a large part of Finland was represented in the study, including urban and rural areas. Participants

come from 44 municipalities, including Finland’s largest cities: Helsinki, Turku, Espoo, Oulu, Jyväskylä, Tampere and Kuopio.

Baseline recruitment was carried out at two time points: in 2011 a pilot study was conducted, in which participants were recruited at home; in 2013–14 the main study went forward, in which participants were recruited at school. The pilot study tested the strategy of home-based recruitment by mailed invitation among 11 000 randomly selected households, but the response rate was 14.5%. Therefore, the main study used a school-based recruitment strategy in which 496 schools agreed to participate and fieldworkers handed out invitations to 27 000 adolescents in those schools. The total participation rate for adolescents at baseline was 30% [14.5%, ($n = 1599$) in the pilot study and 36% ($n = 9808$) in the main study, Figure 1].

An adolescent consent forms had to be signed by each adolescent and one of their parents; participating parents also returned their own, separate consent form. The school-based recruitment strategy did not allow us to obtain any information on non-participants (either no consent or non-response). Therefore, it was not possible to compare information between responders and non-responders.

The Ethics Committee of the Hospital District of Helsinki and Uusimaa approved the Fin-HIT Study

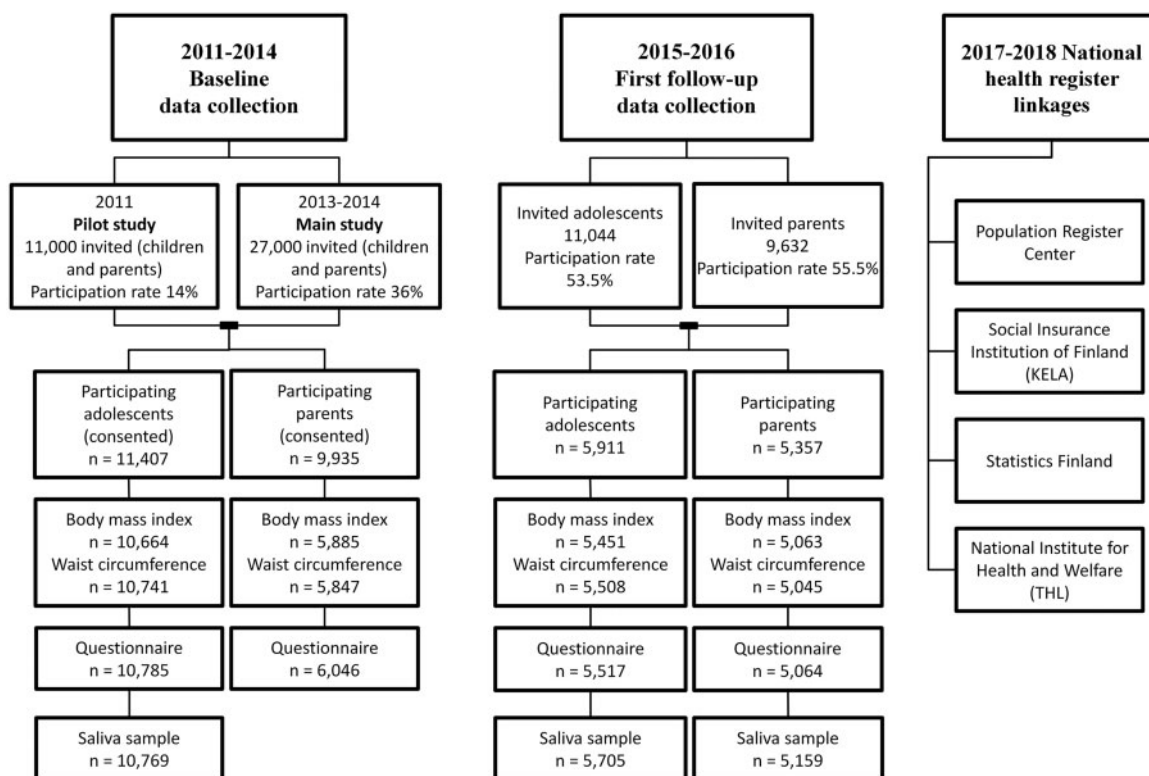


Figure 1. Data collection process and sample size in the Finnish Health in Teens (Fin-HIT) Study.

(decision number 169/13/03/00/10). Research permission to approach the schools was received from each municipality's education administration office. Approval to conduct the study was granted by the principal of each school.

How often have they been followed up?

The first active follow-up took place in 2015–16. Criteria for inclusion in the follow-up study were: valid study consent from both the adolescent and parent; valid body mass index (BMI) and/or saliva sample from the adolescent at baseline; and ability to identify personal information for adolescents and parents in the Population Information Center. Therefore 11 044 adolescents and 9632 parents were invited (Figure 1). There were 5911 adolescents and 5357 parents in the follow-up, corresponding to a participation rate of 53.5% and 55.5%, respectively.

The current ethical approval covers a 25-year follow-up period (i.e. until 2035), to which all participants have consented. This will include active follow-up, that is questionnaires and repeated saliva samples; and passive follow-up, that is linkage to national health registers through the participants' social security number, which will provide us with reliable follow-up data.

What has been measured?

At baseline

Adolescents answered a web questionnaire, provided a saliva sample and had their anthropometric measures (height, weight and waist circumference) taken at the school by fieldworkers. Parents completed a web questionnaire, in which they gave self-reported anthropometric measures. All information collected in the Fin-HIT Study is shown in Table 1.^{21–39}

Questionnaires for adolescents and parents were available in Finnish and Swedish, since they are both official languages in Finland, and the questionnaires covered a range of issues (Table 1). The questions on adolescent physical activity were validated with accelerometers in a sub-study.⁴⁰

The fieldworkers followed a standardized measurement protocol for all adolescents. Height was measured to the nearest 0.1 cm with a portable stadiometer (Seca model 217); weight to the nearest 0.01 kg with portable digital scales (CAS model PB) calibrated daily before each series of measurements; and waist circumference midway between the hip bones and the ribs to the nearest 0.1 cm with a measuring tape calibrated against a measure once a week. BMI was calculated as weight (kg)/height (m)² and

the adolescents were classified as underweight, normal weight, overweight or obese (BMI categories) according to age- and sex-specific cut-offs suggested by International Obesity Task Force (IOTF).⁴¹ Adolescents from the pilot study or those who were absent from school on the day of data collection (approximately 13% of adolescents) returned self-reported body measurements.

At follow-up

Adolescents and parents answered a web questionnaire and provided a saliva sample. Follow-up web questionnaires for both adolescents and parents collected information on lifestyle factors and anthropometric measures (height, weight and waist circumference) (Table 1). This self-reported follow-up information allowed us to study changes in body size and health status over time, including epigenetic and microbial changes and their associations with body size development. The saliva samples enabled us to study common changes and features in the microbiome and epigenome in a household setting.

Biological samples

Unstimulated saliva samples were collected using the Oragene[®] DNA Self-Collection Kit (DNA Genotek Inc., Canada), a high-quality method that has been used in studies of molecular epidemiology.⁴² DNA was extracted for a subset of the saliva samples collected from participants. Two different protocols were used, depending on the research aim. An automated Chemagen protocol (PerkinElmer, UK) was used to enrich human DNA, and both mechanical and enzymatic lysis of all cells was used to ensure access to DNA from all bacteria in the sample.⁴³ We successfully used a targeted bisulphite sequencing (Agilent SureSelect^X, Agilent, CA, USA) to assess DNA methylation ($n = 136$) and 16S rDNA sequencing (1000 baseline saliva samples and 412 follow-up saliva samples) to assess microbial composition using the above-mentioned DNA extracts.

Register data

A proportion of information will be obtained from national health registers. The registers that will be consulted include: (i) the Population Information System at the Population Register Center [https://eevertti.vrk.fi/paivitu_spalvelut], which contains information on social security number, address, and mother tongue; (ii) the Social Insurance Institution of Finland, [<http://www.kela.fi/web/en/492>], which includes information on medical prescriptions, purchases of prescription drugs and patient

Table 1. Information collected in the Fin-HIT Study for adolescents and parents at baseline and follow-up

Adolescent's information	Parent's information
Baseline 2011-14	
Self-administered web questionnaire	Self-administered web questionnaire
Lifestyle and health behaviour: diet, meal patterns, physical activity, parents' attitudes toward physical exercise, screen time, TV-programmes watched, bullying, ²¹ sleep patterns	Adolescent's childhood: family structure, child daycare, child breast-feeding, child feeding and eating behaviour in childhood, child special diets and allergies
Mental health: emotional eating, self-esteem, ^{22,23} anxiety, ²⁴ depression, ²⁵ obsessive compulsive disorder, ²⁶ weight perception, ²⁷ disordered eating symptoms, ²⁸ binge eating symptoms, ³⁷ body image ²⁹	Parent health information: educational level, socioeconomic status, illnesses diagnosed or treated, smoking, use of snuff, alcohol consumption, ^{34,35} general health status, ³⁶ life events, ³¹ depression, ³² weight perception of self and of child, dieting, binge eating symptoms, ³⁷ eating disorder diagnosis and/or treatment of family members, sense of coherence, ³⁸ screen time, potential partner's screen time, magazines read in the family
Adolescent growth environment: parent-child relationship, ^{30,39} parenting practices, life events, ³¹ alone time during school days, children's perception of alcohol consumption among adults in their social environment, puberty onset ³²	
Anthropometric measures ^a	Self-reported anthropometric measures ^a
Self-collected saliva sample ^b	
First follow-up 2015-16	
Self-administered web questionnaire	Self-administered web questionnaire
Meal patterns, diet, self-esteem, physical activity in free time, screen time	Family structure, illnesses diagnosed or treated, physical activity in free time, screen time
Self-reported anthropometric measures ^a	Self-reported anthropometric measures ^a
Self-collected saliva sample ^b	Self-collected saliva sample ^b

^aHeight, weight, waist circumference.

^bOragene[®] DNA Self Collection Kit.

spending on these drugs; (iii) Statistics Finland [http://www.stat.fi/til/asan_kaikki_en.html], which includes information on occupational status, wages and cause of death; and (iv) the National Institute for Health and Welfare (THL) [https://www.thl.fi/en/web/thlfi-en/statistics/information-for-researchers], which manages the Medical Birth Register, the Care Register for Health Care and the Register of Primary Health Care Visits, which contain information on diseases, pregnancy, newborn health, diagnoses, etc.

Descriptive results

The average age of adolescents was 11.2 (\pm 0.8) years at baseline and 13.7 (\pm 1.3) years at follow-up. Of the 11 407 adolescents recruited, 52% (n = 5981) were girls and 48% (n = 5423) were boys, and a similar proportion was found at follow-up (Table 2). This distribution is quite similar to that of the 10–14 years-old Finnish population in 2017 (51.1% boys and 48.8% girls).⁴⁴ Information on sex was obtained from the consent form and confirmed through linkage with the Population Information System at the Population Register Center. Social security number was missing for three participants, for whom we do not have information on sex.

At baseline, the prevalence of overweight in Fin-HIT adolescents was 12.6% (n = 1343) and the prevalence of obesity was 2.6% (n = 274), which is in accordance with other studies.^{45,46} At follow-up there was a similar percentage of adolescents with overweight (12.3%; n = 670) and obesity (2.2%; n = 119). In the total cohort, 4.6% (n = 524) of the adolescents reported Swedish as their first language, which is slightly lower than the proportion in the general Finnish population (5–6%).⁴⁷ Most adolescents reported having reached puberty (65.9%; n = 5614) but there were a lot of missing data for these questions (25%; n = 2892). Of the non-responders, 47% (n = 1355) were represented by adolescents below age 10 years and not targeted to answer these questions, and 53% (n = 1537) did not want to answer these questions (Table 2).

Both at baseline and at follow-up, most participating parents were female (n = 8568, 86.8%; n = 4701, 87.5%, respectively). The average age for parents was 42.0 (\pm 5.5) years at baseline and 44.9 (\pm 5.4) years at follow-up. The prevalence of overweight and obesity among parents at baseline was lower (41.3 %; n = 2431) than the estimated prevalence in the general population in Finland (50% of females and 62% of males).⁴⁸ However, this prevalence was higher at follow-up (45.7%; n = 2313). The majority

Table 2. Distribution of principal characteristics of participants at baseline and follow-up

		Baseline			Follow-up		
		<i>n</i>	%	Missing data	<i>n</i>	%	Missing data
Adolescents							
Sex	Female	5981	52.4%	3 ^a	3125	52.9%	
	Male	5423	47.6%		2786	47.1%	
Age (mean ± SD)		11 312	11.2 ± 0.8	95 ^a	5764	13.7 ± 1.3	147 ^d
Waist circumference (mean ± SD)		10 741	64.3 ± 7.9	666 ^a	5508	70.9 ± 8.3	403 ^d
BMI categories (IOTF)	Underweight	1175	11.0%	761 ^a	412	7.6%	459 ^d
	Normal weight	7854	73.8%		4251	78.0%	
	Overweight	1343	12.6%		670	12.3%	
	Obese	274	2.6%		119	2.2%	
Mother tongue	Finnish	10 555	92.6%	3 ^a	5538	93.7%	
	Swedish	524	4.6%		251	4.2%	
	Other	325	2.8%		122	2.1%	
Puberty phase	Prepubertal	2901	34.1%	2892 ^{a,§}	No information at follow-up		
	Pubertal	5527	64.9%				
	Post-pubertal	87	1.0%				
Parents							
Sex	Female	8568	86.8%	59 ^b	4701	87.5%	
	Male	1308	13.2%		669	12.5%	
Age (mean ± SD)		9884	42.0 ± 5.5	51 ^b	5188	44.9 ± 5.4	182 ^e
Education level	High school/ technical level	2634	45.1%	212 ^c	No information at follow-up		
	University degree	3200	54.9%				
Waist circumference (mean ± SD)		5847	86.4 ± 12.5	199 ^c	5045	87.1 ± 12.3	19 ^f
BMI categories (IOTF)	Underweight	106	1.8%	161 ^c	45	0.9%	1 ^f
	Normal	3348	56.9%		2705	53.4%	
	Overweight	1693	28.8%		1609	31.8%	
	Obese	738	12.5%		704	13.9%	

IOTF, International Obesity Task Force.⁴¹

^aBase for calculation: 11 407 children with consent at baseline.

^bBase for calculation: 9935 parents with consent at baseline.

^cBase for calculation: 6046 parents with consent and who answered the web questionnaire at baseline.

^dBase for calculation: 5911 child participants at follow-up.

^eBase for calculation: 5370 parent participants at follow-up.

^fBase for calculation: 5064 parents who answered the questionnaire at follow-up.

[§]1322 children aged under 10 years who did not answer questions on puberty onset.

of the parents reported that they had a university degree with diploma from a university of applied sciences or a degree from a university (54.9 %; *n* = 3200), and the others reported a high school or technical level of education (45.1%; *n* = 2634) (Table 2).

No substantial differences were found between adolescents with and without their parent's questionnaire information; however, results showed higher participation among prepubescent adolescents in the group with parental information (36.8%; *n* = 1784 compared with 30.5%; *n* = 1117 without parental information) (Table 3).

When some characteristics at baseline were compared between participating and non-participating adolescents in

the follow-up (Table 4), only parental educational level differed somewhat: participating adolescents in the follow-up had parents with a slightly higher educational level (57.5%) than the non-participating ones (49.5%). However, this information was available only from 5834 parents.

Of the 5277 adolescents with information on BMI at baseline and follow-up, 80.5% (*n* = 4247) maintained the same BMI at both time points (Table 5). The highest change was related to adolescents who were underweight at baseline and changed to normal weight at follow-up (6.6%; *n* = 349). Among normal-weight adolescents at baseline, 2.5% (*n* = 130) changed their BMI status to underweight, and 4.7% (*n* = 251) changed to overweight or obese at follow-up.

Table 3. Distribution of principal characteristics of adolescents with or without parental information

Adolescent characteristics	Parental participation in the baseline web questionnaire				
	Adolescents without parental information (<i>n</i> = 5361)		Adolescents with parental information (<i>n</i> = 6046)		
	<i>n</i>	%	<i>n</i>	%	
Age (mean ± SD)	5301	11.2 ± 0.90	6011	11.2 ± 0.78	
Waist circumference (mean ± SD)	4821	64.1 ± 7.92	5920	64.4 ± 7.97	
Sex	Female	2873	53.6%	3108	51.4%
	Male	2485	46.4%	2938	48.6%
BMI categories (baseline, IOTF)	Underweight	537	11.2%	638	10.9%
	Normal weight	3472	72.7%	4382	74.7%
	Overweight	63	13.3%	707	12.0%
	Obese	131	2.7%	143	2.4%
Mother tongue	Finnish	4874	91.0%	5681	94.0%
	Swedish	238	4.4%	286	4.7%
	Other	246	4.6%	79	1.3%
Puberty phase	Pre-pubertal	1117	30.5%	1784	36.8%
	Pubertal	2500	68.2%	3027	62.4%
	Post-pubertal	48	1.3%	39	0.8%

IOTF, International Obesity Task Force.⁴¹

Table 4. Distribution of characteristics of adolescents who did or did not participate in follow-up

	Adolescent participation at follow-up				
	No participation at follow-up (<i>n</i> = 5496)		Participation at follow-up (<i>n</i> = 5911)		
	<i>n</i>	%	<i>n</i>	%	
Age (mean ± SD)	5427	11.9 ± 0.84	5885	11.1 ± 0.83	
Waist circumference (mean ± SD)	4972	64.6 ± 8.44	5769	63.9 ± 7.5	
Gender children	Girl	2856	52.0%	3125	52.9%
	Boy	2637	48.0%	2786	47.1%
BMI categories (baseline, IOTF)	Underweight	517	10.5%	658	11.5%
	Normal	3575	72.7%	4279	74.7%
	Overweight	667	13.6%	676	11.8%
	Obese	161	3.3%	113	2.0%
Mother tongue	Finnish	5017	91.3%	5538	93.7%
	Swedish	273	5.0%	251	4.2%
	Others	203	3.7%	122	2.1%
Puberty phase (at baseline)	Prepubertal	1246	32.0%	1655	35.8%
	Pubertal	2594	66.7%	2933	63.4%
	Post-pubertal	49	1.3%	38	0.8%
Education level	High school/technical level	973	50.5%	1661	42.5%
	University degree	952	49.5%	2248	57.5%

IOTF, International Obesity Task Force.⁴¹

What has it found? Key findings and publications

Published studies and ongoing projects from the Fin-HIT cohort are briefly described below.

Validity of self-reported height, weight and waist circumference

This study assessed the validity of self-reported anthropometric measurements compared with standardized

Table 5. Changes in adolescents' BMI category^a (IOTF)

		BMI categories (follow-up)								Total in each row	
		Underweight		Normal weight		Overweight		Obese			
		<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%		
BMI categories (baseline)	Underweight	270	5.1%	349	6.6%					619	11.7%
	Normal weight	130	2.5%	3547	67.2%	240	4.5%	11	0.2%	3928	74.4%
	Overweight	1	0.01%	217	4.1%	368	7.0%	39	0.7%	625	11.8%
	Obese			4	0.1%	39	0.7%	62	1.2%	105	2.0%
Total in each column		401	7.6%	4117	78.0%	647	12.3%	112	2.1%	5277	100.0%

IOTF, International Obesity Task Force.⁴¹

^aOnly adolescents with information on BMI at baseline and follow-up.

measurements taken at school among adolescents, at baseline. We found no statistically significant difference in height or BMI measured at home and at school.⁴⁹

Maternal alcohol and tobacco consumption and BMI among adolescents

This cross-sectional study aimed to evaluate whether maternal consumption of alcohol or tobacco is associated with their children's BMI. We found that maternal consumption of tobacco and alcohol is associated with their children's BMI. Current maternal smoking was associated with overweight among children, and former maternal smoking was inversely associated with underweight among children.⁵⁰

DNA methylation and body size

DNA methylation (DNAm) has been analysed among 100 adolescents at baseline: 50 underweight girls and 50 girls with overweight. An association was found between differential methylation and body size groups. The two strongest signals were located near *NAV3* and *MC2R*. Many of the associated CpG-sites and genomic regions were co-located with known obesity-related genes, predominantly in the insulin-melanocortin pathway. The overlap with obesity and insulin-related genes, including *MC2R*, *IGFBPL1*, *IP6K1* and *IGF2BP1*, indicate functional connections between the saliva methylome and BMI, and vice-versa.⁵¹ Replication of these results is ongoing.

Identifying eating habits in Finnish adolescents

In a cross-sectional study, we aimed to identify different eating habits among adolescents and to evaluate the association between these eating habits and meal patterns, breakfast consumption and sociodemographic characteristics. We identified three groups: unhealthy eaters (12.3%), fruit and vegetable avoiders (43.3%) and healthy eaters

(44.1%). Unhealthy eaters showed irregular meal and irregular breakfast patterns, and had parents with a low education level. Healthy eaters showed regular meal and regular breakfast patterns, and had parents with high education level (Figueiredo *et al.*, submitted).

Body dissatisfaction and disordered eating symptoms in Finnish pre-adolescents

The purpose of this cross-sectional study was to evaluate whether body dissatisfaction is associated with disordered eating symptoms like dieting or avoiding certain foods, and to determine the effects of gender and BMI on this association. A relevant percentage of adolescents reported body dissatisfaction: 30.0% wanted a smaller body and 9.3% wanted a larger body. Only 2.2% of the participants had disordered eating symptoms. We found that body dissatisfaction was associated with disordered eating symptoms, especially among girls and those who were underweight and normal-weight (Figueiredo *et al.*, submitted).

Reproducibility and repeatability of six high-throughput 16S rDNA sequencing protocols for microbiota profiling

The purpose of the study was to establish methods to investigate the microbiome in saliva samples collected at baseline. One of the challenges when using next-generation sequencing technologies to assess the microbiome is achieving sufficient reproducibility and repeatability of the results. High reproducibility and repeatability are mostly attained through robust polymerase chain reaction (PCR) amplification. We assessed the reproducibility of saliva microbiota profiles produced with simplified, in-house 16S amplicon assays with a large number of barcodes. The assays included primers modified with Truseq (TS-tailed) or Nextera (NX-tailed) adapters, with either dual index or

dual index plus a 6-nt internal index. All amplification protocols produced consistent microbial profiles for the same samples. However, reproducibility was highest for the TS-tailed method, and the repeatability of a TS-tailed, one-step protocol without internal index tested on the HiSeq platform yielded high alpha diversity.

Microbiome and body size

Associations between BMI categories and the saliva microbiome were investigated in 1000 randomly selected saliva samples at baseline. About 104 million 16S rDNA (V3-V4) sequences were obtained and classified into operational taxonomic units (OTUs). Significant differences in microbial abundance at three taxonomic levels (OTU, genus, order) were observed between BMI categories. The following bacteria were significantly more abundant in the BMI categories: *Kingella* in underweight; *Alysiella*, *Caulobacter* and *Acidovorax* in overweight; *Acinetobacter*, *Kingella* and *Enhydrobacter* in overweight and obese; and *Alysiella* and *Acidovorax* in obese. Our results may potentially be used for early identification of persons at risk for developing obesity (Raju *et al.*, submitted).

Diversity in saliva microbiota and body composition of adolescents at baseline and follow-up

We aimed to investigate longitudinal changes in the adolescent saliva microbiome after 4 years of follow-up, and their association with BMI development. The microbiome of 580 follow-up saliva samples will be compared with baseline samples and changes will be studied in four groups: adolescents who maintained normal weight; adolescents who maintained overweight; adolescents who changed from normal weight to overweight; or vice versa; during the 4-year follow-up (Raju *et al.*, in preparation).

Picky eating, a risk factor for underweight in Finnish adolescents

This cross-sectional study focused on the associations of picky eating (PE) and food neophobia (FN) with food consumption and BMI. The overall prevalence of PE and FN in the cohort were 33.6% and 14.1%, respectively. We have shown that PE and FN are real obstacles to healthy eating, as they are clearly associated with unhealthy eating habits. Adolescents with PE and FN had a higher risk for underweight, and those with PE had a lower risk for overweight/obesity (Viljakainen H *et al.*, in preparation).

Eating habits and body size in Finnish adolescents

This cross-sectional study evaluates the associations of eating habits, meal patterns and breakfast consumption with body size, as defined by BMI categories. Fruit and vegetable avoiders were associated with underweight. Adolescents with irregular breakfast consumption had a lower risk of underweight but a higher risk of overweight and obesity (Viljakainen J *et al.*, in preparation).

What are the main strengths and weaknesses

Strengths of the Fin-HIT Study include its sample size, as it is one of the largest prospective population-based studies of 9–12-year-olds and their parents in Finland so far. Moreover, questionnaire data, anthropometric measures and saliva samples are available for both adolescent and parents. The study takes advantage of data linkage from several national registers. The longitudinal study design enables us to observe trends from adolescence to adulthood related to body size, lifestyle factors, the microbiome, genetic and epigenetic aspects and others. The study design also lends to the elaboration of aetiological studies on body size development. The data collection was supervised by trained staff following standard operating procedures, and all management procedures are quality assured.

Weaknesses include a relatively low participation rate at baseline (30%) and first active follow-up, during which only about half of the original 11 407 adolescents participated; thus, selection bias cannot be excluded. Reassuringly, the prevalences of overweight and obesity among Fin-HIT adolescents (13.4%, Table 2) are similar to those observed in other studies.^{45,46} Other studies have reported similar or lower participation rates, which may indicate a more global trend of unwillingness to participate in large epidemiological studies.⁵² Another weakness was that information on principal risk factors were self-reported, which may have some bias and thus may provide weaker evidence of causality. However, some parts of the questionnaire data will be confirmed and complemented with data from national registers.

Can I get hold of the data? Where can I find out more?

The Fin-HIT Study is being conducted at the Folkhälsan Research Center, under the supervision of Professor Elisabete Weiderpass. Details of the cohort can be found at [www.finhit.fi/for-researchers]. We welcome applications to use the Fin-HIT dataset. Interested researchers, please contact Professor Elisabete Weiderpass [e-mail: elisabete.weiderpass@helsinki.fi].

Profile in a nutshell

- The Fin-HIT Study is designed to study environmental, genetic and epigenetic factors in the development of body size and health outcomes over time.
- At baseline (2011–14), 11 407 adolescents aged 9 to 12, living in and around the largest cities in Finland, were enrolled in the study together with 9935 parents.
- The first active follow-up was conducted in 2015–16 and included repeated body measurements and saliva sampling from both adolescents and parents.
- The dataset consists of questionnaire data, anthropometric measures and biological samples. The study database is linked to data from several Finnish national health registers.
- For collaborative studies, please contact Professor Elisabete Weiderpass [e-mail: elisabete.weiderpass@helsinki.fi].

Funding

The Fin-HIT Study is supported by the Folkhälsan Research Foundation, the Academy of Finland [grant number 250704]; Swedish: Medicinska Understödsföreningen Liv och Hälsa [2-147-21], the Swedish Cultural Foundation in Finland [16/2341], the Signe and Ane Gyllenberg Foundation [grant number 40–2847-42] and the Yrjö Jahnsson Foundation [grant number 11486].

Acknowledgements

The study group thanks the adolescents and parents who are participating in the Fin-HIT Study, the teachers and principals of the schools, all the fieldworkers and coordinators who took part in cohort enrolment, Jesper Skand for data management and Stephanie von Kraemer and Catharina Sarkkola for revision of early drafts of this article. We also thank Samfundet Folkhälsan for supporting the study.

Conflict of interest: None declared.

References

1. Non-Communicable Diseases Risk Factor Collaboration. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: A pooled analysis of 2416 population-based measurement studies in 128.9 million children, adolescents, and adults. *Lancet* 2017;390:2627–42.
2. Olds T, Maher C, Zumin S *et al.* Evidence that the prevalence of childhood overweight is plateauing: data from nine countries. *Int J Pediatr Obes* 2011;6:342–60.
3. Park MH, Sovio U, Viner RM, Hardy RJ, Kinra S. Overweight in childhood, adolescence and adulthood and cardiovascular risk in later life: pooled analysis of three British birth cohorts. *PLoS One* 2013;8:e70684.
4. Xu S, Xue Y. Pediatric obesity: causes, symptoms, prevention and treatment (review). *Exp Ther Med* 2016;11:15–20.
5. Hill JO, Wyatt HR, Peters JC. Energy balance and obesity. *Circulation* 2012;126:126–32.
6. Gurnani M, Birken C, Hamilton J. Childhood obesity: causes, consequences, and management. *Pediatr Clin North Am* 2015; 62:821–40.
7. Hallal PC, Andersen LB, Bull FC, Guthold R, Haskell W, Ekelund U. Global physical activity levels: surveillance progress, pitfalls, and prospects. *Lancet* 2012;380:247–57.
8. Bucksch J, Sigmundova D, Hamrik Z *et al.* International trends in adolescent screen-time behaviors from 2002 to 2010. *J Adolesc Health* 2016;58:417–25.
9. Huang T, Hu FB. Gene-environment interactions and obesity: recent developments and future directions. *BMC Med Genomics* 2015;8(Suppl 1):S2.
10. Fall T, Ingelsson E. Genome-wide association studies of obesity and metabolic syndrome. *Mol Cell Endocrinol* 2014;382: 740–57.
11. Hebebrand J, Hinney A. Environmental and genetic risk factors in obesity. *Child Adolesc Psychiatr Clin North Am* 2009;18:83–94.
12. Speliotes EK, Willer CJ, Berndt SI *et al.* Association analyses of 249,796 individuals reveal eighteen new loci associated with body mass index. *Nat Genet* 2010;42:937–48.
13. Lavebratt C, Almgren M, Ekström TJ. Epigenetic regulation in obesity. *Int J Obes Relat Metab Disord* 2012;36:757–65.
14. van Dijk SJ, Molloy PL, Varinli H, Morrison JL, Muhlhauser BS. EpiSCOPE members of. Epigenetics and Human Obesity. *Int J Obes* 2015;39:85.
15. Kuroda A, Rauch TA, Todorov I *et al.* Insulin gene expression is regulated by DNA methylation. *PLoS One* 2009;4:e6953.
16. Ley RE, Turnbaugh PJ, Klein S, Gordon JI. Microbial ecology: human gut microbes associated with obesity. *Nature* 2006;444: 1022.
17. Goodson JM, Groppo D, Halem S, Carpino E. Is obesity an oral bacterial disease? *J Dent Res* 2009;88:519–23.
18. DiBaise JK, Zhang H, Crowell MD, Krajmalnik-Brown R, Decker GA, Rittmann BE. Gut microbiota and its possible relationship with obesity. *Mayo Clin Proc* 2008;83:460–69.
19. Zeigler CC, Persson GR, Wondimu B, Marcus C, Sobko T, Modéer T. Microbiota in the oral subgingival biofilm is associated with obesity in adolescence. *Obesity* 2012;20:157–64.
20. World Health Organization. Health for the World's Adolescents. Geneva:WHO, 2014.
21. Luopa P, Pietikäinen M, Jokela J. *Kouluterveyskysely 1998–2007: Nuorten hyvinvoinnin kehitys ja alueelliset erot [School Health Promotion Study 1998–2007: Development and Regional Differences of Adolescents' well-being]*. Helsinki: Research Reports 23, 2008.
22. Miller H. Cross-cultural validity of a model of self-worth: application to Finnish children. *Soc Behav Pers* 2000;28:105–18.
23. Rosenberg M. *Society and the Adolescent Self-Image*. Princeton, NJ: Princeton University Press, 1965.
24. Birmaher B, Khetarpal S, Brent D *et al.* The Screen for Child Anxiety Related Emotional Disorders (SCARED): scale construction and psychometric characteristics. *J Am Acad Child Adolesc Psychiatry* 1997;36:545–53.
25. Weissman M, Orvaschel H, Padian N. Children's symptom and social functioning self-report scales. Comparison of mothers' and children's reports. *J Nerv Ment Dis* 1980;168:736–40.

26. Uher R, Heyman I, Mortimore C, Frampton I, Goodman R. Screening young people for obsessive compulsive disorder. *Br J Psychiatry* 2007;191:353–54.
27. Brenner N, Kann L, Kinchen S. A *et al.* Methodology of the youth risk behavior surveillance system. *MMWR Recomm Rep* 2004; 53:1–13.
28. Maloney MJ, McGuire JB, Daniels SR. Reliability testing of a children's version of the eating attitude test. *J Am Acad Child Adolesc Psychiatry* 1988;27:541–43.
29. Collins ME. Body figure perceptions and preferences among pre-adolescent children. *Int J Eat Disord* 1991;10:199–208.
30. Steinberg L, Lamborn S, Darling N, Mounts N, Dornbusch S. Over-time changes in adjustment and competence among adolescents from authoritative, authoritarian, indulgent, and neglectful families. *Child Dev* 1994;65:754–70.
31. Johnson J. *Life Events as Stressors in Childhood and Adolescence*. Thousand Oaks, CA: Sage Publications, 1986.
32. Raitasalo R. *Mielialakysely—Suomen Oloihin Beckin Lyhyen Depressiokyselyn Pohjalta Kehitetty Masenmusoireilun Ja Itsetunnon Kysely [Mood Questionnaire. Finnish Modification of the Short form of the Beck Depression Inventory Measuring Depression Symptoms and Self-Esteem]*. Helsinki, 2007.
33. Tanner JM. *Growth in Adolescents*. 2nd edn. Oxford, UK: Blackwell Scientific Publications, 1962.
34. Babor TF, Higgins BJC, Saunders JJB, Monteiro MG. *AUDIT. The Alcohol Use Disorders Identification Test. Guidelines for Use in Primary Care*. Geneva: WHO, 2001.
35. Saunders JB, Aasland OG, Babor TF, De La Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO collaborative project on early detection of persons with harmful alcohol consumption-II. *Addiction* 1993;88: 791–804.
36. Aalto A, Aro A, Teperi J. *RAND-36 Terveysteen Liittyvän Elämänlaadun Mittarina—Mittarin Luotettavuus Ja Suomalaiset Väestöarvot [RAND-36 as a measure of Health-Related Quality of Life. Reliability, Construct Validity and Reference Values in the Finnish General Population]*. Helsinki, 1999.
37. Field AE, Taylor CB, Celio A, Colditz GA. Comparison of self-report to interview assessment of bulimic behaviors among pre-adolescent and adolescent girls and boys. *Int J Eat Disord* 2004; 35:86–92.
38. Antonovsky A. *Unraveling the Mystery of Health: How People Manage Stress and Stay Well*. San Francisco, CA: Jossey-Bass, 1987.
39. Cerdá M, Bordelois P, Keyes KM *et al.* Family ties: maternal-offspring attachment and young adult nonmedical prescription opioid use. *Drug Alcohol Depend* 2014;142:231–38.
40. Määttä S, Nuutinen T, Ray C, Eriksson JG, Weiderpass E, Roos E. Validity of self-reported out-of-school physical activity among Finnish 11-year-old children. *Arch Public Health* 2016;74:11.
41. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. *Pediatr Obes* 2012;7:284–94.
42. Rylander-Rudqvist T, Håkansson N, Tybring G, Wolk A. Quality and quantity of saliva DNA obtained from the self-administered orogene method—a pilot study on the cohort of Swedish men. *Cancer Epidemiol Biomarkers Prev* 2006;15:1742–45.
43. Yuan S, Cohen DB, Ravel J, Abdo Z, Forney LJ. Evaluation of methods for the extraction and purification of DNA from the human microbiome. *PLoS One* 2012;7:e33865.
44. Statistics Finland. *Population Structure*. 2018. https://www.stat.fi/tup/suoluk/suoluk_vaesto_en.html (19 June 2018, date last accessed).
45. Mäki P, Hakulinen-Viitanen T, Kaikkonen R *et al.* Lasten Terveystutkimuksen Perustulokset Lasten Kasvusta, Kehityksestä, Terveystilasta. *Terveystutkimuksista Ja Kasvuympäristöstä [Child Health – Results of the LATE-study on Growth, Development, Health, Health Behavior and Growth Environment]*. National Institute for Health and Welfare (THL), 2010. <http://www.julkari.fi/handle/10024/80056>.
46. Vuorela N, Saha MT, Salo M. Prevalence of overweight and obesity in 5- and 12-year-old Finnish children in 1986 and 2006. *Acta Paediatr* 2009;98:507–12.
47. Volanen S, Suominen S, Lahelma E, Koskenvuo M, Silventoinen K. Sense of coherence and its determinants: a comparative study of the Finnish-speaking majority and the Swedish-speaking minority in Finland. *Scand J Public Health* 2006;34:515–25.
48. Ng M, Fleming T, Robinson M *et al.* Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014;384:766–81.
49. Sarkkola C, Rounge TB, Simola-Ström S, Kraemer SV, Roos E, Weiderpass E. Validity of home-measured height, weight and waist circumference among adolescents. *Eur J Public Health* 2016;2014:1–3.
50. Figueiredo RA, de O, Roos E, Eriksson JG, Simola-Ström S, Weiderpass E. Maternal alcohol and tobacco consumption and the association with their 9 to 14-year-old children's body mass index. *Scand J Public Health* 2017;45:503–10.
51. Rounge TB, Page CM, Lepistö M, Ellonen P, Andreassen BK, Weiderpass E. Genome-wide DNA methylation in saliva and body size of adolescent girls. *Epigenomics* 2016;8:1495–505.
52. Galea S, Tracy M. Participation rates in epidemiologic studies. *Ann Epidemiol* 2007;17:643–53.