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ARTICLE

Pediatrics

Do adolescents with extreme obesity differ according to previous treatment seeking behavior? The Youth with Extreme obesity Study (YES) cohort

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Abstract

Objectives Adolescent extreme obesity is associated with somatic and psychiatric comorbidity, low quality of life, and social dysfunction. Nevertheless, few adolescents seek obesity treatment, thus many may elope appropriate care. We examine whether previous treatment seeking relates to disease burden, and whether previously non-treatment seeking adolescents accept diagnostic and therapeutic offers. This information is important to inform intervention strategies.

Methods The Youth with Extreme obesity Study (YES) is a prospective, multicenter cohort study. We developed a novel recruitment strategy to span medical and vocational ascertainment settings and directly compare previously treatment seeking and non-treatment seeking youth. Participants aged 14–24 years; BMI ≥ 30 kg/m^2 were enrolled at four medical- and one job centers. We present comorbidity and psycho-social baseline data by sex, obesity WHO grade I-III, and treatment-seeking status, defined as self-reported previous participation in a weight-loss program.

Results Of 431 participants, 47% were male; mean age 16.6 (standard deviation 2.3) years, BMI 39.2 (7.5) kg/m^2. Somatic comorbidity increased with obesity grade, $p < 0.05$: hypertension (42, 55, 64%), dyslipidemia (28, 24, 37%,), dysglycemia (9, 19, 20%,), elevated transaminases (15, 26, 30%). Quality of life (EQ5 D) decreased (74, 71, 70). Rates of psychiatric disorders were stable: depression 11%, attention deficit disorder 6%, substance use disorder 2%, self-injurious behavior 5%, suicide attempt 3%. Only 63% (56, 64, 69%) reported previous treatment seeking. Acceptance of the diagnostic (89%) or therapeutic (28%) program, medical or psychosocial situation did not differ by treatment seeking status. Acceptance of the therapeutic program was generally low, but high at the job center (92%).

Conclusion Irrespective of previous treatment seeking, adolescent extreme obesity was associated with high comorbidity and psychosocial burden. Acceptance of the diagnostic program overall and the therapeutic program at the job center were high. This underscores the need of innovative, accessible programs beyond the currently offered care.

Introduction

Extreme adolescent obesity is a serious health problem and associated with high morbidity and mortality [1–3]. Rates of adolescent extreme obesity continue to increase [4–6], and approximately 90% of youth with extreme obesity go on to develop at least WHO grade II obesity in adulthood [7]. Treatment is difficult: adherence to conventional weight-loss programs is as low as 15-20% and decreases with increasing BMI [8–10]. Sustained BMI reduction is characteristically minor (0.05 to 0.5 standard deviation scores [SDS]) after observation periods of 0.5 to 5 years [8, 10–18]. Bariatric surgery shows more promising results, but it

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is invasive and long-term outcomes are not well studied in adolescents [19]. This creates a therapeutic dilemma as to whether and how to treat adolescents with extreme obesity. Presence and severity of comorbidities are key decision factors regarding medical supervision and interventions, because comorbidities can be treated.

Therefore, it is important to capture unbiased comorbidity rates to inform treatment and prevention strategies. This is difficult as only a small percentage of adolescents seek medical attention. Those who do not present for medical care are not evaluated and are not captured in observational studies. Hence, most comorbidity data are derived from younger children, adults, or the subset of adolescents who present to specialized obesity treatment centers. The data are influenced by differences in age and BMI and prone to ascertainment bias. Specifically, reported comorbidity rates in treatment seeking patients may over- or under underestimate the rates in non-treatment seeking populations: e.g. only the sickest adolescents seek obesity treatment versus the most affected youth are unable to present for care due to physical or mental barriers, stigmatization and resignation following unsuccessful weight-loss attempts. Population-based registries generally corroborate the high morbidity rates [3, 7, 20, 21]. However, due to the infrequent occurrence of extreme obesity in adolescence and uncertain participation rates, it remains extremely difficult to systematically assess comorbidity in epidemiological samples [21]. Moreover, direct comparison of treatment seeking participants at obesity centers and non-treatment seeking adolescents captured in registries is limited due to methodological differences in recorded outcome measures. Early comparative studies show higher levels of anxiety and depression in treatment seeking youth [20, 21], supporting the notion of increased burden of disease in the treatment seeking. Somatic outcomes have not been directly compared.

The 'Youth with Extreme obesity Study (YES)' [22], is a prospective multi-center cohort study that specifically focuses on the understudied group of older adolescents and young adults with extreme obesity. We developed a novel recruitment strategy to span medical and non-medical ascertainment settings in an effort to reach treatment and non-treatment seeking youth. The YES is ongoing with the overall aims to characterize health and psychosocial situation of adolescents, test a novel low level obesity intervention [23], describe the outcomes of adolescent bariatric surgery, assess financial burden, and follow adolescents longitudinally into adulthood [22]. Here, we present a summary of baseline demographic, anthropometric, somatic and psychiatric comorbidity data of the cohort, and directly compare participants with different treatment seeking behaviors. Our aims were to determine: (a) whether previous treatment seeking relates to obesity degree, disease burden or psycho-social situation (b) whether previously non-treatment seeking adolescents would accept diagnostic- and therapeutic programs.

Methods

Design

Prospective cohort study.

Recruitment and participants

Adolescents and young adults (henceforth referred to as "adolescents", or "youth") aged 14–24 years with obesity (BMI ≥ 30.0 kg/m^2) and sufficient German language skills to complete surveys were recruited at four university medical centers (study center 1-4) and one job center (study center 5) between June 2012 and November 2014. The medical centers enrolled eligible individuals who presented for obesity treatment. Additional eligible participants were ascertained by study advertisements through the media, health insurances, local job centers and schools, as well as through database search of APV (national Adiposity Patients Registry; captures all obesity-related patient encounters at participating centers) [24] at study center 4. In addition, we used APV to determine patient volume at study centers 1–4 to estimate recruitment drop-out rates. At study center 5 (job center), case managers were instructed to screen all individuals in the specified age range using body silhouette images by Stunkard et al [25]. Ranging from underweight (type 1) to extremely obese (type 9), these silhouettes have been used for self- and external assessment of body type in many studies. A body silhouette type 6 generally corresponds to a BMI of 28–29 kg/m^2 [26] and formed the basis for participant identification. Candidates were given study information and invited to an information session, during which height and weight were measured to confirm eligibility, and consent was obtained. We recorded recruitment source per self-report: All participants were asked by what means they received information of the study (answer choices: physician, health insurance, school, job center, internet, flyer, friends/family, other; see Fig. 1).

Data collection

Participants were offered comprehensive assessments including anthropometric measures; a laboratory evaluation of fasting glucose, insulin, liver enzymes (aspartate aminotransferase [AST], alanine aminotransferase [ALT], gamma-glutamyl transferase [GGT]), serum lipids (total cholesterol [TC], low density lipoprotein cholesterol [LDL-c], high density lipoprotein cholesterol [HDL-c], triglycerides),

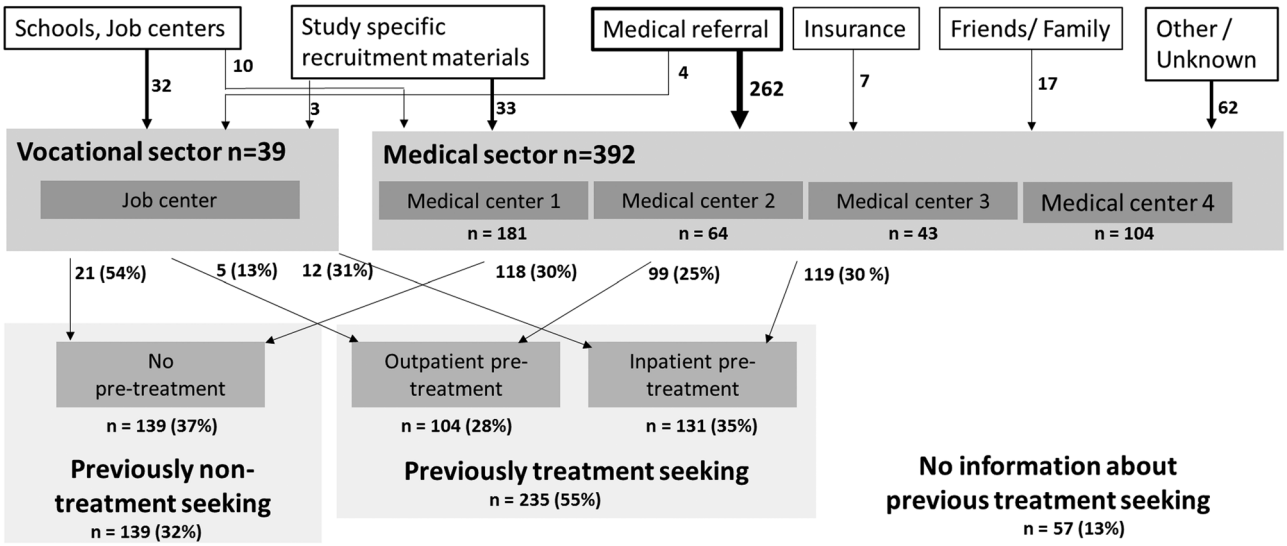

Fig. 1 Recruitment source and ascertainment setting. Recruitment source (as reported by the participant) is listed in the first row, ascertainment setting (vocational versus medical sector) in the second row, and previous treatment seeking status in the third row. Arrows depict number of participants contributed through each recruitment source or ascertainment setting. Numbers of participants are given.

uric acid, and other variables; an oral glucose tolerance test (OGTT); liver ultrasound (data not presented); sleep apnea screening (data not presented); and an array of standardized questionnaires and validated instruments to assess somatic and mental health, socio-demographic situation, and quality of life (excerpt data presented). The evaluation was adapted from the protocol of the Teen-LABS *study* [27] and complied with the German guidelines for adolescents with extreme obesity (http://www.a-g-a.de). Height and weight were obtained by double-measurement using calibrated instruments. Blood pressure was obtained manually by double measurement, using appropriately sized cuffs. Blood samples were obtained after an overnight fast at the initial visit (medical centers 1–3) or at a subsequent visit (medical center 4, job center [study center 5]). Samples were analyzed using standard assays in certified, accredited clinical laboratories.

Self-reported information including: previous participation in weight-loss programs, somatic and psychiatric comorbidity, medication use, socio-demographics, lifestyle variables, and parental anthropometrics was collected per paper questionnaires. Participants were encouraged to consult with caregivers to answer all questions. Questions on socio-demographics, nicotine and alcohol use, physical activity and screen use were adapted from *T*he German Health Interview and Examination Survey for Children and Adolescents (KiGGS-protocols*)* [28]. Quality of life was assessed using the validated instrument *EQ-5D-3L* with 5 items and a visual analog scale (VAS). Depression was assessed using the online Beck Depression Inventory II (BDI-II) with 21 items, each scoring 0–3. Depression severity was characterized according to the sum of item scores: 0–8—none, 9–13—minimal, 14–19—mild, 20–28—moderate, 29–63—severe depression [29]. To test acceptance of a therapeutic program, participants were offered a structured, low-level group intervention based on principles of cognitive behavioral therapy and consisting of six manual-based 90-min sessions over 3–6 months. Contents were administered in a randomized design to include either a novel motivational/behavioral intervention focused on quality of life and psychosocial functioning, or a standard care weight management intervention. Therapists in both arms were briefed on the intervention strategy and received a manual that included powerpoint slides, patient handouts and worksheets. A study monitor held annual visits to assess implementation and model fidelity. See Muehlig et al. [23] for detailed theoretical framework, content, participant adherence and outcomes of the intervention.

Data processing and variables

Baseline data was collected during the 6 months preceding and following enrollment. If more than one value was available, the following data is presented: anthropometrics, blood pressure, self-reported information and OGTT closest to enrollment; laboratory parameters closest to the OGTT (or enrollment date if no OGTT performed). All data were examined visually and outliers outside physiological plausibility removed. Variables were derived from the measured values in relation to age and gender-specific references: BMI SDS*:* based on extrapolated percentiles for ages 0–79 years; [30] hypertension: blood pressure ≥ 95th percentile for age, height and sex [31], or use of antihypertensive medications; dyslipidemia: TC > 200 mg/dl (5.18 mmol/l) or HDL-c < 35 mg/dl (0.91 mmol/L) or LDL-c > 130 mg/dl (3.37 mmol/l), or use of lipid lowering medications;

triglyceridemia: fasting triglycerides > 150 mg/dl (1.69 mmol/L); dysglycemia: fasting blood glucose ≥ 110 mg/dl (6.11 mmol/l) or 2-hour glucose ≥ 140 mg/dl (7.78 mmol/l; WHO definition); Homa-Index: fasting insulin [mU/l] * fasting blood glucose [mg/dl] / [22.5 * 18]; elevated transaminases: AST or ALT > 50 U/l (0.85 µkat/L) or GGT > 50 U/l (0.83 µkat/l). Variables based on self-report were: lower educational track: lowest of three educational tracks in Germany, including special education; low academic achievement: self-reported academic grades predominantly between 4 and 6 (German grading system: 1—very good, 2—good, 3—fair, 4— sufficient, 5— insufficient, 6—fail); absenteeism: often misses or is late for school; screen time > 4 h: daily time spent on TV/video games /movies/gaming console/computer/internet; migration background: at least one parent born abroad and/or status as a foreign citizen; acceptance of the diagnostic program: participation in fasting laboratory evaluation; acceptance of the therapeutic program: agreement to participate in the structured manual based group-intervention.

Group comparison

Adolescents and young adults and were categorized *a* priori (NCT01625325) according to WHO categories for adult obesity: Obesity: WHO Grade I - BMI 30.0–34.9 kg/m^2; Extreme Obesity – WHO Grade II - BMI 35.0–39.9 kg/m^2 and III - BMI ≥ 40.0 kg/m^2. In an alternative model, participants aged 14–19 years were categorized according to recent recommendations for adolescent obesity: Grade I - BMI > 120% of 95th percentile; Grade II - BMI 120- < 140% of 95th percentile and Grade III - ≥ 140% of 95th percentile (online supplement).

Youth were labeled "previously treatment seeking" if they reported previous participation in any weight-loss program. Participants were further sub-divided according to the intensity of pre-treatment as those who had participated in outpatient only versus inpatient programs. We explored additional definitions of treatment seeking using (1). Recruitment strategy: active recruitment (flyers, insurance, job center) = non-treatment seeking versus spontaneous presentation = treatment seeking, (2). Ascertainment setting: vocational sector = non-treatment seeking versus medical sector = treatment seeking. These analyses showed similar results and are not presented.

Statistical analyses

Absolute and relative frequencies as well as means and standard deviations (SD) are reported for participants with available information (number of participants for each variable given in tables). The group-wise comparisons were performed by Chi-Square for nominal variables and Wilcoxon-Mann-Whitney (WMW) tests for continuous variables. Regression models with adjustment for age (linear), sex and BMI (linear for absolute categories, categorical for percentile-based categories), were used. Least square means (LS-means) with 95% confidence intervals (95% CI) were calculated. A two-sided p-value < 0.05 was considered significant. In a sensitivity analysis, we compared data from the job center to participants of similar age (≥ 18 years) from the medical centers. As we observed no evidence for differences between the centers, we report combined data as one study cohort. Analyses were performed using SAS 9.4 software (SAS institute Inc. 2012, Cary, NC).

Ethics

The study was conducted in accordance with the Helsinki Declaration and the ICH-GCP guideline and national regulations and was approved by the ethics committees at the 5 study centers. Written informed consent was obtained from adult participants, or assent and parental consent from adolescents under the age of 18 years.

Registration

clinicaltrials.gov NCT01625325; German Clinical Trials Register (DRKS) DRKS00004172.

Results

Recruitment

A total of 899 eligible individuals presented to the medical centers during the recruitment period according to the APV national database [24], of whom 392 (43%) were enrolled in the study. At the job center, 169 youth were identified with the obese body silhouette. Of these, 80 (48%) expressed interest and were invited for an initial information session, 53 (32%) participated in this session and 34 (20%) were enrolled in the study; five additional participants were ascertained through clinics at study center 5 and referred to the job center study site, for a total of 39 job center participants. Taken together, 431 participants were enrolled across all ascertainment settings. Figure 1 lists all enrolled participants by self-reported recruitment source, ascertainment setting (vocational versus medical sector), and previous treatment seeking status.

Anthropometric, demographic, and psychosocial characteristics

Average age was 16.6 (SD 2.3) years, 47% were male. Mean BMI was 39.2 (7.5) kg/m^2 and mean BMI SDS was

3.02 (0.50) (Table 1, Fig. 2). The diagnostic program was accepted by 89%, and the therapeutic program by 28%. Ten percent of participants with available data were unemployed, 17% were enrolled in vocational training and 73% in school. Among pupils, 25% were in the lower educational track, 27% had school absenteeism, and 15% had low academic achievement. Forty-eight percent reported migration background. Neither parent had a full-time employment in 35%, 81% had at least one obese parent. Sixty-one percent endorsed > 4 h daily screen time, 44% denied recreational physical activity. Seventeen percent reported nicotine and 34% alcohol use.

Job center accrual: a novel strategy to recruit obese youth

The $n = 39$ job center participants were older than the $n = 392$ medical center participants (21.2 [2.3] versus 16.1 [1.7] years, $p < 0.001$). When comparing ≥ 18-year-old job center ($n = 36$) and medical center ($n = 35$) participants in a sensitivity analysis, mean age still differed slightly (21.5 [2.1] versus 20.0 [1.9] years, $p = 0.002$) but mean BMI was similar (45.7 [6.3] versus 44.5 [11.6] kg/m^2, $p = 0.12$). Job center participants were less frequently enrolled in school, vocational training or workforce (28 versus 79%, $p < 0.001$), less frequently had a migration background (25 vs. 54%, $p = 0.01$), and revealed lower previous treatment seeking (43% versus 81%, $p = 0.002$). There was no difference in any of the assessed medical or psychiatric comorbidities. Acceptance of the therapeutic program, which was generally low, was exceptionally high in job center participants (92 versus 23%, $p < 0.001$).

Comorbidity

Somatic comorbidity rates were high, 60% had hypertension, 31% dyslipidemia, 16% dysglycemia, and 25% elevated transaminases. Fifty-seven percent reported back- or leg pain in the past 4 weeks, causing 8% to miss work or school (on average 7 days). Psychiatric disorders were reported by 24%, including depression (11%), attention deficit/hyperactivity disorder (ADHD) (6%) and substance use disorders (2%). Five percent reported self-injurious behavior and 3% had a previous suicide attempt. Mean BDI-II score was 10.4 (9.0), 11% met criteria for mild, 11% for moderate and 6% for severe depression (Table 1). Quality of life (QOL) was low, with an average EQ-5D VAS score of 72 [23].

Sex differences

Upon adjustment for age and BMI, dyslipidemia (38 versus 21%, $p = 0.002$) and elevated transaminases (33 versus

Table 1 YES baseline cohort characteristics

Variable	N^a	Summary statistic
Anthropometrics		
Age, mean (SD), years	431	16. 6 (2.3)
Male, %	431	47
BMI, mean (SD), kg/m^2	431	39.2 (7.5)
BMI SDS, mean (SD)	431	3.02 (0.50)
Socio-demographic Factors		
Migration background, %	396	48
No parent full-time employed, %	376	35
Parents lower education track, %	360	33
At least one parent obese, %	294	81
Highest parental BMI, mean, kg/m^2	294	36.6
Vocational Information		
Unemployed, %	394	10
Vocational training, %	394	17
School enrollment, %	394	73
Lower educational track, %	317	25
Low academic achievement, %	294	15
Absenteeism, %	289	27
Lifestyle		
Cigarette smoking, %	388	17
Alcohol use, %	380	34
Recreational sport or physical activity, %	390	56
Screen time over 4 h per day, %	385	61
Previous treatment seeking behavior		
Previously treatment seeking (inpatient), %	374	35
Previously treatment seeking (outpatient), %	374	28
Previously non-treatment seeking, %	374	37
Medical comorbidity		
Hypertension, %	413	60
Antihypertensive medications, %	431	5
Dyslipidemia, %	391	31
Hypertriglyceridemia, %	381	22
Lipid lowering medications, %	431	0.7
Dysglycemia, %	388	16
HbA1C, mean, %	304	5.35 (0.62)
Homa-index, mean	353	5.64 (4.92)
Antihyperglycemic medications, %	431	5
Elevated transaminases, %	389	25
Hirsutism, %	205	19
Psychiatric comorbidity (self-report), %	353	24
Depression (self-reported), %	353	11
Depression (BDI II-score), mean (SD)	322	10.4 (9.0)
Depression mild, %	322	11
Depression moderate, %	322	11
Depression severe, %	322	6
Quality of life (EQ-5D) VAS mean (SD)	341	72 (23)

Table 1 (continued)

Variable	N^a	Summary statistic
Back or leg pain in the past 4 weeks	375	57
Missed school / work because of pain in the past 4 weeks, %	375	8 (7 days on average)

[a]Number of participants with information available

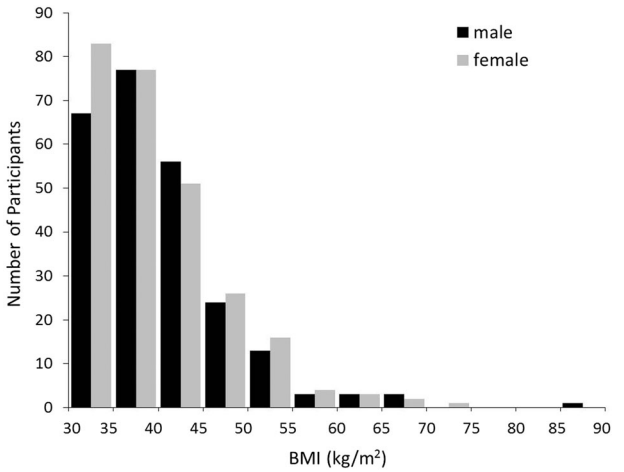

Fig. 2 BMI distribution by sex. Males black, females grey. Both sexes follow a similar BMI distribution pattern

16%, $p < 0.001$) were more common in males, whereas females had more self-injurious behaviors (7 versus 1%, $p = 0.02$), depressive symptoms (mean BDI-score 12.8 (95% CI: 11.5, 14.2) versus 7.9 (6.6, 9.3), $p < 0.001$), higher rates of moderate (15 versus 6%, $p = 0.009$) and severe (11 versus 1%, $p = 0.002$) depression (Table 2), and more back and leg pain (66 versus 47%, $p < 0.001$).

BMI comparison

After adjustment for age and sex, higher obesity grade was associated with lower quality of life assessed by EQ5D VAS (Grade I - 74, Grade II - 71, Grade III – 70, $p = 0.01$), enrollment in the lower education track (11, 25, 39%, $p < 0.001$), lower sports participation (63, 53, 53%, $p = 0.005$) and screen time > 4 h per day (60, 52, 68%, $p = 0.02$) (Table 3). Rates of somatic comorbidity increased with obesity grades: hypertension (42, 55, 64%, $p < 0.001$), dyslipidemia (28, 34, 37%, $p = 0.02$), dysglycemia (9, 19, 20%, $p = 0.005$), elevated transaminases (15, 26, 30%, $p = 0.002$), and back and leg pain (50, 53, 67%, $p = 0.05$). In contrast, rates of self-reported psychiatric disorders and BDI score did not correlate with obesity degree. Alternative analysis based on percentile-based BMI cut-offs for participants aged 14–19 years yielded similar results in most domains, but did not show significant differences in dyslipidemia, previous treatment seeking, lifestyle factors and quality of life (supplement).

Previous treatment seeking

The $N = 139$ reported no prior participation in weight-loss programs and were classified as previously non-treatment seeking; $n = 235$ participants reported prior weight-loss treatment and were classified as previously treatment seeking; $n = 57$ did not provide this information. Previous treatment seeking was slightly more prevalent with increasing obesity Grade I-III (56, 64, 69%, $p = 0.006$, Table 3), and average BMI for the non-treatment versus treatment seeking groups was lower (38.2 vs. 39.8 kg/m^2, $p = 0.03$), mostly due to higher BMI in the inpatient pre-treatment group (Table 4). After adjusting for age, sex and BMI, only the HOMA index was higher in previously treatment compared to non-treatment seeking participants ($p = 0.03$). Quality of life, depression score, and frequencies of diagnostic BDI scores did not differ according to previous treatment seeking behavior. Likewise, acceptance of the diagnostic and therapeutic program did not differ between previously treatment and non-treatment seeking adolescents.

Post-hoc analysis based on the type of prior weight-loss treatment showed that participants with prior inpatient treatment were more commonly in the lower education track compared to participants with prior participation in outpatient weight-loss treatment (26 versus 14%, $p = 0.05$), and had higher rates of self-reported psychiatric disorders (33 versus 19%, $p = 0.02$) and alcohol use (42 versus 27%, $p = 0.02$) compared to participants who had not previously sought treatment (Table 4).

Discussion

We report baseline characteristics of a group of adolescents and young adults with grades I-III obesity recruited for the YES prospective multicenter cohort study. We describe somatic and psychiatric comorbidity according to obesity degree, sex and previous treatment seeking behavior, and examined (a) whether previous treatment seeking relates to obesity degree, disease burden or psycho-social situation (b) whether previously non-treatment seeking adolescents would accept diagnostic- and therapeutic programs.

Previous treatment seeking increased with obesity degree, while acceptance of the diagnostic and therapeutic program was stable. When comparing previously treatment and non-treatment seeking youth, previous treatment seeking was associated with equal acceptance of the therapeutic

Table 2 YES cohort characteristics compared by sex

	$N_{male,female}$ [a]	LS-mean /% (95% CI) [b]		*p*-value [b]
		Male	Female	
Age, mean, years [c]	202, 229	16.3 (16.0,16.7)	16.8 (16.5,17.1)	0.02
BMI, mean, kg/m^2 [c]	202, 229	39.2 (38.2,40.3)	39.2 (38.2,40.1)	0.74
Migration background, %	184, 212	44	52	0.1
No parent full-time employed, %	174, 202	31	38	0.16
Highest parental BMI, %	127, 167	36.6 (35.3,37.9)	36.6 (35.4,37.7)	1
Lower educational track, %	157, 160	25	18	0.13
School absenteeism, %	147, 142	29	25	0.47
Recreational sport or physical activity, %	180, 210	58	55	0.61
Screen time over 4 h per day, %	180, 205	65	57	0.1
Cigarette smoking, %	177, 211	13	18	0.18
Alcohol use, %	175, 205	36	30	0.26
Hypertension, %	192, 221	53	56	0.66
Dyslipidemia, %	185, 206	38	23	0.002
Dysglycemia, %	181, 207	13	17	0.19
HbA1C, mean, %	139, 165	5.34 (5.24,5.44)	5.36 (5.26,5.45)	0.83
Homa-index, mean	164, 189	5.30 (4.57,6.03)	5.93 (5.24,6.61)	0.22
Elevated transaminases, %	182, 207	33	16	< 0.001
Back or leg pain in the past 4 weeks, %	172, 203	47	66	< 0.01
Psychiatric comorbidity (self-report), %	161, 192	25	23	0.61
Depression (self-reported), %	161, 192	11	11	0.79
BDI II-score, mean	161, 161	7.9 (6.6,9.3)	12.8 (11.5,14.2)	< 0.001
Depression mild, %	161, 161	11	10	0.64
Depression moderate, %	161, 161	6	15	0.009
Depression severe, %	161, 161	1	11	0.002
Quality of life (EQ-5D), VAS mean	165,176	72 (68,75)	72 (68,75)	0.98

[a]Number of participants with information available

[b]Adjusted for age (linear) and BMI (linear) [c]Values for age and BMI are reported without adjustment

and diagnostic program, a slightly higher obesity grade, but similar demographic and psychosocial factors and comorbidity.

The high comorbidity rates in our cohort are consistent with the adolescent extreme obesity literature reporting high rates of cardiovascular risk [1, 2, 32–37], diabetes [38–41], nonalcoholic fatty liver disease [42, 43], musculoskeletal disorders [44, 45], depression and suicide attempts [46–49]. The mean EQ5-D score of 72 is very low compared to same-age population means around 95 [50], and scores around 80 in participants with other chronic diseases, e.g. cystic fibrosis [51]. Low quality of life has previously been reported in overweight and obese children and adolescents [52], specifically in treatment seeking populations [53]. With increasing obesity, somatic comorbidity increased, and variables of social and vocational success and quality of life decreased. This aligns with previous studies [48, 54–56] and may be secondary to decreased mobility and other obesity related impairments.

Despite the high BMI and comorbidity rates, only 63% of participants reported previous participation in a weight-loss program and were accordingly classified as previously treatment seeking. Previous treatment seeking was associated with a higher grade of obesity (mostly due to higher BMI in participants with previous inpatient treatment), and higher HOMA index after adjustment for BMI and age. Previously treatment and non-treatment seeking youth had equal acceptance of the diagnostic and therapeutic program, and similar demographic and psychosocial factors, prevalence of somatic and psychiatric co-morbidities, symptoms of depression and health related quality of life. Merely participants with inpatient pre-treatment reported higher psychiatric comorbidity and alcohol use compared to the other two groups. In contrast, previous studies have reported higher rates of anxiety disorders, major depressive disorder and eating disorders in treatment seeking obese adolescents and young adults compared to population controls [20, 21]. This discrepancy may be due to methodological

Table 3 YES cohort characteristics compared by obesity grade

	$n_{\text{grade I, II, III}}$ [a)]	Mean /% (95% CI) [b]			p-value [b]
		Obesity	Extreme obesity		
		Grade I (BMI 30–35 kg/m^2)	Grade II (BMI 35–40 kg/m^2)	Grade III (BMI ≥ 40 kg/m^2)	
Age, mean, years [c]	150, 122, 159	15.7 (15.3,16.0)	16.1 (15.7,16.5)	17.7 (17.4,18.1)	< 0.001
Male, % [c]	150, 122, 159	45	48	48	0.93
Previously non-treatment seeking, %	131, 104, 139	44	36	31	0.006
Acceptance of the diagnostic program, %	150, 122, 159	92	91	88	0.97
Acceptance of the therapeutic program, %	150, 122, 159	23	28	29	0.87
Migration background, %	139, 111, 146	48	50	48	0.52
No parent full-time employed, %	130, 106, 140	38	31	36	0.06
Highest parental BMI, kg/m^2	110, 85, 99	34.2 (32.7,35.6)	35.5 (33.9,37.0)	40.2 (38.7,41.8)	< 0.001
Lower educational track, %	129, 96, 92	11	25	39	< 0.001
School absenteeism, %	125, 87, 77	26	20	36	0.14
Recreational sport or physical activity, %	137, 111, 142	63	53	53	0.005
Screen time over 4 h per day, %	135, 108, 142	60	52	68	0.02
Cigarette smoking, %	136, 109, 143	10	21	17	0.69
Alcohol use, %	131, 107, 142	32	35	32	0.52
Hypertension, %	147, 121, 145	42	55	64	< 0.001
Dyslipidemia, %	141, 115, 135	28	24	37	0.02
Dysglycemia, %	143, 109,136	9	19	20	0.005
HbA1C, mean, %	118, 95, 91	5.24 (5.13,5.35)	5.37 (5.24,5.49)	5.48 (5.35,5.61)	0.01
Homa-index, mean	135, 105, 113	4.23 (3.41,5.05)	5.57 (4.65,6.49)	7.37 (6.46,8.28)	< 0.001
Elevated transaminases, %	138, 114, 137	15	26	30	0.002
Hirsutism, %	72, 56, 77	16	18	23	0.56
Back or leg pain in the past 4 weeks, %	131, 102, 142	50	53	67	0.05
Psychiatric comorbidity (self-report), %	127, 96, 130	25	27	20	0.3
Depression (self-reported), %	127, 96, 130	11	10	11	0.99
BDI II-score, mean	112, 89, 121	10	10	12	0.13
Quality of life (EQ-5D), mean	117, 98, 126	74 (70,78)	71 (66,75)	70 (66,74)	0.01

[a]Number of participants with information available

[b]Adjusted for age (linear) and BMI (linear)

[c]Unadjusted

differences, as discussed in strengths and limitations. It is disconcerting that previously non-treatment seeking adolescents had equally high comorbidity rates compared to their previously treatment seeking peers, because they may have eloped timely diagnosis and treatment. On the other hand, it is promising that these youth had an equally high acceptance of the diagnostic program. While acceptance of the therapeutic program was generally low, it was exceptionally high at the job center. Factors contributing to this difference may be the abundance of alternative therapeutic options at medical centers (e.g. individual treatment), the older age of job-center participants and thus achieved autonomy, a lower exposure rate to previous weight-loss programs, and a different motivation based on current psychosocial status (e.g. job-seeking versusl enrolled in school). While reasons remain speculative, the high acceptance of diagnostic and therapeutic offers at the job center

Table 4 YES cohort characteristics compared by obesity class by self-reported obesity pre-treatment (treatment seeking versus non-treatment seeking participants)

	$n_{no,outp.,inp.}$	Mean /% (95% CI) [a]			*p*-value [a]		
		Previously non-treatment seeking	Previously treatment seeking				
			outpatient program	inpatient program	[c]	[d]	[e]
Age, mean, years [b]	139, 104, 131	16.8 (16.4,17.2)	16.1 (15.7,16.6)	17.0 (16.6,17.4)	0.25	0.004	0.10
Male, % [b]	139, 104, 131	45	49	47	0.57	0.71	0.84
BMI, mean, kg/m^2 [b]	139, 104, 131	38.1 (36.9,39.3)	37.3 (35.9,38.8)	42.1 (40.8,43.4)	0.40	< 0.001	< 0.001 *)
Acceptance of the diagnostic program, %	139, 104, 131	92	87	90	0.25	0.55	0.56
Acceptance of the therapeutic program, %	139, 104, 131	32	23	30	0.14	0.25	0.75
Migration background, %	139, 103, 131	52	47	42	0.49	0.42	0.11
No parent full-time employed, %	135, 99, 125	41	36	27	0.45	0.18	0.03
Highest parental BMI, %	104, 78, 105	36.2 (34.7,37.6)	36.9 (35.2,38.5)	36.6 (35.1,38.0)	0.52	0.80	0.68
Lower educational track, %	113, 88, 102	23	14	26	0.10	0.05	0.64
Absenteeism, %	100, 81, 93	28	30	25	0.76	0.47	0.65
Recreational sport or physical activity, %	138, 100, 130	56	61	54	0.46	0.27	0.68
Screen time over 4 h per day, %	136, 100, 130	60	62	65	0.84	0.55	0.39
Cigarette smoking, %	137, 101, 129	16	15	15	0.95	0.92	0.86
Alcohol use, %	135, 98, 127	27	33	42	0.33	0.24	0.02
Hypertension, %	129, 103, 125	54	56	59	0.76	0.69	0.47
Dyslipidemia, %	125, 93, 118	31	22	35	0.15	0.06	0.61
Dysglycemia, %	127, 94, 114	14	12	18	0.73	0.27	0.40
Homa-index, mean	112, 87, 103	4.92 (4.36,5.49)	5.78 (5.15,6.42)	5.68 (5.08,6.29)	0.05	0.82	0.08 *)
Elevated transaminases, %	125, 92, 118	21	25	26	0.52	0.87	0.39
HbA1C, mean, %	103, 74, 82	5.29 (5.16,5.41)	5.39 (5.25,5.54)	5.43 (5.29,5.57)	0.28	0.71	0.14
Hirsutism, %	66, 46, 66	23	7	17	0.03	0.14	0.38
Back or leg pain in the past 4 weeks	135, 97, 122	55	55	60	0.44	0.97	0.41
Psychiatric comorbidity (self-report), %	130, 94, 113	19	21	33	0.81	0.06	0.02
Depression (self-reported), %	130, 94, 113	9	10	13	0.45	0.76	0.24
Depression (BDI II-score), mean	109, 80, 106	10 (9,12)	10 (8,11)	12 (10,13)	0.48	0.09	0.28
Quality of life (EQ-5D), mean	117, 86, 109	70 (66,74)	74 (69,79)	72 (68,77)	0.18	0.61	0.40

[a]Adjusted for age (linear), sex and BMI (linear), except age, sex and BMI

[b]Unadjusted

[c]Outpatient versus no pretreatment

[d]Inpatient versus outpatient pretreatment

[e]Inpatient versus no pretreatment

*$p < 0.05$ when comparing previously non-treatment versus treatment seeking

suggests a potential role of the vocational sector in obesity care.

Strengths and limitations

To our knowledge, this is the first direct comparison of previously treatment versus non-treatment seeking adolescents with extreme obesity. Other reports on comorbidity are generally based on current treatment seeking and originate from either specialized obesity centers (treatment seeking) or population-based registries (non-treatment seeking). Outcome measures reported for medical cohorts and population-based registries are fundamentally different (e.g. measured blood pressure versus self-reported hypertension) and usually don't allow for direct comparison, with the exception of early psychiatric studies using survey instruments [20, 21].

Limitations of our study include the ascertainment of treatment seeking by self-report, use of absolute BMI cut-offs, and lack of generalizability to the vocational sector. (1) Previous treatment seeking was ascertained by self-report which is prone to recall bias. Timing and intensity of pre-treatment may be heterogeneous, and pre-treatment may have influenced morbidity and quality of life positively due to treatment success, or negatively due to frustration and resignation due to unsuccessful weight-loss attempts. To account for this, we performed additional post-hoc analyses testing different definitions of treatment seeking based on recruitment source versus ascertainment setting and found similar results. (2) Absolute BMI cut-offs for obesity and its grades in adults are well established, but cut-offs for extreme childhood obesity are controversial: the 99th BMI percentile, 99.5th BMI percentile, 120% of the 95th percentile or an absolute cut-off of 35 kg/m^2 have been proposed [57]. BMI percentiles have limitations in adolescents, as there is a step-off from pediatric to adult references [30]. As adolescents approach young adulthood, absolute cut-offs become more appropriate and form the basis for bariatric surgery guidelines [58]. Because the YES contains a surgical arm, we decided *a* priori to use absolute WHO categories for adult obesity for both, adolescents and adults in this cohort. This creates a bias toward including younger participants in the lower obesity categories compared to percentile-based cut-offs. Alternative analyses using percentile-based BMI cut offs - a classification that has become more broadly accepted over recent years - yielded similar results (supplement). 3) Only ~40% of eligible participants were enrolled in the study. We did not systematically assess reasons for non-enrollment, introducing possible selection bias. Moreover, the majority of participants were recruited through medical referral. Few participants responded to study specific recruitment efforts, and only one of the centers ascertained participants via the local job center, limiting generalizability to the vocational sector. Nevertheless, we demonstrate that job centers can participate in accrual of a specific subset of extremely obese youth. More studies are needed to evaluate this approach.

Conclusion

In the prospective multicenter YES, we established a novel recruitment strategy for comparison of previously treatment and non-treatment seeking adolescents and young adults with extreme obesity. The YES cohort includes well-characterized participants from medical and vocational sectors and thereby provides an innovative platform for the study of adolescent extreme obesity. At baseline, we found high somatic and psychiatric comorbidity, increasing somatic comorbidity and decreasing quality of life and vocational success with obesity grade. Previously treatment and non-treatment seeking participants had similarly high comorbidity and psychosocial burden, and equal acceptance of the diagnostic and therapeutic program. This underscores the need of accessible, outcome-oriented programs that can reach these youth, beyond the currently offered programs at medical obesity centers. Given the poor weight-loss achieved in medical obesity programs [8, 10–18], a major focus should be on the timely diagnosis and treatment of comorbidity. Future analyses of the YES will yield longitudinal information on the natural course of obesity and different treatment regimens.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

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