Severe obesity in youth

SEVERE OBESITY IN YOUTH

HEALTH IMPLICATIONS AND
TREATMENT STRATEGIES

Kelly van de Pas

ISBN: 978-94-6483-281-5
Design & layout: Marilou Maes | www.persoonlijkproefschrift.nl
Printed by: Ridderprint | www.ridderprint.nl

The execution and dissemination of this research were financially supported by: Maastricht University, Maastricht University Medical Centre +, Máxima MC, ELAN products, Nutricia, Vitaminenoprecept, Dutch Society of Metabolic Surgery (DSMBS), Research Manager, Chipsoft, ABN AMRO.

SEVERE OBESITY IN YOUTH

HEALTH IMPLICATIONS AND
TREATMENT STRATEGIES

Proefschrift

ter verkrijging van de graad van doctor aan de Universiteit Maastricht,
op gezag van de Rector Magnificus, Prof. dr. Pamela Habibović
volgens het besluit van het College van Decanen,
in het openbaar te verdedigen
op vrijdag 1 maart 2024 om 13.00 uur

door

Kelly Gerardus Helmina van de Pas

Promotor
Prof. dr. A.C.E. Vreugdenhil

Copromotor
Dr. F.M.H. van Dielen (Máxima MC Veldhoven)

Beoordelingscommissie
Prof. dr. E. Dompeling (voorzitter)
Prof. dr. E.L.T. van den Akker (Erasmus MC Rotterdam)
Prof. dr. J.W.M. Greve
Prof. dr. D. Keszthelyi
Dr. S.W. Nienhuijs (Catharina Ziekenhuis Eindhoven)

CONTENTS

CHAPTER 1

GENERAL INTRODUCTION

GENERAL INTRODUCTION

Obesity is a major health crisis that has reached epidemic proportions in both developed and developing countries[1]. The global prevalence of obesity has nearly tripled between 1975 and 2016, and at least 2.8 million people die yearly as a result of being overweight or obese[2]. Currently, 379 million children and adolescents have obesity worldwide and this number is still increasing[3]. In the Netherlands, in 2022, 17.2% of children aged 2 to 25 years suffered from overweight and 4.4% suffered from obesity[4].

Terms and definitions

Overweight and obesity are defined using body mass index (BMI, kg/m^2). In adults, overweight is defined as a BMI ≥ 25 kg/m^2, obesity as a BMI ≥ 30 kg/m^2, and severe obesity as a BMI ≥ 35 kg/m^2. These definitions are more complex in children and adolescents, as age and sex need to be taken into account. For the definition of overweight, obesity, and severe obesity in children and adolescents, the International Obesity Task Force (IOTF) criteria are one of the most commonly used definitions (Figure 1)[5]. The IOTF determined sex- and age-adjusted cutoff values for overweight, obesity, and severe obesity based on national data from six countries, including the Netherlands. When assessing weight loss in children and adolescents, BMI z-scores are utilized rather than BMI. BMI z-scores are measures of relative weight adjusted for age and sex[6]. This thesis focuses on severe obesity in youth. To be more specific, several age definitions are used. Children are defined as those aged up to 11 years and adolescents are defined as those aged 12-17 years[7,8]. Young adults are defined as those aged 18-25 years.

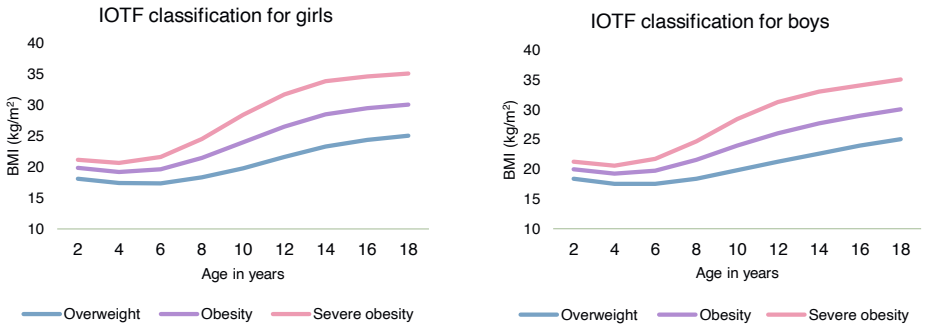


Figure 1. IOTF classification for girls and boys

Etiology

Childhood obesity is a multifactorial disease with a complex pathogenesis[9]. Simplistically, obesity is caused by an imbalance between energy intake and energy expenditure.

However, it is much more complicated, and in light of this Davison and Birch described a contextual model for the development of childhood obesity. In this model, child characteristics and child risk factors; parenting styles and family characteristics; community, demographics and societal characters are involved in the development of childhood obesity[10]. Examples of child characteristics and child risk factors in this model are gender, age, dietary intake and sedentary behavior. Parenting styles and family characteristics include the weight status of the parents, and parental knowledge of a healthy lifestyle. Examples of community, demographics and societal factors are socioeconomic status and physical education programs at school. This model reveals how many factors play a role in the development of obesity. A recent example of a crisis that influenced all these factors was the COVID-19 pandemic. The pandemic resulted in an increase in sedentary time, more mental health issues and an increase of snacking behavior, eventually leading to weight gain[11-13].

The abovementioned multifactorial model contributes to the development of obesity in a large proportion of children and adolescents. However, underlying medical conditions such as endocrine disturbances, syndromes or monogenic defects can also cause or contribute to the development of obesity, albeit less frequently. A recent Dutch study revealed that in 19% of the children with obesity who were referred to a specialized pediatric obesity unit an underlying medical cause was found[14]. Examples of endocrine disturbances associated with obesity include hypothyroidism, Cushing's disease and hypothalamic obesity. Examples of syndromes in which obesity is common are Prader-Willi, Bardet-Biedl and Alström. Another medical cause for obesity can be monogenetic defects; they result from a single gene mutation. Examples of monogenic defects are melanocortin 4 receptor (MC4R) mutations (most common), proopiomelanocortin (POMC) deficiency and leptin receptor mutations[15].

Health consequences

The health consequences of obesity are severe. Childhood obesity is associated with several life-threatening conditions such as cardiovascular disease, diabetes mellitus type 2 (T2DM), sleep apnea, kidney disease and non-alcoholic fatty liver disease (NAFLD)[16,17]. The disease course of T2DM in adolescents is even worse compared to adults, with medical treatment options failing earlier[18]. Besides this, overweight and obesity during adolescence are associated with an increased cardiovascular mortality in adulthood[19]. The abovementioned health consequences are even more pronounced in the children and adolescents with the most severe grade of obesity[17]. Consequently, people with severe obesity have an estimated 5 to 20 years shorter life expectancy[20]. In light of these implications, effective treatment strategies for severe obesity in youth are crucial.

Besides the physical health consequences, obesity is associated with several psychosocial impairments. Children and adolescents with obesity face weight-related stigmatizing and bullying, leading to a negative self-image, depressive symptoms and anxiety complaints[21-23]. Altogether this results in an impaired (health-related) quality of life (HRQoL) in these youth[21,24]. It has even been suggested that adolescents with obesity have a similar HRQoL as those diagnosed with cancer[25]. Despite mounting evidence of an impaired HRQoL in children and adolescents with overweight and obesity, it is unclear which children have the lowest HRQoL and are most negatively affected physically, psychologically and socially[21,24,26,27]. It is important to identify the children and adolescents who are most at risk, in order to tailor treatments according to their needs.

Multidisciplinary lifestyle intervention

Since obesity is such a multifactorial disease, its treatment is challenging. Multidisciplinary lifestyle interventions are the cornerstone of childhood obesity treatment. These interventions are generally family based and focus on lifestyle (including nutrition, physical activity, and sleep) as well as psychosocial components of obesity (including psychological and social wellbeing, and behavioral change)[28,29]. Previous research revealed that these interventions are effective in terms of weight loss in youth with overweight and obesity[7,8]. Furthermore, improvements in cardio metabolic health parameters and blood pressure were observed during a lifestyle intervention[30].

COACH intervention

An example of a multidisciplinary lifestyle intervention is the intervention that has been developed by the Centre for Overweight, Adolescents and Children's Healthcare (COACH)[33]. COACH is a specialized pediatric obesity unit that offers a tailored multidisciplinary lifestyle intervention. The intervention is provided by a multidisciplinary team consisting of pediatricians, dieticians, psychologists, pedagogues, physical activity coaches and care coordinators. Prior to the intervention, children and adolescents receive a baseline assessment to identify obesity-related comorbidities, to gain an understanding of behavior and family functioning, and to determine whether there is an underlying cause of obesity. This baseline assessment includes a broad anamnesis, physical examination, abdominal ultrasound, fasted blood sampling and interviews with a dietician and psychologist. After the assessment the multidisciplinary team develops an individualized, integral treatment plan. Individual guidance focusing on lifestyle changes regarding nutrition, food habits, physical activity, sleep and psychosocial aspects is offered to all families. Initial sessions occur on a monthly basis and are adjusted to the specific needs of individual families. In these sessions motivational interviewing, goal setting and positive reinforcement are utilized to obtain a healthy lifestyle. Moreover, the COACH intervention offers children and adolescents possibilities to participate in food and sport activities. The assessments to monitor the progress of the child and his or her family are offered to the participants each year.

The majority of the conducted studies regarding the effectiveness of lifestyle interventions tend to overlook youth with severe obesity, even though they are the ones with the highest cardio metabolic risk, health consequences and therefore the special focus of this thesis[17]. Two previous studies performed in youth with severe obesity showed that a lifestyle intervention was mainly beneficial in children but less effective in a subgroup of adolescents regarding weight loss[31,32]. These results indicate that for a subgroup of adolescents with severe obesity, for whom a lifestyle intervention is insufficiently effective, additional treatments such as pharmacotherapy or bariatric surgery are warranted.

Pharmacotherapy

In the Netherlands, pharmacotherapy is not a standard treatment for children and adolescents with obesity. However, it can be considered as an additional treatment modality in individual cases when a lifestyle intervention is insufficiently effective[34]. This approach aligns with the recently published guideline of the American Academy of Pediatrics, which specifically recommends it for adolescents with life-threatening comorbidities, and adolescents with severe obesity[29].

Current additional medical treatment options for children and adolescents with obesity in the Netherlands are metformin and liraglutide. Metformin is a biguanide drug that reduces blood glucose and cholesterol levels. Metformin has also weight reducing properties, which are caused by gastrointestinal side effects (e.g. nausea and vomiting), and an increase in anorexigenic hormones (e.g. GLP1 and PYY)[35]. A systematic review reported that the majority of the children who used metformin had a greater reduction in BMI compared to a control group[36]. However, it's worth noting that metformin is used off label as it is not approved by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) as a weight-loss drug[37].

Liraglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist. GLP-1 leads, among other things, to a decrease in gastric emptying and inhibition of food intake[38]. A randomized controlled trial reported that 43.3% of the adolescents achieved a BMI decrease of at least 5%, and 26.1% achieved a BMI decrease of at least 10% after one year of using liraglutide[39]. These results are promising, unfortunately liraglutide is currently not reimbursed by health insurance companies for youth with obesity in the Netherlands. On the other hand, liraglutide is the only weight-loss drug for children and adolescents approved by the FDA and EMA[37].

Bariatric surgery

When it comes to achieving weight loss and the remission of obesity-related comorbidities, bariatric surgery is the most effective treatment for severe obesity in adults[40]. Weight loss after bariatric surgery is generally expressed as percentage total weight loss (TWL); (preoperative weight-postoperative weight)/preoperative weight X 100%. The maximum weight loss is achieved one to two years after surgery and is approximately 32% TWL. Weight loss 15 years after surgery is approximately 27%[41]. Improvements in quality of life are also observed in adults undergoing bariatric surgery[42].

The most commonly performed bariatric procedures worldwide are the Roux-en-Y gastric bypass (RYGB) and the sleeve gastrectomy (SG). In 2018, 38.2% of the bariatric procedures worldwide were RYGB and 46.0% of the procedures were SG[43]. In the Netherlands, RYGB is the gold standard. In 2019, 61% of the procedures were RYGB while 21% were SG[44]. The RYGB is performed by dividing the stomach to create a small gastric pouch is generated (20-30 ml). Afterwards, the mid-jejunum is anastomosed to the gastric pouch, resulting in a gastro-jejunal anastomosis and an alimentary limb which allows food passage. Anastomosis of the biliopancreatic limb with the jejunum enables drainage of digestive juices, which combine with food in the common limb (Figure 2)[45]. By reducing the stomach size and shortening the gastrointestinal tract, RYGB is a restrictive and malabsorptive procedure that limits food intake and decreases nutrient absorption[46,47].

The SG involves transection of the greater curvature of the stomach, hereby removing the fundus and body, to create a tube-like new stomach which is approximately 25% of its original capacity[45,48]. SG is primarily a restrictive procedure as the intake is limited by reducing the size of the stomach (Figure 3).

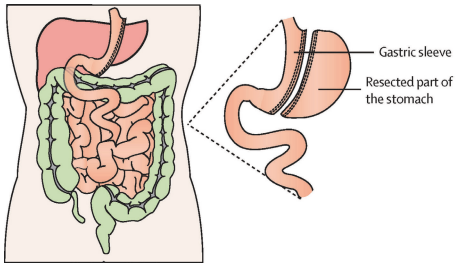


Figure 2. Roux-en-Y gastric bypass

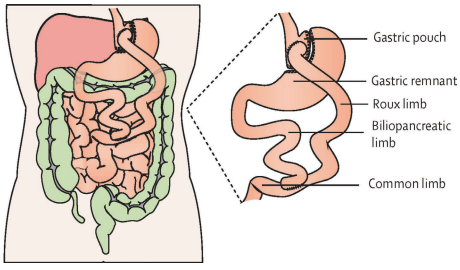


Figure 3. Sleeve gastrectomy

The number of adolescents undergoing bariatric surgery has grown in recent years[49]. A systematic review on bariatric surgery in adolescents revealed that the mean decrease in BMI was 13.3 kg/m^2 three years postoperatively. Besides this, the complication rates were comparable to those in the adult population[50]. A study that compared the outcomes of bariatric surgery between adolescents and adults, found that the weight loss between these age groups was similar up to five years after surgery. However, the adolescents showed greater remission rates with regard to T2DM and hypertension[51]. Overall bariatric surgery seems a safe and effective treatment modality for adolescents with severe obesity. Nevertheless, it may also raise some ethical concerns as invasive and sometimes irreversible procedures are offered to adolescents with life-long consequences[52]. In the Netherlands, adolescent bariatric surgery is currently only allowed in the context of scientific research and when specific criteria are met (Table 1)[53].

Table 1. Eligibility criteria for bariatric surgery in adolescents with severe obesity in the Netherlands

Eligibility criteria
• The causative and maintaining factors of obesity must be well understood.
• Age and sex-adjusted BMI ≥40 kg/m^2, or 35 to 40 kg/m^2 in combination with a severe co-morbidity.
• Counselling of a multidisciplinary lifestyle intervention for at least one year with inadequate results.
• Tanner stage ≥ 4.
• The adolescent is willing to participate in a postoperative multidisciplinary treatment program and lifelong follow-up.

Before bariatric surgery can successfully be implemented in adolescents with severe obesity in the Netherlands, a couple of issues need to be addressed. At first, additional knowledge is required regarding the long-term efficacy and safety of bariatric surgery in the younger age group (e.g. young adults). Secondly, it is important to understand the opinions of the stakeholders such as pediatricians, as they are the ones who will inform and refer adolescents for bariatric surgery. The opinions of the parents and adolescents are also essential, as adolescents need to be willing to undergo bariatric surgery including the necessary behavioral changes, and parents need to support their adolescents in this. Lastly, we must determine what kind of guidance adolescents require when they decide to proceed with bariatric surgery, and subsequently the care must be tailored to their needs. When developing a clinical pathway for adolescent bariatric surgery, consideration should be given to prevailing guidelines and position statements of professional associations[29,53,54].

AIMS AND OUTLINE OF THIS THESIS

This introductory overview illustrates the health implications associated with the most severe grade of obesity in youth, and the challenges associated with its treatment strategies. Both clinical practice and scientific research tend to overlook youth with the most severe grade of obesity. Therefore, the first part of this thesis aims to gain further insight into the impact of severe obesity in youth, and aims to evaluate the effectiveness of the current cornerstone treatment. This first part once more emphasizes that youth with severe obesity are seriously at risk, both physically and mentally. Consequently, for a subgroup of youth with severe obesity other additional treatment strategies such as bariatric surgery are warranted. With the aim of optimizing treatment strategies for youth with severe obesity, the second part of this thesis explores the applicability of bariatric surgery. The second part contributes to a better understanding of the effectiveness of bariatric surgery in young adults and the perspective of stakeholders regarding bariatric surgery in youth. Ultimately, a clinical pathway for bariatric surgery as an integral part of a comprehensive treatment for a selected group of adolescents with severe obesity will be developed.

Part I - Impact of severe obesity and current treatment

In addition to the physical health consequences, obesity is associated with various psychosocial impairments. **Chapter 2** evaluates the health-related quality of life in children and adolescents with overweight, obesity and severe obesity who are referred to a specialized pediatric obesity unit for treatment. It is hypothesized that children and adolescents with the most severe grade of obesity experience the greatest impact on their physical, psychological and social functioning.

Lack of structure (e.g. when schools are closed during a holiday) leads to a deterioration of lifestyle in children and adolescents in general, but especially in those with severe obesity. This eventually results in weight gain. In the recent COVID-19 pandemic the daily structure was disrupted, which hypothetically could have influenced the lifestyle and wellbeing of children and adolescents, particularly those with severe obesity. Therefore, in **chapter 3** in-depth information on the experiences of families regarding lifestyle and wellbeing during the pandemic is obtained.

The current cornerstone treatment for youth with severe obesity is a multidisciplinary lifestyle intervention. However, it remains unclear whether a lifestyle intervention is equally effective in different age groups regarding weight loss and the improvement of cardio metabolic health parameters. Therefore, **chapter 4** compares the effectiveness

of an intensive, tailored multidisciplinary lifestyle intervention between children and adolescents with severe obesity after one and two years of intervention.

Part II - Bariatric surgery

There is a reluctance towards bariatric surgery in young adults, possibly due to a lack of insight regarding long-term efficacy and safety. Therefore, **chapter 5** compares weight loss, complications and the remission of obesity-related comorbidities between young adults and adults who underwent bariatric surgery. Given this knowledge gap, there is also limited information available regarding the optimal bariatric procedure for the younger age group. **Chapter 6** aims to compare RYGB and SG in terms of weight loss, complications and the remission of obesity-related comorbidities in young adults using national data.

Since bariatric surgery was previously unavailable for adolescents with severe obesity in the Netherlands, it is relevant to elucidate the opinions of the stakeholders before implementing this treatment modality. **Chapter 7** reveals the perspective of pediatricians, parents and adolescents on bariatric surgery in youth.

In **chapter 8**, the development of a comprehensive clinical pathway for bariatric surgery in adolescents with severe obesity in the Netherlands is described. This comprehensive clinical pathway includes a multidisciplinary eligibility assessment as well as peri- and postoperative care.

At last, **chapter 9, 10, 11 and 12** summarize the main findings of the presented studies, place them in a broader perspective and discuss clinical implications and future perspectives.

REFERENCES

1. World Health Organization. Obesity 2021. Available from: https://www.who.int/news-room/facts-in-pictures/detail/6-facts-on-obesity.
2. The Lancet Gastroenterology H. Obesity: another ongoing pandemic. Lancet Gastroenterol Hepatol. 2021;6(6):411.
3. World Health Organization. World Obesity Day 2022 – Accelerating action to stop obesity 2022. Available from: https://www.who.int/news/item/04-03-2022-world-obesity-day-2022-accelerating-action-to-stop-obesity.
4. Centraal Bureau voor de Statistiek. Kwart 18- tot 25-jarigen te zwaar. Available from: https://www.cbs.nl/nl-nl/nieuws/2023/22/kwart-18-tot-25-jarigen-te-zwaar#:~:text=Het%20percentage%20kinderen%20en%20jongeren,is%20sinds%202014%20gelijk%20gebleven.
5. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. Pediatr Obes. 2012;7(4):284-94.
6. Must A, Anderson SE. Body mass index in children and adolescents: considerations for population-based applications. Int J Obes (Lond). 2006;30(4):590-4.
7. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6(6):Cd012691.
8. Mead E, Brown T, Rees K, Azevedo LB, Whittaker V, Jones D, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese children from the age of 6 to 11 years. Cochrane Database Syst Rev. 2017;6(6):Cd012651.
9. Lin X, Li H. Obesity: Epidemiology, Pathophysiology, and Therapeutics. Front Endocrinol (Lausanne). 2021;12:706978.
10. Davison KK, Birch LL. Childhood overweight: a contextual model and recommendations for future research. Obes Rev. 2001;2(3):159-71.
11. Ten Velde G, Lubrecht J, Arayess L, van Loo C, Hesselink M, Reijnders D, et al. Physical activity behaviour and screen time in Dutch children during the COVID-19 pandemic: Pre-, during- and post-school closures. Pediatr Obes. 2021;16(9):e12779.
12. Ravens-Sieberer U, Kaman, A., Erhart, M. et al. Impact of the COVID-19 pandemic on quality of life and mental health in children and adolescents in Germany. European Child & Adolescent Psychiatry. 2021.
13. Koletzko B, Holzapfel C, Schneider U, Hauner H. Lifestyle and Body Weight Consequences of the COVID-19 Pandemic in Children: Increasing Disparity. Ann Nutr Metab. 2021;77(1):1-3.
14. Kleinendorst L, Abawi O, van der Voorn B, Jongejan M, Brandsma AE, Visser JA, et al. Identifying underlying medical causes of pediatric obesity: Results of a systematic diagnostic approach in a pediatric obesity center. PLoS One. 2020;15(5):e0232990.
15. Mason K, Page L, Balikcioglu PG. Screening for hormonal, monogenic, and syndromic disorders in obese infants and children. Pediatr Ann. 2014;43(9):e218-24.

16. Kelly AS, Barlow SE, Rao G, Inge TH, Hayman LL, Steinberger J, et al. Severe obesity in children and adolescents: identification, associated health risks, and treatment approaches: a scientific statement from the American Heart Association. Circulation. 2013;128(15):1689-712.
17. Skinner AC, Perrin EM, Moss LA, Skelton JA. Cardiometabolic Risks and Severity of Obesity in Children and Young Adults. N Engl J Med. 2015;373(14):1307-17.
18. Beamish AJ, D'Alessio DA, Inge TH. Controversial Issues: When the drugs don't work, can surgery provide a different outcome for diabetic adolescents? Surg Obes Relat Dis. 2015;11(4):946-8.
19. Twig G, Yaniv G, Levine H, Leiba A, Goldberger N, Derazne E, et al. Body-Mass Index in 2.3 Million Adolescents and Cardiovascular Death in Adulthood. N Engl J Med. 2016;374(25):2430-40.
20. Olshansky SJ, Passaro DJ, Hershow RC, Layden J, Carnes BA, Brody J, et al. A potential decline in life expectancy in the United States in the 21st century. N Engl J Med. 2005;352(11):1138-45.
21. Buttitta M, Iliescu C, Rousseau A, Guerrien A. Quality of life in overweight and obese children and adolescents: a literature review. Qual Life Res. 2014;23(4):1117-39.
22. Puder JJ, Munsch S. Psychological correlates of childhood obesity. Int J Obes (Lond). 2010;34 Suppl 2:S37-43.
23. Rankin J, Matthews L, Cobley S, Han A, Sanders R, Wiltshire HD, et al. Psychological consequences of childhood obesity: psychiatric comorbidity and prevention. Adolesc Health Med Ther. 2016;7:125-46.
24. Meixner L, Cohrdes C, Schienkiewitz A, Mensink GBM. Health-related quality of life in children and adolescents with overweight and obesity: results from the German KIGGS survey. BMC Public Health. 2020;20(1):1722.
25. Schwimmer JB, Burwinkle TM, Varni JW. Health-related quality of life of severely obese children and adolescents. Jama. 2003;289(14):1813-9.
26. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among children and adolescents, assessed using the pediatric quality of life inventory index. J Pediatr. 2013;162(2):280-6.e1.
27. Ottova V, Erhart M, Rajmil L, Dettenborn-Betz L, Ravens-Sieberer U. Overweight and its impact on the health-related quality of life in children and adolescents: results from the European KIDSCREEN survey. Qual Life Res. 2012;21(1):59-69.
28. Overgewicht en obesitas bij volwassenen en kinderen 2022. Available from: https://richtlijnendatabase.nl/richtlijn/overgewicht_en_obesitas_bij_volwassenen_en_kinderen/diagnostiek_ondersteuning_en_zorg_voor_kinderen_met_obesitas.html.
29. Hampl SE, Hassink SG, Skinner AC, Armstrong SC, Barlow SE, Bolling CF, et al. Clinical Practice Guideline for the Evaluation and Treatment of Children and Adolescents With Obesity. Pediatrics. 2023;151(2).
30. Bondyra-Wiśniewska B, Myszkowska-Ryciak J, Harton A. Impact of Lifestyle Intervention Programs for Children and Adolescents with Overweight or Obesity on Body Weight and Selected Cardiometabolic Factors-A Systematic Review. Int J Environ Res Public Health. 2021;18(4).

31. Knop C, Singer V, Uysal Y, Schaefer A, Wolters B, Reinehr T. Extremely obese children respond better than extremely obese adolescents to lifestyle interventions. Pediatr Obes. 2015;10(1):7-14.

32. Danielsson P, Kowalski J, Ekblom Ö, Marcus C. Response of severely obese children and adolescents to behavioral treatment. Arch Pediatr Adolesc Med. 2012;166(12):1103-8.

33. Rijks JM, Plat J, Mensink RP, Dorenbos E, Buurman WA, Vreugdenhil AC. Children With Morbid Obesity Benefit Equally as Children With Overweight and Obesity From an Ongoing Care Program. J Clin Endocrinol Metab. 2015;100(9):3572-80.

34. Behandeling van kinderen met Obesitas. Medicamenteuze behandeling bij kinderen met obesitas. 2020. Available from: https://richtlijnendatabase.nl/richtlijn/behandeling_van_kinderen_met_obesitas/medicamenteuze_behandeling_bij_kinderen_met_obesitas.html.

35. Yerevanian A, Soukas AA. Metformin: Mechanisms in Human Obesity and Weight Loss. Curr Obes Rep. 2019;8(2):156-64.

36. Lentferink YE, Knibbe CAJ, van der Vorst MMJ. Efficacy of Metformin Treatment with Respect to Weight Reduction in Children and Adults with Obesity: A Systematic Review. Drugs. 2018;78(18):1887-901.

37. Calcaterra V, Rossi V, Mari A, Casini F, Bergamaschi F, Zuccotti GV, et al. Medical treatment of weight loss in children and adolescents with obesity. Pharmacol Res. 2022;185:106471.

38. van Rossum EFC, Welling MS, van der Voorn B, van der Valk ES, Abawi O, van den Akker ELT. [Pharmacotherapy for obesity]. Ned Tijdschr Geneeskd. 2021;165.

39. Kelly AS, Auerbach P, Barrientos-Perez M, Gies I, Hale PM, Marcus C, et al. A Randomized, Controlled Trial of Liraglutide for Adolescents with Obesity. N Engl J Med. 2020;382(22):2117-28.

40. English WJ, Williams DB. Metabolic and Bariatric Surgery: An Effective Treatment Option for Obesity and Cardiovascular Disease. Prog Cardiovasc Dis. 2018;61(2):253-69.

41. Sjöström L. Review of the key results from the Swedish Obese Subjects (SOS) trial - a prospective controlled intervention study of bariatric surgery. J Intern Med. 2013;273(3):219-34.

42. Coulman KD, Blazeby JM. Health-Related Quality of Life in Bariatric and Metabolic Surgery. Curr Obes Rep. 2020;9(3):307-14.

43. Welbourn R, Hollyman M, Kinsman R, Dixon J, Liem R, Ottosson J, et al. Bariatric Surgery Worldwide: Baseline Demographic Description and One-Year Outcomes from the Fourth IFSO Global Registry Report 2018. Obes Surg. 2019;29(3):782-95.

44. Dutch Institute for Clinical Auditing. Jaarrapportage 2019 DATO. Available from: https://dica.nl/jaarrapportage-2019/dato.

45. Steenackers N, Vanuytsel T, Augustijns P, Tack J, Mertens A, Lannoo M, et al. Adaptations in gastrointestinal physiology after sleeve gastrectomy and Roux-en-Y gastric bypass. Lancet Gastroenterol Hepatol. 2021;6(3):225-37.

46. Olbers T, Lönroth H, Fagevik-Olsén M, Lundell L. Laparoscopic gastric bypass: development of technique, respiratory function, and long-term outcome. Obes Surg. 2003;13(3):364-70.

47. Pucci A, Batterham RL. Mechanisms underlying the weight loss effects of RYGB and SG: similar, yet different. J Endocrinol Invest. 2019;42(2):117-28.

48. Abu-Jaish W, Rosenthal RJ. Sleeve gastrectomy: a new surgical approach for morbid obesity. Expert Rev Gastroenterol Hepatol. 2010;4(1):101-19.

49. Kyler KE, Bettenhausen JL, Hall M, Fraser JD, Sweeney B. Trends in Volume and Utilization Outcomes in Adolescent Metabolic and Bariatric Surgery at Children's Hospitals. J Adolesc Health. 2019;65(3):331-6.

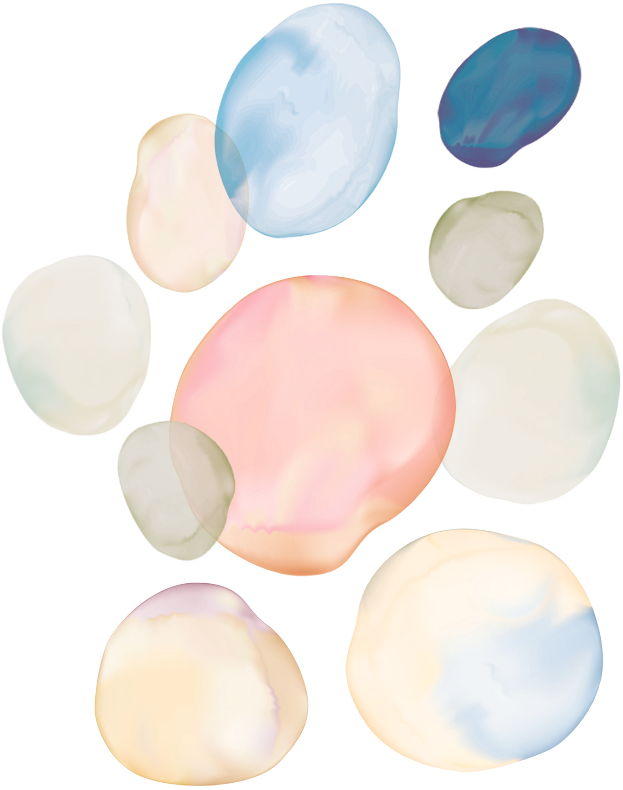
50. Shoar S, Mahmoudzadeh H, Naderan M, Bagheri-Hariri S, Wong C, Parizi AS, et al. Long-Term Outcome of Bariatric Surgery in Morbidly Obese Adolescents: a Systematic Review and Meta-Analysis of 950 Patients with a Minimum of 3 years Follow-Up. Obes Surg. 2017;27(12):3110-7.

51. Inge TH, Courcoulas AP, Jenkins TM, Michalsky MP, Brandt ML, Xanthakos SA, et al. Five-Year Outcomes of Gastric Bypass in Adolescents as Compared with Adults. N Engl J Med. 2019;380(22):2136-45.

52. Martinelli V, Singh S, Politi P, Caccialanza R, Peri A, Pietrabissa A, et al. Ethics of Bariatric Surgery in Adolescence and Its Implications for Clinical Practice. Int J Environ Res Public Health. 2023;20(2).

53. Behandeling van kinderen met Obesitas. Indicatiestelling bariatrische chirurgie bij kinderen met obesitas 2020. Available from: https://richtlijnendatabase.nl/richtlijn/behandeling_van_kinderen_met_obesitas/indicatiestelling_bariatrische_chirurgie_bij_kinderen_met_obesitas.html.

54. Eisenberg D, Shikora SA, Aarts E, Aminian A, Angrisani L, Cohen RV, et al. 2022 American Society of Metabolic and Bariatric Surgery (ASMBS) and International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) Indications for Metabolic and Bariatric Surgery. Obes Surg. 2023;33(1):3-14.



PART I

IMPACT OF SEVERE OBESITY AND CURRENT TREATMENT

CHAPTER 2

HEALTH-RELATED QUALITY OF LIFE IN CHILDREN AND ADOLESCENTS WITH OVERWEIGHT, OBESITY AND SEVERE OBESITY: A CROSS SECTIONAL STUDY

Kelly G.H. van de Pas*
Maartje A.P. de Krom*
Bjorn Winkens
François M.H. van Dielen
Anita C.E. Vreugdenhil

* Both authors contributed equally.

Obesity facts 2023.

ABSTRACT

Introduction

Children and adolescents with overweight and obesity have an impaired health-related quality of life (HRQoL). However, it is unclear which of these children are most affected in their physical, psychological, and social functioning. Therefore, this study aimed to evaluate HRQoL in treatment-seeking children and adolescents with overweight, obesity, and severe obesity.

Methods

A cross-sectional study was performed at the Centre for Overweight Adolescent and Children's Healthcare (COACH). Children and adolescents (8–17 years) with overweight, obesity, and severe obesity were included. The primary outcome was the self-reported HRQoL measured with the KIDSCREEN-27.

Results

A total of 419 participants with overweight (n = 121), obesity (n = 182), and severe obesity (n = 116) were included. One-way ANOVA analysis showed that children and adolescents with severe obesity reported significantly lower physical wellbeing (41.25 ± 13.14) compared to those with overweight (47.91 ± 12.53; $p < 0.001$) and obesity (46.74 ± 11.93; $p < 0.001$). Furthermore, impaired psychological wellbeing was found in the group with severe obesity (45.14 ± 13.27) in comparison to the group with overweight (50.90 ± 9.48; $p < 0.001$) and obesity (49.71 ± 10.95; $p = 0.002$). Multivariable linear regression analysis, while correcting for age, sex, cardio metabolic health risk, and ethnicity, revealed similar results. Additionally, children and adolescents with severe obesity scored lower regarding autonomy and parent relation than those with overweight ($B = 3.95$; $p = 0.009$). In almost all groups and dimensions of the KIDSCREEN-27, caregivers scored lower compared to the children and adolescents themselves. Furthermore, a low child-caregiver agreement seemed to exist, especially in the children and adolescents with overweight.

Conclusion

The HRQoL of treatment-seeking children and adolescents with overweight and obesity was most affected in children and adolescents with the most severe grade of obesity. Following these findings, lifestyle intervention programs targeting childhood obesity should be aware of this even more vulnerable group so that treatments can be tailored according to their needs.

INTRODUCTION

Childhood overweight is recognized as one of the most complex and pressing health challenges that the world is facing today[1]. In 2021, the prevalence of overweight in Dutch children aged between 4 and 17 years was 12.3%, whereas 3.5% of the children had obesity[2]. Although the prevalence of childhood overweight has stabilized over time, the recent COVID-19 pandemic contributed to an increase of more than 3% in the number of children with obesity compared to the pre-pandemic period[3-5]. This is troublesome, as childhood overweight and obesity are associated with several life-threatening conditions including type 2 diabetes mellitus and fatty liver disease[6,7].

Besides the physical consequences, childhood overweight and obesity can result in substantial psychosocial problems[8-12]. Children and adolescents with overweight and obesity have to deal with weight-related social stigmatizing, discrimination and bullying, leading to a negative self-image, body dissatisfaction, depressive and anxiety symptoms, and social isolation[10-12]. These aspects contribute to an impaired health-related quality of life (HRQoL) in children with overweight and obesity compared to peers with normal weight[8,10,13-19]. Schwimmer et al. even found a similar HRQoL in children with obesity and children diagnosed with cancer[8]. Taken together, these results highlight that childhood overweight has a substantial negative impact on daily functioning and wellbeing.

Although there is mounting evidence of an impaired HRQoL in children and adolescents with overweight and obesity, it is unknown which of these children have the lowest HRQoL and are mostly affected in their physical, psychological, and social functioning[8,10,13-19]. A cross-sectional study of 45 treatment-seeking Dutch adolescents observed lower physical functioning and comfort in adolescents with severe obesity compared to adolescents with overweight[20]. In addition to this study, it is important to further identify the children and adolescents whose HRQoL is most affected in order to tailor treatments accordingly. Especially as a previous study showed that a higher HRQoL can improve therapy compliance[21]. Furthermore, it is essential to use a validated questionnaire that is equally understandable for children and adolescents from different cultures, such as the KIDSCREEN-27[22,23]. Therefore, the primary aim of this study was to evaluate HRQoL in treatment-seeking children and adolescents with overweight, obesity, and severe obesity. It was hypothesized that children and adolescents with the most severe grade of obesity had the worst HRQoL. Besides this, the self-reported and caregiver-reported HRQoL scores were compared, and the child-caregiver agreement was evaluated.

MATERIALS AND METHODS

Setting and study design

This cross-sectional study was performed within the setting of the Centre for Overweight Adolescent and Children's Healthcare (COACH) at the Maastricht University Medical Centre + (MUMC+). Within this setting, all children and adolescents with overweight, obesity, and severe obesity underwent a comprehensive pre-intervention assessment. The assessment aimed to exclude syndromic or endocrine conditions of the weight status, to evaluate the presence of obesity-related comorbidities, and to determine the psychological wellbeing of the children and adolescents before the start of the COACH lifestyle intervention[24]. Based on the outcomes, several healthcare professionals including pediatricians, psychologists, and dieticians set up a patient-tailored lifestyle intervention program for each child and adolescent focusing on durable lifestyle changes.

The present study was performed according to the guidelines of the Declaration of Helsinki and approval was given by the Medical Ethical Committee of the MUMC+ (METC-number 13-4-130). The study is registered at ClinicalTrial.gov as NCT02091544. Informed consent was obtained from all parents/legal guardians and children aged 12 years and older.

Study participants

All children and adolescents who received an assessment prior to the start of the COACH lifestyle intervention between May 2014 and December 2021 were considered for inclusion in this study. Children and adolescents aged 8–17 years old with overweight, obesity, and severe obesity were eligible to participate. Children below the age of 8 were not considered for inclusion since the questionnaire measuring our primary outcome was exclusively validated in children aged 8 years and older. Children and adolescents were excluded from the analyses when self-reported HRQoL data were missing.

Participant characteristics

Trained staff performed height and weight measurements during pre-intervention assessment. BMI was determined as the weight in kilograms divided by the height in meters squared. BMI z-scores were calculated using the Growth analyzer (GrowthAnalyser, VE). Participants were divided into the group with overweight, obesity, and severe obesity according to the International Obesity Task Force criteria, which are comparable to a BMI of ≥25 kg/m^2, ≥30 kg/m^2, and ≥35 kg/m^2 in adults[25]. Children were defined as aged 8–11 years, while adolescents were classified as aged 12–17 years[26]. Ethnicity was classified as Dutch, Western, and Non-Western according to the Dutch Central Agency for Statistics[27]. Besides this, parent's educational level was divided into low, moderate, and high[28]. Low parental educational attainment was assigned when

both parents had completed less than secondary vocational education. A high level of parental education was assigned when both parents had completed more than secondary vocational education. In other cases, the parents' educational level was considered moderate. At last, several medical conditions, including chronic/congenital somatic disease (e.g., diabetes mellitus type 1 and asthma), developmental disorders (e.g., Attention Deficit Hyperactivity Disorder and autism spectrum disorders), cancer, and mental health disorders (e.g., anxiety disorders and depression) were noted[29].

Health-related quality of life

The primary outcome was the HRQoL measured with the Dutch version of the validated KIDSCREEN-27 questionnaire. This instrument includes 27 items covering five different HRQoL dimensions. The physical wellbeing dimension (five questions) referred to the general health of a child or adolescent and their level of physical activity, fitness, and energy. The psychological wellbeing dimension included seven questions regarding positive emotions, satisfaction with life, level of self-esteem and the presence of loneliness and/or sadness. The third dimension, autonomy and parent relations (seven questions), explored the relationship between the child or adolescent and their parents or caregivers, level of autonomy, and financial sources. The relationship between the child or adolescent and their peers and the support they experienced from them is discovered in the social support and peers dimension (four questions). The last dimension referred to the school environment which includes four questions regarding the perception of the child or adolescent on their own cognitive capacity and skills, the relationship with teachers and their own feelings about school. A Likert scale with five options, ranging from 1 = "not at all/never" to 5 = "all the way/always" was used. Some items had to be reversed when scoring the questionnaire. Both the participant and caregiver separately completed the questionnaire at home or in the hospital. A scoring algorithm was used to convert the raw scores into T-scores[26]. If at least one item per dimension was left unanswered, the overall dimension score was identified as missing. Higher T-scores reflect better HRQoL.

Cardio metabolic health risk

During the clinical pre-intervention assessment, fasting levels of serum triglycerides, high-density lipoprotein (HDL), and glucose were measured. These levels combined with the average of at least three blood pressure measurements were used to determine the cardio metabolic health risk according to the Dutch Care Standard Obesity which was based on a consensus of the International Diabetes Federation. Triglycerides ≥1.7 mmol/L, HDL <1.03 mmol/L or HDL <1.29 mmol/L (females >16 years of age), and glucose ≥5.6 mmol/L were considered as abnormal values[30,31]. According to a recent guideline, blood pressure was elevated when systolic and/or diastolic blood pressure ≥90th percentile for sex, age, and height[32]. All these values were gathered, and when

participants (≥10 years of age) had at least one abnormal value, they were identified as having an increased cardio metabolic health risk. In line with the Dutch Care Standard Obesity, children <10 years of age were not considered as having an increased cardio metabolic health risk. When two or more values were missing, the cardio metabolic health risk was identified as missing.

Statistical analysis

Statistical analyses were performed with IBM SPSS Statistics, version 26.0, Armonk, NY. Two-sided p values ≤ 0.05 were considered statistically significant. First of all, the numerical baseline characteristics were checked for homoscedasticity with the homogeneity of variances test, and normality using P-P plots and histograms. If the assumptions were not violated, the numerical baseline characteristics were analyzed using one-way ANOVA tests. Categorical baseline characteristics were analyzed using $\chi 2$ or Fisher-Freeman-Halton Exact tests. Both self-reported and caregiver-reported T-scores for the HRQoL data were presented. The self-reported and caregiver-reported T-scores were checked for normality using P-P plots and histograms; homoscedasticity was controlled by the homogeneity of variances test and linearity using scatterplots. Outliers were checked using Cook's distance, a distance >1 indicated an influential outlier. Multicollinearity was assessed by the variance inflation factor, and a variance inflation factor >10 indicated a multicollinearity problem. If the assumptions were not violated, one-way ANOVA and multivariable linear regression analyses were performed to compare the self-reported HRQoL dimensions between the group with overweight, obesity, and severe obesity. In case of a $p \leq 0.05$ in the oneway ANOVA analyses, post hoc tests were conducted using Tukey's method to correct for multiple testing. Results were checked for important patient perceived differences in HRQoL (clinical relevance). Important patient perceived differences in HRQoL between groups were earlier defined as half a standard deviation (SD) of the total group score[33]. In the multivariable linear regression analyses, a top-down procedure was used to obtain the final model. First, interactions between age*weight category and sex*weight category were assessed as the effect of weight category on HRQoL might depend on age and sex. In case of a significant interaction, the effect of weight category was presented for different values of that effect modifier. If the interactions were not significant, the interactions were removed from the model and the main effect of weight category was given. In all models, corrections were made for participants' age, sex, the cardio metabolic health risk, and ethnicity according to literature (8). The group with severe obesity was considered as the reference category. As a sensitivity analysis, the significance level was set at 0.01 to account for multiple testing in the multivariable linear regression analyses. The difference between self-reported and caregiver-reported mean T-scores was evaluated using paired samples t tests and the correlation between these scores was

investigated using Pearson correlations. Furthermore, child-caregiver agreement was evaluated using Bland-Altman plots. In the Bland-Altman plots, the Y-axis represents the difference in self-reported and caregiver-reported T-score, while the X-axis represents the mean of the participants' and caregiver T-score[34].

RESULTS

A total of 583 children and adolescents with overweight, obesity, and severe obesity underwent pre-intervention assessment before the start of the COACH life style intervention. From these, 490 children and adolescents were eligible to participate since they were aged 8–17 years old (Fig. 1). After excluding 71 children and adolescents (14.5%) who did not return or complete the self-reported KIDSCREEN-27 questionnaires, 419 children and adolescents (85.5%) were included. The most frequently mentioned reasons for not completing or returning the KIDSCREEN-27 were misunderstanding of the questionnaire or a language barrier. The response rates between the group with overweight, obesity, and severe obesity were comparable; the response rates were 88.9%, 84.7%, and 83.5%, respectively. The only differences between the 419 included participants and the 71 excluded participants were found in the higher prevalence of non-Western ethnicity and mental health disorders among the excluded children and adolescents (data not shown).

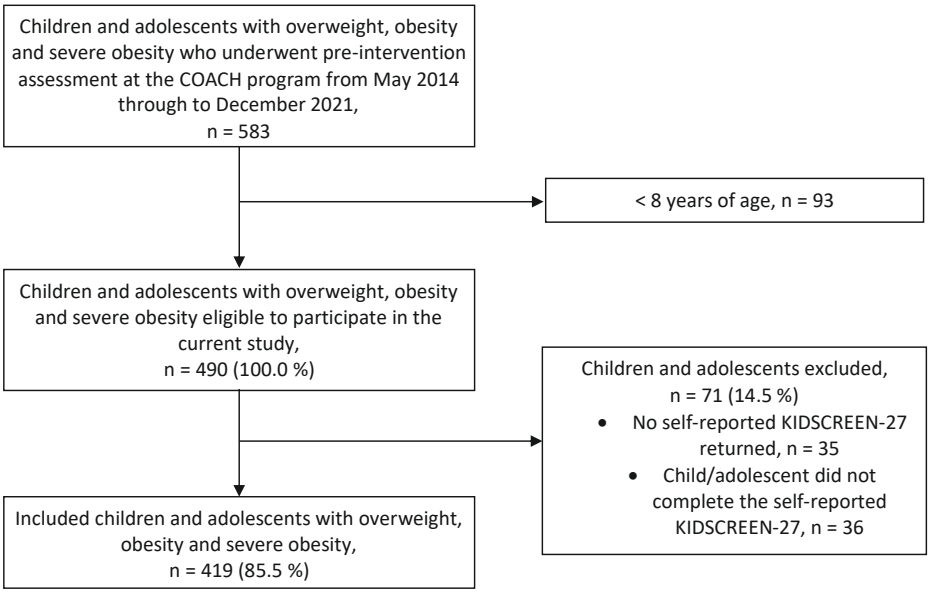


Figure 1. Flow diagram of the inclusion of children and adolescents with overweight, obesity and severe obesity

Table 1. Participant characteristics of the included children and adolescents

	Total n = 419	**Overweight n = 121 (28.9%)**	**Obesity n = 182 (43.4%)**	**Severe obesity n = 116 (27.7%)**	***p* value**
Age (years, mean ± SD)	12.93 ± 2.55	12.47 ± 2.43	12.79 ± 2.54	13.62 ± 2.55	**0.001***
Age category, n. (%)	419	121	182	116	**0.002**
Children	174 (41.5)	61 (50.4)	80 (44.0)	33 (28.4)	
Adolescents	245 (58.5)	60 (49.6)	102 (56.0)	83 (71.6)	
Sex, n. (%)	419	121	182	116	0.707
Female	210 (50.1)	63 (52.1)	87 (47.8)	60 (51.7)	
Male	209 (49.9)	58 (47.9)	95 (52.2)	56 (48.3)	
BMI (kg/m^2, mean ± SD)	29.81 ± 6.21	24.52 ± 2.17	28.79 ± 2.99	36.91 ± 6.26	**<0.001****
BMI z-score (mean ± SD)	3.16 ± 0.69	2.38 ± 0.34	3.17 ± 0.29	3.98 ± 0.41	**<0.001****
Cardio metabolic health risk[a], n. (%)	412	121	180	111	0.266
Yes	174 (42.2)	45 (37.2)	76 (42.2)	53 (47.7)	
No	238 (57.8)	76 (62.8)	104 (57.8)	58 (52.3)	
Ethnicity[b], n. (%)	417	121	180	116	0.693
Dutch	289 (69.3)	90 (74.4)	121 (67.2)	78 (67.2)	
Western	34 (8.2)	8 (6.6)	15 (8.3)	11 (9.5)	
Non-western	94 (22.5)	23 (19.0)	44 (24.4)	27 (23.3)	
Parent's education[b], n. (%)	370	106	157	107	**<0.001**
Low	166 (44.9)	37 (34.9)	67 (42.7)	62 (57.9)	
Moderate	160 (43.2)	47 (44.3)	75 (47.8)	38 (35.5)	
High	44 (11.9)	22 (20.8)	15 (9.6)	7 (6.5)	
Family composition[c], n. (%)	418	121	181	116	0.424
Married	225 (53.8)	73 (60.3)	93 (51.4)	59 (50.9)	
Divorced	176 (42.1)	43 (35.5)	82 (45.3)	51 (44.0)	
Other	17 (4.1)	5 (4.1)	6 (3.3)	6 (5.2)	
Medical history, n. (%)	419	121	182	116	0.366
Chronic/congenital somatic disease	66 (15.8)	17 (14.0)	26 (14.3)	23 (19.8)	0.290
Developmental disorder	78 (18.6)	24 (19.8)	28 (15.4)	26 (22.4)	0.361
Cancer[c]	3 (0.7)	0 (0)	1 (0.5)	2 (1.7)	0.396
Mental health disorder[c]	10 (2.4)	1 (0.8)	5 (2.7)	4 (3.4)	

BMI, Body Mass Index; SD, standard deviation; n, number.

a Triglycerides ≥ 1.7 mmol/L, HDL-cholesterol < 1.03 mmol/L or HDL < 1.29 (for females ≥ 16 years of age), fasting glucose ≥ 5.6 mmol/L (30, 31) or systolic and/or diastolic blood pressure ≥90th percentile for sex, age and height (32).

b According to the Dutch Central Agency for Statistics (27, 28).

c Fisher-Freeman-Halton Exact test.

* Statistically significant difference between participants with severe obesity and those with overweight and obesity.

** Statistically significant difference between all three weight status categories.

Statistically significant differences ($p \leq .05$) are highlighted in boldface.

Participant characteristics

The characteristics of the included children and adolescents with overweight, obesity, and severe obesity are presented in Table 1. The children and adolescents with severe obesity were significantly older compared to those with overweight and obesity ($p = 0.001$ and $p = 0.015$). Furthermore, there were significant differences among the three groups regarding parent's education.

Self-reported HRQoL

Children and adolescents with severe obesity scored on average lower in all dimensions of the self-reported KIDSSCREEN-27 compared to children and adolescents with overweight or obesity (Fig. 2). One-way ANOVA revealed significant differences between groups in the physical and psychological wellbeing dimensions (both $p < 0.001$). Children and adolescents with severe obesity reported significantly lower physical wellbeing (41.25 ± 13.14) compared to those with overweight (47.91 ± 12.53; $p < 0.001$) and obesity (46.74 ± 11.93; $p < 0.001$). Furthermore, impaired psychological wellbeing was found in the group with severe obesity (45.14 ± 13.27) in comparison to the group with overweight (50.90 ± 9.48; $p < 0.001$) and obesity (49.71 ± 10.95; $p = 0.002$). The differences in physical and psychological wellbeing between the children and adolescents with overweight and severe obesity were also clinically relevant (> 0.5 SD). Multivariable linear regression analysis of self-reported T-scores on the KIDSCREEN-27 dimensions between children and adolescents with overweight, obesity, and severe obesity, while adjusting for age, sex, cardio metabolic health risk, and ethnicity, revealed similar results (Table 2). The children and adolescents with severe obesity reported significantly lower physical and psychological wellbeing compared to the group with overweight and obesity. Additionally, participants with severe obesity scored significantly lower regarding autonomy and parent relation than those with overweight ($B = 3.95$; $p = 0.009$). In the sensitivity analysis (using a significance level of 0.01 instead of 0.05 to adjust for multiple testing), the same conclusions were drawn as all significant p values were below 0.01.

Self-reported versus caregiver-reported HRQoL

The self-reported compared to the caregiver-reported mean T-scores on the KIDSCREEN-27 are presented in Table 3. The mean caregiver scores were lower on almost all dimensions of the KIDSCREEN-27 compared to the mean scores of children and adolescents with overweight, obesity, and severe obesity themselves. In the physical wellbeing dimension, the mean caregiver-reported T-scores were significantly lower compared to the self-reported T-scores in all three weight categories. Furthermore, the mean caregiver-reported T-scores were significantly lower in four out of five KIDSCREEN-27 dimensions in the group with overweight. In the group with obesity, significant differences between the caregiver and self-reported mean T-scores were

found in the physical and psychological wellbeing dimensions, whereas in the group with severe obesity a significant difference was only found in the physical wellbeing dimension. Pearson correlation coefficients between self-reported and caregiver-reported T-scores in the KIDSCREEN-27 dimensions ranged from 0.22 to 0.71. Individual child-caregiver agreement was evaluated using Bland-Altman plots (Fig. 3; Supporting Information Fig. S1, www.karger.com/doi/10.1159/000529560). The upper and lower limits of the Bland-Altman plots were relatively broad in all dimensions and weight categories, indicating a low agreement on individual level. Visual interpretation suggests that there is more agreement when the T-scores were higher, as the dots are situated closer to the zero-bias line.

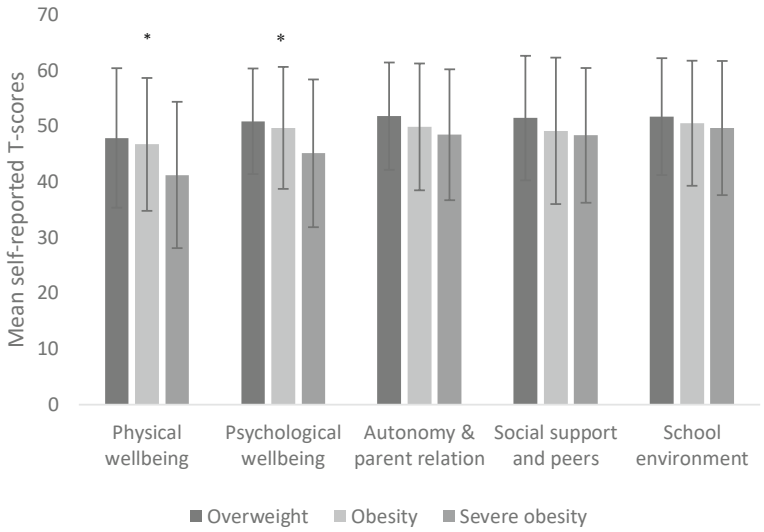


Figure 2. Mean self-reported T-scores (± SD) on KIDSCREEN-27 in the three different weight categories.

SD, standard deviation. Physical wellbeing: overweight n=120; obesity n=178; severe obesity n=116. Psychological wellbeing: overweight n=121; obesity n=181; severe obesity n=115. Autonomy & parent relation: overweight n=120; obesity n=180; severe obesity n=114. Social support and peers: overweight n=120; obesity n=180; severe obesity n=114. School environment: overweight n=119; obesity n=180; severe obesity n=114.

* Statistically significant difference between participants with severe obesity and those with overweight and obesity ($p \leq 0.05$).

Table 2. Multivariable linear regression analysis of self-reported T-scores on the KIDSCREEN-27 dimensions between children and adolescents with overweight, obesity and severe obesity, while correcting for age, sex, cardio metabolic health risk and ethnicity

	Physical wellbeing			**Psychological wellbeing**			**Autonomy & parent relation**			**Social support and peers**			**School environment**		
	B (SE)	β	*p* value	*B (SE)*	β	*p* value	*B (SE)*	β	*p* value	*B (SE)*	β	*p* value	*B (SE)*	β	*p* value
Overweight	**6.46 (1.67)**	**0.23**	**<0.001**	**5.70 (1.52)**	**0.23**	**<0.001**	**3.95 (1.50)**	**0.16**	**0.009**	3.22 (1.68)	0.12	0.055	2.61 (1.53)	0.11	0.089
Obesity	**5.13 (1.52)**	**0.20**	**<0.001**	**4.28 (1.39)**	**0.19**	**0.002**	1.62 (1.37)	0.07	0.237	0.73 (1.53)	0.03	0.632	1.08 (1.39)	0.05	0.440
Severe obesity	Ref.			Ref.			Ref.			Ref.			Ref.		
Age	-0.39 (0.26)	-0.08	0.130	-0.34 (0.23)	-0.08	0.150	0.16 (0.23)	0.04	0.500	-0.22 (0.26)	-0.05	0.389	0.29 (0.23)	0.07	0.219
Boys	-2.13 (1.25)	-0.08	0.089	-0.01 (1.14)	0.00	0.993	-0.51 (1.12)	-0.02	0.654	-0.59 (1.25)	-0.02	0.636	-1.13 (1.14)	-0.05	0.322
Girls	Ref.			Ref.			Ref.			Ref.			Ref.		
Cardio metabolic health risk	-0.68 (1.31)	-0.03	0.601	0.75 (1.18)	0.03	0.529	1.50 (1.17)	0.07	0.199	1.03 (1.30)	0.04	0.430	0.30 (1.19)	0.01	0.799
No cardio metabolic health risk	Ref.			Ref.			Ref.			Ref.			Ref.		
Western ethnicity	2.20 (2.26)	0.05	0.332	-1.44 (2.06)	-0.04	0.485	0.67 (2.08)	0.02	0.747	1.13 (2.27)	0.03	0.617	-0.89 (2.06)	-0.02	0.668
Non-western ethnicity	2.20 (1.51)	0.07	0.146	1.22 (1.38)	0.04	0.378	0.81 (1.35)	0.03	0.548	1.27 (1.52)	0.04	0.403	1.95 (1.38)	0.07	0.159
Dutch ethnicity	Ref.			Ref.			Ref.			Ref.			Ref.		

B, unstandardized regression coefficient indicating the association between this variable and the outcome; *SE,* standard error; β, standardized regression coefficient; ref, reference category. Statistically significant differences (p≤0.05) are highlighted in boldface.

Table 3. Difference and correlation between self-reported and caregiver-reported T-scores on the KIDSCREEN-27 stratified by weight categories

KIDSCREEN-27 T-SCORE	**OVERWEIGHT**					**OBESITY**					**SEVERE OBESITY**				
	n[a]	*Mean self-reported (±SD)*	*Mean caregiver-reported (±SD)*	*p value*	*r*	*n*[a]	*Mean self-reported (±SD)*	*Mean caregiver-reported (±SD)*	*p value*	*r*	*n*[a]	*Mean self-reported (±SD)*	*Mean caregiver-reported (±SD)*	*p value*	*r*
Physical wellbeing	112	47.68 ± 12.77	43.36 ± 15.05	**<0.001**	**0.71**	165	46.49 ± 11.94	41.12 ± 12.54	**<0.001**	**0.51**	107	41.12 ± 13.35	37.06 ± 13.28	**0.001**	**0.61**
Psychological wellbeing	111	51.25 ± 9.40	48.45 ± 11.41	**0.005**	**0.52**	169	49.61 ± 10.93	46.65 ± 11.12	**0.002**	**0.37**	105	45.80 ± 13.09	44.07 ± 13.81	0.140	**0.61**
Autonomy & parent relation	110	51.76 ± 9.66	48.68 ± 9.73	**0.004**	**0.37**	166	49.88 ± 11.57	49.81 ± 9.95	0.944	**0.22**	103	48.86 ± 12.08	48.47 ± 12.64	0.773	**0.38**
Social support and peers	111	52.32 ± 10.46	49.23 ± 11.95	**0.005**	**0.49**	164	49.01 ± 13.45	47.02 ± 13.63	0.088	**0.40**	103	48.10 ± 12.30	46.39 ± 12.56	0.211	**0.39**
School environment	108	51.57 ± 10.61	51.66 ± 11.69	0.924	**0.55**	168	50.58 ± 11.26	50.68 ± 9.67	0.900	**0.50**	104	49.62 ± 11.96	48.15 ± 12.35	0.212	**0.52**

SD, standard deviation; n, number; r, Pearson correlation between self-reported and caregiver-reported T-scores.
[a] Number of participants that both had self-reported and caregiver-reported T-scores on that dimension.
Statistical significance is highlighted in boldface ($p \leq 0.05$).

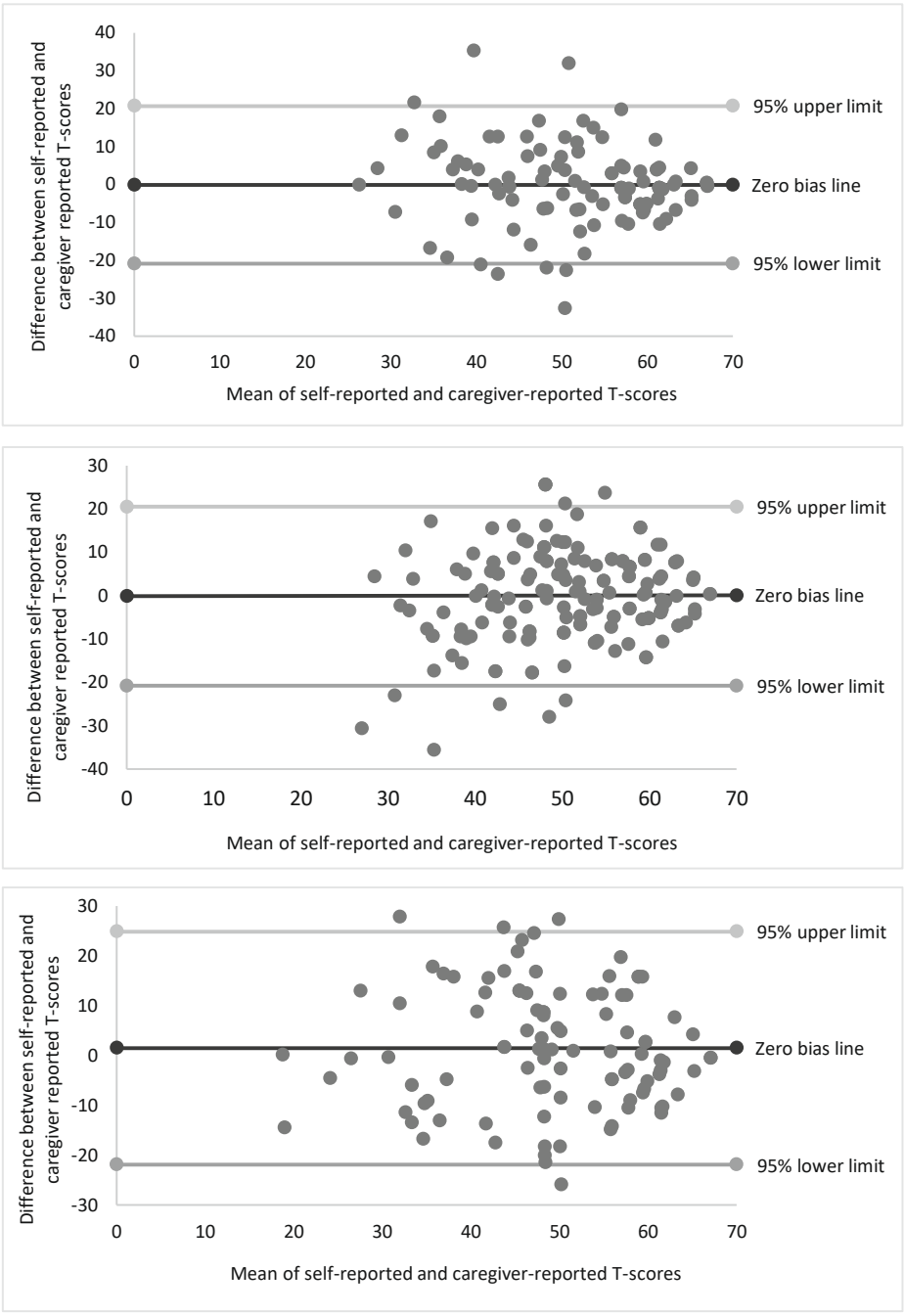


Figure 3. Bland-Altman plots of school environment dimension stratified by weight category

Difference between self-reported (ST) and caregiver reported (CT) T-scores; ST-CT.
Mean of self-reported and caregiver reported T-scores; (ST+CT)/2.

DISCUSSION

The psychosocial consequences of childhood overweight and obesity are severe, resulting in a negative self-image, body dissatisfaction, and social isolation which leads to an impaired HRQoL[10-12]. This study identified that treatment-seeking children and adolescents with the most severe grade of obesity were the most affected in their HRQoL, mainly in the physical, psychological, and autonomy and parent-related dimensions. These findings were also clinically relevant as the children and adolescents with severe obesity had > 0.5 SD lower HRQoL scores compared to children and adolescents with overweight and to a Dutch reference population[35]. Additionally, caregivers felt that their children's HRQoL was worse than the children and adolescents experienced themselves. Besides this, there were large individual discrepancies between caregivers and children, assuming low agreement.

The physical wellbeing dimension is one of the HRQoL dimensions that is most affected by the degree of overweight and obesity in children and adolescents. The pooled analyses of a systematic review revealed a strong inverse relation between physical wellbeing and BMI[36]. Moreover, a recently conducted study among treatment-seeking Dutch adolescents with overweight and obesity observed a lower physical functioning and comfort on the CHQ Child Form 87 and Impact of Weight on Quality of Life-Kids questionnaires in adolescents with obesity grade 3 compared to those with overweight[20]. In line with these studies, the present study found a clinically relevant lower physical wellbeing in children and adolescents with severe obesity compared to those with overweight, and even in comparison to those with obesity. In clinical practice, a lower physical wellbeing resembles less energy, physical activity, and health in general. According to these findings, lifestyle interventions targeting childhood obesity should take into account that children and adolescents with the most severe grade of obesity are less physically active and need extra attention to improve their physical activity. Particularly as a previous study found that long-term changes in physical activity, and not in BMI, explained 30% of the variation in HRQoL[37].

In contrast to physical wellbeing, there is less consensus in literature regarding weight-related psychological wellbeing[10,36]. The present study found a clinically relevant lower psychological wellbeing in the children and adolescents with severe obesity, indicating that these children are less satisfied with themselves and are more often lonely and sad. Remarkably, sex as well as age were not significantly related to psychological wellbeing in our study. This is in contrast with some other reports, which revealed that girls might be more vulnerable to psychological complaints related to their weight status because of higher levels of body dissatisfaction and lower levels of body esteem[38,39]. Besides

this, older children might be more aware of their appearance and social limitations due to their weight and therefore have a lower psychological wellbeing[20]. These conflicting results regarding weight, sex- and age-related psychological wellbeing might be due to different study populations (treatment-seeking or population based), various degrees of overweight and different questionnaires used to evaluate psychological wellbeing. Continued efforts are needed to identify determinants that influence psychological wellbeing, as well as the other quality of life dimensions in children and adolescents with overweight and obesity.

Due to the increased prevalence of chronic somatic and mental disorders among children and adolescents, monitoring of HRQoL has become an important topic in health care[40]. A large population-based study performed in the Netherlands reported a lower HRQoL among children and adolescents with chronic health problems (e.g., asthma, eczema, ADHD, dyslexia, and migraine) compared to those without a chronic condition[41]. Previous research also found an impaired HRQoL in youth with overweight and obesity compared to youth with a normal weight[8,10,13-19]. Our results revealed an even worse HRQoL in children and adolescents with the most severe grade of obesity. Furthermore, a recent meta-analysis estimated the magnitude of the HRQoL impairments measured with the KIDSCREEN questionnaire in children and adolescents with chronic health problems. The largest impairments in HRQoL were found in children with malignant neoplasms, endocrine and metabolic diseases (e.g., obesity), diseases of the nervous system, congenital malformations, and chronic pain[42]. This indicates that childhood obesity is a severe chronic disease with a huge impact on HRQoL and that its psychosocial consequences should be given equal attention and support as other chronic diseases.

When assessing the HRQoL of children and adolescents with overweight and obesity, it is recommended to use both self-reported and caregiver-reported scores to evaluate HRQoL comprehensively[20,43]. Most previous studies focusing on the HRQoL of children and adolescents with overweight and obesity found lower caregiver-reported HRQoL scores compared to self-reported HRQoL scores, which is in line with our results[10,36]. One interesting finding of the current study was that low child-caregiver agreement seemed to exist in the children and adolescents, especially in the ones with overweight. Children and adolescents with overweight might experience fewer obesity-related complaints or do not relate their complaints or wellbeing to their weight status, while caregivers are more aware of the consequences of the weight status of their child[44]. In children and adolescents with severe obesity, the link between symptoms and weight status might be more apparent for both children and caregivers. Following these findings, one should be aware of the discrepancies between how parents and

children with overweight and obesity experience quality of life, especially in children and adolescents with overweight.

The present study has some limitations that should be acknowledged. First, the use of a questionnaire in this study may have led to recall bias. Second, it is questionable whether our results can be generalized to all children and adolescents with overweight and obesity since our study population consisted of treatment-seeking children and adolescents with overweight, obesity, and severe obesity. The HRQoL in our study population might therefore be lower compared to non-treatment-seeking children and adolescents[45]. Finally, due to the cross-sectional design of this study, no conclusions can be drawn regarding the causal relationship between the degree of overweight and obesity and an impaired HRQoL.

CONCLUSION

The HRQoL of treatment-seeking children and adolescents with overweight and obesity was most affected in the children and adolescents with the most severe grade of obesity, especially in the physical and psychological dimensions. Following these findings, lifestyle intervention programs targeting childhood obesity should be aware of this even more vulnerable group so that treatments can be tailored according to their needs. Subsequently, future longitudinal studies should focus on the effect of these programs on the HRQoL of children and adolescents with various degrees of overweight and obesity. Additionally, attention must be caught to discrepancies in HRQoL between children, adolescents, and their caregivers, especially in the group with overweight.

REFERENCES

1. Di Cesare M, Sorić M, Bovet P, Miranda JJ, Bhutta Z, Stevens GA, et al. The epidemiological burden of obesity in childhood: a worldwide epidemic requiring urgent action. BMC Med. 2019;17(1):212.
2. Rijksinstituut voor Volksgezondheid en Milieu. Overgewicht 2022. Available from: https://www.vzinfo.nl/overgewicht/leeftijd-en-geslacht-jongeren.
3. Olds T, Maher C, Zumin S, Péneau S, Lioret S, Castetbon K, et al. Evidence that the prevalence of childhood overweight is plateauing: data from nine countries. Int J Pediatr Obes. 2011;6(5-6):342-60.
4. van Dommelen P, Schönbeck Y, van Buuren S, HiraSing RA. Trends in a life threatening condition: morbid obesity in dutch, Turkish and Moroccan children in The Netherlands. PLoS One. 2014;9(4):e94299.
5. Lange SJ, Kompaniyets L, Freedman DS, Kraus EM, Porter R, Blanck HM, et al. Longitudinal Trends in Body Mass Index Before and During the COVID-19 Pandemic Among Persons Aged 2-19 Years - United States, 2018-2020. MMWR Morb Mortal Wkly Rep. 2021;70(37):1278-83.
6. Daniels SR, Kelly AS. Pediatric severe obesity: time to establish serious treatments for a serious disease. Child Obes. 2014;10(4):283-4.
7. Kelly AS, Barlow SE, Rao G, Inge TH, Hayman LL, Steinberger J, et al. Severe obesity in children and adolescents: identification, associated health risks, and treatment approaches: a scientific statement from the American Heart Association. Circulation. 2013;128(15):1689-712.
8. Schwimmer JB, Burwinkle TM, Varni JW. Health-related quality of life of severely obese children and adolescents. Jama. 2003;289(14):1813-9.
9. Makkes S, Renders CM, Bosmans JE, van der Baan-Slootweg OH, Seidell JC. Cardiometabolic risk factors and quality of life in severely obese children and adolescents in The Netherlands. BMC Pediatr. 2013;13:62.
10. Buttitta M, Iliescu C, Rousseau A, Guerrien A. Quality of life in overweight and obese children and adolescents: a literature review. Qual Life Res. 2014;23(4):1117-39.
11. Puder JJ, Munsch S. Psychological correlates of childhood obesity. Int J Obes (Lond). 2010;34 Suppl 2:S37-43.
12. Rankin J, Matthews L, Cobley S, Han A, Sanders R, Wiltshire HD, et al. Psychological consequences of childhood obesity: psychiatric comorbidity and prevention. Adolesc Health Med Ther. 2016;7:125-46.
13. Meixner L, Cohrdes C, Schienkiewitz A, Mensink GBM. Health-related quality of life in children and adolescents with overweight and obesity: results from the German KIGGS survey. BMC Public Health. 2020;20(1):1722.
14. Ul-Haq Z, Mackay DF, Fenwick E, Pell JP. Meta-analysis of the association between body mass index and health-related quality of life among children and adolescents, assessed using the pediatric quality of life inventory index. J Pediatr. 2013;162(2):280-6.e1.

15. Pinhas-Hamiel O, Singer S, Pilpel N, Fradkin A, Modan D, Reichman B. Health-related quality of life among children and adolescents: associations with obesity. Int J Obes (Lond). 2006;30(2):267-72.
16. Radhakishun NN, de Wit M, van Vliet M, von Rosenstiel IA, Beijnen JH, Brandjes DP, et al. Impaired quality of life in treatment-seeking obese children of Dutch, Moroccan, Turkish and Surinamese descent. Public Health Nutr. 2016;19(5):796-803.
17. Williams J, Wake M, Hesketh K, Maher E, Waters E. Health-related quality of life of overweight and obese children. Jama. 2005;293(1):70-6.
18. Hughes AR, Farewell K, Harris D, Reilly JJ. Quality of life in a clinical sample of obese children. Int J Obes (Lond). 2007;31(1):39-44.
19. Ottova V, Erhart M, Rajmil L, Dettenborn-Betz L, Ravens-Sieberer U. Overweight and its impact on the health-related quality of life in children and adolescents: results from the European KIDSCREEN survey. Qual Life Res. 2012;21(1):59-69.
20. van der Heijden LB, Feskens EJM, Raat H, Janse AJ. Quality of life of children and adolescents with clinical obesity, perspectives of children and parents. Obes Res Clin Pract. 2021;15(5):466-72.
21. Nagasawa H, Tachi T, Sugita I, Esaki H, Yoshida A, Kanematsu Y, et al. The Effect of Quality of Life on Medication Compliance Among Dialysis Patients. Front Pharmacol. 2018;9:488.
22. Solans M, Pane S, Estrada MD, Serra-Sutton V, Berra S, Herdman M, et al. Health-related quality of life measurement in children and adolescents: a systematic review of generic and disease-specific instruments. Value Health. 2008;11(4):742-64.
23. Ravens-Sieberer U, Karow A, Barthel D, Klasen F. How to assess quality of life in child and adolescent psychiatry. Dialogues Clin Neurosci. 2014;16(2):147-58.
24. Rijks JM, Plat J, Mensink RP, Dorenbos E, Buurman WA, Vreugdenhil AC. Children With Morbid Obesity Benefit Equally as Children With Overweight and Obesity From an Ongoing Care Program. J Clin Endocrinol Metab. 2015;100(9):3572-80.
25. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. Pediatr Obes. 2012;7(4):284-94.
26. The Kidscreen Group Europe. KIDSCREEN: healt related quality of life questionnaire for children and young people and their parents. Available from: www.kidscreen.org.
27. Centraal Bureau voor de Statistiek. Persoon met een westerse migratieachtergrond. Available from: www.cbs.nl/nl-nl/onze-diensten/methoden/begrippen/persoon-met-een-westerse-migratieachtergrond.
28. Centraal Bureau voor de Statistiek. Opleidingsniveau. Available from: www.cbs.nl/nl-nl/nieuws/2019/33/verschil-levensverwachting-hoog-en-laagopgeleid-groeit/opleidingsniveau.
29. World Health Organization. Mental disorders 2022. Available from: https://www.who.int/news-room/fact-sheets/detail/mental-disorders.
30. Partnerschap Overgewicht Nederland. Zorgstandaard Obesitas 2010. Available from: https://www.partnerschapovergewicht.nl/wp-content/uploads/2020/03/PON_Zorgstandaard_Obesitas_2011_A4_v1_04.pdf.

31. Alberti KG, Zimmet P, Shaw J. International Diabetes Federation: a consensus on Type 2 diabetes prevention. Diabet Med. 2007;24(5):451-63.

32. Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. Pediatrics. 2017;140(3).

33. Norman GR, Sloan JA, Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. Med Care. 2003;41(5):582-92.

34. Bland JM, Altman DG. Measuring agreement in method comparison studies. Stat Methods Med Res. 1999;8(2):135-60.

35. Teunissen M, Hijmans CT, Cnossen MH, Bronner MB, Grootenhuis MA, Peters M. Quality of life and behavioral functioning in Dutch pediatric patients with hereditary spherocytosis. Eur J Pediatr. 2014;173(9):1217-23.

36. Tsiros MD, Olds T, Buckley JD, Grimshaw P, Brennan L, Walkley J, et al. Health-related quality of life in obese children and adolescents. Int J Obes (Lond). 2009;33(4):387-400.

37. Rank M, Wilks DC, Foley L, Jiang Y, Langhof H, Siegrist M, et al. Health-related quality of life and physical activity in children and adolescents 2 years after an inpatient weight-loss program. J Pediatr. 2014;165(4):732-7.e2.

38. Krause L, Ellert U, Kroll LE, Lampert T. [Health-related quality of life of overweight and obese adolescents: what differences can be seen by socio-economic status and education?]. Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2014;57(4):445-54.

39. Wardle J, Cooke L. The impact of obesity on psychological well-being. Best Pract Res Clin Endocrinol Metab. 2005;19(3):421-40.

40. Van Cleave J, Gortmaker SL, Perrin JM. Dynamics of obesity and chronic health conditions among children and youth. Jama. 2010;303(7):623-30.

41. Bai G, Herten MH, Landgraf JM, Korfage IJ, Raat H. Childhood chronic conditions and health-related quality of life: Findings from a large population-based study. PLoS One. 2017;12(6):e0178539.

42. Silva N, Pereira M, Otto C, Ravens-Sieberer U, Canavarro MC, Bullinger M. Do 8- to 18-year-old children/adolescents with chronic physical health conditions have worse health-related quality of life than their healthy peers? a meta-analysis of studies using the KIDSCREEN questionnaires. Qual Life Res. 2019;28(7):1725-50.

43. Dey M, Landolt MA, Mohler-Kuo M. Assessing parent-child agreement in health-related quality of life among three health status groups. Soc Psychiatry Psychiatr Epidemiol. 2013;48(3):503-11.

44. Firman N, Dezateux C. Does parental concern about their child's future risk of overweight vary by their ethnic background? Cross-sectional analysis of a national cohort study. BMJ Open. 2019;9(8):e027226.

45. Kolotkin RL, Crosby RD, Williams GR. Health-related quality of life varies among obese subgroups. Obes Res. 2002;10(8):748-56.

CHAPTER 3

THE IMPACT OF THE COVID-19 PANDEMIC ON LIFESTYLE AND WELLBEING OF CHILDREN, ADOLESCENTS AND THEIR PARENTS: A QUALITATIVE STUDY

Kelly G.H. van de Pas*
Marijn L. Hesselink*
Robin Schlechtriem
Lisanne Arayess
Johanna M. Kreutz
Anita C.E. Vreugdenhil

* Both authors contributed equally.

Children 2022.

ABSTRACT

Prior studies have shown that changes in daily structure and habits due to the COVID-19 pandemic affected the lifestyle and wellbeing of families. This study aimed to obtain in-depth information on children's and adolescents' experiences regarding their lifestyle and wellbeing during the pandemic. Semi-structured interviews with fifteen families were carried out between May and November 2021. Directed content analysis was used to analyze the transcripts and fundamental qualitative description to describe the results. Children and adolescents revealed an overall unhealthier lifestyle and decreased wellbeing. These negative effects were even larger in adolescents and children with overweight or psychosocial complaints. Our results revealed that parents were actively involved in maintaining a normal daily structure. Furthermore, diet changes were inconsistent and dependent on food availability. An increase in screen time was experienced as inevitable, and external influences were necessary to keep children and adolescents active. Almost no effects were reported on physical health, whereas negative emotions were experienced in varying degrees. Moreover, the decrease in social interactions was reported as the most negative effect of the pandemic. The abovementioned insights may contribute to the development of preventive measures to promote a healthy lifestyle and wellbeing of children and adolescents during future pandemics.

INTRODUCTION

In March 2020 the World Health Organization declared SARS-CoV-2 (COVID-19) as a global pandemic. Since then, national measures to prevent the spread of COVID-19 in the Dutch population have radically changed the lives of children and adolescents in the Netherlands. Governmental regulations were continuously adapted to lower the spread of COVID-19 infections and ease the burden on the healthcare system. These regulations included the closure of sport facilities, public spaces, non-essential shops, restaurants and schools[1]. Since the start of the pandemic, the regulations of schools and sport facilities for children varied from being completely closed to being open when adhering to certain rules. Examples were quarantining when a certain number of infections within a classroom were reached, not allowing sport competitions between clubs and sport facilities with restricted opening hours. Besides this, parents were regularly required to work from home and additionally had to support their children during home schooling. Social distancing further affected the support systems of families as it was advised to limit contact with people outside of the household.

Previous research has shown that changes in daily structure and habits are expected to affect the lifestyle and wellbeing of children, adolescents and their parents. The alterations in daily structure and habits due to governmental regulations during the COVID-19 pandemic resulted in weight gain, increased fatigue, decreased physical activity, increased sedentary time and an increase in mental health problems[2-8]. Interview studies with families in the United States of America and Indonesia revealed similar results and additionally showed that parents played a role in managing the screen time of children and promoting activity during the pandemic[9,10]. Furthermore, a systematic review reported that children and adolescents are more likely to experience high rates of anxiety and depression during and after a pandemic[11]. A Dutch qualitative mixed methods study among children with severe obesity observed an increased demand for food and attributed this to a loss of daily structure, increased stress and boredom. In this study, lower physical activity due to anxiety about a COVID-19 infection was also mentioned. Besides this, parents reported deteriorated emotional wellbeing of their children due to an increase in conflicts, as the whole family was at home all the time[12]. Since these studies only included children with severe obesity who were undergoing treatment for their weight or were conducted in a different country, it is unknown whether the general population of Dutch children and adolescents also encountered these barriers. Therefore, the aim of our study is to obtain in-depth information on the experiences regarding lifestyle and wellbeing of Dutch children, adolescents and their families during the COVID-19 pandemic using semi-structured interviews.

MATERIALS AND METHODS

Setting

Families were selected from the COLC study (Children, Obesity and Lifestyle during COVID-19). The COLC study was a national prospective digital questionnaire study concerning the lifestyle and wellbeing of Dutch children and adolescents during the COVID-19 pandemic. The study was conducted in accordance with the Declaration of Helsinki, approved by the Medical Ethical Committee of the Maastricht University Medical Centre (METC2020-1330-A-1) and registered at clinicaltrials.gov (NCT04411511). Informed consent of parents and children aged 12 years was obtained prior to the start of the study. Families had the opportunity to give additional informed consent to participate in interviews.

Participants

Recruitment of families took place via social media, traditional media, primary and secondary schools. Children aged between four and eighteen years living in the Netherlands during the COVID-19 pandemic were considered for inclusion in this study. Families who participated in the COLC study and gave additional informed consent for an interview were invited by email (n = 262). From May 2021 until November 2021, 25 families responded and after interviewing the first 15 families the researchers collaboratively decided that data saturation was reached. The other 10 families either did not respond to make an appointment or were only available after data saturation was reached.

All the interviewed families had Dutch nationality. During three interviews, both mother and father were present, in one case only the father, and in another case only the adolescent attended the interview. In all the other interviews, only the mother and the children were present. In seven interviews, siblings also participated next to the main child. The characteristics of the included main participants and their families are presented in Table 1. The majority of the children and adolescents had a healthy weight and reported no weight gain during the pandemic. Three adolescents stated that they had gained weight during the pandemic and these were the ones with overweight or severe obesity.

Table 1. Characteristics of the included children, adolescents and their families

	Children, adolescents and their families, n = 15
Age category[1], n.	
Children	7
Adolescents	8
Sex, n.	
Female	9
Male	6
IOTF classification[2], n.	
Healthy weight	12
Overweight	1
Obese	0
Severely obese	2
Weight change during pandemic, n.	
Weight loss or unchanged	12
Weight gain	3
Family composition[3], n.	
Intact	14
Not intact	1
Number of children in family, n.	
One child	3
Two children	6
Three or more children	6
Working status parents[4], n.	
Employed	13
Unemployed	2

Data presented as number. n = number, IOTF = International Obesity Task Force.
[1] Children aged 4-11, adolescents aged ≥12[13,14].
[2] According to International Obesity Task Force[15].
[3] Intact family means parents are in a relationship.
[4] Employed means both parents have a job.

Procedures

Semi-structured interviews of 50 to 70 min were carried out between May 2021 and November 2021 by two female medical students (R.S. and F.B.). There was no relation between the participants and the interviewees prior to the start of the study and the main goal of the research was explained before the start of the interviews. The interviews were conducted via Microsoft Teams, recorded with a digital audio recorder and supervised by three PhD students (K.G.H.v.d.P., M.L.H. and J.M.K.). The interviews covered the topics lifestyle and wellbeing. The interview guide is presented in Supporting Information file S1 (https://www.mdpi.com/article/10.3390/children9121929/s1), and the topics in the guide were based on the questionnaires regarding lifestyle used in the COLC study and a validated questionnaire on quality of life (KIDSCREEN-27)[16].

After a pilot interview and the first two interviews, the interview guide was adjusted to make sure that all relevant topics were covered. The interviews were conducted with all family members simultaneously. The questions were directed towards one child or adolescent as the main participant to gain insight into their experiences during the COVID-19 pandemic. Additionally, parents, and when applicable siblings, were invited to elaborate on the answers of the participating child. The interviews were semi-structured, so that flexibility and responsiveness could be guaranteed whilst still keeping the interview on track. During the interviews field notes regarding non-visual communication and important topics were made. Purposive sampling of children with overweight and obesity was used to ensure that a variety of answers were given, since the majority of the COLC participants had a normal weight. Families were included until no new insights were discovered during the interviews. The Consolidated criteria for Reporting Qualitative research (COREQ) were used as the reporting guidelines[17].

Data analysis

The audio recordings of the interviews were manually transcribed, removing stutters and repetitions, finally resulting in verbatim transcriptions. The transcripts were not returned to the participants for comments or corrections. All transcripts were examined line-by-line and directed content analysis was used to analyze the transcripts[18]. The themes and categories were identified in advance and based on the same topics covered in the interview. The themes were lifestyle and wellbeing: lifestyle was divided into three categories (daily structure, diet and physical activity), as was wellbeing (physical health, mental health and social life). The transcripts were individually coded using Nvivo 14 (version 20.4.0, QSR International Pty Ltd.) by researchers K.G.H.v.d.P. and R.S. The coding was done according to the predefined categories and supplemented with subcategories that came up during the coding (Supporting Information table S1, https://www.mdpi.com/article/10.3390/children9121929/s1). The codes of the transcripts were compared; in case of differences, the code was discussed until an agreement between researchers was reached. Within the categories K.G.H.v.d.P. and M.L.H. analyzed the codes, looking for patterns and answers that were notably different from the overall opinion. Fundamental qualitative description was used to describe the results[19]. Quotes that best reflected this were identified by K.G.H.v.d.P. and M.L.H. and verified by the rest of the research team. In the final stage, the quotes were translated from Dutch to English.

RESULTS

Lifestyle

Families were actively involved in maintaining a normal daily structure - daily structure

The COVID-19 pandemic influenced the daily structure of the interviewed families. However, the majority of the families felt that their daily routine had almost stayed the same. Parents actively tried to keep the daily structure of their children the same as before the pandemic.

> *"I think I am trying to live normal (daily structure comparable to the period before the pandemic) with them" COLC15 (mother)*

One mother indicated that she maintained a daily structure comparable to the period before the pandemic to improve the wellbeing of her children.

> *"Well, they are less irritable now (when maintaining a normal daily structure). And less likely to get angry... It's not just hard for adults but for children too" COLC01 (mother)*

Other reported facilitators for maintaining a daily structure were schools that provided online classes, as children and adolescents had to get up early just like on regular schooldays, and other external factors such as the work of parents and extracurricular care. Notably, maintaining a daily structure seemed harder for adolescents and youth with overweight or psychosocial complaints. These older and vulnerable children more often reported changes in daily structure.

> *"I just went online (for 10 min of school instructions) and after that, I shut down the laptop and I went back to bed, back to sleep again" COLC13 (adolescent)*

With regard to sleeping times, parents mentioned that it is hard to define if the sleeping times altered due to the COVID-19 pandemic or due to their children's aging.

> *"I think he's allowed to go to bed a little later, but would have been able to otherwise, that it's not specifically because of COVID-19" COLC02 (father)*

Other children, adolescents and parents reported that sleeping times shifted due to school starting later and less time spent commuting to school, but that the total sleep duration did not change.

"I think we all went to sleep later. And I do get up later because those classes, they start a little bit later... " COLC04 (adolescent)

Adolescents often mentioned that their sleeping times altered, which might be due to less parental influence in older children. On the contrary, the nature of the child is also important as one adolescent reported that he installed an app on his phone so that he could no longer access his phone after a certain time.

"Yes, I did notice... that especially late, right before bed, I was on my phone and that that also had an effect on how fast I could fall asleep." COLC04 (adolescent)

Changes in diet were dependent on food availability - diet

The COVID-19 pandemic changed the diet and eating behavior of the interviewed families. However, changes were inconsistent. Some families mentioned making healthier choices while other families indicated that snacking behavior of their children increased. Examples of healthier food choices were that children ate more fruit at home than they would at school. Some families mentioned they did groceries locally and cooked dinners at home more often than before the pandemic. Besides this, families reported having a luxurious lunch together more frequently than before the pandemic and this improved family bonding time. However, the products consumed during these lunch breaks were less healthy and children stated that they ate more than they would at school.

"(Did your lunch change?) Yes, she had more waffles, grilled cheese and eggs for lunch. It became more like different, less healthy, and at home you can make it fresh" COLC05 (mother)

The main determinant in the choice for healthy or unhealthy food and the amount of food was the availability and the easy access of food at home. Families that experienced an increased workload due to the COVID-19 pandemic, for example health care workers and schoolteachers, indicated that they tended to make more easy and fast choices. This led to getting more takeout or ready meals for dinner. Families also mentioned that children more frequently asked for snacks.

"Well, I think there were certainly more requests for sweets" COLC06 (mother)

The children themselves indicated that this was out of boredom and easier availability compared to at school. The possibility that children were hungrier because they spent more time playing outside was also mentioned by some families.

"But I also think it's because I have nothing to do at home and at school I don't really think about food, then I'm busy with other things. But at home yes, I generally eat a lot. Because at home, I can always grab something and at school, I only eat during the breaks" COLC05 (adolescent)

Adolescents indicated that they couldn't go to the supermarket with friends during school hours as the schools had closed down. This could have led to buying fewer unhealthy food products. At the same time, they mentioned that they went to get more takeout fast-food as a way of socializing with friends.

"Now, after I had dinner I would go to McDonald's with a friend, there are many other friends and that was the way of seeing them" COLC13 (adolescent)

Notably, a few families mentioned that the father had an unhealthy influence on the groceries that were bought and on the foods that were consumed, which happened due to the father being at home more.

"(speaking to child) When your father did the groceries there was more junk food available at home" COLC11 (mother)

Most families concluded that the positive effects of the COVID-19 pandemic on their diet and food behavior diminished as soon as life went back to how it was before the pandemic. Contrastingly, unhealthy behaviors that started during the COVID-19 pandemic were more difficult to reverse and sometimes remained.

"The structure in my eating pattern is lost. And that still is the case" COLC14 (adolescent)

The increase in screen time was experienced as inevitable – screen time

According to children and adolescents their screen time has inevitably increased during the COVID-19 pandemic. Determinants for the increase in screen time were school, because lessons were offered online, and boredom due to fewer activities. Furthermore, it was reported as the only way to connect with friends, especially for older children.

"The only way of talking to your friends or like anyone that doesn't live with you was via the computer so I guess it only makes sense that you would use the computer a lot more than we used to. Because that's the only connection to the outside world" COLC12 (adolescent)

Some parents also mentioned that they used screens as pastimes or as an easy distraction for their children and adolescents when parents wanted to work, had online meetings or were ill.

> *"Well, during COVID-19 you (children) definitely watched more screens, because if we had an important meeting... Then you had to be quiet" COLC 06 (mother)*

Besides this, the role of schools in limiting screen time diminished during the pandemic. Instead of going to school and participating in physical classes, schools provided online classes.

While most families reported an increase in screen time, some reported that the screen time of their children stayed the same. However, upon further questioning, screen time turned out to be more than before the pandemic, suggesting that it is difficult for families to make an adequate estimation of their screen time during the pandemic.

Keeping children and adolescents active requires external factors – physical activity

The COVID-19 pandemic influenced the physical activity of children and adolescents. However, these changes were inconsistent as younger children reported playing outside more, whereas adolescents did not. External factors such as the organization of alternative activities or the influence of the parents were important for keeping the children active.

At the beginning of the pandemic, all sports activities were cancelled and children and adolescents did not have physical education at school. Additionally, they did not have to cycle or walk to school, possibly leading to a further decline in physical activity. Physical activity reduction resulted in boredom and fewer social interactions among participants. Some children and adolescents also mentioned that they could not release their energy due to this.

> *(Why did you miss sports?) "Then you are with some people from your team again and you learn a little bit. So the fun and you have also exercised. You can release your energy and I like that" COLC04 (adolescent)*

Notably, a couple of children and adolescents said that they missed the competitions the most.

> *"I missed going to the matches actually. Like playing in a match" COLC12 (adolescent)*

As the pandemic proceeded, alternative activities were organized by sport clubs, schools or parents to keep the children and adolescents active. One family bought a trampoline, whereas others tried to do sports, go on a walk or cycle together as a family. However, it was not always easy to motivate children, and it seemed from our observations that younger children were more approachable for this.

> *"But it is not very easy when you have been sitting inside together all day, come on kids we are going to do something fun again (playing tennis). Then it is not like they are always cheering of what a good idea" COLC04 (mother)*

Furthermore, only one adolescent reported that she sought other fulfillment for the reduced physical activity by dancing in her room with her sister.

During the pandemic, the majority of the families mentioned that their children played outside more. This increased due to fewer school hours, no other organized activities and the generally good weather.

> *"You finish school earlier and then you can play outside for longer. Or you just play outside when otherwise you could not, for example field hockey was canceled and instead of this you can play outside" COLC 03 (adolescent)*

It seemed that the children and adolescents who already played outside before the pandemic spent more time playing outside. In line with this, the children who did not play outside before the pandemic did not spend more time playing outside. This was particularly the case in older children. A barrier against playing outside was social control in the neighborhood. Some neighbors did not want children and adolescents playing outside due to the fear of spreading COVID-19.

> *"Because the people in our community were more afraid (of COVID-19), we just did not let the kids play together" COLC10 (mother)*

The important findings with regard to the lifestyle of families during the pandemic are summarized in Table 2.

Table 2. Important findings with regard to the lifestyle of families during the COVID-19 pandemic

	Important findings
Daily structure	• Parents actively tried to maintain their children's daily routine as it was before the pandemic. • Older and vulnerable children (e.g., youth with overweight or psychosocial complaints) often reported changes in their daily structure.
Diet	• Diet changes were inconsistent across families and dependent on the availability of food at home, the workload of parents and boredom of the children. • The positive effects of the pandemic on the food behavior of families diminished as soon as life went back to normal again, whereas the unhealthy behaviors were more difficult to reverse.
Screen time	• The screen time of children and adolescents has inevitably increased according to the families, as school and contact with friends took place online.
Physical activity	• Children and adolescents needed external factors (e.g., influence of parents or organization of alternative activities) to stay active. • The younger children were more approachable for external factors.

Wellbeing

Experienced negative effects of COVID-19 on physical health were limited – physical health

Overall, children and adolescents considered their physical health as good. They did not experience significant differences because of the COVID-19 pandemic. Despite that, almost all children indicated that if they had a cold or any symptoms that could be related to a COVID-19 infection, the effect was more negative than before. They were not allowed to go to school without testing and felt restricted by this.

> *"Because normally when you have a cold you can just go to school and now they had to stay at home" COLC08 (mother)*

Besides this, some feared the impact a COVID-19 infection could have on the health of their elderly family members. Energy levels were reported generally to be similar, compared to before the pandemic, with some exceptions.

> *"Well in my opinion, since the start of the pandemic, you are a little, how to say, more lethargic, like if you are in such a state it is harder for me to get you off the couch" COLC04 (mother)*

One adolescent also indicated that his endurance was lower after he was infected with COVID-19 and that it took a while to regain his fitness.

"After that, you really have to rebuild your condition because of fatigue. And the first time when I was allowed to go back to soccer training, I ran from one side of the penalty area to the other side and I was completely exhausted" COLC08 (adolescent)

Feelings of irritability, anger, loneliness and sadness were experienced in varying degrees – mental health

In general, the children and adolescents were happy and experienced good mental health. However, almost all interviewed families felt that the mental health of their children and adolescents decreased during the pandemic and it decreased even more in adolescents and vulnerable children, e.g., the ones with overweight or psychosocial complaints.

Feelings of irritability, anger, loneliness, sadness, boredom or fear were experienced by almost all children and adolescents, although to varying degrees. Some children mentioned that these feelings were due to a lot of time spent with the same people in the same environment and less social contact.

"I sometimes have moments when I'm just a little angry, but that's.... because all the time when you are home you see you guys (points at father) all day" COLC02 (child)

"Especially that I could not play with my friends, you just could not go on playdates during the pandemic" COLC08 (child)

Others reported boredom as a result of fewer challenges, particularly in school. Notably, one mother indicated that her children learned to become more resilient to alterations and disappointments due to the continued cancellation of activities.

"It was an accumulation of cancelled activities. Then you have to show some resilience as a kid" COLC03 (mother)

One adolescent with severe obesity reported that she was depressed. She was already depressed before the pandemic and her symptoms worsened due to it. For her, it was a struggle to get through each day.

"Normally you go to school and have social contacts around you anyway. And as soon as that is no longer allowed, that you cannot go to school and that your social contacts are taken away from you. Then your depressive phase goes from a normal depression to a more extreme one" COLC13 (adolescent)

Two other families also reported that one of their children had a hard time during the pandemic, e.g., depressive symptoms and excessive worrying. They mentioned that the problems of their children were signaled by the school and that they received help.

Interestingly, when asking children, adolescents and their families about their mental health, the majority attenuated the consequences of the pandemic. They reported that in their case it was not so bad and felt that it was worse in other families.

> *"I did not like it (COVID-19), but I don't like complaining about it seeing that there are people who had it so much worse" COLC12 (adolescent)*

Loss of social interactions was experienced as the most negative effect of COVID-19 – social life

Children and adolescents reported that they had fewer social interactions with friends. The majority stated that this was the most negative effect of the pandemic. Children who played outside indicated they made new friends and met with them more often than before, mainly because they had more time as they spent less time at school. Participants who stayed inside more found it harder to make new friends. It appeared that it was more difficult to arrange meetings with friends without the contact moments at school.

> *"Previously (before the pandemic) I did not meet that often with friend(s) outside of school, so to not meet up with them and to not see each other at school or at the sports club, yes that was hard" COLC04 (adolescent)*

One adolescent reported that he went to the psychologist to receive help in maintaining contacts with friends and getting to know new friends.

Most families were still engaged in social activities with friends and relatives but organized this in a different way than before the pandemic. Examples were video calls and meeting up with each other outside whilst keeping distance. Besides this, they initiated "social bubbles" where they met with the same group of people every time to limit the number of different contacts.

> *"We always had the same social bubble of people who we invited over" COLC08 (mother)*

The amount of contact with others also changed during the pandemic; the more time had passed, the more people became flexible in inviting people over. Particularly after the Dutch government started the vaccination campaign, there were more contacts.

> *"At a certain point we were a bit looser, a bit more flexible. Because sometimes it is more important to see each other anyway" COLC12 (mother)*

The influence of the COVID-19 pandemic on social interactions with relatives also changed. In some families the contact with relatives, for example grandparents, became more intense as they took over care tasks within the family because parents had to work. In the end, some families indicated that they liked the time spent as a family without other people being present. Some children also indicated that they liked the "quieter" days.

> *"Sometimes I just wanted to be at home instead of being with someone else. I saw my best friend a lot. Every week every day, so every now and then I wanted some time for myself" COLC05 (adolescent)*

The important findings with regard to the wellbeing of families during the pandemic are summarized in Table 3.

Table 3. Important findings with regard to the wellbeing of families during the COVID-19 pandemic

	Important findings
Physical health	• Limited influence of the pandemic on the physical health of children and adolescents.
Mental health	• Experienced decrease in mental health of children and adolescents, especially in the older and more vulnerable children, e.g., the ones with overweight or psychosocial complaints. • Feelings of irritability, anger, loneliness, sadness, boredom or fear were reported by almost all children and adolescents.
Social life	• Loss of social contact with friends was the most negative effect of the pandemic according to the children and adolescents. • During the pandemic other ways to stay in touch with friends or family were sought, e.g., "social bubbles" or video calls.

DISCUSSION

The aim of this explorative study was to describe the experiences regarding lifestyle and wellbeing of children, adolescents and their families during the COVID-19 pandemic. Our results revealed the mainly negative effects on lifestyle and wellbeing of families during the pandemic. These negative effects were even larger in adolescents and vulnerable children, e.g., those with overweight or psychosocial complaints. Besides this, we found that parents were actively involved and in general successful in maintaining a normal daily structure for their children. Diet changes were inconsistent and dependent on the availability of food. Furthermore, an increase in screen time was experienced as inevitable as both school and contact with friends took place online. Parents also used screens to keep their children occupied and external influences were necessary to keep children and adolescents active. Fortunately, the experienced negative impact on physical health in children and adolescents was limited, whereas with regard to mental health feelings of irritability, anger, loneliness and sadness were experienced in various degrees. At last, when families were asked for the most negative effect of the pandemic, most reported the decrease in social interactions.

During the COVID-19 pandemic, eating patterns of families changed, both in more and less healthy ways[20,21]. A qualitative report from the United States on family food environment during the pandemic revealed that snacking and food-seeking behavior of children increased and that some parents mentioned that their children gained weight. The parents attributed this to children being home more, increased accessibility to food and boredom[22]. Similar results and determinants were found in the current study among Dutch children and adolescents. Besides this, adolescents with overweight or severe obesity reported a further increase in their weight during the pandemic. This was in contrast to the children and adolescents who had a healthy weight, as they reported no weight gain. Notably, unhealthy eating behaviors that started in the pandemic seemed more difficult to reverse and sometimes remained, whereas the positive effects diminished. This suggests that the abovementioned unhealthy alterations in eating patterns due to the pandemic might have lasting implications for the weight of children and adolescents in the future and mainly in the children with overweight or obesity[23-25].

A daily structure and regular physical activity are important for the health and wellbeing of children and adolescents. During the pandemic, the 'regular' daily routine of the children and adolescents was lost and the usual physical activity diminished. Despite their efforts, children and adolescents seemed unable to maintain their daily routine and physical activity without help. Only the minority reported partially successful attempts to maintain this. Adolescents more often reported a decrease in their physical

activity and an increase in their screen time. Our qualitative data revealed that parents felt the need to help their children in providing a daily structure and to keep them entertained and active by offering alternative activities. Due to less parental influence in the older children, this might be more successful in the younger[26]. Additionally, schools, sports clubs and public health organizations also contributed to this by organizing activities. This enlightens the importance of external factors in maintaining a healthy lifestyle of children and adolescents during the pandemic.

With regard to wellbeing, mental health decreased and the children and adolescents experienced negative emotions such as irritability, anger, loneliness and sadness in varying degrees during the pandemic. An adolescent with depressive symptoms even reported that she went from a 'normal' depression to a more extreme one. This is in line with previous reports that described a lower quality of life, higher anxiety levels and more mental health problems in children and adolescents during the pandemic[12,27,28]. Another nationwide study from Germany concluded that children from families with low education levels and a migration background were more at risk for developing mental health problems[5]. This suggests that the impact on mental health is even worse in the general population compared to our population, as in our study only children and adolescents from Dutch origin participated. Altogether, the pandemic seemed to place an overall burden on the wellbeing of children and adolescents. This is especially worrisome, since childhood is an important period for the social development of children and adolescents.

In previous research, the closure of schools was described as one of the most influential factors during the COVID-19 pandemic on the lifestyle and wellbeing of children and adolescents[27-29]. In our qualitative analysis, school was mentioned as a facilitator for a normal daily structure and normal sleeping times. Going to school also reduced snacking behavior and when children and adolescents go to school instead of having online lessons there is less screen time. Furthermore, schools provide social contact, social and cognitive development and are a safety net for children and adolescents[27]. Lastly, schools ensure physical activity by providing physical education and transport to school, which in the Netherlands is mostly done by biking or walking. Although not all participants identified the closure of schools as one of the main contributors to their changes in lifestyle and wellbeing, the closure of schools can in almost all cases be indirectly linked to these changes, whether participants were aware of this or not. Overall, extended school closures contributed to an unhealthy lifestyle and wellbeing[29].

Besides the burden, families also reported positive experiences due to the pandemic. Examples of positive experiences were increased free time, consumption of more

fruit, more home cooked family dinners and spending more time with family. It was mentioned that due to the pandemic some children became more resilient when faced with challenges. Similar to our study, an Australian study showed that families indicated they enjoyed spending more time together[30]. This emphasizes the differences between how families experienced the pandemic.

By combining the experiences of families during the COVID-19 pandemic, several recommendations can be made with regard to future pandemics or crises. First of all, health promotion programs should not be discontinued without offering an alternative option and should focus on parental involvement. When parents learn how to support their children during crises, they will be more likely to apply this when it is really necessary. Secondly, governmental regulations should be adjusted to the needs of children; especially, adolescents and vulnerable children (e.g., the ones with overweight or psychosocial complaints) might benefit from this. Lastly, governmental regulations to prevent the spread of COVID-19 infections need to be reviewed. Regulations must balance the threat of the pandemic with the impact the regulations have on the children's lifestyle and wellbeing.

This study has several limitations. First, due to the design of the study, selection bias of the interviewed families should be taken into account. Families who volunteered to participate in the study were aware of the subject and might have had stronger opinions on the effect of the COVID-19 pandemic on their lifestyle and wellbeing. Besides this, the families who participated in the study are not entirely representative of the general Dutch population. For example, our study population only consisted of families of Dutch descent, whereas in the general population 26.2% of the Dutch population has a migration background[31]. Besides this, there were three children with overweight (20.0%) and two of them had severe obesity (13.3%), whereas in the general Dutch population the overweight percentage varies from 15.5–18.6% and there are only 2.9–4.3% children with severe obesity[32]. Lastly, the interviews were executed during a broad time range. Ten interviews were done in May and June 2021 and five interviews in October and November 2021. Therefore, the interviews were in different stages of the COVID-19 pandemic. At the end of May 2021, the biggest part of society opened up again, whereas in November 2021 new stricter regulations such as a maximum of four people at home applied[1]. These differences could have led to disparities in recall bias. Families who were interviewed when strict governmental regulations applied, might have experienced more negative feelings with regard to COVID-19 compared to families who were interviewed when almost no governmental regulations applied.

CONCLUSION

Even though children and adolescents appear to be less affected by a COVID-19 infection and most of the interviewed families came from a stable family environment, they faced impactful challenges. The families experienced in general an unhealthier lifestyle and decreased wellbeing, and the older children and the ones with overweight or psychosocial complaints were even more affected. Our qualitative data revealed that children and adolescents are not always able to cope with these challenges without help. External influences, such as the influence of caregivers, schools and public health efforts, are necessary to support them in obtaining a healthy lifestyle and wellbeing. These insights may aid in the development of preventive measures to promote a healthy lifestyle and wellbeing of children and adolescents during future pandemics or other crises. Additionally, it creates awareness of the lasting effects of the COVID-19 pandemic on lifestyle and wellbeing of children and adolescents, even after most regulations were lifted.

REFERENCES

1. Rijksoverheid. Coronavirus tijdlijn 2022. Available from: https://www.rijksoverheid.nl/onderwerpen/coronavirus-tijdlijn.
2. Ten Velde G, Lubrecht J, Arayess L, van Loo C, Hesselink M, Reijnders D, et al. Physical activity behaviour and screen time in Dutch children during the COVID-19 pandemic: Pre-, during- and post-school closures. Pediatr Obes. 2021;16(9):e12779.
3. Xiang M, Zhang Z, Kuwahara K. Impact of COVID-19 pandemic on children and adolescents' lifestyle behavior larger than expected. Prog Cardiovasc Dis. 2020;63(4):531-2.
4. Ravens-Sieberer U, Kaman, A., Erhart, M. et al. Impact of the COVID-19 pandemic on quality of life and mental health in children and adolescents in Germany. European Child & Adolescent Psychiatry. 2021.
5. Ravens-Sieberer UO, C; Kaman, A; Adedeji, A; Devine, J; Napp, A; Erhart, M; Becker, M; Blanck-Stellmacher, U; Löffler, C; Schlack, R; Hurrelmann, K. Mental Health and Quality of Life in Children and Adolescents During the COVID-19 Pandemic - Results of the COPSY study. 2020.
6. Derya Adibelli AS. The effect of the coronavirus (COVID-19) pandemic on health-related quality of life in children. Children and Youth Services Review. 2020;119.
7. Xinyan Xie BQX, MPH; Yu Zhou, BA; et al. Mental Health Status Among Children in Home Confinement During the Coronavirus Disease 2019 Outbreak in Hubei Province, China. JAMA Pediatrics. 2020;174:898-900.
8. Koletzko B, Holzapfel C, Schneider U, Hauner H. Lifestyle and Body Weight Consequences of the COVID-19 Pandemic in Children: Increasing Disparity. Ann Nutr Metab. 2021;77(1):1-3.
9. Neshteruk CD, Zizzi A, Suarez L, Erickson E, Kraus WE, Li JS, et al. Weight-Related Behaviors of Children with Obesity during the COVID-19 Pandemic. Child Obes. 2021;17(6):371-8.
10. Andriyani FD, Biddle SJH, De Cocker K. Adolescents' physical activity and sedentary behaviour in Indonesia during the COVID-19 pandemic: a qualitative study of mothers' perspectives. BMC Public Health. 2021;21(1):1864.
11. Meherali S, Punjani N, Louie-Poon S, Abdul Rahim K, Das JK, Salam RA, et al. Mental Health of Children and Adolescents Amidst COVID-19 and Past Pandemics: A Rapid Systematic Review. Int J Environ Res Public Health. 2021;18(7).
12. Welling MS, Abawi O, van den Eynde E, van Rossum EFC, Halberstadt J, Brandsma AE, et al. Impact of the COVID-19 Pandemic and Related Lockdown Measures on Lifestyle Behaviors and Well-Being in Children and Adolescents with Severe Obesity. Obes Facts. 2022;15(2):186-96.
13. Mead E, Brown T, Rees K, Azevedo LB, Whittaker V, Jones D, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese children from the age of 6 to 11 years. Cochrane Database of Systematic Reviews. 2017(6).
14. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane database of systematic reviews. 2017(6).
15. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. Pediatric obesity. 2012;7(4):284-94.

16. Europe TKG. KIDSCREEN: healt related quality of life questionnaire for children and oung people and their parents. [cited 2021 September 24]. Available from: www.kidscreen.org.
17. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. Int J Qual Health Care. 2007;19(6):349-57.
18. Hsieh HF, Shannon SE. Three approaches to qualitative content analysis. Qual Health Res. 2005;15(9):1277-88.
19. Sandelowski M. Whatever happened to qualitative description? Res Nurs Health. 2000;23(4):334-40.
20. Ruiz-Roso MB, de Carvalho Padilha P, Mantilla-Escalante DC, Ulloa N, Brun P, Acevedo-Correa D, et al. Covid-19 Confinement and Changes of Adolescent's Dietary Trends in Italy, Spain, Chile, Colombia and Brazil. Nutrients. 2020;12(6).
21. Pietrobelli A, Pecoraro L, Ferruzzi A, Heo M, Faith M, Zoller T, et al. Effects of COVID-19 Lockdown on Lifestyle Behaviors in Children with Obesity Living in Verona, Italy: A Longitudinal Study. Obesity (Silver Spring). 2020;28(8):1382-5.
22. Hammons AJ, Robart R. Family Food Environment during the COVID-19 Pandemic: A Qualitative Study. Children (Basel). 2021;8(5).
23. Stavridou A, Kapsali E, Panagouli E, Thirios A, Polychronis K, Bacopoulou F, et al. Obesity in Children and Adolescents during COVID-19 Pandemic. Children (Basel). 2021;8(2).
24. An R. Projecting the impact of the coronavirus disease-2019 pandemic on childhood obesity in the United States: A microsimulation model. J Sport Health Sci. 2020;9(4):302-12.
25. Lubrecht J, Arayess L, Reijnders D, Hesselink ML, Velde GT, Janse A, et al. Weight Gain in Children during the COVID-19 Pandemic and the Protective Effect of Lifestyle Intervention in Children with Obesity. Obes Facts. 2022;15(4):600-8.
26. De Goede IH, Branje SJ, Meeus WH. Developmental changes in adolescents' perceptions of relationships with their parents. J Youth Adolesc. 2009;38(1):75-88.
27. Viner R, Russell S, Saulle R, Croker H, Stansfield C, Packer J, et al. School Closures During Social Lockdown and Mental Health, Health Behaviors, and Well-being Among Children and Adolescents During the First COVID-19 Wave: A Systematic Review. JAMA Pediatr. 2022.
28. Ravens-Sieberer U, Kaman A, Erhart M, Otto C, Devine J, Löffler C, et al. Quality of life and mental health in children and adolescents during the first year of the COVID-19 pandemic: results of a two-wave nationwide population-based study. Eur Child Adolesc Psychiatry. 2021:1-14.
29. Viner R, Bonell C, Blakemore SJ, Hargreaves J, Panovska-Griffiths J. Schools should still be the last to close and first to open if there were any future lockdown. Bmj. 2022;376:o21.
30. Evans S, Mikocka-Walus A, Klas A, Olive L, Sciberras E, Karantzas G, et al. From "It Has Stopped Our Lives" to "Spending More Time Together Has Strengthened Bonds": The Varied Experiences of Australian Families During COVID-19. Front Psychol. 2020;11:588667.
31. Centraal Bureau voor de Statistiek. 3 op 10 vijftienjarigen wonen niet met beide ouders 2018. Available from: https://www.cbs.nl/nl-nl/nieuws/2018/18/3-op-10-vijftienjarigen-wonen-niet-met-beide-ouders#:~:text=In%202017%20woonden%203%20van,een%20of%20beide%20ouders%20overleden.
32. Nederlands Jeugdinstituut. Cijfers over Overgewicht 2023. Available from: https://www.nji.nl/cijfers/overgewicht#:~{}:text=In%202021%20had%2015%2C5,het%20om%2013%2C2%20procent.

CHAPTER 4

THE EFFECT OF A MULTIDISCIPLINARY LIFESTYLE INTERVENTION ON HEALTH PARAMETERS IN CHILDREN VERSUS ADOLESCENTS WITH SEVERE OBESITY

Kelly G.H. van de Pas
Judith W. Lubrecht
Marijn L. Hesselink
Bjorn Winkens
François M.H. van Dielen
Anita C.E. Vreugdenhil

Nutrients 2022.

ABSTRACT

Lifestyle interventions are the common treatment for children and adolescents with severe obesity. The efficacy of these interventions across age groups remains unknown. Therefore, this study aimed to compare the effectiveness of a lifestyle intervention on health parameters between children and adolescents with severe obesity. A longitudinal design was carried out at the Centre for Overweight Adolescent and Children's Healthcare (COACH) between December 2010 and June 2020. Children (2–11 years old, n = 83) and adolescents (12–18 years old, n = 77) with severe obesity received a long-term, tailored, multidisciplinary lifestyle intervention. After one year, 24 children (28.9%) and 33 adolescents (42.9%) dropped out of the intervention. The primary outcome was the change in body mass index (BMI) z-score after one and two years of intervention. The decrease in BMI z-score over time was significantly higher in children compared to adolescents, the mean decrease was 0.15 (0.08–0.23) versus 0.03 (−0.05–0.11) after one year and 0.25 (0.15–0.35) versus 0.06 (−0.06–0.17) after two years of intervention; *p* values for the difference between children and adolescents were 0.035 and 0.012. After two years, multiple improvements in cardio metabolic health parameters were observed, especially in children. In conclusion, during our tailored lifestyle intervention, a positive and maintained effect on health parameters was observed in children with severe obesity. Compared to children, the effect on health parameters was less pronounced in adolescents.

INTRODUCTION

Childhood obesity is a global health crisis that is recognized by the World Health Organization[1]. In 2016, 124 million children and adolescents were affected by obesity[2]. Despite the continuous efforts that are being made to reduce the prevalence of childhood obesity, there is a growing concern about the rapidly growing rates of severe obesity in children and adolescents[3-6]. In particular, the severe grade of obesity is worrisome, since children and adolescents with severe obesity have an increased cardiovascular risk compared to those with obesity[7,8]. As a consequence of this, adolescents with severe obesity have an elevated risk for the development of a fatal cardiac event later in life[9].

Multidisciplinary lifestyle intervention programs that focus on nutrition, physical activity, and behavioral change are the most frequently applied treatment options for children and adolescents with severe obesity. The Centre for Overweight Adolescent and Children's Healthcare (COACH) offers such a lifestyle intervention program that was proven to be successful in reducing health risks in children with overweight, obesity, and severe obesity, all to a similar degree[10].

Research on multidisciplinary lifestyle interventions for children and adolescents with severe obesity is limited, with only a handful of studies examining this specific group[10-17]. A previous study reported a beneficial effect of treatment in children, but almost no effect at group level in adolescents with severe obesity[11]. A similar pattern was found by Danielsson et al., who reported that in 58% of the children with severe obesity (6–9 years old), the body mass index (BMI) z-score reduced at least 0.5 units during a three-year intervention, compared to only 2% of the adolescents (14–16 years old)[12]. Possible reasons for the limited response of adolescents to lifestyle interventions are the suggested decline in parental influence during adolescence and the reduced adherence to these interventions as age increases[18,19].

To date, there is a lack of long-term data comparing the effects of lifestyle interventions between children and adolescents with severe obesity focusing on weight loss and cardio metabolic health parameters. Therefore, this study aimed to compare the effectiveness of the COACH lifestyle intervention on weight loss and cardio metabolic health parameters between children and adolescents with severe obesity after one and two years of intervention. It was hypothesized that the COACH lifestyle intervention would result in significantly greater reductions in BMI z-score and improvements of cardio metabolic health parameters in children compared to adolescents.

MATERIALS AND METHODS

Setting and study design

This study was designed and conducted within COACH at the Maastricht University Medical Centre (MUMC+). A longitudinal design was used to compare the effectiveness of the COACH program between children and adolescents with severe obesity. The study was conducted according to the Declaration of Helsinki, and it was approved by the medical ethical committee of the MUMC+. It is registered at ClinicalTrial.gov as NCT02091544.

All children and adolescents with severe obesity who participated in the COACH program were eligible for inclusion in this study. Severe obesity was defined according to the International Obesity Task Force (IOTF) criteria and is comparable to a BMI ≥ 35 in adults[20]. Children were identified as participants aged 2–11 years of age at baseline, whilst adolescents were classified as those aged 12–18 years[21,22]. The age distribution is based on the transition from primary to secondary school, as it is known that this transition is a major life event and many changes occur during this period[23]. Children and adolescents with available anthropometric data after one year of intervention were included. Inclusion ran from December 2010 through to June 2020. Children and adolescents who underwent baseline assessment after June 2020 were not taken into account as one year follow-up data were not available at the time of analysis. Participants who received a previous intervention at COACH, participants who did not receive a lifestyle intervention or received an intervention elsewhere, and participants who underwent bariatric surgery were excluded.

Intervention

COACH is an obesity expertise center founded in 2010, in which children with overweight or obesity and their families receive a tailored lifestyle intervention from a multidisciplinary team consisting of pediatricians, dieticians, psychologists, pedagogues, physical activity coaches, and nurses. This lifestyle intervention has been extensively described elsewhere[10]. All children and adolescents receive a baseline assessment before starting the intervention. Baseline assessment includes extensive anamnesis, physical examination, fasted blood sampling, abdominal ultrasonography, an interview with a dietician and psychologist, and questionnaires to identify underlying conditions and the presence of obesity-related comorbidities. The assessment establishes an understanding of behavior and family function, and it is offered annually to children and adolescents to monitor comorbidities and weight related risk factors. The obtained information is used by the multidisciplinary team to develop an individualized, integral treatment plan. Individual guidance is offered to all families, with a focus on lifestyle changes pertaining to nutrition, food habits, physical activity, sleep, and psychosocial aspects. With regard

to nutrition and food habits, the general dietary guidelines are followed and special attention is given to healthy snacks, adequate intake of fruits and dairy products, less sugar sweetened beverages, eating breakfast, adequate portion size, and shared family dinners[24]. Regarding physical activity, sleep, and social aspects the intervention focuses on limiting sedentary time, expanding physical activity, sleep hygiene, self-esteem, and emotional eating. Multiple behavioral change strategies such as motivational interviewing, goal setting, positive reinforcement, social support, and relapse prevention are employed. Individual sessions initially occur monthly, with frequency adjusted as the individual progresses through the program depending upon their individual needs. Besides the individual family guidance, the program offers possibilities to participate in sport activities and activities aimed to increase knowledge of nutrition.

Measurements

The primary outcome was the change in BMI z-score after one and two years of intervention between children and adolescents. Secondary outcomes were the change in cardio metabolic health parameters in and between children and adolescents after one and two years of intervention. Outcome measures were collected at baseline, and after one and two years of intervention (±four months). Data that did not fit within these time bands were excluded from analysis.

Anthropometric data

Weight and height were measured barefoot. Weight was determined using digital scales (Seca), and height was measured using a digital stadiometer (De Grood Metaaltechniek). Using this information, BMI was calculated (BMI (kg/m^2) = $weight/height^2$), and BMI z-scores relative to population data from the Dutch Growth Study were obtained using a growth analyzer (Growth Analyzer VE). Children and adolescents were considered as overweight, obese, or severely obese according to the IOTF criteria (20). Clinically significant weight loss was defined as a decrease in BMI z-score ≥0.25, as improvements in body composition and cardio metabolic health parameters can be seen with this decline in BMI z-score[25].

Cardio metabolic health parameters

Fasting serum total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglycerides (TG), glucose, glycated hemoglobin (HbA1c), insulin and alanine aminotransferase (ALT) concentrations were measured. Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated using the formula: fasting glucose (mmol/L) * fasting insulin (mU/L)/22.5[26]. Abnormal values of TC were determined as ≥5.2 mmol/L, for HDL as <1.0 mmol/L, for LDL as ≥3.4 mmol/L, and for TG as ≥1.5 mmol/L[27]. According to the American Diabetes Association abnormal values for fasting

glucose were ≥5.6 mmol/L and for HbA1c ≥5.7% (39 mmol/mol)[28]. Besides this, HOMA-IR values >2.5, and ALT values >22 U/L (0.37 µkat/L) for females and >26 U/L (0.43 µkat/L) for males were identified as not normal[26,29].

Data analysis

All data analyses were carried out using IBM SPSS Statistics for Windows (version 26, IBM Corp. Armonk, NY, USA). A two-sided *p* value ≤ 0.05 was considered statistically significant. Normality was assessed using P-P plots and histograms. Numerical data were analyzed using an independent-samples t-test or a Mann–Whitney U test in case of non-normal distribution and categorical data with a chi-square test to determine differences between groups at baseline. Two marginal models for repeated measures were used to assess and compare the change from baseline in BMI z-score after one and two years of intervention in children and adolescents. Model one included Group (children/adolescents), Time (Year 1 or 2) and Group x Time as fixed factors, where an unstructured covariance structure for repeated measures was used. Next to the fixed factors included in model one, model two adjusted for potential confounders (gender, parent's education, and ethnicity). Estimated marginal means based on restricted maximum likelihood (REML) are reported with corresponding 95% confidence intervals (CI). A likelihood-based approach for missing outcomes was applied, where variables related to missingness (logistic regression analysis) were included in the marginal model to ensure missingness at random (MAR). Due to small sample sizes, especially after one or two years of intervention, independent-samples t-test or Mann–Whitney U test were used to compare changes from baseline in cardio metabolic health parameters between the different age categories. Paired samples t-tests or Wilcoxon signed-rank tests were applied to compare changes from baseline within children and adolescents separately. In addition, abnormal values of cardio metabolic health parameters between age categories were compared using a chi-square test at each time point.

RESULTS

Program retention

A total of 251 children and adolescents with severe obesity underwent baseline assessment between December 2010 and June 2020. All children and adolescents (n = 160) of whom a BMI z-score after one year of intervention was available were included in this study, reporting an exclusion rate of 36.3% (n = 91). Reasons for the missing BMI z-score after one year of intervention are mentioned in Figure 1. The included and excluded children had similar baseline characteristics, except that the included children were younger in comparison to the excluded children (11.6 ± 4.0

versus 12.9 ± 4.2 years; $p = 0.022$). In addition, significantly fewer children compared to adolescents were excluded, 27.8% (n = 32) versus 43.4% (n = 59; $p = 0.011$), respectively.

Fifty-seven children and adolescents (35.6%) included in the study dropped out of the COACH program after the first year of intervention; 24 children (28.9%) versus 33 adolescents (42.9%; $p = 0.080$). Reasons for dropout were lack of motivation, referral for bariatric surgery, or starting a lifestyle intervention elsewhere (Figure 1). A logistic regression analysis was performed to check which variables were associated with dropout of the program, but none were significant.

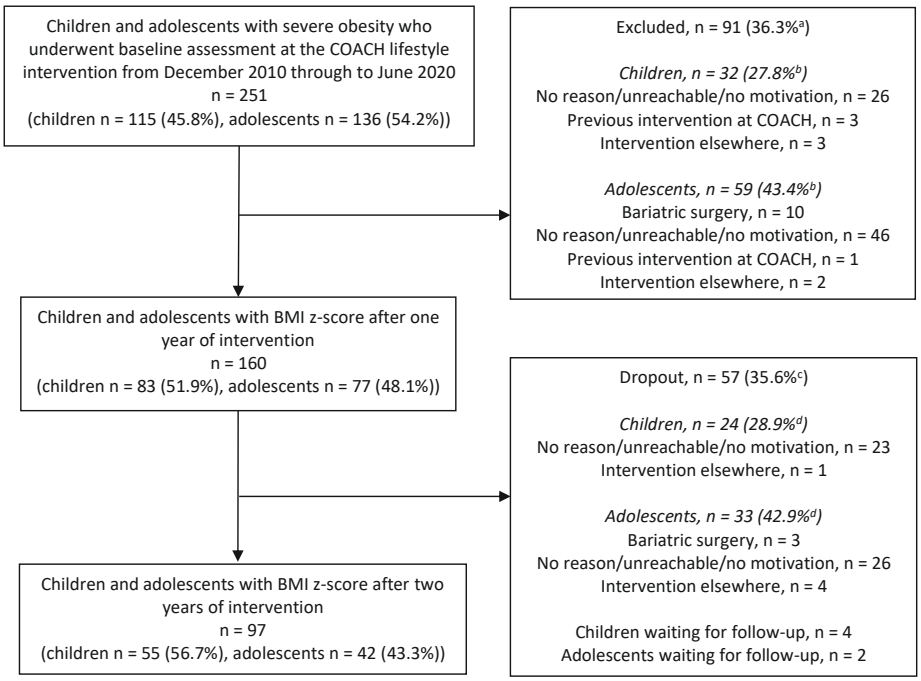


Figure 1. Flow diagram of the exclusion and dropout of children and adolescents with severe obesity from the COACH lifestyle intervention.

[a] Number of excluded participants/number of participants with a baseline assessment from 2010 through 2020.

[b] Number of children or adolescents who were excluded/number of children or adolescents with a baseline assessment from 2010 through 2020

[c] Dropout of the COACH lifestyle intervention after one year of intervention/number of participants with a BMI z- score after one year of intervention

[d] Number of children or adolescents who dropped out of the COACH lifestyle intervention after one year of intervention/number of children or adolescents with a BMI-z-score after one year of intervention

Baseline characteristics

The baseline characteristics of the included children and adolescents were in general similar (Table 1). As expected, age, height, weight, and BMI were significantly higher in the group of adolescents. Besides this, no statistically significant differences were found regarding the cardio metabolic health parameters, except for a higher HOMA-IR and a lower HDL in the group of adolescents.

Table 1. Baseline characteristics of the included children and adolescents with severe obesity

	Children n = 83	**Adolescents n = 77**	***p* value**
Age (years, ±SD)	8.3 ± 2.4	15.2 ± 1.5	<0.001*
Gender, n. (%)			
Female	39 (47.0)	47 (61.0)	0.075
Height (m, ±SD)	1.4 ± 0.2	1.7 ± 0.1	<0.001*
Weight (kg, ±SD)	56.1 ± 20.5	109.4 ± 18.8	<0.001*
BMI (kg/m^2, ±SD)	28.6 ± 4.6	38.9 ± 5.1	<0.001*
BMI z-score (±SD)	4.07 ± 0.55	3.96 ± 0.40	0.139
TC (mmol/L, ±SD)	4.4 ± 0.8	4.4 ± 0.9	0.872
HDL (mmol/L, ±SD)	1.2 ± 0.2	1.1 ± 0.3	0.021*
LDL (mmol/L, ±SD)	2.6 ± 0.7	2.7 ± 0.7	0.546
TG (mmol/L, Q1, Q3)	1.1 [0.7-1.2]	1.0 [0.7-1.3]	0.729
Fasting glucose (mmol/L, ±SD)	4.3 ± 0.6	4.2 ± 0.6	0.605
HbA1c (%, ±SD)	5.3 ± 0.5	5.3 ± 0.4	0.527
HOMA-IR [Q1, Q3]	2.6 [1.4-3.7]	4.0 [2.9-5.5]	<0.001*
ALT (U/l, Q1, Q3)	26.0 [21.0-32.0]	22.0 [16.0-36.0]	0.543
Mother's BMI (kg/m^2, ±SD)	31.6 ± 6.3	31.3 ± 7.0	0.843
Father's BMI (kg/m^2, ±SD)	29.0 ± 4.8	30.3 ± 5.1	0.158
Ethnicity, n. (%)[a]			0.119
Dutch	52 (62.7)	59 (77.6)	
Western	8 (9.6)	4 (5.3)	
Non-Western	23 (27.7)	13 (17.1)	
Parent's education, n. (%)[a]			0.795
Low	34 (42.5)	28 (37.3)	
Middle	34 (42.5)	34 (45.3)	
High	12 (15.0)	13 (17.3)	

Data presented as number (%), mean ± SD or median [Q1, Q3]. * p value ≤ 0.05. n = number, SD = standard deviation, BMI = body mass index, TC = total cholesterol, HDL = high density lipoprotein, LDL = low density lipoprotein, TG = Triglycerides, HbA1c = glycated hemoglobin, HOMA-IR = homeostatic model assessment for insulin resistance, ALT = alanine aminotransferase. [a] According to the Dutch Central Agency for Statistics[30,31].

BMI z-score

Model one revealed that the BMI z-score of children was reduced by an additional 0.12 (0.01–0.23; $p = 0.035$) after one and an additional 0.19 (0.04–0.34; $p = 0.012$) after two years of intervention compared to the BMI z-score of adolescents (Figure 2). Children showed a significant decrease in their BMI z-score after one and two years of intervention compared to baseline, the mean decrease was 0.15 (0.08–0.23; $p < 0.001$) and 0.25 (0.15– 0.35; $p < 0.001$), respectively. Adolescents showed a non-significant reduction in BMI z-score of 0.03 (−0.05–0.11; $p = 0.417$) after one year and 0.06 (−0.06–0.17; $p = 0.316$) after two years of intervention. Model two, adjusting for possible confounders (gender, parent's education, and ethnicity), showed similar results, but only the two-year difference in the change in BMI z-score between children and adolescents was significant. The BMI z-score of children was reduced by an additional 0.10 (−0.01–0.22; $p = 0.069$) and 0.18 (0.03–0.33; $p = 0.018$) after one and two years of intervention compared to adolescents.

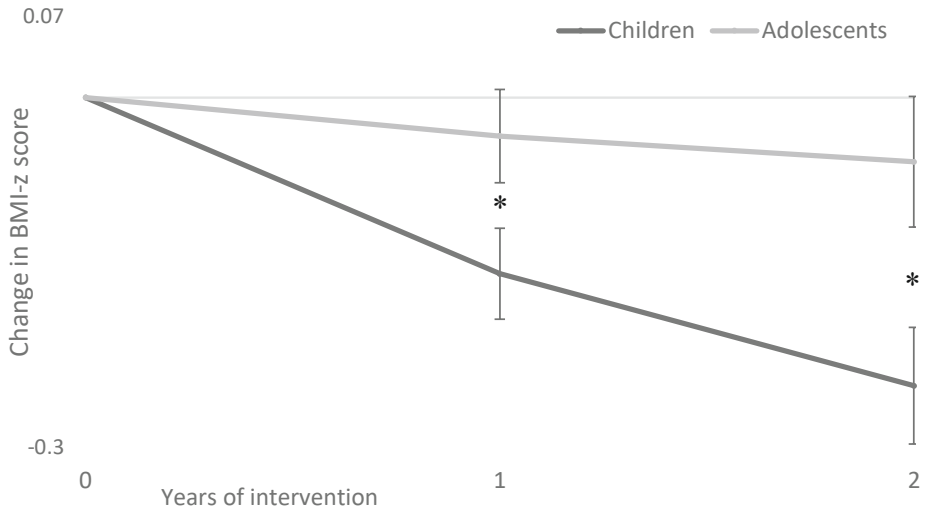


Figure 2. Decrease in BMI z-score after one and two years of intervention in children and adolescents determined by a marginal model for repeated measures (including group, time and their interaction)

Data presented as estimated marginal means and standard error. * p value ≤ 0.05, statistically different between children and adolescents.

After one year of intervention, 21 children (25.3%) and 13 adolescents (16.9%) changed category from severe obesity to obesity, and two adolescents (2.6%) changed to the overweight category. After two years of intervention, 43 children (78.2%) were still severely obese, whereas 11 children (20.0%) switched to the obese category and one child (1.8%) switched to the overweight category compared to baseline. When looking

at the adolescents after two years of intervention; 33 (78.6%) were still severely obese, five (11.9%) changed to the obese category and four (9.5%) changed to the overweight category, compared to baseline (Figure 3).

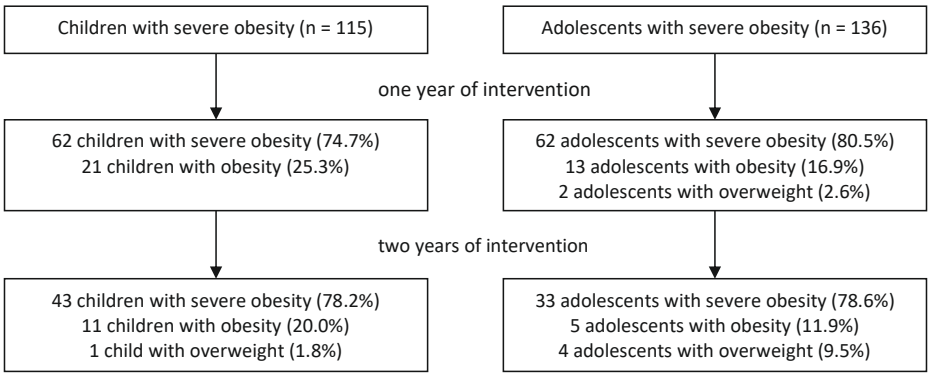


Figure 3. Change in IOTF criteria after one and two years of intervention presented in children and adolescents separately

Data presented as number (%). n = number, IOTF = International Obesity Task Force.

Children more often achieved a clinically significant decrease in their BMI z-score (≥0.25) compared to adolescents; 27 children (32.5%) versus 12 adolescents (15.6%; $p = 0.013$) after one year, and 27 children (49.1%) versus 10 adolescents (23.8%; $p = 0.011$) after two years of intervention. The BMI z-score of children who achieved clinically significant weight loss reduced with 0.50 ± 0.22 after one and 0.53 ± 0.19 after two years of intervention, whereas the BMI z-score of the adolescents with clinically significant weight loss decreased with 0.72 ± 0.50 after one and 0.81 ± 0.53 after two years of intervention. The majority of the children and the adolescents who did not achieve clinically significant weight loss after one year did not obtain this after two years or dropped out of the COACH program, although 12 children (21.4%) and 3 adolescents (4.6%) achieved clinically significant weight loss in the second year of intervention.

Cardio metabolic health parameters

Regarding the changes in cardio metabolic health parameters after one and two years of intervention, no significant differences were found between the two age groups, except for the change in TC concentration after two years of intervention (Table 2). Children had a decrease in TC concentration of 0.6 ± 0.9 mmol/L, whereas adolescents had a TC decrease of 0.1 ± 0.8 mmol/L ($p = 0.044$). In children, no significant changes from baseline in cardio metabolic health parameters were observed after one year of intervention. After two years, significant decreases from baseline in TC concentration (0.6 ± 0.9 mmol/L; $p = 0.003$), LDL concentration (0.5 ± 0.6 mmol/L; $p = 0.004$) and

HbA1c concentration (0.1 ± 0.2%; $p = 0.018$) were found in children. In adolescents, no significant reductions in cardio metabolic health parameters were detected after one and two years of intervention, except for HbA1c. On average, HbA1c decreased 0.2 ± 0.3% ($p < 0.001$) after one and 0.3 ± 0.3% ($p = 0.006$) after two years compared to baseline. At baseline fewer children had abnormal values of HDL and HOMA-IR compared to adolescents; 6.8% (n = 5) versus 27.0% (n = 20; $p = 0.001$) and 51.5% (n = 34) versus 78.3% (n = 54; $p = 0.001$), respectively. After one and two years of intervention, no differences between the number of children and adolescents with abnormal values of cardio metabolic health parameters were observed.

Table 2. Change in cardio metabolic health parameters after one and two years of intervention in and between children and adolescents

	Children		**Adolescents**	
	Baseline – Year 1 Mean ± SD (n)	*Baseline - Year 2 Mean ± SD (n)*	*Baseline – Year 1 Mean ± SD (n)*	*Baseline – Year 2 Mean ± SD (n)*
TC (mmol/L)	- 0.1 ± 0.6 (29)	- 0.6 ± 0.9 (21) * #	- 0.1 ± 0.6 (34)	- 0.1 ± 0.8 (15)
HDL (mmol/L)	0.0 ± 0.2 (29)	- 0.1 ± 0.3 (21)	0.0 ± 0.2 (34)	0.0 ± 0.3 (15)
LDL (mmol/L)	- 0.1 ± 0.6 (29)	- 0.5 ± 0.6 (21) *	- 0.1 ± 0.7 (33)	- 0.1 ± 0.8 (15)
TG (mmol/L)	0.0 ± 0.4 (29)	- 0.3 ± 0.6 (21)	0.1 ± 0.7 (33)	0.0 ± 0.6 (15)
Fasting glucose (mmol/L)	0.2 ± 0.6 (27)	- 0.1 ± 0.7 (20)	0.2 ± 0.8 (34)	0.1 ± 0.9 (15)
HbA1c (%)	- 0.1 ± 0.4 (27)	- 0.1 ± 0.2 (21) *	- 0.2 ± 0.3 (34) *	- 0.3 ± 0.3 (15) *
HOMA-IR	0.5 ± 2.5 (23)	0.0 ± 2.5 (15)	0.5 ± 2.2 (29)	- 0.3 ± 1.9 (11)
ALT (U/L)	- 3.0 [-17.0-3.3] (28)	-6.5 [-27.8-0.8] (21)	0.0 [-4.0-2.0] (34)	5.0 [-13.0-22.0] (15)

Data presented as mean ± SD or median [Q1, Q3].
* p value ≤ 0.05, statistically different change at year 1 or 2 compared to baseline in children and adolescents separately.
# p value ≤ 0.05, statistically different between children and adolescents.
n = number, SD = standard deviation, TC = total cholesterol, HDL = high density lipoprotein, LDL = low density lipoprotein, TG = Triglycerides, HbA1c = glycated hemoglobin, HOMA-IR = homeostatic model assessment for insulin resistance, ALT = alanine aminotransferase.

DISCUSSION

Global authorities have recognized the need for strategies to prevent and treat severe obesity in children, as children and adolescents with severe obesity face immediate and long-term health risks[1,8,9]. This study compared the effectiveness of the COACH lifestyle intervention on health parameters between children and adolescents with severe obesity. During the long-term tailored lifestyle intervention health parameters improved in children with severe obesity, especially after two years of intervention.

Compared to this younger age group, fewer improvements in health parameters were observed in adolescents with severe obesity.

The findings of the present study are in line with the findings of previously conducted research, demonstrating a larger response of lifestyle interventions in children compared to adolescents with severe obesity[11,12]. Knop et al. reported that 48.5% of the children with severe obesity reached clinically significant weight loss (defined as a BMI z-score decline of > 0.25) after a one-year lifestyle intervention, whereas only 20.0% of the adolescents achieved this weight loss[11]. Our study revealed that 32.5% of the children versus 15.6% of the adolescents achieved clinically significant weight loss after one year of intervention, and 49.1% of the children versus 23.8% of the adolescents after two years of intervention. These results suggest that a selected group of adolescents respond minimally to lifestyle interventions. Therefore, future research should focus on identifying this selected group of non-responsive adolescents. For this particular group other treatment options should be sought such as enhanced lifestyle interventions or additional medical and surgical interventions.

Although not well understood, the difference in the effectiveness of lifestyle interventions between children and adolescents might be explained by, amongst others, a declined influence of parents during adolescence[18]. Previous research has shown the importance of parental involvement in childhood obesity interventions[8]. The diminished parental influence and the increasing autonomy of the adolescents may also explain the high dropout rates in our study. Secondly, adolescence is a developmental period characterized by physical and cognitive development that is accompanied by stress. Stress is associated with an increased risk of mental and cardio metabolic dysfunction and food related coping mechanisms that might contribute to the limited effectiveness of lifestyle interventions in adolescents with severe obesity[32,33]. Thirdly, decreased physical activity in older compared to younger children could also partly explain the difference in the effectiveness of lifestyle interventions between children and adolescents[33].

In addition to weight loss, it is important to evaluate the effect of lifestyle interventions on cardio metabolic health parameters to assess the health risks of children and adolescents with severe obesity. Previous literature revealed the positive effects of lifestyle interventions on cardio metabolic health parameters in children and adolescents with severe obesity[10,14,15]. However, these studies did not differentiate between younger and older age groups, while it is known that the younger age group has a larger BMI z-score decrease during these interventions compared to the older age group[11,12]. Although the numbers of children and adolescents with abnormal cardio metabolic health parameters in our study were small, children had a greater decrease

in TC concentration compared to adolescents after two years of intervention. Besides this, significant decreases of TC, LDL and HbA1c concentrations were found after two years of intervention in children, and in adolescents significant decreases of HbA1c were seen. In the other cardio metabolic health parameters similar trends were found although not significant, especially in the children after two years of intervention. However, the changes in cardio metabolic health parameters were small. This could be due to normal baseline values of cardio metabolic health parameters in most children and adolescents. Therefore, future studies with a larger number of participants with abnormal values of cardio metabolic health parameters are warranted to evaluate differences in the effectiveness of lifestyle interventions on cardio metabolic health parameters between children and adolescents with severe obesity.

This study has several limitations. The first limitation is the absence of a control group without a lifestyle intervention. Therefore, our study could not take into account the natural course of the weight of children and adolescents with severe obesity over time. Although, the exact natural course is unknown, it is established that youth with severe obesity are at greater risk of becoming obese in adulthood compared to youth with obesity[3]. Secondly, the two age groups may be different in terms of hereditary contributions and psychosocial factors. Unfortunately, due to the design of the study, not all these influential factors could be taken into account. Another limitation is the higher exclusion and dropout rate in the group of adolescents. Whilst this may be seen as a study limitation, it also points out an important bottleneck in the daily practice of healthcare professions, namely a lowered adherence to intervention as age increases[19]. Besides this, the available amount of data with regard to cardio metabolic health parameters after one and two years of intervention was limited. At last, body composition measurements in combination with BMI z-score and cardio metabolic health parameters would have been a more reliable indicator for weight loss and general health instead of BMI z-score and cardio metabolic health parameters alone.

CONCLUSION

During our tailored lifestyle intervention, a positive and maintained effect on health parameters was observed in children with severe obesity. Compared to children, the effect on health parameters was less pronounced in adolescents with severe obesity. Although a small subgroup of adolescents achieved clinically significant weight loss during the current lifestyle intervention, the majority of the adolescents were unresponsive. These results advocate starting treatment for severe obesity at an early age. Additionally, for a selected group of adolescents, enhanced lifestyle interventions possibly supplemented with medical or surgical treatment options are needed.

REFERENCES

1. World Health Organization. Report of the commission on ending childhood obesity 2017. Available from: https://www.who.int/end-childhood-obesity/publications/echo-plan-executive-summary/en/.
2. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. Lancet. 2017;390(10113):2627-42.
3. Bass R, Eneli I. Severe childhood obesity: an under-recognised and growing health problem. Postgrad Med J. 2015;91(1081):639-45.
4. Wabitsch M, Moss A, Kromeyer-Hauschild K. Unexpected plateauing of childhood obesity rates in developed countries. BMC Med. 2014;12:17.
5. van Dommelen P, Schönbeck Y, van Buuren S, HiraSing RA. Trends in a life threatening condition: morbid obesity in dutch, Turkish and Moroccan children in The Netherlands. PLoS One. 2014;9(4):e94299.
6. Skelton JA, Cook SR, Auinger P, Klein JD, Barlow SE. Prevalence and trends of severe obesity among US children and adolescents. Acad Pediatr. 2009;9(5):322-9.
7. van Emmerik NM, Renders CM, van de Veer M, van Buuren S, van der Baan-Slootweg OH, Kist-van Holthe JE, et al. High cardiovascular risk in severely obese young children and adolescents. Arch Dis Child. 2012;97(9):818-21.
8. Kelly AS, Barlow SE, Rao G, Inge TH, Hayman LL, Steinberger J, et al. Severe obesity in children and adolescents: identification, associated health risks, and treatment approaches: a scientific statement from the American Heart Association. Circulation. 2013;128(15):1689-712.
9. Twig G, Yaniv G, Levine H, Leiba A, Goldberger N, Derazne E, et al. Body-Mass Index in 2.3 Million Adolescents and Cardiovascular Death in Adulthood. N Engl J Med. 2016;374(25):2430-40.
10. Rijks JM, Plat J, Mensink RP, Dorenbos E, Buurman WA, Vreugdenhil AC. Children With Morbid Obesity Benefit Equally as Children With Overweight and Obesity From an Ongoing Care Program. J Clin Endocrinol Metab. 2015;100(9):3572-80.
11. Knop C, Singer V, Uysal Y, Schaefer A, Wolters B, Reinehr T. Extremely obese children respond better than extremely obese adolescents to lifestyle interventions. Pediatr Obes. 2015;10(1):7-14.
12. Danielsson P, Kowalski J, Ekblom Ö, Marcus C. Response of severely obese children and adolescents to behavioral treatment. Arch Pediatr Adolesc Med. 2012;166(12):1103-8.
13. Kalarchian MA, Levine MD, Arslanian SA, Ewing LJ, Houck PR, Cheng Y, et al. Family-based treatment of severe pediatric obesity: randomized, controlled trial. Pediatrics. 2009;124(4):1060-8.
14. van der Baan-Slootweg O, Benninga MA, Beelen A, van der Palen J, Tamminga-Smeulders C, Tijssen JG, et al. Inpatient treatment of children and adolescents with severe obesity in the Netherlands: a randomized clinical trial. JAMA Pediatr. 2014;168(9):807-14.

15. Makkes S, Renders CM, Bosmans JE, van der Baan-Slootweg OH, Hoekstra T, Seidell JC. One-year effects of two intensive inpatient treatments for severely obese children and adolescents. BMC Pediatr. 2016;16:120.

16. Anderson YC, Wynter LE, O'Sullivan NA, Wild CEK, Grant CC, Cave TL, et al. Two-year outcomes of Whānau Pakari, a multi-disciplinary assessment and intervention for children and adolescents with weight issues: A randomized clinical trial. Pediatr Obes. 2021;16(1):e12693.

17. Skodvin VA, Lekhal S, Kommedal KG, Benestad B, Skjåkødegård HF, Danielsen YS, et al. Lifestyle intervention for children and adolescents with severe obesity - results after one year. Tidsskr Nor Laegeforen. 2020;140(9).

18. De Goede IH, Branje SJ, Meeus WH. Developmental changes in adolescents' perceptions of relationships with their parents. J Youth Adolesc. 2009;38(1):75-88.

19. Danielsson P, Svensson V, Kowalski J, Nyberg G, Ekblom O, Marcus C. Importance of age for 3-year continuous behavioral obesity treatment success and dropout rate. Obes Facts. 2012;5(1):34-44.

20. Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. Pediatr Obes. 2012;7(4):284-94.

21. Mead E, Brown T, Rees K, Azevedo LB, Whittaker V, Jones D, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese children from the age of 6 to 11 years. Cochrane Database Syst Rev. 2017;6(6):Cd012651.

22. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6(6):Cd012691.

23. Divya Jindal-Snape EFSH, Dianne Cantali, William Barlow, Stephen MacGillivray. Systematic literature review of primary-secondary transitions: International research. Review of Education. 2020;8(2):526-66.

24. Richtlijnen Goede Voeding 2015. Available from: https://www.gezondheidsraad.nl/documenten/adviezen/2015/11/04/richtlijnen-goede-voeding-2015.

25. Ford AL, Hunt LP, Cooper A, Shield JP. What reduction in BMI SDS is required in obese adolescents to improve body composition and cardiometabolic health? Arch Dis Child. 2010;95(4):256-61.

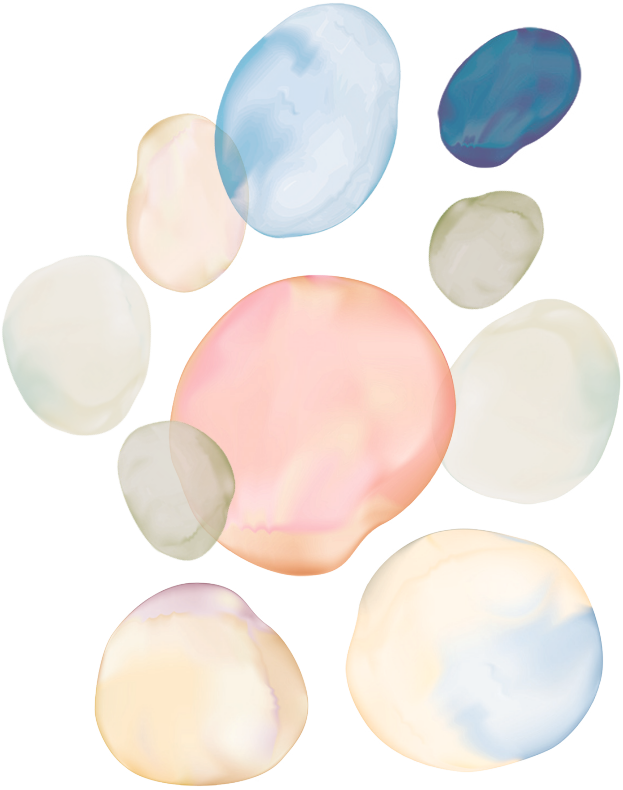
26. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28(7):412-9.

27. Expert panel on integrated guidelines for cardiovascular health and risk reduction in children and adolescents: summary report. Pediatrics. 2011;128 Suppl 5(Suppl 5):S213-56.

28. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2020. Diabetes Care. 2020;43(Suppl 1):S14-s31.

29. Vos MB, Abrams SH, Barlow SE, Caprio S, Daniels SR, Kohli R, et al. NASPGHAN Clinical Practice Guideline for the Diagnosis and Treatment of Nonalcoholic Fatty Liver Disease in Children: Recommendations from the Expert Committee on NAFLD (ECON) and the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN). J Pediatr Gastroenterol Nutr. 2017;64(2):319-34.

30. Centraal Bureau voor de Statistiek. Persoon met een westerse migratieachtergrond. Available from: www.cbs.nl/nl-nl/onze-diensten/methoden/begrippen/persoon-met-een-westerse-migratieachtergrond.
31. Centraal Bureau voor de Statistiek. Opleidingsniveau. Available from: www.cbs.nl/nl-nl/nieuws/2019/33/verschil-levensverwachting-hoog-en-laagopgeleid-groeit/opleidingsniveau.
32. Dimitratos SM, Swartz JR, Laugero KD. Pathways of parental influence on adolescent diet and obesity: a psychological stress-focused perspective. Nutr Rev. 2022;80(7):1800-10.
33. Ten Velde G, Plasqui G, Dorenbos E, Winkens B, Vreugdenhil A. Objectively measured physical activity and sedentary time in children with overweight, obesity and morbid obesity: a cross-sectional analysis. BMC Public Health. 2021;21(1):1558.



PART II

BARIATRIC SURGERY

CHAPTER 5

A POPULATION-BASED COHORT STUDY ON EFFICACY AND SAFETY OF BARIATRIC SURGERY IN YOUNG ADULTS VERSUS ADULTS

Kelly G.H. van de Pas
Aliyar Esfandiyari Noushi
Loes Janssen
Anita C.E. Vreugdenhil
Wouter K.G. Leclercq
François M.H. van Dielen

Obesity surgery 2023.

ABSTRACT

Introduction

Bariatric surgery is the most effective treatment for severe obesity in adults and has shown promising results in young adults. Lack of insight regarding efficacy and safety outcomes might result in delayed bariatric surgery utilization in young adults. Therefore, this study aimed to assess the efficacy and safety of bariatric surgery in young adults compared to adults.

Methods

This is a nationwide population-based cohort study utilizing data from the Dutch Audit Treatment of Obesity (DATO). Young adults (aged 18–25 years) and adults (aged 35–55 years) who underwent primary Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG) were included. Primary outcome was percentage total weight loss (%TWL) until five years postoperatively.

Results

A total of 2,822 (10.3%) young adults and 24,497 (89.7%) adults were included. The follow-up rates of the young adults were lower up to five years postoperatively (46.2% versus 56.7% three years postoperatively; $p < 0.001$). Young adults who underwent RYGB showed superior %TWL compared to adults until four years postoperatively (33.0 ± 9.4 versus 31.2 ± 8.7 three years after surgery; $p < 0.001$). Young adults who underwent SG showed superior %TWL until five years postoperatively (29.9 ± 10.9 versus 26.2 ± 9.7 three years after surgery; $p < 0.001$). Postoperative complications ≤ 30 days were more prevalent among adults, 5.3% versus 3.5% ($p < 0.001$). No differences were found in the long-term complications. Young adults revealed more improvement of hypertension (93.6% versus 78.9%), dyslipidemia (84.7% versus 69.2%) and musculoskeletal pain (84.6% versus 72.3%).

Conclusion

Bariatric surgery appears to be at least as safe and effective in young adults as in adults. Based on these findings the reluctance towards bariatric surgery in the younger age group seems unfounded.

INTRODUCTION

Bariatric surgery has proven to be the most effective treatment for severe obesity in adults and has shown promising results in young adults in achieving weight loss and remission of obesity-related comorbidities[1,2]. A potential benefit of bariatric surgery at a younger age is a shorter exposure to obesity-related comorbidities, such as type 2 diabetes mellitus (T2DM), which can lead to less medical complications and treatment resistance[3,4]. It might also limit the obesity-related psychosocial 'challenges' such as bullying and stigmatizing at this vulnerable age[5]. However, bariatric surgery utilization in young adults lags behind. This might among others be attributed to a lack of understanding regarding efficacy and safety outcomes in this younger age group[6]. The number of young adults that underwent bariatric surgery in the United States even slightly decreased in the last couple of years. In 2006 22.4% of all patients who underwent bariatric surgery were young adults compared to 20.3% in 2015[7].

Prior research has mainly focused on the efficacy and safety of bariatric surgery in the whole group of adults. Only a small number of studies addressed the effects of bariatric surgery in the younger age group. Many of these studies targeted adolescents (generally ≤ 19 years old) and revealed at least comparable results when it comes to weight loss, and equal or more surgery related complications compared to adults[8-12]. In line with this, a Swedish national registry study among 3,531 young adults (aged 18–25 years) and 17,137 adults (aged ≥ 26 years) observed superior weight loss in young adults compared to adults up to five years postoperatively. Besides this, serious adverse events, defined as a Clavien-Dindo ≥ 3b, were more prevalent among young adults between 6 weeks and up to 5 years after a Roux-en-Y gastric bypass (RYGB)[13]. Young adults and adults who underwent a sleeve gastrectomy (SG) were excluded from the study, despite it being the most frequently performed bariatric procedure worldwide along with the RYGB[14].

In order to obtain a better understanding on the efficacy and safety of bariatric surgery in the younger age group, this study aimed to compare weight-related outcomes and complications between young adults (aged 18–25 years) and adults (aged 35–55 years) who underwent a RYGB or SG.

METHODS

Study design

This nationwide population-based cohort study was conducted with pseudo-anonymized data derived from the Dutch Audit Treatment of Obesity (DATO). The DATO is a national mandatory registry for all bariatric procedures performed in the Netherlands starting in 2015 and including all 20 bariatric surgical centers[15]. The Institutional Review Board of the Máxima MC approved this study. Patient consent was not required for this retrospective cohort study according to Dutch law (Medical Research Involving Human Subjects Act).

Setting and participants

Eligibility for bariatric surgery in the Netherlands is assessed according to the Dutch guideline surgical treatment of obesity[16]. The bariatric surgery candidates are evaluated by a multidisciplinary team and need to be ≥ 18 years and have a pre-operative body mass index (BMI) ≥ 40 kg/m^2 or a BMI ≥ 35 kg/m^2 accompanied by an obesity-related comorbidity. Young adults (aged 18–25 years) and adults (aged 35–55 years) who received a primary RYGB or SG between 2015 and 2020 were screened for inclusion in this study. A time range of 10 years around the mean age of adults undergoing bariatric surgery (45 years) was chosen as the control group for the young adults[17]. Participants were excluded when they underwent a two-stage procedure, had a missing body weight 12 months after surgery or had a BMI < 35 kg/m^2.

Outcome parameters – weight loss

Outcome parameters were collected at baseline and one to five years (± three months) after surgery during outpatient clinic visits. Percentage total weight loss (%TWL) one to five years after surgery was the primary outcome and was calculated using the following formula: (preoperative weight-postoperative weight)/preoperative weight * 100%. Secondary outcomes were successful weight loss and weight regain. Percentage TWL ≥ 20% was considered as successful weight loss[18,19]. Weight regain was defined as ≥ 20% regain of a patients' lost weight at their last follow-up visit after initial successful weight loss one year after surgery[18,19].

Outcome parameters – complications

Complications were divided into perioperative complications, postoperative complications ≤ 30 days and postoperative complications > 30 days. The Clavien-Dindo (CD) classification of surgical complications was used to classify the postoperative complications[20]. In case of multiple complications in one patient, only the highest CD complication was used in the CD and readmission analyses. In the other analyses all complications were used.

Outcome parameters – comorbidities

Secondary outcomes included the obesity-related comorbidities, e.g., T2DM, hypertension, dyslipidemia, gastroesophageal reflux disease (GERD), obstructive sleep apnea (OSA), and musculoskeletal pain. The postoperative comorbidity status was classified as cured or improved, and equal or worsened according to the DATO, and compared to the preoperative comorbidity status[21]. The comorbidity status of one and two years after surgery was combined, the last status was chosen. This outcome was only assessed up to two years postoperatively, as the comorbidity status was frequently missing at three, four and five years after surgery which led to small numbers in the young adults group.

Statistical analysis

Statistical analyses were conducted using IBM SPSS statistic software, version 25.0, Armonk, NY. Numerical data (baseline characteristics, weight loss) were analyzed using independent-samples t-test and presented as mean ± standard deviation (SD). Categorical data (baseline characteristics, complications, revision procedures and obesity-related comorbidities) were analyzed using chi-square test and presented as number (percentage). Linear mixed model (LMM) analysis was used to assess %TWL one to five years after surgery between adults and young adults. In this model the factor-analytic covariance matrix and restricted maximum likelihood estimation were utilized. In the model, an interaction variable for age category and bariatric procedure was added, since %TWL might depend on the type of bariatric procedure. In case of a significant interaction, the effect of age category was presented separately for RYGB and SG. Furthermore, corrections were made based on the variables having a significant association with %TWL in univariate analyses. At last, a sensitivity analysis was performed in which %TWL was only assessed up to three years after surgery due to the large lost to follow-up four and five years after surgery. In a second sensitivity analysis, the %TWL until three years after surgery was compared between participants with four- and five-year follow-up data and participants with only one-to-three-year follow-up data using an independent-samples t-test. All data were analyzed according to the intention to treat principle and p values ≤ 0.05 were considered statistically significant.

RESULTS

A total of 33,934 young adults and adults underwent a primary RYGB or SG between 2015 and 2020 in the Netherlands. Of them 27,319 (80.5%) were included, 925 young adults (24.7%) and 5690 adults (18.8%) were excluded due to various reasons such as a

BMI < 35 kg/m^2 or a missing weight 12 months after surgery (Fig. 1). In this study 2,822 (10.3%) young adults and 24,497 (89.7%) adults were included. No clinically relevant differences were found between the in- and excluded young adults and adults regarding their age, gender, BMI and obesity-related comorbidities (data not shown). Compared to the adults, the follow-up rates of the young adults were lower (all $p < 0.001$). Two through five-year follow-up rates in the young adults group were 62.9%, 46.2%, 36.8% and 28.3%, respectively. Whereas in the adult group, two through five-year follow-up rates were 71.4%, 56.7%, 45.8% and 38.4%.

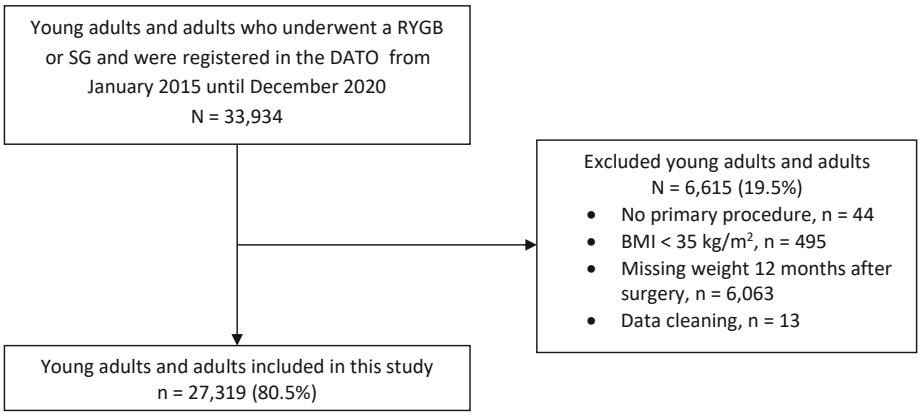


Figure 1. Flow diagram of the inclusion and exclusion of participants

Young adults = aged 18-25 years, adults = aged 35-55 years, RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy, DATO = Dutch Audit Treatment of Obesity.

Baseline characteristics and operative features

In the young adults group, there were more females compared to the adults group, 87.0% versus 79.1% ($p < 0.001$). Furthermore, the preoperative BMI was higher in the young adults, whereas all the preoperative comorbidities were more prevalent among the adults (Table 1). In 2015 only 8.6% of the bariatric procedures were performed in young adults, this increased over time and became 12.3% in 2020. Young adults more often underwent a SG compared to adults (45.8% versus 22.9%; $p < 0.001$). The number of young adults undergoing bariatric surgery increased by age year. Only 2.3% (n = 66) of the young adults were 18 years old, whereas 20.1% (n = 567) were 25 years old. On the contrary, the mean BMI of the young adults who underwent bariatric surgery generally decreased by age year. The mean BMI of the 18-year-olds was 46.0 ± 5.8 kg/m^2, whereas the mean BMI of the 25-year-olds was 44.5 ± 5.2 kg/m^2. This trend regarding number of bariatric procedures and BMI was not observed in the adults group.

Table 1. Baseline characteristics and operative features of the included young adults and adults

	Young adults, n = 2,822 (10.3%)	**Adults, n = 24,497 (89.7%)**	***p* value**
Age (years, ±SD)	22.5 ± 2.0	45.9 ± 5.8	<0.001*
Sex, n. (%)			
Female	2,455 (87.0)	19,381 (79.1)	<0.001*
Male	367 (13.0)	5,116 (20.9)	
Preoperative BMI (kg/m^2, ±*SD)*	44.4 ± 4.9	42.8 ± 5.2	<0.001*
Preoperative comorbidities, n. (%)			
T2DM	97 (3.4)	4,510 (18.4)	<0.001*
Hypertension	137 (4.9)	8,709 (35.6)	<0.001*
Dyslipidemia	145 (5.1)	4,761 (19.4)	<0.001*
GERD	248 (8.8)	4,012 (16.4)	<0.001*
OSA	119 (4.2)	4,508 (18.4)	<0.001*
Musculoskeletal pain	881 (31.2)	11,140 (45.5)	<0.001*
Year of surgery, n. (%)[1]			<0.001*
2015	394 (8.6)	4,203 (91.4)	
2016	483 (9.3)	4,704 (90.7)	
2017	508 (10.7)	4,218 (89.3)	
2018	510 (10.7)	4,241 (89.3)	
2019	525 (11.0)	4,257 (89.0)	
2020	402 (12.3)	2,874 (87.7)	
Bariatric procedure, n. (%)			<0.001*
RYGB	1,529 (54.2)	18,890 (77.1)	
SG	1,293 (45.8)	5,607 (22.9)	
Length of hospital stay in days [Q1, Q3]	1 [1 - 2]	1 [1 - 2]	0.632

Data presented as number (%), mean (±SD) or median [Q1, Q3]. *p value is below the threshold of ≤0.05.
Young adults = aged 18-25 years, adults = aged 35-55 years, n = number, BMI = body mass index, T2DM = type 2 diabetes mellitus, GERD = gastroesophageal reflux disease, OSA = obstructive sleep apnea, RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy.
[1] (number of operated young adults or adults/total number of bariatric procedures during that year) * 100.

Weight loss

Both when young adults underwent a RYGB or SG, %TWL was superior compared to the %TWL of adults one to five years after surgery (Table 2). In a sensitivity analysis, in which %TWL until three years postoperatively was compared between participants with four- and five-year follow-up data and participants with only one-to-three-year follow-up data, similar results were found. Furthermore, successful weight loss (≥ 20% TWL) was more prevalent among young adults one to two years after surgery in the ones who received a RYGB and one to three years after surgery in the ones who received a SG (Table 2). Weight regain occurred in 148 young adults (15.7%) and 2,351 adults (17.6%; p = 0.136) who underwent a RYGB, and in 175 young adults (21.2%) and 1,038 adults (26.3%; p = 0.002) who underwent a SG.

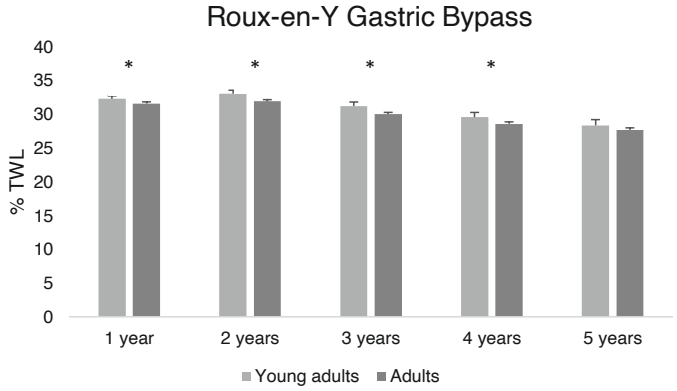
Table 2. Percentage TWL and successful weight loss between young adults and adults who underwent a primary RYGB or SG

	Young adults		**Adults**		***p* value**
	RYGB		*RYGB*		
TWL	n.	% ±SD	n.	% ±SD	
1 year	1,529	34.4 ± 7.2	18,890	32.6 ± 7.2	<0.001*
2 years	813	35.2 ± 8.4	11,927	33.1 ± 8.3	<0.001*
3 years	452	33.0 ± 9.4	7,622	31.2 ± 8.7	<0.001*
4 years	280	31.0 ± 10.4	4,717	29.6 ± 8.9	0.024*
5 years	160	29.7 ± 10.6	2,788	28.8 ± 9.2	0.282
Successful weight loss[1]	n.	%	n.	%	
1 year	1,487	97.3	18,143	96.0	0.018*
2 years	776	95.4	11,179	93.7	0.048*
3 years	404	89.4	6,849	89.9	0.744
4 years	238	85.0	4,048	85.8	0.704
5 years	134	83.8	2,310	82.9	0.770
	SG		*SG*		
TWL	n.	% ±SD	n.	% ±SD	
1 year	1,293	32.1 ± 8.4	5,607	29.3 ± 8.0	<0.001*
2 years	709	32.1 ± 10.1	3,516	28.4 ± 9.2	<0.001*
3 years	423	29.9 ± 10.9	2,221	26.2 ± 9.8	<0.001*
4 years	230	28.7 ± 12.3	1,294	25.6 ± 9.8	<0.001*
5 years	88	28.3 ± 14.4	636	24.3 ± 10.6	0.012*
Successful weight loss[1]	n.	%	n.	%	
1 years	1,188	91.9	4,948	88.2	<0.001*
2 years	626	88.3	2,886	82.1	<0.001*
3 years	343	81.1	1,640	73.8	0.002*
4 years	173	75.2	920	71.1	0.201
5 years	63	71.6	407	64.0	0.162

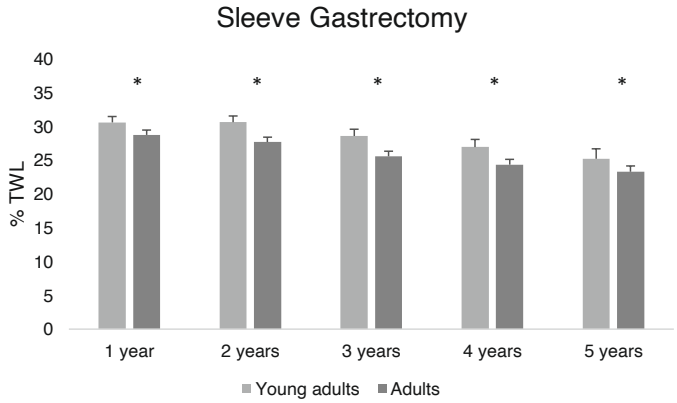
Data presented as mean (±SD) and n (%). * p value is below the threshold of ≤0.05.
Young adults = aged 18-25 years, adults = aged 35-55 years, RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy, TWL = total weight loss, n = number.
[1] Defined as ≥ 20% TWL.

A linear mixed model (LMM) analyzed the association between %TWL and age category (young adults versus adults). This analysis was stratified for bariatric procedure, since age category and bariatric procedure revealed a significant interaction effect on %TWL. Besides this, corrections were made for sex, hypertension, T2DM, OSA, dyslipidemia, BMI and postoperative complications > 30 days as these variables were significantly associated with %TWL in univariate analyses (Supporting Information Table S1, https://link.springer.com/article/10.1007/s11695-023-06673-5#MOESM1). After adjusting for these variables, LMM revealed a higher %TWL one to four years after surgery for young adults who underwent a RYGB and one to five years after surgery for young adults who underwent a SG (Fig. 2). In a sensitivity analysis, in which %TWL was only assessed until

three years after surgery due to the large lost to follow-up four and five years after surgery, similar results were found.



A



B

Figure 2. Percentage TWL between young adults and adults until five years after surgery, stratified for bariatric procedure (RYGB = panel A, SG = panel B) and determined by a linear mixed model (including age category, time and their interaction)

Data presented as estimated marginal means and 95% confidence intervals. * *p* value is below the threshold of ≤0.05.

RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy, TWL = total weight loss, young adults = aged 18-25 years, adults = aged 35-55 years.

Complications

As shown in Table 3, more peroperative gastrointestinal perforations were observed in the adults compared to the young adults; 85 (0.3%) versus 1 (0.0%; $p = 0.005$). Furthermore, the total number of postoperative complications and severe postoperative

complications (CD ≥ III) ≤ 30 days were higher in the adults group. When looking into the postoperative complications ≤ 30 days, major bleedings and anastomotic leakages were more prevalent among adults compared to young adults; 393 (1.6%) versus 20 (0.7%; $p < 0.001$), and 133 (0.5%) versus 4 (0.1%; $p = 0.004$). No differences between the incidence of postoperative complications > 30 days were found between the two age groups.

Table 3. Comparison of per- and postoperative complications between young adults and adults who underwent a primary RYGB or SG

	Young adults, n = 2,822	**Adults, n = 24,497**	***p* value**
Peroperative complications, n. (%)	19 (0.7)	235 (1.0)	0.138
Perforation	1 (0.0)	85 (0.3)	0.005*
Bleeding	7 (0.2)	63 (0.3)	0.935
Spleen injury	3 (0.1)	34 (0.1)	1.000
Liver injury	2 (0.1)	32 (0.1)	0.575
Number of readmissions ≤30 days[1], n. (%)	58 (2.1)	595 (2.4)	0.219
Postoperative complications ≤30 days[1], n. (%)			
CD grade I	14 (0.5)	192 (0.8)	0.094
CD grade II	23 (0.8)	201 (0.8)	0.976
CD grade III	30 (1.1)	470 (1.9)	0.001*
CD grade IV	3 (0.1)	116 (0.5)	0.005*
Total number of postoperative complications ≤30 days, n. (%)	98 (3.5)	1,303 (5.3)	<0.001*
Type of surgical complications ≤30 days, n. (%)			
Major bleeding	20 (0.7)	393 (1.6)	<0.001*
Anastomotic leakage	4 (0.1)	133 (0.5)	0.004*
Intra-abdominal abscess	2 (0.1)	55 (0.2)	0.090
Intestinal obstruction	8 (0.3)	57 (0.2)	0.600
Anastomotic stricture	4 (0.1)	15 (0.1)	0.124
Stomach ulcer	0 (0)	6 (0.0)	NA
Bowel injury	0 (0)	19 (0.1)	NA
Number of readmissions >30 days[1], n. (%)	120 (4.3)	1,032 (4.2)	0.921
Postoperative complications > 30 days[1], n. (%)			
CD grade I	4 (0.1)	51 (0.2)	0.456
CD grade II	10 (0.4)	96 (0.4)	0.761
CD grade III	119 (4.2)	1000 (4.1)	0.732
CD grade IV	1 (0)	8 (0)	0.939
Total number of postoperative complications >30 days, n. (%)	177 (6.3)	1,512 (6.2)	0.835

Data presented as number (%). *p value is below the threshold of ≤0.05.
Young adults = aged 18-25 years, adults = aged 35-55 years, RYGB = Roux-en-Y Gastric Bypass, SG = sleeve gastrectomy, n = number, CD = Clavien–Dindo classification, I is any deviation from the normal postoperative course without intervention, except some drugs such as anti-emetics, antipyretics, analgesics, diuretics and electrolytes; II is a complication requiring pharmacological treatment other than such allowed for grade I; III is a complication requiring intervention under anesthesia; IV is a complication resulting in organ failure, NA = not applicable.
[1] = only the highest CD complication has been registered for each patient.

Revision surgery

A total of 418 young adults and adults underwent revision surgery until December 2021, of which 54 were young adults (1.9%) and 364 were adults at the time of the primary procedure (1.5%; $p = 0.080$). The mean duration between primary and revision procedure was 27.7 months for young adults and 31.0 months for adults. Of the revision procedures 335 were primarily a SG (4.9% of the total number of SG) and 83 a RYGB (0.4% of the total number of RYGB; $p < 0.001$). In the young adult group, the most commonly performed revision procedure was a conversion to a gastric bypass (n = 39, 72.2%) and the main reason for revision was technical failure (n = 29, 53.7%) followed by weight regain (n = 12, 22.2%). In adults, the most frequently executed procedure was a conversion to a gastric bypass (n = 230, 63.2%) and the main reasons for revision procedures were also technical failure (n = 201, 55.2%) and weight regain (n = 64, 17.6%). Furthermore, in the adult group nine adults underwent a second revision procedure and one adult received a third revision procedure, whereas this wat not seen in the young adults.

Obesity-related comorbidities

With regard to the regression of obesity-related comorbidities one and two year after surgery, the young adults revealed more curation or improvement of hypertension, dyslipidemia and musculoskeletal pain (Table 4). No differences between the two age groups were found in the other obesity-related comorbidities.

DISCUSSION

Young adults are less likely to undergo bariatric surgery compared to adults, and this might be due to a lack of insight regarding long-term efficacy and safety outcomes[6]. Therefore, this study aimed to increase knowledge on the efficacy and safety of bariatric surgery in young adults using the Dutch National registry. In our study young adults revealed at least comparable weight loss results compared to adults during five years follow-up, both after a RYGB and SG. Moreover, no more postoperative complications and revision procedures were observed. Young adults even had less short-term postoperative complications and more improvement of hypertension, dyslipidemia and musculoskeletal pain.

Table 4. The regression of obesity-related comorbidities between young adults and adults who received a primary RYGB or SG

	Young adults 1-2 years after surgery			Adults 1-2 years after surgery			
	n. (%) [1]	Cured or improved n. (%)	Equal or worsened n. (%)	n.[1]	Cured or improved n. (%)	Equal or worsened n. (%)	*p* value
T2DM	64 (66.0)	57 (89.1)	7 (10.9)	3,714 (82.4)	3,377 (90.9)	339 (9.1)	0.607
Hypertension	109 (79.6)	102 (93.6)	7 (6.4)	7,363 (84.5)	5,812 (78.9)	1,551 (21.1)	<0.001*
Dyslipidemia	111 (76.6)	94 (84.7)	17 (15.3)	3,836 (80.6)	2,656 (69.2)	1,180 (30.8)	<0.001*
GERD	143 (57.7)	114 (79.7)	29 (20.3)	1,935 (48.2)	1,588 (82.1)	347 (17.9)	0.482
OSAS	69 (58.0)	57 (82.6)	12 (17.4)	3,562 (79.0)	2,983 (83.7)	579 (16.3)	0.800
Musculoskeletal pain	571 (64.8)	483 (84.6)	88 (15.4)	7,614 (68.3)	5,506 (72.3)	2,108 (27.7)	<0.001*

Data presented as number (%). * *P* value is below the threshold of ≤0.05.
Young adults = aged 18-25 years, adults = aged 35-55 years, RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy, n = number, T2DM = type 2 diabetes mellitus, GERD = gastroesophageal reflux disease, OSA = obstructive sleep apnea.
[1] Number of patients with comorbidity status at 1 or 2 years after surgery (patients with postoperative comorbidity status/number of patients with preoperative comorbidity* 100).

Bariatric surgery is at least as effective in young adults as in adults with regard to weight loss. Accordingly, a Dutch cohort study revealed similar %TWL up to three years after surgery between young adults (aged 18–25 years) and adults (aged 35–55 years) who underwent a SG and superior %TWL in young adults after a RYGB[22]. This study revealed similar results and even found superior %TWL between young adults and adults up to 5 years postoperatively. Potential reasons for the favorable weight loss in young adults might be the decline in energy expenditure due to a lower resting metabolic rate and a less active lifestyle later in life[23,24]. Based on our findings, bariatric surgery seems an effective treatment for severe obesity in young adults and even for adolescents as previous literature revealed comparable weight loss results between adolescents and adults[11,12]. However, not only weight loss is an important outcome measure of bariatric surgery and therefore future prospective studies should also focus on quality of life and monitor the long-term effects of bariatric surgery in this younger age group closely.

The low adherence and follow-up rates of young adults after bariatric surgery have raised concerns. A qualitative study among Dutch young adults who underwent bariatric surgery revealed that young adults find it hard to adhere to postoperative behavioral, dietary and physical recommendations[25]. In line with this, a Swedish national registry study found an increase of missed appointments and loss to follow up in young adults who underwent bariatric surgery compared to adults[13]. Similar results were seen in the five-year follow-up duration of this study. A possible explanation for the lower follow-up rates could lie in the developmental stage the young adults are in. They are more likely to move and go to college compared to adults. Nevertheless, the low follow-up rates of young adults might eventually lead to missed physical or psychological complications. Also, insufficient weight loss might not be detected at an early stage, nor can treatments such as dietary or psychological counseling be provided. A previous study also found that adolescents had more micronutrient deficiencies after bariatric surgery compared to adults, suggesting a lower adherence to multivitamin supplementation[11]. Therefore, clinical practice should focus on optimizing follow-up and compliance rates in the younger age group, for example by adjusting the clinical visits to the need of the young population, e.g., online visits and counseling or group sessions.

Inconsistent findings with regard to postoperative complications after bariatric surgery in young adults are described in pre-existing literature. The Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) database revealed that bariatric surgery is safe in youth and young adults (aged 15–24 years), as low rates of reoperation (1.1%), reintervention (1.1%) and readmission (3.7%) within 30 days were found[6]. A Dutch retrospective cohort study in 130 young adults (aged 18–25 years) observed similar complication rates between adults and young adults up to

three years after surgery[22]. In contrast to a large Swedish database study, in which more complications (including serious adverse events (CD 3b-5)) were observed in the young adults (aged 18–25 years) between 6 weeks until 5 years after surgery[13]. This study showed less postoperative complications < 30 days in the young adults group, whereas no differences between the two age groups were found regarding the long-term complications. These differences between complication rates might be explained by study design (cohort study versus database study), subdivision of long- and short-term complications, definition of young adults, and prevalence's of preoperative obesity-related comorbidities.

The effectiveness of bariatric surgery does not depend on weight loss alone and other factors such as the remission of obesity-related comorbidities are just as important. The Teen-Longitudinal Assessment of Bariatric Surgery study revealed similar rates of dyslipidemia remission and more remission of T2DM and hypertension in adolescents compared to adults[11]. In this study, more improvement of hypertension, dyslipidemia and musculoskeletal pain were found in the young adults. Abovementioned results favor bariatric surgery at a younger age, especially as a previous study showed that medical treatments for T2DM fail earlier in youth[26]. Nevertheless, our results should be interpreted with caution as there might be differences in the assessment and registration of obesity -related comorbidities among different Dutch hospitals and no long-term data were analyzed.

There are certain limitations to this registry study, inherent to its retrospective cohort design. There might be differences in the registration of data among the different hospitals and errors are likely to occur. Furthermore, some in depth information on operating techniques, obesity-related comorbidities, quality of life and physical and psychological complications (e.g., mental health issues, alcohol abuse) are missing in the national database. At last, there was a large loss to follow-up four and five years after surgery and especially in the young adults. This might have caused selection bias, as a previous study revealed that poor weight loss could be a reason for loss to follow-up[27]. However, a sensitivity analysis showed similar weight loss results at three years follow-up between patients with and without four- and five-year follow-up data, rendering large selection bias unlikely.

CONCLUSION

Bariatric surgery appears to be at least as safe and effective in young adults as in adults. Compared to adults, even favorable results regarding the improvement of obesity-related comorbidities and short-term complications were found in the younger age group. Based on these findings, the reluctance towards bariatric surgery in young adults seems unfounded. Furthermore, clinical practice should focus on optimizing follow-up and adherence rates so that weight regain, physical and psychosocial complications can be prevented or recognized and treated at an early stage.

REFERENCES

1. English WJ, Williams DB. Metabolic and Bariatric Surgery: An Effective Treatment Option for Obesity and Cardiovascular Disease. Prog Cardiovasc Dis. 2018;61(2):253-69.
2. van de Pas KGH, Bonouvrie DS, Janssen L, Romeijn MM, Luijten A, Leclercq WKG, et al. Roux-en-Y Gastric Bypass Versus Sleeve Gastrectomy in Young Adults: a Dutch Registry Study. Obes Surg. 2022;32(3):763-70.
3. Zeitler P, Hirst K, Pyle L, Linder B, Copeland K, Arslanian S, et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. N Engl J Med. 2012;366(24):2247-56.
4. Kahn SE, Haffner SM, Heise MA, Herman WH, Holman RR, Jones NP, et al. Glycemic durability of rosiglitazone, metformin, or glyburide monotherapy. N Engl J Med. 2006;355(23):2427-43.
5. Jebeile H, Cardel MI, Kyle TK, Jastreboff AM. Addressing psychosocial health in the treatment and care of adolescents with obesity. Obesity (Silver Spring). 2021;29(9):1413-22.
6. Mocanu V, Lai K, Dang JT, Switzer NJ, Birch DW, Ball GDC, et al. Evaluation of the Trends, Characteristics, and Outcomes in North American Youth Undergoing Elective Bariatric Surgery. Obes Surg. 2021;31(5):2180-7.
7. Alalwan AA, Friedman J, Park H, Segal R, Brumback BA, Hartzema AG. US national trends in bariatric surgery: A decade of study. Surgery. 2021;170(1):13-7.
8. Aryannezhad S, Hosseinpanah F, Khalaj A, Mahdavi M, Valizadeh M, Akhavirad SMB, et al. Comparison of the one-year outcomes of bariatric surgery in adolescents and young adults: a matched case-control study, Tehran Obesity Treatment Study (TOTS). Surg Today. 2021;51(11):1764-74.
9. Stanford FC, Mushannen T, Cortez P, Campoverde Reyes KJ, Lee H, Gee DW, et al. Comparison of Short and Long-Term Outcomes of Metabolic and Bariatric Surgery in Adolescents and Adults. Front Endocrinol (Lausanne). 2020;11:157.
10. Benedix F, Krause T, Adolf D, Wolff S, Lippert H, Manger T, et al. Perioperative Course, Weight Loss and Resolution of Comorbidities After Primary Sleeve Gastrectomy for Morbid Obesity: Are There Differences Between Adolescents and Adults? Obes Surg. 2017;27(9):2388-97.
11. Inge TH, Courcoulas AP, Jenkins TM, Michalsky MP, Brandt ML, Xanthakos SA, et al. Five-Year Outcomes of Gastric Bypass in Adolescents as Compared with Adults. N Engl J Med. 2019;380(22):2136-45.
12. Olbers T, Beamish AJ, Gronowitz E, Flodmark CE, Dahlgren J, Bruze G, et al. Laparoscopic Roux-en-Y gastric bypass in adolescents with severe obesity (AMOS): a prospective, 5-year, Swedish nationwide study. Lancet Diabetes Endocrinol. 2017;5(3):174-83.
13. Dreber H, Thorell A, Torgerson J, Reynisdottir S, Hemmingsson E. Weight loss, adverse events, and loss to follow-up after gastric bypass in young versus older adults: A Scandinavian Obesity Surgery Registry study. Surg Obes Relat Dis. 2018;14(9):1319-26.
14. Lee Y, Doumouras AG, Yu J, Aditya I, Gmora S, Anvari M, et al. Laparoscopic Sleeve Gastrectomy Versus Laparoscopic Roux-en-Y Gastric Bypass: A Systematic Review and Meta-analysis of Weight Loss, Comorbidities, and Biochemical Outcomes From Randomized Controlled Trials. Ann Surg. 2021;273(1):66-74.

15. Poelemeijer YQM, Liem RSL, Nienhuijs SW. A Dutch Nationwide Bariatric Quality Registry: DATO. Obes Surg. 2018;28(6):1602-10.
16. Nederlandse Vereniging voor Heelkunde. Chirurgische behandeling van obesitas 2020. Available from: https://richtlijnendatabase.nl/richtlijn/chirurgische_behandeling_van_obesitas/startpagina_-_chirurgische_behandeling_van_obesitas.html.
17. Bonouvrie DS, van de Pas KGH, Janssen L, Leclercq WKG, Greve JWM, van Dielen FMH. Safety of bariatric surgery in the elderly: results from the Dutch National Registry. Surg Obes Relat Dis. 2022.
18. Dutch Institute for Clinical Auditing. Jaarrapportage 2019 DATO. Available from: https://dica.nl/jaarrapportage-2019/dato.
19. Uittenbogaart M. A216 Defining an international standard for primary and secondary non-response following bariatric surgery for research purposes: a modified Delphi consensus. Surgery for Obesity and Related Diseases. 2019;15(10):76.
20. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240(2):205-13.
21. Akpinar EO, Liem RSL, Nienhuijs SW, Greve JWM, Marang-van de Mheen PJ. Metabolic effects of bariatric surgery on patients with type 2 diabetefs: a population-based study. Surg Obes Relat Dis. 2021;17(7):1349-58.
22. Cooiman MI, Aarts EO, Janssen IMC, Hazebroek EJ, Berends FJ. Weight Loss, Remission of Comorbidities, and Quality of Life After Bariatric Surgery in Young Adult Patients. Obes Surg. 2019;29(6):1851-7.
23. Manini TM. Energy expenditure and aging. Ageing Res Rev. 2010;9(1):1-11.
24. Scozzari G, Passera R, Benvenga R, Toppino M, Morino M. Age as a long-term prognostic factor in bariatric surgery. Ann Surg. 2012;256(5):724-8; discussion 8-9.
25. de Jong MMC, Hinnen C. Bariatric surgery in young adults: a multicenter study into weight loss, dietary adherence, and quality of life. Surg Obes Relat Dis. 2017;13(7):1204-10.
26. Beamish AJ, D'Alessio DA, Inge TH. Controversial Issues: When the drugs don't work, can surgery provide a different outcome for diabetic adolescents? Surg Obes Relat Dis. 2015;11(4):946-8.
27. Luca P, Nicolas C, Marina V, Sarah B, Andrea L. Where Are My Patients? Lost and Found in Bariatric Surgery. Obes Surg. 2021;31(5):1979-85.

CHAPTER 6

ROUX-EN-Y GASTRIC BYPASS VERSUS SLEEVE GASTRECTOMY IN YOUNG ADULTS: A DUTCH REGISTRY STUDY

Kelly G.H. van de Pas
Daniëlle S. Bonouvrie
Loes Janssen
Marleen M. Romeijn
Arijan A. P. M. Luijten
Wouter K.G. Leclercq
François M.H. van Dielen

Obesity surgery 2022.

ABSTRACT

Introduction

The most commonly performed bariatric procedures worldwide are Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG), yet outcomes following these procedures in young adults are limited. Therefore, the objective of this study was to compare weight loss outcomes between RYGB and SG in young adults.

Methods

This is a nationwide retrospective cohort study of young adults, aged 18–25 years, who underwent RYGB or SG between 2015 and 2019, with data from the Dutch Audit Treatment of Obesity (DATO). The primary outcome was weight loss expressed as percentage total weight loss (%TWL) in a period of three years after surgery. Secondary outcomes were the incidence of complications (<30 days) and progression of obesity-related comorbidities.

Results

In total, 2,313 patients were included, 1,246 in the RYGB group and 1,067 in the SG group. Percentage TWL was significantly higher in the RYGB group compared to the SG group at one, two and three years after surgery (respectively 2.4%, 2.9%, and 3.3% higher, $p < 0.001$). RYGB was associated with an on-average 2.75 higher %TWL compared to SG in females ($p < 0.001$), although this was not seen in males ($\beta = 0.63$, $p = 0.514$). No differences were found in the incidence of complications, nor the progression of obesity-related comorbidities except for gastroesophageal reflux disease (GERD). There was more improvement or resolution of GERD in the RYGB group (95.2% vs. 56.3%, $p < 0.001$).

Conclusion

Similar numbers of RYGB and SG were performed in young adults, whereas RYGB was associated with greater weight loss in the short- and midterm, particularly in females.

INTRODUCTION

The obesity epidemic is a serious and chronic problem. Obesity leads to impaired quality of life, overall health, and life expectancy[1]. The prevalence of severe obesity has increased substantially worldwide; this trend is also seen in youth and young adults[2,3]. Consequently, an alarming shift in the early onset of obesity-related comorbidities has been noted, illustrating the need for effective treatment options to achieve enduring weight loss and improvement of obesity-related comorbidities early in life[4-7].

In the majority of adults with severe obesity, bariatric surgery has proven to be the most effective and long-lasting treatment[8-11]. The most commonly performed bariatric procedures worldwide are Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG)[11]. RYGB has traditionally been the gold standard and remains the most frequently performed bariatric procedure in the Netherlands with 61% of all procedures in 2019[12,13]. However, SG has grown in popularity due to its technical ease and the belief that it leads to fewer complications[14].

To date, several randomized controlled trials (RCTs) and meta-analyses have been performed in adults comparing RYGB and SG[11,15,16]. A recently published meta-analysis demonstrated that patients who underwent RYGB had a significantly greater decrease in body mass index (BMI) when compared to SG at one and three years after surgery[11]. Nevertheless, most studies in the field of bariatric surgery have only focused on adults and not on young adults[11,15,16]. Due to possible variations in metabolism and compliance rates, the results between RYGB and SG for young adults may differ from adults[17-19]. In light of this possibility, a small cohort study retrospectively evaluated weight loss after bariatric surgery in young adults, aged 18–25 years. RYGB and SG were compared in these young adults, and no differences in terms of weight loss were found. However, the number of included young adults was low (n = 103), and based on this retrospective study with an impaired number of included patients, no firm conclusions can be drawn[20]. Therefore, the aim of this nationwide population-based cohort study was to compare RYGB and SG in terms of weight loss in young adults with severe obesity. Secondary objectives were the incidence of complications and progression of obesity-related comorbidities. It was hypothesized that RYGB might lead to greater weight loss and improvement of obesity-related comorbidities, as well as more complications in comparison with SG in young adults.

METHODS

The methods of this study are in line with the methods of a similar study performed by our research group[21].

Study design

This is a national population-based cohort study of young adults, aged 18–25 years, who received a RYGB or SG in the Netherlands. Pseudo-anonymized data was derived from the Dutch Audit Treatment of Obesity (DATO). The DATO is a nationwide mandatory quality registry covering all bariatric procedures performed in the Netherlands since January 2015[12]. Young adults were included if they received primary RYGB or SG between 01 January 2015 and 31 December 2019 and had a preoperative BMI ≥ 40 kg/m^2 or a BMI ≥ 35 kg/m^2 accompanied by an obesity-related comorbidity. Eligibility for surgery was evaluated by a multidisciplinary team and was according to the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) guidelines[22]. Exclusion criteria were two-stage or revision procedures or a missing body weight one year after surgery. The one-year range was defined as an outpatient clinic visit between 9 and 15 months postoperatively. The study was presented to our local Medical Ethical Research Committee, and no formal approval was necessary according to Dutch law (Medical Research Involving Human Subjects Act).

Study outcomes

The primary outcome was weight loss expressed as %TWL at one, two and three years after surgery. Percentage TWL was calculated as (preoperative weight − postoperative weight)/preoperative weight) × 100%. Secondary outcomes were change in BMI and %TWL in a period of five years after surgery, successful weight loss, weight regain, the incidence of complications, and progression of obesity-related comorbidities. Change in BMI was calculated as preoperative BMI–postoperative BMI. In addition, successful weight loss was defined as ≥ 20% TWL according to the DATO, and weight regain was defined as ≥ 20% regain of a patients' lost weight at their last follow-up visit after initial successful weight loss one year after surgery[13,23]. Perioperative and postoperative complications within 30 days were registered. Postoperative complications were defined according to the Clavien-Dindo (CD) classification of surgical complications[24]. Obesity-related comorbidities included T2DM, hypertension, dyslipidemia, gastroesophageal reflux disease (GERD), obstructive sleep apnea syndrome (OSAS), and musculoskeletal pain. The obesity-related comorbidities were assessed at one and two years after surgery. The latter comorbidity status was compared with the status before surgery and classified as resolved or improved, unchanged or deteriorated, or de novo according to the ASMBS guideline[25]. Previous research based on the DATO described the

classification of the comorbidities extensively[26]. The comorbidity status was frequently missing at three, four and five years after surgery; therefore, this outcome was only assessed up to two years postoperatively.

Statistical analysis

All statistical analyses were conducted using IBM SPSS statistic software, version 25.0. A two-sided p value < 0.05 was considered statistically significant. Continuous variables are presented as mean ± standard deviation (SD), and categorical variables are presented as absolute number (percentage). Outcomes between RYGB and SG were compared using an independent samples t-test for continuous variables and $\chi 2$ test for categorical variables. The associations between bariatric procedure (RYGB versus SG) and %TWL at one, two and three years after surgery were analyzed using linear mixed model (LMM) analyses. In the LMM, the factor-analytic covariance matrix and restricted maximum likelihood estimation were used. Within these analyses, an interaction variable for bariatric procedure and gender was added, and corrections were made for known confounders. Known confounders were based on literature (preoperative BMI) and variables that had a confounding effect in the univariate analysis[27].

RESULTS

A total of 2,341 young adults with a one year follow-up weight were registered from 2015 until 2019; 28 (1.2%) were excluded due to a two-stage procedure or revision surgery. Of the 2,313 young adults who were included, 1,246 received a RYGB (53.9%) and 1,067 received a SG (46.1%). Two-year follow-up in the RYGB group was available in 583 (60.0%) of the 971 young adults who had surgery in or before 2018. Three-, four-, and five-year follow-up was obtained from 331/751 (44.1%), 185/528 (35.0%), and 78/262 (29.8%) of the young adults, respectively. Two-year follow-up in the SG group was available in 542 (64.9%) of the 835 young adults who had surgery in or before 2018. Three-, four-, and five-year follow-up was obtained from 265/575 (46.1%), 113/302 (37.4%), and 33/110 (30.0%) of the young adults, respectively.

The baseline characteristics of the study population were in general similar (Table 1). Notably, young adults who received a RYGB had a lower preoperative BMI compared to young adults who received a SG (44.1 kg/m2 vs. 45.3 kg/m2, p < 0.001). Besides this, preoperative T2DM, dyslipidemia, and musculoskeletal pain were significantly more represented in the RYGB group.

Table 1. Baseline characteristics of the included young adults

	RYGB, n = 1,246	**SG, n = 1,067**	***p* value**
Age (years, ±SD)	23.1 ± 2.0	22.9 ± 2.1	0.002*
Gender, n. (%)			
Female	1,073 (86.1)	925 (86.7)	0.687
Preoperative weight (kg, ±SD)	127.3 ± 18.0	130.4 ± 19.4	<0.001*
Preoperative BMI (kg/m^2, ±SD)	44.1 ± 4.7	45.3 ± 5.1	<0.001*
Preoperative comorbidities, n. (%)			
T2DM	56 (4.5)	30 (2.8)	0.033*
Hypertension	67 (5.4)	52 (4.9)	0.585
Dyslipidemia	88 (7.1)	29 (2.7)	<0.001*
GERD	102 (8.2)	71 (6.7)	0.163
OSAS	60 (4.8)	46 (4.3)	0.563
Musculoskeletal pain	431 (34.6)	311 (29.1)	0.005*

Data presented as number (%) or mean (SD). **p* value is below the threshold of <0.05.
RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy, BMI = body mass index, T2DM = type 2 diabetes mellitus, GERD = gastroesophageal reflux disease, OSAS = obstructive sleep apnea syndrome.

Weight loss

Percentage TWL was significantly higher in the RYGB group compared to the SG group at one, two and three years after surgery. One year after surgery, TWL was 34.3% in the RYGB group versus 31.9% in the SG group, 35.0% versus 32.1% two years after surgery, and 33.1% versus 29.8% three years after surgery (all $p < 0.001$). This trend is preserved four and five years after surgery, although not significant. Similar patterns were found for change in BMI (Table 2). Next to this, the percentage of young adults who achieved successful weight loss (≥ 20% TWL) after a RYGB was higher compared to young adults after a SG, respectively 97.2% versus 91.3% one year after surgery and 95.7% versus 88.7% two years after surgery (all $p < 0.001$). Weight regain after initial successful weight loss was equally seen in the two groups, 14.7% in the RYGB group and 17.6% in the SG group ($p = 0.160$) (Table 2). LMM was used to analyze the association between bariatric procedure (RYGB versus SG) and %TWL. LMM analyses were stratified for gender, since gender and bariatric procedure showed a significant interaction effect on %TWL (Table 3). In female young adults, bariatric procedure, after adjustment for confounders, was significantly associated with %TWL at one, two and three years after surgery. RYGB had an on-average 2.75 higher %TWL compared to SG ($p < 0.001$) in females. Interestingly, this association was not found in male young adults ($\beta = 0.63$, $p = 0.514$).

Table 2. Weight loss outcomes comparing RYGB and SG in young adults

	RYGB		**SG**		
	n.[1]	*% ±SD*	*n.*[1]	*% ±SD*	*p value*
TWL 1 year	1,246/1,246	34.3 ±7.3	1,067/1,067	31.9 ±8.5	<0.001*
TWL 2 years	583/971	35.0 ±8.3	542/835	32.1 ±10.0	<0.001*
TWL 3 years	331/751	33.1 ±9.2	265/575	29.8 ±11.5	<0.001*
TWL 4 years	185/528	30.9 ±10.4	113/302	29.9 ±12.9	0.521
TWL 5 years	78/262	29.5 ±11.2	33/110	26.5 ±15.1	0.307
	n.[1]	*kg/m² ±SD*	*n.*[1]	*kg/m² ±SD*	
Change in BMI 1 year	1,246/1,246	15.1 ±3.6	1,067/1,067	14.4 ±4.3	<0.001*
Change in BMI 2 years	583/971	15.4 ±4.1	542/835	14.6 ±5.2	0.003*
Change in BMI 3 years	331/751	14.6 ±4.6	265/575	13.6 ±5.8	0.024*
Change in BMI 4 years	185/528	13.6 ±5.0	113/302	13.9 ±7.1	0.676
Change in BMI 5 years	78/262	13.1 ±5.2	33/110	12.4 ±7.1	0.589
	n. in analysis	*n. (%)*	*n. in analysis*	*n. (%)*	
Successful weight loss 1 year[2]	1,246	1211 (97.2)	1,067	974 (91.3)	<0.001*
Successful weight loss 2 years[3]	583	558 (95.7)	542	481 (88.7)	<0.001*
Weight regain[4]	673	99 (14.7)	620	109 (17.6)	0.160

Data presented as mean (±SD). * *p* value is below the threshold of <0.05.
[1] Number of patients in analysis/number of patients who could have had a follow-up visit.
[2] Defined as ≥20% TWL at 1 year after surgery.
[3] Defined as ≥20% TWL at 2 years after surgery.
[4] Defined as ≥20% weight regain of a patients' lost weight at their last follow-up visit, with a minimum of two years after surgery, and after initial successful weight loss (≥20% TWL) at 1 year follow-up.
RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy, TWL = total weight loss, BMI = body mass index.

Table 3. Stratified for gender linear mixed model analysis of variables associated with %TWL after RYGB or SG at one to three years after surgery

	Female			**Male**		
	Beta coefficient	*95% CI*	*p value*	*Beta coefficient*	*95% CI*	*p value*
Bariatric procedure (RYGB vs. SG)	2.75	2.07 – 3.44	<0.001*	0.63	-1.27 – 2.53	0.514
Follow-up compared to 1 year after surgery						
2 years	0.43	0.10 – 0.75	0.010*	0.38	-0.52 – 1.28	0.404
3 years	-1.34	-1.86 – -0.83	<0.001*	-1.82	-3.17 – -0.47	0.009*
Preoperative BMI (kg/m²)	-0.07	-0.14 – 0.00	0.064	0.16	-0.01 – 0.34	0.064
Preoperative T2DM (yes vs. no)	-4.44	-6.35 – -2.54	<0.001*	-2.49	-6.59 – 1.60	0.232
Preoperative hypertension (yes vs. no)	-1.37	-3.04 – 0.31	0.110	-3.81	-6.85 – -0.78	0.014*
Preoperative OSAS (yes vs. no)	-2.05	-3.85 – -0.26	0.025*	-3.33	-6.55 – -0.12	0.042*

* *p* value is below the threshold of < 0.05.
RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy, BMI = body mass index, T2DM = type 2 diabetes mellitus, OSAS = obstructive sleep apnea syndrome.

Complications

No significant differences were detected between RYGB and SG in perioperative complications, nor in postoperative complications within 30 days (Table 4). Furthermore, no mortality was reported in both groups.

Table 4. Perioperative and postoperative complications (<30 days) comparing RYGB and SG in young adults

	RYGB, n = 1246	**SG, n = 1067**	***p* value**
Perioperative complications, n. (%)			
Perforation	1 (0.1)	0 (0)	NA
Bleeding	4 (0.3)	2 (0.2)	NA
Spleen injury	1 (0.1)	1 (0.1)	NA
Liver injury	1 (0.1)	1 (0.1)	NA
Total	10 (0.8)	7 (0.7)	0.681
Number of readmissions within 30 days, n. (%)	30 (2.4)	18 (1.7)	0.225
Therapeutic intervention for complication within 30 days, n. (%)	10 (0.8)	6 (0.6)	0.487
Clavien-Dindo classification, n. (%)			
CD grade I	7 (0.6)	7 (0.7)	0.771
CD grade II	8 (0.6)	8 (0.7)	0.755
CD grade III	14 (1.1)	9 (0.8)	0.499
CD grade IV	3 (0.2)	0 (0)	NA
Postoperative complication within 30 days, n. (%)			
Major bleeding	10 (0.8)	6 (0.6)	0.487
Anastomotic leakage	0 (0)	2 (0.2)	NA
Intra-abdominal abscess	0 (0)	1 (0.1)	NA
Wound infection	2 (0.2)	2 (0.2)	1.000
Intestinal obstruction	5 (0.4)	0 (0)	NA
Anastomotic stricture	1 (0.1)	1 (0.1)	1.000
Non-surgical complications	15 (1.2)	18 (1.7)	0.329

Data presented as number (%). **p* value is below the threshold of < 0.05.
RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy, NA = not applicable, CD = Clavien–Dindo classification, I is any deviation from the normal postoperative course without intervention, except some drugs such as anti-ememetics, antipyretics, analgesics, diuretics and electroytes; II is a complication requiring pharmacological treatment other than such allowed for grade I; III is a complication requiring intervention under anesthesia IV is a complication resulting in organ failure.

Obesity-related comorbidities

Regarding the progression of obesity-related comorbidities, no differences were found between the two groups in terms of T2DM, hypertension, dyslipidemia, OSAS, and musculoskeletal pain (Table 5). However, in the RYGB group, more resolution or improvement of GERD compared to the SG group was found (95.2% vs. 56.3%, $p < 0.001$). In line with this, the RYGB group had two (0.18%) de novo developments of GERD compared to 14 (1.38%) in the SG group.

Table 5. Progression of obesity-related comorbidities comparing RYGB and SG in young adults

	RYGB 1-2 years of follow-up			**SG 1-2 years of follow-up**			
	n. [1]	*Resolved or improved*[2] *n. (%)*	*Unchanged or deteriorated*[2] *n. (%)*	*n.*[1]	*Resolved or improved*[2] *n. (%)*	*Unchanged or deteriorated*[2] *n. (%)*	*p value*
T2DM	37/56	31 (83.8)	6 (16.2)	20/30	20 (100.0)	0 (0)	0.081
Hypertension	55/67	47 (85.5)	8 (14.5)	39/52	37 (94.9)	2 (5.1)	0.187
Dyslipidemia	69/88	58 (84.1)	11 (15.9)	19/29	16 (84.2)	3 (15.8)	1.000
GERD	62/102	59 (95.2)	3 (4.8)	32/71	18 (56.3)	14 (43.8)	<0.001*
OSAS	35/60	28 (80.0)	7 (20.0)	19/46	15 (78.9)	4 (21.1)	1.000
Musculoskeletal pain	306/431	261 (85.3)	45 (14.7)	171/311	146 (85.4)	25 (14.6)	0.980

Data presented as number (%). * *p* value is below the threshold of < 0.05.

[1] Number of patients from which comorbidity status is known at 1 or 2 years follow-up with a preoperative comorbidity/number of patients with preoperative comorbidity.

[2] Based on the number of patients with preoperative comorbidity and known status at 1 or 2 years of follow-up .

RYGB = Roux-en-Y gastric bypass, SG = sleeve gastrectomy, T2DM = type 2 diabetes mellitus, GERD = gastroesophageal reflux disease, OSAS = obstructive sleep apnea syndrome.

DISCUSSION

Several studies and meta-analyses have been performed comparing RYGB and SG, yet so far the young adults were underrepresented[11,15,16,28]. To our knowledge, this is the first nationwide population-based cohort study comparing weight loss outcomes between RYGB and SG in young adults (18–25 years). We demonstrated that RYGB is associated with an on-average higher %TWL at one, two and three years after surgery compared to SG, particularly in females. This study also indicates that in general, bariatric surgery appeared to be safe in young adults and that RYGB more often resulted in resolution or improvement of GERD.

In terms of short- and midterm weight loss, this study suggests that RYGB should be favored as surgical technique in young adults rather than SG. This is supported by a recent meta-analysis among adults, demonstrating that RYGB led to a significantly greater decrease in BMI compared to SG at one and three years after surgery (1.25 kg/m^2 and 1.71 kg/m^2). In a sensitivity analysis, this favorable effect of RYGB was also seen five years after surgery (11). Besides this, a large cohort study of three national quality registries revealed that more adults who underwent RYGB achieved successful weight loss (≥ 20% TWL) one year after surgery (95.8% vs. 84.6%)[28]. Similar findings were found in this study, 95.7% of the young adults who received a RYGB achieved successful weight loss versus 88.7% of the young adults who received a SG. However, it should be noted that in our study, no significant differences were found in weight loss four and five years after surgery, presumably because there was a large loss to follow-up of approximately 64% and 70% which may have affected the outcomes. In order to assess the superiority of the RYGB in young adults in the long term, a large comparative study should be designed in which long-term complications, physical wellbeing, and quality of life will also be included, especially in this population, since young adults with obesity are expected to have a reduced quality of life, lower educational attainment, and are more likely to stay single[29,30].

One unexpected finding was that RYGB was significantly associated with higher %TWL compared to SG in female young adults, whereas this effect was not seen in male young adults. Previously, this has not been reported in young adults, and the current literature on gender differences in bariatric surgery reveals significant heterogeneity. One study indicated that SG was more effective in men[31]. On the contrary, a large retrospective cohort study of 20,296 patients showed no gender differences in patients who received SG, nor in patients who received RYGB[32]. Gender differences between females and males might be caused by variations in fat metabolism, eating habits, or compliance

rates but are in general not well understood[33]. Therefore, continued efforts are needed to gain more insights into gender-specific differences in bariatric surgery.

Regarding the postoperative complications after bariatric surgery in young adults, the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program (MBSAQIP) of North America recently published an overview[34]. In 21,592 young adults, it was shown that the rate of readmissions and reinterventions within 30 days was low (all below < 5%), and that serious complications such as bleedings (0.4%) were rarely documented. Besides this, they reported that young adults who received RYGB had threefold higher rates of reoperation, intervention, and serious complications. The complication rate in this study was also low; perioperative and postoperative complications within 30 days were all below 5%. In contrary to the report of the MBSAQIP, the current study revealed no differences between RYGB and SG in postoperative complications within 30 days. A possible explanation for this could be the lower presence of preoperative comorbidities, or it could be due to the fact that this study did not have enough power to assess these outcome measures.

In the last couple of years, the development of GERD after SG has raised concerns. There is a growing body of evidence that SG could lead to the development of GERD and eventually Barrett's esophagus[35,36]. This might be due to the increased intra-gastric pressure, the final shape of the sleeve, or the disruption of the anatomical anti-reflux barrier after SG[36,37]. So far, there is limited evidence comparing RYGB and SG on the development of GERD. Our study revealed more resolution or improvement of GERD after RYGB. Nevertheless, these results need to be interpreted with caution, as there could be differences in the assessment, interpretation, and registration of the obesity-related comorbidities among the different Dutch centers since this study was based on a registry. Future studies are therefore recommended, especially in the young adult population as they could be of greater risk due to their extended exposure.

This study has certain limitations. The first limitation is the significant loss to follow-up, which might have led to a selection bias of the results, as poorer weight loss outcomes could be a possible reason for loss to follow-up[38]. Another limitation of this study is the fact that the study is based on a registry; this might have caused differences in the interpretation and registration of the data entry in the different Dutch centers. Thirdly, our study only assessed the short-term complications, and mainly due to the extended exposure of this young population, the long-term complications would be of interest for future research. Despite these limitations, we believe that this study gained insights into the weight loss outcomes, complications, and progression of obesity-related comorbidities between RYGB and SG in young adults.

CONCLUSION

Population-based data revealed that similar numbers of RYGB and SG were performed in young adults in the Netherlands and appeared to be safe. On the short- and midterm RYGB was associated with greater weight loss, particularly in females. Besides this, RYGB resulted in more improvements of GERD compared to SG. Based on these findings, RYGB might be favored in female young adults. However, future research with an extended follow-up is needed to definitively assess the superiority of the RYGB in the long term. This research should ideally also focus on complications (> 30 days), physical wellbeing, and quality of life, especially in this young population.

REFERENCES

1. Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ, et al. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9·1 million participants. Lancet. 2011;377(9765):557-67.
2. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;384(9945):766-81.
3. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. Lancet. 2017;390(10113):2627-42.
4. Beamish AJ, D'Alessio DA, Inge TH. Controversial Issues: When the drugs don't work, can surgery provide a different outcome for diabetic adolescents? Surg Obes Relat Dis. 2015;11(4):946-8.
5. Shah AS, D'Alessio D, Ford-Adams ME, Desai AP, Inge TH. Bariatric Surgery: A Potential Treatment for Type 2 Diabetes in Youth. Diabetes Care. 2016;39(6):934-40.
6. Gordon-Larsen P, The NS, Adair LS. Longitudinal trends in obesity in the United States from adolescence to the third decade of life. Obesity (Silver Spring). 2010;18(9):1801-4.
7. Bendor CD, Bardugo A, Pinhas-Hamiel O, Afek A, Twig G. Cardiovascular morbidity, diabetes and cancer risk among children and adolescents with severe obesity. Cardiovasc Diabetol. 2020;19(1):79.
8. Sjöström L, Lindroos AK, Peltonen M, Torgerson J, Bouchard C, Carlsson B, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med. 2004;351(26):2683-93.
9. Olbers T, Beamish AJ, Gronowitz E, Flodmark CE, Dahlgren J, Bruze G, et al. Laparoscopic Roux-en-Y gastric bypass in adolescents with severe obesity (AMOS): a prospective, 5-year, Swedish nationwide study. Lancet Diabetes Endocrinol. 2017;5(3):174-83.
10. Inge TH, Courcoulas AP, Jenkins TM, Michalsky MP, Helmrath MA, Brandt ML, et al. Weight Loss and Health Status 3 Years after Bariatric Surgery in Adolescents. N Engl J Med. 2016;374(2):113-23.
11. Lee Y, Doumouras AG, Yu J, Aditya I, Gmora S, Anvari M, et al. Laparoscopic Sleeve Gastrectomy Versus Laparoscopic Roux-en-Y Gastric Bypass: A Systematic Review and Meta-analysis of Weight Loss, Comorbidities, and Biochemical Outcomes From Randomized Controlled Trials. Ann Surg. 2021;273(1):66-74.
12. Poelemeijer YQM, Liem RSL, Nienhuijs SW. A Dutch Nationwide Bariatric Quality Registry: DATO. Obes Surg. 2018;28(6):1602-10.
13. Dutch Institute for Clinical Auditing. Jaarrapportage 2019 DATO. Available from: https://dica.nl/jaarrapportage-2019/dato.

14. Major P, Wysocki M, Dworak J, Pędziwiatr M, Pisarska M, Wierdak M, et al. Analysis of Laparoscopic Sleeve Gastrectomy Learning Curve and Its Influence on Procedure Safety and Perioperative Complications. Obes Surg. 2018;28(6):1672-80.

15. Salminen P, Helmiö M, Ovaska J, Juuti A, Leivonen M, Peromaa-Haavisto P, et al. Effect of Laparoscopic Sleeve Gastrectomy vs Laparoscopic Roux-en-Y Gastric Bypass on Weight Loss at 5 Years Among Patients With Morbid Obesity: The SLEEVEPASS Randomized Clinical Trial. Jama. 2018;319(3):241-54.

16. Peterli R, Wölnerhanssen BK, Peters T, Vetter D, Kröll D, Borbély Y, et al. Effect of Laparoscopic Sleeve Gastrectomy vs Laparoscopic Roux-en-Y Gastric Bypass on Weight Loss in Patients With Morbid Obesity: The SM-BOSS Randomized Clinical Trial. Jama. 2018;319(3):255-65.

17. McVay MA, Friedman KE, Applegate KL, Portenier DD. Patient predictors of follow-up care attendance in Roux-en-Y gastric bypass patients. Surg Obes Relat Dis. 2013;9(6):956-62.

18. Colquitt JL, Pickett K, Loveman E, Frampton GK. Surgery for weight loss in adults. Cochrane Database Syst Rev. 2014(8):Cd003641.

19. Jenkins TM, Xanthakos SA, Zeller MH, Barnett SJ, Inge TH. Distance to clinic and follow-up visit compliance in adolescent gastric bypass cohort. Surg Obes Relat Dis. 2011;7(5):611-5.

20. Cooiman MI, Aarts EO, Janssen IMC, Hazebroek EJ, Berends FJ. Weight Loss, Remission of Comorbidities, and Quality of Life After Bariatric Surgery in Young Adult Patients. Obes Surg. 2019;29(6):1851-7.

21. Romeijn MM, van Hoef S, Janssen L, van de Pas KGH, van Dielen FMH, Luijten AAPM, Göttgens KWA, Greve JWM, Leclercq WKG. Comparison of linear versus circular-stapled gastroenterostomy in Roux-en-Y gastric bypass: a nationwide population-based cohort study. Obes Surg. 2021;31(8):3579–87.

22. Fried M, Yumuk V, Oppert JM, Scopinaro N, Torres A, Weiner R, et al. Interdisciplinary European guidelines on metabolic and bariatric surgery. Obes Surg. 2014;24(1):42-55.

23. Uittenbogaart M. A216 Defining an international standard for primary and secondary non-response following bariatric surgery for research purposes: a modified Delphi consensus. Surgery for Obesity and Related Diseases. 2019;15(10):76.

24. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240(2):205-13.

25. Brethauer SA, Kim J, el Chaar M, Papasavas P, Eisenberg D, Rogers A, et al. Standardized outcomes reporting in metabolic and bariatric surgery. Surg Obes Relat Dis. 2015;11(3):489-506.

26. Akpinar EO, Liem RSL, Nienhuijs SW, Greve JWM, Marang-van de Mheen PJ. Metabolic effects of bariatric surgery on patients with type 2 diabetes: a population-based study. Surg Obes Relat Dis. 2021;17(7):1349-58.

27. Nielsen MS, Christensen BJ, Schmidt JB, Tækker L, Holm L, Lunn S, et al. Predictors of weight loss after bariatric surgery-a cross-disciplinary approach combining physiological, social, and psychological measures. Int J Obes (Lond). 2020;44(11):2291–302.

28. Poelemeijer YQM, Liem RSL, Våge V, Mala T, Sundbom M, Ottosson J, et al. Gastric Bypass Versus Sleeve Gastrectomy: Patient Selection and Short-term Outcome of 47,101 Primary Operations From the Swedish, Norwegian, and Dutch National Quality Registries. Ann Surg. 2020;272(2):326-33.
29. de Jong MMC, Hinnen C. Bariatric surgery in young adults: a multicenter study into weight loss, dietary adherence, and quality of life. Surg Obes Relat Dis. 2017;13(7):1204-10.
30. Dey M, Gmel G, Mohler-Kuo M. Body mass index and health-related quality of life among young Swiss men. BMC Public Health. 2013;13:1028.
31. Perrone F, Bianciardi E, Benavoli D, Tognoni V, Niolu C, Siracusano A, et al. Gender Influence on Long-Term Weight Loss and Comorbidities After Laparoscopic Sleeve Gastrectomy and Roux-en-Y Gastric Bypass: a Prospective Study With a 5-Year Follow-up. Obes Surg. 2016;26(2):276-81.
32. Coleman KJ, Huang YC, Hendee F, Watson HL, Casillas RA, Brookey J. Three-year weight outcomes from a bariatric surgery registry in a large integrated healthcare system. Surg Obes Relat Dis. 2014;10(3):396-403.
33. Ketterer C, Heni M, Stingl K, Tschritter O, Linder K, Wagner R, et al. Polymorphism rs3123554 in CNR2 reveals gender-specific effects on body weight and affects loss of body weight and cerebral insulin action. Obesity (Silver Spring). 2014;22(3):925-31.
34. Mocanu V, Lai K, Dang JT, Switzer NJ, Birch DW, Ball GDC, et al. Evaluation of the Trends, Characteristics, and Outcomes in North American Youth Undergoing Elective Bariatric Surgery. Obes Surg. 2021;31(5):2180-7.
35. Sebastianelli L, Benois M, Vanbiervliet G, Bailly L, Robert M, Turrin N, et al. Systematic Endoscopy 5 Years After Sleeve Gastrectomy Results in a High Rate of Barrett's Esophagus: Results of a Multicenter Study. Obes Surg. 2019;29(5):1462-9.
36. Genco A, Soricelli E, Casella G, Maselli R, Castagneto-Gissey L, Di Lorenzo N, et al. Gastroesophageal reflux disease and Barrett's esophagus after laparoscopic sleeve gastrectomy: a possible, underestimated long-term complication. Surg Obes Relat Dis. 2017;13(4):568-74.
37. Lazoura O, Zacharoulis D, Triantafyllidis G, Fanariotis M, Sioka E, Papamargaritis D, et al. Symptoms of gastroesophageal reflux following laparoscopic sleeve gastrectomy are related to the final shape of the sleeve as depicted by radiology. Obes Surg. 2011;21(3):295-9.
38. Luca P, Nicolas C, Marina V, Sarah B, Andrea L. Where Are My Patients? Lost and Found in Bariatric Surgery. Obes Surg. 2021;31(5):1979-85.

CHAPTER 7

BARIATRIC SURGERY IN YOUTH: THE PERSPECTIVE OF DUTCH PEDIATRICIANS, PARENTS, AND ADOLESCENTS

Kelly G.H. van de Pas
Daniëlle S. Bonouvrie
Loes Janssen
Yvonne G.M. Roebroek
Bas S.H.J. Zegers
Wouter K.G. Leclercq
Anita C.E. Vreugdenhil
François M.H. van Dielen

Obesity Surgery 2021.

ABSTRACT

Introduction

Recent studies have indicated that bariatric surgery is effective for the treatment of youth with severe obesity. The attitudes of pediatricians, parents, and adolescents regarding this topic remains unclear. Therefore, the aim of this study was to assess the current thoughts and beliefs of Dutch pediatricians, parents, and adolescents regarding bariatric surgery in youth.

Methods

An online survey containing twenty questions on bariatric surgery in youth was distributed to pediatricians of the Dutch Society of Pediatrics. Parents and adolescents who participated in an interdisciplinary care program for overweight, obesity, and severe obesity filled out an online survey of twelve questions.

Results

One hundred and twenty-one pediatricians, 49 parents, and 19 adolescents completed the surveys. Seventy-two pediatricians (59.5%) considered bariatric surgery to be an effective treatment for youth with severe obesity when conventional treatment fails, and intend to refer patients for bariatric surgery. The most frequently suggested conditions for bariatric surgery were a minimum age of 16 years (n = 59, 48.7%), a BMI threshold of 40 kg/m^2 (n = 51, 42.2%), and a minimum Tanner stage of IV (n = 59, 48.8%). Thirty parents (61.2%) and fourteen adolescents (73.7%) responded that bariatric surgery should become available for youth with severe obesity.

Conclusion

Dutch pediatricians, parents, and adolescents increasingly accept bariatric surgery as a treatment modality in youth with severe obesity who do not respond successfully to lifestyle interventions. Whether pediatricians will actually refer youth for bariatric surgery remains to be seen when this treatment option will be implemented in the Netherlands.

INTRODUCTION

The worldwide prevalence of overweight and obesity in youth has increased substantially in the last decades; in 2015 more than 100 million children and adolescents were obese[1-3]. Although the rising trends of overweight and obesity have plateaued, the rates of severe obesity are still growing with data from 2009 indicating that 0.59% of Dutch boys and 0.53% of Dutch girls were affected by severe obesity[4]. This upward trend is concerning when considering the substantial short- and long-term health risks related to severe obesity, such as type 2 diabetes mellitus (T2DM), hypertension, fatty liver disease, and dyslipidemia, even when compared to youth with obesity[5-9].

The standard treatment for youth with obesity in the Netherlands comprises of multimodal lifestyle intervention programs focusing on dietary behavior, physical activity, and underlying individual and systemic factors, provided by a pediatric multidisciplinary team. These programs have shown to result in a significant decrease in body mass index (BMI) and improvement of cardio metabolic risk parameters in youth with overweight, obesity, and severe obesity[10-13]. At the same time, a quarter of treated youth do not experience weight loss and adolescents with severe obesity have proven to be particularly difficult to treat[11,12].

As bariatric surgery is commonplace in the treatment of adult obesity, it can be considered in youth with severe obesity to achieve similar long-lasting weight loss and concurrent improvement of comorbidities when conventional treatment fails. A meta-analysis by Shoar et al. reported that bariatric surgery is safe and effective in the treatment of severe obesity in adolescents aged 12 to 19 years old[14]. However, long-term follow-up is lacking[14-16]. A recently published guideline for the treatment of youth with overweight and obesity in the Netherlands advised reticence towards bariatric surgery, advocating its use in youth only in the context of scientific research. Furthermore, this guideline stated that referral should be considered by pediatricians of obesity expertise centers and after the unsuccessful completion of at least one year of multidisciplinary lifestyle intervention at named centers. A successful intervention is defined as weight loss of ≥ 10%[17]. In line with the cautious approach of this guideline, the opinions of professionals, parents, and adolescents worldwide on this subject are divided[18-23]. Studies among pediatricians from the USA dating from 2007 to 2009 reported that 47.0% and 88.5% of pediatricians would not refer patients for bariatric surgery[19,20]. Another qualitative report revealed that Dutch obesity specialists experience reluctance to refer youth for bariatric surgery as they endorse concerns that surgery might not treat the underlying psychological or behavioral problems. On the other hand, the obesity specialists, parents, and adolescents who felt that the etiology of obesity was

predominantly somatic were more in favor of bariatric surgery[21]. However, the current perspective of Dutch pediatricians, parents, and adolescents remains unclear.

With the goal of further investigating the efficacy and feasibility of bariatric surgery in youth, our aim was to explore the current attitudes of Dutch pediatricians towards these topics[24]. A secondary aim was to discover the thoughts and beliefs of Dutch parents and adolescents regarding bariatric surgery in youth.

METHODS

Study design

In January 2020, an online survey was distributed to all practicing members of the Dutch Society of Pediatrics in the Netherlands. To optimize response rates, a reminder was sent to the pediatric departments of all Dutch hospitals from September to November 2020.

Adolescents (13–18 years) who were treated for their overweight, obesity, or severe obesity in the outpatient, family based, interdisciplinary care program of the obesity expertise Centre for Overweight Adolescent and Children's Healthcare (COACH) at the Maastricht University Medical Centre (MUMC+) were asked to fill out a survey during their follow-up visits from September to December 2020. Their parents, as well as parents to children under 13 years of age who were treated for their overweight, obesity, or severe obesity in the COACH program, were asked to fill out a survey in the same period[11]. To optimize response rates, an email was sent to distribute the survey to the parents and adolescents.

The study protocol was submitted to our local Medical Ethical Research Committee, who deemed formal approval not necessary according to Dutch law (Medical Research Involving Human Subjects Act).

Survey

Anonymous surveys were designed using an online platform for questionnaires and surveys (Survey Monkey Inc., San Mateo, CA, USA) (Supporting Information file 1, https://link.springer.com/article/10.1007/s11695-021-05648-8#MOESM1). The surveys were self-administered and the study aim was explained before the start of all the surveys.

The survey for pediatricians consisted of 20 questions covering demographics, the current practice of youth with severe obesity including the results of this treatment,

and the opinions of the respondents regarding bariatric surgery in youth. Youth was defined as persons aged <18 years old, and severe obesity defined as a BMI ≥40 kg/m^2 or a BMI ≥ 35kg/m^2 with an obesity-related co-morbidity, both adjusted for gender and age according to the International Obesity Task Force cut off points[25]. Regarding the questions on bariatric surgery in youth, the pediatricians had to assume that the youth followed a lifestyle intervention program for at least 12 months without successful weight loss, and that they had stable and supportive families.

The survey for parents and adolescents consisted of twelve questions covering their current treatment and their perspectives on bariatric surgery in youth. A short introduction was given to the parents and adolescents regarding bariatric surgery. Types of questions included dichotomous, multiple-choice, and Likert scale questions. In all surveys, some questions allowed textual remarks.

Statistical analysis

The sample size was based on the most important question; a dichotomous question regarding the willingness of pediatricians to refer for bariatric surgery. Accepting a maximal margin of error of 0.1 (precision) for proportions in our population of interest, we required a minimum sample size of 97 pediatricians to estimate proportions close to 0.5 with sufficient precision[26]. All completed surveys were used for analysis. Continuous data are presented as mean ± standard deviation (SD). Categorical

data are presented as number (percentage). Statistical analysis was performed using IBM SPSS Statistics version 25 (IBM, Armonk, NY, USA).

RESULTS

The results of the pediatricians, parents, and adolescents are presented separately.

Pediatricians

Of the 1,461 pediatricians who are affiliated with the Dutch Society of Pediatrics, 176 (12.0%) filled in the questionnaire including 128 complete responses. After excluding the seven responses of pediatric residents, 121 responses were analyzed. Most of the pediatricians were general pediatricians, working in a non-academic hospital and currently treating one to five children for severe obesity (Table 1).

Table 1. Baseline characteristics of respondents and their practice

	Pediatricians
Number of complete responses - n	121
Years of working experience including residency (mean ± SD)	18.8 ± 8.2
Differentiation – n (%)	
General pediatrician	96 (79.3%)
Pediatric endocrinologist	2 (1.7%)
Pediatric gastro-enterologist	5 (4.1%)
Other	18 (14.9%)
Hospital – n (%)	
Centre of expertise for children with obesity	10 (8.3%)
Non-academic hospital	95 (78.5%)
Academic hospital	11 (9.1%)
Other	5 (4.1%)
Children currently on treatment for severe obesity – n (%)	
None	16 (13.2%)
1-5 children	51 (42.2%)
6-15 children	18 (14.9%)
16-30 children	6 (5.0%)
More than 30 children	16 (13.2%)
Other	14 (11.6%)

n = number, SD = standard deviation.

Current practice

One hundred and thirteen pediatricians (93.4%) reported that they always offered lifestyle advice to youth with severe obesity, and 84 pediatricians (69.4%) responded that they always referred to a dietician for dietary advice (Fig. 1).

Different norms of treatment success were observed; 54 respondents (44.6%) considered stabilization of bodyweight after 12 months of intervention as successful and 33 (27.3%) considered improvement of obesity-related comorbidities as a successful treatment, independent of bodyweight change. Twenty-six (21.5%) and eight pediatricians (6.6%) reported that they considered a weight loss of respectively ≥5% or ≥10% after 12 months of intervention as successful. Ninety-three pediatricians (76.9%) estimated that ≤25% of the youth with severe obesity were treated successfully in their hospital. If their treatment was unsuccessful, referral to an obesity expertise center could be the "add on" treatment according to 56 pediatricians (46.3%). Eighteen pediatricians (14.9%) reported that they would refer for inpatient treatment, and ten (8.3%) for bariatric surgery, assuming this would be an option. Seven out of the ten pediatricians who would refer for bariatric surgery were working at a pediatric obesity expertise center.

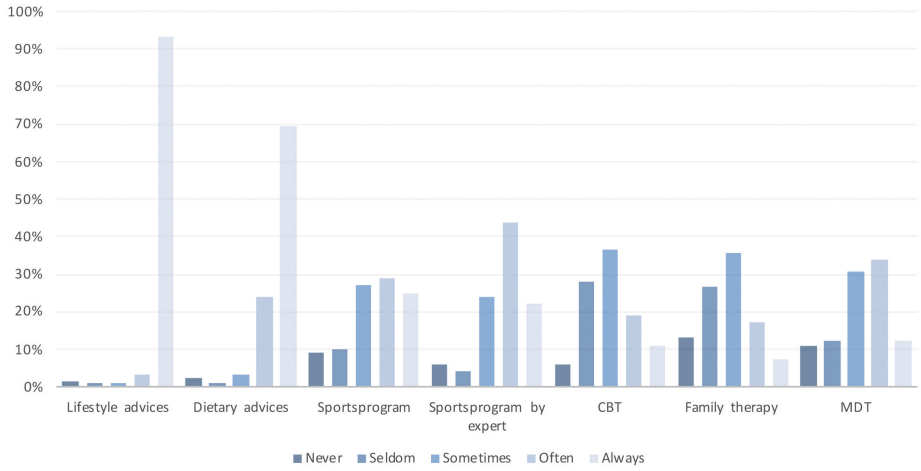


Figure 1. Reported frequency of providing different treatment modalities in youth with severe obesity
CBT = cognitive behavioral therapy, MDT = multidisciplinary treatment.

Pediatricians' perspective on bariatric surgery in youth

Seventy-two pediatricians (59.5%) shared the opinion that bariatric surgery may be effective in treating youth with severe obesity that were unsuccessfully treated with lifestyle interventions. These pediatricians would also refer for bariatric surgery. Eleven pediatricians (9.1%) did not believe bariatric surgery could be an effective treatment and 38 (31.4%) were inconclusive. Forty-nine pediatricians (40.5%) responded that they would not refer for bariatric surgery, with the reasons varying from "lack of evidence and experience" to "referral via an obesity expertise center."

The majority (n = 113, 93.4%) of the respondents reported that there should be a minimum age for bariatric surgery in youth, with 59 pediatricians suggesting a minimum age of 16 years (48.7%). Regarding a BMI threshold for surgery, 51 pediatricians (42.2%) suggested a lower limit of 40 kg/m^2 (sex and age adjusted) without comorbidities, whereas 38 respondents (31.4%) would prefer a BMI of 35 kg/m^2 without comorbidities. When comorbidities are present, the BMI threshold declined for 106 respondents (87.6%). Most often, T2DM was chosen as an influential comorbidity, followed by non-alcoholic fatty liver disease/non-alcoholic steatohepatitis (NAFLD/NASH), obstructive sleep apnea (OSA), and hypertension (Fig. 2). Besides BMI and the presence of comorbidities, also physical development expressed by Tanner stage appeared to be of importance. According to 59 (48.8%) and 46 pediatricians (38.0%), a Tanner stage of IV or V respectively was the minimum for bariatric surgery in youth.

The majority of the respondents (n = 82, 67.7%) reported that bariatric surgery should become a common treatment modality for selected adolescents with severe obesity who do not benefit from a lifestyle intervention. The most common reasons for reluctance were that "it should not become a common treatment modality, only a last resort treatment option" and "lack of evidence."

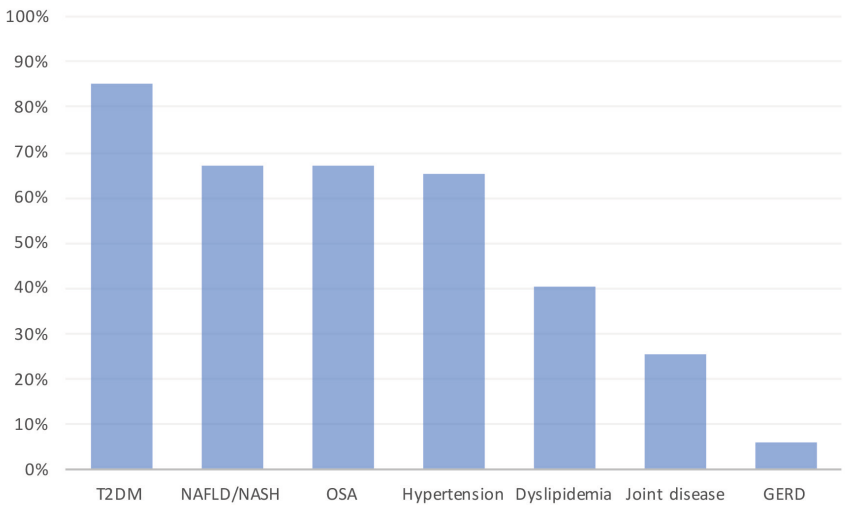


Figure 2. Comorbidities associated with a lower limit of BMI for bariatric surgery in youth

T2DM = type 2 diabetes mellitus, NAFLD/NASH = non-alcoholic fatty liver disease/non-alcoholic steatohepatitis, OSA = obstructive sleep apnea, GERD = gastroesophageal reflux disease.

Parents of youth with overweight, obesity, or severe obesity

Of the 159 parents whose children were treated at COACH and were approached, 56 (35.2%) filled in the questionnaire including 49 complete responses. The children of the respondents were affected by overweight, obesity, or severe obesity for at least one year, the majority for three to five years (n = 20, 40.8%) or six to ten years (n = 18, 36.7%). Thirty-three (67.3%) of their children were treated for their overweight, obesity, or severe obesity at the COACH program for at least one year.

Thirty parents (61.2%) reported that bariatric surgery should be available for youth with severe obesity if a lifestyle intervention is not successful, and 22 (44.9%) would allow their child to be referred for bariatric surgery if the current treatment fails. Reasons for not allowing their child to be referred varied from "being too young" to "children are still growing." Twenty-six parents (53.1%) were in favor of a minimum age for bariatric surgery, with a minimum age of 16 and 18 years both answered most frequently (n = 8, 16.3%).

Twenty-nine parents (59.2%) responded that their child could decide to undergo bariatric surgery without the approval of their parents, after reaching the age of 16 or 17 years. Almost all respondents reported that bariatric surgery should be offered alongside a family-based program around surgery (n = 45, 91.8%). The most frequently reported main goal for surgery was weight loss according to the parents (n = 20, 40.8%), followed by improvement of obesity-related comorbidities (n = 10, 20.4%) and self-esteem (n = 10, 20.4%).

Adolescents with overweight, obesity, or severe obesity

Of the 30 adolescents who were treated at COACH and were approached, 19 (63.3%) completed the questionnaire. The adolescents had a mean age of 15.5 ± 1.6 years. All adolescents were affected by overweight, obesity, or severe obesity for at least one year, with a majority of twelve adolescents (63.2%) for six years or longer. Eleven (57.9%) of the adolescents were treated for their overweight, obesity, or severe obesity at the COACH program for at least one year.

Fourteen adolescents (73.7%) reported that bariatric surgery should be available, and 11 (61.1%) wanted to undergo bariatric surgery themselves if their current lifestyle intervention is not effective. Eight of the ten adolescents (80.0%) who were 16 years or older responded that they could make the decision for bariatric surgery independently of their parents. There was no consensus on the program around bariatric surgery in youth; 31.6% of the adolescents would prefer an individual program (n = 6), 36.8% a program with involvement of the parents (n = 7), and 31.6% a program with involvement of parents, brothers, and sisters (n = 6). The main goal of bariatric surgery reported by the adolescents was weight loss (n = 12, 63.2%), followed by improvement of self-esteem (n = 4, 21.0%) and improvement of obesity-related comorbidities (n = 3, 15.8%).

DISCUSSION

To the best of our knowledge, this is the first study in the Netherlands to have surveyed the current attitudes of pediatricians, parents, and adolescents towards bariatric surgery in youth. Our findings demonstrate that the majority of responding pediatricians consider bariatric surgery as a potentially effective treatment for youth with severe obesity. An even larger proportion agreed that it should be a common treatment modality for selected adolescents with severe obesity who are not responding to lifestyle interventions. Besides insufficient response to lifestyle interventions, pediatricians proposed a lower limit of BMI ≥40 kg/m^2 (sex and age adjusted) without comorbidities, a minimum age of 16 years old, and a minimum Tanner stage of IV as

criteria for bariatric surgery. This proposed minimum age criterion was comparable to the minimum age proposed by the parents.

Only a few studies have previously investigated the attitudes of pediatricians towards bariatric surgery in youth, revealing significant heterogeneity[19-21]. In 2009, an American report on pediatricians and family practitioners showed that 88.5% would be unlikely to, or would never refer a child for a bariatric procedure[19]. Conversely, another American study performed in 2007 with pediatricians reported that only 47.0% would decline referral for bariatric surgery[20]. In Europe, no studies have been conducted that have examined attitudes among pediatricians alone. However, a recent study among European pediatric surgeons reported that 65.7% considered bariatric surgery to be a valuable contribution to obtain long-term weight loss in adolescents with severe obesity[27]. The findings in our study among pediatricians are most comparable to the European study among pediatric surgeons, revealing that 59.5% of the pediatricians would refer for bariatric surgery, and 67.7% supporting bariatric surgery as an acceptable treatment modality for a selected group of adolescents with obesity. We assume that that the accumulating evidence on safety and efficacy of bariatric surgery in youth explains why pediatricians are increasingly accepting this treatment modality[14-16].

Based on current American guidelines and Dutch guidelines, bariatric surgery in youth is accompanied by different selection criteria, including a lower limit of BMI[17,28]. No age limit has been set in these selection criteria. Although, in different explorative studies, professionals have indicated their preference for a minimum age for bariatric surgery, yet this has ranged from 12 to 19 years old[18-20,29,30]. The proposed age of 16 years for bariatric surgery in our study is in line with the preferred age reported by a survey among members of the British Obesity and Metabolic Surgery Society and general practitioners[30]. Currently there is no evidence on limiting access to bariatric surgery in youth based on age[28]. The preference of professionals for a minimum age for bariatric surgery in youth could be due to a lack of knowledge about the procedures and their consequences. Education for pediatricians who treat youth with severe obesity would therefore be recommended. Education of pediatricians might lead to fewer barriers in referring youth for bariatric surgery, and eventually lead to better treatment of youth with severe obesity[31].

Until now, the thoughts and beliefs of parents and adolescents regarding bariatric surgery in youth have not been studied extensively[21-23,32,33]. A recent study by Singh et al. reported that 84.6% of parents would consider bariatric surgery after counselling by pediatricians, compared with only 34.5% of the parents without counselling[22]. In our study, 61.2% of parents stated that bariatric surgery should be available for youth with

severe obesity, whereas only 44.9% of parents would allow their child to be referred for bariatric surgery if the current treatment was insufficiently effective. This discrepancy suggests that counselling by pediatricians could play a crucial role when discussing bariatric surgery in youth, which is supported by a qualitative study of parents and adolescents who underwent gastric banding[23].

Another important aspect of bariatric surgery in youth is family involvement, as concluded by Inge et al. in 2004, a motivated and supportive family is pivotal for successful bariatric surgery in youth[34]. This is in line with our findings that the majority of the parents and adolescents stated that bariatric surgery should only be offered in combination with a perioperative family-based program.

A limitation of this study is the low response rate of the pediatricians. This might have led to selection bias of the results. To minimize this, the hospitals where the respondents worked at were compared with the hospitals where all the members of the Dutch Society of Pediatrics worked at, and the respondents more often worked at a non-academic hospital. Nevertheless, we still believe that this distribution of pediatricians across the Netherlands has provided an insight into their thoughts and beliefs regarding bariatric surgery in youth, as the pediatricians in non-academic hospitals are treating more youth with severe obesity compared to academic hospitals. Another potential limitation is that the parents and adolescents surveyed might not be a representative group, since they are being treated for their overweight, obesity, or severe obesity. Therefore, they may experience more positive attitudes regarding bariatric surgery in youth compared to the general population with overweight, obesity, or severe obesity. The third limitation is the small sample size and the limited response rate of the parents and adolescents. To minimize selection bias, the characteristics of the parents and adolescents were compared to the general COACH population, and they were comparable in terms of age and treatment duration.

CONCLUSION

Dutch pediatricians increasingly accept bariatric surgery as a treatment modality in youth with severe obesity who do not respond successfully to lifestyle interventions, as long as conditions such as a minimum BMI, age, and Tanner stage are met. Whether pediatricians will actually refer for bariatric surgery remains to be seen when this treatment option will be implemented in the Netherlands.

REFERENCES

1. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet. 2014;384(9945):766-81.
2. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. Lancet. 2017;390(10113):2627-42.
3. Lee EY, Yoon KH. Epidemic obesity in children and adolescents: risk factors and prevention. Front Med. 2018;12(6):658-66.
4. van Dommelen P, Schönbeck Y, van Buuren S, HiraSing RA. Trends in a life threatening condition: morbid obesity in dutch, Turkish and Moroccan children in The Netherlands. PLoS One. 2014;9(4):e94299.
5. Bendor CD, Bardugo A, Pinhas-Hamiel O, Afek A, Twig G. Cardiovascular morbidity, diabetes and cancer risk among children and adolescents with severe obesity. Cardiovasc Diabetol. 2020;19(1):79.
6. Pinhas-Hamiel O, Zeitler P. The global spread of type 2 diabetes mellitus in children and adolescents. J Pediatr. 2005;146(5):693-700.
7. Beamish AJ, Olbers T. Bariatric and Metabolic Surgery in Adolescents: a Path to Decrease Adult Cardiovascular Mortality. Curr Atheroscler Rep. 2015;17(9):53.
8. Beamish AJ, D'Alessio DA, Inge TH. Controversial Issues: When the drugs don't work, can surgery provide a different outcome for diabetic adolescents? Surg Obes Relat Dis. 2015;11(4):946-8.
9. Shah AS, D'Alessio D, Ford-Adams ME, Desai AP, Inge TH. Bariatric Surgery: A Potential Treatment for Type 2 Diabetes in Youth. Diabetes Care. 2016;39(6):934-40.
10. Karnebeek K, Thapar S, Willeboordse M, van Schayck OCP, Vreugdenhil ACE. Comorbidities in Primary vs Secondary School Children With Obesity and Responsiveness to Lifestyle Intervention. J Clin Endocrinol Metab. 2019;104(9):3803-11.
11. Rijks JM, Plat J, Mensink RP, Dorenbos E, Buurman WA, Vreugdenhil AC. Children With Morbid Obesity Benefit Equally as Children With Overweight and Obesity From an Ongoing Care Program. J Clin Endocrinol Metab. 2015;100(9):3572-80.
12. Danielsson P, Kowalski J, Ekblom Ö, Marcus C. Response of severely obese children and adolescents to behavioral treatment. Arch Pediatr Adolesc Med. 2012;166(12):1103-8.
13. Peirson L, Fitzpatrick-Lewis D, Morrison K, Warren R, Usman Ali M, Raina P. Treatment of overweight and obesity in children and youth: a systematic review and meta-analysis. CMAJ Open. 2015;3(1):E35-46.
14. Shoar S, Mahmoudzadeh H, Naderan M, Bagheri-Hariri S, Wong C, Parizi AS, et al. Long-Term Outcome of Bariatric Surgery in Morbidly Obese Adolescents: a Systematic Review and Meta-Analysis of 950 Patients with a Minimum of 3 years Follow-Up. Obes Surg. 2017;27(12):3110-7.

15. Olbers T, Beamish AJ, Gronowitz E, Flodmark CE, Dahlgren J, Bruze G, et al. Laparoscopic Roux-en-Y gastric bypass in adolescents with severe obesity (AMOS): a prospective, 5-year, Swedish nationwide study. Lancet Diabetes Endocrinol. 2017;5(3):174-83.
16. Inge TH, Courcoulas AP, Jenkins TM, Michalsky MP, Helmrath MA, Brandt ML, et al. Weight Loss and Health Status 3 Years after Bariatric Surgery in Adolescents. N Engl J Med. 2016;374(2):113-23.
17. Behandeling van kinderen met obesitas 2020. Available from: https://richtlijnendatabase.nl/richtlijn/behandeling_van_kinderen_met_obesitas/startpagina_-_behandeling_van_kinderen_met_obesitas.html.
18. Roebroek YGM, Talib A, Muris JWM, van Dielen FMH, Bouvy ND, van Heurn LWE. Hurdles to Take for Adequate Treatment of Morbidly Obese Children and Adolescents: Attitudes of General Practitioners Towards Conservative and Surgical Treatment of Paediatric Morbid Obesity. World J Surg. 2019;43(4):1173-81.
19. Iqbal CW, Kumar S, Iqbal AD, Ishitani MB. Perspectives on pediatric bariatric surgery: identifying barriers to referral. Surg Obes Relat Dis. 2009;5(1):88-93.
20. Woolford SJ, Clark SJ, Gebremariam A, Davis MM, Freed GL. To cut or not to cut: physicians' perspectives on referring adolescents for bariatric surgery. Obes Surg. 2010;20(7):937-42.
21. van Geelen SM, Bolt IL, van der Baan-Slootweg OH, van Summeren MJ. The controversy over pediatric bariatric surgery: an explorative study on attitudes and normative beliefs of specialists, parents, and adolescents with obesity. J Bioeth Inq. 2013;10(2):227-37.
22. Singh UD, Chernoguz A. Parental attitudes toward bariatric surgery in adolescents with obesity. Surg Obes Relat Dis. 2020;16(3):406-13.
23. Willcox K, Warren N, O'Brien P, Brown W, Nottle P, Winnett J, et al. Patient and Parent Perspectives of Adolescent Laparoscopic Adjustable Gastric Banding (LAGB). Obes Surg. 2016;26(11):2667-74.
24. Bonouvrie DS, Beamish AJ, Leclercq WKG, van Mil E, Luijten A, Hazebroek EJ, et al. Laparoscopic roux-en-Y gastric bypass versus sleeve gastrectomy for teenagers with severe obesity - TEEN-BEST: study protocol of a multicenter randomized controlled trial. BMC Surg. 2020;20(1):117.
25. Bervoets L, Massa G. Defining morbid obesity in children based on BMI 40 at age 18 using the extended international (IOTF) cut-offs. Pediatr Obes. 2014;9(5):e94-8.
26. Senn S. Review of Fleiss, statistical methods for rates and proportions. Res Synth Methods. 2011;2(3):221-2.
27. Roebroek YGM, Pruijssers SR, Bouvy ND, van Heurn E. Current Opinions and Practices of Bariatric Surgery in Adolescents: A Survey among Pediatric Surgeons. Eur J Pediatr Surg. 2020;30(1):117-21.
28. Pratt JSA, Browne A, Browne NT, Bruzoni M, Cohen M, Desai A, et al. ASMBS pediatric metabolic and bariatric surgery guidelines, 2018. Surg Obes Relat Dis. 2018;14(7):882-901.
29. Thenappan A, Nadler E. Bariatric Surgery in Children: Indications, Types, and Outcomes. Curr Gastroenterol Rep. 2019;21(6):24.
30. Penna M, Markar S, Hewes J, Fiennes A, Jones N, Hashemi M. Adolescent bariatric surgery--thoughts and perspectives from the UK. Int J Environ Res Public Health. 2013;11(1):573-82.

31. Malhotra S, Czepiel KS, Akam EY, Shaw AY, Sivasubramanian R, Seetharaman S, et al. Bariatric surgery in the treatment of adolescent obesity: current perspectives in the United States. Expert Rev Endocrinol Metab. 2021;16(3):123-34.

32. Woolford SJ, Clark SJ, Sallinen BJ, Geiger JD, Freed GL. Bariatric surgery decision making challenges: the stability of teens' decisions and the treatment failure paradox. Pediatr Surg Int. 2012;28(5):455-60.

33. Childerhose JE, Eneli I, Steele KE. Adolescent bariatric surgery: a qualitative exploratory study of US patient perspectives. Clin Obes. 2018;8(5):345-54.

34. Inge TH, Krebs NF, Garcia VF, Skelton JA, Guice KS, Strauss RS, et al. Bariatric surgery for severely overweight adolescents: concerns and recommendations. Pediatrics. 2004;114(1):217-23.

CHAPTER 8

DEVELOPMENT OF A CLINICAL PATHWAY FOR BARIATRIC SURGERY AS AN INTEGRAL PART OF A COMPREHENSIVE TREATMENT FOR ADOLESCENTS WITH SEVERE OBESITY IN THE NETHERLANDS

Kelly G.H. van de Pas
Anita. C.E. Vreugdenhil
Loes Janssen
Wouter K.G. Leclercq
Meeike Kusters
Malika Chegary
Inès von Rosenstiel
Eric J. Hazebroek
Edgar G.A.H. van Mil
Renske Wassenberg
Linda M.W. Hover
Wim G. van Gemert
François M.H. van Dielen

Submitted.

CHAPTER 9

GENERAL DISCUSSION

GENERAL DISCUSSION

Childhood obesity is a major health crisis associated with a variety of life-threatening medical conditions and psychosocial impairments[1,2]. Particularly children and adolescents with the most severe grade of obesity face substantial physical and psychosocial consequences[3]. Despite this, they are underrepresented in clinical practice and scientific research compared to youth with overweight or obesity. This thesis focused specifically on this vulnerable group, and aimed to gain insight into the impact of the most severe grade of obesity in youth. We also examined the effectiveness of a tailored multidisciplinary lifestyle intervention, which is the current cornerstone treatment for children and adolescents with severe obesity. In a subgroup of youth with severe obesity, tailored multidisciplinary lifestyle interventions are insufficiently effective. For this particular group additional treatment strategies are warranted. The second part of this thesis focused on optimizing treatment strategies for youth with severe obesity and explored the applicability of bariatric surgery. As a result, a clinical pathway for bariatric surgery as an integral part of a comprehensive treatment was developed for adolescents with severe obesity in the Netherlands. Below, the main findings of this thesis are discussed as well as its clinical implications and future perspectives.

Impact of severe obesity in youth

Severe obesity during childhood is associated with several medical conditions such as type 2 diabetes mellitus (T2DM)[1,3]. With increasing weight, the consequences of these conditions worsen with medical treatments failing earlier and a reduced life expectancy by up to 20 years[4,5]. In **chapter 4**, we found that insulin resistance was present in 51.5% of children, and 78.3% of adolescents with severe obesity. Elevated liver enzymes were observed in 53.4% of children and 48.6% of adolescents. Childhood obesity is also associated with psychosocial impairments, leading to a lower health-related quality of life (HRQoL)[2,6,7]. **Chapter 2** reported a study indicating that children and adolescent with the most severe grade of obesity had a lower physical and psychological wellbeing than their peers with less severe forms of obesity. Lower physical and psychological wellbeing results in decreased energy levels, and increased feelings of loneliness and sadness. A recent study among 803 children and adolescents confirmed these findings. This study found that youth with the most severe grade of obesity had lower scores on all HRQoL dimensions (physical, social, emotional and school functioning)[8]. Lower scores indicate that it is harder for youth with severe obesity to exercise. There is a greater likelihood that these children and adolescents will be bullied, and feel anxious in comparison to children and adolescents with overweight and obesity. In addition, they are more forgetful and attend school less frequently. These findings highlight that youth

with severe obesity are negatively impacted, both physically and psychosocially. As a result, severe obesity is associated with the development of psychological problems and high school dropout compared to peers with a normal weight[2,9]. These studies once again implicate the enormous implications of the global health crisis of childhood obesity.

As mentioned previously, severe obesity has an immense impact on the lifestyle, health and wellbeing of youth. Other factors, such as the COVID-19 pandemic, also affect youth's lifestyle, health and wellbeing[10,11]. In **chapter 3,** fifteen families were interviewed, and these families reported an overall unhealthier lifestyle and decreased wellbeing during the pandemic. The negative effects of the pandemic were even more pronounced among vulnerable children and adolescents, including those with severe obesity. Two adolescents with severe obesity participated in this study. They reported an increase in weight compared to none of the children with a normal weight (n = 12). Previous studies have shown that children and adolescents with obesity are at risk for weight gain during a pandemic[12,13]. Our results suggest that this risk could be higher for those with the most severe grade of obesity. These results highlight the need for special attention (e.g., additional counseling) for children and adolescents with severe obesity during future crises and pandemics, especially as long-term participation in a lifestyle intervention can protect against weight gain[13].

Besides the negative consequences on the health and wellbeing of youth with severe obesity, the societal consequences are enormous. Childhood obesity contributes to socio-economic inequalities. A lower socio-economic position is associated with the development and/or maintenance of obesity[14,15]. Additionally, obesity is accompanied by considerable costs to society. The average costs to society of a person with overweight or obesity comprises 11,463 euros annually. These costs include healthcare expenses, productivity losses (absence from work due to sickness), and patient and family costs (diet books, personal training). Of these annual societal costs, productivity loss constitutes the largest portion (4,519 euros), while healthcare represents the smallest (2,907 euros). The total costs to society are significantly higher for individuals with obesity compared to those with overweight[16]. Following these findings, children and adolescents with severe obesity will impose significant costs on society, as they experience weight related complaints more frequently compared to those with obesity. Additionally, the majority of the children and adolescents with severe obesity are likely to remain severely obese in adulthood[17]. If youth suffer from severe obesity for an extended period, these societal costs could escalate to as much as a million euros per individual. This underscores the importance of addressing severe obesity as early as possible.

Multidisciplinary lifestyle intervention

A multidisciplinary lifestyle intervention is the current cornerstone treatment for children and adolescents with severe obesity[18,19]. However, research evaluating this intervention mostly focused on youth with overweight and obesity. Studies only focusing on youth with severe obesity are scarce. Therefore, in **chapter 4** the effectiveness of a long-term, tailored multidisciplinary lifestyle intervention in children and adolescents with severe obesity was evaluated. Children (aged up to 11 years) experienced more weight loss compared to adolescents (aged 12-17 years) after one and two years of intervention. Besides this, more children achieved a clinically significant decrease in their BMI z-score (≥0.25) and improvements in cardio metabolic health parameters. It appears that lifestyle interventions are more effective at an early age. Possible explanations for this include the decline in parental influence and increased autonomy during adolescence[20]. Some adolescents may have difficulties assessing the long-term health consequences of severe obesity and might require parental guidance to adopt a healthy lifestyle. Also, adolescents tend to be less physically active compared to younger children[21]. These factors make adolescents with severe obesity a particularly challenging group to treat, as confirmed by previous studies[22,23]. For a selected group of adolescents for whom an intensive, tailored multidisciplinary lifestyle intervention is insufficiently effective, additional treatment strategies such as bariatric surgery are warranted. In line with these thoughts, a randomized controlled trial was conducted in Sweden comparing the outcomes of bariatric surgery to a lifestyle intervention in adolescents with severe obesity. The adolescents who underwent bariatric surgery had a BMI decrease of 12.6 kg/m^2 after two years, whereas the lifestyle intervention group had a BMI decrease of 0.2 kg/m^2. Moreover, improvements in cardio metabolic health parameters and physical aspects of quality of life were observed in the surgical group. Postoperative complications were few and mild[24]. Based on these results bariatric surgery might be an effective additional treatment modality for a selected group of adolescents with severe obesity.

Bariatric surgery

Bariatric surgery appears to be safe and effective in the treatment of severe obesity in youth[25-30]. However, it remains controversial as adolescents are offered irreversible interventions with lifelong consequences. Therefore, bariatric surgery should only be performed in a controlled setting and in a selected group of adolescents who do not benefit sufficiently from a multidisciplinary lifestyle intervention. In the Netherlands, bariatric surgery in adolescents (aged <18 years) is only allowed in the context of scientific research.

A number of issues had to be addressed before bariatric surgery could become available for adolescents with severe obesity in the Netherlands. First, more knowledge was needed regarding the efficacy and safety of bariatric surgery in young adults. This lack of knowledge might be one of the reasons why the utilization of bariatric surgery in the younger population lags behind[31]. Using nationwide population-based data from the Netherlands, **chapter 5** showed that bariatric surgery was at least as safe and effective in young adults (aged 18-25 years) as in adults (aged 35-55 years) up to five years after surgery. In **chapter 6** the two most commonly performed bariatric procedures (Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG)) in young adults were compared. Up to three years after surgery, the RYGB showed more weight loss and especially in females. However, to draw firm conclusions for an optimal bariatric procedure for young adults, more prospective long-term research is needed. We might speculate that a single 'one size fits all' type of bariatric procedure for the younger population does not exist, and advocate a tailored approach taking into account patient characteristics. But most importantly, the abovementioned findings suggest that the reluctance towards bariatric surgery in the younger age group seems unfounded. Subsequently, bariatric surgery should be offered to a selected group of adolescents with severe obesity.

A second issue to be clarified were the opinions of Dutch pediatricians, parents, and adolescents towards bariatric surgery in youth. Pediatricians should inform and refer adolescents for bariatric surgery. Also, adolescents and their parents must be willing to undergo bariatric surgery, as well as commit to the necessary behavioral changes and follow-up trajectory. **Chapter 7** found that 59.5% of the Dutch pediatricians would refer youth with severe obesity for bariatric surgery, and 67.7% of them supported bariatric surgery as an acceptable treatment modality for a selected group of adolescents. Of the parents and adolescents surveyed, 61.2% and 73.7% felt that bariatric surgery should be available for youth with severe obesity, whereas only 44.9% of the parents would allow their child to be referred for bariatric surgery and 61.1% of the adolescents wanted to undergo surgery themselves. Taking previous research into account, it seems that this treatment modality is gaining acceptance, as more than 60% of the stakeholders indicated that bariatric surgery should be available for adolescents with severe obesity in the Netherlands[32,33]. However, there is a discrepancy between the percentage of stakeholders in favor of bariatric surgery and those who would refer for surgery or want to undergo surgery. Educating stakeholders on the diligently developed clinical pathway related to adolescent bariatric surgery in the Netherlands could be an opportunity to bridge this gap. As a result, potentially more pediatricians will refer suitable adolescents for bariatric surgery and more eligible adolescents want to undergo surgery themselves.

The findings in **chapter 5, 6 and 7** suggest that bariatric surgery can be an effective additional treatment modality for youth with severe obesity in the Netherlands. However, there was a third issue that needed to be addressed: the care for adolescents with severe obesity who want to undergo bariatric surgery was not established in the Netherlands. Several guidelines do mention that this care needs to be multidisciplinary[19,34]. The Dutch guideline reports that adolescents should be willing to participate in a postoperative lifestyle intervention and lifelong follow-up, meaning that bariatric surgery should be integrated into a comprehensive treatment for adolescents with severe obesity[18]. With these thoughts in mind a clinical pathway for bariatric surgery in adolescents was developed and reported in **chapter 8.** The clinical pathway consists of an eligibility assessment, as well as peri- and postoperative care. The eligibility assessment involves evaluation by a specialized pediatric obesity unit, and an anonymous evaluation by a national board consisting of independent experts in the field of adolescent bariatric surgery. The final decision for surgery is made by the multidisciplinary team for adolescent bariatric surgery, taking into account whether the adolescent will adhere to postoperative counselling and follow-up. Globally, there is no consensus on how adolescents should be selected for bariatric surgery. To be diligent, we involved all relevant stakeholders in designing a multidisciplinary eligibility assessment[18,19,34]. The multidisciplinary team for adolescent bariatric surgery consists of various disciplines; a bariatric surgeon, a pediatrician, a pediatric psychologist, a dietician and a care coordinator. All team members should be dedicated and have expertise in childhood obesity as well as bariatric surgery[27]. The multidisciplinary team for adolescent bariatric surgery provides the peri- and postoperative care in cooperation with the lifestyle intervention the adolescents participated in before surgery. Whether the designed clinical pathway is sufficiently effective and careful should be assessed in the future. Currently, the first adolescents have been enrolled and underwent bariatric surgery.

As mentioned previously, in the Netherlands, bariatric surgery in adolescents is only allowed in the context of scientific research. Therefore, the TEEN-BEST study was designed, currently being the only authorized study for adolescent bariatric surgery in the Netherlands[35]. The original design of the TEEN-BEST study was an international, multicenter, randomized controlled trial (RCT). The TEEN-BEST was supposed to be the first study to compare the two most commonly performed surgical techniques in adolescent bariatric surgery (RYGB versus SG). However, the study design changed due to a number of reasons. The first reason was that a SG is relatively contra-indicated in case of GERD given the risk of developing esophagitis and subsequent Barrett esophagus with its eventual malignant potential[36,37]. Randomization means that adolescents do not have a free choice regarding the type of bariatric procedure. Subsequently, eligible

adolescents with GERD would be excluded from the TEEN-BEST study, depriving them of the only chance to undergo bariatric surgery in the Netherlands. Additionally, a shared opinion in the participating centers was that adolescents should not be denied a choice between the two surgical procedures. Patients today are increasingly encouraged to actively participate in decision-making and more likely have a treatment preference. These strong treatment preferences of patients, which might be the case in adolescent bariatric surgery, call for another study design then a RCT[38]. Therefore, the design of the TEEN-BEST study changed to a prospective cohort study, allowing adolescents to choose between RYGB or SG based on their personal preferences. In case an adolescent has GERD, a RYGB is recommended by the bariatric surgeons. The TEEN-BEST study aims to implement and assess the feasibility, efficacy and safety of bariatric surgery in adolescents with severe obesity in the Netherlands. Secondary aims are to implement and assess the feasibility of the comprehensive clinical pathway and to evaluate quality of life, obesity-related comorbidities and body composition up to five years after surgery. A subgroup analysis based on the type of bariatric procedure will also be performed in which various weight-related outcome measures will be taken into account. This subgroup analysis will gain more insight into the optimal choice of bariatric procedure according to specific characteristics and conditions in adolescent bariatric surgery. The first results are expected in 2028.

Clinical implications and future perspectives

The findings of the studies reported in this thesis have implications for both clinical practice and future research. These implications and future perspectives are presented separately for a lifestyle intervention as well as for bariatric surgery.

Multidisciplinary lifestyle intervention

Quality of life has become an important topic in healthcare. Improving quality of life should be one of the main goals in the treatment of childhood obesity, as physical and psychosocial wellbeing (measured by quality of life) are likely to be as important to youth as weight loss[39]. However, the majority of the interventions primarily focus on weight loss and the improvement of cardio metabolic health parameters[40,41]. Two meta-analyses have indicated that multidisciplinary lifestyle interventions have minimal or slightly positive effects on quality of life in children and adolescents with overweight and obesity[39,42]. Furthermore, weight loss was not associated with improvements in quality of life[39]. This suggests that other factors play a crucial role in enhancing quality of life. To date, there has been limited research on other determinants (such as parental involvement or number of consultations) influencing quality of life in children and adolescents with overweight and obesity participating in a lifestyle intervention. Therefore, our research group is conducting a study among children and

adolescents with overweight, obesity and severe obesity to assess whether quality of life improves during a tailored multidisciplinary lifestyle intervention and whether this improvement depends on weight loss or other determinants. Once this study is performed, determinants that improve quality of life can be used by healthcare professionals treating childhood obesity. This is of utmost importance as a lower quality of life can lead to reduced adherence to treatment, making it even more challenging to treat obesity[43].

Severe obesity has a significant impact on children, adolescents and their parents, stressing the need for effective treatment strategies. Our findings suggest that initiating treatment for severe obesity at a young age is crucial, as younger children are more likely to benefit from a multidisciplinary lifestyle intervention compared to older children. Healthcare providers who identify children and adolescents with severe obesity should not hesitate to discuss the impact of severe obesity with them and their families. Besides this, health care providers should take the initiative to start treatment or refer these youth to specialized pediatric obesity units. Additionally, future research is warranted as a subgroup of youth with severe obesity do not sufficiently benefit from a lifestyle intervention. Continued efforts are needed to identify those children and adolescents. By identifying them at an early age, we can intensify their treatment or prepare them for additional interventions such as pharmacotherapy or bariatric surgery. It is important to note that this thesis did not evaluate the additional value of pharmacotherapy in combination with a multidisciplinary lifestyle intervention. Glucagon like peptide-1 analogs (liraglutide and semaglutide) and glucose-dependent insulinotropic polypeptide analog (tirzepatide) have shown promising results. In adults, semaglutide and tirzepatide have resulted in weight loss of 15 to 20%[44-46]. Although pharmacotherapy rises hope, future research is needed to assess the long-term efficacy of pharmacotherapy in youth with severe obesity, including the impact on quality of life and safety.

Bariatric surgery

Adolescent bariatric surgery requires merging the care of various disciplines to provide the optimal treatment for these vulnerable youth. The TEEN-BEST study, along with the presented comprehensive clinical pathway, has made bariatric surgery available in trial setting for adolescents with severe obesity in the Netherlands. Clinical practice and future evaluation of the study results must reveal whether the clinical pathway, as currently designed, is sufficiently effective to select suitable candidates and adequately guide them through the pre- and postoperative trajectory. It is our hope that the delicately designed clinical pathway as provided paves the way to the implementation of adolescent bariatric surgery into regular care. However, there are still certain

aspects of adolescent bariatric surgery that require attention. To date, there is only one multidisciplinary team for adolescent bariatric surgery, which is located at Máxima MC and the Maastricht University Medical Centre+/Centre for Overweight Adolescent and Children's Healthcare (COACH). To ensure that bariatric surgery is accessible to all eligible adolescents, it is imperative to establish more multidisciplinary teams for adolescent bariatric surgery across the Netherlands, thereby eliminating geographical barriers.

As previously mentioned, bariatric surgery is still considered a controversial novel treatment approach for adolescents with severe obesity in the Netherlands. Also, bariatric surgery is accompanied by stigma, which acts as a barrier for adolescents considering bariatric surgery as a treatment option[47]. To successfully implement adolescent bariatric surgery, it is essential to focus on educating and gaining the trust of various stakeholders, including the Dutch population. Stakeholders and the Dutch population must be informed about the fact that not every adolescent with severe obesity is eligible for bariatric surgery, and that the clinical pathway for adolescent bariatric surgery has been carefully developed. Those adolescents who do qualify for bariatric surgery are currently not responding to the current cornerstone treatment, motived to adhere to long-term lifestyle adjustments and require care because they already suffer from obesity-related comorbidities. By disseminating this information, the stigma surrounding adolescent bariatric surgery will hopefully diminish. Additionally, healthcare professionals (e.g., pediatricians, bariatric surgeons and general practitioners) should be educated on which adolescents might be suitable for bariatric surgery, the comprehensive clinical pathway, and how to refer adolescents for bariatric surgery. This education should ensure that all eligible adolescents have access to bariatric surgery. Furthermore, healthcare professionals should receive training on recognizing and treating the most common complications after bariatric surgery, enabling early intervention. At last, adolescents who may qualify for bariatric surgery should be informed about the healthcare providers they can consult regarding this treatment modality.

Another crucial area that warrants attention is the reimbursement of adolescent bariatric surgery[48]. In the Netherlands, bariatric surgery below the age of 18 is currently not reimbursed by healthcare insurance companies. Presently, two major health insurance companies authorized reimbursement based on a policy rule for innovation of the Dutch Health Authority. However, not all insurance companies reimburse adolescent bariatric surgery and at some point, this policy rule ends. Therefore, healthcare professionals should convince health insurance companies that this care needs to be reimbursed for all eligible adolescents. This is of considerable importance,

as adolescents with severe obesity including their families are often unable to bear the costs for bariatric surgery themselves. We implore health care insurance companies to put short term costs in perspective and enact a durable policy, as bariatric surgery is a cost-effective treatment modality for adolescents five years after surgery[48].

At last, it must be emphasized that prevention is superior to cure. This thesis has specifically aimed to shed light on the impact- and improve the treatment of severe obesity in youth, a condition that is partly preventable through a healthy lifestyle. It is imperative that we continue to actively and collectively strive towards preventing childhood obesity. This requires a joint effort from society in its entirety, including policy makers, health care professionals, supermarkets, families, and beyond. This combined effort is a prerequisite to ensure a healthier future for the next generation.

REFERENCES

1. Kelly AS, Barlow SE, Rao G, Inge TH, Hayman LL, Steinberger J, et al. Severe obesity in children and adolescents: identification, associated health risks, and treatment approaches: a scientific statement from the American Heart Association. Circulation. 2013;128(15):1689-712.
2. Rankin J, Matthews L, Cobley S, Han A, Sanders R, Wiltshire HD, et al. Psychological consequences of childhood obesity: psychiatric comorbidity and prevention. Adolesc Health Med Ther. 2016;7:125-46.
3. Skinner AC, Perrin EM, Moss LA, Skelton JA. Cardiometabolic Risks and Severity of Obesity in Children and Young Adults. N Engl J Med. 2015;373(14):1307-17.
4. Beamish AJ, D'Alessio DA, Inge TH. Controversial Issues: When the drugs don't work, can surgery provide a different outcome for diabetic adolescents? Surg Obes Relat Dis. 2015;11(4):946-8.
5. Olshansky SJ, Passaro DJ, Hershow RC, Layden J, Carnes BA, Brody J, et al. A potential decline in life expectancy in the United States in the 21st century. N Engl J Med. 2005;352(11):1138-45.
6. Buttitta M, Iliescu C, Rousseau A, Guerrien A. Quality of life in overweight and obese children and adolescents: a literature review. Qual Life Res. 2014;23(4):1117-39.
7. Puder JJ, Munsch S. Psychological correlates of childhood obesity. Int J Obes (Lond). 2010;34 Suppl 2:S37-43.
8. van der Voorn B, Camfferman R, Seidell JC, Halberstadt J. Health-related quality of life in children under treatment for overweight, obesity or severe obesity: a cross-sectional study in the Netherlands. BMC Pediatr. 2023;23(1):167.
9. Gensthaler L, Felsenreich DM, Jedamzik J, Eichelter J, Nixdorf L, Bichler C, et al. Trends of Overweight and Obesity in Male Adolescents: Prevalence, Socioeconomic Status, and Impact on Cardiovascular Risk in a Central European Country. Obes Surg. 2022;32(4):1024-33.
10. Ravens-Sieberer U, Kaman, A., Erhart, M. et al. Impact of the COVID-19 pandemic on quality of life and mental health in children and adolescents in Germany. European Child & Adolescent Psychiatry. 2021.
11. Koletzko B, Holzapfel C, Schneider U, Hauner H. Lifestyle and Body Weight Consequences of the COVID-19 Pandemic in Children: Increasing Disparity. Ann Nutr Metab. 2021;77(1):1-3.
12. Vogel M, Geserick M, Gausche R, Beger C, Poulain T, Meigen C, et al. Age- and weight group-specific weight gain patterns in children and adolescents during the 15 years before and during the COVID-19 pandemic. Int J Obes (Lond). 2022;46(1):144-52.
13. Lubrecht J, Arayess L, Reijnders D, Hesselink ML, Velde GT, Janse A, et al. Weight Gain in Children during the COVID-19 Pandemic and the Protective Effect of Lifestyle Intervention in Children with Obesity. Obes Facts. 2022;15(4):600-8.
14. Bouthoorn SH, Wijtzes AI, Jaddoe VW, Hofman A, Raat H, van Lenthe FJ. Development of socioeconomic inequalities in obesity among Dutch pre-school and school-aged children. Obesity (Silver Spring). 2014;22(10):2230-7.

15. Shrewsbury V, Wardle J. Socioeconomic status and adiposity in childhood: a systematic review of cross-sectional studies 1990-2005. Obesity (Silver Spring). 2008;16(2):275-84.
16. Hecker J, Freijer K, Hiligsmann M, Evers S. Burden of disease study of overweight and obesity; the societal impact in terms of cost-of-illness and health-related quality of life. BMC Public Health. 2022;22(1):46.
17. Gordon-Larsen P, The NS, Adair LS. Longitudinal trends in obesity in the United States from adolescence to the third decade of life. Obesity (Silver Spring). 2010;18(9):1801-4.
18. Nederlandse Vereniging voor Kindergeneeskunde. Behandeling van kinderen met obesitas 2020. Available from: https://richtlijnendatabase.nl/richtlijn/behandeling_van_kinderen_met_obesitas/startpagina_-_behandeling_van_kinderen_met_obesitas.html.
19. Hampl SE, Hassink SG, Skinner AC, Armstrong SC, Barlow SE, Bolling CF, et al. Clinical Practice Guideline for the Evaluation and Treatment of Children and Adolescents With Obesity. Pediatrics. 2023;151(2).
20. De Goede IH, Branje SJ, Meeus WH. Developmental changes in adolescents' perceptions of relationships with their parents. J Youth Adolesc. 2009;38(1):75-88.
21. Ten Velde G, Plasqui G, Dorenbos E, Winkens B, Vreugdenhil A. Objectively measured physical activity and sedentary time in children with overweight, obesity and morbid obesity: a cross-sectional analysis. BMC Public Health. 2021;21(1):1558.
22. Knop C, Singer V, Uysal Y, Schaefer A, Wolters B, Reinehr T. Extremely obese children respond better than extremely obese adolescents to lifestyle interventions. Pediatr Obes. 2015;10(1):7-14.
23. Danielsson P, Kowalski J, Ekblom Ö, Marcus C. Response of severely obese children and adolescents to behavioral treatment. Arch Pediatr Adolesc Med. 2012;166(12):1103-8.
24. Järvholm K, Janson A, Peltonen M, Neovius M, Gronowitz E, Engström M, et al. Metabolic and bariatric surgery versus intensive non-surgical treatment for adolescents with severe obesity (AMOS2): a multicentre, randomised, controlled trial in Sweden. Lancet Child Adolesc Health. 2023;7(4):249-60.
25. Shoar S, Mahmoudzadeh H, Naderan M, Bagheri-Hariri S, Wong C, Parizi AS, et al. Long-Term Outcome of Bariatric Surgery in Morbidly Obese Adolescents: a Systematic Review and Meta-Analysis of 950 Patients with a Minimum of 3 years Follow-Up. Obes Surg. 2017;27(12):3110-7.
26. Inge TH, Courcoulas AP, Jenkins TM, Michalsky MP, Brandt ML, Xanthakos SA, et al. Five-Year Outcomes of Gastric Bypass in Adolescents as Compared with Adults. N Engl J Med. 2019;380(22):2136-45.
27. Beamish AJ, Harper ER, Järvholm K, Janson A, Olbers T. Long-term outcomes following adolescent metabolic and bariatric surgery. J Clin Endocrinol Metab. 2023.
28. McClelland PH, Kabata K, Gorecki W, Jano A, Zenilman ME, Gorecki P. Long-term weight loss after bariatric procedures for morbidly obese adolescents and youth: a single-institution analysis with up to 19-year follow-up. Surg Endosc. 2023;37(3):2224-38.
29. Hoeltzel GD, Swendiman RA, Tewksbury CM, Parks EP, Williams NN, Dumon KR. How safe is adolescent bariatric surgery? An analysis of short-term outcomes. J Pediatr Surg. 2022;57(8):1654-9.

30. Goldenshluger M, Iluz R, Beck T, Adileh M, Segev L, Froilych D, et al. Laparoscopic Sleeve Gastrectomy in Adolescents: Ten-Years Follow-up. Obes Surg. 2023;33(1):32-7.

31. Mocanu V, Lai K, Dang JT, Switzer NJ, Birch DW, Ball GDC, et al. Evaluation of the Trends, Characteristics, and Outcomes in North American Youth Undergoing Elective Bariatric Surgery. Obes Surg. 2021;31(5):2180-7.

32. Roebroek YGM, Talib A, Muris JWM, van Dielen FMH, Bouvy ND, van Heurn LWE. Hurdles to Take for Adequate Treatment of Morbidly Obese Children and Adolescents: Attitudes of General Practitioners Towards Conservative and Surgical Treatment of Paediatric Morbid Obesity. World J Surg. 2019;43(4):1173-81.

33. Iqbal CW, Kumar S, Iqbal AD, Ishitani MB. Perspectives on pediatric bariatric surgery: identifying barriers to referral. Surg Obes Relat Dis. 2009;5(1):88-93.

34. Eisenberg D, Shikora SA, Aarts E, Aminian A, Angrisani L, Cohen RV, et al. 2022 American Society of Metabolic and Bariatric Surgery (ASMBS) and International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) Indications for Metabolic and Bariatric Surgery. Obes Surg. 2023;33(1):3-14.

35. Bonouvrie DS, Beamish AJ, Leclercq WKG, van Mil E, Luijten A, Hazebroek EJ, et al. Laparoscopic roux-en-Y gastric bypass versus sleeve gastrectomy for teenagers with severe obesity - TEEN-BEST: study protocol of a multicenter randomized controlled trial. BMC Surg. 2020;20(1):117.

36. Nederlandse Vereniging voor Heelkunde. Chirurgische behandeling van obesitas 2020. Available from: https://richtlijnendatabase.nl/richtlijn/chirurgische_behandeling_van_obesitas/startpagina_-_chirurgische_behandeling_van_obesitas.html.

37. Yeung KTD, Penney N, Ashrafian L, Darzi A, Ashrafian H. Does Sleeve Gastrectomy Expose the Distal Esophagus to Severe Reflux?: A Systematic Review and Meta-analysis. Ann Surg. 2020;271(2):257-65.

38. Brewin CR, Bradley C. Patient preferences and randomised clinical trials. Bmj. 1989;299(6694):313-5.

39. Murray M, Pearson JL, Dordevic AL, Bonham MP. The impact of multicomponent weight management interventions on quality of life in adolescents affected by overweight or obesity: a meta-analysis of randomized controlled trials. Obes Rev. 2018;20(2):278-89.

40. Al-Khudairy L, Loveman E, Colquitt JL, Mead E, Johnson RE, Fraser H, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese adolescents aged 12 to 17 years. Cochrane Database Syst Rev. 2017;6(6):Cd012691.

41. Mead E, Brown T, Rees K, Azevedo LB, Whittaker V, Jones D, et al. Diet, physical activity and behavioural interventions for the treatment of overweight or obese children from the age of 6 to 11 years. Cochrane Database Syst Rev. 2017;6(6):Cd012651.

42. Ligthart KA, Paulis WD, Djasmo D, Koes BW, van Middelkoop M. Effect of multidisciplinary interventions on quality of life in obese children: a systematic review and meta-analysis. Qual Life Res. 2015;24(7):1635-43.

43. Nagasawa H, Tachi T, Sugita I, Esaki H, Yoshida A, Kanematsu Y, et al. The Effect of Quality of Life on Medication Compliance Among Dialysis Patients. Front Pharmacol. 2018;9:488.

44. Kelly AS, Auerbach P, Barrientos-Perez M, Gies I, Hale PM, Marcus C, et al. A Randomized, Controlled Trial of Liraglutide for Adolescents with Obesity. N Engl J Med. 2020;382(22):2117-28.

45. Wilding JPH, Batterham RL, Calanna S, Davies M, Van Gaal LF, Lingvay I, et al. Once-Weekly Semaglutide in Adults with Overweight or Obesity. N Engl J Med. 2021;384(11):989-1002.

46. Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, et al. Tirzepatide Once Weekly for the Treatment of Obesity. N Engl J Med. 2022;387(3):205-16.

47. Campbell EG, Alasmar A, Lawrence R, Kurpius-Brock M, DeCamp M, Kovar A, et al. Barriers to metabolic bariatric surgery in adolescents: results of a qualitative study. Surg Obes Relat Dis. 2022;18(6):794-802.

48. Klebanoff MJ, Chhatwal J, Nudel JD, Corey KE, Kaplan LM, Hur C. Cost-effectiveness of Bariatric Surgery in Adolescents With Obesity. JAMA Surg. 2017;152(2):136-41.

CHAPTER 10

IMPACT

IMPACT

Scientific impact

"Scientific impact is the contribution of results from scientific research to the understanding and advancement of science"

The first aim of this thesis was to gain insight into the impact of severe obesity in youth. The second aim was to optimize treatment strategies for those with the most severe grade of obesity by exploring the applicability of bariatric surgery. The first part of this thesis revealed that youth with severe obesity are negatively impacted, both physically and psychosocially. Besides this, youth with severe obesity are among the most vulnerable groups when a pandemic occurs. In these children and adolescents with severe obesity, a multidisciplinary lifestyle intervention had a positive and sustained effect on health parameters. These effects were even more pronounced in the younger age group. However, for a subgroup of adolescents with severe obesity a lifestyle intervention was insufficiently effective. For these adolescents with severe obesity, additional treatment strategies are warranted. The second part of this thesis displayed that bariatric surgery is as safe and effective in young adults as in adults. Additionally, the majority of the pediatricians, parents and adolescents revealed positive attitudes towards bariatric surgery in youth. Consequently, a clinical pathway for bariatric surgery as an integral part of a comprehensive treatment for adolescents with severe obesity was developed.

Socio-economic impact

"Socio-economic impact is the contribution of results from scientific research to changes in or development of socio-economic sectors and to socio-economic challenges"

Globally, there are 379 million children and adolescents with obesity, and this number continues to rise[1]. In addition to the physical consequences associated with obesity, youth with obesity are more likely to fail in high school, become unemployed, remain single or develop psychosocial problems[2-4]. This illustrates the enormous social impact of childhood obesity. According to this thesis, youth with severe obesity are more affected compared to youth with less severe forms of obesity. By highlighting the vulnerability of youth with severe obesity, this thesis creates awareness of the importance of effective, long-lasting treatment strategies at an early age in this often overlooked population.

The current cornerstone treatment for severe obesity is a multidisciplinary lifestyle intervention. However, in a subgroup of adolescents with severe obesity, this treatment

proves to be insufficiently effective. Bariatric surgery in addition to a multidisciplinary lifestyle intervention might provide an effective treatment strategy in this group. This thesis explored the applicability of bariatric surgery in youth. We developed a comprehensive clinical pathway for adolescent bariatric surgery. As a result, the studies described in this thesis enriched the care for youth with severe obesity with an additional treatment modality. Currently, adolescent bariatric surgery is only available in the context of scientific research. It is our hope that the delicately designed clinical pathway as provided in this thesis paves the way to its implementation into regular care.

Beyond the social impact of childhood obesity, the economic burden is enormous. A recent meta-analysis revealed that the total annual medical costs of a child with obesity are approximately $300 higher compared to a child with a normal weight[5]. It can be presumed that these costs are even higher for youth with severe obesity as they more often suffer from weight related complaints compared to those with obesity. The expected excess lifetime healthcare costs are 3.7 times higher for men and 5 times higher for woman who suffered from overweight or obesity during childhood[6]. This thesis contributed to the development of a comprehensive clinical pathway for adolescent bariatric surgery. In this clinical pathway, eligible adolescents with severe obesity are carefully selected for bariatric surgery. The eligible adolescents receive extensive counselling and follow-up, ensuring the surgery's benefits are maximized in terms of both health related and financial outcomes. While the initial costs of bariatric surgery may be high, it is expected that adolescent bariatric surgery will prove to be cost-effective in the long term. Especially as a previous study suggests that adolescent bariatric surgery is cost-effective five years after surgery[7].

Target audience

The target audience of this thesis are healthcare professionals who treat childhood obesity, as well as youth with severe obesity including their families. Healthcare professionals include, among others, general practitioners, dieticians, psychologists, pediatricians, bariatric surgeons as well as pediatric surgeons. These stakeholders were engaged by presenting the results of this thesis at several national and international meetings. The findings have also been published in multiple scientific journals focusing on obesity. Hereby, creating awareness for the impact of severe obesity in youth, and the challenges associated with its treatment strategies. Additionally, the national media reported several times on adolescent bariatric surgery[8]. Consequently, both healthcare professionals and youth with severe obesity have been informed about the availability of bariatric surgery as a treatment option, albeit in a research context, for a select group of adolescents with severe obesity in the Netherlands. At last, some of the chapters in this thesis were summarized, translated to Dutch and published in the monthly journal of 'Bariatrie Groep Nederland', which is a patient federation of bariatric surgery patients.

REFERENCES

1. World Health Organization. World Obesity Day 2022 – Accelerating action to stop obesity 2022. Available from: https://www.who.int/news/item/04-03-2022-world-obesity-day-2022-accelerating-action-to-stop-obesity.
2. Kelly AS, Barlow SE, Rao G, Inge TH, Hayman LL, Steinberger J, et al. Severe obesity in children and adolescents: identification, associated health risks, and treatment approaches: a scientific statement from the American Heart Association. Circulation. 2013;128(15):1689-712.
3. Rankin J, Matthews L, Cobley S, Han A, Sanders R, Wiltshire HD, et al. Psychological consequences of childhood obesity: psychiatric comorbidity and prevention. Adolesc Health Med Ther. 2016;7:125-46.
4. Gensthaler L, Felsenreich DM, Jedamzik J, Eichelter J, Nixdorf L, Bichler C, et al. Trends of Overweight and Obesity in Male Adolescents: Prevalence, Socioeconomic Status, and Impact on Cardiovascular Risk in a Central European Country. Obes Surg. 2022;32(4):1024-33.
5. Ling J, Chen S, Zahry NR, Kao TA. Economic burden of childhood overweight and obesity: A systematic review and meta-analysis. Obes Rev. 2023;24(2):e13535.
6. Sonntag D, Ali S, Lehnert T, Konnopka A, Riedel-Heller S, König HH. Estimating the lifetime cost of childhood obesity in Germany: Results of a Markov Model. Pediatr Obes. 2015;10(6):416-22.
7. Klebanoff MJ, Chhatwal J, Nudel JD, Corey KE, Kaplan LM, Hur C. Cost-effectiveness of Bariatric Surgery in Adolescents With Obesity. JAMA Surg. 2017;152(2):136-41.
8. van der Geest M. Eerste maagverkleiningen bij Nederlandse obese jongeren vanaf 13 jaar 2023. Available from: https://www.volkskrant.nl/wetenschap/eerste-maagverkleiningen-bij-nederlandse-obese-jongeren-vanaf-13-jaar~b760c52d/#:~:text=Nederlandse%20jongeren%20van%2013%20tot,ingepast%20in%20de%20reguliere%20zorg.

CHAPTER 11

SUMMARY

SUMMARY

Childhood obesity is one of the most pressing health challenges. In children and adolescents, overweight, obesity and severe obesity are defined using the International Obesity Task Force criteria, corresponding to an adult BMI of ≥25 kg/m^2, ≥30 kg/m^2, and ≥35 kg/m^2, respectively. This thesis specifically focused on severe obesity in youth. Although this particular group suffers from tremendous physical and psychological consequences, they are often overlooked in clinical practice and scientific research. More specifically, the following age definitions are used: children are defined as those aged up to 11 years, adolescents are defined as those aged 12-17 years, and young adults are defined as those aged 18-25 years.

The first part of this thesis aimed to gain insight into the impact of the most severe grade of obesity in youth, and aimed to evaluate the effectiveness of the current cornerstone treatment; a multidisciplinary lifestyle intervention. The second part of this thesis aimed to optimize treatment strategies for youth with severe obesity and explored the applicability of bariatric surgery.

Part I - Impact of severe obesity and current treatment

Childhood obesity is linked to medical conditions such as hypertension, type 2 diabetes mellitus, and cardiovascular disease. In youth with the most severe grade of obesity, these health implications are even more pronounced compared to those with overweight or obesity. Besides this, childhood obesity is associated with psychosocial impairments such as depressive symptoms and body dissatisfaction, which lead to a lower health-related quality of life (HRQoL). However, it is unclear which children and adolescents are most affected in their physical, psychological, and social functioning. **Chapter 2** evaluated the HRQoL of children and adolescents with overweight, obesity and severe obesity who were referred to the Centre for Overweight Adolescent and Children's Healthcare (COACH), a specialized pediatric obesity unit, for treatment. Youth with severe obesity displayed lower physical and psychological wellbeing compared to those with overweight and obesity. Additionally, caregivers reported lower HRQoL scores compared to the children and adolescents themselves. The abovementioned results reveal that the quality of life of treatment-seeking children and adolescents with overweight and obesity was most affected in those with the most severe grade of obesity.

Obesity has a major impact on the lifestyle, health and wellbeing of youth. Youth's lifestyle, health and wellbeing might also be affected by other factors, such as the recent COVID-19 pandemic. **Chapter 3** obtained in-depth information on families' experiences

regarding their lifestyle and wellbeing during a pandemic using semi-structured interviews. The interviewed children and adolescents revealed an unhealthier lifestyle and decreased wellbeing during the pandemic. In vulnerable youth, such as those with severe obesity, these negative effects were more pronounced. External influences, such as the input from caregivers or schools, seemed necessary to support children and adolescents in obtaining a healthy lifestyle and wellbeing. These insights may contribute to the development of preventive measures to promote a healthy lifestyle and wellbeing of youth during future pandemics. These measures must attribute attention to the most vulnerable children and adolescents as they prove to be most at risk.

The current cornerstone treatment for children and adolescents with severe obesity is a multidisciplinary lifestyle intervention, which focuses on nutrition, physical activity, sleep and psychosocial aspects of obesity. However, the efficacy of this intervention across different age groups remains unknown. **Chapter 4** compared the effectiveness of the COACH intervention on health parameters between children and adolescents with severe obesity. Children had a significantly larger decrease in their BMI z-score after one and two years of intervention. Besides this, more children achieved clinically significant weight loss compared to adolescents. After two years, multiple improvements in cardio metabolic health parameters were observed, especially in the children. These results advocate starting treatment for severe obesity at an early age. They also suggest that for a subgroup of adolescents with severe obesity enhanced lifestyle interventions, possibly supplemented with medical or surgical treatment options, are needed.

Part II - Bariatric surgery

Bariatric surgery is the most effective treatment for severe obesity in adults, and has shown promising results in younger populations. However, bariatric surgery is not yet available for adolescents below the age of 18 in the Netherlands, and is only allowed in the context of scientific research. To enable safe and effective implementation of bariatric surgery in adolescents with severe obesity in the Netherlands, a number of issues need to be addressed. The first issue is the reluctance towards bariatric surgery in young adults and adolescents. This reluctance might be attributed to a lack of insight regarding efficacy and safety outcomes of bariatric surgery in this young population. **Chapter 5** compared weight-related outcomes between young adults (aged 18-25 years) and adults (aged 35-55 years) who underwent a primary Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG) using data from a national registry. This nationwide population-based cohort study showed that young adults had at least comparable results regarding weight loss up to five years after surgery compared to adults. However, the follow-up rates were lower in the young adult population. Besides this, postoperative short-term complications were more prevalent among adults, and

the young adults revealed more improvement of hypertension, dyslipidemia and musculoskeletal pain. **Chapter 6** focused on the optimal bariatric procedure in young adults, and compared the two most commonly used bariatric procedures; RYGB and SG, using the same national registry. On the short- and midterm, this study among 2,313 young adults revealed more weight loss for young adults who underwent a RYGB compared to young adults who received a SG. These results were more pronounced in the female group. RYGB also resulted in more remission of gastro-esophageal reflux disease (GERD) compared to SG. No differences were found in terms of complications. Based on these findings the reluctance towards bariatric surgery in the younger population seems unfounded. Bariatric surgery might even be offered to a selected group of adolescents with severe obesity. However, future prospective research in this young population is required, and should preferably focus on optimizing follow-up rates, long-term results and quality of life.

Chapter 5 and **6** revealed that bariatric surgery is safe and effective in the younger population. However, the attitude of pediatricians, adolescents and parents towards bariatric surgery in youth remains unclear, posing a second issue. It is important to clarify the opinions of the stakeholders, as pediatricians need to refer potential candidates for bariatric surgery. In addition, adolescents and their families need to be willing to undergo bariatric surgery including the necessary behavioral changes. In **chapter 7** Dutch pediatricians, parents and adolescents who participated in the COACH intervention were surveyed on their opinion on bariatric surgery in youth. Two thirds of the pediatricians reported that bariatric surgery should become a common treatment modality for a selected group of adolescents with severe obesity. Almost 60% of pediatricians intended to refer adolescents for bariatric surgery. More than 60% of the parents and more than 70% of the adolescents responded that bariatric surgery should become available for youth with severe obesity. These results suggest that Dutch stakeholders increasingly share a positive view towards bariatric surgery in youth.

The final issue is the absence of a clinical pathway for adolescent bariatric surgery in the Netherlands. In **chapter 8** the development of a comprehensive clinical pathway for adolescent bariatric surgery is described. An eligibility assessment and perioperative and postoperative care are included in the clinical pathway. The eligibility assessment involves, among others, an evaluation by a specialized pediatric obesity unit, and an anonymous evaluation by a national board. The final decision for bariatric surgery is made by the multidisciplinary team for adolescent bariatric surgery. Among important factors considered in this final decision are the potential to adhere to necessary behavioral changes and postoperative counselling and follow-up. When an adolescent is deemed eligible for bariatric surgery, he or she receives intensive

peri- and postoperative counselling by a pediatrician, bariatric surgeon, dietician and psychologist. In this intensive guidance, several regular appointments are made, and additional care will be provided based on the needs of the adolescent and his or her family. Whether the clinical pathway is sufficiently effective to select suitable adolescents for bariatric surgery and adequately guide them through the peri- and postoperative course is currently being evaluated in the TEEN-BEST study.

CHAPTER 12

SAMENVATTING

SAMENVATTING

Obesitas bij kinderen is een gezondheidscrisis. Bij kinderen en adolescenten worden overgewicht, obesitas en ernstige obesitas gedefinieerd aan de hand van de International Obesity Task Force criteria, die vergelijkbaar zijn met een BMI van respectievelijk ≥25 kg/m^2, ≥30 kg/m^2, en ≥35 kg/m^2 bij volwassenen. Dit proefschrift heeft zich specifiek gericht op jongeren met ernstige obesitas. Jongeren met ernstige obesitas hebben te kampen met enorme lichamelijke en psychische klachten en toch worden ze vaak over het hoofd gezien in de klinische praktijk en het wetenschappelijk onderzoek. Om specifieker te zijn, worden de volgende leeftijdsdefinities gebruikt: kinderen worden gedefinieerd als personen tot 11 jaar, adolescenten worden gedefinieerd als personen van 12-17 jaar en jongvolwassenen worden gedefinieerd als personen van 18-25 jaar.

Het eerste deel van dit proefschrift heeft zich gericht op het verkrijgen van inzicht in de gevolgen van de ernstigste vorm van obesitas bij jongeren. Dit deel heeft ook de effectiviteit van de huidige standaardbehandeling geëvalueerd; een multidisciplinaire leefstijlinterventie. Het tweede deel van dit proefschrift heeft zich gericht op het optimaliseren van behandelstrategieën voor jongeren met ernstige obesitas en heeft de toepasbaarheid van bariatrische chirurgie onderzocht.

Deel I - Gevolgen van ernstige obesitas en de huidige behandeling

Obesitas bij jongeren is geassocieerd met medische aandoeningen zoals een hoge bloeddruk, suikerziekte en hart- en vaatziekten. Bij jongeren met de ernstigste vorm van obesitas zijn deze gevolgen voor de gezondheid nog groter ten opzichte van jongeren met overgewicht of obesitas. Daarnaast is obesitas bij jongeren ook geassocieerd met psychosociale klachten zoals depressieve symptomen en ontevredenheid over het lichaam. Deze klachten leiden tot een lagere kwaliteit van leven. Het is echter onduidelijk welke jongeren het meest worden beïnvloed in hun fysiek, psychologisch en sociaal functioneren. Daarom is in **hoofdstuk 2** de kwaliteit van leven onderzocht van kinderen en adolescenten met overgewicht, obesitas en ernstige obesitas die voor behandeling werden doorverwezen naar het Centre for Overweight Adolescent and Children's Healthcare (COACH), een obesitas expertisecentrum. Kinderen en adolescenten met ernstige obesitas hadden een lager fysiek en psychologisch welzijn in vergelijking met kinderen en adolescenten met overgewicht of obesitas. Ouders rapporteerden een lagere kwaliteit van leven ten opzichte van de kinderen en adolescenten zelf. Deze resultaten laten zien dat de kwaliteit van leven het meest is aangedaan in de kinderen en adolescenten met de ernstigste vorm van obesitas.

Obesitas heeft een grote invloed op de leefstijl, gezondheid en het welzijn van jongeren. Andere factoren, zoals de recente COVID-19 pandemie, kunnen ook van invloed zijn op de leefstijl, gezondheid en het welzijn van jongeren. Het onderzoek beschreven in **hoofdstuk 3** heeft aan de hand van semigestructureerde interviews informatie verkregen over de ervaringen van gezinnen met betrekking tot hun leefstijl en welzijn tijdens de pandemie. De geïnterviewde kinderen en adolescenten rapporteerden een ongezondere leefstijl en een verminderd welzijn gedurende deze periode. Deze negatieve effecten waren meer uitgesproken in de kwetsbare jongeren, bijvoorbeeld diegenen met ernstige obesitas. Externe invloeden, zoals de invloed van ouders of school, leken noodzakelijk om jongeren te ondersteunen bij het verkrijgen van een gezonde leefstijl en het verbeteren van hun welzijn. Deze inzichten kunnen bijdragen aan de ontwikkeling van preventieve maatregelen ter bevordering van de leefstijl en het welzijn van jongeren tijdens toekomstige pandemieën. Hierbij moet extra aandacht worden besteed aan de meest kwetsbare kinderen en adolescenten.

De huidige standaardbehandeling voor kinderen en adolescenten met ernstige obesitas is een multidisciplinaire leefstijlinterventie. Deze interventie richt zich op voeding, beweging, slaap en psychosociale aspecten van obesitas. De effectiviteit van deze interventie in verschillende leeftijdsgroepen is echter onbekend. In **hoofdstuk 4** is de effectiviteit van de COACH interventie op gezondheidsparameters vergeleken tussen kinderen en adolescenten met ernstige obesitas. Kinderen hadden een grotere daling in hun BMI z-score zowel na één als twee jaar interventie. Daarnaast bereikten meer kinderen een klinisch relevant gewichtsverlies ten opzichte van de adolescenten. Na twee jaar werden meerdere verbeteringen in cardio metabole gezondheidsparameters waargenomen, vooral bij de kinderen. Deze resultaten pleiten voor het starten van de behandeling van ernstige obesitas op jonge leeftijd. Verder suggereren de resultaten dat voor een deel van de adolescenten met ernstige obesitas een geoptimaliseerde leefstijlinterventie nodig is. Deze leefstijlinterventie dient te worden afgestemd op de behoefte van de adolescent en eventueel worden aangevuld met medicamenteuze of chirurgische behandelopties.

Deel II - Bariatrische chirurgie

Bariatrische chirurgie is de meest effectieve behandeling voor ernstige obesitas bij volwassenen. Daarnaast heeft bariatrische chirurgie ook veelbelovende resultaten laten zien bij adolescenten. In Nederland is bariatrische chirurgie echter nog niet beschikbaar voor adolescenten en is het alleen toegestaan in het kader van wetenschappelijk onderzoek. Om een veilige en effectieve implementatie van bariatrische chirurgie bij adolescenten met ernstige obesitas in Nederland mogelijk te maken, moeten er een aantal hordes worden genomen. Het eerste probleem is de terughoudendheid

ten aanzien van bariatrische chirurgie bij jongvolwassenen en adolescenten. Mogelijk komt deze terughoudendheid door te weinig kennis ten aanzien van de veiligheid en effectiviteit van bariatrische chirurgie bij jongeren. Daarom zijn in **hoofdstuk 5** de gewichtsgerelateerde uitkomsten vergeleken tussen jongvolwassenen (18-25 jaar) en volwassenen (35-55 jaar) die een Roux-en-Y gastric bypass (RYGB) of sleeve gastrectomie (SG) kregen. Deze landelijke cohortstudie toonde aan dat jongvolwassenen tot vijf jaar na de operatie een vergelijkbaar gewichtsverlies hadden ten opzichte van volwassenen. Daarnaast kwamen postoperatieve korte termijncomplicaties minder vaak voor bij jongvolwassenen en lieten de jongvolwassenen meer verbetering van hypertensie, dyslipidemie en gewrichtsklachten zien. Het onderzoek beschreven in **hoofdstuk 6** heeft de optimale bariatrische procedure in de jongvolwassen populatie onderzocht. In dit hoofdstuk werden de twee meest gebruikte bariatrische procedures vergeleken; de RYGB en de SG, waarbij gebruik werd gemaakt van dezelfde landelijke registratie als in hoofdstuk 5. Op de korte en middellange termijn liet dit onderzoek onder 2.313 jongvolwassenen meer gewichtsverlies zien bij jongvolwassenen die een RYGB kregen. Dit effect was nog duidelijker te zien in de vrouwelijke groep. De RYGB liet ook meer remissie van refluxziekte zien ten opzichte van de SG. Er werden geen verschillen gevonden tussen de twee technieken wat betreft complicaties. Op basis van deze bevindingen lijkt de terughoudendheid ten opzichte van bariatrische chirurgie in de jongere populatie ongegrond en zou het zelfs aangeboden kunnen worden aan een selecte groep adolescenten met ernstige obesitas. Toekomstig prospectief onderzoek in deze jonge populatie is echter gerechtvaardigd en zou zich moeten richten op het optimaliseren van de follow-up percentages, lange termijn resultaten en de kwaliteit van leven.

Hoofdstuk 5 en **6** hebben laten zien dat bariatrische chirurgie veilig en effectief is in de jongere populatie. De mening van de kinderartsen, adolescenten en ouders ten aanzien van bariatrische chirurgie bij adolescenten blijft echter onduidelijk en dit vormt een tweede horde. De mening van kinderartsen is belangrijk, omdat zij adolescenten moeten doorverwijzen voor bariatrische chirurgie. Daarnaast is de mening van adolescenten en hun families belangrijk, omdat zij bereid moeten zijn om bariatrische chirurgie, inclusief de noodzakelijke gedragsveranderingen te ondergaan. In **hoofdstuk 7** werden Nederlandse kinderartsen, ouders en adolescenten die deelnamen aan de COACH interventie gevraagd naar hun mening over bariatrische chirurgie bij jongeren. Tweederde van de kinderartsen gaf aan dat bariatrische chirurgie een gebruikelijke behandelmogelijkheid zou moeten worden voor een selecte groep adolescenten met ernstige obesitas. Bijna 60% van de kinderartsen was van plan om adolescenten door te verwijzen voor bariatrische chirurgie. Meer dan 60% van de ouders en meer dan 70% van de adolescenten gaven aan dat bariatrische chirurgie beschikbaar zou

moeten worden voor jongeren met ernstige obesitas. Deze resultaten suggereren dat Nederlandse betrokkenen bariatrische chirurgie steeds meer accepteren als behandelmogelijkheid voor jongeren met ernstige obesitas waarbij leefstijlinterventies onvoldoende effectief zijn.

De laatste horde is dat het zorgpad voor bariatrische chirurgie bij adolescenten nog niet was opgezet in Nederland. In **hoofdstuk 8** is de ontwikkeling van een uitgebreid zorgpad voor bariatrische chirurgie bij adolescenten beschreven. Het zorgpad bestaat uit een geschiktheidsbeoordeling en peri- en postoperatieve zorg. De geschiktheidsbeoordeling omvat onder andere een evaluatie door een obesitas expertisecentrum en een anonieme evaluatie door een nationaal platform dat bestaat uit onafhankelijke deskundigen op het gebied van bariatrische chirurgie bij adolescenten. Het multidisciplinaire team voor bariatrische chirurgie bij adolescenten neemt de uiteindelijke beslissing voor bariatrische chirurgie, waarbij wordt beoordeeld of de adolescent zich zal houden aan de postoperatieve begeleiding en follow-up. Als een adolescent in aanmerking komt voor bariatrische chirurgie, krijgt deze intensieve peri- en postoperatieve begeleiding van een kinderarts, bariatrisch chirurg, diëtist en psycholoog. In deze intensieve begeleiding worden verschillende standaard afspraken gemaakt en wordt aanvullende zorg verleend op basis van de behoeften van de adolescent en de familie. Of het ontwikkelde zorgpad voldoende effectief is om geschikte adolescenten te selecteren voor bariatrische chirurgie en deze adolescenten daarnaast adequaat te begeleiden tijdens het peri- en postoperatieve traject wordt momenteel onderzocht in de TEEN-BEST studie.

APPENDICES

DANKWOORD
LIST OF PUBLICATIONS
CURRICULUM VITAE

DANKWOORD

Een proefschrift schrijf je niet alleen, een proefschrift is een teamprestatie. Hieronder wil ik dan ook graag een aantal mensen uit 'mijn team' bedanken.

Beste **Anita**, wat heb ik veel van jou mogen leren. Jij hebt me geleerd groots te denken en te denken in mogelijkheden in plaats van beperkingen. Je gedrevenheid en daadkracht zijn een voorbeeld voor velen. Jij doet geen water bij de wijn, want water is voor vissen. Ik wens je alle goeds voor de toekomst en ben ervan overtuigd dat 2024 jouw jaar gaat worden.

Beste **François**, jouw energie, enthousiasme en positieve instelling zijn inspirerend, zowel op het werk als daarbuiten. Bovendien ben je een echte grammarnazi, die mij het belang van interpunctie heeft bijgebracht (best lastig als je het liefste zinnen van 4 regels maakt). Het afgelopen jaar heeft heel Nederland gehoord over 'jouw kindje' de TEEN-BEST studie, laat die 150 inclusies nu maar komen!

Lieve **Loes**, zonder jouw hulp was dit proefschrift er niet geweest. Voor mij ben je dan ook een tweede copromotor. Jij stond altijd voor mij klaar met een pragmatische oplossing. Nieuw studie design voor de TEEN-BEST? Geen probleem dan herschrijven we het protocol gewoon. Je bent een aanwinst voor de onderzoeksgroep, zowel qua kennis, organisatorische skills als gezelligheid.

Beste **Wouter**, jouw kritische blik heeft dit proefschrift 'gemáximaliseerd'. Daarnaast wil ik je ook bedanken voor de goede zorgen voor mijn oma. Ondanks dat het niet altijd goed nieuws betrof, keek zij uit naar de afspraken bij jou. Ik hoop dat ik ook ooit zo'n dokter mag worden voor mijn patiënten.

Prof. Dompeling, **Prof. Greve**, **Prof. van den Akker**, **Prof. Keszthelyi** en **dr. Nienhuijs**, geachte leden van de beoordelingscommissie, hartelijk dank voor jullie tijd en inspanning met betrekking tot het beoordelen van dit proefschrift.

Veel dank aan alle **patiënten** die hebben deelgenomen aan de onderzoeken in dit proefschrift. Zonder jullie was dit proefschrift er niet geweest.

Aan alle **co-auteurs** en leden van het **TEEN-BEST studieteam**, dank voor jullie kritische blik en de tomeloze inzet voor de adolescenten bariatrie in Nederland.

Lieve **Marieke** en **Eline**, er was geen moment twijfel, jullie zouden mijn paranimfen zijn! Wij gaan altijd diep, of we dit nu willen of niet. Ik kan me geen betere vriendinnen wensen die tijdens mijn promotie aan mijn zijde zullen fladderen. Wanneer gaan we dat weekendje champagne nu eens plannen?

Lieve **collega-onderzoekers van het Máxima MC** en **COACH/MUMC+**, waaronder **Louisa**, **Marleen**, **Muriel**, **Monica**, **Margot**, **Charissa**, **Aliyar**, **David**, **Tom**, **Quirine**, **Kay**, **Judith**, **Marijn**, **Johanna**, **Maartje** en **Lisanne.** Wat een geluk dat ik deel mocht uitmaken van twee fantastische onderzoeksteams. Ik kijk met plezier terug op alle koffiemomenten, writing retreats, en wijn- en karaokeavonden. Op naar nog veel meer promoties en bedankt voor de heerlijke tijd!

Lief **COACH-team**, en in het bijzonder **Cara**, **Ronny** en **Pauline**, wat fijn dat ik bij zo'n gedreven team mocht horen en van jullie kon leren. Jullie toewijding aan COACH en jullie inzet voor de zorg van kinderen met overgewicht en obesitas werkte aanstekelijk. Op dat we in de toekomst nog veel meer kinderen mogen helpen.

Beste medewerkers van het **obesitas centrum van het Máxima MC** (onder andere **Myrthe, Aniek, Jolanda** en **Ina**), dank dat jullie altijd voor mij klaar stonden om logistieke zaken te regelen, maar ook zeker voor een niet werk gerelateerd praatje en een hopje. Zonder jullie is er geen OBC.

Aan alle **chirurgen van het Máxima MC** en in het bijzonder **Arijan,** dank voor jullie geloof in mij, van semi-arts tot ANIOS en promovendus. Door jullie kan ik met voldoende bagage en een gerust hart uitvliegen naar het VieCuri.

Aan al mijn **vriendinnen**, voor, tijdens en na mijn studietijd, onder andere de **Hangovers** en **Primavera**, wat heb ik een geluk dat ik het leven met jullie mag vieren.

Lieve **schoonfamilie**, bedankt voor jullie oprechte interesse in mij en in dit proefschrift. De weekenden in Friesland zijn een feest en ik hoop dat we dit nog heel veel jaren kunnen blijven doen.

Lieve **oma's,** jullie zijn mijn voorbeeld. Jullie levenslust, zorgzaamheid en positieve uitstraling zijn uniek. Wanneer gaan we weer op vakantie?

Lieve **opa**, bedankt voor alle wijze lessen en goede zorgen. Wie het kleine niet eert is het grote niet weert?! Helaas ben jij niet meer hier, maar daardoor niet minder belangrijk, ik denk aan je.

Lieve **Sem**, kleine grote zus. Wij zijn tegenpolen, maar vullen elkaar daardoor juist aan. Bedankt voor je zorgzaamheid en dat ik mij nu tante mag noemen. Ik ben trots op je.

Lieve **pap** en **mam**, dank voor jullie onvoorwaardelijke steun, vertrouwen en vooral ook liefde. Ook al lopen onze wegen niet altijd synchroon, ik weet dat jullie altijd achter mij zullen staan. De veilige thuishaven op de boerderij, jullie en mijn thuis, voelt als een plek waar ik mezelf kan zijn en tot rust kan komen. Bedankt voor alles!

Lieve **Wald**, waar moet ik beginnen? Jij bent mijn rots in de branding, jij krijgt me rustig (wat best knap is), zorgt dat ik kan relativeren en houdt me op de juiste koers. Het allerfijnste vind ik dat we altijd samen kunnen geinen en overal over kunnen praten. Op naar nog veel meer mooie jaren en ik hou tot de maan en terug van je!

LIST OF PUBLICATIONS

1. **van de Pas KGH**, Esfandiyari Noushi A, Janssen L, Vreugdenhil ACE, Leclercq WKG, van Dielen FMH; Dutch Audit for Treatment of Obesity Research Group. A Population-Based Cohort Study on Efficacy and Safety of Bariatric Surgery in Young Adults Versus Adults. Obes Surg. 2023 Aug;33(8):2475-2484.

2. Bonouvrie DS**, van de Pas KGH**, Janssen L, Leclercq WKG, Greve JWM, van Dielen FMH; Dutch Audit for the Treatment of Obesity Research Group. Safety of bariatric surgery in the elderly: results from the Dutch National Registry. Surg Obes Relat Dis. 2023 Apr;19(4):335-343.

3. **van de Pas KGH***, de Krom MAP*, Winkens B, van Dielen FMH, Vreugdenhil ACE. Health-Related Quality of Life in Children and Adolescents with Overweight, Obesity, and Severe Obesity: A Cross-Sectional Study. Obes Facts. 2023;16(3):282-292.

4. **van de Pas KGH***, Hesselink ML*, Schlechtriem R, Arayess L, Kreutz JM, Vreugdenhil ACE. The Impact of the COVID-19 Pandemic on Lifestyle and Wellbeing of Children, Adolescents and Their Parents: A Qualitative Study. Children (Basel). 2022 Dec 8;9(12):1929.

5. Bol ME, Huckriede JB, **van de Pas KGH**, Delhaas T, Lorusso R, Nicolaes GAF, Sels JEM, van de Poll MCG. Multimodal measurement of glycocalyx degradation during coronary artery bypass grafting. Front Med (Lausanne). 2022 Nov 29;9:1045728.

6. **van de Pas KGH**, Lubrecht JW, Hesselink ML, Winkens B, van Dielen FMH, Vreugdenhil ACE. The Effect of a Multidisciplinary Lifestyle Intervention on Health Parameters in Children versus Adolescents with Severe Obesity. Nutrients. 2022 Apr 25;14(9):1795.

7. **van de Pas KGH**, Bonouvrie DS, Janssen L, Romeijn MM, Luijten AAPM, Leclercq WKG, van Dielen FMH; Dutch Audit for Treatment of Obesity Research Group. Roux-en-Y Gastric Bypass Versus Sleeve Gastrectomy in Young Adults: a Dutch Registry Study. Obes Surg. 2022 Mar;32(3):763-770.

8. van der Heijden JAG, **van de Pas KGH**, van den Broek FJC, van Dielen FMH, Slooter GD, Maaskant-Braat AJG. Oncological and functional outcomes of transanal total mesorectal excision in a teaching hospital in the Netherlands. Ann Coloproctol. 2022 Feb;38(1):28-35.

9. **van de Pas KGH**, Bonouvrie DS, Janssen L, Roebroek YGM, Zegers BSHJ, Leclercq WKG, Vreugdenhil ACE, van Dielen FMH. Bariatric Surgery in Youth: the Perspective of Dutch Pediatricians, Parents, and Adolescents. Obes Surg. 2021 Nov;31(11):4821-4828.

10. Romeijn MM, van Hoef S, Janssen L, **van de Pas KGH**, van Dielen FMH, Luijten AAPM, Göttgens KWA, Greve JWM, Leclercq WKG. Comparison of Linear versus Circular-Stapled Gastroenterostomy in Roux-en-Y Gastric Bypass: A Nationwide Population-Based Cohort Study. Obes Surg. 2021 Aug;31(8):3579-3587.

11. **van de Pas KGH**, Smit JV, Snel-Bongers J. Otologische symptomen als primaire presentatie van granulomatose met polyangiitis. Nederlands Tijdschrift voor Keel-Neus-Oorheelkunde. 2021 nr 2.

* Both authors contributed equally.

Collaboratives

1. Singhal R, Omar I, Madhok B, Rajeev Y, Graham Y, Tahrani AA, Ludwig C, Wiggins T, Mahawar K; GENEVA Collaborators. Safety of Bariatric Surgery in ≥ 65-Year-Old Patients During the COVID-19 Pandemic. Obes Surg. 2022 Jul;32(7):1-13.

2. Singhal R, Omar I, Madhok B, Ludwig C, Tahrani AA, Mahawar K; GENEVA Collaborators. Effect of BMI on safety of bariatric surgery during the COVID-19 pandemic, procedure choice, and safety protocols - An analysis from the GENEVA Study. Obes Res Clin Pract. 2022 May-Jun;16(3):249-253.

3. Singhal R, Cardoso VR, Wiggins T, Super J, Ludwig C, Gkoutos GV, Mahawar K; GENEVA Collaborators. 30-day morbidity and mortality of sleeve gastrectomy, Roux-en-Y gastric bypass and one anastomosis gastric bypass: a propensity score-matched analysis of the GENEVA data. Int J Obes (Lond). 2022 Apr;46(4):750-757.

4. STARSurg Collaborative and EuroSurg Collaborative. Validation of the OAKS prognostic model for acute kidney injury after gastrointestinal surgery. BJS Open. 2022 Jan 6;6(1):zrab150.

5. Singhal R, Wiggins T, Super J, Alqahtani A, Nadler EP, Ludwig C, Tahrani A, Mahawar K; GENEVA Collaborative. 30-Day morbidity and mortality of bariatric metabolic surgery in adolescence during the COVID-19 pandemic - The GENEVA study. Pediatr Obes. 2021 Dec;16(12):e12832.

6. GENEVA collaborators. 30-Day Morbidity and Mortality of Bariatric Surgery During the COVID-19 Pandemic: a Multinational Cohort Study of 7704 Patients from 42 Countries. Obes Surg. 2021 Oct;31(10):4272-4288.

7. Singhal R, Tahrani AA, Ludwig C, Mahawar K; GENEVA collaborators. Global 30-day outcomes after bariatric surgery during the COVID-19 pandemic (GENEVA): an international cohort study. Lancet Diabetes Endocrinol. 2021 Jan;9(1):7-9.

8. EuroSurg Collaborative. Timing of nasogastric tube insertion and the risk of postoperative pneumonia: an international, prospective cohort study. Colorectal Dis. 2020 Dec;22(12):2288-2297.

9. EuroSurg Collaborative. Safety of hospital discharge before return of bowel function after elective colorectal surgery. Br J Surg. 2020 Apr;107(5):552-559.

10. EuroSurg Collaborative. Safety and efficacy of non-steroidal anti-inflammatory drugs to reduce ileus after colorectal surgery. Br J Surg. 2020 Jan;107(2):e161- e169.

CURRICULUM VITAE

Kelly van de Pas was born on the 6th of June 1994 in Venlo, the Netherlands. She grew up on a farm with her family in Kessel. In her youth, she developed a special interest for horse riding, in which she won several regional and national championships. After graduating from high school (Bouwens van der Boijecollege, Panningen) she studied Medical Sciences and Technology at the Eindhoven University of Technology in which she completed the first year with honors. In 2013, she enrolled into Medical School at the Maastricht University, where she developed her first interest into surgery. After 6 years, she graduated from Medical School and started working as a general surgery resident not in training at the Máxima MC. In 2020, she enrolled as a PhD candidate under the guidance of prof. dr. A.C.E. Vreugdenhil and dr. F.M.H van Dielen at the Maastricht University Medical Centre+ and the Máxima MC. In her thesis she focused on the impact of severe obesity in youth and the optimization of treatment strategies for youth with severe obesity. Currently, Kelly works as a general surgery resident not in training at the VieCuri Medical Centre in Venlo.