HRQoL changes in pediatric patients with severe obesity that were offered an integrated care approach with additional diagnostics in secondary or tertiary care.

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Abstract

Introduction

The occurrence of childhood obesity has witnessed substantial growth, which is alarming due to its potential to negatively impact the HRQoL. In the Netherlands, the recommended treatment for pediatric patients with severe obesity is a multi-disciplinary care approach with additional diagnostics in secondary or tertiary care center (ICCO+). This study aims to determine whether the generic- and weight-specific HRQoL changed after a year of receiving the personalized ICCO+ treatmentplan and determine which baseline characteristics are associated with these changes. Additionally, the correlation between ΔHRQoL and ΔBMI was examined.

Method

This prospective observational study included 392 pediatric patients with severe obesity that received the personalized ICCO+ treatmentplan and returned for evaluation one year later. Three points in time were designated for measurements: T0 = diagnostic multidisciplinary assessment, T1 = personalized ICCO+ treatmentplan, and T2 = one year follow-up.

ΔGeneric- and weight-specific HRQoL were used as primary outcome measurements. Additionally, age, gender, ethnicity, SEP, SDS-BMI, PSQ, SDSC, BVB and NVE were assessed before the treatmentplan was offered and were used as secondary measurements. For the analyses, a paired T test, a Pearson correlation and linear regressions were used.

Results

Generic HRQoL ($T = 4.98$, $p<0.001$) and weight-specific HRQoL ($T = -2.16$, $p<0.04$) have both significantly improved after a year of receiving the personalized ICCO+ treatmentplan. Furthermore, there was no correlation between ΔSDS-BMI and Δgeneric HRQoL ($r = -0.06$, $p = 0.29$), as well as weight-specific HRQoL ($r = -0.10$, $p = 0.50$). Lastly, the variables generic HRQoL at intake (T1), SDS-BMI, SDSC, PSQ and NVE emotional have a significant association with Δgeneric HRQoL ($p<0.05$).

Conclusion

This study demonstrates positive changes in generic- and weight-specific HRQoL in pediatric patients with severe obesity after a year of receiving the personalized ICCO+ treatmentplan**.** These changes are associated with various psychosocial and lifestyle variables at intake (T1), but not correlated with the changes in SDS-BMI.

Introduction

Obesity has emerged as one of the most significant health problems of our time (Swinburg et al., 2019). In the Netherlands, the percentage of children and adolescents between 4 and 17 years of age classified as obese (Body Mass Index (BMI) equivalent to an adult ≥ 30 kg/m2) rose from 2.2% in 2019 to 3.6% in 2021 (CBS, 2022; Federatie Medisch specialisten, 2020; VWS, 2022). And, although not objectified with data, generally when the prevalence of obesity increases, there also tends to be an increase in severe obesity (BMI equivalent to an adult ≥ 35 kg/m2) (Cole, 2000; Halberstadt, 2015; van Dommelen et al., 2014).

The increased prevalence of severe childhood obesity is alarming, due to its potential to negatively impact a child's life in various ways. Not only does a higher BMI value increase the risk of physical and mental health problems later in life (Spinelli et al., 2019; Quek et al., 2017), but it also poses immediate physical health consequences, such as a poorer cardiometabolic risk profile and early signs of vascular dysfunction (Freedman et al., 2007; Gidding et al., 2004). Additionally, children with severe obesity may face mental problems such as teasing, bullying, discrimination, and weight stigmatization (Luppino et al., 2010; Makkes et al., 2013; Quek et al., 2017). Rather than the severe obesity itself, stigmatization may have an additional detrimental impact on psychological problems such as depressive symptoms and lower self-esteem (Rubino, 2020; Wu & Berry, 2018).

The physical and psychological problems of children and adolescents (later called pediatric patients: 4 - 18 years old) with higher degrees of obesity have consistently been found to contribute to a further decrease in health-related quality of life (HRQoL) (Buttitta et al., 2014; Noordam et al., 2016; Schwimmer et al., 2003; van der Voorn et al., 2022; Wu & Berry, 2018). In this study, HRQoL is defined as ‘the impact of health or disease on physical, mental, and social well-being from the patient’s point of view’ (Testa & Simonson, 1996). The decreased HRQoL can reach levels comparable to those observed in pediatric patients coping with cancer (Schwimmer et al., 2003; Varni et al., 2007).

In the Netherlands, the recommended treatment for pediatric patients with overweight and obesity, that aims to decrease BMI and increase the HRQoL, is a multi-disciplinary care approach based on the national model “Integrated Care for Childhood Obesity” (ICCO) (Halberstadt et al., 2023; Sijben, 2018). This approach emphasizes the principle of ‘stepped and matched care’ (Halberstadt et al., 2023). This entails adjusting the duration and intensity of care based on weight status, weight-related health risk and level of self-management. Where the underlying motto is to provide healthcare as less as possible and as much as needed (Seidell et

al., 2012). Notably, the approach will be structurally funded from the beginning of 2024 (Halberstadt et al., 2023; Seidell et al., 2012; VWS, 2023)

Pediatric patients with severe obesity often necessitate a personalized intensive treatment approach, due to the weight-related health risks and the possibility of an underlying medical condition (Kleinendorst et al., 2020; Reinehr et al. 2007; Seidell et al., 2012). For example, Hoedjes et al. (2018) has intensified treatment by incorporating a therapeutical admission and found a positive effect on the HRQoL. The ICCO emphasizes an intensified treatment by providing personalized diagnostics of underlying factors and/or determining weight-related health risks in a secondary or tertiary obesity care center (later called : personalized ICCO+ treatmentplan) when necessary (Halberstadt et al., 2023). This may improve patients' comprehension of their condition, diminish societal stigma, and help healthcare professionals to offer a personalized treatment approach (Kleinendorst et al., 2020; van den Akker et al., 2018; van der Valk et al., 2019).

For evaluating treatment effectiveness, it has been suggested to use patient-reported outcome measurements (PROMs) for both generic- and weight-specific HRQoL, in addition to changes in biomedical health (Ahuja et al., 2014; Noordam et al., 2016; van der Voorn et al., 2022; Federatie Medisch specialisten, 2022; Hoedjes et al., 2018; Seidell et al., 2012; Tsiros et al., 2009). The Pediatric Quality of Life Inventory (PedsQL) 4.0 and the Impact of Weight on Quality of Life for Kids (IWQoL) are examples of valid HRQoL PROMs (Noordam et al., 2016). The PedsQL is a sensitive instrument to measure changes in generic HRQoL in pediatric patients with severe obesity and the IWQoL is a suitable instrument to gain insights into changes in weight-specific HRQoL in pediatric patients with severe obesity participating in a weight management program (Hoedjes et al., 2018).

This study aims to investigate if the generic- and weight-specific HRQoL of pediatric patients (4 – 18 years) with severe obesity changes after one year of receiving the personalized ICCO+ treatmentplan. Even for these more complex and severely diseased cases it is hypothesized that there will be an increase in HRQoL after receiving the personalized treatment advice since the intensive treatment of Hoedjes et al. (2018) with a therapeutical admission has a positive effect on the HRQoL of pediatric patients with severe obesity (Hoedjes et al., 2018).

In addition, this study aims to analyze if HRQoL changes are correlated with changes in BMI in pediatric patients with severe obesity receiving the personalized ICCO+ treatmentplan. It is hypothesized that there is a negative correlation between the HRQoL changes and the changes in BMI (Buttitta et al. (2013).

Lastly, this study aims to investigate which baseline characteristics are negatively or positively associated with a change in generic- and weight-specific HRQoL in pediatric patients receiving a personalized ICCO+ treatmentplan. It is hypothesized to find associations consistent with previous literature, including a negative relationship between changes in HRQoL and the variables age, gender, ethnicity, BMI, eating behavior, and PedsQL intake (T1) and positive associations between changes in HRQoL and the variables social economic position (SEP), sleep problems, stress, and physical (in)activity (Zolotarjova et al., 2018; van den Eynde, 2020; van der Voorn et al., 2022; Grasaas et al., 2022; Roeser et al., 2012; Halberstadt, 2015; Lacy et al., 2012).

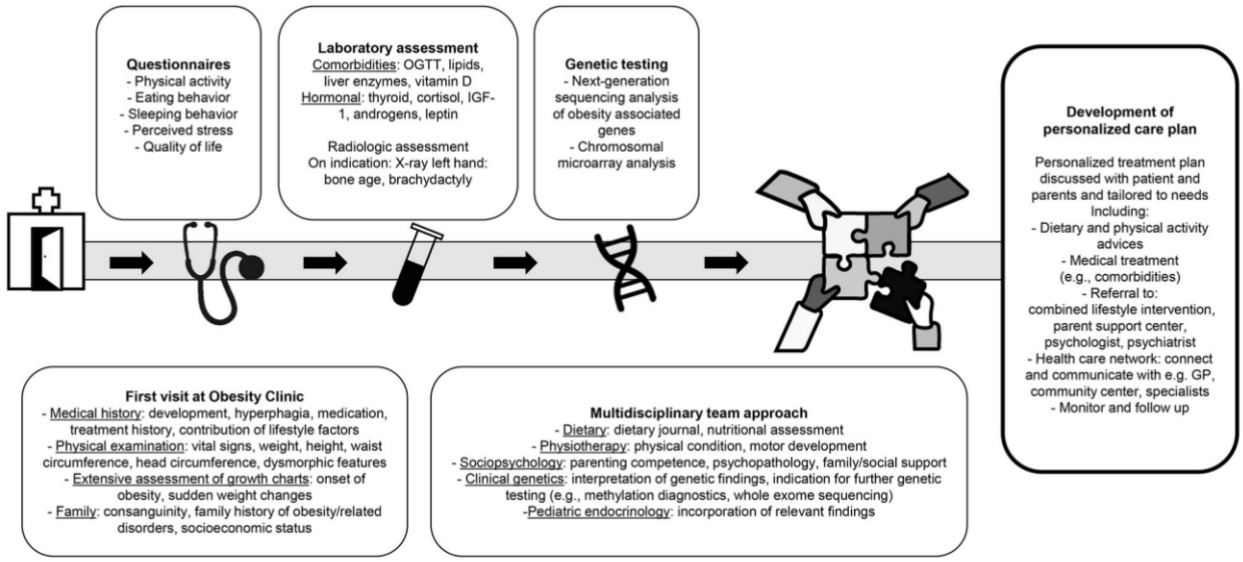
Method

Study population & Study design

This study was a prospective observational study that included 392 pediatric patients between 4 and 18 years, whom all received the personalized ICCO+ treatmentplan between 2015 and 2023, including guidance coordinated by the Obesity Center CGG (Dutch: *Centrum Gezond Gewicht*; English: *Centre for Healthy Weight*). The Obesity Center CGG is a referral center in the Netherlands that offers a multidisciplinary diagnostic approach and treatment plan. It involves a partnership between the academic hospital Erasmus MC and the general hospitals, Maasstad Ziekenhuis and Franciscus Gasthuis. In this study, all patients received their diagnostic work-up and treatment advice at Maasstad Ziekenhuis or Erasmus MC.

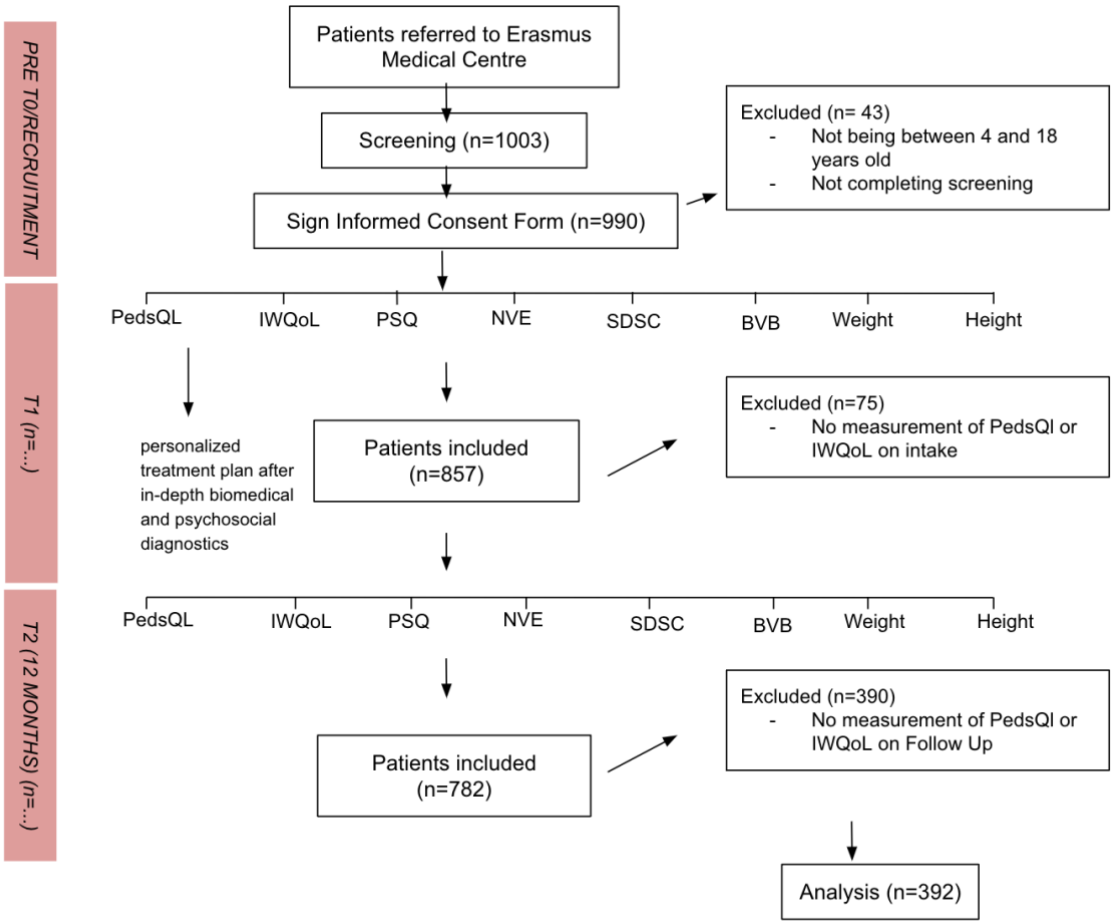
Due to suspicion of underlying reasons for obesity, non-response to a combined lifestyle intervention or other circumstances that necessitated a personalized multidisciplinary therapeutic advice from an Obesity Center of Expertise, patients in this cohort were directed to the obesity Center CGG by their pediatrician. This trajectory began with a diagnostic assessment by a specialized pediatrician, dietician, physical therapist, and pedagogue (T0). Subsequently, a multidisciplinary consultation took place to discuss the case, and personalized advice was provided to the pediatrician using the obesity guideline for pediatricians (Dutch: *Obesitas, leidraad voor kinderartsen*) (Federatie Medisch specialisten, 2020) (T1) (Figure 1). Following this, CGG collaborated with the patient and their family to identify a local coordinating professional who took responsibility for coordinating support and care by involving various local professionals, motivating the child and its primary caregivers, tracking the progress, and taking additional actions if necessary (Halberstadt et al., 2023). After a year, a follow-up took place (T2). At T0 and T2 demographics were assessed, while participants completed multiple questionnaires at T1 and T2 (see Figure 2).

Only those who gave informed consent after providing information and fulfilled the following criteria: age ≥ 4 till 18 and having two valid measurements of the PedsQL questionnaire and/ or the IWQoL questionnaire at T1 and T2, were included in the research (Figure 2). Patients who were unable to provide informed consent or were lost to follow-up were excluded from the study.



Note. Taken from "Identifying underlying medical causes of pediatric obesity: Results of a systematic diagnostic approach in a pediatric obesity center", by Kleinendorst et al., 2020, *PloS one, 15*(5) (https://doi.org/10.1371/journal.pone.0232990)

Figure 1: Systematic diagnostic approach for children and adolescents with severe obesity and a suspicion of an underlying medical cause.



Note. Pediatric Quality of Life Inventory 4.0 *(PedsQL),* Impact of Weight on Quality of Life for Kids *(IWQoL),* Perceived Stress Questionnaire *(PSQ),* Dutch Eating Behavior Questionnaire *(NVE),* Sleep Disturbance Scale for Children *(SDSC),* Dutch Exercise Behavior Questionnaire *(BVB).*

Figure 2: Study flow chart. *Flow chart indicating the in- and exclusion of participants in this cohort.*

Primary Outcome Measures

Generic HRQoL

To measure generic HRQoL, the Dutch version of the valid and reliable "Pediatric Quality of Life Inventory 4.0" (PedsQL) (Cronbach's α = 0.89) was used (Varni, 2003). This questionnaire was completed by the adolescents or participating care givers via paper (until 2020) or digitally (using Gemstracker). The PedsQL questionnaire contained 23 questions divided into four categories: Physical Functioning (FYS), Emotional Functioning (EMO), Social Functioning (SOC), and School Functioning (EDU) (Varni, 2003). The responses were converted into a

scale ranging from 0 to 100, where a score of "0" represented low generic HRQoL and a score of "100" represented high generic HRQoL.

Weight-specific HRQoL

To measure weight-specific HRQoL, the Dutch version of the "Impact of Weight on Quality of Life for Kids" (IWQoL) (Cronbach's α = 0.96) was used (Kolotkin et al., 2006). This questionnaire was completed by the adolescents or participating care givers via paper (until 2020) or digitally (using Gemstracker). The IWQoL questionnaire contained 27 questions divided into four categories: Physical Comfort (PC), Body Esteem (BE), Social Life (SL), and Family Relationships (FR) (Kolotkin et al., 2006). The responses were converted into a scale ranging from 0 to 100 where a score of "0" represented low weight-specific HRQoL and a score of "100" represented high weight-specific HRQoL. The variable was not normally distributed. Therefore, a reversed logarithm transformation was performed. This means that the logarithm of weight-specific HRQoL is negatively associated with the baseline measures of weight-specific HRQoL.

Additional Measurements

Demographics

For healthcare purposes, personal information and demographic variables were collected. Age was filled in in years with decimals, ethnicity was answered in Dutch (0) and non-Dutch (1) and gender in male (0) and female (1).

Social economic position

The social economic position (SEP) was measured through status score; a composite measure of a specific postal code area, which takes into account three indicators: income, level of education, and level of unemployment (CBS, 2019). The status score was a continues variable were < 0 indicates below-average SEP and a status score ≥ 0 indicates above-average SEP. For this study, the variable was dichotomized into below average (0) and above average (1).

Stress

To measure the perceived stress level of the population during the last four weeks, the validated questionnaire "Perceived Stress Questionnaire" (PSQ) (Cronbach's α = 0.84) was used (Levenstein, 1993). It consisted of 20 items divided into four subdomains (4-point Likert scales), representing worries, tension, joy and demands. The responses were converted into a

total scale ranging from 0 to 1, where higher scores on the scale indicated an increased level of stress. The commonly used cutoff levels for stress classification using the PSQ are as follows: low stress (< 0.33), medium stress (0.33–0.45), moderate stress (0.45–0.60), and severe stress (> 0.60) (Levenstein, 1993).

Physical (in)activity

To measure physical (in)activity, the validated questionnaire "Dutch Exercise Behavior Questionnaire" (in Dutch: 'Basis Vragenlijst Bewegen', BVB) was used (Van Wieringen, 2009). This instrument consisted of 7 or 12 multiple choice items (depending on age) about different aspects of exercise and screentime (Van Wieringen, 2009). The responses were converted to the average amount of minutes a child spends on being active per week and the average amount of minutes a child spends on watching TV/computer per week. The first variable 'physical activity' was categorized according to the Dutch norm of physical activity into 2 categories (Gezondheidsraad, 2017). Whereby 0 represented not norm-active (< 420 min/week), and 1 represented norm-active (≥ 420 minutes/week). The second variable 'physical inactivity' was categorized according to the norm of physical inactivity into two categories (American Academy of Pediatrics, 2001). Whereby 0 represented above norm-inactivity (> 840 minutes/week) and 1 represented under norm-inactivity (< 840 minutes/week) (American Academy of Pediatrics, 2001).

Sleep problems

To measure sleep problems, the validated questionnaire "Sleep Disturbance Scale for Children" (SDSC) (Cronbach's $\alpha = 0.661$) was used (Bruni et al., 1996). This instrument consisted of 26 items (5-point Likert scale) about six aspects related to sleep, which can help identify the risk of sleep disorders or disturbances in children and adolescents. The responses were converted into a scale ranging from 0 to 100, where a score of "0" represented low risk of developing sleep problems and a score of "100" represented high risk of developing sleep problems. The variable was not normally distributed. Therefore, a logarithm transformation has been performed. Still a higher value of the log-transformed variable indicated a higher risk of developing sleep problems (Bruni et al., 1996).

Eating behavior

To measure eating behavior, the validated questionnaire "Dutch Eating Behavior Questionnaire" (in Dutch: 'Nederlandse Vragenlijst Eten', NVE) (Cronbach's $\alpha = 0.91$) was

used (Van Strien et al., 1986). This instrument consisted of 33 items (5-point Likert scale) about the three aspects: emotional, external, and restrained eating. The responses were converted into a scale ranging from 0 to 1, where higher scores indicated a higher frequency of the specific behavior or attitude. These higher scores suggested greater sensitivity to emotional states, responsiveness to external cues, and levels of dietary restraint. Due to the worsened distribution after a logarithm transformation and low statistical power precluding categorization, the variable was analyzed in a non-normally distributed state.

Standard Deviation Score of Body Mass Index (SDS-BMI)

The weight of pediatric patients was measured in kilograms (kg) by a calibrated scale while participants stand without shoes and wear light clothing. Height was measured in centimeters (cm) using a stadiometer. BMI was calculated by dividing weight in kilograms by height in meters squared (kg/m2). In this study, the SDS-BMI (Standard Deviation Score-BMI) was used to express the BMI. The SDS-BMI represents a BMI value adjusted by the mean standard deviation, as determined by the fourth Dutch nationwide growth study (Halberstadt et al., 2013). Hereby, an SDS-BMI of ≥ 3, or ≥ 2.3 in combination with obesity-related comorbidity is indicative of severe obesity (CDC, 2023; Halberstadt et al., 2013).

Statistical analyses

The statistical analyses were executed using IBM SPSS version 27. The significance level for all analyses was set at $p \leq 0.05$. To describe the baseline characteristics the mean, standard deviation (SD), median, interquartile range (IQR), frequential, and percentage were used. Unless explicitly stated otherwise, all variables were normally distributed.

For the first aim, a paired T-test was used to examine if the generic- and weight-specific HRQoL significantly changed between intake and follow-up.

For the second aim, a Pearson correlation was used to examine if there was a correlation between the changes in HRQoL (ΔHRQoL) and the changes in SDS-BMI (ΔSDS-BMI).

For the last aim, a univariate linear regression analysis was executed to analyze the association between changes in generic- and weight-specific HRQoL between T1 and T2 and the baseline characteristics. ΔHRQoL was used as the dependent variable and baseline characteristics or lifestyle measurements as the independent variable. Furthermore, all univariate models that were statistically significant were analyzed in the different subdomains of the two HRQoL questionnaires to assess which subdomain is most associated with the changes in HRQoL. Additionally, all univariate models that were statistically significant were

analyzed in a multiple linear regression by adjusting them for confounders. These variables were defined as confounders according to the literature: age (Zolotarjova et al., 2018), gender (Zolotarjova et al., 2018), ethnicity (Houben- van Herten et al., 2015), SEP (Zeller & Modi., 2016), and SDS-BMI (Ul-haq et al., 2013). Due to the correlations (observed using Pearson correlation) between the variables generic HRQOL, sleep problems, and stress scores, it was decided to be cautious when including all variables in the analysis. Although multicollinearity is more commonly a concern when correlations exceed 0.9, the decision was made to include only the theoretical variables, along with one strongly associated variable, as potential confounders in the multiple regression analyses (Tabachnick & Fidell, 2007).

Lastly based on the existing literature, it is widely acknowledged that a linear regression model lacks sufficient statistical power when the number of observations falls below 10 (Twisk, 2016). To ensure the reliability of the results, no analyses were performed between the variables PSQ (n=10), SDSC (n=9) and ΔIWQoL.

Ethical Considerations

This study was conducted after approval of the Medical Ethical Review Committee. Prior to the study, all participants received an explanation of the study and its purpose. Additionally, participants received information about the use and storage of the data. All outcomes were anonymized, and privacy was guaranteed. A written informed consent form was signed by all participants, knowing that they are free to leave the study at all times. After anonymization it was approved to use the data for this specific research.

Results

The baseline characteristics of the final sample for analysis are presented in Table 1. This table shows that the majority of the included sample filled in the PedsQL questionnaire (99%) above the IWQoL questionnaire (13%). Of all the pediatric patients who filled in the PedsQL, 58% identified themselves as female. They reported a mean SDS-BMI of 3.97 (±0.8) and a mean age of 11.23 (±3.7) year. Additionally, the median of the SDSC is 41 (±18) and the mean of the PSQ is 0.27 (±0.14). Of all pediatric patients who filled in the IWQoL questionnaire, two participants only filled in the IWQoL and 50 filled in both questionnaires. The IWQoL completers have a positive mean of ΔSDS-BMI (0.02 (±0.6)) and most of the group scores under average on status score (42% versus 40%). Additionally, the median score of the SDSC was 48 (±12.0).

Table 1

Baseline Characteristics of the study population (n = 392).

	ΔPedsQL	ΔIWQoL
N (%)	390 (99.5)	52 (13.3)
SDS-BMI intake (T1) – Mean (SD)	3.79 (0.79)	3.74 (0.68)
ΔSDS-BMI – Mean (SD)	- 0.12 (0.52)	0.02 (0.61)
Age – Mean (SD)	11.23 (3.66)	11.53 (3.94)
Gender – N (%)		
Male	165 (42.31)	22 (42.31)
Female	225 (57.70)	30 (57.69)
Ethnicity – N (%)		
Dutch	193 (49.49)	29 (55.77)
Non-Dutch	101 (25.90)	13 (25.0)
Status score – N (%)		
Below average	150 (38.46)	22 (42.31)
Above average	147 (37.70)	21 (40.38)
BVB Activity – N (%)		
Not Norm-active	68 (17.44)	19 (36.64)
Norm-active	128 (32.82)	30 (57.69)
BVB Inactivity – N (%)		
Above norm-inactivity	115 (29.49)	31 (59.62)
Under norm-inactivity	84 (21.54)	20 (38.46)
SDSC – Median (IQR)	41 (18)	48.0 (12.0)
PSQ – Mean (SD)	0.27 (0.14)	0.21 (0.10)
NVE – Median (IQR)		
External	0.61 (0.65)	0.57 (0.74)
Emotional	0.45 (0.57)	0.55 (0.68)
Restrained	0.82 (0.45)	0.84 (0.42)

Changes in generic- and weight-specific Health Related Quality of Life

The examined differences of generic- and weight-specific HRQoL between intake and follow-up are presented in Table 2. These results show an average change of 3.00 (95% CI: 1.81, 4.18) in generic HRQoL and an average change of 1.50 (95% CI: -2.22, 5.21) in weight-specific HRQoL. Because of the not normally distributed weight-specific HRQoL variable, the reversed logarithm of weight-specific HRQoL is used to analyze the paired T-test. The utilization of a reversed logarithm for weight-specific HRQoL results in a negative association that paradoxically signifies an increase in weight-specific HRQoL. The increase on both ΔPedsQL ($p<0.01$) and ΔIWQoL ($p = 0.04$) were statistically significant. When analyzing the changes in generic HRQoL in subdomains, all subdomains show a significant increase ($p<0.003$). Additionally, when analyzing the changes in weight-specific HRQoL in subdomains, only the subdomains IWQoL SL and IWQoL FR remain statistically significant ($p = 0.01$).

Table 2

Changes in HRQoL scores from intake (T1) to directly after the 1-year treatment (T2)

	Mean (SD) - Intake	Mean (SD) – Follow-up	Mean (SD) - Delta	Ttest	Two-sided P
PedsQL	70.22 (15.66)	73.15 (16.18)	3.00 (11.88)	4.98	< 0.001
FYS	72.67 (19.67)	75.42 (20.10)	2.76 (15.30)	3.56	< 0.001
EMO	68.14 (19.24)	70.92 (20.31)	2.78 (17.32)	3.17	0.002
SOC	69.74 (21.10)	73.54 (21.16)	3.79 (17.45)	4.30	< 0.001
EDU	68.93 (18.13)	71.65 (18.74)	2.71 (17.83)	3.01	0.003
	Median (IQR) - Intake	Median (IQR) - Followup	Median (IQR) - Delta	Ttest of log.	Two-sided P
IWQoL	80.56 (20.14)	83.80 (27.08)	1.39 (11.81)	- 2.16	0.04
PC	77.08 (29.17)	79.17 (45.83)	0.00 (16.67)	-1.32	0.19
BE	75.00 (30.56)	76.39 (40.97)	1.39 (21.53)	-1.04	0.30
SL	85.42 (29.17)	87.50 (32.29)	0.00 (16.67)	-2.57	0.01
FR	85.42 (29.17)	87.50 (32.29)	0.00 (16.67)	-2.57	0.01

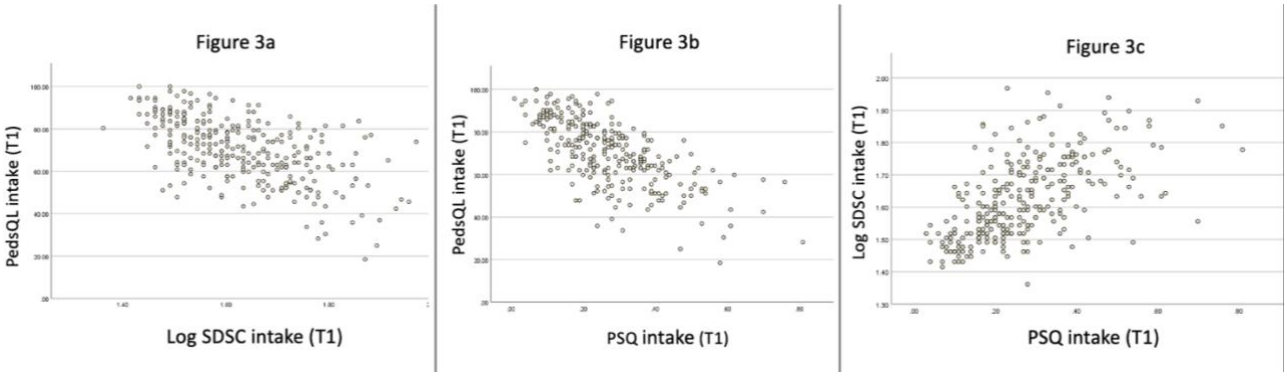
Note. Physical Functioning *(FYS),* Emotional Functioning *(EMO),* Social Functioning *(SOC),* School Functioning *(EDU),* Physical Comfort *(PC),* Body Esteem *(BE),* Social Life *(SL),* and Family Relationships *(FR)*

Correlation between ΔHealth Related Quality of Life and ΔBody Mass Index

The analysis conducted to examine the correlation between the changes in generic- and weight-specific HRQoL indicates that both ΔPedsQL ($r = -0.06$, $p = 0.29$) and ΔIWQoL ($r = -0.10$, $p = 0.50$) are not significantly correlated with ΔSDS-BMI. Additionally, the correlations between the ΔPedsQL subdomains and ΔSDS-BMI, as well as the ΔIWQoL subdomains and ΔSDS-BMI, were not significant ($p > 0.05$).

Correlation between Pediatric Quality of Life Inventory (T1), Sleep Disturbance Scale for Children (T1) and Perceived Stress Questionnaire (T1)

The correlation analysis conducted on the variables in the multiple regression analyses reveals significant correlations among three questionnaires. As shown in figure 3a, there is a significant negative correlation between PedsQL intake (T1) and log(SDSC) intake (T1) ($r = -0.59$, $p = <0.001$). In addition, Figure 3b shows a significant negative correlation between PedsQL intake (T1) and PSQ intake (T1) ($r = 0.69$, $p = <0.001$). Furthermore, Figure 3c shows a significant positive correlation between log(SDSC) intake (T1) and PSQ intake (T1) ($r = 0.58$, $p = <0.001$). Considering SDS-BMI is not significantly correlated with PedsQL intake (T1) ($p = 0.53$), log(SDSC) ($p = 0.82$) or PSQ ($p = 0.53$), only PedsQL intake (T1) is included in de adjusted analysis for SDS-BMI.



Note. All figures are presented in their actual size in Appendix 1.

Figure 3a, 3b and 3c: Scatter plots that show a negative and positive correlation between PedsQL intake (T1), log(SDSC) intake (T1) and PSQ intake (T1)

Association between ΔHealth Related Quality of Life and baseline characteristics

To analyze the association between Δgeneric- and weight-specific HRQoL and different variables, a univariate linear regression analysis was executed. Only the results of the significant crude analyses are presented in Table 3 along with their adjusted estimates in different subdomains.

Regarding the PedsQL score (T1), there is a statistically significant negative association with the ΔPedsQL score in both crude and adjusted estimates. The adjusted estimate indicated a negative association (β -0,27, 95% CI: -0.36, 0.18). Similar associations were found with the ΔPedsQL subdomain scores. Furthermore, the crude association between PedsQL intake (T1) and ΔIWQoL is not statistically significant, as indicated by the crude estimate of -0.10 (95% CI: -0.32, 0.12).

Secondly, there is an adjusted statistically significant negative association between the SDS-BMI intake (T1) score and ΔPedsQL, with a decrease of -1.91 (95% CI: -3.82, -0.01). When examining subdomains, only the adjusted association of ΔPedsQL EMO remains statistically significant (β = -2.87, 95% CI: -5.65, -0.06). Additionally, the crude association between SDS-BMI intake (T1) and ΔIWQoL was not statistically significant, as indicated by the crude estimate of -0.58 (95% CI: -5.38, 4.21).

Thirdly, there is a statistically significant positive association between the ΔPedsQL and both log(SDSC) intake (T1) (β 13.91, 95% CI: 0.97, 26.86) and PSQ intake (T1) (β 16.23, 95% CI: 4.33, 28.14) in the adjusted estimates. When analyzing these association within the subdomains of ΔPedsQL, it was observed that several crude and adjusted estimates exhibited statistical significance or showed potential trends. In addition, the crude association between

log(SDSC) intake (T1) (β 43.44, 95% CI: -45.60, 123.48) or PSQ intake (T1) (β 54.74, 95% CI: -11.61, 121.10) and ΔIWQoL is not statistically significant.

Fourthly, when adjusting for other variables, there only a noteworthy trend of a positive association between the NVE emotional score and ΔPedsQL remains, indicating an increase of 5.13 (95% CI: -0.50, 10.67). Among the subdomains, only the adjusted positive association of ΔPedsQL EDU is statistically significant (B = 10.59, 95% CI: 2.34 to 18.84). Additionally, the crude positive association between intake NVE emotional and ΔIWQoL is not statistically significant, with an estimate of 0.65 (95% CI: -11.03, 12.33).

Lastly, the variables of age, gender, ethnicity, status score, BVB activity, BVB inactivity, and NVE external and restrained did not show statistically significant associations with either ΔPedsQL or ΔIWQoL, as none of the crude estimates fell inside the respective confidence intervals of 95%.

Table 3: Regression models of the Association between PedsQL intake (T1), SDS-BMI, SDSC, PSQ, NVE emo and ΔPedsQL– Crude and Adjusted models

	ΔPedsQL total	ΔPedsQL FYS	ΔPedsQL EMO	ΔPedsQL SOC	ΔPedsQL EDU
PedsQL intake	B [CI]	B [CI]	B [CI]	B [CI]	B [CI]
Crude	-0.25 [-0.33, -0.18]**	-0.23 [-0.33, -0.13]**	-0.19 [-0.29, -0.08]**	-0.34 [-0.45, -0.24]**	-0.28 [-0.33, -0.18]**
Adjusted[a]	-0.27 [-0.36, -0.18]**	-0.23 [-0.35, -0.11]**	-0.23 [-0.36, -0.10]**	-0.33 [-0.46, -0.20]**	-0.29 [-0.42, -0.15]**
SDS-BMI intake	-1.54	-1.18	-1.41	-1.85	-1.97
Crude	[-3.05, -0.02]*	[-3.13, 0.78]	[-3.64, 0.82]	[-4.09, 0.40]	[-4.26, 0.32]+
Adjusted[b]	-1.91 [-3.82, -0.01]*	-2.17 [-4.67, 0.36]+	-2.87 [-5.65, -0.06]*	-1.19 [-3.94, 1.56]	-1.34 [-4.21, 1.53]
SDSC (log)	16.00	9.22	16.28	21.63	19.99
Crude	[4.89, 27.12]**	[-5.20, 23.64]	[0.03, 32.52]*	[5.11, 38.15]**	[3.38, 36.60]*
Adjusted[a]	13.91 [0.97, 26.86]*	3.58 [-12.97, 20.13]	14.56 [-4.21, 33.33]	19.22 [0.51, 37.93]*	23.52 [4.83, 42.22]*
PSQ	15.56	10.94	13.93	21.31	18.68
Crude	[5.35, 25.77]**	[-1.99, 23.86]+	[-0.75, 28.61]+	[6.40, 36.23]**	[3.77, 33.60]*
Adjusted[a]	16.23 [4.33, 28,14]**	13.08 [-2.08, 28.24]+	14.64 [-2.48, 31.77]+	21.18 [3.97, 38.39]*	17.54 [0.26, 34.81]*
NVE – emo	6.32	3.83	4.41	7.84	10.64
Crude	[2.56, 10.08]**	[1.09, 8.75]	[-1.21, 10.02]	[2.31, 13.38]**	[5.09, 16.19]**
Adjusted[b]	5.13 [-0.50, 10.76]+	-0.59 [-8.03, 6.85]	8.12 [-0.22, 16.45]+	5.93 [-2.15, 14.00]	10.58 [2.34, 18.82]*

*Note. B = beta coefficient. CI = 95% confidence interval. * p ≤.05, ** p ≤.01, + ≤.10. [a]Model was adjusted for gender, age and ethnicity, and SEP. [b]Model was adjusted for gender, age and ethnicity, SEP and PedsQL intake (T1).*

Discussion

Changes in generic- and weight-specific Health Related Quality of Life

The first aim of this study was to investigate the change in generic HRQoL (ΔPedsQL) and weight-specific HRQoL (ΔIWQoL) in pediatric patients with severe obesity a year after receiving in depth diagnostics for underlying causes and limiting factors of which the results formed a multidisciplinary treatment advice. This tertiary care guidance was in accordance with the integrated care approach based on the national model ICCO. The findings of this study revealed improvements in both generic- and weight-specific HRQoL among pediatric patients with severe obesity. These findings are in line with the prior study of Hoedjes et al. (2018) which has shown beneficial effect on the HRQol of pediatric patients with severe obesity after receiving an intensive diagnostic process leading to a personalized network approach including a combined lifestyle intervention started during a therapeutic admission. To our knowledge, this was the only study examining changes in HRQoL among pediatric patients with severe obesity receiving an intensive diagnostic approach.

In accordance with Hoedjes et al. (2018), we found significant improvements in the subdomain scores FYS-, EMO- and SOC generic HRQoL, as well as SL for weight-specific HRQOL. On the other hand, differences in subdomain improvement scores were found when comparing the two studies: this study also found an increased EDU generic HRQoL and FR weight-specific HRQoL, while Hoedjes et al. (2018) also found increases in the PC- and BE weight-specific HRQoL. Overall, both studies showed positive changes in both generic- and weight-specific HRQoL scores after a year. Differences may have appeared due to the fact that the characteristics of participants differed between our study and the cohort of Hoedjes et al. (2018), i.e., age (mean 11 years versus 15 years) and SEP. Next to, it may be due to the in-patient approach that Hoedjes et al. offered.

Correlation between ΔHealth Related Quality of Life and ΔBody Mass Index

The second aim of this study was to investigate if there is a correlation between the changes in generic- as well as weight-specific HRQoL and the changes in SDS-BMI a year after receiving the personalized ICCO+ treatmentplan. Interestingly, we did not find a correlation between change in HRQoL and SDS-BMI. This suggests that improvements in HRQoL can be achieved even if there is no weight reduction and vice versa. This is not in line with our hypothesis since Buttitta et al. (2013) showed multiple studies that documented a negative correlation. However, according to the systematic review of Kolotkin and Andersen (2017) the literature is inconsistent about this correlation. This inconsistency may be attributed to variations in; the

effectiveness of different interventions in inducing weight loss, quality of reporting, or study population (Kolotkin & Andersen, 2017). Given that our study population was referred to an obesity center of expertise based on suspicions of underlying causes for obesity/severe obesity or non-response to a combined lifestyle intervention, it is plausible that this specific population encounters extra challenges in losing weight. This can potentially explain the absence of a correlation between changes in SDS-BMI and changes in HRQoL, at the one-year follow-up. Longer term follow-up might show more effect on SDS-BMI changes, subsequentially after psychosocial factors have improved.

Association between ΔHealth Related Quality of Life and baseline characteristics

The last aim of this study was to identify baseline characteristics that are associated with changes in generic- and weight-specific HRQoL.

No association was found between generic HRQoL and the demographic variables age, gender, ethnicity, SEP and physical (in)activity. These findings indicate that a specific age, gender, ethnicity, SEP, or physical (in)activity does not appear to affect the ability to improve generic HRQoL scores after receiving the personalized ICCO+ treatmentplan. Associations with treatment success in similar studies are inconsistent: the influence of age and gender (Zolotarjova et al., 2018) ethnicity (Wiegand et al., 2014), SEP (Killedar et al., 2020) and physical (in)activity (Lacy et al. 2012). We labeled, in comparison to most other studies, the positive change of generic HRQoL as treatment success instead of weight loss. Since these variables are not correlated in this cohort, it is possible that there is an association with the changes in SDS-BMI but not with the changes in generic HRQoL.

In addition, the findings of this study revealed a negative association between the generic HRQoL intake (T1), and the changes observed in all subdomains of generic HRQoL. These findings suggest that individuals with a higher generic HRQoL intake (T1) experience relatively smaller increases in their changes in generic HRQoL in all subdomains after receiving a personalized ICCO+ treatmentplan. The study of van den Eynde et al. (2020) showed the same association after a 10-week lifestyle intervention in children with overweight or obesity. These findings may be attributed to a ceiling effect: children who already scored high did not have much room for improvement (Salkind, 2010).

Furthermore, the results show an association between SDS-BMI intake (T1) score and changes in both total and EMO generic HRQoL. However, for the remaining subdomains, only a tendency towards association is observed or no association is found. These findings are not in line with the cross-sectional study of van der Voorn et al. (2022) that showed an association

between SDS-BMI and all subdomains of generic HRQoL intake (T1). One explanation could be that the study of van der Voorn et al. (2022) did not account for changes in HRQoL during the intervention. The second explanation could be that selection bias played a roll, i.e., all included children had an SDS-BMI above +2.3, whereas van der Voorn et al. (2022) had included children with overweight, obesity and severe obesity.

In addition, the findings of this study revealed a positive association between both an increased level of stress as well as a higher risk of developing sleep problems and the changes in generic HRQoL. However, when examining the association within subdomains, only SOC- and EDU generic HRQoL showed a positive association. These results suggest that individuals with higher stress levels or a higher risk of sleep problems experience greater improvement in total, SOC, and EDU generic HRQoL scores after receiving ICCO+ intervention. According to Grasaas et al. (2022) and Roeser et al. (2012) there is a cross-sectional negative association between stress as well as higher risk of developing sleep problems and generic HRQoL. A possible explanation for this inconsistency is related to the findings of Taylor et al. (2023), which demonstrate that improving sleep through an intervention leads to a corresponding improvement in HRQoL. Children with initially poor sleep scores have the opportunity to improve their sleep during the intervention, resulting in a faster and greater increase in HRQoL compared to those with already satisfactory sleep scores. It is worth noting that the overall cohort scored well on both questionnaires, making it difficult to determine the effects of high stress levels and higher risk of developing sleep problems on the changes of generic HRQoL.

Additionally, we found a positive association between having emotional eating behavior and the changes in the subdomain EDU generic HRQoL. No associations with other eating behavior styles were found. These findings indicate that individuals with more emotional eating behavior at intake (T1) are more likely to experience improvement in their EDU generic HRQoL after receiving the personalized ICCO+ treatmentplan. Halberstadt (2015) showed large variations in long-term weight change in different eating styles at intake (T1) but did not correlate these with the changes in generic HRQoL. It is worth noting that the non-normal distribution of the NVE in our study may have affected the validity of the results.

Lastly, no association was found between any variable and the changes in weight-specific HRQoL. It is possible that this is due to a too small sample size in the analyses since the IWQoL questionnaire was first administered in 2021 and therefore not many pediatric patients have filled in both intake and follow-up. To say something about the impact of the variables on the weight-specific HRQoL further research is necessary.

Although it was not initially the focus of this study, it is noteworthy to highlight that a strong correlation was found between the generic HRQoL, the SDSC and PSQ at intake (T1). This provides valuable insights into the interconnectedness of these factors within the studied population. Further investigation and analysis of this correlation could offer a deeper understanding of the impact of sleep and psychosocial well-being on the overall quality of life of pediatric patients in similar contexts.

Strengths and limitations

Several strengths and limitations of the study should be acknowledged. The first strength is that the study's sample size to analyze generic HRQoL was adequately large, enabling the detection of meaningful effects and reducing the likelihood of Type II error. This contributes to increased confidence in the validity and reliability of the study's findings.

Secondly, the population of this research comprises individuals with severe obesity. This specific subgroup is growing but remains relatively small on population level, representing the tip of the iceberg. Consequently, conducting research on this population poses considerable challenges, i.e., complexity of the cases. However, the study's notable large sample size and comprehensive phenotyping of patients and their disease enhance the generalizability of the results to other practices.

The first limitation is that we asked all parents of children <12 years to complete the questionnaires, together with their child, and children >12 years to complete the questionnaires themselves. Proxy- and self-reports may have distinct scores (Eiser & Varni, 2013). Although we accounted for age as confounder, we could not fully exclude the potential effect of that.

Secondly, it was not possible to attribute the observed improvements in HRQoL to specific aspects of the personalized ICCO+ treatmentplan due to a lack of detailed insights regarding the exact care and support that was offered throughout the year. Accordingly, we analyzed intention-to-treat- and not per-protocol effects.

Thirdly, the analysis examining the relationship between baseline characteristics and weight-specific HRQoL possibly lacked sufficient statistical power, affecting observed associations. It is plausible that an association exists in reality, but it was not detected within this small sample.

Lastly, the study population in this research represents a very specific subgroup within obesity care. Consequently, the unique characteristics and circumstances of the population limits the applicability and generalizability beyond the scope of this specific group.

Recommendations

Our findings have some important implications for the practice. For healthcare professionals, healthcare insurance companies and policymakers, it is important to know that the personalized ICCO+ treatmentplan for pediatric patients with severe obesity can lead to improvements in generic and weight-specific HRQoL, independent of baseline characteristics. These improvements are of particular importance, since this approach will be structurally funded from the beginning of 2024 (VWS, 2023). In addition, several recommendations can be made based on our insights. It is advisable to reevaluate associations with weight-specific HRQoL once a larger sample size is attained. Furthermore, to establish a more conclusive link between the personalized ICCO+ treatmentplan and HRQoL enhancements, a randomized controlled trial could be helpful. This trial should include a control group consisting of pediatric patients with severe obesity who either received the standard ICCO without additional diagnostics in a tertiary care center, or no care at all. Additionally, while the primary aim of this research did not focus on investigating the correlation between the different baseline variables influencing changes in HRQoL, our analysis has revealed indications of potential correlations. Therefore, it is recommended to conduct further research specifically examining the correlation between SDS-BMI, generic HRQoL, sleep problems, and stress. Lastly, future research could investigate specific elements of the personalized ICCO+ treatmentplan and social factors associated with changes in HRQoL by incorporating additional questionnaires, such as self-esteem and experiences of bullying (Houben-van Herten et al., 2015). Understanding the potential association can provide valuable insights into the factors that influence HRQoL outcomes and help inform targeted interventions for pediatric patients with severe obesity.

Conclusion

In conclusion, this study shows a positive change of the generic- and weight-specific HRQoL in pediatric patients with severe obesity after a year of receiving the personalized ICCO+ treatmentplan, independent of baseline characteristics. It is found that a high score of generic HRQoL, SDS-BMI, higher risk of sleep problems, stress, and emotional eating behavior at intake (T1) are associated with more positive changes in generic HRQoL. In contrast other baseline characteristics did not show an association with the changes in Generic HRQoL. Furthermore, in this cohort there was no correlation between the changes in SDS-BMI and the changes of both generic- and weight-specific HRQoL, after one year follow-up.

Reference

Ahuja, B., Klassen, A. F., Satz, R., Malhotra, N., Tsangaris, E., Ventresca, M., & Fayed, N. (2014). A review of patient-reported outcomes for children and adolescents with obesity. *Quality of life research: an international journal of quality of life aspects of treatment, care and rehabilitation*, *23*(3), 759–770. https://doi.org/10.1007/s11136-013-0459-9

American Academy of Pediatrics. Committee on Public Education (2001). American Academy of Pediatrics: Children, adolescents, and television. *Pediatrics*, *107*(2), 423–426. https://doi.org/10.1542/peds.107.2.423

Bruni, O., Ottaviano, S., Guidetti, V., Romoli, M., Innocenzi, M., Cortesi, F., & Giannotti, F. (1996). The Sleep Disturbance Scale for Children (SDSC). Construction and validation of an instrument to evaluate sleep disturbances in childhood and adolescence. *Journal of sleep research*, *5*(4), 251–261. https://doi.org/10.1111/j.1365-2869.1996.00251.x

Buttitta M, Iliescu C, Rousseau A, Guerrien A. (2014) Quality of life in overweight and obese children and adolescents: a literature review. Qual Life Res; 23(4):1117-39. doi: 10.1007/s11136-013-0568-5. Epub 2013 Nov 19. PMID: 24249217.

CBS. (2019). *Sociaal-economische status per postcode, 2019*. Retrieved June 23, 2023 from https://www.cbs.nl/nl-nl/maatwerk/2022/26/sociaal-economische-status-per-postcode-2019

CBS. (2022). Lengte en gewicht van personen, ondergewicht en overgewicht; vanaf 198. Retrieved February 5, 2023 from https://opendata.cbs.nl/statline/#/CBS/nl/dataset/81565NED/table?ts=1553851467369

Cole, T. J., Bellizzi, M. C., Flegal, K. M., & Dietz, W. H. (2000). Establishing a standard

definition for child overweight and obesity worldwide: international survey. *BMJ (Clinical research ed.)*, *320*(7244), 1240–1243. https://doi.org/10.1136/bmj.320.7244.1240

Eiser, C., & Varni, J. W. (2013). Health-related quality of life and symptom reporting: similarities and differences between children and their parents. European journal of pediatrics, 172(10), 1299–1304. https://doi.org/10.1007/s00431-013-2049-9

Federatie Medisch specialisten. (2020). *Behandeling van kinderen met obesitas*. Richtlijnendatabase. Retrieved 28 March, 2023 from Https://richtlijnendatabase.nl/richtlijn/behandeling_van_kinderen_met_obesitas/startpagina_-_behandeling_van_kinderen_met_obesitas.html

Federatie medisch specialisten. (2022). *Richtlijn overgewicht en obesitas bij volwassenen en kinderen*. Richtlijnendatabase. Retrieved 7 April, 2023 from https://richtlijnendatabase.nl/richtlijn/overgewicht_en_obesitas_bij_volwassenen_en_kinderen/startpagina_-_overgewicht_en_obesitas_bij_volwassenen_en_kinderen.html

Freedman, D. S., Mei, Z., Srinivasan, S. R., Berenson, G. S., & Dietz, W. H. (2007). Cardiovascular risk factors and excess adiposity among overweight children and adolescents: the Bogalusa Heart Study. The Journal of pediatrics, 150(1), 12–17.e2. https://doi.org/10.1016/j.jpeds.2006.08.042

Gezondheidsraad (2017). Beweegrichtlijnen 2017. The Hague: Gezondheidsraad.

Gidding, S. S., Nehgme, R., Heise, C., Muscar, C., Linton, A., & Hassink, S. (2004). Severe obesity associated with cardiovascular deconditioning, high prevalence of cardiovascular risk factors, diabetes mellitus/hyperinsulinemia, and respiratory compromise. *The Journal of pediatrics*, *144*(6), 766–769. https://doi.org/10.1016/j.jpeds.2004.03.043

Grasaas, E., Skarstein, S., Mikkelsen, H. T., Småstuen, M. C., Rohde, G., Helseth, S., &

Haraldstad, K. (2022). The relationship between stress and health-related quality of life and the mediating role of self-efficacy in Norwegian adolescents: a cross-sectional study. Health and quality of life outcomes, 20(1), 162. https://doi.org/10.1186/s12955-022-02075-w

Halberstadt, J., Koetsier, L.W., Sijben, M. et al. The development of the Dutch "National model integrated care for childhood overweight and obesity". BMC Health Serv Res 23, 359 (2023). https://doi.org/10.1186/s12913-023-09284-z

Halberstadt, J., Makkes, S., de Vet, E., Jansen, A., Nederkoorn, C., van der Baan-Slootweg, O. H., & Seidell, J. C. (2013). The role of self-regulating abilities in long-term weight loss in severely obese children and adolescents undergoing intensive combined lifestyle interventions (HELIOS); rationale, design and methods. *BMC pediatrics*, *13*, 41. https://doi.org/10.1186/1471-2431-13-41

Halberstadt, J. (2015). Long-term weight management in children and adolescents with severe obesity: psychological aspects. [PhD-Thesis - Research and graduation internal, Vrije Universiteit Amsterdam].

Hoedjes, M., Makkes, S., Halberstadt, J., Noordam, H., Renders, C. M., Bosmans, J. E., van der Baan-Slootweg, O. H., & Seidell, J. C. (2018). Health-Related Quality of Life in Children and Adolescents with Severe Obesity after Intensive Lifestyle Treatment and at 1-Year Follow-Up. *Obesity facts*, *11*(2), 116–128. https://doi.org/10.1159/000487328

Houben-van Herten, M., Bai, G., Hafkamp, E., Landgraf, J. M., & Raat, H. (2015). Determinants of health-related quality of life in school-aged children: a general population study in the Netherlands. *PloS one*, *10*(5), e0125083. https://doi.org/10.1371/journal.pone.0125083

Killedar, A., Lung, T., Petrou, S., Teixeira-Pinto, A., Tan, E. J., & Hayes, A. (2020). Weight

status and health-related quality of life during childhood and adolescence: effects of age and socioeconomic position. *International journal of obesity (2005)*, *44*(3), 637–645. https://doi.org/10.1038/s41366-020-0529-3

Kleinendorst, L., Abawi, O., van der Voorn, B., Jongejan, M. H. T. M., Brandsma, A. E., Visser, J. A., van Rossum, E. F. C., van der Zwaag, B., Alders, M., Boon, E. M. J., van Haelst, M. M., & van den Akker, E. L. T. (2020). Identifying underlying medical causes of pediatric obesity: Results of a systematic diagnostic approach in a pediatric obesity center. *PloS one*, *15*(5), e0232990. https://doi.org/10.1371/journal.pone.0232990

Kolotkin, R. L., & Andersen, J. R. (2017). A systematic review of reviews: exploring the relationship between obesity, weight loss and health-related quality of life. *Clinical obesity*, *7*(5), 273–289. https://doi.org/10.1111/cob.12203

Kolotkin, R. L., Zeller, M., Modi, A. C., Samsa, G. P., Quinlan, N. P., Yanovski, J. A., Bell, S. K., Maahs, D. M., de Serna, D. G., & Roehrig, H. R. (2006). Assessing weight-related quality of life in adolescents. *Obesity (Silver Spring, Md.)*, *14*(3), 448–457. https://doi.org/10.1038/oby.2006.59

Lacy, K. E., Allender, S. E., Kremer, P. J., de Silva-Sanigorski, A. M., Millar, L. M., Moodie, M. L., Mathews, L. B., Malakellis, M., & Swinburn, B. A. (2012). Screen time and physical activity behaviours are associated with health-related quality of life in Australian adolescents. *Quality of life research : an international journal of quality of life aspects of treatment, care and rehabilitation*, *21*(6), 1085–1099. https://doi.org/10.1007/s11136-011-0014-5

Levenstein, S., Prantera, C., Varvo, V., Scribano, M. L., Berto, E., Luzi, C., & Andreoli, A.

(1993). Development of the Perceived Stress Questionnaire: a new tool for psychosomatic research. *Journal of psychosomatic research*, *37*(1), 19–32. https://doi.org/10.1016/0022-3999(93)90120-5

Luppino, F. S., de Wit, L. M., Bouvy, P. F., Stijnen, T., Cuijpers, P., Penninx, B. W., & Zitman, F. G. (2010). Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. *Archives of general psychiatry*, *67*(3), 220–229. https://doi.org/10.1001/archgenpsychiatry.2010.2

Makkes, S., Renders, C. M., Bosmans, J. E., van der Baan-Slootweg, O. H., & Seidell, J. C. (2013). Cardiometabolic risk factors and quality of life in severely obese children and adolescents in The Netherlands. *BMC pediatrics*, *13*, 62. https://doi.org/10.1186/1471-2431-13-62

Noordam, H., Halberstadt, J., & Seidell, J. C. (2016). *Kwaliteit van leven als uitkomstmaat in de zorg voor kinderen (4-19 jaar) met obesitas. Tijdschrift Voor Gezondheidswetenschappen, 94(8), 300–304.* doi:10.1007/s12508-016-0107-1

Quek, Y. H., Tam, W. W. S., Zhang, M. W. B., & Ho, R. C. M. (2017). Exploring the association between childhood and adolescent obesity and depression: a meta-analysis. *Obesity reviews : an official journal of the International Association for the Study of Obesity*, *18*(7), 742–754. https://doi.org/10.1111/obr.12535

Roeser, K., Eichholz, R., Schwerdtle, B., Schlarb, A. A., & Kübler, A. (2012). Relationship of sleep quality and health-related quality of life in adolescents according to self- and proxy ratings: a questionnaire survey. *Frontiers in psychiatry*, *3*, 76. https://doi.org/10.3389/fpsyt.2012.00076

Rubino, F., Puhl, R. M., Cummings, D. E., Eckel, R. H., Ryan, D. H., Mechanick, J. I., Nadglowski, J., Ramos Salas, X., Schauer, P. R., Twenefour, D., Apovian, C. M., Aronne, L. J., Batterham, R. L., Berthoud, H. R., Boza, C., Busetto, L., Dicker, D., De

Groot, M., Eisenberg, D., Flint, S. W., … Dixon, J. B. (2020). Joint international consensus statement for ending stigma of obesity. *Nature medicine*, *26*(4), 485–497. https://doi.org/10.1038/s41591-020-0803-x

Salkind, N. J. (2010). *Encyclopedia of Research Design* (1st ed.). SAGE Publications, Inc. https://doi.org/10.4135/9781412961288

Schwimmer, J. B., Burwinkle, T. M., & Varni, J. W. (2003). Health-related quality of life of severely obese children and adolescents. *JAMA*, *289*(14), 1813–1819. https://doi.org/10.1001/jama.289.14.1813

Seidell, J. C., Halberstadt, J., Noordam, H., & Niemer, S. (2012). An integrated health care standard for the management and prevention of obesity in The Netherlands. *Family practice*, *29 Suppl 1*, i153–i156. https://doi.org/10.1093/fampra/cmr057

Sijben, M., van der Velde, M., van Mil, E., Stroo, J. & Halberstadt, J. (2018). Landelijk model ketenaanpak voor kinderen met overgewicht en obesitas. Amsterdam: Care for Obesity

Spinelli, A., Buoncristiano, M., Kovacs, V. A., Yngve, A., Spiroski, I., Obreja, G., Starc, G., Pérez, N., Rito, A. I., Kunešová, M., Sant'Angelo, V. F., Meisfjord, J., Bergh, I. H., Kelleher, C., Yardim, N., Pudule, I., Petrauskiene, A., Duleva, V., Sjöberg, A., Gualtieri, A., … Breda, J. (2019). Prevalence of Severe Obesity among Primary School Children in 21 European Countries. *Obesity facts*, *12*(2), 244–258. https://doi.org/10.1159/000500436

Tabachnick, B. G., & Fidell, L. S. (2007). Using multivariate statistics (5 ed. Vol. 5). Boston, MA: Pearson Education.

Taylor, R. W., Haszard, J. J., Jackson, R., Morrison, S., Beebe, D. W., Meredith-Jones, K. A., Elder, D. E., & Galland, B. C. (2023). Effect of Sleep Changes on Health-Related Quality of Life in Healthy Children: A Secondary Analysis of the DREAM Crossover

Trial. *JAMA network open*, *6*(3), e233005. https://doi.org/10.1001/jamanetworkopen.2023.3005

Testa, M. A., & Simonson, D. C. (1996). Assessment of quality-of-life outcomes. *The New England journal of medicine*, *334*(13), 835–840. https://doi.org/10.1056/NEJM199603283341306

Tsiros, M. D., Olds, T., Buckley, J. D., Grimshaw, P., Brennan, L., Walkley, J., Hills, A. P., Howe, P. R., & Coates, A. M. (2009). Health-related quality of life in obese children and adolescents. *International journal of obesity (2005)*, *33*(4), 387–400. https://doi.org/10.1038/ijo.2009.42

Twisk, J. W. R. (2016). Inleiding in de toegepaste biostatistiek. In *Bohn Stafleu van Loghum eBooks*. https://doi.org/10.1007/978-90-368-1534-5

Ul-Haq, Z., Mackay, D. F., Fenwick, E., & Pell, J. P. (2013). Meta-analysis of the association between body mass index and health-related quality of life among adults, assessed by the SF-36. *Obesity (Silver Spring, Md.)*, *21*(3), E322–E327. https://doi.org/10.1002/oby.20107

Van den Eynde, E., Camfferman, R., Putten, L. R., Renders, C. M., Seidell, J. C., & Halberstadt, J. (2020). Changes in the Health-Related Quality of Life and Weight Status of Children with Overweight or Obesity Aged 7 to 13 Years after Participating in a 10-Week Lifestyle Intervention. *Childhood obesity (Print)*, *16*(6), 412–420. https://doi.org/10.1089/chi.2020.0070

van der Valk, E. S., van den Akker, E. L. T., Savas, M., Kleinendorst, L., Visser, J. A., Van Haelst, M. M., Sharma, A. M., & van Rossum, E. F. C. (2019). A comprehensive diagnostic approach to detect underlying causes of obesity in adults. *Obesity reviews : an official journal of the International Association for the Study of Obesity*, *20*(6), 795–804. https://doi.org/10.1111/obr.12836

Van der Voorn, B., Camfferman, R., Seidell, J., & Halberstadt, J. (2022). Health-related Quality of Life in Children under Treatment for Overweight, Obesity or Severe Obesity: a cross-sectional study in the Netherlands. *Research Square*. https://doi.org/10.21203/rs.3.rs-1956402/v1

van Dommelen, P., Schönbeck, Y., van Buuren, S., & HiraSing, R. A. (2014). Trends in a life threatening condition: morbid obesity in dutch, Turkish and Moroccan children in The Netherlands. *PloS one*, *9*(4), e94299. https://doi.org/10.1371/journal.pone.0094299

Van Strien, T., Frijters, J.E.R., Bergers, G.P.A., & Defares, P.B. (1986). Nederlandse Vragenlijst voor eetgedrag (NVE). Handleiding. Lisse: Swets & Zeitlinger

Van Wieringen JCM (2009). *Standpunt Beweegstimulering door de jeugdgezondheidszorg.* Rijksinstituut voor Volksgezondheid en Milieu (RIVM) Bilthoven, The Netherlands: Dutch Ministry of Health, Welfare and Sport; p. 45-53. Available from https://www.rivm.nl/bibliotheek/rapporten/295002001.pdf.

Varni, J. W., Burwinkle, T. M., Seid, M., & Skarr, D. (2003). The PedsQL 4.0 as a pediatric population health measure: feasibility, reliability, and validity. *Ambulatory pediatrics : the official journal of the Ambulatory Pediatric Association*, *3*(6), 329–341. https://doi.org/10.1367/1539-4409(2003)003<0329:tpaapp>2.0.co;2

Varni, J. W., Limbers, C. A., & Burwinkle, T. M. (2007). Impaired health-related quality of life in children and adolescents with chronic conditions: a comparative analysis of 10 disease clusters and 33 disease categories/severities utilizing the PedsQL 4.0 Generic Core Scales. *Health and quality of life outcomes*, *5*, 43. https://doi.org/10.1186/1477-7525-5-43

VWS (Ministerie van Volksgezondheid, Welzijn en Sport)(2022). *Overgewicht | Leeftijd en geslacht jongeren*. Public Health and Care. Retrieved 3 April, 2023 from https://www.vzinfo.nl/overgewicht/leeftijd-en-geslacht-jongeren

VWS (Ministerie van Volksgezondheid, Welzijn en Sport) (2023). *Structurele bekostiging voor aanpak kinderen met overgewicht en obesitas*. Newspaper | Dutch healthcare authority. Retrieved 15 June, 2023 from https://www.nza.nl/actueel/nieuws/2023/05/24/structurele-bekostiging-voor-aanpak-kinderen-met-overgewicht-en-obesitas

Wu, Y. K., & Berry, D. C. (2018). Impact of weight stigma on physiological and psychological health outcomes for overweight and obese adults: A systematic review. *Journal of advanced nursing*, *74*(5), 1030–1042. https://doi.org/10.1111/jan.13511

Zeller, M. H., & Modi, A. C. (2006). Predictors of health-related quality of life in obese youth. *Obesity (Silver Spring, Md.)*, *14*(1), 122–130. https://doi.org/10.1038/oby.2006.15

Zolotarjova, J., Ten Velde, G., & Vreugdenhil, A. C. E. (2018). Effects of multidisciplinary interventions on weight loss and health outcomes in children and adolescents with morbid obesity. *Obesity reviews : an official journal of the International Association for the Study of Obesity*, *19*(7), 931–946. https://doi.org/10.1111/obr.12680

Appendix 1

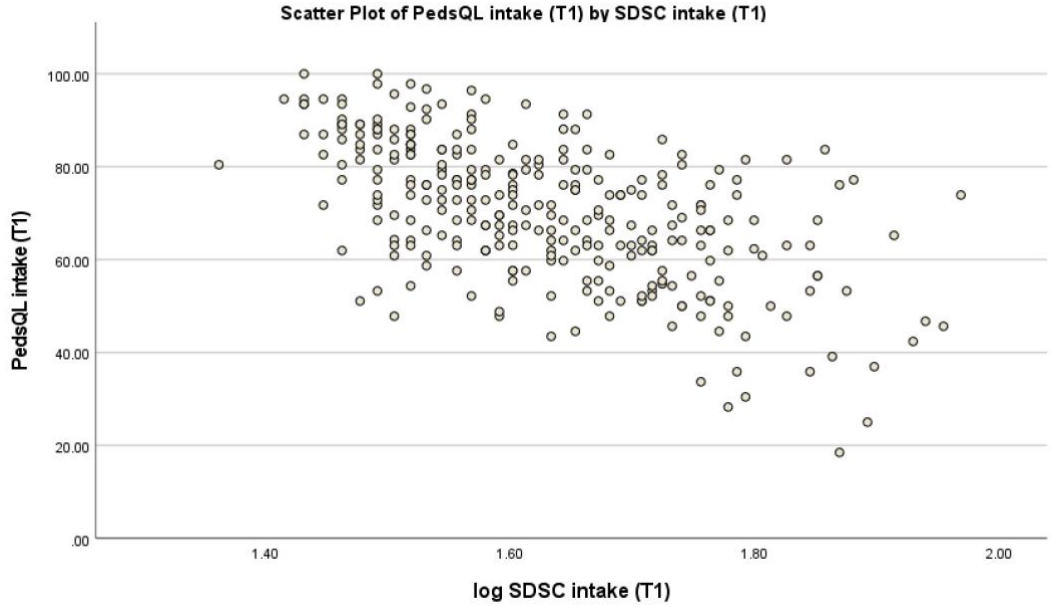


Figure 3a: Negative correlation between PedsQL intake (T1) and log SDSC intake (T1)

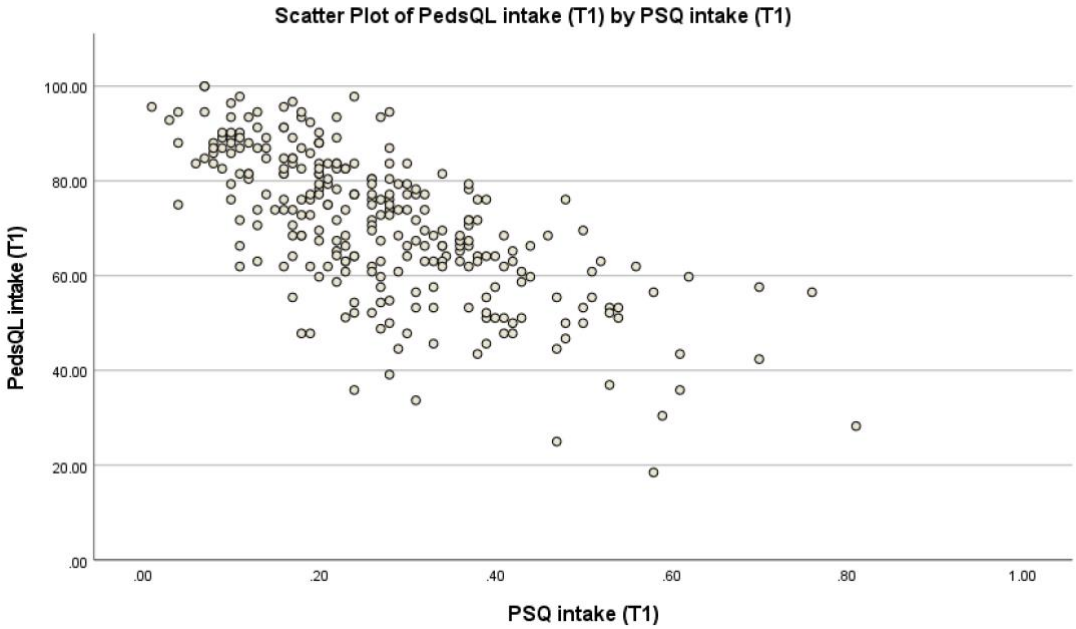


Figure 3b: Negative correlation between PedsQL intake (T1) and PSQ intake (T1)

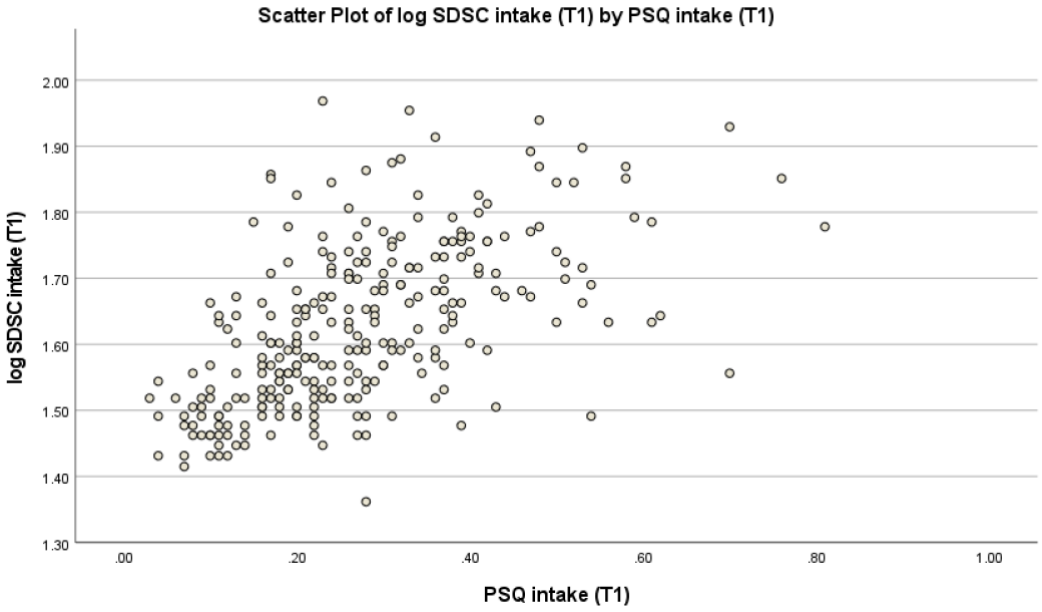


Figure 3c: Positive correlation between log(SDSC) and PSQ