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Early detection of childhood overweight and related complications in a Danish population-based cohort aged 2–8 years

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ABSTRACT

Background: Overweight in early childhood often tracks into adolescence and adulthood and early childhood is a critical period for developing sustained overweight. This study aims to investigate the early detection of childhood overweight (including obesity) and related cardiometabolic complications in a Danish population-based cohort of children aged 2.5–8 years in collaboration with primary care municipal dental clinics and public health nurses.

Methods: In this prospective population-based cohort study, 335 pre-school children (age 2.5 and 5 years) were recruited from municipal dental clinics, and 657 school children (age 6–8 years) by public health nurses. A subgroup of 392 children (40%) participated in additional hospital-based examinations including blood pressure measurement and a blood sample. Children were re-examined approximately one year later.

Results: The prevalence of overweight was 13.73% in pre-school children and 13.69% in school children at baseline. In the pre-school children, differences in cardiometabolic risk markers between children with and without overweight were minor, whereas in school children with overweight, cardiometabolic derangements were manifest including significantly higher levels of fasting glucose, insulin, homoeostasis model of assessment for insulin resistance, triglycerides, and alanine aminotransferase and lower levels of high-density lipoprotein cholesterol. During follow-up the prevalence of overweight did not change in pre-school children but increased to 17.0% in school children.

Conclusions: Existing contacts with the primary health care sector, including dental care, can successfully be used for detection of overweight. This study suggests that early detection should be initiated at pre-school ages since overweight-related complications are already established by school ages.

1. Introduction

Even in childhood, multiple severe complications from overweight

can occur. Children with overweight can have several concurrent complications, including dyslipidemia, fatty liver disease, hypertension, insulin resistance, and type 2 diabetes that may develop into long-term

Abbreviations: BMI, Body mass index; SDS, Standard deviation score; HDL, High-density lipoprotein; ALT, Alanine transaminase; LDL, Low-density lipoprotein; HOMA-IR, Homoeostasis model of assessment – insulin resistance; IOTF, International Obesity Task Force.

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negative health consequences [1]. However, early childhood is a window of opportunity for preventing sustained overweight and its related comorbidities since it is a critical period for developing overweight and its related cardiometabolic risk [2–4]. As a part of normal physiological development, children's body mass index (BMI) increases during infancy, declines, and then rises again typically by 6 years of age [5]. The timing and steepness of this BMI increase in childhood are associated with later overweight [6] and cardiometabolic disease [7,8]. Nonetheless, there are indications that risks associated with overweight in childhood can be mitigated, as overweight at seven years of age is associated with increased risks of adult type 2 diabetes only if overweight is sustained until puberty or later [9]. Therefore, the timely identification of children at risk is crucial as treatment prior to the development of overt comorbidities may prevent sustained overweight and its related complications.

In Denmark and other Northern European countries, the primary health care sector has continuous contact with the paediatric population, thus making it an existing system in which early evaluation of children at risk is possible. In Denmark, children are in contact with municipal dental care and public health nurses who visit the child's home during infancy and see them in the schools. Thus, introducing the early detection of childhood overweight into the existing and functioning primary health care sector is likely feasible and economically prudent. Although using dental clinics as a system for detecting overweight in children has been proposed in reviews on the subject [10,11], actual studies are sparse [12,13].

This study aims to examine the prevalence of overweight and related complications in a Danish population-based cohort of pre-school children aged 2.5 and five years and school children aged 6–8 years investigated in collaboration with municipal dental care and public health nurses in the primary sector.

2. Methods

2.1. Design and study population

In Denmark, childhood dental care and health care provided by public health nurses are coordinated at the municipal level. The number and timing of these contacts is set by national law. Based upon this framework, in this prospective study, a population-based cohort of children was recruited using the children and family's existing contacts with the primary sector including municipal dental care and public health nurses in Holbæk municipality, Denmark from March 2015 until June 2016. To obtain a deeper phenotype than what was possible in the primary sector setting, the participants were subsequently invited to an additional examination at Copenhagen University Hospital Holbæk from March 2015 to October 2016. Approximately one year later, this setup was repeated with follow-up in both the primary sector and the hospital setting.

2.2. Training of paediatric dental assistants and public health care nurses

Paediatric dental assistants ($n = 4$) and public health nurses ($n = 19$) were provided training on how to assess overweight by medical doctors and a paediatric nurse experienced in this area. Training included education about how to accurately measure anthropometrics (height, weight, hip-, waist-, and neck circumferences) as to reduce error and inter-investigator variation. It also included training on how to communicate messages about overweight in a paediatric population.

2.3. Primary sector visits

Based upon the existing schedule of municipal dental care consultations, pre-school children aged 2.5 years (born in 2013) and five years (born in 2010) were invited to participate in the study. Similarly, based upon existing health consultations in the schools with public health

nurses, school children aged 6–8 years at school entry in 2014/15 and 2015/16 (birth years 2007–2009) were invited to participate in the study.

When receiving standard invitations for the existing primary sector health care visits, the families were informed about the study. Children from the relevant birth years were invited and a total of 3408 children were eligible for inclusion. There were no exclusion criteria in the study. However, study information was only provided in Danish.

When possible in the primary sector, the follow-up examination took place using existing contacts. Children who had been included through the dental clinics at age 5 were re-examined at school entry by the public health nurses and the baseline school children were re-examined in second grade at an existing consultation. A new consultation was created for the baseline 2.5-year-old children in the dental clinics at age 3.5 years.

2.4. Outcome measures in the primary sector visit

During the visit in the primary sector, trained staff measured the child's height, weight, hip-, waist-, and neck circumferences. Before the visit, the child's parents filled in a health questionnaire that included questions about self-perceived ethnic origin, socioeconomic status, exposure to passive smoking, and questions regarding precocious puberty. At follow-up, the same outcome measures were assessed including the questionnaire.

2.5. Outcome measures in the hospital setting

All participants were invited to participate in an additional hospital-based examination, which included blood pressure measurement, a venous blood sample after an overnight fast and repeated measurements of height and weight. Blood samples were collected only on children five years or older for ethical reasons. These outcomes were assessed again at follow-up.

2.6. Anthropometrics

Stadiometers and weight scales were provided to the dental clinics and public health nurses if needed, and all equipment was calibrated. Height was measured by stadiometer to the nearest 1 mm. Weight was measured to the nearest 100 g on a Tanita® BWN-800 SMA scale or Radwag® WPT 60/150 O/OW scale in the primary sector and on Tanita® BC418 scale in the hospital setting. Measurements were performed wearing light indoor clothes and without shoes. Waist circumference was measured at the umbilical level in a standing position and post-exhalation and hip circumference was measured at the level with the largest circumference around thighs/buttocks. Both circumferences were measured to the nearest 5 mm. Neck circumference was measured just below the laryngeal prominence with a stretch resistant measuring tape to the nearest 0.1 cm. Blood pressure was measured three times on the right upper arm with an electronic sphygmomanometer, Omron 705IT® after five minutes of rest in a supine position. An average value was calculated from the last two measurements.

2.7. Blood samples and biochemical analyses

Venous blood samples were drawn between 7 and 9 AM after an overnight fast. If requested, the venipuncture was performed after application of a topical anaesthetic (lidocaine/prilocain mixture). The samples were processed immediately and analysed within six to eight hours after sampling.

Serum insulin and C-peptide concentrations were measured on a Cobas 6000 Analyzer (Roche Diagnostics, Denmark). Concentrations of plasma glucose, total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, and alanine aminotransferase (ALT) were determined on a Dimension Vista 1500 Analyzer (Siemens Healthcare, Erlangen,

Germany). The Friedewald formula was used for calculation of low-density lipoprotein (LDL) cholesterol (LDL-C = total cholesterol–HDL-C–TG/5) [14]. Homoeostasis model of assessment - insulin resistance (HOMA-IR) was calculated as insulin (mIU/L) × glucose (mmol/L)/22.5 [15].

2.8. Degree of overweight assessment

If the child had a BMI > 90th percentile for age and sex at any of the examinations, the parents were informed that the child had overweight and that there was an available treatment option within the municipality [16]. This community overweight treatment programme was based upon The Children's Obesity Clinic Treatment protocol, a tertiary multidisciplinary childhood obesity treatment as described in detail here [17].

2.9. Ethics

All parents gave informed written and oral consent. The study was approved by the Ethics Committee of Region Zealand, Denmark (no. SJ-104) and the Danish Data Protection Agency. The study was conducted in accordance with the Helsinki Declaration of 1975 as revised in 2013. The study is part of The Danish Childhood Obesity Biobank; ClinicalTrials.gov ID-no.: NCT00928473.

2.10. Statistics

The International Obesity Task Force (IOTF) reference was used to calculate BMI SDS [18]. Height SDS were calculated according to an American reference [19]. Socioeconomic status was categorised into five groups depending on parental occupation using a national classification [20]. Blood pressure was expressed as SD scores according to the American Academy of Pediatrics reference [21]. The cohort was analysed in two groups based upon where the children were recruited from (dental clinic or school). Histograms and qq-plots were used to evaluate the normality of data. Student's t-test, Wilcoxon rank-sum test or chi-square test were used to examine differences between the groups. Statistical analyses were performed in R statistical software (v.3.5.2) [22].

3. Results

3.1. Demographic data

The study included 992 children (494 boys) at the baseline visit in the primary sector; 335 pre-school children were included from municipal dental clinics and 656 from schools (Table 1). Subsequently, 392 children (192 boys; 40% of the initial population) participated in additional examinations in the hospital setting (Table 2).

3.2. Baseline visit in the primary sector

At the baseline visit, the prevalence of overweight (including obesity) was 13.73% in the pre-school children aged 2.5 and 5 years and 13.69% in the school children aged 6–8 years (Table 1). The distributions of ethnic origin, socioeconomic status, and exposure to passive smoking were similar between the two groups and all participants were pre-pubertal (Table 1).

3.3. Baseline additional examinations in hospital setting

The additional examinations occurred after a median of 36 days, and 150 pre-school and 242 school children from the initial cohort participated. Of these children, 10.0% and 11.2%, respectively, exhibited overweight. Fasting blood values of glucose metabolism, lipids, and liver parameters were similar in the two groups. Diastolic blood pressure SDS

Table 1

Descriptive characteristics of the baseline visit in the primary sector.

Characteristic	N missing data	Pre-school children (2.5 and 5 years old) N = 335	School children (6–8 years old) N = 657	P-value
Sex (% boys)	–	49.0	50.2	0.78
Age (years)	–	2.7 [2.6, 5.2]	6.8 [6.4, 7.1]	–
Anthropometrics				
Height SDS	–	0.48 (0.93)	0.51 (0.91)	–
Weight (kg)	–	15.7 [13.9, 19.5]	23.6 [21.7, 26.3]	–
Waist circumference (cm)	4	53.0 [50.8, 56.0]	57.6 [55.1, 61.0]	–
Hip circumference (cm)	4	59.0 [56.5, 62.9]	65.2 [62.0, 68.3]	–
Neck circumference (cm)	8	25.0 [24.0, 26.0]	26.5 [25.7, 27.7]	–
Degree of obesity ^a				
BMI SDS	–	0.33 (0.92)	0.34 (0.90)	0.87
BMI SDS > 90th percentile (%)	–	13.73 (46)	13.69 (90)	1.00
Ethnic origin, %	–			0.97
North-European white	–	96.7	96.7	–
Middle Eastern	–	2.4	2.4	–
Asian	–	0.3	0.5	–
African	–	0.6	0.5	–
Socioeconomic status (%)	359			0.43
1 (highest)	–	24.8	28.3	–
2	–	46.6	41.0	–
3	–	20.4	21.5	–
4	–	6.3	5.2	–
5	–	1.9	4.0	–
Passive smoking (%)	–	16.4 (55)	18.9 (124)	0.39

Data are medians and interquartile ranges in brackets or means and standard deviations in parenthesis. Abbreviations: BMI SDS: Body mass index standard deviation score.

^a IOTF reference used for percentiles, see main text.

was higher in the pre-school group ($P < 0.001$), although it should be noted there were some challenges in adhering to the measurement protocol in the youngest children (Table 2).

3.4. Comparison of children with and without overweight at baseline

In the pre-school children with overweight, fasting glucose was lower ($P = 0.028$), while HDL-cholesterol ($P = 0.030$) and ALT ($P = 0.018$) were higher than in children without overweight (Table 3). In the school children with overweight, levels of ALT were also higher ($P < 0.001$) and, in contrast to the pre-school children, levels of fasting glucose were higher ($P = 0.002$) and HDL-cholesterol were lower ($P = 0.007$) than in school children without overweight (Table 3). Further, the school children with overweight were taller ($P = 0.002$) and exhibited higher levels of insulin, C-peptide, HOMA-IR ($P < 0.001$ for all), and triglycerides ($P = 0.029$) than school children without overweight (Table 3). Nonetheless, it should be noted that all median concentrations in both pre-school and school children were within normal ranges.

3.5. Follow-up in the primary sector

Follow-up examinations in the primary sector were conducted in the pre-school ($n = 223$) and school children ($n = 518$) after a median of 14.7 and 20.5 months, respectively. In this subgroup of children, at baseline 13.0% of the pre-school children had overweight and 12.4% of the school children had overweight. At the follow-up, the prevalence of overweight in the pre-school children was 12.6%, and this did not differ

Table 2

Descriptive characteristics of the additional examinations at baseline in the hospital setting.

Characteristic	N missing data	Pre-school children (2.5 and 5 years old) N = 150	School children (6–8 years old) N = 242	P-value
Sex (% boys)	–	47.3	50.0	0.68
Age (years)	–	3.0 [2.8, 5.4]	6.9 [6.7, 7.3]	–
Anthropometrics				
Height SDS	–	0.62 (0.96)	0.65 (0.93)	–
Weight (kg)	–	16.4 [13.9, 19.6]	24.2 [22.0, 26.6]	–
Degree of obesity^a				
BMI SDS	–	-0.05 (0.96)	0.17 (1.01)	0.040
BMI SDS > 90th percentile (%)	–	10.0 (15)	11.2 (27)	0.85
Blood pressure				
Systolic BP SDS	8	0.14 [– 0.24, 0.78]	0.18 [– 0.24, 0.64]	0.69
Diastolic BP SDS	8	0.56 [0.12, 1.05]	-0.00 [– 0.28, 0.38]	< 0.001
Venous blood samples^b				
Glucose (mmol/L)	46	4.7 [4.5, 4.9]	4.7 [4.5, 5.0]	0.95
HbA1c (mmol/mol)	42	33.0 [31.0, 35.0]	33.0 [31.0, 35.0]	0.88
Insulin (pmol/L)	49	27.1 [18.2, 37.6]	27.8 [18.0, 40.5]	0.55
C-peptide (nmol/L)	46	0.3 [0.3, 0.4]	0.3 [0.3, 0.4]	0.37
HOMA-IR	54	0.9 [0.6, 1.4]	1.0 [0.6, 1.5]	0.53
Triglycerides (mmol/L)	36	0.6 [0.5, 0.7]	0.5 [0.4, 0.7]	0.44
Cholesterol (mmol/L)	36	3.8 [3.4, 4.1]	3.8 [3.4, 4.3]	0.66
HDL-C (mmol/L)	36	1.4 [1.3, 1.6]	1.5 [1.3, 1.7]	0.96
LDL-C (mmol/L)	36	2.1 [1.7, 2.3]	2.1 [1.8, 2.5]	0.47
ALT (U/l)	36	23.0 [20.0, 25.2]	22.0 [19.0, 26.0]	0.45

Data are medians and interquartile ranges in brackets or means and standard deviations in parenthesis. Abbreviations: BMI SDS: Body mass index standard deviation score; BP: Blood pressure; HbA1c: Haemoglobin A1c; HOMA-IR: Homoeostasis model of assessment - insulin resistance; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; ALAT: Alanine transaminase.

^a IOTF reference used for percentiles, see main text.

^b Blood sampling was not conducted in children below 5 years of age (n = 97).

from baseline levels. However, in the school children the prevalence increased to 17.0% at follow-up (P = 0.043) (Table 4A).

3.6. Follow-up in the hospital setting

Follow-up examinations in the hospital setting were conducted in 92 pre-school and 148 school children after a median of 11.8 and 12.1 months, respectively. In the pre-school children, only diastolic blood pressure changed. In the school children, glucose (P = 0.018), insulin (P < 0.001), C-peptide (P = 0.028), HOMA-IR (P < 0.001), total cholesterol (P = 0.008), and HDL cholesterol (P = 0.033) increased (Table 4B).

3.7. Comparison of children with and without overweight at follow-up

In pre-school children, minor changes occurred during follow-up regardless of overweight status. In the school children with overweight (n = 16), no changes in BMI SDS, blood pressure, or blood sample parameters were detected during the follow-up time, whereas insulin (P < 0.001), HOMA-IR (P < 0.001), total cholesterol (P = 0.009), and HDL cholesterol (P = 0.036) increased in the school children without overweight (n = 132) (Supplementary Table 1).

Table 3

Comparison of anthropometrics, degree of obesity, blood pressure, and venous blood samples between children with and without overweight at baseline.

Characteristic	Pre-school children			School children		
	BMI SDS < P90 N = 135	BMI SDS > P90 N = 15	P-value	BMI SDS < P90 N = 215	BMI SDS > P90 N = 27	P-value
Sex (% boys)	45.9	60.0	0.45	51.6	37.0	0.22
Age (years)	3.1 [2.8, 5.4]	2.9 [2.7, 5.4]	0.68	7.0 [6.7, 7.3]	6.9 [6.7, 7.1]	0.86
Anthropometrics						
Height SDS	0.61 (0.99)	0.76 (0.73)	0.58	0.59 (0.88)	1.11 (1.19)	0.006
Weight (kg)	15.8 [13.8, 19.4]	18.3 [16.5, 22.1]	0.004	23.7 [21.8, 25.6]	31.6 [28.9, 35.8]	< 0.001
Degree of obesity^a						
BMI SDS	-0.24 (0.78)	1.72 (0.37)	< 0.001	-0.06 (0.80)	1.99 (0.58)	< 0.001
Blood pressure						
Systolic BP SDS	0.08 [– 0.24, 0.80]	0.43 [0.37, 0.67]	0.96	0.11 [0.28, 0.58]	0.57 [0.24, 1.09]	0.001
Diastolic BP SDS	0.56 [0.08, 1.09]	0.66 [0.40, 0.84]	0.66	-0.00 [– 0.31, 0.35]	0.08 [0.24, 0.55]	0.31
Venous blood samples^b						
Glucose (mmol/L)	4.7 [4.6, 5.0]	4.4 [4.2, 4.6]	0.028	4.7 [5.0]	5.0 [5.1]	0.002
HbA1c (mmol/mol)	33.0 [31.0, 35.0]	34.5 [33.8, 35.0]	0.28	33.0 [31.0, 35.0]	32.5 [31.8, 34.0]	0.48
Insulin (pmol/L)	27.1 [18.2, 37.6]	25.8 [19.4, 33.6]	0.94	25.4 [16.4, 37.1]	58.6 [37.1, 81.7]	< 0.001
C-peptide (nmol/L)	0.3 [0.3, 0.4]	0.3 [0.3, 0.4]	0.53	0.3 [0.3, 0.4]	0.5 [0.4, 0.7]	< 0.001
HOMA-IR	0.9 [0.6, 1.4]	0.9 [0.6, 1.1]	0.74	0.9 [1.3]	2.2 [3.2]	< 0.001
Triglycerides (mmol/L)	0.6 [0.5, 0.7]	0.4 [0.4, 0.5]	0.10	0.5 [0.4, 0.7]	0.6 [0.5, 0.7]	0.029
Cholesterol (mmol/L)	3.8 [3.40, 4.10]	4.2 [3.9, 4.6]	0.12	3.8 [3.4, 4.3]	3.8 [3.6, 4.1]	0.88
HDL-C (mmol/L)	1.4 [1.3, 1.6]	1.8 [1.6, 2.0]	0.030	1.5 [1.3, 1.7]	1.3 [1.1, 1.5]	0.007
LDL-C (mmol/L)	2.1 [1.7, 2.3]	2.4 [2.0, 2.7]	0.29	2.1 [1.7, 2.5]	2.2 [2.0, 2.5]	0.16
ALT (U/l)	22.0 [20.0, 25.0]	27.5 [26.5, 32.0]	0.018	22.0 [19.0, 25.0]	27.0 [22.8, 29.0]	< 0.001

Data are medians and interquartile ranges in brackets or means and standard deviations in parenthesis. Abbreviations: BMI SDS: Body mass index standard deviation score; P: Percentile; BP: Blood pressure; HbA1c: Haemoglobin A1c; HOMA-IR: Homoeostasis model of assessment - insulin resistance; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; ALAT: Alanine transaminase.

^a IOTF reference used for percentiles, see main text.

^b Blood sampling was not conducted in children below 5 years of age (n = 97).

Table 4
Comparison between baseline and follow-up.

A. Anthropometrics and degree of obesity in the primary sector						
Characteristic	Pre-school children N = 223			School children N = 518		
	Baseline	Follow-up	P-value	Baseline	Follow-up	P-value
Sex (% boys)	50.2	50.2	–	51.0	51.0	–
Age (years)	2.8 [2.6, 5.3]	4.0 [3.7, 6.8]	–	6.7 [6.4, 7.0]	8.5 [8.1, 8.8]	–
Anthropometrics						
Height SDS	0.46 (0.92)	0.52 (0.91)	0.49	0.50 (0.89)	0.48 (0.89)	0.73
Weight (kg)	16.4 [13.7, 19.8]	19.0 [16.2, 23.4]	–	23.4 [21.5, 26.1]	29.3 [26.2, 33.0]	–
Waist circumference (cm)	53.5 [50.9, 56.0]	55.0 [52.9, 58.1]	< 0.001	57.5 [55.1, 60.5]	60.4 [57.0, 64.7]	< 0.001
Hip circumference (cm)	59.5 [56.5, 63.0]	61.0 [57.5, 65.0]	0.001	65.0 [61.6, 68.0]	70.0 [66.1, 74.0]	< 0.001
Neck circumference (cm)	25.1 [24.0, 26.1]	25.9 [25.1, 26.8]	< 0.001	26.5 [25.6, 27.5]	27.7 [26.8, 29.0]	< 0.001
Degree of obesity ^a						
BMI SDS	0.31 (0.90)	0.24 (0.93)	0.44	0.31 (0.87)	0.40 (0.90)	0.090
BMI SDS > 90th percentile (%)	13.0 (29)	12.6 (28)	1.00	12.4 (64)	17.0 (88)	0.043
B. Anthropometrics, degree of obesity, blood pressure, and venous blood samples in the hospital-setting						
Characteristic	Pre-school children N = 92			School children N = 148		
	Baseline	Follow-up	P-value	Baseline	Follow-up	P-value
Sex (% boys)	46.7	46.7	–	51.4	51.4	–
Age (years)	2.9 [2.8, 5.4]	3.9 [3.7, 6.3]	–	6.9 [6.7, 7.4]	8.0 [7.7, 8.4]	–
Anthropometrics						
Height SDS	0.56 (0.95)	0.71 (0.94)	0.27	0.73 (0.99)	0.70 (0.90)	0.80
Weight (kg)	16.1 [13.8, 19.3]	17.9 [16.0, 21.9]	–	24.2 [22.0, 26.8]	27.6 [24.9, 31.0]	–
Degree of obesity ^a						
BMI SDS	-0.05 (0.96)	-0.05 (0.88)	0.97	0.17 (0.93)	0.19 (1.07)	0.87
BMI SDS > 90th percentile (%)	12.0 (11)	5.4 (5)	0.19	10.8 (16)	12.2 (18)	0.86
Blood pressure						
Systolic BP SDS	0.15 [- 0.24, 0.78]	0.15 [- 0.25, 0.51]	0.27	0.19 [- 0.19, 0.59]	0.16 [- 0.27, 0.57]	0.69
Diastolic BP SDS	0.55 [0.18, 1.13]	0.27 [- 0.05, 0.76]	0.009	0.02 [- 0.30, 0.35]	-0.07 [- 0.38, 0.25]	0.40
Venous blood samples ^b						
Glucose (mmol/L)	4.7 [4.5, 5.0]	4.7 [4.6, 4.9]	0.55	4.8 [4.5, 5.0]	4.9 [4.7, 5.0]	0.018
HbA1c (mmol/mol)	33.0 [31.0, 35.0]	33.0 [32.0, 34.0]	0.79	33.0 [31.0, 35.0]	33.0 [31.0, 34.0]	0.45
Insulin (pmol/L)	27.1 [16.4, 41.6]	29.9 [22.8, 37.9]	0.43	26.1 [17.9, 38.0]	36.2 [26.2, 45.5]	< 0.001
C-peptide (nmol/L)	0.3 [0.3, 0.4]	0.3 [0.3, 0.4]	0.83	0.3 [0.3, 0.4]	0.4 [0.3, 0.4]	0.028
HOMA-IR	0.9 [0.6, 1.4]	1.0 [0.8, 1.4]	0.55	0.9 [0.6, 1.4]	1.3 [0.9, 1.6]	< 0.001
Triglycerides (mmol/L)	0.6 [0.5, 0.6]	0.5 [0.4, 0.6]	0.13	0.5 [0.4, 0.7]	0.6 [0.5, 0.7]	0.13
Cholesterol (mmol/L)	4.0 [3.6, 4.1]	3.6 [3.3, 4.4]	0.72	3.8 [3.5, 4.3]	4.1 [3.6, 4.5]	0.008
HDL-C (mmol/L)	1.5 [1.3, 1.7]	1.6 [1.4, 1.9]	0.18	1.4 [1.3, 1.7]	1.6 [1.3, 1.8]	0.033
LDL-C (mmol/L)	2.1 [1.8, 2.3]	1.9 [1.7, 2.3]	0.37	2.1 [1.8, 2.4]	2.3 [1.9, 2.6]	0.11
ALT (U/l)	22.0 [19.0, 26.5]	21.5 [19.0, 28.8]	0.89	23.0 [19.8, 27.0]	22.0 [19.0, 26.0]	0.55

This table includes the children who participated in both baseline and follow-up investigations. Data are medians and interquartile ranges in brackets or means and standard deviations in parenthesis. Abbreviations: BMI SDS: Body mass index standard deviation score; BP: Blood pressure; HbA1c: Haemoglobin A1c; HOMA-IR: Homoeostasis model of assessment - insulin resistance; HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; ALT: Alanine transaminase.

^a IOTF reference used for percentiles, see main text.

^b Blood sampling was not conducted in children below 5 years of age (n = 97).

4. Discussion

The early identification of paediatric overweight prior to development of overt comorbidities is important in the prevention of overweight and its related complications although achieving this is difficult. In this study, we successfully examined a population-based cohort of children aged 2.5–8 years who were included through existing contacts with the primary sector – both the municipal dental care and public health nurses – and evaluated the degree of overweight as well as related complications at baseline and at follow-up.

We detected a prevalence of overweight of 13.73% and 13.69% in the pre-school and school children at baseline, respectively. We found that derangements in measures of glucose and lipid metabolism and liver function were present in school children with overweight but not yet in the pre-school children. So, despite the prevalence of overweight being the same in the pre-school- and school children, the prevalence of overweight-related complications was higher in the school children. In children who were followed up, during a median of 14.7 and 20.5 months of follow-up respectively, the prevalence of overweight did not change in the pre-school children, but it rose to 17.0% in the school children. Further, measures of glucose metabolism and lipids increased in the school children. Even though these levels were below thresholds for defining disease, they highlight that deleterious changes may be detectable even within the normal range. These findings highlight the

critical importance of timely detection of childhood overweight and its related complications.

Our findings that 13.73% and 13.69% of the children in this cohort had overweight in 2015 is in agreement with national estimates [23,24] and accordingly a major finding of this study is the illustration of the usefulness of using primary care dental assistants and public health nurses in screening for paediatric overweight. In the pre-school children, the prevalence of overweight did not change and almost no changes in the cardiometabolic risk factors were detected from baseline to follow-up. In contrast, after follow-up in the school children we identified increases in the prevalence of overweight and cardiometabolic risk factors. It remains possible that we were unable to detect differences due to a lack of power as we had few young children with overweight. Although we can only speculate as to why the overweight and cardiometabolic risk-factor profile deteriorated at these particular ages, it possibly reflects that there is a necessary time and/or exposure threshold in order to develop overweight and cardiometabolic derangements. The differences in the increase in the degree of overweight between pre-school and school children in the present study highlights the findings from the literature describing how the timing of overweight in childhood plays a major role determining obesity-related morbidity later in life. This study demonstrated an increasing prevalence of overweight in school children, this suggests there is an age threshold before which prevention and/or treatment should be initiated.

As children grow older, markers of glucose metabolism, lipids, and liver function vary with growth and development as shown in references for these parameters from our own group based on a comparable paediatric population-based cohort [14,25,26]. Therefore, whether the observed changes of cardiometabolic risk factors reflect a true increased cardiometabolic risk or normal physiological development induced variation in biochemical markers requires further studies of both paediatric cohorts with overweight and further exploration of normal age-dependent variation in paediatric biomarkers.

A major finding of our study is that existing contacts in the primary sector with municipal dental care and public health nurses can successfully be used for evaluating the degree of overweight in pre-school and school children. The success of this detection in dental clinics is especially encouraging as they have contact with a large group of children who are seen regularly from as early as one year of age. Partnering with dental clinics is mutually beneficial as there are associations between overweight and periodontal disease [27].

Although screening for medical conditions such as diabetes and cardiovascular disease in adults can be feasible and effective in a dental setting [28–30], studies addressing childhood overweight in a dental setting are sparse. One pilot study investigated anthropometric screening in community dental clinics in 139 children aged 6–13 years and found that healthy weight intervention was feasible and well-accepted in a paediatric dental setting [13]. In Denmark, public health care nurses already play a key role in detecting overweight in children as they are in contact with the families regularly from early childhood and we found that working with public health nurses in schools was effective in the present study.

In our study, we successfully worked with paediatric dental assistants to detect childhood overweight. We provided them with training on how to assess anthropometry and how to communicate with parents. By doing this, we overcame barriers identified in other studies which include concerns about a lack of adequate training, offending patients and caregivers and stigmatisation of the child [28,31,32]. Working with the dental clinics provided access to a paediatric population at young ages before overweight-related complications have emerged.

The partnership between the dental clinics, the public health nurses, and the paediatric department is a great strength of this study that has enabled the recruitment of a large population-based cohort of Danish children and thereby this collaboration has entailed a greater outreach than what a single clinic could encompass. Another strength is the extensive phenotyping and the assessment of biochemical markers in a relatively larger number of children including collection of follow-up information. Furthermore, the careful collection and the analyses of blood samples in the same laboratory minimised pre-analytical and analytical variations.

Limitations to this study include missing information on children and families who declined to participate and the participants who were lost to follow-up. A differential loss to follow-up between the age groups also could have affected the number of children with overweight in this study. In our cohort, 96.7% of the children were of ethnic Danish origin. This is a higher percentage than in the overall Holbæk municipality where 91.6% of children and adolescents are of Danish origin [33]. We likely had a higher proportion of Danish children in the cohort since information materials were only available in Danish, thus our results may not be generalisable to the other ethnic groups in this community. We only collected venous blood samples on children > 5 years for ethical reasons. Additionally, measuring blood pressure of children aged 2–3 years was sometimes challenging and it was not always possible to follow the protocol of pre-measurement rest and supine positioning in this age group.

Identification of overweight and related cardiometabolic derangements prior to development of overt comorbidities is important in the prevention of overweight and related physical and psychosocial complications. The present study suggests that early childhood – as early as age 2–5 years – is the time to detect these conditions, as complications

from overweight including derangements in glucose metabolism may become evident when the children are just a few years older. Furthermore, the present study shows how using existing contacts with the primary health care sector including dental care may be a useful tool in the early detection of childhood overweight.

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Ethical statement

All parents gave informed written and oral consent. The study was approved by the Ethics Committee of Region Zealand, Denmark (no. SJ-104) and the Danish Data Protection Agency. The study was conducted in accordance with the Helsinki Declaration of 1975 as revised in 2013. The study is part of The Danish Childhood Obesity Biobank; ClinicalTrials.gov ID-no.: NCT00928473.

Conflict of interest

All authors declare no conflict of interest.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.orcp.2022.04.001](https://doi.org/10.1016/j.orcp.2022.04.001).

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